



Desk Reference Guide

Updated: September 25, 2019

Click bottom right corner to
return to Table of Contents



Table of Contents

#

5-HTP CR

5-MTHF

5-MTHF Plus B12

5-MTHF ES

6 Day Detox Kits

A

ActivEssentials

ActivEssentials for Women

ActivEssentials with Calcium

ActivEssentials with OncoPLEX & D3

ActivNutrients

ActivNutrients Chewable

ActivNutrients without Copper & Iron

ActivNutrients without Copper & Iron

Multivitamin Powder

ActivNutrients without Iron

Adrenal Essence

AdrenaLiv

Adrenal Manager

AdrenaMax

ALAMax CR

AllerDHQ

AngiNOX

Appe-Curb

ATP Ignite

ATP Ignite Workout

B

B Activ

Berbemycin

Benfotiamine

Bio C 1:1

BrainSustain

BrainSustain for Kids

C

Calcium D-Glucarate

Candididal

CarniteX

CheleX

CholeRex

CinnDromeX

Cogniquil

ColonX

ConjuLean 1000

CoQmax ME

CoQmax-100 ME

CoQmax Omega

CoQmax Ubiquinol

Corticare B

Cortisolv

CurcuPlex CR

CurcuPlex-95



Table of Contents

D

D3 2000

D3 5000

D3 Liquid

DHA from Algae

DHA from Algae for Kids

DIMension 3

DioVasc

Drainage

E

Effektiv

F

Femquil

FIT Food Lean

FIT Food Lean Complete

FIT Food Lean Complete Sugar & Stevia
Free

FIT Food Lean Whey

FlashArrest

Foundation Essentials

G

GarliX

GastrAcid

GI Protect

GlutAloeMine

Green Tea 600

H

HistDAO

Hormone Protect

I

i5

i5 Energize

IG 26 DF

IG 26 Plus DF

IgG 2000 CWP

IgG Pure

Immune Essentials

ImmunotiX 250

ImmunotiX 500

Iron Glycinate

I-Sight

K

K2-45

K2-D3

K-Mg Citrate

KetonX

L

Leptin Manager

LipotropiX

Liver Protect

L-Glutamine

L-Lysine



Table of Contents

L-Theanine

M

Magnesium Citrate

MCT Powder

MedCaps DPO

MedCaps GI

MedCaps IS

MedCaps Menopause

MedCaps T3

Melatonin

Melatonin CR

MemorAll

MenoFem

Methylcobalamin

Methyl Protect

MinRex

Mitochondrial Renewal Kit

Mood Food

Mood Food ES

N

N.O.max ER

NAC

Nattokinase

NeuroActives BrainSustain

NiaVasc

NiaVasc 750

Nrf2 Activator

O

OlivDefense

Omega MonoPure Curcumin EC

Omaga MonoPure DHA EC

Omega MonoPure 650 EC

Omega MonoPure 1300 EC

OmegaPure 600 EC

OmegaPure 780 EC

OmegaPure 820

OmegaPure 900 EC

OmegaPure 900-TG

OmegaPure DHA

OmegaPure EPA

OmegaPure Krill

OncoPLEX

OncoPLEX ES

OptiCleanse GHI

OptiCleanse GHI Sugar- & Stevia-F ree

OptiCleanse Plus

OptiFiber Lean

OptiMag 125

OptiMag Neuro

OptiMag Plus Calcium

OptiMetaboliX

OptiMetaboliX 2:1

Oraxinol

OrganiX Bars



Table of Contents

OrganiX PhytoFood

OSApdex

OSApdex CF

OSApdex MK-7

Ossopan 1100

Ossopan MD

OsteoBlox CF

P

PanXyme pH

PepciX

PhosphaLine

PMS Soothe

Prenatal Essentials

ProbioMax 350 DF & Complete DF

ProbioMax DF

ProbioMax Daily DF

ProbioMax for Toddlers

ProbioMax IG 26 DF

ProbioMax Lean DF

ProbioMax Plus DF

ProbioMax Sb DF

Probio Defense

Prostate FLO

ProteoXyme

R

RegeneMax Liquid

RegeneMax Plus

RelaxMax

Resveratin Plus

S

S-Acetyl Glutathione

Saccharomycin DF

Saloxicin

SAM-e

SAMe & TMG

SedaLin

SynovX AI

SynovX Calm

SynovX DJD

SynovX Metabolic

SynovX Performance

SynovX Recovery

SynovX Tendon & Ligament

T

T-150

TestoPlex Plus

U

UritraX



Table of Contents

V

VegaPro

Vinpocetine

Viragraphis

VitalVasc

X

Xcellent C

Xcellent E

XenoProtX

XymoBoIX

XymoDine

XymoZyme

Z

Zinc Glycinate



5-HTP CR

Controlled-Release 5-Hydroxytryptophan Formula



Available in 60 tablets

Discussion

5-hydroxytryptophan (5-HTP) is a precursor to serotonin. In the body, the essential amino acid tryptophan (when acted upon by the enzyme tryptophan hydroxylase) converts to 5-HTP. The compound is subsequently decarboxylated to serotonin, thereby elevating extracellular serum serotonin levels. Supplementing with 5-HTP bypasses the somewhat limiting conversion of tryptophan to 5-HTP.^[1,2] Oral 5-HTP is well-absorbed in the intestine without the need for a transporter; other amino acids do not compete with it for absorption. It easily crosses the blood-brain barrier, is not degraded by the enzymes that degrade tryptophan, and it is excreted through the kidneys.*^[1,3]

Mood and Comfort Serotonin regulates many normal brain activities, increases norepinephrine and dopamine, and is important in regulating mood and behavior. Adequate levels of serotonin are associated with normal calmness and relaxation.*^[1-5]

Several studies have demonstrated that 5-HTP supports a healthy frame of mind, good energy levels, ease of movement, and restful sleep.^[1,6,7] Published studies (dose~100-600 mg/day) have also demonstrated the effectiveness of 5-HTP supplementation in supporting cerebral comfort.*^[8-10]

Appetite Used in a high dose (i.e., 300 mg/three times a day), 5-HTP decreased food consumption and reduced weight. This result may relate to the effect of 5-HTP in supporting normal hypothalamic regulation, which includes appetite homeostasis.^[11] However, nausea at this relatively high dose was a common complaint.^[12,13] In other research, sublingual 5-HTP administered five times per day for eight weeks in adult overweight women significantly supported feelings of post-meal hunger satisfaction.*^[14]

Hormones and Sleep 5-HTP is thought to effect the HPA axis, as it has the ability to raise plasma cortisol levels, to cause transient increase in growth hormone (at 150 mg dose), and in men only, to support healthy levels of thyroid stimulating hormone.^[15,16] Serotonin is also converted to melatonin; thus, supplementation has similar

Clinical Applications

- » Supports Healthy Biosynthesis of Serotonin*
- » Supports Healthy Mood and Positive Outlook*
- » Supports Normal Appetite*
- » Supports Restful Sleep Pattern*

*5-HTP CR has a delivery system that releases 5-HTP slowly and steadily over a period of time. 5-HTP is a drug-free amino acid derived from a plant that naturally increases the body's level of serotonin, the chemical messenger that affects emotions, behavior, appetite, and sleep. Today's stress-filled lifestyles and dietary practices may negatively affect how the body handles serotonin. Regular use of XYMOGEN®'s 5-HTP CR helps promote a more positive outlook and greater appetite control.**

effects. Support of sleep quality is likely related to 5-HTP's ability to increase the length of rapid eye movement (REM).^[3,17] In children, supplementation with 5-HTP may help modulate arousal level and support peaceful sleep.*^[18]

5-HTP CR Supplement Facts

Serving Size: 1 Tablet

	Amount Per Serving	%Daily Value
Calcium (as dicalcium phosphate)	22 mg	2%
5-HTP (5-Hydroxytryptophan)(from <i>Griffonia simplicifolia</i> (seed))	100 mg	**

** Daily Value not established.

Other Ingredients: Cellulose, hypromellose, stearic acid, silica, magnesium stearate, methylcellulose, and glycerin.**DIRECTIONS:** Take one tablet, up to two times daily, with a meal. Do not exceed recommended dose.

Consult your healthcare practitioner prior to use if you have, or suspect you have, a medical condition or are taking prescription drugs for depression, migraines, Parkinson's disease, or psychiatric disorders. Not for use by children.

CAUTIONS: Do not take if you are, or suspect you are, pregnant or if you are lactating, or under 18 years of age.**STORAGE:** Keep closed in a cool, dry place out of reach of children.**DOES NOT CONTAIN:** Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, artificial colors, artificial sweeteners, or artificial preservatives.**References**

- Juhl JH. Fibromyalgia and the serotonin pathway. *Altern Med Rev.* 1998 Oct;3(5):367-75. [PMID: 9802912]
- Gutknecht L, Jacob C, Strobel A, et al. Tryptophan hydroxylase-2 gene variation influences personality traits and disorders related to emotional dysregulation. *Int J Neuropsychopharmacol.* 2007 Jun;10(3):309-20. [PMID: 17176492]
- Birdsall TC. 5-Hydroxytryptophan: a clinically-effective serotonin precursor. *Altern Med Rev.* 1998 Aug;3(4):271-80. [PMID: 9727088]
- Agren H, Reibring L, Hartvig P, et al. Low brain uptake of L-[11C]5-hydroxytryptophan in major depression: a positron emission tomography study on patients and healthy volunteers. *Acta Psychiatr Scand.* 1991;83(6):449-55. [PMID: 1882697]
- Zmilacher K, Battagay R, Gastpar M. L-5-hydroxytryptophan alone and in combination with a peripheral decarboxylase inhibitor in the treatment of depression. *Neuropsychobiology.* 1988;20(1):28-35. [PMID: 3265988]
- Caruso I, Sarzi Puttini P, Cazzola M, et al. Double-blind study of 5-hydroxytryptophan versus placebo in the treatment of primary fibromyalgia syndrome. *J Int Med Res.* 1990 May-Jun;18(3):201-09. [PMID: 2193835]
- Puttini S, Caruso I. Primary fibromyalgia syndrome and 5-hydroxy-L-tryptophan: a 90-day open study. *J Int Med Res.* 1992 Apr;20(2):182-89. [PMID: 1521674]
- Ribeiro CA. L-5-hydroxytryptophan in the prophylaxis of chronic tension-type headache: a double-blind, randomized, placebo controlled study. *Headache.* 2000 Jun;40(6):451-56. [PMID: 10849040]
- Nagata E, Shibata M, Hamada J, et al. Plasma 5-hydroxytryptamine (5-HT) in migraine during an attack-free period. *Headache.* 2006 Apr;46(4):592-96. [PMID: 16643553]
- Nicolodi M, Sicuteri F. L-5-hydroxytryptophan can prevent nociceptive disorders in man. *Adv Exp Med Biol.* 1999;467:177-82. [PMID: 10721054]
- Schott DA, Nicolai J, de Vries JE, et al. Disorder in the serotonergic system due to tryptophan hydroxylation impairment: a cause of hypothalamic syndrome? *Horm Res Paediatr.* 2010;73(1):68-73. [PMID: 20190542]
- Cangiano C, Ceci F, Cascino A, et al. Eating behavior and adherence to dietary prescriptions in obese adult subjects treated with 5-hydroxytryptophan. *Am J Clin Nutr.* 1992 Nov;56:863-67. [PMID: 1384305]
- Cangiano C, Laviano A, Del Ben M, et al. Effects of oral 5-hydroxy-tryptophan on energy intake and macronutrient selection in non-insulin dependent diabetic patients. *Int J Obes Relat Metab Disord.* 1998 Jul;22(7):648-54. [PMID: 9705024]
- Rondanelli M, Klersy C, Iadarola P, et al. Satiety and amino-acid profile in overweight women after a new treatment using a natural plant extract sublingual spray formulation. *Int J Obes (Lond).* 2009 Oct;33(10):1174-82. [PMID: 19752879]
- Lee MA, Nash JF, Barnes M, et al. Inhibitory effect of ritanserin on the 5-hydroxytryptophan-mediated cortisol, ACTH and prolactin secretion in humans. *Psychopharmacology (Berl).* 1991;103(2):258-64. [PMID: 1851310]
- Mashchak CA, Kletzky OA, Spencer C, et al. Transient effect of L-5-hydroxytryptophan on pituitary function in men and women. *J Clin Endocrinol Metab.* 1983 Jan;56(1):170-76. [PMID:6600170]
- Wyatt RJ, Zarcone V, Engelman K, et al. Effects of 5-hydroxytryptophan on the sleep of normal human subjects. *Electroencephalogr Clin Neurophysiol.* 1971 Jun;30(6):505-09. [PMID: 4105646]
- Bruni O, Ferri R, Miano S, et al. L-5-hydroxytryptophan treatment of sleep terrors in children. *Eur J Pediatr.* 2004 Jul;163(7):402-07. [PMID:15146330]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

5-MTHF

Bioactive Folate Formulas



5-MTHF and 5-MTHF ES are available in 60 capsules
5-MTHF Plus B12 is available in 30 tablets and 60 tablets

Discussion

5-MTHF (5-methyltetrahydrofolate)

5-MTHF is the most biologically active form of folate. It is the predominant type of folate present in food and the form into which the body must convert all other forms of folate.^[1] Along with vitamin B12, folate serves as a donor of methyl groups. The body utilizes methyl groups in many nervous system and metabolic processes, including the conversion of homocysteine to methionine, the synthesis of monoamine neurotransmitters, the production of melatonin, and the synthesis of DNA. In addition, sufficient folate is necessary for brain and nervous system functions and for a healthy pregnancy outcome.*

5-MTHF—Preferred Over Folic Acid

Folic acid is the synthetic form of folate that is used to fortify foods. It is often found in dietary supplements as well. Despite some research showing that folic acid and 5-MTHF have equivalent bioavailability, 5-MTHF is often the preferred form to replenish folate. This is due, primarily, to the presence of digestive or metabolic variabilities that can affect the conversion of folic acid to 5-MTHF.^[2-4] Furthermore, studies have shown that 5-MTHF increased plasma folate more effectively than folic acid irrespective of genetic differences in metabolism.^[1,5] A study in women of childbearing age showed that 5-MTHF was more effective than folic acid in improving overall folate status.*^[6]

Using 5-MTHF instead of folic acid has several important advantages. 5-MTHF provides the biologically active form of folate, reduces the potential for masking hematological symptoms of vitamin B12 deficiency, reduces interactions with drugs that inhibit dihydrofolate reductase, overcomes folate metabolism challenges associated with functioning of methylenetetrahydrofolate reductase (MTHFR), and prevents the potential negative effects of UMFA in the peripheral circulation.*^[7]

Clinical Applications

- » Support Methylation*
- » Support Nervous System Health*
- » Support Normal Cellular Proliferation (Including Red Blood Cells)*
- » 5-MTHF Does Not Contribute to Unmetabolized Folic Acid Accumulation (UMFA)*
- » 5-MTHF Supports Healthy Serum Folate Levels*
- » 5-MTHF Supports a Healthy Pregnancy Outcome*

*5-MTHF is the most biologically active form of the water-soluble B vitamin, folate. It is the preferred form of folate supplementation due to an array of conditions that can limit conversion or absorption of folic acid. Data indicate that supplementing with 5-MTHF increases plasma folate more effectively than folic acid. MecobalActive™, which is found in the 5-MTHF plus B12 formula, is a highly pure form of methylcobalamin that does not use any harmful solvents during manufacture.**

Quatrefolic®

In XYMOGEN's formulas, 5-MTHF is provided as Quatrefolic—the glucosamine salt of 5-MTHF. Quatrefolic is proven to have greater stability, solubility, and bioavailability over the commonly used calcium salt form of 5-MTHF. In a randomized crossover study, subjects received 400 mcg/d of Quatrefolic or 5-MTHF calcium salt. Titer-normalized Cmax and AUC demonstrated a 10% higher bioavailability of Quatrefolic.^[8] Quatrefolic has several in vitro and in vivo preclinical and clinical studies to characterize and assure the safety profile of the product.*^[9]

5-MTHF Plus B12

XYMOGEN's 5-MTHF Plus B12 formula combines Quatrefolic and vitamin B12 as MecobalActive™ in cherry-flavored, quick-dissolve tablets. MecobalActive is a pure form of methylcobalamin. Many vitamin B12 supplements on the market contain cyanocobalamin. The liver is able to convert a small amount of cyanocobalamin to methylcobalamin; however, methylcobalamin is the preferred form because it is the bioactive form and is therefore better utilized.^[10] Another point of interest regarding B12 supplementation is the commonly held belief that intramuscular injections of B12 are more effective than oral supplementation. In fact, oral supplementation is just as effective and carries the added benefits of lower cost and ease of administration.^[11,12] Unlike other sources of methylcobalamin on the market, MecobalActive does not use any harmful solvents during its manufacture. The patented, advanced production methods used to create MecobalActive also result in a methylcobalamin with greater purity and lower moisture, which translates to greater stability.*

Functions of B12

Vitamin B12 supports healthy methylation through its roles in the synthesis of methionine from homocysteine and synthesis of S-adenosylmethionine (SAMe). As an example of its importance in homocysteine metabolism, one study showed that the addition of B12 to a folate regimen had a greater impact (7%) on homocysteine than did folate alone.^[13] Like folate, erythroblasts require vitamin B12

Continued on next page

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

5-MTHF Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Folate (as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt)	2000 mcg DFE	500%

Other Ingredients: Microcrystalline cellulose, HPMC (capsule), stearic acid, magnesium stearate, and silica.

DIRECTIONS: Take one to two capsules daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.



Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,662.

**5-MTHF ES Supplement Facts**

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Folate (as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt)	10,000 mcg DFE	2500%

Other Ingredients: Microcrystalline cellulose, HPMC (capsule), stearic acid, magnesium stearate, and silica.

DIRECTIONS: Take one to two capsules daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.



Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,662.

**5-MTHF Plus B12 Supplement Facts**

Serving Size: 1 Quick-Dissolve Tablet

	Amount Per Serving	%Daily Value
Folate (as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt)	1000 mcg DFE	250%
Vitamin B12 (as MecobalActive™ methylcobalamin)	2500 mcg	104,167%

Other Ingredients: Xylitol, ascorbyl palmitate, silica, and natural cherry flavor.

DIRECTIONS: Take one cherry-flavored tablet daily, or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.



Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,662.



MecobalActive™ is a trademark of Ferrer Health Tech. The active form of B₁₂

for proliferation during their differentiation.^[14] B12 is important for neurological health, and chronic insufficiency can affect the spinal cord, peripheral nerves, the optic nerve, and the brain. Research also supports a role for methylcobalamin supplementation in modulating melatonin secretion, enhancing light sensitivity, normalizing circadian rhythms, and improving sleep-wake cycles.*^[15,16]

References

1. Prinz-Langenohl R, Brämswig S, Tobolski O, et al. [6S]-5-methyltetrahydrofolate increases plasma folate more effectively than folic acid in women with the homozygous or wild-type 677C->T polymorphism of methylenetetrahydrofolate reductase. *Br J Pharmacol.* 2009 Dec;158(8):2014-21. [PMID: 19917061]
2. Yakut M, Ustün Y, Kabaçam G, et al. Serum vitamin B12 and folate status in patients with inflammatory bowel diseases. *Eur J Intern Med.* 2010 Aug;21(4):320-23. [PMID: 20603044]
3. Venn BJ, Green TJ, Moser R, et al. Comparison of the effect of low-dose supplementation with L-5-methyltetrahydrofolate or folic acid on plasma homocysteine: a randomized placebo-controlled study. *Am J Clin Nutr.* 2003 Mar;77(3):658-62. [PMID: 12600857]
4. 5-methyltetrahydrofolate. Monograph. *Altern Med Rev.* 2006 Dec;11(4):330-37. [PMID: 17176169]
5. Willems FF, Boers GH, Blom HJ, et al. Pharmacokinetic study on the utilisation of 5-methyltetrahydrofolate and folic acid in patients with coronary artery disease. *Br J Pharmacol.* 2004 Mar;141(5):825-30. [PMID: 14769778]
6. Lamers Y, Prinz-Langenohl R, Brämswig S, et al. Red blood cell folate concentrations increase more after supplementation with [6S]-5-methyltetrahydrofolate than with folic acid in women of childbearing age. *Am J Clin Nutr.* 2006 Jul;84(1):156-61. [PMID: 16825690]
7. Scaglione F, Panzavolta G. Folate, folic acid and 5-methyltetrahydrofolate are not the same thing. *Xenobiotica.* 2014 May;44(5):480-8. [PMID: 24494987]
8. Crossover Comparative Bioavailability Study of 5-Methyltetrahydrofolate Glucosamine Salt (GN10G) Compared to the Reference Metafolin® in Healthy Volunteers. IPAS-5MTHFA-583-09 final report. Desio, Italy: Gnosis S.p.A.; March 15, 2010: 1-33. [available from the manufacturer Gnosis S.p.A. upon request]
9. Thomas J, Heimbach, J, Soni M. Determination of the Generally Recognized as Safe (GRAS) Status of (6S)-5-Methyltetrahydrofolic acid Glucosamine Salt. Expert panel statement. Desio, Italy: Gnosis S.p.A.; July, 2010: 1-46. [available from the manufacturer Gnosis S.p.A. upon request]
10. Methylcobalamin. *Altern Med Rev.* 1998 Dec;3(6):461-3. Erratum in: *Altern Med Rev* 1999 Feb;4(1):9. [PMID: 9855571]
11. Kuzminski AM, Del Giacco EJ, Allen RH, et al. Effective treatment of cobalamin deficiency with oral cobalamin. *Blood.* 1998 Aug 15;92(4):1191-98. [PMID: 9694707]
12. Kim HI, Hyung WJ, Song KJ, et al. Oral vitamin B12 replacement: an effective treatment for vitamin B12 deficiency after total gastrectomy in gastric cancer patients. *Ann Surg Oncol.* 2011 Dec;18(13):3711-17. [PMID: 21556950]
13. Lowering blood homocysteine with folic acid based supplements: meta-analysis of randomised trials. Homocysteine Lowering Trialists' Collaboration. *BMJ.* 1998 Mar;316(7135):894-98. [PMID: 9569395]
14. Koury MJ, Ponka P. New insights into erythropoiesis: the roles of folate, vitamin B12, and iron. *Annu Rev Nutr.* 2004;24:105-31. [PMID:15189115]
15. Kiuchi T, Sei H, Seno H, et al. Effect of vitamin B12 on the sleep-wake rhythm following an 8-hour advance of the light-dark cycle in the rat. *Physiol Behav.* 1997 Apr;61(4):551-54. [PMID: 9108574]
16. Honma K, Kohsaka M, Fukuda N, et al. Effects of vitamin B12 on plasma melatonin rhythm in humans: increased light sensitivity phase-advances the circadian clock? *Experientia.* 1992 Aug 15;48(8):716-20. [PMID: 1516676]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

6 Day Detox Kit Family

Biotransformation Program



6 Day Detox Micro Kit includes 10 single serving packets of OptiCleanse GHI Vanilla Delight Sugar- & Stevia-Free[‡], 1 bottle of ColonX 60c, 1 carton of ProbioMax Daily DF 30c, and 1 bottle of Drainage 1 fl oz.

6 Day Detox Kit includes 1 bottle of OptiCleanse GHI Vanilla Delight, 1 bottle of ColonX 60c, 1 carton of ProbioMax Daily DF 30c, 1 bottle of Drainage 1 fl oz, and 1 20 oz Shaker Bottle.

Discussion

While other detoxification kits that are found in the marketplace focus simply on liver detoxification, the reach of XYMOGEN's 6 Day Detox Kit extends far beyond the liver. Of course, supporting phase I and phase II liver detoxification pathways and antioxidant activity, as accomplished by OptiCleanse GHI, is critical; but there are multiple systems and organs involved in detoxification. For this reason, a detox program cannot be truly comprehensive without addressing the whole body.*

For instance, the movement of food and waste through the digestive system is an important aspect of cleansing and detoxification. Food must be well-digested, and it must move at a healthy pace through the intestines and colon. The longer the transit time, the longer the toxic waste matter sits in the bowel, and the more likely that toxins will be reabsorbed. XYMOGEN's 6 Day Detox Kit includes the regularity-supporting action of ColonX not only to complement the liver-detoxing functions of OptiCleanse GHI but also because bowel movements should be regular before the start of a detox program.*

Probiotics are another critical aid to the detoxification process. Probiotics may help reduce toxin production in the intestines, and they also help directly eliminate toxins. An animal study showed that compared to controls, rats supplemented with probiotics had a significant decrease in blood BPA (bisphenol A) concentration after BPA administration, a 2.4 times greater excretion of BPA in feces, and a significantly higher percentage of BPA bound to the sediment fraction of the feces.^[1] Laboratory tests suggest that probiotics are able to adsorb or metabolize NMDA (N-nitrosodimethylamine), nitrate, HCA (heterocyclic aromatic amines), and a variety of organophosphorus pesticides.^[2-5] Furthermore, certain gut microbiota, such as lactobacilli, can bind and sequester heavy metals,^[6,7] which can result in eventual removal of the metals through defecation.*^[6,8]

By including probiotics with formulas that specifically promote good digestion, drainage, regular bowel elimination, GI health, balanced phase I and phase II detoxification, and powerful antioxidant

Clinical Applications

- » Supports Natural Detoxification Mechanisms*
- » Helps Maintain a Healthy Intestinal Microecology*
- » Supports the Body's Natural Immune Response*
- » Supports a Balanced Cytokine Profile*
- » Supports Digestion, Assimilation, and Elimination*
- » Supports Lactose Digestion*
- » Promotes Gastrointestinal Health, Motility, Stool Bulk, and Bowel Regularity*

*6 Day Detox Kit is designed to renew and enhance the body's cleansing and detoxification capabilities. It combines four specially selected XYMOGEN formulations: ColonX™, Drainage™, ProbioMax® Daily DF, and OptiCleanse® GHI. When taken together, as recommended within the 6-Day Detox Guide, these complementary formulas work in concert to encourage the various detox-linked systems and organs of the body to process and eliminate waste and toxins.**

protection, 6 Day Detox Kit is a truly complete and thoughtful approach to detoxification. Each formula addresses different aspects of whole body detoxification:

OptiCleanse GHI is a comprehensive, fructose-free, low-allergy-potential dietary supplement designed to support GI function and balanced detoxification.^[9-12] OptiCleanse GHI contains macro- and micronutrients, as well as a host of specialized ingredients (some patented or proprietary) that help moderate phase I detoxification and upregulate and support phase II pathways.^[13-15] Generous antioxidant support combats the free radicals produced during phase I activation; and activated cofactors support mitochondrial energy production, which is needed for biotransformation and detoxification. Additionally, this multifaceted formula supports healthy eicosanoid metabolism and cytokine production.*

In addition to a host of phytonutrients, amino acids, and antioxidant nutrients, OptiCleanse GHI features VegaPro™, XYMOGEN's proprietary amino acid and pea/rice protein blend; Aminogen®, an enzyme matrix that facilitates protein absorption; Preventium®, a patented form of potassium hydrogen d-glucarate that supports glucuronidation; Albion mineral amino acid chelates; and activated B vitamins, including Quatrefolic® and methylcobalamin.*

ColonX is designed to support GI regularity and complement dietary fiber intake. GI regularity and function is vital to physiological balance and overall well-being. How well the body digests and assimilates metabolic fuel and eliminates metabolic waste determines health at the cellular level. Toxins that enter the body must be detoxified and their metabolites must exit the body. Gastrointestinal elimination plays a major role in detoxification by expelling the remnants of toxic molecules. If these harmful remnants are not eliminated, they can recirculate throughout the body.*

Continued on next page

EXCLUSIVE • PATENTED

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

Antioxidant Activity

Detoxification

Cytokine Balance Support

Gastrointestinal Support

Immune System Support

Liver Support

Antioxidant Activity

Detoxification

Cytokine Balance Support

Gastrointestinal Support

Immune System Support

Liver Support

OptiCleanse® GHI Vanilla Delight Sugar- & Stevia Free† Single Serving Packet Supplement Facts

Serving Size: 1 Packet

	Amount Per Serving	%DV
Calories	210	
Total Fat	8 g	10%*
Saturated Fat	2 g	10%*
Total Carbohydrate	10 g	4%*
Dietary Fiber	4 g	14%
Protein	26 g	
Vitamin A (as natural beta-carotene)	750 mcg	83%
Vitamin C (as sodium ascorbate)	250 mg	278%
Thiamin (as thiamine HCl)	15 mg	1250%
Riboflavin (as riboflavin 5'-phosphate sodium)	5 mg	385%
Niacin (as niacinamide and niacin)	40 mg	250%
Vitamin B6 (as pyridoxal 5'-phosphate)	5 mg	294%
Folate (as Quatrefolic® (6S)-5-methyltetrahydrofolate acid, glucosamine salt)	200 mcg DFE	50%
Vitamin B12 (as methylcobalamin)	50 mcg	2083%
Biotin	150 mcg	500%
Pantothenic Acid (as d-calcium pantothenate)	35 mg	700%
Choline (as choline bitartrate)	100 mg	18%
Calcium (as DimaCal® di-calcium malate and ingredients with naturally occurring calcium)	225 mg	17%
Iron (naturally occurring)	5 mg	28%
Iodine (as potassium iodide)	60 mcg	40%
Magnesium (as Albion® di-magnesium malate)	140 mg	33%
Zinc (as TRAACS® zinc bisglycinate chelate)	10 mg	91%
Selenium (as Albion® selenium glycinate complex)	100 mcg	182%
Manganese (as TRAACS® manganese bisglycinate chelate)	2 mg	87%
Chromium (as TRAACS® chromium nicotinate glycinate chelate)	60 mcg	171%
Molybdenum (as TRAACS® molybdenum glycinate chelate)	35 mcg	78%
Sodium (from ingredients with naturally occurring sodium, sodium sulfate anhydrous, and sodium ascorbate)	560 mg	24%
Potassium (from tripotassium citrate and ingredients with naturally occurring potassium)	455 mg	10%
Stabilized Flaxseed	5.6 g	**
Typical Alpha-Linolenic Acid	1.28 g	**
Typical Linoleic Acid	392 mg	**
Pomegranate Extract (<i>Punica granatum</i>)(hull)(40% ellagic acid)	400 mg	**
Betaine Anhydrous (trimethylglycine)	250 mg	**
Lemon Bioflavonoid Complex (<i>Citrus x limon</i>)(fruit peel)(25% bioflavonoids)	250 mg	**
Quercetin (as quercetin dihydrate from <i>Dimorphandra mollis</i> (pod))	250 mg	**
Preventium® (potassium d-glucarate)	250 mg	**
Rutin (from <i>Sophora japonica</i>)(bud)	200 mg	**
BCM-95® Turmeric Extract (<i>Curcuma longa</i>)(rhizome)(95% total curcuminoids complex, including curcumin, curcuminoids, and volatile oils)(86% curcuminoids)(65% curcumin)	200 mg	**
N-Acetyl-L-Cysteine	150 mg	**
Ginger (<i>Zingiber officinale</i>)(rhizome)	150 mg	**
Methylsulfonylmethane (MSM)	120 mg	**
Sodium Sulfate Anhydrous	100 mg	**
Watercress (<i>Nasturtium officinale</i>)(aerial parts)	100 mg	**
Green Tea Aqueous Extract (<i>Camellia sinensis</i>)(leaf)(80% polyphenols, 60% catechins, 30% EGCG, 6% caffeine)	82 mg	**

* Percent Daily Values are based on a 2,000 calorie diet.

** Daily Value (DV) not established.

Other Ingredients: VegaPro™ (XYMOGEN's proprietary blend of pea protein isolate, taurine, glycine, rice protein concentrate, and L-glutamine), sunflower oil, natural flavors (no MSG), medium-chain triglyceride oil, cellulose gum, xanthan gum, Aminogen® fungal proteases, monk fruit extract, guar gum, and silica.

DIRECTIONS: Blend, shake, or briskly stir the contents of one packet (53 g) into 10-12 ounces chilled, pure water (or mix amount for desired thickness) and consume once daily, or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner.

STORAGE: Store in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

†This formula is not a low-calorie dietary supplement. Please see the Supplement Facts panel for more details.

BCM-95® is a registered trademark of DolCas Biotech, Ltd. Protected under US patents 7,883,728; 7,736,679; and 7,879,373.

Preventium® is a registered trademark of Applied Food Sciences, LLC. (US patents 4,845,123, 5,364,644, 5,561,160).

6 Day Detox Kit contains OptiCleanse GHI Vanilla Delight which has all of the same active ingredients found in OptiCleanse GHI Vanilla Delight Sugar- & Stevia Free†. However, it contains sugar and stevia, and does not contain monk fruit extract.

ColonX features magnesium citrate for its promotion of muscle relaxation and effective elimination of feces through the bowel. Magnesium citrate is also highly bioavailable.^[16] Cape aloe is added to support normal GI transit time and stool bulk.^[17] Triphala, a balanced blend of astringent fruits used extensively in Ayurveda, is present to support all phases of digestion, assimilation, and elimination.*^[18]

Drainage combines homeopathic “drainers” with homeopathic remedies that support excretory function and address symptoms of toxicity. Cleansing itself of by-products and waste that accumulate is an essential function of the body. Homeopathic drainage, specifically, is a process of detoxifying the body that involves opening the emunctories and elimination channels and discharging toxic accumulation. Emunctories are organs of elimination: liver, kidneys, lungs, stomach, intestines, pancreas, skin, nose, genitals. Toxic accumulation can occur from external sources, such as pesticides, insecticides, and herbicides, and from internal sources, such as stress and inadequate nutrition, which lead to undesirable changes in metabolic function.*

ProbioMax Daily DF is a vegetarian, dairy- and gluten-free, four-strain probiotic formula totaling 30 billion CFU (colony forming units) per capsule. Supplementation with probiotics assists with many mechanisms of action that benefit health, including (1) supporting metabolic activity, such as the production of short-chain fatty acids and vitamins, nutrient absorption, and the digestion of lactose; (2) adhering to intestinal epithelial cells to help maintain a healthy balance of organisms in the intestinal tract; (3) helping to establish populations of good bacteria after disruption in balance; (4) supporting immune function; (5) promoting intestinal epithelial cell survival; (6) supporting healthy bowel function; and (7) degrading oxalates.^[19-25] Additionally, the role of probiotics in direct detoxification and elimination of unwanted substances is scientifically supported, as discussed earlier.*^[1-8]

ProbioMax Daily DF provides four researched strains of beneficial bacteria: *Lactobacillus acidophilus* La-14®, *Lactobacillus plantarum* Lp-115®, *Bifidobacterium longum* BI-05™, and the extensively studied HN019 strain of *Bifidobacterium lactis*. These live microorganisms have proven health benefits and well-established safety, and have been tested for epithelial cell adhesion and/or resistance to low pH.*

Each vegetarian capsule is sealed in nitrogen-purged aluminum blister packs that serve as protection from factors proven to compromise probiotic stability, such as heat, moisture, and oxygen. To further support resistance to low pH and assist the delivery of microorganisms to the small intestine, XYMOGEN employs DRcaps™ gastro-resistant capsules. These specially designed, innovative capsules help slow the exposure of actives to stomach acid and ensure more targeted release.*



Albion®, DimaCal®, TRAACS®, and the Albion Gold Medallion® are registered trademarks of Albion Laboratories, Inc. Malates covered by US patent 6,706,904.



Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,662.



AMINOGEN® is a registered trademark of Innophos Nutrition, Inc. AMINOGEN is protected under U.S. patent 5,387,422.



EXCLUSIVE • PATENTED

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

ColonX™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Magnesium (as magnesium citrate)	200 mg	48%
Triphala Extract (<i>Embilica officinalis</i>)(fruit), (<i>Terminalia bellerica</i>)(fruit), (<i>Terminalia chebula</i>)(fruit)(45% tannins)	250 mg	**
Cape Aloe (<i>Aloe ferox</i>)(leaf)	50 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, silica, and medium-chain triglycerides.

DIRECTIONS: Take one to two capsules at bedtime with 8 oz of water, or as directed by your healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn protein, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, artificial colors, artificial sweeteners, or preservatives.

CAUTIONS: Consult your healthcare practitioner before use. **DO NOT USE IF YOU ARE PREGNANT OR NURSING.** Discontinue use if diarrhea or abdominal pain develops. Intended for occasional support of bowel movements.

STORAGE: Keep tightly closed in a cool, dry place out of reach of children.



ProbioMax® Daily DF Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Proprietary Blend <i>Lactobacillus acidophilus</i> La-14® <i>Bifidobacterium longum</i> BI-05™ <i>Lactobacillus plantarum</i> Lp-115®	174 mg (15 Billion CFU) [†]	**
HOWARU® Bifido (<i>Bifidobacterium lactis</i> HN019®)	50 mg (15 Billion CFU) [†]	**

** Daily Value not established.

Other Ingredients: Microcrystalline cellulose, HPMC (acid-resistant capsule), stearic acid, magnesium stearate, and silica.

[†] Colony-Forming Unit

DIRECTIONS: Take one capsule with water daily, or as directed by your healthcare practitioner.

Children and pregnant or lactating women should consult their healthcare practitioner prior to use.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or preservatives.

STORAGE: No refrigeration necessary. Keep closed in a cool, dry place out of reach of children.

HOWARU®

HOWARU and the HOWARU logo are registered trademarks of DuPont or its affiliates.

HN019 is a registered trademark of Fonterra Limited and is licensed to DuPont Nutrition Biosciences.



Drainage

DIRECTIONS: Ages 12 and up, take 6 drops by mouth (ages 0 to 11, give 3 drops) at bedtime, or use as directed by your healthcare practitioner.

ACTIVE INGREDIENTS: Equal parts of Cynara 6x, Solidago 6x, Taraxacum 6x, Benzoicum ac. 15x, Berber. vulg. 15x, Bryonia 15x, Cantharis 15x, Carduus ben. 15x, Carduus mar. 15x, Ceanothus 15x, Chelidonium maj. 15x, Chionanthus 15x, Cinchona 15x, Dioscorea 15x, Dolichos 15x, Iris vers. 15x, Juniperus com. 15x, Nux vom. 15x, Ptelea 15x, Taraxacum 15x, Uricum ac. 15x.

INACTIVE INGREDIENTS: USP purified water; USP gluten-free, non-GMO, organic cane alcohol 20%.

WARNING: Keep out of reach of children. Do not use if tamper-evident seal is broken or missing. If symptoms worsen or persist for more than a few days, consult a doctor. If pregnant or breast-feeding, ask a doctor before use.

References

- Oishi K, Sato T, Yokoi W, et al. Effect of probiotics, *Bifidobacterium breve* and *Lactobacillus casei*, on bisphenol A exposure in rats. *Biosci Biotechnol Biochem*. 2008 Jun;72(6):1409-15. [PMID: 18540113]
- Islam SM, Math RK, Cho KM, et al. Organophosphorus hydrolase (OpdB) of *Lactobacillus brevis* WCP902 from kimchi is able to degrade organophosphorus pesticides. *J Agric Food Chem*. 2010 May 12;58(9):5380-86. [PMID: 20405842]
- Cho KM, Math RK, Islam SM, et al. Biodegradation of chlorpyrifos by lactic acid bacteria during kimchi fermentation. *J Agric Food Chem*. 2009 Mar 11;57(5):1882-89. [PMID: 19199784]
- Nowak A, Kuberski S, Libudzisz Z. Probiotic lactic acid bacteria detoxify N-nitrosodimethylamine. *Food Addit Contam Part A Chem Anal Control Expo Risk Assess*. 2014;31(10):1678-87. [PMID: 25010287]
- Sobko T, Reinders CI, Jansson E, et al. Gastrointestinal bacteria generate nitric oxide from nitrate and nitrite. *Nitric Oxide*. 2005 Dec;13(4):272-78. [PMID: 16183308]
- Robinson JB, Tuovinen OH. Mechanisms of microbial resistance and detoxification of mercury and organomercury compounds: physiological, biochemical, and genetic analyses. *Microbiol Rev*. 1984 Jun;48(2):95-124. [PMID: 6377034]
- Halttunen T, Salminen S, Tahvonen R. Rapid removal of lead and cadmium from water by specific lactic acid bacteria. *Int J Food Microbiol*. 2007 Feb 28;114(1):30-35. [PMID: 17184867]
- Monachese M, Burton JP, Reid G. Bioremediation and tolerance of humans to heavy metals through microbial processes: a potential role for probiotics? *Appl Environ Microbiol*. 2012 Sep;78(18):6397-404. [PMID: 22798364]
- Smith RJ, Wilmore DW. Glutamine nutrition and requirements. *JPN J Parenter Enteral Nutr*. 1990 Jul-Aug;14(4 Suppl):94S-99S. Review. [PMID: 2119461]
- Lantz RC, Chen GJ, Sarihan M, et al. The effect of extracts from ginger rhizome on inflammatory mediator production. *Phytomedicine*. 2007 Feb;14(2-3):123-28. [PMID: 16709450]
- Adolphe JL, Whiting SJ, Juurlink BH, et al. Health effects with consumption of the flax lignan secoisolariciresinol diglucoside. *Br J Nutr*. 2010 Apr;103(7):929-38. Review. [PMID: 20003621]
- Hofmann T, Kuhnert A, Schubert A, et al. Modulation of detoxification enzymes by watercress: in vitro and in vivo investigations in human peripheral blood cells. *Eur J Nutr*. 2009 Dec;48(8):483-91. [PMID: 19636603]
- Barch DH, Rundhaugen LM, Stoner GD, et al. Structure-function relationships of the dietary anticarcinogen ellagic acid. *Carcinogenesis*. 1996 Feb;17(2):265-69. [PMID: 8625448]
- Akhlaghi M, Bandy B. Dietary green tea extract increases phase 2 enzyme activities in protecting against myocardial ischemia-reperfusion. *Nutr Res*. 2010 Jan;30(1):32-39. [PMID: 20116658]
- Amália PM, Possa MN, Augusto MC, et al. Quercetin prevents oxidative stress in cirrhotic rats. *Dig Dis Sci*. 2007 Oct;52(10):2616-21. [PMID: 17431769]
- Walker AF, Marakis G, Christie S, et al. Mg citrate found more bioavailable than other Mg preparations in a randomised, double-blind study. *Magnes Res*. 2003 Sep;16(3):183-91. [PMID: 14596323]
- Wintola OA, Sunmonu TO, Afolayan AJ. The effect of *Aloe ferox* Mill. in the treatment of loperamide-induced constipation in Wistar rats. *BMC Gastroenterol*. 2010 Aug 19;10:95. [PMID: 20723249]
- Mukherjee PK, Rai S, Bhattacharyya S, et al. Clinical study of "triphala" – a well-known phytomedicine from India. *Iranian J Pharmacol Ther*. 2006 Jan;5(1):51-54. <http://www.bioline.org.br/request?pt06008>. Accessed June 18, 2012.
- Vanderpool C, Yan F, Folk DB. Mechanisms of probiotic action: Implications for therapeutic applications in inflammatory bowel diseases. *Inflamm Bowel Dis*. 2008 Nov;14(11):1585-96. [PMID: 18623173]
- Abratt VR, Reid SJ. Oxalate-degrading bacteria of the human gut as probiotics in the management of kidney stone disease. *Adv Appl Microbiol*. 2010;72:63-87. [PMID: 20602988]
- Masood MI, Qadir MI, Shirazi JH, et al. Beneficial effects of lactic acid bacteria on human beings. *Crit Rev Microbiol*. 2011 Feb;37(1):91-98. [PMID: 21162695]
- Turroni S, Vitali B, Bendazzoli C, et al. Oxalate consumption by lactobacilli: evaluation of oxalyl-CoA decarboxylase and formyl-CoA transferase activity in *Lactobacillus acidophilus*. *J Appl Microbiol*. 2007 Nov;103(5):1600-09. [PMID: 17953571]
- Shu Q, Lin H, Rutherford KJ, et al. Dietary *Bifidobacterium lactis* (HN019) enhances resistance to oral *Salmonella typhimurium* infection in mice. *Microbiol Immunol*. 2000;44(4):213-22. [PMID: 10832963]
- Gopal P, Prasad J, Gill H. Effects of the consumption of *Bifidobacterium lactis* HN019 (DR10TM) and galacto-oligosaccharides on the microflora of the gastrointestinal tract in human subjects. *Nutr Res*. 2003;23(10):1313-28. [http://www.nrjournal.com/article/S0271-5317\(03\)00134-9/abstract](http://www.nrjournal.com/article/S0271-5317(03)00134-9/abstract). Accessed December 22, 2014.
- Waller PA, Gopal PK, Leyer GJ, et al. Dose-response effect of *Bifidobacterium lactis* HN019 on whole gut transit time and functional gastrointestinal symptoms in adults. *Scand J Gastroenterol*. 2011 Sep;46(9):1057-64. [PMID: 21663486]

Additional references available upon request

EXCLUSIVE • PATENTED

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

ActivEssentials™

Daily Dose-Pack Nutrition



Available in 60 packets

Discussion

The average diet can be lacking in complete nutrition due to modern food-production techniques, poor food choices, and nutrient-depleting preparation methods.^[1-3] Combine these with the toll of lifestyle stress and oxidizing chemicals—found in foods and the environment—and it becomes essential to ensure comprehensive foundation nutrition for the body. To achieve this, each cellophane-wrapped package of ActivEssentials contains the following XYMOGEN® formulas:*

ActivNutrients® without Iron This high-quality, hypoallergenic multivitamin/mineral blend is provided in vegetable capsules and not only features activated vitamin cofactors and patented Albion® chelated mineral complexes, but it also provides folate as 5-MTHF as well as methylcobalamin as MecobalActive™. The form of 5-MTHF is Quatrefolic®, which is proven to have greater stability, solubility, and bioavailability when compared to calcium salt forms of 5-MTHF.^[4] MecobalActive is a patented form of methylcobalamin that has very high purity; no harmful solvents are used in its production.^[5] The balanced nutrient profile in ActivNutrients without Iron supports vitamin/mineral synergistic activity; antioxidant protection with vitamins C and E, selenium, and carotenoids; and phase I detoxification.*

Oraxinol™ This innovative blend contains oxidation-fighting botanicals derived from a variety of fruits. The technique known as ORAC (oxygen radical absorbance capacity) measures antioxidant capacity, and units of an ORAC value are expressed as micromoles Trolox equivalents per gram of a substance. Consuming an average of five to nine servings per day of a variety of fruits and vegetables yields 6000 Trolox equivalents. This same amount is supplied by just two capsules (1000 mg) of Oraxinol.*^[6]

OmegaPure 600 EC™ Each enteric-coated softgel contains 1 g of fish oil, delivering 360 mg of eicosapentaenoic acid (EPA) and 240 mg of docosahexaenoic acid (DHA). A rigorous, proprietary, temperature-controlled/vacuum technology is used for purification and manufacturing. Stringent verification processes reduce any potential health risks that may otherwise result from the oil's exposure to rancid fats, toxins, bacteria, molds, yeasts, or very high levels of fat-soluble vitamins, such as vitamin A.

Clinical Applications

- » Provide Foundation Micronutrition for a Variety of Protocols*
- » Support Improved Dietary Nutrient Intake*
- » Provide Antioxidant Support*

ActivEssentials™ is a convenient way to get daily comprehensive nutritional support. Each daily dose packet contains several different supplements that provide Albion® chelated minerals; activated B vitamins, including 5-MTHF as Quatrefolic® and methylcobalamin as MecobalActive™; botanicals for antioxidant protection; and fresh, pure IFOS five-star certified fish oils. ActivEssentials™ for Women contains iron and additional calcium while ActivEssentials™ with Calcium contains extra calcium without iron.

XYMOGEN is proud to provide this International Fish Oil Standards (IFOS) five-star certified formula, which assures the highest level of purity, stability, and potency in fish oils. In addition to complying with a host of federal and state regulations, our supplier also agrees to adhere to voluntary guidelines for manufacturing and to a code of ethics as members of the Council for Responsible Nutrition. Research suggests that consumption of EPA and DHA omega-3 fatty acids may support cardiovascular health.^[7] Studies have also shown that fish oils may support healthy cytokine production, promote optimal joint function,^[8] and support overall brain and nervous system function.*^[9]

Notes

ActivEssentials™ with Calcium contains the same nutrients in the same amounts that are present in ActivEssentials, plus each packet contains one capsule of XYMOGEN's Ossopan™ for added calcium. Ossopan is microcrystalline hydroxyapatite concentrate (MCHC), a complex crystalline compound that contains calcium, phosphorus, bioactive growth factors, type I collagen, amino acids, glycosaminoglycans, and essential trace elements that naturally comprise healthy bone. Each Ossopan capsule contains 275 mg of calcium which, in addition to the 50 mg of calcium delivered in ActivEssentials from DimaCal® dicalcium malate and calcium ascorbate, brings the total amount of calcium to 325 mg per packet. This amount of calcium comprises 33% daily value (DV). One capsule of Ossopan also provides 99 mg of phosphorus, which is 10% DV.

ActivEssentials™ for Women contains the same nutrients in the same amounts as found in ActivEssentials with Calcium. Each packet of ActivEssentials for Women also contains 2.5 mg of iron and comprises 14% DV. The iron in this formula is Albion's Ferrochel® (ferrous bisglycinate chelate), a well-studied, 100% fully-reacted, and patented form of iron that has higher bioavailability, lower toxicity, fewer food interactions, and a longer shelf life than any other common form of iron.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

ActiveEssentials™ Supplement Facts

Serving Size: 1 Packet

	2 ActivNutrients® without Iron Capsules		1 Oraxinol™ 1 Capsule		1 OmegaPure 600 EC™ Softgel	
	Amount Per Serving	%DV	Amount Per Serving	%DV	Amount Per Serving	%DV
Calories					10	
Total Fat					1 g	1%†
Vitamin A (75% as natural beta-carotene and 25% as retinyl palmitate)	1120 mcg	124%				
Vitamin C (as sodium ascorbate, potassium ascorbate, zinc ascorbate, and calcium ascorbate)	125 mg	139%				
Vitamin D3 (cholecalciferol)	2.5 mcg (100 IU)	13%				
Vitamin E (as d-alpha tocopheryl succinate and mixed tocopherols)	67 mg	447%				
Thiamin (as thiamine mononitrate)	10 mg	833%				
Riboflavin (as riboflavin 5'-phosphate sodium)	10 mg	769%				
Niacin (as niacinamide and niacin)	32 mg	200%				
Vitamin B6 (as pyridoxal 5'-phosphate)	10 mg	588%				
Folate (as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt)	200 mcg DFE	50%				
Vitamin B12 (as MecobalActive™ methylcobalamin)	250 mcg	10,417%				
Biotin	500 mcg	1667%				
Pantothenic Acid (as d-calcium pantothenate)	100 mg	2000%				
Choline (as choline dihydrogen citrate)	18 mg	3%				
Calcium (as DimaCal® di-calcium malate, d-calcium pantothenate, and calcium ascorbate)	50 mg	4%				
Iodine (as potassium iodide)	50 mcg	33%				
Magnesium (as Albion® di-magnesium malate)	50 mg	12%				
Zinc (as TRAACS® zinc bisglycinate chelate)	6.5 mg	59%				
Selenium (as Albion® selenium glycinate complex)	50 mcg	91%				
Copper (as TRAACS® copper bisglycinate chelate)	0.5 mg	56%				
Manganese (as TRAACS® manganese bisglycinate chelate)	0.25 mg	11%				
Chromium (as TRAACS® chromium nicotinate glycinate chelate)	250 mcg	714%				
Molybdenum (as TRAACS® molybdenum glycinate chelate)	25 mcg	56%				
Potassium (as Albion® potassium glycinate complex and potassium ascorbate)	49.5 mg	1%				
Fish Oil Concentrate					1 g	**
Total Omega-3 Fatty Acids					650 mg	**
EPA (eicosapentaenoic acid)					360 mg	**
DHA (docosahexaenoic acid)					240 mg	**
Oraxinol (proprietary blend of grape (<i>Vitis vinifera</i>) (seed, skin, and pulp), pomegranate (<i>Punica granatum</i>) (whole fruit), blueberry (<i>Vaccinium uliginosum</i>) (whole berry), chokeberry (<i>Aronia arbutifolia</i>) (whole berry), mangosteen (<i>Garcinia mangostana</i>) (skin), cranberry (<i>Vaccinium macrocarpon</i>) (whole berry), goji berry (<i>Lycium barbarum</i>) (whole berry), apple (<i>Malus pumila</i> Mill.) (skin), bilberry (<i>Vaccinium myrtillus</i>) (whole berry)) (6,000 µmol TE/g)			500 mg	**		
Inositol	18 mg	**				
PABA (<i>para</i> -aminobenzoic acid)	6.5 mg	**				
Vanadium (as TRAACS® vanadium nicotinate glycinate chelate)	375 mcg	**				

† Percent Daily Values are based on a 2,000 calorie diet.

** Daily Value (DV) not established.

Other Ingredients for ActivNutrients without Iron: HPMC (capsule), microcrystalline cellulose, ascorbyl palmitate, silica, and medium-chain triglyceride oil.

Other Ingredients for Oraxinol: HPMC (capsule), vegetable stearic acid, vegetable magnesium stearate, and silica.

Other Ingredients for OmegaPure 600 EC: Softgel (tilapia fish gelatin, vegetable glycerin, and purified water), GRAS enteric coating (purified water, ethylcellulose, sodium alginate, ammonium hydroxide, medium-chain triglyceride oil, oleic acid, and vegetable stearic acid), and mixed natural tocopherols.

Contains: Fish (Alaska pollock, Pacific whiting [sources of fish oil], tilapia [source of fish gelatin]) from certified sustainable sources.

DIRECTIONS: Consume the contents of one packet daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication, especially blood thinners, should discuss potential interactions with their healthcare practitioner.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, dairy products, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

 Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,662.

 MecobalActive™ is a trademark of Ferrer Health Tech. The active form of B₁₂.

 Albion, DimaCal, TRAACS and the Albion Medallion design are registered trademarks of Albion Laboratories, Inc. Malates covered by U.S. Patent 6,706,904 and patents pending.

 VEGETARIAN CAPS

References

1. National Health and Nutrition Examination Survey. Centers for Disease Control and Prevention. <http://www.cdc.gov/nchs/nhanes.htm>. Accessed February 22, 2011.
2. What we eat in America. USDA Agricultural Research Service http://www.ars.usda.gov/main/site_main.htm?modecode=12-35-50-00. Accessed February 22, 2011.
3. Worthington V. Nutritional quality of organic versus conventional fruits, vegetables, and grains. *J Altern Complement Med*. 2001 Apr;7(2):161-73. [PMID: 11327522]
4. Quatrefolic. <http://www.quatrefolic.com/4thGeneration.html>. Accessed May 22, 2014.
5. Sallares J, Petschen I, Camps X, inventors; Ferrar Internacional, S.A., applicant. Process for the production of methylcobalamin. International publication number [English] WO 2006100059 A1. September 28, 2006.
6. Price JA, Sanny CG, Shevlin D. Application of manual assessment of oxygen radical absorbent capacity (ORAC) for use in high throughput assay of "total" antioxidant activity of drugs and natural products. *J Pharmacol Methods*. 2006 July-Aug;54(1):56-61. [PMID: 16337142]
7. FDA announces qualified health claims for omega-3 fatty acids. U.S. Food and Drug Administration Department of Health and Human Services. <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2004/ucm108351.htm>. Accessed February 27, 2011.
8. Proudman SM, Cleland LG, James MJ. Dietary omega-3 fats for treatment of inflammatory joint disease: efficacy and utility. *Rheum Dis Clin North Am*. 2008 May;34(2):469-79. [PMID: 18638687]
9. Cole GM, Ma QL, Frautschy SA. Dietary fatty acids and the aging brain. *Nutr Rev*. 2010 Dec;68(suppl 2):S102-11. [PMID: 21091943]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

ActivEssentials™ with OncoPLEX™ & D3

Daily Dose-Pack Nutrition



Available in 60 packets

Discussion

The average diet can be lacking in complete nutrition due to modern food-production techniques, poor food choices, and nutrient-depleting preparation methods.^[1-3] Combine these with the toll of lifestyle stress and oxidizing chemicals—found in foods and the environment—and it becomes essential to ensure comprehensive foundation nutrition for the body. To help achieve this, each cellophane-wrapped packet of ActivEssentials with OncoPLEX & D3 contains the following XYMOGEN formulas and ingredient combinations:*

ActivNutrients® without Iron This high-quality, hypoallergenic multivitamin/mineral blend provided in vegetable capsules not only features activated vitamin cofactors and patented Albion® chelated mineral complexes, but it also includes folate as 5-MTHF as well as methylcobalamin as MecobalActive™. The form of 5-MTHF is Quatrefolic®, which is proven to have greater stability, solubility, and bioavailability compared to calcium salt forms of 5-MTHF.^[4] MecobalActive is a patented form of methylcobalamin that has very high purity; no harmful solvents are used in its production.^[5] The balanced nutrient profile in ActivNutrients™ without Iron supports vitamin/mineral synergistic activity; antioxidant protection with vitamins C and E, selenium, and carotenoids; and phase I detoxification.*

Omega MonoPure® 650 EC is made using a proprietary MaxSimil composition containing monoglyceride fish oil with no additional ingredients, carriers, or excipients. Each fish-gelatin softgel is enteric-coated, and every batch of fish oil is IFOS five-star certified to ensure the world's highest standards for purity, potency, and freshness. The fish oil is non-GMO, certified sustainable from Scandinavia, and antibiotic-free. Additionally, it is eco-friendly because the greater absorption of EPA and DHA ultimately means that fewer grams of fish oil need to be harvested for the same benefit. Research suggests that consumption of EPA and DHA omega-3 fatty acids may support cardiovascular health.^[6] Studies have also shown that fish oils may support healthy cytokine production, promote optimal joint function^[7], and support overall brain and nervous system function.*^[8]

Clinical Applications

- » Provide Foundation Micronutrition for a Variety of Protocols*
- » Support Improved Dietary Nutrient Intake*
- » Provide Long-Lasting Antioxidant Support*
- » Support Individuals with Higher Vitamin D Requirements*

*ActivEssentials™ with OncoPLEX™ & D3 is a conveniently dose-packaged combination of three formulas that provide comprehensive nutritional support for health and well-being especially when higher vitamin D intake and long-lasting antioxidant support against free radical damage is desirable.**

OncoPLEX™ and D3 This combination contains truebroc® glucoraphanin, a patented phytochemical derived from broccoli extract that is featured in XYMOGEN's OncoPLEX formulas, and bioactive D3. These two nutrients continue to be the focus of much research for their protective roles at both system and cellular levels.*

OncoPLEX delivers 15 mg of glucoraphanin, the glucosinolate in broccoli that converts to sulforaphane in the body. Extensive research suggests that when glucoraphanin is enzymatically converted to sulforaphane (its active form), it safely and effectively supports the Nrf2 system, antioxidant systems, and vital phase II detoxification enzymes.^[9,10] This process provides protection from common toxins and xenobiotics. In addition, sulforaphane has been shown to support normal cell-life regulation.^[11-14] It has also been shown to support the body's response to harmful microbes, a healthy response to aging-associated changes in cytokine production, and eye and cardiovascular health.*^[15-19]

D3 is provided as 2000 IU of cholecalciferol, identical to the form in which it is derived in the body from cholesterol and synthesized by sunlight on the skin. Although vitamin D forms are similar biochemically, a recent study reported D3 to be approximately 87% more potent in raising and maintaining serum 25-hydroxyvitamin D (25[OH]D) concentrations and in producing two- to threefold greater storage of vitamin D than did equimolar D2 (ergocalciferol).^[20] In addition to musculoskeletal benefits, research now suggests that optimal serum levels of vitamin D support normal cell differentiation, cardiovascular health, normal immune function, good balance, healthy mood, normal fetal development, neuronal growth and neurodevelopment, healthy glucose metabolism, periodontal health, and normal intestinal immune responses.*^[21-23]

EXCLUSIVE • PATENTED

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

Bone Health Support

Cardiovascular Support

Cell-Life Regulation

Cytokine Balance Support

Immune System Support

Multivitamins & Minerals

ActivEssentials™ with OncoPLEX™ & D3 Supplement Facts

Serving Size: 1 Packet

	2 ActivNutrients® without Iron Capsules		1 OncoPLEX™ & D3 Capsule MonoPure® 650 EC Softgel		1 Omega 650 EC Softgel	
	Amount Per Serving	%DV	Amount Per Serving	%DV	Amount Per Serving	%DV
Calories					5	
Total Fat					0.5 g	1%†
Vitamin A (75% as natural beta-carotene and 25% as retinyl palmitate)	1120 mcg	124%				
Vitamin C (as sodium ascorbate, potassium ascorbate, zinc ascorbate, and calcium ascorbate)	125 mg	139%				
Vitamin D3 (as cholecalciferol)	2.5 mcg (100 IU)	13%	50 mcg (2000 IU)	250%		
Vitamin E (as d-alpha tocopheryl succinate and mixed tocopherols)	67 mg	447%				
Thiamin (as thiamine mononitrate)	10 mg	833%				
Riboflavin (as riboflavin 5'-phosphate sodium)	10 mg	769%				
Niacin (as niacinamide and niacin)	32 mg	200%				
Vitamin B6 (as pyridoxal 5'-phosphate)	10 mg	588%				
Folate (as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt) DFE	200 mcg	50%				
Vitamin B12 (as MecobalActive™ methylcobalamin)	250 mcg	10,417%				
Biotin	500 mcg	1667%				
Pantothenic Acid (as d-calcium pantothenate)	100 mg	2000%				
Choline (as choline dihydrogen citrate)	18 mg	3%				
Calcium (as DimaCal® di-calcium malate, d-calcium pantothenate, and calcium ascorbate)	50 mg	4%				
Iodine (as potassium iodide)	50 mcg	33%				
Magnesium (as Albion® di-magnesium malate)	50 mg	12%				
Zinc (as TRAACS® zinc bisglycinate chelate)	6.5 mg	59%				
Selenium (as Albion® selenium glycinate complex)	50 mcg	91%				
Copper (as TRAACS® copper bisglycinate chelate)	0.5 mg	56%				
Manganese (as TRAACS® manganese bisglycinate chelate)	0.25 mg	11%				
Chromium (as TRAACS® chromium nicotinate glycinate chelate)	250 mcg	714%				
Molybdenum (as TRAACS® molybdenum glycinate chelate)	25 mcg	56%				
Potassium (as Albion® potassium glycinate complex and potassium ascorbate)	49.5 mg	1%				
MaxSimil® Fish Oil Concentrate					650 mg	**
Total Omega-3 Fatty Acids					430 mg	**
EPA (eicosapentaenoic acid)					300 mg	**
DHA (docosahexaenoic acid)					130 mg	**
Inositol	18 mg	**				
truebroc® Glucoraphanin (from broccoli extract) (<i>Brassica oleracea italica</i>) seed)			15 mg	**		
PABA (<i>para</i> -aminobenzoic acid)	6.5 mg	**				
Vanadium (as TRAACS® vanadium nicotinate glycinate chelate)	375 mcg	**				

† Percent Daily Values are based on a 2,000 calorie diet.
 ** Daily Value (DV) not established.

Other Ingredients for ActivNutrients without Iron: HPMC (capsule), microcrystalline cellulose, ascorbyl palmitate, silica, and medium-chain triglyceride oil.

Other Ingredients for OncoPLEX & D3 capsule: Microcrystalline cellulose, HPMC (capsule), vegetable stearic acid, vegetable magnesium stearate, and silica.

Other Ingredients for Omega MonoPure 650 EC: Softgel (fish gelatin, vegetable glycerin, and purified water), GRAS enteric coating (ethylcellulose, sodium alginate, purified water, medium-chain triglycerides, oleic acid, vegetable stearic acid, and ammonium hydroxide), and mixed natural tocopherols.

Contains: Fish (anchovy and/or sardine [sources of fish oil], tilapia and/or pangasius [sources of fish gelatin]).

DIRECTIONS: Consume the contents of one packet daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication, especially blood thinners, should discuss potential interactions with their healthcare practitioner. Do not use if packet is damaged.

STORAGE: Keep tightly closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, dairy products, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

 Produced under US patent 6,521,816 licensed from Brassica Protection Products LLC. truebroc is a registered trademark of Brassica Protection Products LLC.

 Albion, DimaCal, TRAACS, and the Albion Medallion design are registered trademarks of Albion Laboratories, Inc. Malates covered by US patent 6,706,904.

 Quatrefolic® is a registered trademark of Genesis S.p.A. Produced under US patent 7,947,662.

 VEGETARIAN CAPS

 MecobalActive™ is a trademark of Ferrer Health Tech.

Manufactured using MaxSimil® fish oil. MaxSimil® is a registered trademark of Ingenutra Inc. Protected under US patents 8,119,690 and 8,198,324; Canadian patents 2672513 and 2677670.

References

- National Health and Nutrition Examination Survey. Centers for Disease Control and Prevention. <http://www.cdc.gov/nchs/nhanes.htm>. Accessed February 22, 2011.
- What we eat in America. USDA Agricultural Research Service. http://www.ars.usda.gov/main/site_main.htm?modecode=80-40-05-30. Accessed September 16, 2015.
- Worthington V. Nutritional quality of organic versus conventional fruits, vegetables, and grains. *J Altern Complement Med*. 2001 Apr;7(2):161-73. [PMID: 11327522]
- Quatrefolic. <http://www.quatrefolic.com/4thGeneration.html>. Accessed May 22, 2014.
- Sallares J, Petschen I, Camps X, inventors; Ferrar Internacional, S.A., applicant. Process for the production of methylcobalamin. International publication number [English] WO 2006100059 A1. September 28, 2006.
- FDA announces qualified health claims for omega-3 fatty acids. U.S. Food and Drug Administration Department of Health and Human Services. <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2004/ucm108351.htm>. Accessed February 27, 2011.
- Proudman SM, Cleland LG, James MJ. Dietary omega-3 fats for treatment of inflammatory joint disease: efficacy and utility. *Rheum Dis Clin North Am*. 2008 May;34(2):469-79. [PMID: 18638687]
- Cole GM, Ma QL, Frautschy SA. Dietary fatty acids and the aging brain. *Nutr Rev*. 2010 Dec;68(suppl 2):S102-11. [PMID:21091943]
- Ping Z, Liu W, Kang Z, et al. Sulforaphane protects brains against hypoxic-ischemic injury through induction of Nrf2-dependent phase 2 enzyme. *Brain Res*. 2010 Jul 9;1343:178-85. [PMID: 20417626]
- Vauzour D, Buonfiglio M, Corona G, et al. Sulforaphane protects cortical neurons against 5-S-cysteinyldopamine-induced toxicity through the activation of ERK1/2, Nrf-2 and the upregulation of detoxification enzymes. *Mol Nutr Food Res*. 2010 Apr;54(4):532-42. [PMID: 20166144]
- Cheung KL, Kong AN. Molecular targets of dietary phenethyl isothiocyanate and sulforaphane for cancer chemoprevention. *AAPS J*. 2010 Mar;12(1):87-97. [PMID: 20013083]
- Shapiro TA, Fahey JW, Wade KL, et al. Chemoprotective glucosinolates and isothiocyanates of broccoli sprouts: metabolism and excretion in humans. *Cancer Epidemiol Biomarkers Prev*. 2001 May;10(5):501-08. [PMID: 11352861]
- Ho E, Clarke JD, Dashwood RH. Dietary sulforaphane, a histone deacetylase inhibitor for cancer prevention. *J Nutr*. 2009 Dec;139(12):2393-96. [PMID: 19812222]
- Chu WF, Wu DM, Liu W, et al. Sulforaphane induces G2-M arrest and apoptosis in high metastasis cell line of salivary gland adenoid cystic carcinoma. *Oral Oncol*. 2009 Nov;45(11):998-1004. [PMID: 19589718]
- Yanaka A, Fahey JW, Fukumoto A, et al. Dietary sulforaphane-rich broccoli sprouts reduce colonization and attenuate gastritis in Helicobacter pylori-infected mice and humans. *Cancer Prev Res (Phila Pa)*. 2009 Apr;2(4):353-60. [PMID: 19349290]
- Zakkar M, Van der Heiden K, Luong le A, et al. Activation of Nrf2 in endothelial cells protects arteries from exhibiting a proinflammatory state. *Arterioscler Thromb Vasc Biol*. 2009 Nov;29(11):1851-57. [PMID: 19729611]
- Noyan-Ashraf MH, Sadeghnejad Z, Juurink BH. Dietary approach to decrease aging-related CNS inflammation. *Nutr Neurosci*. 2005 Apr;8(2):101-10. [PMID: 16053242]
- Gao X, Talalay P. Induction of phase 2 genes by sulforaphane protects retinal pigment epithelial cells against photooxidative damage. *Proc Natl Acad Sci USA*. 2004 July;101(28):10446-51. [PMID: 15229324]
- Wu L, Noyan Ashraf MH, Facci M, et al. Dietary approach to attenuate oxidative stress, hypertension, and inflammation on the cardiovascular system. *Proc Natl Acad Sci USA*. 2004 May;101(18):7094-99. [PMID: 15103025]
- Heaney RP, Recker RR, Grote J, et al. Vitamin d3 is more potent than vitamin d2 in humans. *J Clin Endocrinol Metab*. 2011 Mar;96(3):E447-52. [PMID: 21177785]
- Toubi E, Shoenfeld Y. The role of vitamin D in regulating immune responses. *Isr Med Assoc J*. 2010 Mar;12(3):174-75. [PMID: 20684184]
- Cannell JJ, Hollis BW. Use of vitamin D in clinical practice. *Altern Med Rev*. 2008 Mar;13(1):6-20. [PMID: 18377099]
- Heany RP. Vitamin D in health and disease. *Clin J Am Soc Nephrol*. 2008 Sep;3(5):1535-41. [PMID: 18525006]

Additional references available upon request

EXCLUSIVE • PATENTED

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

ActivNutrients®

Hypoallergenic Multivitamin/Mineral Formula for Wellness Support*



ActivNutrients is available in 120 and 240 capsules
ActivNutrients without Iron is available in 60, 120, and 240 capsules
ActivNutrients without Copper & Iron is available in 120 capsules

Discussion

Good nutrition is a basis for wellness, and good nutrition usually translates into a stronger immune system and better health. An important aspect of good nutrition is micronutrition (vitamins and minerals).^[1-4] Micronutrients participate in converting food to energy; building and repairing tissues and DNA; manufacturing neurotransmitters, hormones, and other modulators in the body; breaking down and detoxifying xenobiotics and medications; and maintaining growth, reproduction, and health. According to research by the USDA and other organizations, the American diet is lacking micronutrients.^[5-8] In fact, nine out of 10 Americans are missing key micronutrients.^[7] Mass food production, storage techniques, poor food choices, and nutrient-depleting preparation methods may contribute to inadequacies. The bottom line is that children and adults are not consuming enough nutrient-rich foods to meet all their most basic vitamin and mineral needs.^[6] What's more, some scientists feel that the recommended intakes (e.g., %DV, DRIs, EARs, RDAs) may not meet the requirements of all individuals, especially the chronically ill.*

There are numerous reasons to select ActivNutrients formulas:

Balanced Profile Vitamins and minerals work synergistically and cooperatively when present in proper amounts. However, imbalances between micronutrients can disrupt this synergistic relationship, possibly leading to instances of competitive intestinal absorption or displacement at the metabolic/cellular level, which can produce relative excesses and insufficiencies. For this reason, ActivNutrients formulas feature a balanced nutrient profile that includes calcium and magnesium, zinc and copper, vitamins C and E, bioactive folate, vitamin B12, B vitamin complex, beta-carotene, and trace elements.*

Bioavailability The micronutrients are provided in bioavailable forms so that they can be better absorbed and utilized. ActivNutrients formulas contain a full complement of Albion® patented mineral chelates and complexes. Albion is a recognized world leader in mineral amino acid chelate nutrition and manufactures highly

Clinical Applications

- » Foundation Nutrition for a Variety of Protocols*
- » Basic “Insurance” Formulas for Wellness*
- » Supports Antioxidant Protection*
- » Supports Detoxification*
- » Supports Health in Individuals with Poor Nutrient Intake*
- » Supports Individuals with Stressful Lifestyles*

*This high-quality, hypoallergenic, multivitamin/mineral blend includes activated vitamins; folate as Quatrefolic® (5-MTHF) for optimal utilization; and patented Albion® TRAACS® chelated mineral complexes in vegetarian capsules. The comprehensive nutrient profile in **ActivNutrients®** supports foundational wellness; antioxidant activity with vitamins C and E, selenium, and beta-carotene; and phase I detoxification.**

bioavailable nutritional mineral forms that are validated by third-party research and clinical studies. Not only do these formulas contain natural vitamin E, which has been proven to be up to 100% more bioavailable than synthetic dl-alpha-tocopherol, but it is also provides mixed tocopherols to more closely approximate how one might consume vitamin E in healthful foods.^[9,10] Folate is provided as 5-methyltetrahydrofolate (5-MTHF)—the most bioactive form of folate.^[11] ActivNutrients formulas feature 5-MTHF as Quatrefolic®, which is proven to have greater stability, solubility, and bioavailability over calcium salt forms of 5-MTHF. Vitamin B12 is provided as MecobalActive™. This patented form of methylcobalamin has very high purity; no harmful solvents are used in its production.^[12] Vitamins B2 and B6 are also provided in activated forms.*

Energy Production ActivNutrients formulas provide generous levels of B vitamins, which serve as prime coenzymes in glycolysis and oxidative phosphorylation and as cofactors in amino acid and lipid metabolism. The balanced presence of B vitamins is essential to their cooperative functioning and excellent for those with stressful lifestyles.*

Antioxidant Protection Vitamins E and C, selenium, zinc, beta carotene, and trace elements provide broad-spectrum antioxidant activity. Their combined presence supports their ability to regenerate each other and maintain consistent levels of antioxidant activity both intra- and extracellularly.*

Detoxification Support Xenobiotics, including environmental pollutants and medications, must undergo biotransformation into molecules that can be easily excreted from the body. There are significant levels of bioavailable riboflavin, niacin, folate, and B12 present in these formulas to support phase I detoxification. Beta carotene, vitamin C, tocopherols, selenium, copper, zinc, and manganese are present to protect tissues from reactive intermediates formed between phase I and phase II detoxification.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

ActivNutrients® Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%DV
Vitamin A (75% as natural beta-carotene and 25% as retinyl palmitate)	1120 mg	124%
Vitamin C (as sodium ascorbate, potassium ascorbate, zinc ascorbate, and calcium ascorbate)	125 mg	139%
Vitamin D3 (cholecalciferol)	2.5 mcg (100 IU)	13%
Vitamin E (as d-alpha tocopheryl succinate and mixed tocopherols)	67 mg	447%
Thiamin (as thiamine mononitrate)	10 mg	833%
Riboflavin (as riboflavin 5'-phosphate sodium)	10 mg	769%
Niacin (as niacinamide and niacin)	32 mg	200%
Vitamin B6 (as pyridoxal 5'-phosphate)	10 mg	588%
Folate (as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt)	200 mcg DFE	50%
Vitamin B12 (as MecobalActive™ methylcobalamin)	250 mcg	10,417%
Biotin	500 mcg	1667%
Pantothenic Acid (as d-calcium pantothenate)	100 mg	2000%
Choline (as choline dihydrogen citrate)	18 mg	3%
Calcium (as DimaCal® di-calcium malate, d-calcium pantothenate, and calcium ascorbate)	50 mg	4%
Iron (as Ferrochel® ferrous bisglycinate chelate)	2.5 mg	14%
Iodine (as potassium iodide)	50 mcg	33%
Magnesium (as Albion® di-magnesium malate)	50 mg	12%
Zinc (as TRAACS® zinc bisglycinate chelate)	6.5 mg	59%
Selenium (as Albion® selenium glycinate complex)	50 mcg	91%
Copper (as TRAACS® copper bisglycinate chelate)	0.5 mg	56%
Manganese (as TRAACS® manganese bisglycinate chelate)	0.25 mg	11%
Chromium (as TRAACS® chromium nicotinate glycinate chelate)	250 mcg	714%
Molybdenum (as TRAACS® molybdenum glycinate chelate)	25 mcg	56%
Potassium (as Albion® potassium glycinate complex and potassium ascorbate)	49.5 mg	1%
Inositol	18 mg	**
PABA (<i>para</i> -aminobenzoic acid)	6.5 mg	**
Vanadium (as TRAACS® vanadium nicotinate glycinate chelate)	375 mcg	**

** Daily Value (DV) not established.

Other Ingredients: HPMC (capsule), microcrystalline cellulose, ascorbyl palmitate, silica, and medium-chain triglyceride oil.**DIRECTIONS:** Take two capsules twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

WARNING: Accidental overdose of iron-containing products is a leading cause of fatal poisoning in children under 6. Keep this product out of reach of children. In case of accidental overdose, call a doctor or poison control center immediately.**STORAGE:** Keep closed in a cool, dry place out of reach of children.**DOES NOT CONTAIN:** Wheat, gluten, yeast, soy protein, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.**Also Available in:**

ActivNutrients® without Copper & Iron

Activated Vitamin Cofactors in a Hypoallergenic Proprietary Blend with Patented Mineral Chelates*The same great formula as ActivNutrients, but without copper or iron. Folate is provided as a blend of calcium folinate and Quatrefolic.*

ActivNutrients® without Iron

Hypoallergenic Multivitamin/Mineral Formula for Wellness Support**The same great formula as ActivNutrients, but without iron.*

Albion, DimaCal, Ferrochel, TRAACS and the Albion Medallion design are registered trademarks of Albion Laboratories, Inc. Malates covered by U.S. Patent



Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,662.

 MecobalActive™ is a trademark of Ferrer Health Tech. The active form of B₁₂.**References**

- Ames BN. A role for supplements in optimizing health: the metabolic tune-up. *Arch Biochem Biophys*. 2004 Mar 1;423(1):227-34. [PMID: 14989256]
- Toffanello ED, Inelmen EM, Minicuci N, et al. Ten-year trends in vitamin intake in free-living healthy elderly people: the risk of subclinical malnutrition. *J Nutr Health Aging*. 2011 Feb;15(2):99-103. [PMID: 21365161]
- Block G, Jensen CD, Norkus EP, et al. Usage patterns, health, and nutritional status of long-term multiple dietary supplement users: a cross-sectional study. *Nutr J*. 2007 Oct 24;6:30. [PMID: 17958896]
- Fletcher RH, Fairfield KM. Vitamins for chronic disease prevention in adults: clinical applications. *JAMA*. 2002 Jun 19;287(23):3127-29. [PMID: 12069676]
- Moshfegh AJ, Goldman JD, Ahuja JK, et al. U.S. Department of Agriculture, Agricultural Research Service. What we eat in America, Nhanes 2005-2006. Usual nutrient intakes from food and water compared to 1997 dietary reference intakes for vitamin D, calcium, phosphorus, and magnesium. http://www.ars.usda.gov/SP2UserFiles/Place/12355000/pdf/0506/usual_nutrient_intake_vitD_ca_phos_mg_2005-06.pdf Published July 2009. Accessed February 22, 2011.
- What we eat in America. WIN Notes. Weight Control Information Network. <http://win.niddk.nih.gov/notes/winter99/artcl6.htm>. Accessed July 22, 2011.
- Milk Processor Education Program. What America's Missing: A 2011 Report on the Nation's Nutrient Gap. Why Milk.com. http://www.whymilk.com/pdfs/what_americas_missing.pdf. Accessed August 3, 2011.
- Alexy U, Libuda L, Mersmann S, Kersting M. Convenience foods in children's diet and association with dietary quality and body weight status. *Eur J Clin Nutr*. 2011 Feb;65(2):160-66. [PMID: 21139631]
- Kiyose C, Muramatsu R, Kameyama Y, et al. Biodiscrimination of alpha-tocopherol stereoisomers in humans after oral administration. *Am J Clin Nutr*. 1997 Mar;65(3):785-89. [PMID: 9062530]
- Burton GW, Traber MG, Acuff RV, et al. Human plasma and tissue alpha-tocopherol concentrations in response to supplementation with deuterated natural and synthetic vitamin E. *Am J Clin Nutr*. 1998 Apr;67(4):669-84. [PMID: 9537614]
- Venn BJ, Green TJ, Moser R, et al. Comparison of the effect of low-dose supplementation with L-5-methyltetrahydrofolate or folic acid on plasma homocysteine: a randomized placebo-controlled study. *Am J Clin Nutr*. 2003 Mar;77(3):658-62. [PMID: 12600857]
- Sallares J, Petschen I, Camps X, inventors; Ferrar Internacional, S.A., applicant. Process for the production of methylcobalamin. International publication number [English] WO 2006100059 A1. September 28, 2006.

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

ActivNutrients® Chewable

Children's Multivitamin/Mineral



Available in 60 and 120 chewable tablets

Discussion

Good nutrition in childhood and adolescence is essential for achieving optimal growth and normal development. It also greatly impacts overall health and well-being, including resistance to infection and achieving peak bone mass.^[1] Not only does good nutrition impact health, but it also influences socialization, self-esteem, and academic performance.^[2,3] Unfortunately, the diets of many American children fall considerably short of recommended dietary standards.^[4] For instance, vitamins A, C, D, and E as well as folate, calcium, and magnesium are all underconsumed relative to the estimated average requirements (EARs).^[5]

Finding a children's multivitamin and mineral formula that comprises nutrients in their most highly absorbable form, such as 5-MTHF instead of folic acid^[6,7]; is free of toxic additives and preservatives; and tastes great without using corn syrup can be very challenging. XYMOGEN has met this challenge with ActivNutrients Chewable.

Clean ActivNutrients Chewable is free of the common allergens wheat, gluten, yeast, soy protein, dairy products, fish, shellfish, peanuts, tree nuts, and egg. It does not contain hydrogenated oils, dyes, artificial colors, or other additives, such as high-fructose corn syrup; nor does it contain artificial flavors, sweeteners, or preservatives.

Quality, Naturally ActivNutrients Chewable micronutrients are provided in bioavailable forms so that they can be better absorbed and utilized. The formula features a full complement of Albion® patented mineral chelates and complexes.^[8] It not only provides natural vitamin E, which has been proven to be up to 100% more bioavailable than synthetic dl-alpha-tocopherol, but it also delivers mixed tocopherols to more closely approximate how one might consume vitamin E in healthful foods.^[9,10] Folate is provided as Quatrefolic—5-methyltetrahydrofolate (5-MTHF) glucosamine salt. 5-MTHF is the most bioactive form of folate.^[11] K2 is delivered in the form of menaquinone-7. Vitamin B12 is provided as MecobalActive™, a form of methylcobalamin that has very high purity; no harmful solvents are used in its production.^[12] Vitamins B2 and B6 are also provided in activated forms.*

Clinical Applications

- » Supports Micronutrition for Optimal Growth, Normal Development, and Long-Term Health*
- » Helps Ensure That Children Who Are Picky Eaters, Have Poor Appetites, or Are on Restricted Diets Get the Nutrients They Might Be Missing*
- » Helps Bridge Nutritional Gaps Resulting from Diets Low in Healthful Fruits and Vegetables and High in Processed Foods and Sugar*
- » Provides Micronutrients Important for Healthy Immunity to Fight Common Ailments*
- » Ideal for Children and Adolescents Who Cannot Swallow Capsules*

*ActivNutrients® Chewable is formulated to address children's unique nutritional needs for growth, development, and vitality and to help close the nutritional gaps that commonly result from suboptimal diets. Each great-tasting tablet provides 23 important vitamins and minerals in active, highly bioavailable forms and is free of artificial colors and flavors, preservatives, and high-fructose corn syrup.**

Taste To get children to take a supplement, it must taste good. The mixed berry flavor makes it easy to incorporate ActivNutrients Chewable into kids' daily routines; they will never notice all the great B vitamins and other micronutrients they are getting. Its delicious blend of blackberry, blueberry, strawberry, raspberry, and cherry flavors has the perfect balance of sweetness and tartness—one doesn't overpower the other. There's also no stevia. ActivNutrients Chewable is sweetened by xylitol and monk fruit extract.*^[13]

Complete Many vitamins and minerals work synergistically and cooperatively. ActivNutrients Chewable features a 23-nutrient profile that includes calcium and magnesium, zinc and copper, vitamins C and E, B vitamin complex, beta-carotene, and trace elements.*

Divided Dosing Unlike one-a-day multivitamins, ActivNutrients Chewable doses can be divided throughout the day to allow better utilization of the nutrients. This is particularly important for water-soluble nutrients like vitamin C and the B vitamins.*

Energy Production Kids need energy to perform well in school and keep up with their extracurricular activities. ActivNutrients Chewable provides generous levels of B vitamins, which serve as prime coenzymes in glycolysis and oxidative phosphorylation and as cofactors in amino acid and lipid metabolism. Many functional medicine practitioners believe that the balanced presence of B vitamins is essential to their cooperative functioning.*

Antioxidant Protection Vitamins E and C, selenium, zinc, trace elements, and 1,275 mg of mixed carotenoids (beta-carotene, alpha-carotene, lutein, lycopene, and zeaxanthin) provide broad-spectrum antioxidant activity. The combined presence of all of these nutrients supports their ability to regenerate each other and maintain consistent levels of antioxidant activity both intra- and extracellularly.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

ActivNutrients® Chewable Supplement Facts

Serving Size: 4 Chewable Tablets

	Amount Per Serving	%DV for Children 1 through 3 Years of Age	%DV for Adults and Children 4 or more Years of Age
Calories	15		
Total Carbohydrate	6 g	4%†	2%†
Vitamin A (300 mcg (50%) as natural beta-carotene and 300 mcg (50%) as retinyl palmitate)	600 mcg	200%	67%
Vitamin C (ascorbic acid)	250 mg	1667%	278%
Vitamin D3 (cholecalciferol)	12.5 mcg (500 IU)	83%	63%
Vitamin E (as d-alpha tocopheryl succinate)	33.5 mg	558%	223%
Vitamin K2 (as menaquinone-7)	15 mcg	50%	13%
Thiamin (as thiamine HCl)	5 mg	1000%	417%
Riboflavin (as riboflavin and riboflavin 5'-phosphate sodium)	5 mg	1000%	385%
Niacin (as niacinamide)	10 mg	167%	63%
Vitamin B6 (as pyridoxine HCl and pyridoxal 5'-phosphate)	2.5 mg	500%	147%
Folate (as Quatrefolic® (6S)-5-methyltetrahydrofolate acid, glucosamine salt)	200 mcg DFE	133%	50%
Vitamin B12 (as methylcobalamin)	50 mcg	5556%	2083%
Biotin	150 mcg	1875%	500%
Pantothenic Acid (as d-calcium pantothenate)	10 mg	500%	200%
Calcium (as Albion® calcium citrate malate)	50 mg	7%	4%
Iron (as Albion® ferric glycinate)	3 mg	43%	17%
Iodine (as potassium iodide)	75 mcg	83%	50%
Magnesium (as Albion® di-magnesium malate)	50 mg	63%	12%
Zinc (as TRAACS® zinc bisglycinate chelate)	7.5 mg	250%	68%
Selenium (as Albion® selenium glycinate complex)	50 mcg	250%	91%
Copper (as TRAACS® copper bisglycinate chelate)	0.5 mg	167%	56%
Manganese (as TRAACS® manganese bisglycinate chelate)	0.5 mg	42%	22%
Chromium (as TRAACS® chromium nicotinate glycinate chelate)	50 mcg	455%	143%
Molybdenum (as TRAACS® molybdenum glycinate chelate)	50 mcg	294%	111%
Natural Mixed Tocopherols	18 mg	**	**
Natural Mixed Carotenoids	1.275 mg	**	**
Typical Composition:			
Beta-Carotene	600 mcg	**	**
Alpha-Carotene	250 mcg	**	**
Lutein	246 mcg	**	**
Lycopene	123 mcg	**	**
Zeaxanthin	12 mcg	**	**

†Percent Daily Values are based on a 2,000 calorie diet.

‡Percent Daily Values are based on a 1,000 calorie diet.

* Daily Value (DV) not established.

Other Ingredients: Xylitol, natural flavors (no MSG), vegetable stearic acid, citric acid, silica, vegetable magnesium stearate, monk fruit extract, and malic acid.**DIRECTIONS:** Children 1-3 years: one to two tablets twice daily; children 4 years or more: two to four tablets twice daily, or take as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

WARNING: Accidental overdose of iron-containing products is a leading cause of fatal poisoning in children under 6. Keep this product out of reach of children. In case of accidental overdose, call a doctor or poison control center immediately.**DOES NOT CONTAIN:** Wheat, gluten, yeast, soy protein, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

 Albion®, DimaCal®, TRAACS®, and the Albion Gold Medallion® are registered trademarks of Albion Laboratories, Inc. Di-Magnesium Malate covered by US patent 6,706,904.


 Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,662.
References

1. Story M, Stang J. Nutrition Needs in Adolescents. In: Stang J, Story M, eds. *Guidelines for Adolescent Nutrition Services*. Minneapolis, MN: Center for Leadership, Education and Training in Maternal and Child Nutrition, Division of Epidemiology and Community Health, School of Public Health, University of Minnesota; 2005. http://www.epi.umn.edu/let/pubs/img/adol_ch3.pdf. Accessed February 21, 2017.
2. Nutrition-Related Health Concerns, Dietary Intakes, and Eating Behaviors of Children and Adolescents. In: Stallings V, Yaktine A, eds. *Nutrition Standards for Foods in Schools: Leading the Way Toward Healthier Youth*. Washington, DC: The National Academies Press; 2007. <http://www.nap.edu/read/11899/chapter/4>. Accessed February 21, 2017.
3. Stuber, N. *Nutrition and Students' Academic Performance*. Saint Paul, MN: Wilder Research; January 2014. <https://www.wilder.org/Wilder-Research/Publications/Studies/Fueling%20Academic%20Performance%20-%20Strategies%20to%20Foster%20Healthy%20Eating%20Among%20Students/Nutrition%20and%20Students'%20Academic%20Performance.pdf>. Accessed February 21, 2017.
4. Stallings V, Yaktine A, eds. *Nutrition Standards for Foods in Schools: Leading the Way Toward Healthier Youth*. Washington, DC: The National Academies Press; 2007. <http://www.nap.edu/read/11899/chapter/1>. Accessed August 8, 2016.
5. US Department of Agriculture. Part D. Chapter 1: Food and Nutrient Intakes, and Health: Current Status and Trends. In: *Scientific Report of the 2015 Dietary Guidelines Advisory Committee*. <https://health.gov/dietaryguidelines/2015-scientific-report/PDFs/06-Part-D-Chapter-1.pdf>. Accessed February 21, 2017.
6. Scaglione F, Panzavolta G. Folate, folic acid and 5-methyltetrahydrofolate are not the same thing. *Xenobiotica*. 2014 May;44(5):480-88. [PMID: 24494987]
7. Miraglia N, Agostinetti M, Bianchi D, et al. Enhanced oral bioavailability of a novel folate salt: comparison with folic acid and a calcium folate salt in a pharmacokinetic study in rats. *Minerva Ginecol*. 2016 Apr;68(2):99-105. [PMID: 27008238]
8. TRAACS®: The real amino acid chelate system. Albion® *Research Notes*. <http://www.albionhumannutrition.com/research-notes/134-traacs-the-real-amino-acid-chelate-system>. Accessed February 21, 2017.
9. Kiyose C, Muramatsu R, Kameyama Y, et al. Biodiscrimination of alpha-tocopherol stereoisomers in humans after oral administration. *Am J Clin Nutr*. 1997 Mar;65(3):785-89. [PMID: 9062530]
10. Burton GW, Traber MG, Acuff RV, et al. Human plasma and tissue alpha-tocopherol concentrations in response to supplementation with deuterated natural and synthetic vitamin E. *Am J Clin Nutr*. 1998 Apr;67(4):669-84. [PMID: 9537614]
11. Venn BJ, Green TJ, Moser R, et al. Comparison of the effect of low-dose supplementation with L-5-methyltetrahydrofolate or folic acid on plasma homocysteine: a randomized placebo-controlled study. *Am J Clin Nutr*. 2003 Mar;77(3):658-62. [PMID: 12600857]
12. Sallares J, Petschen I, Camps X, inventors; Ferrar Internacional, S.A., applicant. Process for the production of methylcobalamin. International publication number [English] WO 2006100059 A1. September 28, 2006.
13. Li XE, Lopetcharat K, Drake MA. Parents' and children's acceptance of skim chocolate milks sweetened by monk fruit and stevia leaf extracts. *J Food Sci*. 2015 May;80(5):S1083-92. [PMID: 25847181]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

© XYMOGEN
DRS-309
Rev. 06/25/19

ActivNutrients® without Copper & Iron Multivitamin Powder

Great-Tasting, Flexible-Dosing for All Ages



Available in Natural Fruit Punch

Discussion

Good nutrition is a basis for wellness, and good nutrition usually translates into a stronger immune system and better health. An important aspect of good nutrition is micronutrition (vitamins and minerals).^[1-4] Micronutrients participate in converting food into energy; building and repairing tissues and DNA; manufacturing neurotransmitters, hormones, and other modulators in the body; breaking down and detoxifying xenobiotics and medications; and maintaining growth, reproduction, and health.*

According to research by the USDA and other organizations, Americans are lacking key micronutrients.^[5-6] Mass food production, storage techniques, poor food choices, and nutrient-depleting preparation methods may contribute to inadequacies. Nutrient intake data from a representative sample of the US population aged 2 years and older indicate that vitamins A, D, E, C, and folate, calcium, and magnesium are underconsumed relative to the estimated average requirements (EARs). What's more, some functional medicine practitioners believe that the recommended intakes (e.g., %DV, DRIs, EARs, RDAs) may not meet the requirements of all individuals, especially the chronically ill. The bottom line is that children and adults are not consuming enough nutrient-rich foods to meet all their most basic vitamin and mineral needs.*^[6]

There are numerous reasons to select ActivNutrients without Copper and Iron Multivitamin Powder:

Complete, Minus Copper and Iron This formula features a wide variety of important nutrients in significant amounts, including calcium and magnesium, vitamins C and E, bioactive folate, B complex, beta-carotene, and trace elements. ActivNutrients without Copper and Iron Multivitamin Powder provides the option to add copper and/or iron only when needed, such as when indicated by laboratory testing.*

Bioavailability The micronutrients are provided in forms that can be optimally absorbed and utilized. ActivNutrients without Copper and Iron Multivitamin Powder contains a full complement of Albion® patented mineral chelates and complexes. Albion is a recognized world leader in mineral amino acid chelate nutrition and manufactures highly bioavailable minerals that are validated by third-party research and clinical studies.*

Clinical Applications

- » Basic "Insurance" Formula for Wellness*
- » Supports Antioxidant Protection*
- » Supports Detoxification*
- » Supports Health in Individuals with Poor Nutrient Intake*
- » Supports Individuals with Stressful Lifestyles*

*ActivNutrients® without Copper and Iron Multivitamin Powder is a high-quality, hypoallergenic multivitamin formula designed to help meet the daily nutritional needs of children and adults. The formula's delicious, natural fruit punch flavor and its powdered form make it easy to use. It features natural and activated forms of vitamins, such as beta-carotene, cholecalciferol, folate as 5-MTHF (5-methyltetrahydrofolate), and B12 as methylcobalamin as well as patented Albion® chelated mineral complexes. The activated nutrient profile supports vitamin/mineral synergistic activity; antioxidant protection with vitamins C and E, selenium, and carotenoids; healthy immune activity; cellular metabolism; and detoxification.**

Not only does this formula contain natural vitamin E, which has been proven to be up to 100% more bioavailable than synthetic dl-alpha-tocopherol, but it also provides mixed tocopherols to more closely approximate how vitamin E occurs naturally in whole foods.^[9,10] Folate is provided as 5-methyltetrahydrofolate (5-MTHF), the most bioactive form of folate.^[11] This formula features 5-MTHF as Quatrefolic®, which is proven to have greater stability, solubility, and bioavailability when compared to the calcium salt form of 5-MTHF.^[12] Vitamin B12 is provided as MecobalActive™. This patented form of methylcobalamin has very high purity; no harmful solvents are used in its production.^[13] Vitamins B2 and B6 are also provided in activated forms.*

Energy Production ActivNutrients without Copper and Iron Multivitamin Powder provides generous levels of B vitamins, which serve as prime coenzymes in glycolysis and oxidative phosphorylation (steps in energy production) and as cofactors in amino acid and lipid metabolism. The balanced presence of B vitamins is essential to their cooperative functioning and excellent for growing children as well as adults with stressful lifestyles.*

Antioxidant Protection Vitamins E and C; selenium; zinc; lemon bioflavonoids; mixed carotenoids, including alpha- and beta-carotene, gamma-carotene, and lycopene; and trace elements provide broad-spectrum antioxidant activity. The combination of these nutrients provides broad spectrum intra- and extracellular antioxidant support.*

Detoxification Support Xenobiotics, including environmental pollutants and medications, must undergo biotransformation into molecules that can be easily excreted from the body. Artificial colors and flavors, additives, preservatives, and pesticides all increase demands on the body's detoxification processes, which require vitamins and minerals. There are significant levels of bioavailable riboflavin, niacin, folate, and B12 present in these formulas to support phase I detoxification. Beta carotene, vitamin C, tocopherols, selenium, and zinc are present to protect tissues from reactive intermediates formed between phase I and phase II detoxification.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

ActivNutrients® without Copper & Iron Multivitamin Powder Supplement Facts

Serving Size: 2 Scoops (about 6.1 g)

	Amount Per Serving	%DV for Children 1 through 3 Years of Age	%DV for Adults and Children 4 or more Years of Age
Calories	20		
Total Carbohydrate	4 g	3% [†]	1% [†]
Vitamin A (600 mcg (76%) as retinyl palmitate and 190 mcg (24%) as natural beta-carotene and alpha-carotene)	790 mcg	263%	88%
Vitamin C (ascorbic acid)	600 mg	4000%	667%
Vitamin D3 (cholecalciferol)	40 mcg (1600 IU)	267%	200%
Vitamin E (as d-alpha tocopheryl succinate)	100 mg	1667%	667%
Vitamin K2 (as menaquinone-7)	30 mcg	100%	25%
Thiamin (as thiamine HCl)	12.5 mg	2500%	1042%
Riboflavin (as riboflavin and riboflavin 5'-phosphate sodium)	10 mg	2000%	769%
Niacin (as niacinamide)	20 mg	333%	125%
Vitamin B6 (as pyridoxine HCl and pyridoxal 5'-phosphate)	5 mg	1000%	294%
Folate (as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt)	400 mcg DFE	267%	100%
Vitamin B12 (as MecobalActive™ methylcobalamin)	100 mcg	11,111%	4167%
Biotin	300 mcg	3750%	1000%
Pantothenic Acid (as d-calcium pantothenate)	50 mg	2500%	1000%
Choline (as choline dihydrogen citrate)	30 mg	15%	5%
Calcium (as Albion® calcium citrate malate)	100 mg	14%	8%
Iodine (as potassium iodide)	150 mcg	167%	100%
Magnesium (as Albion® di-magnesium malate)	125 mg	156%	30%
Zinc (as TRAACS® zinc bisglycinate chelate)	15 mg	500%	136%
Selenium (as Albion® selenium glycinate complex)	100 mcg	500%	182%
Manganese (as TRAACS® manganese bisglycinate chelate)	0.5 mg	42%	22%
Chromium (as TRAACS® chromium nicotinate glycinate chelate)	125 mcg	1136%	357%
Molybdenum (as TRAACS® molybdenum glycinate chelate)	100 mcg	588%	222%
Sodium	45 mg	3%	2%
Potassium (as Albion® potassium glycinate complex)	66 mg	2%	1%
Natural Mixed Tocopherols	140 mg	**	**
Lemon Bioflavonoids (from <i>Citrus x limon</i>) (peel)	60 mg	**	**
Inositol	15 mg	**	**
Natural Mixed Carotenoids	2.59 mg	**	**
Typical Composition:			
Beta-Carotene	1.85 mg	**	**
Alpha-Carotene	925 mcg	**	**
Gamma-Carotene	9.25 mcg	**	**
Lycopene	2.8 mcg	**	**
Boron (as Albion® bororganic glycine)	750 mcg	**	**

[†]Percent Daily Values are based on a 2,000 calorie diet.[†]Percent Daily Values are based on a 1,000 calorie diet.

** Daily Value (DV) not established.

Other Ingredients: Beet juice concentrate (color), natural flavors, citric acid, stevia leaf extract, malic acid, and sea salt.

DIRECTIONS: *Children 1-3:* a half scoop twice daily; *children 4 or more:* one scoop twice daily; *adults:* three to four scoops divided into two daily doses. Mix thoroughly in 8 oz of water and consume, or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



Albion, DimaCal, TRAACS, and the Albion Medallion design are registered trademarks of Albion Laboratories, Inc. Malates covered by US patent 6,706,904 and patents pending.



Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,662.

MecobalActive™ is a trademark of Ferrer Health Tech.
The active form of B₁₂.

References

- Ames BN. A role for supplements in optimizing health: the metabolic tune-up. *Arch Biochem Biophys.* 2004 Mar 1;423(1):227-34. [PMID: 14989256]
- Ward E. Addressing nutritional gaps with multivitamin and mineral supplements. *Nutr J.* 2014 Jul 15;13:72. [PMID: 25027766]
- Block G, Jensen CD, Norkus EP, et al. Usage patterns, health, and nutritional status of long-term multiple dietary supplement users: a cross-sectional study. *Nutr J.* 2007 Oct 24;6:30. [PMID: 17958896]
- Lam LF, Lawlis TR. Feeding the brain - The effects of micronutrient interventions on cognitive performance among school-aged children: A systematic review of randomized controlled trials. *Clin Nutr.* 2016 Jun 23. [PMID: 27395329]
- Moshfegh AJ, Goldman JD, Ahuja JK, et al. U.S. Department of Agriculture, Agricultural Research Service. What we eat in America, Nhanes 2005-2006. Usual nutrient intakes from food and water compared to 1997 dietary reference intakes for vitamin D, calcium, phosphorus, and magnesium. http://www.ars.usda.gov/SP2UserFiles/Place/12355000/pdf/0506/usual_nutrient_intake_vitD_ca_phos_mg_2005-06.pdf Published July 2009. Accessed September 22, 2016.
- Fulgoni VL 3rd, Keast DR, Bailey RL, et al. Foods, fortificants, and supplements: Where do Americans get their nutrients? *J Nutr.* 2011 Oct;141(10):1847-54. [PMID: 21865568]
- Milk Processor Education Program. What America's Missing: A 2011 Report on the Nation's Nutrient Gap. <https://milklife.com/articles/nutrition/what-americas-missing>. Accessed September 23, 2016.
- Alexy U, Libuda L, Mersmann S, et al. Convenience foods in children's diet and association with dietary quality and body weight status. *Eur J Clin Nutr.* 2011 Feb;65(2):160-66. [PMID: 21139631]
- Kiyose C, Muramatsu R, Kameyama Y, et al. Biodiscrimination of alpha-tocopherol stereoisomers in humans after oral administration. *Am J Clin Nutr.* 1997 Mar;65(3):785-89. [PMID: 9062530]
- Burton GW, Traber MG, Acuff RV, et al. Human plasma and tissue alpha-tocopherol concentrations in response to supplementation with deuterated natural and synthetic vitamin E. *Am J Clin Nutr.* 1998 Apr;67(4):669-84. [PMID: 9537614]
- Venn BJ, Green TJ, Moser R, et al. Comparison of the effect of low-dose supplementation with L-5-methyltetrahydrofolate or folic acid on plasma homocysteine: a randomized placebo-controlled study. *Am J Clin Nutr.* 2003 Mar;77(3):658-62. [PMID: 12600857]
- Crossover Comparative Bioavailability Study of 5-Methyltetrahydrofolate Glucosamine Salt (GN10G) Compared to the Reference Metafolin® in Healthy Volunteers. IPAS-5MTHFA-583-09 final report. Desio, Italy: Gnosis S.p.A.; March 15, 2010: 1-33. [available from the manufacturer Gnosis S.p.A. upon request]
- Sallares J, Petschen I, Camps X, inventors; Ferrar Internacional, S.A., applicant. Process for the production of methylcobalamin. International publication number [English] WO 2006100059 A1. September 28, 2006.

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Adrenal Essence®

Adaptogenic Herbal & Vitamin Supplement*



Available in 60 capsules and 120 capsules

Discussion

Cordyceps sinensis (cordyceps) As a highly regarded cornerstone of Chinese medicine, cordyceps has been used for centuries for its far-reaching restorative effects. It is a safe, highly valued herb with activities that support nearly every physiological system impacted by the body's response to normal everyday stressors, including the immune and cardiovascular systems.^[1-4] Cordyceps has been used to support good balance, strength, and a healthy body weight. It is also widely and traditionally used to increase energy and enhance stamina.^[1,2] It has a positive effect on blood sugar and fat metabolism, which is important because fats and sugars are actively mobilized during activation of the stress response to supply the body with extra energy.^[1,4] Traditional Chinese Medicine (TCM) practitioners also recommend the regular use of cordyceps to strengthen the body.^[1] Furthermore, the cell-protective and antioxidant activities of cordyceps have been documented.*^[1,4-7]

Rhodiola rosea (rhodiola) This adaptogenic herb has been used traditionally in Eastern Europe and Asia for centuries to increase stamina, maintain a healthy mood, support the nervous and immune systems, and maintain healthy male sexual function.^[8,9] According to Panossian et al, experimental studies performed on isolated organs, tissues, cells, and enzymes demonstrate that rhodiola preparations exhibit adaptogenic effects that support nerve, brain, and heart health and are calming, longevity-enhancing, and central nervous system-stimulating.^[9] In addition, experimental animal models suggest that the root extract may be able to support normal heart rhythm.^[10] Rhodiola may also have a positive effect on brain neurotransmitters, such as dopamine and serotonin, and may influence endogenous opioid levels.^[8] According to a review of the literature on rhodiola, supplementation supports healthy work performance, quality of sleep, appetite, and energy levels subsequent to intense physical or intellectual strain. Salidroside and rosavin have been identified as primary actives. The rhodiola extract in this formula is standardized to provide no less than 1%-3% salidroside and 3% rosavin.*

Clinical Applications

- » Helps Support Healthy Energy Levels*
- » Supports the Body's Adaptogenic Response*
- » Supports Healthy Immune Function*
- » Supports Antioxidant and Cell-Protective Activity*

*Adrenal Essence® is a comprehensive blend of standardized extracts of the highest-quality adaptogenic herbs plus three B vitamins. These ingredients aid in adrenal hormone production and support the body's adaptogenic response. The formula is designed to support healthy energy levels, antioxidant activity, and healthy immune function.**

Panax ginseng (ginseng) As an important herbal remedy in TCM, ginseng has been used for thousands of years, primarily for energy production. The main active agents have been identified as ginsenosides, and they are the focus of much published research.^[11] Experimental models show that ginseng and ginsenosides have beneficial effects in supporting the adrenal glands; protecting the gastric mucosa; and supporting healthy body weight, blood hormones, and the gene expression of catecholamine-synthesizing enzymes.^[11-15] Ginsenosides also have immune-supporting and cytokine-modulating activities.*^[12,16]

Vitamin B6, Pantothenic Acid, and Para-Aminobenzoic Acid (PABA) Pantothenic acid is essential to the adrenal glands for production of the glucocorticoids. It forms pantothenic acid in the body, which then converts to coenzyme-A—the most active metabolic enzyme in the human body needed to produce cellular energy.^[17] D-calcium pantothenate contains 91.96% pantothenic acid and is the usual supplemental form. Vitamin B6, acting as a coenzyme, has a role in the conversion of muscle glycogen to glucose, which is needed for a proper response to stressors; the synthesis of serotonin; and the support of the immune function.^[18] PABA has a role in amino acid metabolism and is needed to manufacture folic acid.*

The Thyroid Connection The interplay between healthy adrenal function and healthy thyroid function has long been recognized by functional medicine practitioners. In fact, cortisol acts in concert with thyroid hormone at the receptor-gene level, and a normal physiologic amount of cortisol is important for normal thyroid function.*^[19]

Adrenal Essence® Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Vitamin B6 (as pyridoxine HCl)	25 mg	1471%
Pantothenic Acid (as d-calcium pantothenate)	50 mg	1000%
Cordyceps Extract (<i>Cordyceps sinensis</i>)(mycelium)(7% cordycepic acids)	400 mg	**
Rhodiola Extract (<i>Rhodiola rosea</i>)(root)(3% rosavins and 1% salidroside)	100 mg	**
PABA (<i>para</i> -aminobenzoic acid)	25 mg	**
Asian Ginseng Extract (<i>Panax ginseng</i>)(herb)(80% ginsenosides)	20 mg	**

** Daily Value not established.
Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, silica, and medium-chain triglyceride oil.

DIRECTIONS: Take one capsule twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.



References

- Holliday J, Cleaver M. Medicinal value of the caterpillar fungi species of the genus *Cordyceps* (Fr.) Link (Ascomycetes). A review. *International Journal of Medicinal Mushrooms*. 2008;10(3):219-34. http://www.alohamedicinals.com/Cordyceps_Ascmycetes.pdf. Accessed May 3, 2011.
- Zhu JS, Halpern GM, Jones K. The scientific rediscovery of a precious ancient Chinese herbal regimen: *Cordyceps sinensis*: part II. *J Altern Complement Med*. 1998;4(3):289-303. [PMID: 9884180]
- Mei QB, Tao JY, Gao SB, et al. [Antiarrhythmic effects of *cordyceps sinensis* (Berk.) Sacc] [in Chinese]. *Zhongguo Zhong Yao Za Zhi*. 1989 Oct;14(10):616-18, 640. [PMID: 2597326]
- Li SP, Zhang GH, Zeng Q, et al. Hypoglycemic activity of polysaccharide, with antioxidation, isolated from cultured *Cordyceps mycelia*. *Phytomedicine*. 2006 Jun;13(6):428-33. [PMID: 16716913]
- Marchbank T, Ojubo E, Playford CJ, et al. Reparative properties of the traditional Chinese medicine *Cordyceps sinensis* (Chinese caterpillar mushroom) using HT29 cell culture and rat gastric damage models of injury. *Br J Nutr*. 2011 May;105(9):1303-10. [PMID: 21272405]
- Ji NF, Yao LS, Li Y, et al. Polysaccharide of *Cordyceps sinensis* enhances cisplatin cytotoxicity in non-small cell lung cancer H157 cell line. *Integr Cancer Ther*. 2011 Mar 7. [Epub ahead of print] [PMID: 21382957]
- Shen W, Song D, Wu J, et al. Protective effect of a polysaccharide isolated from a cultivated *Cordyceps mycelia* on hydrogen peroxide-induced oxidative damage in PC12 cells. *Phytother Res*. 2011 May;25(5):675-80. doi: 10.1002/ptr.3320. [PMID: 21043033]
- Chan SW. *Panax ginseng Rhodiola rosea* and *Schisandra chinensis*. *Int J Food Sci Nutr*. 2012 Mar;63 Suppl 1:75-81. [PMID: 22039930]
- Panossian A, Wikman G, Sarris J. Rosenroot (*Rhodiola rosea*): traditional use, chemical composition, pharmacology and clinical efficacy. *Phytomedicine*. 2010 Jun;17(7):481-93. [PMID: 20378318]
- Maslov LN, Lishmanov luB. [Cardioprotective and antiarrhythmic properties of *Rhodiole roseae* preparations] [in Russian]. *Eksp Klin Farmakol*. 2007 Sep-Oct;70(5):59-67. [PMID: 18074810]
- Kiefer D, Pantuso T. *Panax ginseng*. *Am Fam Physician*. 2003 Oct 15;68(8):1539-42. [PMID: 14596440]
- Jia L, Zhao Y, Liang XJ. Current evaluation of the millennium phytomedicine-ginseng (II): Collected chemical entities, modern pharmacology, and clinical applications emanated from traditional Chinese medicine. *Curr Med Chem*. 2009;16(22):2924-42. [PMID: 19689273]
- Kim Y, Choi EH, Doo M, et al. Anti-stress effects of ginseng via down-regulation of tyrosine hydroxylase (TH) and dopamine β -hydroxylase (DBH) gene expression in immobilization-stressed rats and PC12 cells. *Nutr Res Pract*. 2010 Aug;4(4):270-75. [PMID: 20827341]
- Tachikawa E, Kudo K, Hasegawa H, et al. In vitro inhibition of adrenal catecholamine secretion by steroidal metabolites of ginseng saponins. *Biochem Pharmacol*. 2003 Dec 1;66(11):2213-21. [PMID: 14609746]
- Rai D, Bhatia G, Sen T, et al. Anti-stress effects of *Ginkgo biloba* and *Panax ginseng*: a comparative study. *J Pharmacol Sci*. 2003 Dec;93(4): 458-64. [PMID: 14737017]
- Lee DC, Lau AS. Effects of *Panax ginseng* on tumor necrosis factor- α -mediated inflammation: a mini-review. *Molecules*. 2011 Mar 30;16(4):2802-16. [PMID: 21455094]
- National Institutes of Health. Office of Dietary Supplements. Dietary Supplement Fact Sheet: Vitamin B6. <http://ods.od.nih.gov/factsheets/VitaminB6-HealthProfessional/>. Updated September 15, 2011. Accessed March 29, 2012.
- University of Maryland Medical Center. Vitamin B5 (Pantothenic acid). www.umm.edu/altmed/articles/vitamin-b5-000336.htm. Accessed May 10, 2011.
- Perrone MH, Greer TL, Hinkle PM. Relationships between thyroid hormone and glucocorticoid effects in GH3 pituitary cells. *Endocrinology*. 1980 Feb;106(2):600-05. [PMID: 6243541]

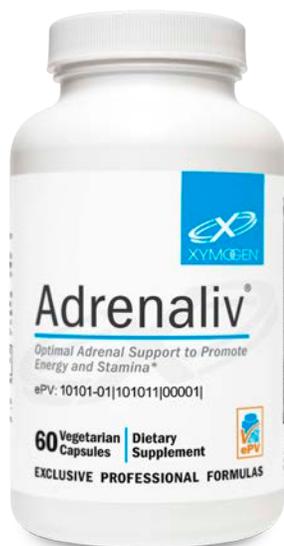
Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Adrenaliv®

Optimal Adrenal Support to Promote Energy and Stamina*



Available in 60 capsules and 120 capsules

Discussion

Cortisol is one of the main stress-mediating glucocorticoid hormones produced by the adrenal gland. It acts to maintain blood glucose levels necessary for normal brain and physical functions. Typically, cortisol levels spike in the morning and gradually decrease throughout the day. When the body is under stress, cortisol production increases. With prolonged increased levels of cortisol, the body produces more glucose leading to an increase in risk for depressed immune function, increased production of cytokines, insulin resistance, weight gain, and other potentially chronic conditions. Eventually, the adrenal production of cortisol weakens resulting in “adrenal fatigue,” which causes feelings of tiredness, mild depression, and general malaise. Adrenaliv® is formulated to support individuals who present with cortisol levels that are low throughout the day and are sometimes referred to as being in the “burnout” or “flat-line” stage of adrenal fatigue.*

Vitamin C

The release of adrenocorticotropic hormone (ACTH) from the pituitary gland in tandem with the body's physiological response to stress will deplete the relatively large amount of vitamin C typically stored in the adrenal cortex.^[1,2] This vitamin is essential for the synthesis of epinephrine, the hormone secreted by the adrenal medulla in response to stress. Epinephrine, in turn, plays a role in the synthesis of aldosterone, the hormone that regulates blood pressure, volume, and pH.*

Vitamin B6, Pantothenic Acid

Vitamin B6, acting as a coenzyme, has a role in the conversion of muscle glycogen to glucose, which is needed for a proper response to stressors, the synthesis of serotonin, and the support of the immune function.^[3] Physiologically, vitamin B6 influences the adrenal glucocorticoid receptor, stimulates the secretion of adrenal catecholamines, and aids in sodium and potassium balance.*^[2]

Pantothenic acid is essential to the adrenal glands for the production of glucocorticoids. It forms pantothenine in the body, which then converts to coenzyme-A—the most active metabolic enzyme in the human body needed to produce cellular energy.^[4] Pantothenic acid plays a critical role in the utilization of fats and carbohydrates in energy production and in the manufacture of adrenal hormones and red blood cells.*^[5]

Asian Ginseng (Panax)

As an important herbal remedy in traditional Chinese medicine, *Panax ginseng* has been used for thousands of years, primarily for energy production. The main active agents have been identified as ginsenosides, and they are the focus of much published research.^[6] Experimental models show that ginseng and ginsenosides have beneficial effects in supporting the adrenal glands; protecting

Clinical Applications

- » Promotes Energy Production and Stamina*
- » Supports the Body's Adaptogenic Response*
- » Supports the Body's Response to Stress*
- » Promotes Adrenal Physiological Functions*

*Adrenaliv® features a comprehensive blend of nutrients and botanical extracts targeted to supporting the body's adaptogenic response to promote optimal energy production, stamina, and the management of everyday stressors. Adrenal glandular tissue, sourced from Argentinian bovine to safeguard purity, rounds out the ingredient profile.**

the gastric mucosa; and supporting healthy body weight, blood hormones, and the gene expression of catecholamine-synthesizing enzymes.^[6-10] Ginsenosides also have immune-supporting and cytokine-modulating activities.*^[7,11]

Eleuthero

In the 1950s, Russian researchers investigated the properties of eleuthero and discovered that it had “adaptogenic” activity. An adaptogen refers to a substance that supports the body's ability to adapt and promote healthy physiological functioning, most notably in relation to stress. This balancing effect has been evaluated in numerous human clinical trials that demonstrate the ability of eleuthero to increase stamina, mental alertness, and the capability of the participants to handle stress.*^[12,19]

Rhodiola

This adaptogenic herb has been used traditionally in Eastern Europe and Asia for centuries to increase stamina, maintain a healthy mood, support the nervous and immune systems, and maintain healthy male sexual function.^[13,14] According to Panossian et al, experimental studies performed on isolated organs, tissues, cells, and enzymes demonstrated that rhodiola preparations exhibit adaptogenic effects that support nerve, brain, and heart health and instill calm, enhance longevity, and stimulate the nervous system.^[14] Rhodiola may also have a positive effect on brain neurotransmitters, such as dopamine and serotonin, and may influence endogenous opioid levels.^[13] According to a review of the literature on rhodiola, supplementation supports healthy work performance, quality of sleep, appetite, and energy levels subsequent to intense physical or intellectual strain. Salidroside and rosavin have been identified as primary actives. The rhodiola extract in Adrenaliv is standardized to provide no less than 1% salidroside and 3% rosavin.*

Schisandra

Schisandra has been widely studied for its effect on helping the body adapt to psychological and physical stressors. It has been suggested that schisandra affects the basal levels of nitric oxide and cortisol, which promote endurance and accuracy of movement, mental performance, and working capacity.*^[15,16]

Schisandra is commonly used in combination with other adaptogens. In a double-blind placebo-controlled trial with rhodiola and eleuthero, improvement in attention as well as speed and accuracy on cognitive tasks was noted.*^[17]

Adrenal Gland (from Argentina bovine), Licorice Root

Adrenal gland derived from pure Argentinian bovine is a complementary ingredient traditionally used to replenish adrenal function.^[18] Licorice contains triterpenoid saponins that influence cortisol balance, and it is a staple herb for supporting adrenal insufficiency.*^[19]

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

Adrenalin® Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Vitamin C (ascorbic acid)	125 mg	139%
Vitamin B6 (as pyridoxal 5'-phosphate)	15 mg	882%
Pantothenic Acid (as d-calcium pantothenate)	150 mg	3000%
Adrenal Gland (from bovine)(Argentina)	125 mg	**
Asian Ginseng Extract (<i>Panax ginseng</i>)(root)(5% ginsenosides)	75 mg	**
Eleuthero Extract (<i>Eleutherococcus senticosus</i>)(root)(0.8% eleutheroside)	50 mg	**
Licorice (<i>Glycyrrhiza glabra</i>)(roots)	50 mg	**
Schisandra 4:1 Extract (<i>Schisandra chinensis</i>)(fruit)	50 mg	**
Rhodiola Extract (<i>Rhodiola rosea</i>)(root)(3% rosavins and 1% salidroside)	50 mg	**
** Daily Value not established.		

Other Ingredients: Capsule (hypromellose and water), ascorbyl palmitate, medium-chain triglyceride oil, silica, and maltodextrin.

DIRECTIONS: Take one capsule twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

**References:**

- Murray RK, Granner DK, Mayes PA, et al. *Harper's Biochemistry*. 25th ed. Stamford, CT: Appleton & Lange; 2000.
- Head KA, Kelly GS. Nutrients and botanicals for treatment of stress: adrenal fatigue, neurotransmitter imbalance, anxiety, and restless sleep. *Altern Med Review*. 2009 June;14(2): 114-140. [PMID: 19594222]
- Vitamin B5 (Pantothenic acid). University of Maryland Medical Center. <http://www.umm.edu/health/medical/altmed/supplement/vitamin-b5-pantothenic-acid>. Updated July 16, 2013. Accessed September 12, 2017.
- National Institutes of Health. Office of Dietary Supplements. Dietary Supplement Fact Sheet: Vitamin B6. <https://ods.od.nih.gov/factsheets/VitaminB6-HealthProfessional/> Updated February 11, 2016. Accessed September 11, 2017.
- Kelly CJ. Invigorating the context and content of nutrition in medical education. *Aca Med*. 2011 Nov;86(11):1340. [PMID: 22030639]
- Kiefer D, Pantuso T. Panax ginseng. *Am Fam Physician*. 2003 Oct 15;68(8):1539-42. [PMID: 14596440]
- Jia L, Zhao Y, Liang XJ. Current evaluation of the millennium phytomedicine ginseng (II): Collected chemical entities, modern pharmacology, and clinical applications emanated from traditional Chinese medicine. *Curr Med Chem*. 2009;16(22):2924-42. [PMID: 19689273]
- Kim Y, Choi EH, Doo M, et al. Anti-stress effects of ginseng via down-regulation of tyrosine hydroxylase (TH) and dopamine β-hydroxylase (DBH) gene expression in immobilization-stressed rats and PC12 cells. *Nutr Res Pract*. 2010 Aug;4(4):270-75. [PMID: 20827341]
- Tachikawa E, Kudo K, Hasegawa H, et al. In vitro inhibition of adrenal catecholamine secretion by steroidal metabolites of ginseng saponins. *Biochem Pharmacol*. 2003 Dec 1;66(11):2213-21. [PMID: 14609746]
- Rai D, Bhatia G, Sen T, et al. Anti-stress effects of Ginkgo biloba and Panax ginseng: a comparative study. *J Pharmacol Sci*. 2003 Dec;93(4):458-64. [PMID: 14737017]
- Lee DC, Lau AS. Effects of Panax ginseng on tumor necrosis factor-α-mediated inflammation: a mini-review. *Molecules*. 2011 Mar 30;16(4):2802-16. [PMID: 21455094]
- Panossian A, Wikman G. Effects of adaptogens on the central nervous system and the molecular mechanisms associated with their stress-protective activity. *Pharmaceuticals*. 2010 Jan 19;3(1):188-224. [PMID: 27713248]
- Chan SW. Panax ginseng Rhodiola rosea and Schisandra chinensis. *Int J Food Sci Nutr*. 2012 Mar;63 Suppl 1:75-81. [PMID: 22039930]
- Panossian A, Wikman G, Sarris J. Rosenroot (Rhodiola rosea): traditional use, chemical composition, pharmacology and clinical efficacy. *Phytomedicine*. 2010 Jun;17(7):481-93. [PMID: 20378318]
- Panossian A, Wikman G. Pharmacology of Schisandra chinensis Bail.: an overview of Russian research and uses in medicine. *J Ethnopharmacol*. 2008 July;118(2):183-212. [PMID: 18515024]
- Upton R, ed. *Schisandra Berry (Schisandra chinensis): Analytical, Quality Control and Therapeutic Monograph*. Santa Cruz, CA: American Herbal Pharmacopoeia; 1999:1-25. <http://cms.herbalgram.org/herbclip/pdfs/011007-185.pdf>.
- Aslanyan G, Amroyan E, Gabrielyan E, et al. Double-blind, placebo-controlled, randomised study of single dose effects of ADAPT-232 on cognitive functions. *Phytomedicine*. 2010 June;17(7):494-499. [PMID: 20374974]
- Ronzio R. A rationale for the use of glandular products. Stichting Sci Nutrition. http://tuesdayminute.net/A-Rationale_for_the_use_of_glandular_products.pdf. Revised October 2006. Accessed September 11, 2017.
- Panossian AG. Adaptogens: Tonic herbs for fatigue and stress. *Altern Complement Ther*. 2004 July;9(6):327-331. https://www.researchgate.net/publication/244889830_Adaptogens_Tonic_Herbs_for_Fatigue_and_Stress. Accessed September 19, 2017.

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Adrenal Manager™

Stress Response Support*



Available in 60 capsules and 120 capsules

Discussion

Stress is caused by physiological, psychological, or emotional triggers (stressors) that cause a disturbance in the homeostasis of an organism. How we respond to those stressors (physiologically and psychologically) influences how well we cope with change and with ongoing stress. Structural or physical trauma, distress, poor diet, infection, toxic exposure, leaky gut, births, deaths, lack of sleep, temperature changes, electromagnetic radiation, and allergies or food sensitivities are all potential stressors. Combined, they amount to a total stress level and can ultimately disrupt homeostasis with direct effects on the autonomic nervous system, the hypothalamic-pituitary-adrenal (HPA) axis, and the cardiovascular, metabolic, and immune systems.^[1] Specifically, research reveals that prolonged stress has a profound effect on the adrenal glands, lymph nodes, thymus gland, and gastrointestinal system.^[2] Endocrinologist Hans Selye identified the various stages of the stress response (alarm, resistance, and exhaustion) and described the entire phenomenon as the general adaptation syndrome (GAS).

Micronutrients, such as vitamins, minerals, and antioxidants, are involved in the majority of metabolic functions in the body. B vitamins are especially important to energy generation within the cellular mitochondria, and a deficiency of any B vitamin can compromise mitochondrial function.^[3,4] Riboflavin supports the respiratory chain, niacin supplies protons for oxidative phosphorylation, and pantothenic acid is required for coenzyme A production, metabolic enzyme complex formation, and fatty acid oxidation. Stressors can increase metabolic demand, energy expenditure, and micronutrient needs.^[5] Micronutrient sufficiency and balance have been established as crucial to helping maintain a healthy psychological and physiological response to stress.^[6] Unfortunately, experts estimate that a significant proportion of the general population does not consume adequate dietary levels of several micronutrients. Experts suggest that exogenous supplementation can improve micronutrient status and sufficiency and help support a healthy response to stress.^{*[7]}

Clinical Applications

- » Supports the Body's Response to Stress*
- » Supports Energy Production and Metabolic Function*

*Adrenal Manager™ pairs glandulars with targeted nutrients to support the body's response to everyday stressors. Among the comprehensive blend of nutrients are high-potency pantothenic acid and vitamin C, activated B vitamins, and mineral amino acid chelates. Gland and organ tissues are derived from an Argentinian bovine source that ensures safety and purity.**

Clinical research supports the premise that micronutrient supplementation can favorably support the stress response in a variety of circumstances.^[7] In a randomized, double-blind, placebo-controlled (RDBPC) trial, high-potency doses of B vitamins and vitamin C along with an array of minerals were studied for their effects on perceived stress scores (measuring one's self perception of stress) in 215 males aged 30 to 55 years. Results revealed significant improvements on the perceived stress scale (PSS), the profile of mood states (POMS), and the general health questionnaire (GHQ-12) for those taking the multivitamin/mineral supplement.^[8] Another RDBPC study of 80 males revealed consistent and statistically significant modulation in anxiety and perceived stress in the men who took a high-potency multivitamin/mineral supplement compared to those who took the placebo. Participants taking the supplement also reported feeling less tired and better able to concentrate compared to their placebo-taking counterparts.^[9] Similar results were achieved in a double-blind, placebo-controlled, double-center study of 300 subjects taking a multivitamin/mineral supplement, with significant improvement in baseline stress scores.^[6] The levels of vitamin C, riboflavin, B6, pantothenic acid, and zinc provided in the recommended dose of two Adrenal Manager capsules twice daily meets or exceeds the levels used in these clinical studies. The recommended daily dose of four capsules also provides 30 mg of niacin (compared to 50 mg used in studies) and 90 mg of magnesium (compared to 100 mg used in studies).*

Adrenal Manager also contains a blend of complementary nutrients and purified glandulars. *Rhodiola rosea*, chlorella, grape seed extract, magnesium, zinc, chromium, bioflavonoids, and L-tyrosine are present at levels that allow for additional supplementation to round out their profile. Activated B vitamins and Albion® TRAACS® (the real amino acid chelate system) mineral amino acid chelates, along with other chelated minerals, are key features of the formula. Adrenal, parotid, thymus, and spleen glandulars are extracted from an Argentinian bovine source that ensures safety and purity.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Adrenal Manager™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%DV
Vitamin C (ascorbic acid)	175 mg	194%
Riboflavin (as riboflavin 5'-phosphate sodium)	15 mg	1154%
Niacin (as niacinamide)	15 mg	94%
Vitamin B6 (as pyridoxal 5'-phosphate)	10 mg	588%
Pantothenic Acid (as d-calcium pantothenate)	105 mg	2100%
Magnesium (as magnesium citrate)	45 mg	11%
Zinc (as TRAACS® zinc bisglycinate chelate)	5 mg	45%
Chromium (as TRAACS® chromium nicotinate glycinate chelate)	50 mcg	143%
Potassium (as potassium glycinate complex)	2 mg	0%
Lemon Bioflavonoid Complex (<i>Citrus x limon</i>)(fruit peel)	225 mg	**
L-Tyrosine	175 mg	**
Parotid (from bovine)(Argentina)	80 mg	**
Thymus (from bovine)(Argentina)	70 mg	**
Chlorella (<i>Chlorella vulgaris</i>)	50 mg	**
Adrenal Gland (from bovine)(Argentina)	25 mg	**
Rhodiola Extract (<i>Rhodiola rosea</i>)(root)(3% rosavins and 1% salidroside)	25 mg	**
Spleen (from bovine)(Argentina)	20 mg	**
Grape Extract (<i>Vitis vinifera</i>)(seed)(95% proanthocyanidins)	1 mg	**

Other Ingredients: HPMC (capsule), microcrystalline cellulose, vegetable stearic acid, vegetable magnesium stearate, medium-chain triglyceride oil, and silica.

DIRECTIONS: Take two capsules daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.

Albion and TRAACS are registered trademarks of Albion Laboratories, Inc.

**References**

1. Brame AL, Singer M. Stressing the obvious? An allostatic look at critical illness. *Crit Care Med.* 2010 Oct;38(10 Suppl):S600-7. [PMID: 21164403]
2. Szabo S, Tache Y, Somogyi A. The legacy of Hans Selye and the origins of stress research: a retrospective 75 years after his landmark brief "letter" to the editor of *Nature*. *Stress.* 2012 Sep;15(5):472-8. [PMID: 22845714]
3. Depeint F, Bruce WR, Shangari N, et al. Mitochondrial function and toxicity: role of the B vitamin family on mitochondrial energy metabolism. *Chem Biol Interact.* 2006 Oct 27;163(1-2):94-112. [PMID: 16765926]
4. Angelo G. What is metabolism? Linus Pauling Institute. <http://lpi.oregonstate.edu/ss13/metabolism.html>. Accessed October 19, 2013.
5. Askew EW. Environmental and physical stress and nutrient requirements. *Am J Clin Nutr.* 1995 Mar;61(3 Suppl):631S-637S. Review. [PMID: 7879730]
6. Schlebusch L, Bosch BA, Polglase G, et al. A double-blind, placebo-controlled, double-centre study of the effects of an oral multivitamin-mineral combination on stress. *S Afr Med J.* 2000 Dec;90(12):1216-23. [PMID: 11234653]
7. Drake V. Micronutrients and Cognitive Function. Linus Pauling Institute. <http://lpi.oregonstate.edu/infocenter/cognition.html>. Accessed October 12, 2013
8. Kennedy DO, Veasey R, Watson A, et al. Effects of high-dose B vitamin complex with vitamin C and minerals on subjective mood and performance in healthy males. *Psychopharmacology (Berl).* 2010 Jul;211(1):55-68. [PMID: 20454891]
9. Carroll D, Ring C, Suter M, et al. The effects of an oral multivitamin combination with calcium, magnesium, and zinc on psychological well-being in healthy young male volunteers: a double-blind placebo-controlled trial. *Psychopharmacology (Berl).* 2000 Jun;150(2):220-5. [PMID: 10907676]

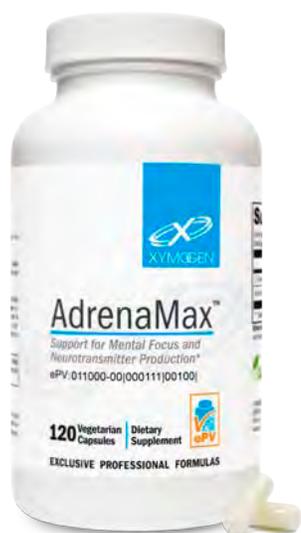
Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

AdrenaMax™

Support for Mental Focus and Neurotransmitter Production*



Available in 120 capsules

Discussion

Tyrosine, or 4-hydroxyphenylalanine, a proteogenic, non-essential amino acid that can be synthesized in the body from phenylalanine, is converted into dopamine, epinephrine, and norepinephrine. Although present in foods such as dairy, eggs, soy, peanuts, sesame, seaweed, avocados, bananas, poultry, lima beans, and others, tyrosine, when consumed in food, must compete for absorption with the other amino acids present. Taken as a supplement, tyrosine does not have to compete with other amino acids and, therefore, its full benefits can be realized.*

Stress conditions, such as a cold environment, psychological stress, sleep deprivation, and strenuous, prolonged athletic activity, appear to reduce the body's ability to convert phenylalanine to tyrosine. This underproduction may manifest itself as poor memory and performance. Tyrosine, as a precursor for catecholamine synthesis, presumably augments brain catecholamine levels and improves working memory under stress. Tyrosine also supports adrenal and pituitary function, and may increase thyroid hormone. Additionally, it is necessary for production of the skin pigment, melanin. Oral contraceptives may cause a decline in tyrosine plasma levels, possibly because estrogen can increase glucocorticoid levels. This, in turn, elevates levels of tyrosine aminotransferase, which degrades tyrosine in the liver.*

Although increased dopamine may be beneficial in some circumstances, excessive synthesis of this neurotransmitter generates hydroxy radicals that stress glutathione levels. N-acetyl cysteine (NAC), a derivative of the amino acid, L-cysteine, is the precursor to glutathione and helps augment the body's reserve of this important antioxidant. It has been included in this formula primarily to protect the neurons against dopamine toxicity. However, NAC also lessens the load on the methylation cycle, thereby decreasing the load on the THB cycle and promoting the conversion of tyrosine to dopamine.*

Only a percentage of the tyrosine consumed will make it into the brain for conversion to catecholamines. The rest will be picked up for

Clinical Applications

- » Maintain Healthy Levels of Dopamine, Norepinephrine and Epinephrine*
- » Supports Memory Under Stressful Conditions*
- » Supports Mental Focus and Alertness*
- » Supports Individuals with Polymorphism in Dopamine Receptors*
- » Supports Healthy Mood*

*Each AdrenaMax™ capsule contains 400 mg of L-tyrosine, a conditionally essential amino acid the body can convert to the neurotransmitters dopamine, epinephrine, and norepinephrine. These neurotransmitters are found to increase mental alertness and focus and also preserve normal memory under stressful conditions. N-acetyl-L-cysteine is present to support glutathione production, antioxidant activity, and neuronal protection.**

structural protein usage, etc. The only component that needs to be balanced with a glutathione precursor is the portion of tyrosine that is converted into catecholamines. For this reason, less NAC than tyrosine is present.*

AdrenaMax™ Supplement Facts

Serving Size: 3 Capsules

	Amount Per Serving	%Daily Value
L-Tyrosine	1.2 g	**
N-Acetyl-L-Cysteine	400 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, and silica.**DIRECTIONS:** Take one to three capsules one to three times per day, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.

**References**

1. Growdon JH. Effects of oral L-tyrosine administration on CSF tyrosine and homovanillic acid levels in patients with Parkinson's disease. *Life Sci.* 1982 Mar 8;30(10):827-32. [PMID: 6175872]
2. O'Brien C, et al. Dietary tyrosine benefits cognitive and psychomotor performance during body cooling. *Physiol Behav.* 2007 Feb 28;90(2-3):301-7. Epub 2006 Oct 31. [PMID: 17078981]
3. Palinkas LA. Mental and cognitive performance in the cold. *Int J Circumpolar Health.* 2001 Aug;60(3):430-9. [PMID: 11590885]
4. Deijen JB, Orlebeke JF. Effect of tyrosine on cognitive function and blood pressure under stress. *Brain Res Bull.* 1994;33(3):319-23. [PMID: 8293316]
5. Magill RA, et al. Effects of tyrosine, phentermine, caffeine D-amphetamine, and placebo on cognitive and motor performance deficits during sleep deprivation. *Nutr Neurosci.* 2003 Aug;6(4):237-46. [PMID: 12887140]
6. Rose DP, Cramp DG. Reduction of Plasma Tyrosine by Oral Contraceptives and Oestrogens: A Possible Consequence of Tyrosine Aminotransferase Induction. *Clin Chim Acta.* 1970;29:49-53. [PMID: 5500691]
7. Lee M, et al. Effects of hydrogen sulfide-releasing L-DOPA derivatives on glial activation: potential for treating Parkinson's disease. *Biol Chem.* 2010 Jun 4;285(23):17318-28. Epub 2010 Apr 5. [PMID: 20368333]
8. Clark J, et al. Oral N-acetyl-cysteine attenuates loss of dopaminergic terminals in alpha-synuclein overexpressing mice. *PLoS One.* 2010 Aug 23;5(8). pii: e12333.[PMID: 20808797]

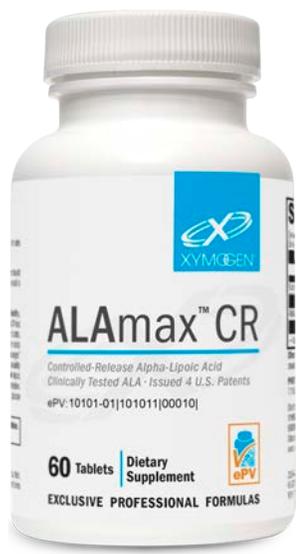
Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

ALAmax™ CR

Controlled-Release Alpha-Lipoic Acid



Available in 60 & 120 tablets

Discussion

Alpha-lipoic acid (ALA) is an eight-carbon disulfide water- and fat-soluble compound that is synthesized in small quantities in the liver and other tissues. Oral supplementation readily crosses the blood brain barrier after it is absorbed in the small intestine, goes into the portal vein, and is distributed via systemic circulation. Once in the tissues, ALA can be found inside and outside the cells including inside the mitochondria where it functions naturally as a coenzyme for the oxidation of pyruvate, alpha ketoglutarate, and branched-chain amino acids.*

Researchers recently identified lipoic acid's mechanisms of action related to maintaining metabolic health. It has a direct binding site at the insulin receptor tyrosine kinase domain. ALA appears to modulate 5'-AMP-activated protein kinase and PPAR-regulated genes, to activate PPAR-alpha and PPAR-gamma, and to support expression of PPAR-gamma mRNA and protein in heart tissue and smooth muscle of the aorta.*^[2]

Controlled-release technology supports efficacy of alpha-lipoic acid in helping to maintain blood sugar already in the normal range. Data from a 12-week clinical study indicate that supplementation with ALAmax™ CR (1200 mg per day, divided doses) may support healthy C-peptide levels. C-peptide is used as an indication of insulin sensitivity.*^[3,4]

Alpha-lipoic acid effectively neutralizes a variety of free radicals, including oxygen radicals and ionized metals. This action is particularly beneficial for people who have higher levels of oxidative stress. Alpha-lipoic acid regenerates vitamins C and E, increases tissue levels of glutathione, and helps maintain the proper ratio of reduced to oxidized coenzyme Q10 in the mitochondria. In addition, alpha-lipoic acid may help the body rid itself of heavy metals.*

Clinical Applications

- » Provides Fat-Soluble and Water-Soluble Antioxidant Activity*
- » Coenzyme for Whole-Body Glucose Utilization*
- » Supports Healthy Intracellular Glutathione Levels*
- » Supports Regeneration of Vitamins C and E*
- » Helps Maintain a Balance Between Oxidized and Reduced CoQ10*

*ALAmax™ CR provides whole-body, multifunctional antioxidant activity that helps to maintain healthy, well-functioning cells. ALAmax CR is designed to neutralize free radicals in both the water-based and lipid-based portion of cells, help the body synthesize glutathione, and recharge important antioxidants. Unlike regular alpha-lipoic acid, ALAmax CR's patented, controlled-release formulation provides extended protection. In addition, biotin supports the function of alpha-lipoic acid in glucose metabolism.**

Healthy endothelial-mediated vasodilation is accepted as a surrogate marker for cardiovascular health and can be affected by synthesis, bioavailability, or action of nitric oxide (NO). Increased oxidative stress appears to play a significant role in neutralizing or inactivating NO. ALA's antioxidant properties, along with its demonstrated safety and potency, qualify it as a prime candidate to evaluate for its ability to support healthy endothelial function.*^[5]

The ability of alpha-lipoic acid to improve energy metabolism and decrease oxidative stress alludes to its ability to support healthy mitochondrial function with age.*

Biotin has been added because chronic administration of lipoic acid lowers the activities of pyruvate carboxylase and beta-methylcrotonyl-CoA carboxylase in vivo by competing with biotin.*^[6]

ALMax™ CR Supplement Facts

Serving Size: 1 Tablet

	Amount Per Serving	%Daily Value
Biotin	450 mcg	1500%
Alpha-Lipoic Acid (thioctic acid)	600 mg	**

Other Ingredients: Cellulose and cellulose derivatives, silica, magnesium stearate, stearic acid, glycerin, and dicalcium phosphate.

PROTECTED BY U.S. PATENTS: 6,191,162(B1); 6,197,340(B1); 6,572,888(B2); 7,118,762(B2)

DIRECTIONS: Take one tablet 30 minutes before breakfast and one tablet 30 minutes before dinner, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, corn, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

References

1. Teichert J, Kern J, Tritschler HJ, Ulrich H, Preiss R: Investigations on the pharmacokinetics of alpha-lipoic acid in healthy volunteers. *Int.J.Clin. Pharmacol.Ther.* 36:625-628, 1998
2. Pershadsingh HA. Alpha-lipoic acid: physiologic mechanisms and indications for the treatment of metabolic syndrome. *Expert Opin Investig Drugs.* 2007 Mar;16(3):291-302 [PMID: 17302524]
3. Evans JL, Goldfine ID: α -Lipoic acid: a multi-functional antioxidant that improves insulin sensitivity in patients with type 2 diabetes. *Diabetes Technol Therap* 2:401-413, 2000
4. Jacob S, Ruus P, et al. Oral administration of RAC-alpha-lipoic acid modulates insulin sensitivity in patients with type 2 diabetes mellitus: a placebo-controlled pilot trial. *Free Radic Biol Med* 27:309-314, 1999
5. Bojunga J, et al. Antioxidative treatment reverses imbalances of nitric oxide synthase isoform expression and attenuates tissue-cGMP activation in diabetic rats. *Biochem Biophys Res Commun.* 2004 Apr 9;316(3):771-80 [PMID: 15033467]
6. Zemleni J, Trusty TA, Mock DM. Lipoic acid reduces the activities of biotin-dependent carboxylases in rat liver. *J Nutr.* 1997 Sep;127(9):1776-81 [PMID: 9278559]
7. Foster TS. Efficacy and safety of {alpha}-lipoic acid supplementation in the treatment of symptomatic diabetic neuropathy. *Diabetes Educ.* 2007 Jan-Feb;33(1):111-7 [PMID: 17272797]
8. Alpha Lipoic Acid. www.naturaldatabase.com {accessed 3.06.07}
9. Diesel B. et. al. Alpha-lipoic acid as a directly binding activator of the insulin receptor: protection from hepatocyte apoptosis. *Biochemistry.* 2007 Feb 27;46(8):2146-2155. Epub 2007 Feb 3 [PMID: 17274632]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Antioxidant Activity

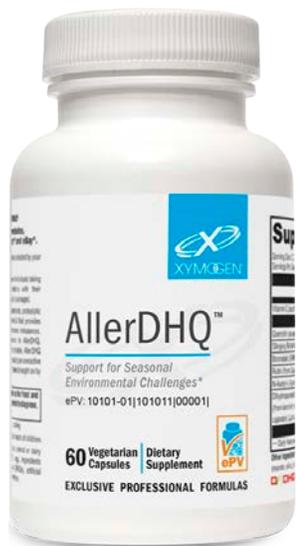
Blood Sugar Support

Cell-Life Regulation

Liver Support

AllerDHQ™

Support for Seasonal Environmental Challenges*



Available in 60 capsules and 120 capsules

Discussion

Individuals with hypersensitive immune reactions often experience physical, mental, and functional decline even with moderate onset of discomfort.^[1] AllerDHQ provides fast-acting, natural support for hypersensitivity reactions, including watery, itchy eyes and runny nose, as well as other manifestations of histamine release. Formulated with a synergistic combination of vitamins, bioflavonoids, amino acids, herbs, and bromelain, AllerDHQ addresses the distressing signs of immune hypersensitivity.*

Vitamin C (ascorbic acid) Vitamin C is essential to humans and must be obtained exogenously. While most mammals are able to synthesize ascorbic acid, humans lack one of the enzymes required for this process and can quickly become deficient if dietary or supplemental intake is inadequate. Stress, smoking, pollution, and temperature changes increase our requirement for vitamin C. Well-known functions of vitamin C include antioxidant protection from damaging free radicals and the synthesis of collagen, carnitine, and neurotransmitters. Vitamin C also plays a lesser-known role in the deactivation of histamine.*^[2,3]

Bioflavonoids Quercetin, dihydroquercetin (DHQ), and rutin are active bioflavonoids incorporated into AllerDHQ for their role in moderating an exaggerated immune response. Bioflavonoids work synergistically with other antioxidants to protect tissues from the negative effects of oxidation and inflammation often observed during hyperimmune reactions.^[4] Immune-moderating effects include inhibition of mast-cell degranulation and prevention of histamine release during hypersensitive episodes.*^[1,5,6]

Dihydroquercetin DHQ supports the activities of other antioxidants, protects erythrocytes and capillaries, supports bronchial function, and assists in chelation of metals.^[7] DHQ was also found to moderate pro-inflammatory pathways by inhibiting inducible ICAM-1 expression.^[8] The FlavitPURE™⁺ form of DHQ in AllerDHQ is a bioactive, natural form that is significantly more absorbable than quercetin alone. The inclusion of FlavitPURE in AllerDHQ creates a clear advantage over products containing only quercetin, as fewer capsules are required

Clinical Applications

- » Supports Hypersensitive Individuals*
- » Supports Nasal and Sinus Passages*
- » Provides Antioxidant Support and Protection*

*AllerDHQ™ incorporates bioflavonoids, micronutrients, proteolytic enzymes, and herbs into a comprehensive formula that provides multifaceted support for individuals with immune imbalances. Dihydroquercetin (DHQvital™), a key component in AllerDHQ, inhibits oxidation, is bioactive, and is highly absorbable. AllerDHQ supports the body's regulating function in addressing an overactive or distressed histamine response that are sometimes brought on by the environment.**

for effective results. This specific form of DHQ boasts an impressive ORAChydro value of 28,000+ μM TE/g and a CAP-e assay of 9.9-10.5 units per gram,^[7,9] indicative of effective antioxidant protection within the cell. ORAChydro reflects oxygen radical absorbance capacity for water-soluble antioxidants, and CAP-e refers to cell-based antioxidant protection in erythrocytes.*

Rutin A source of naturally occurring flavonoids, rutin reduces capillary permeability and edema, which can reduce mucus fluid buildup or “runny nose.”^[10] Rutin's protective effect against oxidation is amplified by ascorbic acid, also present in AllerDHQ.*^[4]

N-Acetyl-Cysteine NAC is the acetylated form of the conditionally essential amino acid L-cysteine. As a precursor to the “master antioxidant” glutathione, NAC plays a significant role in detoxification and antioxidant protection. NAC also functions as a natural mucolytic, reducing the viscosity of mucus commonly produced during a hyperimmune response.*^[11,12]

Stinging Nettle Extract (*Urtica dioica*) Stinging nettle leaf has been found to regulate a variety of inflammatory activities associated with hyperimmune response, including mast-cell degranulation, prostaglandin formation, and histamine action.*^[13-15]

Bromelain Bromelain refers to an enzyme complex extracted from the stem and fruit of the pineapple plant (*Ananas comosus*). Its modulation of the inflammatory response is thought to exert a beneficial effect in combating hypersensitive immune reactions, earning it approved status by the German Commission E for “micro-inflammations” and related discomforts.^[15,16] Early studies identified its positive effects on controlling edema, tissue permeability, and vasodilation.^[17] Bromelain is also found to enhance the absorption of quercetin.*^[18]

Research indicates that the natural components in AllerDHQ, including vitamin C, bioflavonoids, DHQ, NAC, and bromelain, work synergistically to moderate unpleasant immune reactions.*^[1,4]

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

AllerDHQ™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Vitamin C (ascorbic acid)	200 mg	222%
Quercetin (as quercetin dihydrate)(from <i>Sophora japonica</i>)(bud)	400 mg	**
Stinging Nettle Aqueous Extract (<i>Urtica dioica</i>)(aerial parts)(1% silica)	200 mg	**
Bromelain (2400 GDU/g)(from <i>Ananas comosus</i>)(stem)	100 mg	**
Rutin (from <i>Sophora japonica</i>)(bud)	100 mg	**
N-Acetyl-L-Cysteine	100 mg	**
DHQvital™ Dihydroquercetin (from larch tree extract)(<i>Larix dahurica</i> , <i>Larix gmelinii</i> , <i>Larix sibirica ledeb.</i> , <i>Larix cajanderi</i> , <i>Larix czekanowskii</i> , <i>Larix russica</i> , <i>Larix sukaczewii</i>)(saw logs)	40 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), dicalcium phosphate, stearic acid, magnesium stearate, silica, and medium-chain triglyceride oil.**DIRECTIONS:** Take one to two capsules daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

CAUTIONS: Do not use if you are pregnant or lactating.**STORAGE:** Keep closed in a cool, dry place out of reach of children.**DOES NOT CONTAIN:** Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives. DHQvital is a trademark of Berg Imports, LLC**References:**

1. Thornhill SM, Kelly AM. Natural treatment of perennial allergic rhinitis. *Altern Med Rev.* 2000 Oct;5(5):448-54. [PMID: 11056414]
2. Johnston CS. The antihistamine action of ascorbic acid. *Subcell Biochem.* 1996;25:189-213. [PMID: 8821975]
3. Strohle A, Wolters M, Hahn A. Micronutrients at the interface between inflammation and infection—ascorbic acid and calciferol: part 1, general overview with a focus on ascorbic acid. *Inflamm Allergy Drug Targets.* 2011 Feb;10(1):54-63. [PMID: 21184650]
4. Skaper SD, Fabris M, Ferrari V, et al. Quercetin protects cutaneous tissue-associated cell types including sensory neurons from oxidative stress induced by glutathione depletion: cooperative effects of ascorbic acid. *Free Radic Biol Med.* 1997;22(4):669-78. [PMID: 9013129]
5. Middleton E Jr, Drzewiecki G, Krishnarao D. Quercetin: an inhibitor of antigen-induced human basophil histamine release. *J Immunol.* 1981 Aug;127(2):546-50. [PMID: 6166675]
6. Park HH, Lee S, Son HY, et al. Flavonoids inhibit histamine release and expression of proinflammatory cytokines in mast cells. *Arch Pharm Res.* 2008 Oct;31(10):1303-11. [PMID: 18958421]
7. <http://www.vitalavita.us> Accessed July 31, 2011.
8. Bito T, Roy S, Sen CK, et al. Flavonoids differentially regulate IFN gamma-induced ICAM-1 expression in human keratinocytes: molecular mechanisms of action. *FEBS Lett.* 2002 Jun 5;520(1-3):145-52. [PMID: 12044887]
9. Ou B, Hampsch-Woodill M, Prior RL. Development and validation of an improved oxygen radical absorbance capacity assay using fluorescein as the fluorescent probe. *J Agric Food Chem.* 2001 Oct;49(10):4619-26. [PMID: 11599998]
10. Turner RB, Fowler SL, Berg K. Treatment of the common cold with roxerutin. *APMIS.* 2004 Sep;112(9):605-11. [PMID: 15601310]
11. Kelly GS. Clinical applications of N-acetylcysteine. *Altern Med Rev.* 1998 Apr;3(2):114-27. [PMID: 9577247]
12. Ziment I. Acetylcysteine: a drug that is much more than a mucokinetic. *Biomed Pharmacother.* 1988;42(8):513-9. [PMID: 3066412]
13. Roschek B Jr, Fink RC, McMichael M, Alberte RS. Nettle extract (*Urtica dioica*) affects key receptors and enzymes associated with allergic rhinitis. *Phytother Res.* 2009 Jul;23(7):920-6. [PMID: 19140159]
14. Riehemann K, Behnke B, Schulze-Osthoff K. Plant extracts from stinging nettle (*Urtica dioica*), an antirheumatic remedy, inhibit the proinflammatory transcription factor NF-kappaB. *FEBS Lett.* 1999 Jan 8;442(1):89-94. [PMID: 9923611]
15. Blumenthal M. *The Complete German Commission E Monographs: Therapeutic Guide to Herbal Medicines.* Austin, TX: American Botanical Council; 2000.
16. Maurer HR. Bromelain: biochemistry, pharmacology and medical use. *Cell Mol Life Sci.* 2001 Aug;58(9):1234-45. [PMID: 11577981]
17. Ryan RE. A double-blind clinical evaluation of bromelains in the treatment of acute sinusitis. *Headache.* 1967 Apr;7(1):13-7. [PMID: 4859824]
18. Lakhanpal, P, Rai DK. Quercetin: A Versatile Flavonoid. *IJMU.* 2007 Jul-Dec;2(2):22-37.

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

AngiNOX™

Effervescent Nitric Oxide Formula



Available in 30 scoops & 60 scoops

Discussion

Nitric oxide (NO) is produced by various body cells from the amino acid L-arginine through the enzymatic action of nitric oxide synthase (NOS). NO has critical roles in regulating the function of organs and systems throughout the body. It is well known that NO production by vascular endothelium plays a critical role in blood flow regulation and that the abnormal production of NO can adversely affect blood flow, delivery of nutrients and oxygen, and other vascular functions.

L-Arginine is the principal substrate for the family of NOS enzymes that catalyze the biosynthesis of NO. Some of L-arginine's benefits include support of immune response, ammonia detoxification, growth hormone secretion (during rest), improved exercise performance (at 6 g/d), wound healing, reduced platelet aggregation, and vasodilation.^[1,2] ADMA (asymmetric dimethylarginine) is a newly identified factor confronting cardiovascular health. As an endogenous NOS inhibitor, accumulation of ADMA impairs NO formation by competing with L-arginine for NOS binding. Under these conditions, supplementation with L-arginine may support maintenance of near-normal levels.^[1] New research also suggests that ADMA accumulation in oxidized low-density lipoproteins (OxLDL) may signal vascular smooth muscle cell (VSMC) migration—which plays a critical role in the etiology of intimal thickening—and L-arginine markedly blocked ADMA-induced VSMC migration.^[3]

L-Citrulline is a precursor to L-arginine that readily permeates the intestinal wall and enters the bloodstream. L-citrulline is processed by the kidney, where it is converted to L-arginine; and oral L-citrulline supplementation in humans has been shown to increase plasma L-arginine availability for NO synthesis.^[4] In an animal study, oral supplementation with "L-arginine, L-citrulline, and/or antioxidants (vitamins C and E) showed marked support of endothelium-dependent vasorelaxation and blood flow, maintenance of a healthy endothelium, and decrease in superoxide production and oxidation-sensitive gene expression ..."^[5]

Clinical Applications

- » Optimize Flow of Blood and Oxygen to Peripheral Tissues*
- » Helps Maintain Healthy Male Sexual Function*
- » Supports Lean Body Mass/Athletic Performance*
- » Supports Healthy Dilatation of Blood Vessels*
- » Supports the Healthy Flow of Blood and Oxygen to the Brain for Healthy Mood, Mind, and Memory*

*AngiNOX™ is XMOGEN's exciting formula based on the latest Nobel Prize-winning research on nitric oxide, a naturally occurring compound in the body. Nitric oxide is an important messenger that signals a variety of responses at the cellular level which are beneficial to circulatory, immune, and nervous system functions. AngiNOX is a refreshing, effervescent powder that offers therapeutic levels of L-arginine and L-citrulline, two amino acids the body uses to make nitric oxide.**

Quercetin A major flavonoid naturally occurring in plants, quercetin has been shown in a study on mice using microarray DNA analyses and pathway analyses to inhibit LPS-induced expression of IL-1beta, IL-1alpha, IL-6, TNF-alpha, IL-12, iNOS, VCAM1, ICAM1, COX2, IL-1RA, TRAF1 and CD40.^[6] Experimental models suggest that quercetin prevents the redox imbalance associated with decreased intracellular NO levels and superoxide overproduction, and it prevents the overexpression of inducible NOS (iNOS).^[7,8]

Folic Acid Research suggests that homocysteine may decrease the bioavailability of NO.^[9] Therefore, folate's deleterious effect on homocysteine may provide the added benefit of increasing NO levels through enhancing NO bioavailability. Another role of folic acid in NO production relates to tetrahydrobiopterin (THBP, also known as BH4)—an essential cofactor for NOS. Inadequate folate may impair the synthesis of THBP,^[10] and 5-MTHF (bioactive folate) may normalize the activity of NOS in THBP-depleted endothelial cells.^[11] In a placebo-controlled study of patients receiving 400 mcg/d of folic acid for seven weeks before coronary artery bypass grafting, improved vascular function was observed and attributed to improved availability of THBP for NOS and reduced vascular oxidative stress.^[12]

Vitamins C and E Free-radical injury reduces NO availability, and antioxidants appear to preserve NO. In addition, healthy endothelial function is associated with low oxidative stress, particularly decreased superoxide production and reduced oxidized LDL (OxLDL), which, if elevated, can reduce endothelium-derived NO activity. Vitamins C and E administration can reduce both superoxide and OxLDL, thereby improving NO activity.^[13] According to Heller et al, "The effect of alpha-tocopherol seems to be dependent on tissue saturation with ascorbic acid, and both vitamins may act synergistically to provide optimal conditions for endothelial NO formation."^[14]

"More than any other single factor, nitric oxide may be the key to living a longer, healthier life." – Dr. Louis Ignarro, 1998 Nobel Prize Laureate

AngiNOX™ Supplement Facts

Serving Size: 1 Scoop (about 8 g)

	Amount Per Serving	%Daily Value
Calories	20	
Total Carbohydrate	3 g	1%†
Vitamin C (ascorbic acid)	300 mg	333%
Folate	3,333 mcg DFE (2,000 mcg folic acid)	833%
Sodium	220 mg	10%
L-Arginine	2 g	**
L-Citrulline	500 mg	**
Quercetin (as quercetin dihydrate) (from <i>Sophora japonica</i>)(bud)	500 mg	**
Mixed Tocopherols d-Gamma Tocopherol	230 mg 160 mg	** **

†Percent Daily Values are based on a 2,000 calorie diet.
** Daily Value not established.

Other Ingredients: Citric acid, dried cane syrup, sodium bicarbonate, natural orange flavor (no MSG), silica, and stevia leaf extract.

DIRECTIONS: Pour one level scoop of powder into a tall, empty glass. Add 3 oz of chilled water and lightly stir. Let stand one minute. Add 3 more oz of chilled water and lightly stir. Let stand one minute and drink. Take once daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, artificial colors, artificial sweeteners, or artificial preservatives.

CAUTIONS: Do NOT use if you have low blood pressure.

STORAGE: Keep closed in a cool, dry place out of reach of children.

References

1. Böger RH. The pharmacodynamics of L-arginine. *J Nutr.* 2007 Jun;137(6 Suppl 2):1650S-55S. [PMID: 17513442]
2. Bailey SJ, Winyard PG, Vanhatalo A, et al. Acute L-arginine supplementation reduces the O₂ cost of moderate-intensity exercise and enhances high-intensity exercise tolerance. *J Appl Physiol.* 2010 Nov;109(5):1394-403. [PMID: 20724562]
3. Sun L, Zhang T, Yu X, et al. Asymmetric dimethylarginine confers the communication between endothelial and smooth muscle cells and leads to VSMC migration through p38 and ERK1/2 signaling cascade. *FEBS Lett.* 2011 Sep 2;585(17):2727-34. [PMID: 21821030]
4. Sureda A, Cordova A, Ferrer MD, et al. Effects of L-citrulline oral supplementation on polymorphonuclear neutrophils oxidative burst and nitric oxide production after exercise. *Free Radic Res.* 2009 Sep;43(9):828-35. [PMID: 19585317]
5. Hayashi T, Juliet PA, Matsui-Hirai H, et al. L-Citrulline and L-arginine supplementation retards the progression of high-cholesterol-diet-induced atherosclerosis in rabbits. *Proc Natl Acad Sci U S A.* 2005 Sep 20;102(38):13681-86. [PMID: 16157883]
6. Qureshi AA, Tan X, Reis JC, et al. Inhibition of nitric oxide in LPS-stimulated macrophages of young and senescent mice by delta-tocotrienol and quercetin. *Lipids Health Dis.* 2011 Dec 20;10(1):239. [Epub ahead of print] [PMID: 22185406]
7. Kostyuk VA, Potapovich AI, Suhan TO, et al. Antioxidant and signal modulation properties of plant polyphenols in controlling vascular inflammation. *Eur J Pharmacol.* 2011 May 11;658(2-3):248-56. [PMID: 21371465]
8. Zhang ZJ, Cheang LC, Wang MW, et al. Quercetin exerts a neuroprotective effect through inhibition of the iNOS/NO system and pro-inflammation gene expression in PC12 cells and in zebrafish. *Int J Mol Med.* 2011 Feb;27(2):195-203. [PMID: 21132259]
9. Tawakol A, Forgiione MA, Stuehlinger M, et al. Homocysteine impairs coronary microvascular dilator function in humans. *J Am Coll Cardiol.* 2002 Sep 18;40(6):1051-58. [PMID: 12354427]
10. Crabtree MJ, Channon KM. Synthesis and recycling of tetrahydrobiopterin in endothelial function and vascular disease. *Nitric Oxide.* 2011 Aug 1;25(2):81-88. [PMID: 21550412]
11. McCarty MF. Coping with endothelial superoxide: potential complementarity of arginine and high-dose folate. *Med Hypotheses.* 2004;63(4):709-18. [PMID: 15325022]
12. Shirodaria C, Antoniadis C, Lee J, et al. Global improvement of vascular function and redox state with low-dose folic acid: implications for folate therapy in patients with coronary artery disease. *Circulation.* 2007 May 1;115(17):2262-70. [PMID: 17420345]
13. Carr A, Frei B. The role of natural antioxidants in preserving the biological activity of endothelium-derived nitric oxide. *Free Radic Biol Med.* 2000 Jun 15;28(12):1806-14. [PMID: 10946222]
14. Heller R, Werner-Felmayer G, Werner ER. Alpha-Tocopherol and endothelial nitric oxide synthesis. *Ann N Y Acad Sci.* 2004 Dec;1031:74-85. [PMID: 15753135]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Appe-Curb™

Combatting Cravings Naturally*



Available in 120 capsules & 240 capsules

Discussion

5-Hydroxytryptophan (“5-HTP”) is a naturally-occurring amino acid precursor to serotonin. Numerous studies during the ‘90s, including those randomized, double-blind, and placebo-controlled, confirmed the safety and efficacy of 5-HTP in reducing appetite and food intake in obese healthy and non-insulin-dependent diabetic individuals.^[1,2,3] A 2006 study in mice concluded, “5-HTP-induced anorexia may be mediated by facilitation of leptin secretion.”^[4] Vitamins B6 and C are important cofactors in the 5-HTP to serotonin pathway. Among the several serotonin receptors thus identified, the 5HT2C receptors are suspected in control of food intake. Mice without this receptor exhibit increased food intake and become obese.^{*[5]}

DL-Phenylalanine (DLPA) is a combination of the d- and the l- forms of this essential amino acid. Phenylalanine suppresses appetite by regulating the release of cholecystokinin, which in turns signals satiety in the brain. D-phenylalanine increases endorphins, while L-phenylalanine is an amphetamine-like stimulatory compound. DLPA has been found to elevate mood, curb appetite and reduce pain.*

L-Tyrosine, an essential amino acid is needed for conversion into the catecholamine neurotransmitters stress depletes: dopamine, norepinephrine, and epinephrine. It is also a precursor for thyroxine. Doctors use tyrosine as a mood elevator, to increase alertness after sleep deprivation and as an appetite suppressant; although support for the latter appears anecdotal.^{*[6]}

L-Glutamine, well-recognized for gut and immune support, has also been espoused to reduce carbohydrate cravings and support alcohol withdrawal, although the mechanism of action for these benefits is not known.^{*[7,8]}

Chromium, as chromium picolinate is widely used to optimize insulin function; thereby preventing swings in blood glucose levels that may be responsible for carbohydrate cravings. The mineral in the form present was indeed demonstrated to reduce carbohydrate cravings in a double-blind, placebo-controlled study.^{*[9,10]}

Clinical Applications

- » Nutritional Support for Carbohydrate, Alcohol & Drug Cravings*
- » Supports Healthy Weight (by reducing carbohydrate cravings)*
- » Improve Sense of Wellbeing and Energy*
- » Supports Healthy Serotonin Levels*

*Appe-Curb™ contains key amino acids to support the biosynthesis of neurotransmitters involved in appetite control, carbohydrate or fat cravings, and mood. Chromium is present to support healthy glucose metabolism and support food intake regulation.**

Appe-Curb™ Supplement Facts

Serving Size: 4 Capsules

	Amount Per Serving	%Daily Value
Vitamin C (ascorbic acid)	500 mg	556%
Vitamin B6 (as pyridoxine HCl)	37.5 mg	2206%
Chromium (as TRAACS® chromium nicotinate glycinate chelate)	60 mcg	171%
DL-Phenylalanine	1 g	**
L-Tyrosine	750 mg	**
L-Glutamine	375 mg	**
5-HTP (5-hydroxytryptophan)(from <i>Griffonia simplicifolia</i>)(seed)	75 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, medium-chain triglyceride oil, and silica.

DIRECTIONS: Take four capsules before breakfast and four capsules before 3 PM, or use as directed by your healthcare practitioner. Do not take after 3 PM.

Consult your healthcare practitioner prior to use if you have, or suspect you have, a medical condition or are taking prescription drugs for depression, migraines, Parkinson's disease, or psychiatric disorders. Not for use by children. Do not use if tamper seal is damaged.

CAUTIONS: Do not take if you are, or suspect you are, pregnant or if you are lactating.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



TRAACS® and the Gold Medallion® are registered trademarks of Balchem Corporation or its subsidiaries.

**References**

1. Cangiano C, et al. Eating behavior and adherence to dietary prescriptions in obese adult subjects treated with 5-hydroxytryptophan. *Am J Clin Nutr* 1992 Nov;56(5):863-7
2. Cangiano C Effects of oral 5-hydroxy-tryptophan on energy intake and macronutrient selection in non-insulin dependent diabetic patients. *Int J Obes Relat Metab Disord* 1998 Jul;22(7):648-544
3. Amamoto T, Sarai K. On the tryptophan-serotonin metabolism in manic-depressive disorders. Changes in plasma 5-HT and 5-HIAA levels and urinary 5-HIAA excretion following oral loading of L-5HTP in patients with depression. *Hiroshima J Med Sci.* 1976 Sep;25(2-3):135-40 [PMID: 1088369]
4. Yamada J, Sugimoto Y, Ujikawa M. Involvement of leptin in hypophagia induced by the serotonin precursor 5-hydroxytryptophan (5-HTP) in mice. *Biol Pharm Bull.* 2006 Mar;29(3):557-9 [PMID: 16508167]
5. Rogers PJ, Blundell JE. Reanalysis of the effects of phenylalanine, alanine, and aspartame on food intake in human subjects. *Physiol Behav.* 1994 Aug;56(2):247-50 [PMID: 7938234]
6. <http://web.indstate.edu/thcme/mwking/aminoacidderivatives.html> {accessed 09 July 07}
7. Goodwin, F. APA Psychiatric News, Dec 5, 1986 in Atkins, R. Dr. Atkins Vita-Nutrient Solution. *Simon & Schuster*, NY 1998 p169
8. Rogers, L., Pelton, R. Quarterly Journal of Studies of Alcohol, 1957;18(4):581-87 in Atkins, R. Dr. Atkins Vita-Nutrient Solution. *Simon & Schuster*, NY 1998 p169
9. Broadhurst CL, Domenico P. Clinical studies on chromium picolinate supplementation in diabetes mellitus--a review. *Diabetes Technol Ther.* 2006 Dec;8(6):677-87 [PMID: 17109600]
10. Docherty JP, et al. A double-blind, placebo-controlled, exploratory trial of chromium picolinate in atypical depression: effect on carbohydrate craving. *J Psychiatr Pract.* 2005 Sep;11(5):302-14 [PMID: 16184071]

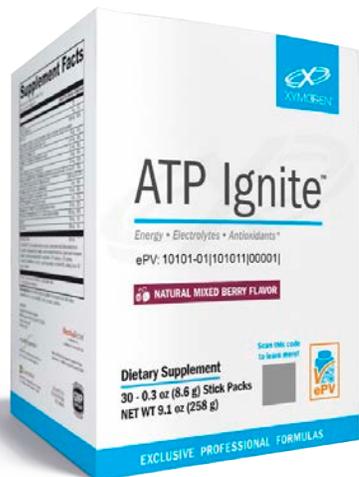
Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

ATP Ignite™

Energy • Electrolytes • Antioxidants*



Available in Natural Mixed Berry & Natural Citrus

Discussion

PUREENERGY™

Purenergy is an innovative patent-protected ingredient that combines caffeine with pTeroPure® pterostilbene—a highly bioavailable analog of resveratrol—to form a unique co-crystal structure. It appears that this unique structure affects the way the body utilizes caffeine. As such, it may offer significant advantages over caffeine alone.*

Study Findings

In a rat study (n=6), the half-life of the caffeine from Pureenergy was eight hours, while that of ordinary caffeine was just three hours.^[1] In a preliminary, four-week, single-blind, crossover human study (n=12) that compared 232 mg of Pureenergy (providing 99.76 mg of caffeine) to 100 mg of ordinary caffeine, the following effects were demonstrated^[2,3]:

- » Pureenergy delivered almost 30% more caffeine into the blood than ordinary caffeine.*
- » The absorption rate of the caffeine from Pureenergy was significantly slower by approximately 30% compared to ordinary caffeine.*
- » The half-life of the caffeine from Pureenergy was extended significantly by approximately 25% compared to ordinary caffeine.*
- » At 4 hours, serum showed 45% more caffeine from Pureenergy compared to ordinary caffeine.*
- » At 6 hours, serum showed 51% more caffeine from Pureenergy compared to ordinary caffeine.*
- » Pureenergy had no adverse effect.*

While the results of these studies are promising, larger studies are needed to validate the findings and determine if these findings translate into a lengthened energy effect.*

More Energy

Taken together, data from these studies suggest that the effects of caffeine from Pureenergy may last longer than the effects from ordinary caffeine and point to a potential for reducing total caffeine intake due to Pureenergy's more efficient delivery and slower absorption rate. These are encouraging factors for people who wish to reduce their caffeine intake.*

Slower Caffeine "Finish"

Scientists are researching whether or not the extended half-life and slower absorption rate of caffeine from Pureenergy can produce a more moderated and gradual finish. This may

Clinical Applications

- » Designed to Support a Healthy Energy Level*
- » Supports Electrolyte Replacement*
- » Helps Fight Free Radicals with Antioxidant Nutrients, Including S-Acetyl-L-Glutathione and 500 mg of Vitamin C*
- » Provides an Alternative to Ordinary Caffeine*
- » Provides Ingredients That Support ATP Biosynthesis*

*ATP Ignite™ transforms water into a great-tasting, revitalizing energy drink. Each stick provides a combination of B vitamins, electrolytes, trace minerals, amino acids, herbs, and antioxidants to fuel your body's energy production. Building on these important nutrients, ATP Ignite also features Pureenergy™, a technology-driven, patent-protected ingredient that combines caffeine and pTeroPure® pterostilbene. Initial reports suggest that Pureenergy's caffeine may be absorbed more slowly and stay in your system longer than regular caffeine, which may help your energy last longer. With just 5 g of carbohydrate per serving and zero sugars, ATP Ignite simply gives your body what it needs to produce energy.**

help prevent the "crash" associated with regular caffeinated energy products and may give ATP Ignite an advantage over formulas that use ordinary caffeine.*

All-Natural, No Sugars

ATP Ignite relies on natural ingredients, not ephedra or artificial stimulants. Furthermore, it provides only five grams of carbohydrates and zero sugars. By using natural flavors and stevia in place of sugar and other carbohydrates, the typical "sugar high" that is associated with many energy drinks can be avoided. Equally important, ATP Ignite contains no artificial colors.*

Caffeine, in General

In animal and human studies, caffeine has demonstrated positive effects on athletic performance, fatigue, and cognitive functions, such as supporting a healthy memory.^[4-8] According to Meeusen et al, research on caffeine suggests its performance-enhancing effect is related to antagonism of the adenosine receptors that influence the dopaminergic and other neurotransmitter systems.*^[9]

Pterostilbene

In the aforementioned human study, Pureenergy also delivered approximately 50% more total pterostilbene into the blood than pTeroPure delivered alone,^[2] thus potentially enhancing the functional benefits of pterostilbene. Pterostilbene is a highly bioavailable analog of resveratrol—a stilbenoid found in blueberries and grapes. Compared to resveratrol, pterostilbene is four times more bioavailable,^[10] has a seven times greater half-life,^[11] exhibits greater oral absorption and metabolic stability (pterostilbene is more lipophilic), and produces two to four times greater cellular uptake.^[12] Aside from resveratrol's well-known antioxidant benefits that support cardiovascular health, pterostilbene is also known to activate certain proteins (i.e., *SIRT1* and PGC-1 α) involved in increasing mitochondrial biogenesis and therefore ATP (energy) production.*^[13-15]

Electrolytes and Antioxidants

Electrolytes—including sodium, potassium, and magnesium—are important for energy production, nerve transmission, muscle contractions, pH balance, fluid balance, and more. Conditions that promote excessive sweating and increased metabolic activity can require replacement of these important minerals and increase the need for antioxidants. ATP Ignite provides 130 mg of sodium, 280 mg of potassium, and 150 mg of magnesium in each serving. To support protection from free radicals, ATP Ignite

Continued on next page

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

ATP Ignite™ Natural Mixed Berry Supplement Facts

Serving Size: 1 Stick Pack (about 8.6 g)

	Amount Per Serving	%Daily Value
Calories	20	
Total Carbohydrate	5 g	2%†
Vitamin C (as sodium ascorbate, potassium ascorbate, calcium ascorbate, and zinc ascorbate)	500 mg	556%
Vitamin E (as d-alpha tocopheryl succinate)	10 mg	67%
Thiamin (as thiamine HCl)	0.45 mg	38%
Riboflavin (as riboflavin 5'-phosphate sodium)	0.5 mg	38%
Niacin	10 mg	63%
Vitamin B6 (as pyridoxal 5'-phosphate)	2.6 mg	153%
Folate (as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt)	40 mcg DFE	10%
Vitamin B12 (as MecobalActive™ methylcobalamin)	2500 mcg	104,167%
Pantothenic Acid (as d-calcium pantothenate)	3 mg	60%
Magnesium (as Albion® di-magnesium malate)	150 mg	36%
Zinc (as TRAACS® zinc bisglycinate chelate)	3 mg	27%
Manganese (as TRAACS® manganese bisglycinate chelate)	0.5 mg	22%
Chromium (as TRAACS® chromium nicotinate glycinate chelate)	100 mcg	286%
Sodium	130 mg	6%
Potassium	280 mg	6%
Proprietary Blend	465 mg	**
PUREENERGY™ (caffeine pterostilbene cocrystal), whole coffee fruit (<i>Coffea arabica</i>) (whole fruit) (40% chlorogenic acid), taurine, L-arginine alpha-ketoglutarate, organic green tea aqueous extract (<i>Camellia sinensis</i>) (leaf) (25% polyphenols, 15% catechins, <10% caffeine), s-acetyl-L-glutathione, and acetyl-L-carnitine (as acetyl-L-carnitine HCl), yielding a total of 95 mg of caffeine.		

† Percent Daily Values are based on a 2,000 calorie diet.

** Daily Value not established.

Other Ingredients: Maltodextrin, citric acid, malic acid, potassium bicarbonate, natural grape powder, sodium bicarbonate, natural flavors (no MSG), stevia leaf extract, and silica.

DIRECTIONS: Dissolve the contents of one stick pack in 6-12 oz of water according to preferred sweetness. Consume the effervescent drink once daily, or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Caffeine should not be combined with synephrine or ephedrine. Use cautiously if you have a history of abnormal heart rhythm. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

 Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,662.

Albion and TRAACS are registered trademarks of Albion Laboratories, Inc. Malate covered by US patent 6,706,904.



PUREENERGY™ is a trademark of ChromaDex, Inc. Patents: See www.ChromaDexPatents.com

 MecobalActive™ is a trademark of Ferrer Health Tech. The active form of B₁₂.

provides 500 mg of vitamin C in the form of four mineral ascorbates, as well as natural vitamin E, selenium, green tea extract, and s-acetyl-L-glutathione (SAG). SAG is an orally stable glutathione that has been shown to cross the membrane of the mitochondria, which increases the organelle's activity and helps minimize reactive oxygen species.*

Herbs and Amino Acids

ATP Ignite combines Pureenergy in a proprietary blend with various herbs and amino acids, including green tea extract, coffee fruit extract, taurine, and L-arginine alpha-ketoglutarate. This proprietary blend is designed to complement the activities of Pureenergy. Furthermore, some of these individual ingredients taken in high doses have roles in mitochondrial biogenesis or are known to have a positive influence on exercise performance.*^[16-18]

B Vitamins

As essential parts of coenzymes, these water-soluble nutrients are integral to the complex biochemical processes that convert food to glucose and ATP—the energy used by cells. Vitamin B12 also works closely with folate to help make red blood cells and facilitate the work of iron in the body. Iron helps carry oxygen to all cells, including muscle cells, for use in the generation of energy.*

References

1. Single-dose comparative pharmacokinetic study of pterostilbene, caffeine and combination of pterostilbene caffeine co-crystal in SD rats by oral route. Study report. Study No: VLL/0912/NG/DO33; Version No.: 1.0. Genome Valley, Hyderabad, India: Vimta Labs Limited; November 2012:1-25. [on file]
2. A crossover, clinical evaluation to determine the relative bioavailability, pharmacokinetics and safety of PUREENERGY™ and pTeroPure® in healthy adult males. PK study summary. Miami, FL/Irvine, CA: Miami Research Associates/ChromaDex Inc.; 2013:1-34. [on file]
3. Pureenergy™: A novel next-generation caffeine alternative. Irvine, CA: ChromaDex Inc.; September 10, 2014:1-5. [on file]
4. Stadheim HK, Spencer M, Olsen R, et al. Caffeine and performance over consecutive days of simulated competition. *Med Sci Sports Exerc.* 2014 Sep;46(9):1787-96. [PMID: 25134002]
5. Pérez-López A, Salinero JJ, Abian-Vicen J, et al. Caffeinated energy drinks improve volleyball performance in elite female players. *Med Sci Sports Exerc.* 2014 Jul 18. [Epub ahead of print] [PMID: 2505139]
6. Burke LM. Caffeine and sports performance. *Appl Physiol Nutr Metab.* 2008 Dec;33(6):1319-34. [PMID: 19088794]
7. Costa MS, Botton PH, Mioranza S, et al. Caffeine improves adult mice performance in the object recognition task and increases BDNF and TrkB independent on phospho-CREB immunoccontent in the hippocampus. *Neurochem Int.* 2008 Sep;53(3-4):89-94. [PMID: 18620014]
8. Ronen A, Oron-Gilad T, Gershon P. The combination of short rest and energy drink consumption as fatigue countermeasures during a prolonged drive of professional truck drivers. *J Safety Res.* 2014 Jun;49:39-43. [PMID: 24913484]
9. Meeusen R, Roelands B, Spriet LL. Caffeine, exercise and the brain. *Nestle Nutr Inst Workshop Ser.* 2013;76:1-12. [PMID: 23899750]
10. Kapetanovic IM, Muzzio M, Huang Z, et al. Pharmacokinetics, oral bioavailability, and metabolic profile of resveratrol and its dimethylether analog, pterostilbene, in rats. *Cancer Chemother Pharmacol.* 2011 Sep;68(3):593-601. [PMID: 21116625]
11. Remsberg CM, Yáñez JA, Ohgami Y, et al. Pharmacometrics of pterostilbene: preclinical pharmacokinetics and metabolism, anticancer, antiinflammatory, antioxidant and analgesic activity. *Phytother Res.* 2008 Feb;22(2):169-79. [PMID: 17726731]
12. Nutakul W, Sobers HS, Qiu P, et al. Inhibitory effects of resveratrol and pterostilbene on human colon cancer cells: a side-by-side comparison. *J Agric Food Chem.* 2011 Oct 26;59(20):10964-70. [PMID: 21936500]
13. Ljubicic V, Burt M, Lunde JA, et al. Resveratrol induces expression of the slow, oxidative phenotype in mdx mouse muscle together with enhanced activity of the SIRT1-PGC-1α axis. *Am J Physiol Cell Physiol.* 2014 Jul 1;307(1):C66-82. [PMID: 24760981]
14. Jian B, Yang S, Chaudry IH, et al. Resveratrol restores sirtuin 1 (SIRT1) activity and pyruvate dehydrogenase kinase 1 (PDK1) expression after hemorrhagic injury in a rat model. *Mol Med.* 2014 Mar 13;20:10-6. [PMID: 24395567]
15. Alcain FJ, Villalba JM. Sirtuin activators. *Expert Opin Ther Pat.* 2009 Apr;19(4):403-14. Review. [PMID: 19441923]
16. Campbell B, Roberts M, Kerkick C, et al. Pharmacokinetics, safety, and effects on exercise performance of L-arginine alpha-ketoglutarate in trained adult men. *Nutrition.* 2006 Sep;22(9):872-81. [PMID: 16928472]
17. Flôres MF, Martins A, Schmidt HL, et al. Effects of green tea and physical exercise on memory impairments associated with aging. *Neurochem Int.* 2014 Sep 6. [PMID: 25195719]
18. Pandareesh MD, Anand T. Ergogenic effect of dietary L-carnitine and fat supplementation against exercise induced physical fatigue in Wistar rats. *J Physiol Biochem.* 2013 Dec;69(4):799-809. [PMID: 23661316]

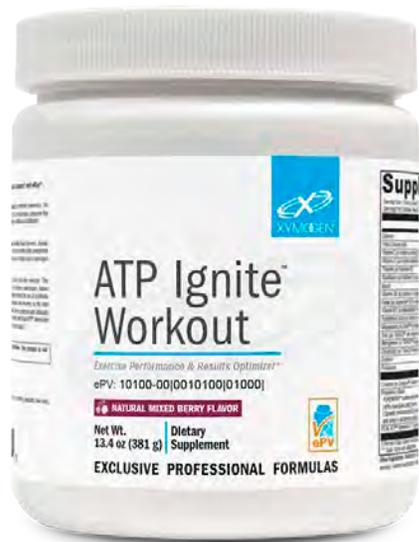
Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

ATP Ignite™ Workout

Exercise Performance & Results Optimizer*



Available in Natural Mixed Berry

Discussion

All-Natural, No Sugars

ATP Ignite Workout relies on natural ingredients, not ephedra or artificial stimulants, to help maximize exercise performance. Furthermore, it provides only five grams of carbohydrates and zero sugars. By using natural flavors and stevia in place of sugar and other carbohydrates, the typical “sugar high” that is associated with many energy drinks can be avoided. Equally important, ATP Ignite Workout contains no artificial colors.*

Peak ATP®

Oral supplementation of ATP (adenosine triphosphate) combined with resistance training has demonstrated ergogenic benefits.^[1] Peak ATP is a patented form of ATP disodium that has been shown in human studies to enhance muscular growth, power, and strength while improving recovery. Proposed mechanisms of action include increased muscular excitability, improved blood flow, and increased anabolic signaling.^[1-4] As a result of these effects, Peak ATP helps athletes push themselves to greater levels of performance.*

Peak ATP supplementation (400 mg/d) has been shown to increase post-exercise ATP levels and athletic performance following repeated sprint bouts. Peak ATP also significantly increased vasodilation and blood flow after acute arm exercise bouts.^[5,6] In a double-blind, placebo-controlled, crossover study, 400 mg of Peak ATP for 15 days “tended to reduce muscle fatigue while improving muscle low-peak torque through sets of exhaustive exercise.”^[7] A double-blind placebo-controlled study showed that resistance-trained participants taking Peak ATP for 12 weeks experienced several benefits over placebo, such as increased strength (147%), increased power (30%), increased lean body mass (100%), and increased muscle thickness (96%). Additionally, body fat decreased in the supplemented group.^[3] Data also suggests that Peak ATP helped prevent performance declines seen in overreaching.^[3] Adding to these findings, in a randomized, double-blind, placebo-controlled study (n=42), Purpura et al found that 400 mg of Peak ATP for two weeks prevented exercise-induced declines in ATP and its metabolites and enhanced peak power and muscle excitability.*^[7]

Creapure® Creatine Monohydrate

Creatine supplementation increases the amount of creatine in muscle tissue, heightens energy production, decreases muscle fatigue, and reduces lactic acid output. Significant improvements in body mass, fat-free body mass, oxygen uptake, sprint performance, weightlifting volumes, and overall exercise performance following creatine supplementation have been demonstrated.^[8-10] In ATP Ignite Workout, a compounding effect of several ingredients is expected. In fact, the combinatory effects of caffeine, creatine, and amino acids have produced improvements in time to exhaustion (TTE) and peak velocity (PV) in humans.*^[11]

Clinical Applications

- » Enhances Exercise Performance*
- » Helps Reduce Muscle Fatigue and Supports Muscle Power, Strength, and Growth with Peak ATP*
- » Supports Recovery*
- » Supports ATP Biosynthesis and Muscular Excitability*
- » Provides an Alternative to Ordinary Caffeine*
- » Supports Electrolyte Replacement*
- » Provides Antioxidant Support with S-Acetyl-L-Glutathione and Vitamin C*

*ATP Ignite™ Workout is designed to meet the demanding needs of the body during and after exercise. This great-tasting drink mix provides a low-carb, zero-sugar combination of bioactive B vitamins, electrolytes, Albion TRAACS® chelated trace minerals, key amino acids, herbs, and powerful antioxidants without the use of synthetic sweeteners or artificial ingredients. To fuel muscular excitability and take performance and recovery to the next level, ATP Ignite Workout features a unique blend of natural exercise enhancers that are patented and clinically tested. These include Purenergy™ caffeine/pterostilbene co-crystal, Creapure® creatine, and Peak ATP® adenosine triphosphate. Let ATP Ignite Workout help you maximize your exercise time and your energy output.**

Creapure is premium, 100% pure creatine monohydrate that has been used with confidence for over 20 years. The Creapure brand is recognized for careful selection of raw materials, patented high-performance technology, sophisticated process engineering under GMP conditions, and precise chemical analysis to ensure consistency and purity.

PUREENERGY™

Purenergy is an innovative patent-protected ingredient that combines caffeine with pTeroPure® pterostilbene—a highly bioavailable analog of resveratrol—to form a unique co-crystal structure. It appears that this unique structure affects the way the body utilizes caffeine. As such, it may offer significant advantages over caffeine alone. In a rat study (n=6), the half-life of caffeine from Purenergy was eight hours, while that of ordinary caffeine was just three hours.^[12] In a preliminary, four-week, single-blind, crossover human study (n=12) that compared 232 mg of Purenergy (providing 99.76 mg of caffeine) to 100 mg of ordinary caffeine, the absorption of caffeine from Purenergy was approximately 30% slower and Purenergy delivered 30% more caffeine to the bloodstream. Furthermore, at six hours, 51% more caffeine from Purenergy was detected in serum compared to ordinary caffeine.*^[13,14]

These data suggest that the effects of caffeine from Purenergy may last longer than the effects from ordinary caffeine and point to a potential for reducing total caffeine intake. Additionally, the extended half-life and slower absorption rate of caffeine from Purenergy may produce a more moderated and gradual finish, thereby preventing the “crash” associated with regular caffeinated energy products. While the results of these studies are promising, larger studies are needed to validate the findings and determine if these findings translate into a lengthened energy effect. Of interest, chlorogenic acids from coffee have been found to positively affect human fecal microbiota, including *Bifidobacterium* species, which could benefit host health.*^[15]

Herbs and Amino Acids

ATP Ignite Workout combines Purenergy in a proprietary blend with various herbs and amino acids, including green tea extract, coffee fruit extract, taurine, and L-arginine alpha-ketoglutarate. This proprietary blend is designed to complement the activities of Purenergy. Furthermore, some of these individual ingredients taken in high doses have roles in mitochondrial biogenesis and are known to have a positive influence on exercise performance.*^[16-18]

Electrolytes and Antioxidants

Electrolytes—including sodium, potassium, and magnesium—are important for energy production, nerve transmission, muscle contractions, pH balance, fluid balance, and more. Conditions that promote excessive sweating and increased metabolic activity

Continued on next page

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

ATP Ignite™ Workout Supplement Facts

Serving Size: 1 Scoop (about 12.7 g)

	Amount Per Serving	%Daily Value
Calories	25	
Total Carbohydrate	5 g	2%†
Vitamin C (as sodium ascorbate, potassium ascorbate, calcium ascorbate, and zinc ascorbate)	500 mg	556%
Vitamin E (as d-alpha tocopheryl succinate)	10 mg	67%
Thiamin (as thiamine HCl)	0.45 mg	38%
Riboflavin (as riboflavin 5'-phosphate sodium)	0.5 mg	38%
Niacin	10 mg	63%
Vitamin B6 (as pyridoxal 5'-phosphate)	2.6 mg	153%
Folate (as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt)	40 mcg DFE	10%
Vitamin B12 (as MecobalActive™ methylcobalamin)	2500 mcg	104,167%
Pantothenic Acid (as d-calcium pantothenate)	3 mg	60%
Magnesium (as Albion® di-magnesium malate)	150 mg	36%
Zinc (as TRAACS® zinc bisglycinate chelate)	3 mg	27%
Manganese (as TRAACS® manganese bisglycinate chelate)	0.5 mg	22%
Chromium (as TRAACS® chromium nicotinate glycinate chelate)	100 mcg	286%
Sodium	135 mg	6%
Potassium	310 mg	7%
Creatine (as Creapure® creatine monohydrate)	3 g	**
Proprietary Blend	465 mg	**
PUREENERGY™ (caffeine pterostilbene cocrystal), whole coffee fruit (<i>Coffea arabica</i>) (whole fruit) (40% chlorogenic acid), taurine, L-arginine alpha-ketoglutarate, organic green tea aqueous extract (<i>Camellia sinensis</i>) (leaf) (25% polyphenols, 15% catechins, <10% caffeine), s-acetyl-L-glutathione, and acetyl-L-carnitine (as acetyl-L-carnitine HCl), yielding a total of 95 mg of caffeine.		
PEAK ATP® Adenosine 5' Triphosphate Disodium	400 mg	**
† Percent Daily Values are based on a 2,000 calorie diet.		
** Daily Value not established.		

Other Ingredients: Maltodextrin, citric acid, malic acid, natural flavors (no MSG), potassium bicarbonate, natural grape powder, sodium bicarbonate, stevia leaf extract, and silica.

DIRECTIONS: Dissolve the contents of one scoop in 6-12 oz of water according to preferred sweetness. On non-workout days, consume the effervescent drink in the AM on an empty stomach. On workout days, consume the effervescent drink once daily 30 minutes prior to workout, or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication, especially blood thinners, should discuss potential interactions with their healthcare practitioner. Caffeine should not be combined with synephrine or ephedrine. Use cautiously if you have a history of abnormal heart rhythm. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, artificial colors, artificial sweeteners, or artificial preservatives.

 Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,662.

Albion and TRAACS are registered trademarks of Albion Laboratories, Inc. Malates covered by US patent 6,706,904 and patents pending.



PUREENERGY™ is a trademark of ChromaDex, Inc. Patents: See www.ChromaDexPatents.com

 MecobalActive™ is a trademark of Ferrer Health Tech. The active form of B₁₂.



PEAK ATP is a registered trademark of TSI, Inc. and is used under license.

Creapure® is a registered trademark of AlzChem AG, Germany, US Reg. No 2715915.

can require replacement of these important minerals and increase the need for antioxidants. ATP Ignite Workout provides 130 mg of sodium, 280 mg of potassium, and 150 mg of magnesium in each serving. To support protection from free radicals, ATP Ignite Workout provides 500 mg of vitamin C in the form of four mineral ascorbates, as well as natural vitamin E, selenium, green tea extract, and s-acetyl-L-glutathione (SAG). SAG is an orally stable glutathione that has been shown to cross the membrane of the mitochondria, which increases the organelle's activity and helps minimize reactive oxygen species.*

B Vitamins

The B vitamins provided in ATP Ignite Workout are in their activated forms to optimize bioavailability and utilization. As essential parts of coenzymes, these water-soluble nutrients are integral to the complex biochemical processes that convert food to glucose and ATP—the energy used by cells. Vitamin B12 also works closely with folate to help make red blood cells and facilitate the work of iron in the body. Iron helps carry oxygen to all cells, including muscle cells, for use in the generation of energy.*

References

- Rathmacher JA, Fuller JC Jr, Baier SM, et al. Adenosine-5'-triphosphate (ATP) supplementation improves low peak muscle torque and torque fatigue during repeated high intensity exercise sets. *J Int Soc Sports Nutr.* 2012 Oct 9;9(1):48. [PMID: 23046855]
- Jäger R, Roberts MD, Lowery RP, et al. Oral adenosine-5'-triphosphate (ATP) administration increases blood flow following exercise in animals and humans. *J Int Soc Sports Nutr.* 2014 Jun 13;11:28. [PMID: 25006331]
- Wilson JM, Joy JM, Lowery RP, et al. Effects of oral adenosine-5'-triphosphate supplementation on athletic performance, skeletal muscle hypertrophy and recovery in resistance-trained men. *Nutr Metab (Lond).* 2013 Sep 22;10(1):57. [PMID: 24330670]
- Kichenin K, Decollogne S, Angignard J, et al. Cardiovascular and pulmonary response to oral administration of ATP in rabbits. *J Appl Physiol* (1985). 2000 Jun;88(6):1962-8. [PMID: 10846006]
- Rauch J, Lowery RP, Silva J, et al. The oral bioavailability of ATP following an intense sprinting protocol. In: National Strength and Conditioning Association 2014 Annual Meeting, Las Vegas, NV. *J Strength Cond Res.* 2014;28(suppl 2):S53-S54. http://journals.lww.com/nsca-jscr/Fulltext/2014/12001/NSCA_2014_Annual_Meeting.1.aspx. Accessed September 29, 2015.
- Lowery R, Roberts M, Booth F, et al. Oral ATP administration improves blood flow responses to exercise in both animal and human training models. In: Proceedings of the Tenth International Society of Sports Nutrition (ISSN) Conference and Expo, Colorado Springs, CO. *J Int Soc Sports Nutr.* 2013;10(suppl 1):P16. <http://www.issn.com/content/10/S1/P16>. Accessed September 29, 2015.
- Purpura M, Rathmacher JA, Sharp MH, et al. Oral adenosine-5'-triphosphate (ATP) administration increases postexercise ATP levels, muscle excitability, and athletic performance following a repeated sprint bout. *J Am Coll Nutr.* 2017 Jan 12:1-7. [PMID: 28080323]
- Smith RN, Agharkar AS, Gonzales EB. A review of creatine supplementation in age-related diseases: more than a supplement for athletes. *F1000Res.* 2014 Sep 15;3:222. [PMID: 25664170]
- Aguar AF, Januário RS, Junior RP, et al. Long-term creatine supplementation improves muscular performance during resistance training in older women. *Eur J Appl Physiol.* 2013 Apr;113(4):987-96. [PMID: 23053133]
- Bemben MG, Lamont HS. Creatine supplementation and exercise performance: recent findings. *Sports Med.* 2005;35(2):107-25. [PMID: 15707376]
- Fukuda DH, Smith AE, Kendall KL, et al. The possible combinatory effects of acute consumption of caffeine, creatine, and amino acids on the improvement of anaerobic running performance in humans. *Nutr Res.* 2010 Sep;30(9):607-14. [PMID: 20934602]
- Single-dose comparative pharmacokinetic study of pterostilbene, caffeine and combination of pterostilbene caffeine co-crystal in SD rats by oral route. Study report. Study No: VLL/0912/NG/DO33; Version No.: 1.0. Genome Valley, Hyderabad, India: Vimta Labs Limited; November 2012:1-25. [on file]
- A crossover, clinical evaluation to determine the relative bioavailability, pharmacokinetics and safety of PUREENERGY™ and pTeroPure® in healthy adult males. PK study summary. Miami, FL/Irvine, CA: Miami Research Associates/ChromaDex Inc.; 2013:1-34. [on file]
- Pureenergy™: A novel next-generation caffeine alternative. Irvine, CA: ChromaDex Inc.; September 10, 2014:1-5. [on file]
- Mills CE, Tzounis X, Oruna-Concha MJ, et al. In vitro colonic metabolism of coffee and chlorogenic acid results in selective changes in human faecal microbiota growth. *Br J Nutr.* 2015 Apr 28;113(8):1220-27. [PMID: 25809126]
- Campbell B, Roberts M, Kerkisick C, et al. Pharmacokinetics, safety, and effects on exercise performance of L-arginine alpha-ketoglutarate in trained adult men. *Nutrition.* 2006 Sep;22(9):872-81. [PMID: 16928472]
- Flôres MF, Martins A, Schimidt HL, et al. Effects of green tea and physical exercise on memory impairments associated with aging. *Neurochem Int.* 2014 Sep 6. [PMID: 25195719]
- Pandareesh MD, Anand T. Ergogenic effect of dietary L-carnitine and fat supplementation against exercise induced physical fatigue in Wistar rats. *J Physiol Biochem.* 2013 Dec;69(4):799-809. [PMID: 23661316]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

(RV) DRS-299
Rev. 03/06/17

B Activ[®]

B Complex with Benfotiamine and Quatrefolic[®]



Available in 90 and 180 capsules

Discussion

The water-soluble B vitamins have to be absorbed in the small intestine and then go to the liver where they are biotransformed into their active coenzyme forms. B Activ contains vitamins B1 (thiamine), B2 (riboflavin), B6 (pyridoxine), and B12 (methylcobalamin) in their physiologically-active form making them easier to absorb and “ready-for-use.” For example, in patients receiving pyridoxine HCl, only 33 percent responded with an increase in plasma pyridoxal-5'-phosphate (P5P); however, the level increased in all of the patients receiving P5P.*^[1]

Folate is provided as 5-methyltetrahydrofolate (5-MTHF), which bypasses metabolic steps to folate bioactivity. Despite research showing that folic acid and 5-MTHF have equivalent bioavailability and that supplementation with large doses of folic acid can “force” its conversion to the more active form, 5-MTHF may be the preferred form to replenish folate. This may be especially applicable to those with digestive challenges or genetic variations in folate metabolism.^[2-4] In this formula, 5-MTHF is provided as Quatrefolic—the glucosamine salt of 5-MTHF. In vitro and in vivo studies have proven that Quatrefolic has greater stability, solubility, and bioavailability over calcium salt forms of 5-MTHF. Folate is stored in small amounts in red blood cells (RBC), and RBC folate has been shown to be higher after supplementation with 5-MTHF compared to folic acid and placebo. Likewise, patients given 5 mg of 5-MTHF experienced plasma levels of 5-MTHF 700% greater than patients given folic acid.*^[5]

Another unique ingredient in this formula is benfotiamine (S-benzoylthiamine O-monophosphate), a safe, fat-soluble analog of thiamine. One study showed that it not only raised blood and tissue levels of thiamine at least five times higher than the water-soluble salt, but it also remained bioavailable after oral administration up to 3.6 times longer than thiamine salt.^[6] Benfotiamine is the most potent of a class of thiamine-derived compounds present in small quantities in members of the *Allium* genus. The superiority of its biological activity compared to thiamine rests in its structure—a thiazole ring

Clinical Applications

- » Supports Carbohydrate Metabolism*
- » Supports Healthy Nervous System/Adrenal/Immune Function*
- » Supports Cardiovascular Health*
- » Supports Healthy Mental Function and Mood*

*B Activ[®] contains the entire spectrum of B vitamins to support adrenal and neurological functions. It features activated forms of vitamins B2, B6, and B12; benfotiamine, a fat soluble, more physiologically active form of thiamine; and folate as Quatrefolic[®], which is proven to have greater stability, solubility, and bioavailability over calcium salt forms of 5-MTHF.**

opens to allow easy diffusion through a membrane and then closes to become structurally active.*

Benfotiamine increases transketolase activity, thereby diverting from three natural, yet destructive metabolic pathways: 1) it decreases the glucose metabolites that lead to the buildup of certain types of detrimental advanced glycation end products (AGEs); 2) it normalizes protein kinase C activity; 3) it protects the retina by preventing the activation of NF-kappaB therein.^[7] Research suggests it may also protect the kidneys and endothelial cells.^[8] Benfotiamine is useful for replenishing thiamine, this may be especially true in individuals that use the vitamin at a higher rate or in those with lifestyle habits that deplete it.*^[9-11]

B Activ® Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Thiamin (as thiamine HCl)	20 mg	1667%
Riboflavin (as riboflavin 5'-phosphate sodium)	20 mg	1538%
Niacin (130 mg as niacinamide and 10 mg as niacin)	140 mg	875%
Vitamin B6 (as pyridoxal 5'-phosphate)	20 mg	1176%
Folate (as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt)	400 mcg DFE	100%
Vitamin B12 (as MecobalActive™ methylcobalamin)	400 mcg	16,667%
Biotin	400 mcg	1333%
Pantothenic Acid (as d-calcium pantothenate)	150 mg	3000%
Choline (as choline dihydrogen citrate)	30 mg	5%
Benfotiamine	20 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, and silica.**DIRECTIONS:** Take one capsule once or twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.**STORAGE:** Keep closed in a cool, dry place out of reach of children.

 Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,662.


 MecobalActive™ is a trademark of Ferrer Health Tech.
The active form of B₁₂
References

1. Labadarios D, Rossouw JE, McConnell JB, et al. Vitamin B6 deficiency in chronic liver disease – evidence for increased degradation of pyridoxal-5-phosphate. *Gut*. 1977;18:23-27. [PMID: 838399]
2. Yakut M, Ustün Y, Kabaçam G, et al. Serum vitamin B(12) and folate status in patients with inflammatory bowel diseases. *Eur J Intern Med*. 2010 Aug;21(4):320-23. [PMID: 20603044]
3. Halsted CH, Villanueva JA, Devlin AM. Folate deficiency, methionine metabolism, and alcoholic liver disease. *Alcohol*. 2002 Jul;27(3):169-72. [PMID: 12163145]
4. Kluijtmans LA, Van den Heuvel LP, Boers GH, et al. Molecular genetic analysis in mild hyperhomocysteinemia: a common mutation in the methylenetetrahydrofolate reductase gene is a genetic risk factor for cardiovascular disease. *Am J Hum Genet*. 1996 Jan;58(1):35-41. [PMID:8554066]
5. Willems FF, Boers GH, Blom HJ, et al. Pharmacokinetic study on the utilisation of 5-methyltetrahydrofolate and folic acid in patients with coronary artery disease. *Br J Pharmacol*. 2004 Mar;41(5):825-30. [PMID: 14769778]
6. Loew D. Pharmacokinetics of thiamine derivatives especially of benfotiamine. *Int J Clin Pharmacol Ther*. 1996 Feb;34(2): 47-50. [PMID: 8929745]
7. Thornalley PJ. The potential role of thiamine (vitamin B1) in diabetic complications. *Curr Diabetes Rev*. 2005 Aug;1(3):287-98. [PMID: 18220605]
8. Stirban A, Negrean M, Stratmann B, et al. Benfotiamine prevents macro- and microvascular endothelial dysfunction and oxidative stress following a meal rich in advanced glycation end products in individuals with type 2 diabetes. *Diabetes Care*. 2006 Sep;29(9):2064-71. [PMID: 16936154]
9. Woelk H, Lehl S, Bitsch R, et al. Benfotiamine in treatment of alcoholic polyneuropathy: an 8-week randomized controlled study (BAP I Study). *Alcohol*. 1998 Nov-Dec;33(6):631-38. [PMID: 9872352]
10. Ayazpoor U. Chronic alcohol abuse. Benfotiamine in alcohol damage is a must [in German]. *MMW Fortschr Med*. 2001 Apr 19;143(16):53. [PMID: 11367995]
11. Schupp N, Schmid U, Heidland A, et al. New approaches for the treatment of genomic damage in end-stage renal disease. *J Ren Nutr*. 2008 Jan;18(1):127-33. [PMID: 18089459]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration.
 This product is not intended to diagnose, treat, cure, or prevent any disease.

Benfotiamine

Lipid-Soluble, Highly Bioavailable Thiamin Derivative*



Available in 120 capsules

Clinical Applications

- » Supports Healthy Thiamin Status*
- » Supports Vascular Health*
- » Supports Nerve Health*

*Benfotiamine is a lipid-soluble derivative of thiamin that demonstrates improved absorption and duration of activity compared to water-soluble thiamin. Benfotiamine activates transketolase activity, thereby facilitating conversion of harmful glucose metabolites and positively affecting AGE formation. It supports peripheral nerve health and may support vascular health, including the microvasculature of the retina and kidney. Benfotiamine is also an excellent way to improve thiamin status.**

Discussion

The excellent pharmacokinetic profile of lipid-soluble benfotiamine (S-benzoylthiamine O-monophosphate) is the reason why many practitioners select it in preference to other forms of supplemental thiamin, especially for protocols requiring high levels of the B vitamin. Its effectiveness, however, has been demonstrated even in low doses (i.e. 150 mg/d).^[1] As compared to thiamin hydrochloride administration, maximum plasma levels are approximately five times higher and bioavailability is, at maximum, approximately 3.6 times as high. These plasma levels are also better than lipophilic thiamin derivatives.^[2]

Pathways of Glucose-Metabolite-Induced Damage High intracellular sugars can lead to an accumulation of intermediate metabolic products. These metabolic products activate certain pathways.^[3,4] These pathways are: (1) polyol pathway flux; (2) increased formation of AGEs (advanced glycation end-products); (3) increased expression of the receptor for AGEs (RAGEs) and its activating ligands; (4) activation of protein kinase C (PKC) isoforms; and (5) overactivity of the hexosamine pathway.^[4] Together, these mechanisms can impact vascular tissue and target particularly susceptible capillary endothelial cells of the retina, mesangial cells in the renal glomerulus, neuronal cells, and Schwann cells.^{*[3-7]}

Benfotiamine Supports Diversion to Different Pathway

Benfotiamine has been shown to enhance the activity of transketolase, an enzyme that catalyzes the conversion of harmful glucose-intermediate metabolites in the pentose phosphate pathway.^[4-7] In vitro research showed treatment with benfotiamine had an impressive effect on transketolase activity (454% increase from control).^[5] Researchers further indicated that increasing transketolase activity supports the diversion of intermediate metabolites away from three of the major pathways (including AGE formation) discussed above.^[5] Benfotiamine was shown to have a positive influence on AGE formation and PKC activity. It is thought to prevent NF-kappaB activation in the rat retina as well as inhibit change in the number of retinal acellular capillary segments.^{*[5]}

This research has been supported by a human pilot study wherein subjects given benfotiamine (600 mg/d) plus alpha-lipoic acid (1200 mg/d) demonstrated healthy changes in AGE formation, monocyte hexosamine-modified proteins, and prostacyclin synthase activity.^{*[8]}

Nerve Tissue Health Microvasculature feeding peripheral nerves can be affected by the pathways discussed herein. Furthermore, lower AGE formation is associated with healthier nerve tissue. The role of benfotiamine in diverting glucose metabolites to a less harmful metabolic pathway may well be the underlying reason it has been used successfully in Germany for over a decade to support nerve health. Results suggest that benfotiamine is most effective in large doses (320-600 mg/d), although effectiveness is still achieved in smaller daily dosages (150 mg/d).^{*[1,9,10]}

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Benfotiamine Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Benfotiamine	300 mg	**
**Daily Value not established.		

Other Ingredients: Microcrystalline cellulose, HPMC (capsule), ascorbyl palmitate, silica, and medium-chain triglyceride oil.

DIRECTIONS: Take two capsules in the morning and two capsules in the evening, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.

**References**

1. Winkler G, Pál B, Nagybégyani E, et al. Effectiveness of different benfotiamine dosage regimens in the treatment of painful diabetic neuropathy. *Arzneimittelforschung*. 1999 Mar;49(3):220-24. [PMID: 10219465]
2. Loew D. Pharmacokinetics of thiamine derivatives especially of benfotiamine. *Int J Clin Pharmacol Ther*. 1996 Feb; 34(2):47-50. [PMID: 8929745]
3. Brownlee M. The pathobiology of diabetic complications: a unifying mechanism. *Diabetes*. 2005 Jun;54(6):1615-25. [PMID: 15919781]
4. Giacco F, Brownlee M. Oxidative stress and diabetic complications. *Circ Res*. 2010 Oct 29;107(9):1058-70. [PMID: 21030723]
5. Hammes HP, Du X, Edelstein D, et al. Benfotiamine blocks three major pathways of hyperglycemic damage and prevents experimental diabetic retinopathy. *Nat Med*. 2003 Mar;9(3):294-99. [PMID: 12592403]
6. Balakumar P, Rohilla A, Krishan P, et al. The multifaceted therapeutic potential of benfotiamine. *Pharmacol Res*. 2010 Jun;61(6):482-88. [PMID: 20188835]
7. Thornalley PJ. The potential role of thiamine (vitamin B1) in diabetic complications. *Curr Diabetes Rev*. 2005 Aug;1(3):287-98. [PMID: 18220605]
8. Du X, Edelstein D, Brownlee M. Oral benfotiamine plus alpha-lipoic acid normalises complication-causing pathways in type 1 diabetes. *Diabetologia*. 2008 Oct;51(10):1930-32. [PMID: 18663426]
9. Haupt E, Ledermann H, Köpcke W. Benfotiamine in the treatment of diabetic polyneuropathy—a three-week randomized, controlled pilot study (BEDIP study). *Int J Clin Pharmacol Ther*. 2005 Feb;43(2):71-77. [PMID: 15726875]
10. Stracke H, Gaus W, Achenbach U, et al. Benfotiamine in diabetic polyneuropathy (BENDIP): results of a randomised, double blind, placebo-controlled clinical study. *Exp Clin Endocrinol Diabetes*. 2008 Nov;116(10):600-05. [PMID: 18473286]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Berbemycin™

Microbial Balance/Immune Support*



Available in 120 vegetarian capsules

Discussion

Many plants have been used throughout history for their ability to influence microbial activity and support healthy immune function. Potency is an important aspect in achieving the benefits imparted by an herbal supplement. The herbs in Berbemycin are concentrated to a 4:1 end ratio. This means that the equivalent raw herb conversion is 4 kg raw herb to 1 kg of extracted material. All actives are provided in easy-dissolving vegetarian capsules.*

***Berberis aquifolium* (Oregon grape)** Berberine is a plant alkaloid derived from a variety of herbs, including Oregon grape root. This phytochemical constituent has a long history of use in Chinese and Ayurvedic medicine owing to its effectiveness and safety. Berberine extracts have demonstrated significant ability to influence the activity of a variety of organisms that affect human health.^[1-3] Mechanisms of action may include effects on organism adhesion and intracellular invasion, metabolic activity, maturation, and enterotoxin formation.^[1,4] Berberine can also address the intestinal secretion of water and electrolytes induced by certain organism toxins, thereby supporting healthy stool formation.^[1] Furthermore, it may reduce smooth muscle contraction and intestinal motility, and delay intestinal transit time. Both in vitro and animal research suggest that berberine can affect COX-2 protein.*^[1]

***Myrica cerifera* (bayberry)** The root bark and berry of bayberry have been traditionally used as an astringent and circulatory stimulant. Like the berry, the root bark contains tannin constituents that are responsible for its astringent action.^[5,6] Astringent herbs are traditionally used to maintain the already normal release or secretion of perspiration, stool, essence (the body's reproductive and regenerative substance), and urine. As a circulatory stimulant, bayberry helps to increase body energy levels and supports toxin elimination. Myricitin, a flavonoid isolated from bayberry, exhibits antioxidant activity, particularly in the colon.*^[7]

***Citrus x paradisi* (grapefruit)** The seed extract of grapefruit, commonly known as GSE, is widely used as an oral supplement to

Clinical Applications

- » Supports Healthy Microbial Activity in the GI Tract*
- » Supports Healthy Immune Function*
- » Promotes GI Mucous Membrane Health*
- » Stimulates Circulation*

Berbemycin™ features a concentrated 4:1 extract of Oregon grape root, which supplies berberine—a plant alkaloid that influences the activities of microorganisms in the gastrointestinal tract, supports immune function, and may influence cytokine balance. The 4:1 extracts of bayberry bark and grapefruit seed complement the actions of berberine to support healthy microbial activity, stimulate circulation, and promote mucous membrane health. Zinc is included in this formula for its immune-supportive effects.*

maintain healthy gut ecology. GSE is employed by the food processing and agricultural industries for a diversity of applications. It is important to note that GSE contains a variety of phenolic substances with antioxidant activity including vitamin C, hesperidin, limonoids, tocopherols, serols, citric acid, and other trace minerals.*^[8,9]

Zinc The supportive effects of zinc on immunity and microbial balance are well documented.^[10,11] Zinc ions are thought to work directly in the GI tract, affecting microbial activity therein. Immune cells, due to their high rate of proliferation and differentiation, need a constant and sufficient supply of zinc. Although further study is needed, zinc supplementation also shows promise in its ability to support healthy stool formation. In this formula, zinc is provided as Albion® TRAACS® zinc glycinate chelate for optimal absorption and utilization.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Berbemycin™ Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Zinc (as TRAACS® zinc bisglycinate chelate)	5 mg	45%
Oregon Grape 4:1 Extract (<i>Berberis aquifolium Pursh</i>) (roots)	200 mg	**
Bayberry 4:1 Extract (<i>Myrica cerifera</i>)(bark)	200 mg	**
Grapefruit 4:1 Extract (<i>Citrus × paradisi</i>)(seed)	50 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, silica, and medium-chain triglyceride oil.**DIRECTIONS:** Take one capsule daily, or as directed by your healthcare practitioner. Do not use if tamper seal is damaged.**DOES NOT CONTAIN:** Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.**CAUTIONS:** Do not use if you are pregnant or lactating.**STORAGE:** Keep closed in a cool, dry place out of reach of children.

TRAACS® is a registered trademark of Albion Laboratories, Inc.

**References**

1. Vuddanda PR, Chakraborty S, Singh S. Berberine: a potential phytochemical with multispectrum therapeutic activities. *Expert Opin Investig Drugs*. 2010 Oct;19(10):1297-307. [PMID: 20836620]
2. Yu HH, Kim KJ, Cha JD, et al. Antimicrobial activity of berberine alone and in combination with ampicillin or oxacillin against methicillin-resistant *Staphylococcus aureus*. *J Med Food*. 2005 Winter;8(4):454-61. [PMID: 16379555]
3. Rohrer U, Kunz EM, Lenkeit K, et al. Antimicrobial activity of *Mahonia aquifolium* and two of its alkaloids against oral bacteria. *Schweiz Monatsschr Zahnmed*. 2007;117(11):1126-31. [PMID: 18072463]
4. Saha P, Bhattacharjee S, Sarkar A, et al. Berberine chloride mediates its anti-leishmanial activity via differential regulation of the mitogen activated protein kinase pathway in macrophages. *PLoS One*. 2011 Apr 5;6(4):e18467. [PMID: 21483684]
5. *Myrica cerifera*. Withlacoochee Permaculture Guild. <http://wcpemaculture.org/plants/myrica-cerifera>. Accessed August 2, 2011.
6. Grieve M. Bayberry. A Modern Herbal. Botanical.com. <http://botanical.com/botanical/mgmh/b/bayber20.html>. Accessed August 2, 2011.
7. Asano N, Kuno T, Hirose Y, et al. Preventive effects of a flavonoid myricitrin on the formation of azoxymethane-induced premalignant lesions in colons of rats. *Asian Pac J Cancer Prev*. 2007 Jan-Mar;8(1):73-76. [PMID: 17477776]
8. Jayaprakasha GK, Girenavar B, Patil BS. Radical scavenging activities of Rio Red grapefruits and Sour orange fruit extracts in different in vitro model systems. *Bioresour Technol*. 2008 Jul;99(10):4484-94. [PMID: 17935981]
9. Manthey JA. Biological properties of flavonoids pertaining to inflammation. *Microcirculation*. 2000;7(6 Pt 2):S29-34. [PMID: 11151968]
10. Puertollano MA, Puertollano E, de Cienfuegos GÁ, et al. Dietary antioxidants: immunity and host defense. *Curr Top Med Chem*. 2011;11(14):1752-66. [PMID: 21506934]
11. Knoell DL, Liu MJ. Impact of zinc metabolism on innate immune function in the setting of sepsis. *Int J Vitam Nutr Res*. 2010 Oct;80(4-5):271-77. [PMID: 21462110]

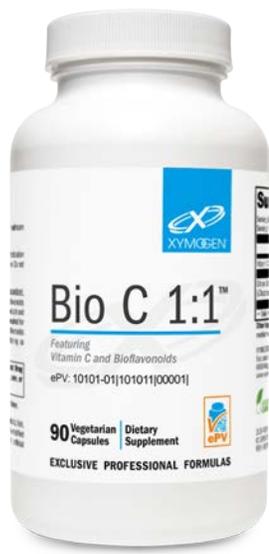
Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

<p>*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.</p>
--

Bio C 1:1™

Featuring Vitamin C and Bioflavonoids



Available in 90 capsules

Discussion

Bio C 1:1 is formulated to provide antioxidant protection, enhance immune function, and support synthesis and function of collagen, carnitine, and neurotransmitters. Each capsule of Bio C 1:1 provides 500 mg of vitamin C and 500 mg of citrus bioflavonoid complex in a one-to-one ratio.*

Vitamin C (ascorbic acid) is a water-soluble antioxidant vitamin that is essential to humans. While most mammals are able to synthesize vitamin C, humans must obtain it exogenously. Stress, smoking, pollution, radiation and heavy metal exposure, immune challenge, and temperature change all increase the human requirement for vitamin C.^[1] Well-known functions of this ubiquitous vitamin include antioxidant protection from free radicals and oxidative processes; synthesis of collagen, carnitine, and neurotransmitters; adrenal support; and immune stimulation and support.^[2-4] Vitamin C serves as a cofactor for several metabolic enzymes, including hydroxylase and oxygenase (hydroxylation reactions).^{*[5]}

Vitamin C has long been recognized for its contribution to immune support.^[3] Immune cells absorb and concentrate vitamin C. Immune cell activity, particularly T-cell function and phagocytosis, is found to be enhanced by this essential vitamin.^[6-7] In early 1972, a randomized, double-blind, placebo-controlled study of 1000 subjects taking 1000 mg of vitamin C per day provided support for the use of vitamin C supplementation for common immune challenges. The study results revealed that the supplementation group missed significantly fewer days from work/activities and had fewer days per episode of immune challenge; in addition, significantly more subjects taking vitamin C remained symptom free throughout the study.^[8] Optimal intake of vitamin C for humans continues to be debated, though normal vitamin C synthesis in mammals such as the rat is calculated to be 26-58 mg/kg/day. Dr. Linus Pauling, in his 1970 article on evolution and vitamin C requirements, recommended a minimum intake of 2300 mg per 2500 kilocalorie intake per day for humans.^{*[9]}

Vitamin C has far-reaching effects on a number of tissues in the

Clinical Applications

- » Antioxidant support*
- » Healthy Connective Tissue and Blood Vessel Synthesis*
- » Support of Normal Immune System Function*
- » Synthesis of Carnitine, Neurotransmitters, and Collagen*

*Bio C 1:1™ combines high-potency vitamin C with a standardized, full-spectrum, citrus bioflavonoid complex. Both vitamin C and bioflavonoids have been extensively researched for their roles in supporting antioxidant and immune function. In addition, research indicates that vitamin C is required for the synthesis of collagen, neurotransmitters, and carnitine. Bioflavonoids appear to support healthy metabolism and cognition by functioning as cell-signaling agents.**

body because it is required for the synthesis of collagen.^[4] Collagen is a fundamental component of bones, tendons, ligaments, blood vessels, skin, gums, and joints. Ultimately, the health of these tissues depends on vitamin C. Energy generation from fatty acids is vitamin C-dependent as well since synthesis of carnitine (the molecule that shuttles long-chain fatty acids into the mitochondria) requires this versatile vitamin. Vitamin C is maintained in relatively high concentrations in the brain; it is essential to maintaining healthy mood and brain function because it facilitates conversion of dopamine to norepinephrine and enhances interneuronal communication.^{*[10]}

Bioflavonoids (also known as flavonoids) are phytochemicals that are often found together with vitamin C in nature and are generally considered to be among the most important and interesting classes of biologically active compounds in contemporary research. More than 4000 bioflavonoids have been identified. Intake of flavonoids is associated with healthy cardiovascular status, the body's normal response to inflammation, and positive microbial balance.^{*[11,12]}

Citrus bioflavonoids are commonly used in Europe for blood vessel and lymph system support. US practitioners utilize bioflavonoids in protocols to support tissue and joint comfort and the body's normal response to inflammation,^[13-15] respiratory^[16,17] and eye health,^[18] and maintenance of cardiovascular health.^[19-21] Citrus bioflavonoids are able to cross the blood-brain barrier and have been recognized for their neuroprotective effects.^[22] As cell-signaling agents, bioflavonoids are believed to support healthy cell growth and normal cell-life regulation, stimulate detoxification enzymes, decrease vascular cell adhesion molecules, increase vasodilation, and support healthy platelet function.^{*[23]}

The combination of vitamin C and citrus bioflavonoids in Bio C 1:1 ensures that a wide range of metabolic functions will be supported.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Bio C 1:1™ Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Vitamin C (ascorbic acid)	500 mg	556%
Citrus Bioflavonoid Complex (<i>Citrus aurantium</i>)(skin)(50% citrus bioflavonoids)	500 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, medium-chain triglyceride oil, and silica.

DIRECTIONS: Take one capsule daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms, artificial colors, artificial sweeteners, or artificial preservatives.



References

1. Whitney EN, Rolfes SR. *Understanding Nutrition*. 8th ed. Belmont, CA: Wadsworth; 1998:321.
2. NIH Office of Dietary Supplements. Dietary Supplement Fact Sheet: Vitamin C. <http://ods.od.nih.gov/factsheets/VitaminC-HealthProfessional/>. Accessed December 10, 2012.
3. Schlueter AK, Johnston CS. Vitamin C: overview and update. *Journal of Evidence-Based Complementary & Alternative Medicine (JEBCAM)*. 2011; 16(1):49-57. <http://chp.sagepub.com/content/16/1/49.full.pdf+html>. Accessed December 10, 2012.
4. Linus Pauling Institute. Vitamin C. <http://lpi.oregonstate.edu/infocenter/vitamins/vitaminC/>. Updated November 2009. Accessed December 10, 2012.
5. Naidu KA. Vitamin C in human health and disease is still a mystery? An overview. *Nutr J*. 2003 Aug 21;2:7. [PMID: 14498993]
6. Chatterjee M, Dikshit M. Vitamin C mediated resistance to pathogenic invasions: possible implications during infections for better health. *Proceedings of the National Academy of Sciences India*. Section B, Biological Sciences. 2009; 79(1):15-25.
7. Ströhle A, Wolters M, Hahn A. Micronutrients at the interface between inflammation and infection—ascorbic acid and calciferol: part 1, general overview with a focus on ascorbic acid. *Inflamm Allergy Drug Targets*. 2011 Feb;10(1):54-63. [PMID: 21184650]
8. Anderson TW, Reid DB, Beaton GH. Vitamin C and the common cold: a double-blind trial. *Can Med Assoc J*. 1972 Sep 23;107(6):503-8. [PMID: 5057006]
9. Pauling L. Evolution and the need for ascorbic acid. *Proc Natl Acad Sci USA*. 1970 Dec;67(4):1643-8. [PMID: 5275366]
10. Rebec GV, Pierce RC. A vitamin as neuromodulator: ascorbate release into the extracellular fluid of the brain regulates dopaminergic and glutamatergic transmission. *Prog Neurobiol*. 1994 Aug;43(6):537-65. Review. [PMID: 7816935]
11. Tripoli E, La Guardia M, Giammanco S, et al. Citrus flavonoids: Molecular structure, biological activity and nutritional properties: A review. *Food Chemistry*. 2007; 104(2):466-79.
12. Middleton E Jr, Kandaswami C, Theoharides TC. The effects of plant flavonoids on mammalian cells: implications for inflammation, heart disease, and cancer. *Pharmacol Rev*. 2000 Dec;52(4):673-751. Review. [PMID: 11121513]
13. Guardia T, Rotelli AE, Juárez AO, et al. Anti-inflammatory properties of plant flavonoids. Effects of rutin, quercetin and hesperidin on adjuvant arthritis in rats. *Farmacol*. 2001 Sep;56(9):683-7. [PMID: 11680812]
14. Rotelli AE, Guardia T, Juárez AO, et al. Comparative study of flavonoids in experimental models of inflammation. *Pharmacol Res*. 2003 Dec;48(6):601-6. [PMID: 14527825]
15. Lin N, Sato T, Takayama Y, et al. Novel anti-inflammatory actions of nobiletin, a citrus polymethoxy flavonoid, on human synovial fibroblasts and mouse macrophages. *Biochem Pharmacol*. 2003 Jun 15;65(12):2065-71. [PMID: 12787887]
16. Pijnenburg MW, Hoffhuis W, Hop WC, et al. Exhaled nitric oxide predicts asthma relapse in children with clinical asthma remission. *Thorax*. 2005 Mar; 60(3):215-8. [PMID: 15741438]
17. Lee NK, Choi SH, Park SH, et al. Antiallergic activity of hesperidin is activated by intestinal microflora. *Pharmacology*. 2004 Aug;71(4):174-80. [PMID: 15240993]
18. Majumdar S, Srirangam R. Potential of the bioflavonoids in the prevention/treatment of ocular disorders. *J Pharm Pharmacol*. 2010 Aug;62(8):951-65. Review. [PMID: 20663029]
19. Wright B, Spencer JP, Lovegrove JA, et al. Insights into dietary flavonoids as molecular templates for the design of anti-platelet drugs. *Cardiovasc Res*. 2012 Nov 1. [Epub ahead of print] [PMID: 23024269]
20. Mulvihill EE, Huff MW. Citrus flavonoids and the prevention of atherosclerosis. *Cardiovasc Hematol Disord Drug Targets*. 2012 Oct 1. [Epub ahead of print] [PMID: 23030447]
21. Soory M. Nutritional antioxidants and their applications in cardiometabolic diseases. *Infect Disord Drug Targets*. 2012 Nov 16. [Epub ahead of print] [PMID: 23167714]
22. Hwang SL, Shih PH, Yen GC. Neuroprotective effects of citrus flavonoids. *J Agric Food Chem*. 2012 Feb 1;60(4):877-85. doi: 10.1021/jf204452y. Epub 2012 Jan 23. Review. [PMID: 22224368]
23. Linus Pauling Institute. Micronutrient Information Center. Flavonoids. <http://lpi.oregonstate.edu/infocenter/phytochemicals/flavonoids/>. Updated June 2008. Accessed December 10, 2012.

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

BrainSustain™ & BrainSustain™ for Kids

Comprehensive Brain Support Formulas*



Available in Creamy Chocolate & Vanilla Delight
BrainSustain™ for Kids is available in Vanilla Delight

Discussion

EVNol™, currently found in Creamy Chocolate and Vanilla Delight and not in BrainSustain for Kids, is a patented, full-spectrum, pure d-mixed-tocotrienols complex. This advanced tocotrienol ingredient is derived from sustainable red palm fruit oil—a scientifically validated source. It is primarily composed of the four tocotrienol isomers (alpha, beta, gamma, and delta) in natural ratios. EVNol also provides d-alpha tocopherol and phytonutrients that are naturally extracted with the tocotrienols. The result is a natural and wholesome tocotrienol complex. The extraordinary protective benefits of tocotrienols on brain cells (e.g., white matter) and neurons have been demonstrated in in vitro, animal, and human studies.^[1-3] A large, placebo-controlled human trial investigated the effects of tocotrienols on white matter lesions (WML). Individuals taking the placebo showed an increase in WML volume, while those taking 200 mg of EVNol twice a day (equivalent to approximately 68 mg pure d-mixed tocotrienols) remained essentially unchanged.^[2] Scientists later determined that in order to achieve brain protection, the required plasma level of tocotrienols is just 588.6 nanomolar, which equates to approximately 31.25 mg of pure d-mixed tocotrienols/day.^{*[4,5]}

Furthermore, several studies have shown that good vitamin E status, especially tocotrienols, is associated with cognitive health and reduced risk of cognitive impairment in older adults.^[5,6] In a cross-sectional multicenter study on elderly subjects, researchers at the Aging Research Center at Karolinska Institutet in Stockholm found that cognitively normal individuals had better mean plasma levels of vitamin E, especially tocotrienols, and lower oxidative damage markers.^[5] Other research has demonstrated that combined tocopherol and tocotrienol administration supports healthy liver conditions and liver triglyceride metabolism.^{*[7-10]}

EVNol has a self-affirmed GRAS (generally recognized as safe) designation. It is 100% vegetarian-based and is derived from non-GMO sources.

N-Acetyl-Cysteine (NAC) is a precursor to glutathione—a tripeptide active in detoxification and antioxidant systems. Research suggests

Clinical Applications

- » Support Brain Health and Healthy Recall Ability*
- » Provide Nutrients That Support Antioxidant Mechanisms*
- » Supply Protein and Amino Acids for Neurotransmitter Production*

*BrainSustain™ & BrainSustain™ for Kids represent more than 30 years of neuroscience research. Designed to address brain health, structure, and function, these formulas contain a variety of nutrients and cofactors that support mitochondrial energy production, antioxidant systems, neurotransmitter production, and cell membrane integrity.**

that NAC hinders the formation of free radicals that can contribute to oxidative stress in the brain.^{*[11]}

Phosphatidylserine (PS) is a phospholipid that is highly concentrated in the brain and plays a key role in neuronal energy production and communication. The body must synthesize the PS it needs for brain health because very little is found in food. Supplementation can help maintain normal brain levels of PS and thereby support brain functions that are dependent on this vital phospholipid.^[12-14] For some individuals, changes in brain function may be related to “age-related decline in nutrition,”^[15] and early nutrition intervention may be warranted. These BrainSustain formulas contain safe-source PS from non-GMO soy.*

Acetyl-L-Carnitine (ALCAR) supports nerve health.^[16] It is able to cross the blood-brain barrier where it stabilizes cell membranes, provides antioxidant support, and helps maintain brain cell health.^[17-19] In addition, ALCAR supports neuronal energy production, facilitates transport of fuel and waste products into and out of mitochondria, and supports production of acetylcholine, a neurotransmitter essential to the processes of learning and concentration.^{*[18,20]}

Alpha-Lipoic Acid has fat- and water-soluble properties and therefore imparts intracellular and extracellular protection against oxidative stress. With its low molecular weight, alpha-lipoic acid is easily absorbed in the gastrointestinal tract. It then enters circulation, crosses the blood-brain barrier, and reaches the brain where it can support antioxidant activity and regenerate glutathione, vitamin E, and vitamin C.^{*[21,22]}

Coenzyme Q10 (CoQ10) plays a pivotal role in energy generation because it transports electrons in the mitochondrial electron transport chain. CoQ10 also donates electrons, helping to protect the brain from oxidative stress and further supporting neuronal cell health.^{*[23]}

Continued on page 3

BrainSustain™ Vanilla Delight Supplement Facts

Serving Size: 1 Packet (about 48 g)
 Servings Per Container: 15

	Amount Per Serving	%Daily Value
Calories	180	
Total Fat	5 g	6%*
Saturated Fat	1.5 g	8%*
Total Carbohydrate	17 g	6%*
Dietary Fiber	6 g	21%
Total Sugars	6 g	**
Includes 5g Added Sugars		10%
Protein	19 g	
Vitamin C (as calcium ascorbate)	400 mg	444%
Vitamin D3 (cholecalciferol)	25 mcg (1000 IU)	125%
Vitamin E (as d-alpha tocopheryl succinate)	134 mg	893%
Riboflavin (as riboflavin 5' phosphate sodium)	25 mg	1923%
Niacin (as niacinamide)	200 mg	1250%
Vitamin B6 (as pyridoxal 5'-phosphate)	50 mg	2941%
Folate (400 mcg as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt and 400 mcg as calcium folinate)	800 mcg DFE	200%
Vitamin B12 (as methylcobalamin)	1000 mcg	41,667%
Calcium (as calcium ascorbate and ingredients with naturally occurring calcium)	60 mg	5%
Iron (naturally occurring)	4 mg	22%
Phosphorus (as dipotassium phosphate)	50 mg	4%
Magnesium (as Albion® di-magnesium malate)	50 mg	12%
Sodium (naturally occurring)	410 mg	18%
Potassium (from dipotassium phosphate and ingredients with naturally occurring potassium)	155 mg	3%
Acetyl-L-Carnitine (as acetyl-L-carnitine HCl)	800 mg	**
N-Acetyl-L-Cysteine	300 mg	**
Sharp•PS® GREEN Phosphatidylserine	200 mg	**
Alpha-Lipoic Acid	200 mg	**
Kaneka Q10® Coenzyme Q10 (as ubiquinone)	200 mg	**
life'sDHA® DHA (docosahexaenoic acid from algal oil)	50 mg	**
EVNoI™ Mixed Tocotrienols	50 mg	**
Benfotiamine	50 mg	**
trubroc® Glucoraphanin (from broccoli extract)(<i>Brassica oleracea italica</i>)(seed)	30 mg	**
Mixed Tocopherols	18 mg	**

* Percent Daily Values are based on a 2,000 calorie diet.
 ** Daily Value not established.

Other Ingredients: VegaPro™ (XYMOGEN®'s proprietary blend of pea protein isolate, taurine, glycine, rice protein concentrate, and L-glutamine), dried cane syrup, inulin (from chicory), sunflower oil, natural flavors (no MSG), medium-chain triglyceride oil, cellulose gum, xanthan gum, Aminogen® fungal proteases, guar gum, stevia leaf extract, and silica.

DIRECTIONS: Blend, shake, or briskly stir the contents of one packet (48 g) into 8-12 oz chilled water and consume once daily, or as directed by your healthcare practitioner. Adjust amount of water to desired sweetness and thickness.

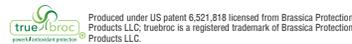
Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, dairy products, shellfish, peanuts, tree nuts, egg, artificial colors, or artificial sweeteners.



life'sDHA® is a trademark of DSM.



Produced under US patent 6,521,818 licensed from Brassica Protection Products LLC. true/broc is a registered trademark of Brassica Protection Products LLC.



AMINOGEN® is a registered trademark of Innophos Nutrition, Inc. AMINOGEN® is protected under US patent 5,387,422.



EVNoI™ (formerly known as Tocotrienol) is a trademark of EcoVite. Tocotrienols are extracted and concentrated from sustainably sourced Malaysian red palm oil. Protected by US patent 5,157,132.



Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,662.



Sharp•PS® GREEN is a registered trademark of Enzymotec Ltd.

Albion is a registered trademark of Albion Laboratories, Inc

Kaneka Q10® is a registered trademark of Kaneka Corp.

Typical Amino Acid Profile Per Serving:

Alanine	930 mg	Methionine	240 mg
Arginine	1,870 mg	Phenylalanine	1,180 mg
Aspartic Acid	2,470 mg	Proline	970 mg
Cysteine	220 mg	Serine	1,140 mg
Glutamic Acid	3,620 mg	Threonine	840 mg
Glycine	1,380 mg	Taurine	500 mg
Histidine	540 mg	Tryptophan	220 mg
Isoleucine	970 mg	Tyrosine	820 mg
Leucine	1,810 mg	Valine	1,080 mg
Lysine	1,540 mg		

BrainSustain™ for Kids Vanilla Delight Supplement Facts

Serving Size: 1 Scoop (About 17 g)
 Servings Per Container: About 15

	Amount Per Serving	%Daily Value
Calories	80	
Total Fat	3 g	4%†
Saturated Fat	1 g	5%†
Total Carbohydrate	7 g	3%†
Dietary Fiber	2 g	7%
Total Sugars	3 g	**
Includes 3g Added Sugars		6%
Protein	6 g	
Iron (naturally occurring)	1 mg	6%
Sodium (naturally occurring)	130 mg	6%
N-Acetyl-L-Cysteine	100 mg	**
life'sDHA® DHA (docosahexaenoic acid from algal oil)	50 mg	**
Kaneka Q10® Coenzyme Q10 (as ubiquinone)	50 mg	**
trubroc® Glucoraphanin (from broccoli extract)(<i>Brassica oleracea italica</i>)(seed)	30 mg	**
Sharp•PS® GREEN Phosphatidylserine	25 mg	**
Alpha-Lipoic Acid	20 mg	**

† Percent Daily Values are based on a 2,000 calorie diet.
 ** Daily Value not established.

Other Ingredients: VegaPro™ (XYMOGEN®'s proprietary blend of pea protein isolate, rice protein concentrate, L-glutamine, and glycine), sunflower oil, dried cane syrup, natural flavors (no MSG), inulin (from chicory), medium-chain triglyceride oil, Aminogen® fungal proteases, cellulose gum, xanthan gum, guar gum, stevia leaf extract, and silica.

DIRECTIONS: For children four years of age or older, blend, shake, or briskly stir 1 level scoop (17 grams) of BrainSustain™ for Kids into 4-6 oz chilled water or other beverage, or as directed by your healthcare practitioner. Adjust amount of water to desired sweetness and/or thickness.

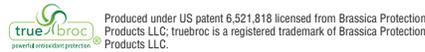
Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, artificial colors, artificial sweeteners, or artificial preservatives.



life'sDHA® is a trademark of DSM.



Produced under US patent 6,521,818 licensed from Brassica Protection Products LLC. true/broc is a registered trademark of Brassica Protection Products LLC.



AMINOGEN® is a registered trademark of Innophos Nutrition, Inc. AMINOGEN® is protected under US patent 5,387,422.



Sharp•PS® GREEN is a registered trademark of Enzymotec Ltd.

Kaneka Q10® is a registered trademark of Kaneka Corp.

Typical Amino Acid Profile Per Serving:

Alanine	330 mg
Arginine	650 mg
Aspartic Acid	860 mg
Cysteine	80 mg
Glutamic Acid	1,270 mg
Glycine	333 mg
Histidine	190 mg
Isoleucine	340 mg
Leucine	630 mg
Lysine	530 mg
Methionine	90 mg
Phenylalanine	410 mg
Proline	340 mg
Serine	400 mg
Threonine	290 mg
Tryptophan	80 mg
Tyrosine	290 mg
Valine	380 mg

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas

800-647-6100 | www.xymogen.com

Glucoraphanin (previously Brassica's SGS™, now Brassica's truebroc®) is a patented phytochemical derived from broccoli extract. Extensive research suggests that when glucoraphanin is enzymatically converted to sulforaphane (its active form), it safely and effectively supports the Nrf2 system, antioxidant systems, and vital phase II detoxification enzymes.^[24,25] This process provides protection from common toxins and xenobiotics.*

DHA (docosahexaenoic acid) is a conditionally essential fatty acid and the main polyunsaturated fatty acid in the brain. DHA supports the structure and function of brain cell membranes, and hence plays a fundamental role in neuronal communication.^[26] Studies suggest that DHA supports the biosynthesis and accumulation of PS in neuronal and glial cells as well.*^[27]

VegaPro™ is XYMOGEN's proprietary and lactose-free pea/rice protein blend. In BrainSustain and BrainSustain for Kids, VegaPro is coupled with Aminogen®, an enzyme complex that facilitates protein digestion and absorption. Amino acids from protein metabolism provide the precursors needed for neurotransmitter production.*

Micronutrients complete the adult version of this formula's comprehensive design. These include magnesium, calcium, phosphorus, vitamin D3, vitamin E (as mixed tocopherols), and activated B vitamins riboflavin 5'-phosphate (B2), pyridoxal 5'-phosphate (B6), methylcobalamin (B12), and folate as 5-MTHF (5-methyltetrahydrofolate). 5-MTHF supports healthy folate nutrition, especially in individuals with genetic variations in folate metabolism. 5-MTHF is provided as Quatrefolic® for enhanced stability, solubility, and bioavailability.^[28,29] In addition, two scoops of BrainSustain adult formula provide the same amount of NAC, PS, ALCAR, alpha-lipoic acid, CoQ10, and glucoraphanin as eight capsules of NeuroActives™ BrainSustain™.*

References

- Selvaraju TR, Khaza'ai H, Vidyadaran S, et al. The neuroprotective effects of tocotrienol rich fraction and alpha tocopherol against glutamate injury in astrocytes. *Bosn J Basic Med Sci.* 2014 Nov 16;14(4):195-204. [PMID: 25428670]
- Gopalan Y, Shuaib IL, Magosso E, et al. Clinical investigation of the protective effects of palm vitamin E tocotrienols on brain white matter. *Stroke.* 2014 May;45(5):1422-28. [PMID: 24699052]
- Rink C, Christoforidis G, Khanna S, et al. Tocotrienol vitamin E protects against preclinical canine ischemic stroke by inducing arteriogenesis. *J Cereb Blood Flow Metab.* 2011 Nov;31(11):2218-30. [PMID: 21673716]
- Khosla P, Patel V, Whinter JM, et al. Postprandial levels of the natural vitamin E tocotrienol in human circulation. *Antioxid Redox Signal.* 2006 May-Jun;8(5-6):1059-68. [PMID: 16771695]
- Mangialasche F, Xu W, Kivipelto M, et al. Tocopherols and tocotrienols plasma levels are associated with cognitive impairment. *Neurobiol Aging.* 2012 Oct;33(10):2282-90. [PMID: 22192241]
- Mangialasche F, Solomon A, Kåreholt I, et al. Serum levels of vitamin E forms and risk of cognitive impairment in a Finnish cohort of older adults. *Exp Gerontol.* 2013 Dec;48(12):1428-35. [PMID: 24113154]
- Muto C, Yachi R, Aoki Y, et al. Gamma-tocotrienol reduces the triacylglycerol level in rat primary hepatocytes through regulation of fatty acid metabolism. *J Clin Biochem Nutr.* 2013 Jan;52(1):32-37. [PMID: 23341695]
- Yachi R, Muto C, Ohtaka N, et al. Effects of tocotrienol on tumor necrosis factor- α /d-galactosamine-induced steatohepatitis in rats. *J Clin Biochem Nutr.* 2013 Mar;52(2):146-53. [PMID: 23526264]
- Magosso E, Ansari MA, Gopalan Y, et al. Tocotrienols for normalisation of hepatic echogenic response in nonalcoholic fatty liver: a randomised placebo-controlled clinical trial. *Nutr J.* 2013 Dec 27;12(1):166. [PMID: 24373555]
- Thendiono EJ, Arguillas M. The effect of vitamin E (mixed tocotrienol) on the liver stiffness measurement measured by transient elastography (fibroscan) among NAFLD patients. Poster presented at APASL Liver Week; June 6-10, 2013; Suntec, Singapore.
- Sansone RA, Sansone LA. Getting a knack for NAC: N-acetyl-cysteine. *Innov Clin Neurosci.* 2011 Jan;8(1):10-14. [PMID: 21311702]
- Kato-Kataoka A, Sakai M, Ebina R, et al. Soybean-derived phosphatidylserine improves memory function of the elderly Japanese subjects with memory complaints. *J Clin Biochem Nutr.* 2010 Nov;47(3):246-55. [PMID: 21103034]
- Richter Y, Herzog Y, Cohen T, et al. The effect of phosphatidylserine-containing omega-3 fatty acids on memory abilities in non-demented elderly with subjective memory complaints: a pilot study. *Clin Interv Aging.* 2010 Nov 2;5:313-16. [PMID: 21103402]
- Vakhapova V, Cohen T, Richter Y, et al. Phosphatidylserine containing omega-3 fatty acids may improve memory abilities in non-demented elderly with memory complaints: a double-blind placebo-controlled trial. *Dement Geriatr Cogn Disord.* 2010;29(5):467-74. [PMID: 20523044]
- Suchy J, Chan A, Shea TB. Dietary supplementation with a combination of alpha-lipoic acid, acetyl-L-carnitine, glycerophosphocoline, docosahexaenoic acid, and phosphatidylserine reduces oxidative damage to murine brain and improves cognitive performance. *Nutr Res.* 2009 Jan;29(1):70-74. [PMID: 19185780]
- Picconi B, Barone I, Pisani A, et al. Acetyl-L-carnitine protects striatal neurons against in vitro ischemia: the role of endogenous acetylcholine. *Neuropharmacology.* 2006 Jun;50(8):917-23. [PMID: 16500685]
- Steffen V, Santiago M, de la Cruz CP, et al. Effect of intraventricular injection of 1-methyl-4-phenylpyridinium: protection by acetyl-L-carnitine. *Hum Exp Toxicol.* 1995 Nov;14(11):865-71. [PMID: 8588946]
- Sorbi S, Forleo P, Fani C, et al. Double-blind, crossover, placebo-controlled clinical trial with L-acetylcarnitine in patients with degenerative cerebellar ataxia. *Clin Neuropharmacol.* 2000 Mar-Apr;23(2):114-18. [PMID: 10803803]
- Jones LL, McDonald DA, Borum PR. Acylcarnitines: role in brain. *Prog Lipid Res.* 2010 Jan;49(1):61-75. Review. [PMID: 19720082]
- Kobayashi S, Iwamoto M, Kon K, et al. Acetyl-L-carnitine improves aged brain function. *Geriatr Gerontol Int.* 2010 Jul;10 Suppl 1:S99-106. [PMID: 20590847]
- Packer L, Tritschler HJ, Wessel K. Neuroprotection by the metabolic antioxidant alpha-lipoic acid. *Free Radic Biol Med.* 1997;22(1-2):359-78. Review. [PMID: 8958163]
- Liu J. The effects and mechanisms of mitochondrial nutrient alpha-lipoic acid on improving age-associated mitochondrial and cognitive dysfunction: an overview. *Neurochem Res.* 2008 Jan;33(1):194-203. Review. [PMID: 17605107]
- Mancuso M, Orsucci D, Volpi L, et al. Coenzyme Q10 in neuromuscular and neurodegenerative disorders. *Curr Drug Targets.* 2010 Jan;11(1):11-21. Review. [PMID: 20017723]
- Ping Z, Liu W, Kang Z, et al. Sulforaphane protects brains against hypoxic-ischemic injury through induction of Nrf2-dependent phase 2 enzyme. *Brain Res.* 2010 Jul 9;1343:178-85. [PMID: 20417626]
- Vauzour D, Buonfiglio M, Corona G, et al. Sulforaphane protects cortical neurons against 5-S-cysteinyl-dopamine-induced toxicity through the activation of ERK1/2, Nrf-2 and the upregulation of detoxification enzymes. *Mol Nutr Food Res.* 2010 Apr;54(4):532-42. [PMID: 20166144]
- Chang CY, Ke DS, Chen JY. Essential fatty acids and human brain. *Acta Neurol Taiwan.* 2009 Dec;18(4):231-41. Review. [PMID: 20329590]
- Guo M, Stockert L, Akbar M, et al. Neuronal specific increase of phosphatidylserine by docosahexaenoic acid. *J Mol Neurosci.* 2007 Sep;33(1):67-73. [PMID: 17901548]
- Prinz-Langenohl R, Brämwig S, Tobolski O, et al. [6S]-5-methyltetrahydrofolate increases plasma folate more effectively than folic acid in women with the homozygous or wild-type 677C->T polymorphism of methylenetetrahydrofolate reductase. *Br J Pharmacol.* 2009 Dec;158(8):2014-21. [PMID: 19917061]
- Quatrefolic®. <http://quatrefolic.com>. Accessed April 30, 2012.

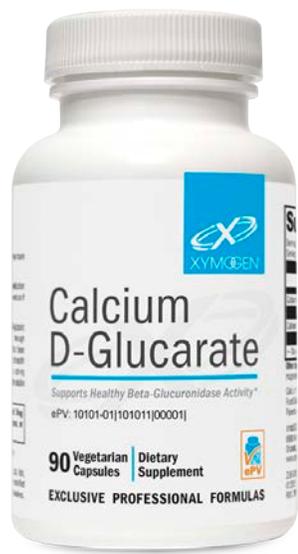
Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Calcium D-Glucarate

Supports Healthy Beta-Glucuronidase Activity*



Available in 90 capsules

Discussion

XYMOGEN's Calcium D-Glucarate is the patented calcium salt of D-glucaric acid, a substance produced naturally in very small amounts in the body and found in many fruits and vegetables. Researchers at the MD Anderson Cancer Center, who studied the effects and realized the benefits of D-glucaric acid, quickly moved to patent its supplemental form, calcium D-glucarate (CGT). Oral supplementation of CGT has been shown to indirectly inhibit beta-glucuronidase.^[1-3] This activity ultimately increases glucuronidation (phase II detoxification) and the excretion of toxins and harmful metabolites.*

Glucuronidation and Beta-Glucuronidase During phase II detoxification, unwanted chemicals or compounds are conjugated with glucuronic acid in the liver (glucuronidation) to form glucuronide conjugates that can then be excreted via the urine or bile. Glucuronidation is the pathway used by estrogens and androgens; some steroid hormones; lipid-soluble toxins, such as polycyclic aromatic hydrocarbons; and some nitrosamines, heterocyclic amines, and aromatic amines. This pathway also represents a major means of converting most drugs to water-soluble substances that can be excreted.*

Beta-glucuronidase, an enzyme produced by intestinal bacteria, cleaves glucuronic acid from the glucuronide conjugates formed during phase II detoxification. This cleaving activity frees the unwanted compounds (e.g., toxins), allowing their reabsorption by the ileal mucosa. When this happens, the body is re-exposed to toxins for prolonged periods, which can increase their potential to harm. CGT is converted metabolically to an inhibitor of beta-glucuronidase in the intestine, thereby preventing deconjugation and reabsorption of toxins while increasing their elimination.^[1,3] Because elevated levels of sex hormones have been linked to unwanted cellular changes, researchers studied the effects of CGT on steady-state hormones and glucuronidation. They found that female rats on a CGT diet had reduced levels of serum estradiol and 17-ketosteroid by 23% and 55%, respectively.^[4] Furthermore, urinary excretion of 17-ketosteroids in the rats placed on the 10% CGT diet increased by 200% on the

Clinical Applications

- » Provides the Patented Form of Supplemental D-Glucaric Acid
- » Reduces Beta-Glucuronidase Activity for Increased Glucuronidation of Unwanted Compounds*
- » Increased Glucuronidation Supports Detoxification and Elimination of Chemicals, Steroid Hormones (Estrogens, Androgens), and Lipid-Soluble Toxins*

*Calcium D-Glucarate is the supplemental, patented calcium salt form of D-glucaric acid—a substance produced naturally in the body and obtained through consumption of certain fruits and vegetables. Calcium D-glucarate has been extensively studied by researchers at the MD Anderson Cancer Center, and its health benefits are largely attributed to inhibition of beta-glucuronidase; this activity supports the body's ability to detoxify estrogens, xenobiotics, and fat-soluble toxins.**

second day and then dropped. After one week, excretion had reached a new steady-state level, which was lower by approximately 50% than that of the rats fed the regular chow diet.*

Modulating Beta-Glucuronidase Activity As stated earlier, CGT does not inhibit beta-glucuronidase directly. Taken orally, it dissolves in the stomach and forms D-glucaric acid, from which the potent beta-glucuronidase inhibitor D-glucaro-1,4-lactone is derived.^[5] Unfortunately, the body rapidly clears D-glucaro-1,4-lactone. However, oral calcium D-glucarate can be considered a sustained release form of the D-glucaro-1,4-lactone.^[4] Animals given a single dose of oral calcium D-glucarate showed a 50% inhibition of beta-glucuronidase for five hours.^[2] In vitro and animal studies suggest that the inhibition of beta-glucuronidase protects cells and supports normal cell replication and death (apoptosis).^[3] These benefits of D-glucaric acid and its salts have been observed in tissues of the colon, prostate, lung, liver, skin, and breast in animal-model studies.^[3,6,7] These in vitro and animal data are promising, and researchers postulate that controlled human trials will reflect similar results.*

Antioxidant Activity Although the mechanisms of action have not been clearly elucidated, the antioxidant effects of CTG have been demonstrated.^[8-10] For instance, Olas et al showed that D-glucaro-1,4-lactone was protective against oxidative/nitrative modifications of plasma proteins.*^[9]

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Calcium D-Glucarate Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Calcium (as calcium D-glucarate)	60 mg	5%
Calcium D-Glucarate	500 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), stearic acid, microcrystalline cellulose, magnesium stearate, and silica.
Calcium D-glucarate is licensed from Applied Food Sciences, Inc. and is protected by US patent 7,662,863.

DIRECTIONS: Take one capsule twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



References

1. Zóttaszek R, Hanausek M, Kiliańska ZM, et al. The biological role of D-glucaric acid and its derivatives: potential use in medicine [in Polish]. *Postepy Hig Med Dosw* (Online). 2008 Sep 5;62:451-62. [PMID: 18772850]
2. Dwivedi C, Heck WJ, Downie AA, et al. Effect of calcium glucarate on beta-glucuronidase activity and glucarate content of certain vegetables and fruits. *Biochem Med Metab Biol*. 1990 Apr;43(2):83-92. [PMID: 2346674]
3. Calcium-D-glucarate. *Altern Med Rev*. 2002 Aug;7(4):336-39. [PMID: 12197785]
4. Walaszek Z, Hanausek-Walaszek M, Minton JP, et al. Dietary glucarate as anti-promoter of 7,12-dimethylbenz[a]anthracene-induced mammary tumorigenesis. *Carcinogenesis*. 1986 Sep;7(9):1463-36. [PMID: 3091283]
5. Walaszek Z, Szemraj J, Narog M, et al. Metabolism, uptake, and excretion of a D-glucaric acid salt and its potential use in cancer prevention. *Cancer Detect Prev*. 1997;21(2):178-90. [PMID: 9101079]
6. Abou-Issa H, Moeschberger M, el-Masry W, et al. Relative efficacy of glucarate on the initiation and promotion phases of rat mammary carcinogenesis. *Anticancer Res*. 1995 May-Jun;15(3):805-10. [PMID: 7645962]
7. Singh J, Gupta KP. Calcium glucarate prevents tumor formation in mouse skin. *Biomed Environ Sci*. 2003 Mar;16(1):9-16. [PMID: 12747003]
8. Saluk-Juszczak J, Olas B, Nowak P, et al. Protective effects of D-glucaro-1,4-lactone against oxidative modifications in blood platelets. *Nutr Metab Cardiovasc Dis*. 2008 Jul;18(6):422-28. [PMID:17933501]
9. Olas B, Saluk-Juszczak J, Nowak P, et al. Protective effects of D-glucaro 1,4-lactone against oxidative/nitrative modifications of plasma proteins. *Nutrition*. 2007 Feb;23(2):164-71. [PMID: 17234507]
10. Kolodziejczyk J, Saluk-Juszczak J, Wachowicz B. In vitro study of the antioxidative properties of the glucose derivatives against oxidation of plasma components. *J Physiol Biochem*. 2011 Jun;67(2):175-83. [PMID: 21086198]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Candididal™

Natural Support for GI Balance*



Available in 60 capsules

Discussion

Candididal™ offers a functional approach to achieving and maintaining balance in gastrointestinal flora, a primary component of GI health.^[1] The complementary blend of ingredients is formulated to support antioxidant activity, microbial balance, and gastrointestinal function.*

Origanox™+WS The water-soluble form of Origanox (Origanox WS) is a natural plant extract from the edible herb *Origanum vulgare* (oregano). Essential oils and phytonutrients from oregano, including rosmarinic acid and quercetin, have been studied closely for their role in supporting antioxidant mechanisms and healthy microbial balance in the body.^[2,3] The ORAC (oxygen radical absorbance capacity) value of Origanox is 5,800 units per gram.^[4] The ORAC scale, developed by scientists at the National Institute of Aging, is a measure of the scavenging capacity of antioxidants against free radicals that cause oxidative stress.*

Sodium Caprylate, a derivative of caprylic acid, is a medium-chain fatty acid with a long research history. Research indicates that it has the potential to support healthy microbial balance in the intestines without adversely affecting beneficial GI flora. Studies also suggest that it may have direct effects on cellular integrity and growth, further supporting gastrointestinal health.*^[5,6]

Ginger (*Zingiber officinale*) plays an important role in Candididal, offering support for gastrointestinal, immune, and antioxidant systems.^[7-9] Ginger has been used for centuries for support of normal gastric function and activity.*

Turmeric Extract Turmeric (*Curcuma longa*) has been used historically to support normal muscular contraction/relaxation and digestion. This ancient herb is rich in curcumin, which has been researched considerably for its protective effects,^[10,11] as well as its ability to support healthy cytokine balance.^[12,13] The addition of turmeric to Candididal provides additional support for GI function and balance.*

Clinical Applications

- » Supports Healthy Microbial Balance*
- » Provides Nutrients That Support Antioxidant Activity*
- » Supports Gastrointestinal Health*

*Candididal™ offers a complementary blend of herbs, essential oils, and sodium caprylate, a naturally occurring fatty acid. Candididal is formulated to support the body's immune system as well as a healthy gastrointestinal (GI) flora. This comprehensive formula contains Origanox™ WS—a GRAS, phenolic-rich ingredient extracted from the edible herb Origanum vulgare—as well as herbs to support digestion and a healthy GI system.**

Olive Leaf Extract from the traditional medicinal plant *Olea europaea* is known for its array of healthful attributes, including support for immune and antioxidant activities. While studying the attributes of olive leaf, scientists in the late 19th century isolated oleuropein,^[14] which is converted in the body to the active component elenolic acid. By the late 1960s, research focused on the role of both oleuropein and elenolic acid. Oleuropein and rutin in olive leaf may contribute to maintaining healthy gastrointestinal microflora.^[15] Olive leaf extract in Candididal is standardized to 20% oleuropein, while less concentrated formulas are standardized to as little as 6% oleuropein.*

Candididal is a comprehensive formula designed to support GI tract health and microflora balance while concurrently supporting antioxidant systems and tissue health.*

Candididal™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Oregano Extract (<i>Origanum vulgare</i>)(herb) (≥23% phenolics) (Origanox™ WS)	300 mg	**
Sodium Caprylate	300 mg	**
Ginger (<i>Zingiber officinale</i>)(rhizome)	300 mg	**
Turmeric Extract (<i>Curcuma longa</i>)(root)(95% curcuminoids)	200 mg	**
Olive Extract (<i>Olea europaea</i>)(leaf)(20% oleuropein)	100 mg	**
** Daily Value not established.		

Other Ingredients: HPMC (capsule), dicalcium phosphate dihydrate, stearic acid, calcium silicate, magnesium stearate, silica, and medium-chain triglyceride oil. Origanox™ is a trademark of Barrington Nutritionals.

DIRECTIONS: Take one to two capsules, once daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged. The labeling on this product does not comply with California's Proposition 65. Therefore, this product may not be sold in California.

CAUTIONS: Do not use if you are pregnant or lactating.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.

**References:**

- Pizzorno LU, Pizzorno JE, Murray MT. *Natural Medicine Instructions for Patients*. London, England: Churchill Livingstone; 2002.
- Tampieri MP, Galuppi R, Macchioni F, et al. The inhibition of *Candida albicans* by selected essential oils and their major components. *Mycopathologia*. 2005 Apr;159(3):339-45. [PMID: 15883716]
- Chun SS, Vattem DA, Lin YT, et al. Phenolic antioxidants from clonal oregano (*Origanum vulgare*) with antimicrobial activity against *Helicobacter pylori*. *Process Biochem*. 2005;40(2):809-16.
- www.origanox.info. Accessed August 9, 2011.
- Adams JN, Painter BG, Payne WJ. Effects of Sodium Caprylate on *Candida Albicans*. I. Influence of Concentration on Ultrastructure. *J Bacteriol*. 1963 Sep;86:548-57. [PMID: 14066435]
- Payne WJ, Bannister ER. Effects of Sodium Caprylate on *Candida Albicans*. II. Influence of Various Concentrations on Biochemical Changes. *J Bacteriol*. 1963 Sep;86:558-62. [PMID: 14066436]
- Lantz RC, Chen GJ, Sarihan M, et al. The effect of extracts from ginger rhizome on inflammatory mediator production. *Phytomedicine*. 2007 Feb;14(2-3):123-8. [PMID: 16709450]
- Ernst E, Pittler MH. Efficacy of ginger for nausea and vomiting: a systematic review of randomized clinical trials. *Br J Anaesth*. 2000 Mar;84(3):367-71. [PMID: 10793599]
- Ali BH, Blunden G, Tanira MO, Nemmar A. Some phytochemical, pharmacological and toxicological properties of ginger (*Zingiber officinale* Roscoe): a review of recent research. *Food Chem Toxicol*. 2008 Feb;46(2):409-20. [PMID: 17950516]
- Neelofar K, Shreaz S, Rimple B, et al. Curcumin as a promising anticandidal of clinical interest. *Can J Microbiol*. 2011 Mar;57(3):204-10. [PMID: 21358761]
- Martins CV, da Silva DL, Neres AT, et al. Curcumin as a promising antifungal of clinical interest. *J Antimicrob Chemother*. 2009 Feb;63(2):337-9. [PMID: 19038979]
- Jurenka JS. Anti-inflammatory properties of curcumin, a major constituent of *Curcuma longa*: a review of preclinical and clinical research. *Altern Med Rev*. 2009 Jun;14(2):141-53. [PMID: 19594223]
- Jagetia GC, Aggarwal BB. "Spicing up" of the immune system by curcumin. *J Clin Immunol*. 2007 Jan;27(1):19-35. [PMID: 17211725]
- Ritchason J. *Olive Leaf Extract*. Salt Lake City, UT: Woodland Publishing Incorporated; 2007.
- Pereira AP, Ferreira IC, Marcelino F, et al. Phenolic compounds and antimicrobial activity of olive (*Olea europaea* L. Cv. Cobrançosa) leaves. *Molecules*. 2007 May 26;12(5):1153-62. [PMID: 17873849]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

CarniteX™

Ultra-Pure L-Carnitine



Available in 60 capsules

Discussion

L-carnitine is a conditionally essential micronutrient synthesized from the essential amino acids L-lysine and L-methionine primarily in the human brain, liver, and kidney. Production is a multi-step process and requires adequate niacin, pyridoxine, vitamin C, and iron. Once synthesized, carnitine is transported to other parts of the body, especially cardiac and skeletal muscle where 98% of total body carnitine is confined.*^[1]

Carnitine plays an important role in fat and carbohydrate metabolism and energy production by transporting long-chain fatty acids into the mitochondria where beta-oxidation of the fatty acids produces energy in the form of ATP (adenosine-5'-triphosphate). It transports short- and medium-chain fatty acids out of the mitochondria and assists in the liberation of coenzyme A, further promoting ATP synthesis. Carnitine facilitates oxidation of glucose, branched-chain amino acids, and ketones, and is required for the oxidation of medium-chain fatty acids in cardiac and skeletal muscle, tissues that use fatty acids as their primary fuel.*^[1,2]

Carnitine requirements may vary under certain conditions—for example, overnutrition or aging—and supplementation may support energy and glucose metabolism during these times. Researchers studying carnitine function and requirements utilized supplementation to support energy and substrate metabolism in an animal model. The results suggested that orally administered L-carnitine does indeed support complete fatty acid oxidation, normal mitochondrial fuel metabolism, and glucose tolerance.^[3] According to the Council for Responsible Nutrition, the observed safe level for carnitine supplementation in humans appears to be 2,000 mg per day, although higher doses have been tested and tolerated.*^[4]

Muscle fuel metabolism also depends on carnitine when fatty acids become the primary energy source for muscles during ongoing low to moderate exercise. Increasing total muscle carnitine content in healthy humans may support physiological function by reducing muscle glycolysis and increasing glycogen storage, fat oxidation, and

Clinical Applications

- » Supports Cardiovascular, Neurological, and Endocrine System Health*
- » Supports Fat Utilization and Energy Generation*
- » Supports Post-Exercise Muscle Recovery*
- » Provides 680 mg of Stabilized L-Carnitine per Two-Capsule Dose*

*CarniteX™, a highly stabilized form of the amino acid L-carnitine, supports cardiovascular health, pulmonary function, and muscle recovery from exercise. L-carnitine supports fat utilization and energy production in the mitochondria and is found in abundance in heart and skeletal muscle. CarniteX contains 60% pure L-carnitine and 32% natural L-tartaric acid.**

work output.^[5,6] A randomized, placebo-controlled human subject study suggested that carnitine can improve exercise tolerance and inspiratory muscle strength, as well as reduce lactate production.^[7] A six-month, randomized, double-blind, placebo-controlled study of 50 children suggested that oral supplementation with L-carnitine helped support normal carnitine levels in the body with statistically significant positive effects on support of lung function.*^[8]

The role of carnitine in normal fertility has been investigated with meta-analysis of nine randomized controlled trials suggesting that carnitine may be effective in improving pregnancy rate and sperm kinetics, though further research is warranted.^[9] In some individuals, carnitine supplementation may support cardiovascular health and triglyceride and HDL levels already within the normal range.*^[10,11]

Carnitine participates in cell volume and fluid balance, liver lipid metabolism, and antioxidant activity. Ongoing research suggests that carnitine supplementation may effectively help maintain the health and function of the cardiovascular, nervous, immune, and endocrine systems, as well as the kidneys and the liver.*^[12]

CarniteX™ Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
L-Carnitine (as L-carnitine L-tartrate)	340 mg	**
** Daily Value not established.		

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, and silica.**DIRECTIONS:** Take one capsule twice daily between meals, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

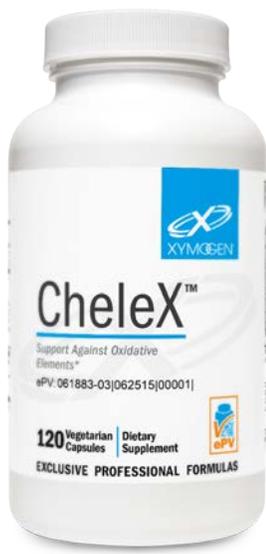
DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.**STORAGE:** Keep closed in a cool, dry place out of reach of children.**References**

1. Natural Standard Database. www.NaturalStandard.com. Accessed February 24, 2012.
2. Linus Pauling Institute. <http://lpi.oregonstate.edu/infocenter/othernuts/carnitine/>. Accessed February 24, 2012.
3. Noland RC, Koves TR, Seiler SE, et al. Carnitine insufficiency caused by aging and overnutrition compromises mitochondrial performance and metabolic control. *J Biol Chem*. 2009 Aug 21;284(34):22840-52. [PMID: 19553674]
4. Hathcock JN, Shao A. Risk assessment for carnitine. *Regul Toxicol Pharmacol*. 2006 Oct;46(1):23-8. Review. [PMID: 16901595]
5. Stephens FB, Constantin-Teodosiu D, Greenhaff PL. New insights concerning the role of carnitine in the regulation of fuel metabolism in skeletal muscle. *J Physiol*. 2007 Jun 1;581(Pt 2):431-44. Review. [PMID: 17331998]
6. Wall BT, Stephens FB, Constantin-Teodosiu D, et al. Chronic oral ingestion of L-carnitine and carbohydrate increases muscle carnitine content and alters muscle fuel metabolism during exercise in humans. *J Physiol*. 2011 Feb 15;589(Pt 4):963-73. [PMID: 21224234]
7. Borghi-Silva A, Baldissera V, Sampaio LM, et al. L-carnitine as an ergogenic aid for patients with chronic obstructive pulmonary disease submitted to whole-body and respiratory muscle training programs. *Braz J Med Biol Res*. 2006 Apr;39(4):465-74. [PMID: 16612469]
8. Al-Biltagi M, Isa M, Bediwy AS, et al. L-carnitine improves the asthma control in children with moderate persistent asthma. *J Allergy (Cairo)*. 2012;2012:509730. [PMID: 22162707]
9. Zhou X, Liu F, Zhai S. Effect of L-carnitine and/or L-acetyl-carnitine in nutrition treatment for male infertility: a systematic review. *Asia Pac J Clin Nutr*. 2007;16 Suppl 1:383-90. Review. [PMID: 17392136]
10. Vacha GM, Giorcelli G, Siliprandi N, et al. Favorable effects of L-carnitine treatment on hypertriglyceridemia in hemodialysis patients: decisive role of low levels of high-density lipoprotein-cholesterol. *Am J Clin Nutr*. 1983 Oct;38(4):532-40. [PMID: 6624695]
11. Kender BS. Supplemental conditionally essential nutrients in cardiovascular disease therapy. *J Cardiovasc Nurs*. 2006 Jan-Feb;21(1):9-16. Review. [PMID: 16407731]
12. Flanagan JL, Simmons PA, Vehige J, et al. Role of carnitine in disease. *Nutr Metab (Lond)*. 2010 Apr 16;7:30. [PMID: 20398344]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

<p>*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.</p>
--



Available in 120 capsules

Discussion

Himalayan Shilajit Extract (*Asphaltum punjabinum*) is a purified form of shilajit also known as salajit, shilajatu, mimie, or mummiyo. This naturally occurring phytocomplex is found in high mountain rocks, especially those of the Himalayas and Hindu Kush ranges of the Indian subcontinent. It is formed from decomposed plant material that has been preserved in the dark pressure of rocky crevasses. As the sun warms the rocks and the snow melts, the shilajit seeps out and is scraped from the stone by hand. XYMOGEN's shilajit is meticulously harvested at high altitudes to ensure the purest product possible. It is then low-temperature dried and tested to be free of pollutants. Shilajit is composed mainly of humic substances, including fulvic acid, plus some oligoelements (minute amounts of trace elements). It has a rich history of use in the Indian Ayurvedic and Siddha systems of medicine, and it is known as a rasayana because of its rejuvenating qualities.*^[1]

Modern research suggests that shilajit has powerful antioxidant activity.^[1-3] As an example, in an animal model, processed shilajit increased superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) activities in a dose-dependent manner.^[3] Furthermore, humic substances, as found in shilajit, have been shown to affect the distribution, metabolism, and absorption of heavy metals, such as cadmium and lead.^[4-7] One human study showed that the daily consumption of humic acid with bound complex micro-elements for six weeks decreased uptake and increased urinary excretion of cadmium in alkaline battery production workers.*^[8]

EDTA (ethylenediaminetetraacetic acid) is a synthetic amino acid compound and perhaps the most well-known and often-used intravenous chelating agent. Oral EDTA is poorly absorbed, but it is thought to support detoxification of metals largely in the gastrointestinal tract.^[9,10] More studies are needed to validate oral administration. It is believed that there is a benefit in combining EDTA with other chelators because EDTA acts slowly and could potentially lead to redeposition of metals.^[11] Due to EDTA's metal-binding ability, it is important to replace beneficial minerals, such as zinc, copper, iron, cobalt, and manganese.*

Clinical Applications

- » Helps Protect Tissues from Oxidative Stress*
- » Supports Detoxification*

*CheleX™ is designed to help the body rid itself of damaging oxidative elements. It features specialized ingredients, such as EDTA, Himalayan shilajit extract (50% fulvic acid), chlorella, coriander, and antioxidant-stimulating nutrients. These ingredients perform in concert to support your health when your body is challenged by environmental toxins, such as heavy metals.**

Coriander Seed Extract (water-extracted) (*Coriandrum sativum*), also known as cilantro, appears to suppress the deposition of lead and arsenic by chelating these metals.^[12,13] In a study, lead-induced histological changes in the testis of albino mice were prevented to some extent by concomitant daily administration of *C sativum* extracts, perhaps due to a reduction in associated oxidative stress.^[14] In another study, tissue-specific amelioration of lead-induced oxidative stress occurred in the brains of Wistar rats after administration of hydroalcoholic seed extract of *C sativum*.*^[15]

Allicin is the main biologically active component of garlic clove extracts and has promising effects on toxic metal accumulation in experimental research.^[16] In animal and in vitro models, garlic was able to reduce cellular exposure to, or accumulation of, lead, cadmium, and mercury.^[17-22] Furthermore, various extracts and forms of garlic have demonstrated garlic's ability to positively affect detoxification pathways.*^[22]

Chlorella is a naturally occurring micro-algae and an excellent source of chlorophyll—a detoxifying substance that is also thought to bind toxic metals. The positive effect of chlorella supplementation on toxic metals, including methylmercury, cadmium, and lead, is supported by animal research.^[23,24] For example, testing its metal chelating ability, researchers observed a dramatic 66.03% reduction in blood lead levels in mice receiving chlorella extract (50 mg/kg/day) concurrent with lead exposure compared to lead-exposed, non-treated mice.*^[23]

N-Acetyl-L-Cysteine (NAC) and Alpha-Lipoic Acid (ALA) are well-known for their antioxidant activity. Exposure to heavy metals increases free radical production and oxidative stress.^[25] Research suggests that there is a beneficial role for free radical scavengers in reducing the oxidative stress that is common with toxic metal exposure.^[26] NAC has the ability to interact with reactive oxygen species (ROS) and stimulate the body to produce glutathione. This can enhance cell survival after exposure to heavy metals or toxins.^[27] In addition, ALA may directly chelate or reduce the oxidative capacity of metals, such as copper, arsenic, cadmium, and mercury.*^[28-31]

CheleX™ Supplement Facts

Serving Size: 4 Capsules

	Amount Per Serving	%Daily Value
Himalayan Shilajit Extract (<i>Asphaltum punjabinum</i>)(mineral extract)(50% fulvic acid)	600 mg	**
Calcium Disodium EDTA	300 mg	**
Chlorella (<i>Chlorella vulgaris</i>)	300 mg	**
Coriander 4:1 (<i>Coriandrum sativum</i>)(seeds)	300 mg	**
N-Acetyl-L-Cysteine	200 mg	**
Alpha-Lipoic Acid	100 mg	**
Allicin (from garlic extract)(<i>Allium sativum</i>)(bulb)	6 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), stearic acid, microcrystalline cellulose, magnesium stearate, and silica.

DIRECTIONS: Take two to four capsules daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking blood thinners, insulin, or other medication should discuss potential interactions with their healthcare practitioner. Do not take if you are pregnant or lactating. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



References

1. Carrasco-Gallardo C, Guzmán L, Maccioni RB. Shilajit: a natural phytocomplex with potential procognitive activity. *Int J Alzheimers Dis.* 2012;2012:674142. [PMID: 22482077]
2. Mittal P, Kaushik D, Gupta V. Therapeutic potentials of "shilajit rasayana": a review. *Int J Pharm Clin Res.* 2009;1(2):47-49. <http://www.rudramani.com/research/shilajit-as-a-medicine-for-general-physical-strengthening-anti-aging-and-much-more.pdf>. Accessed August 1, 2014.
3. Bhattacharya SK, Sen AP, Ghosal S. Effects of shilajit on biogenic free radicals. *Phyto Res.* 1995 Feb;9(1):56-59. doi:10.1002/ptr.2650090113.
4. Glynn AW. Fulvic and humic acids decrease the absorption of cadmium in the rat intestine. *Arch Toxicol.* 1995;70(1):28-33. [PMID: 8750902]
5. Lind Y, Glynn AW. The influence of humic substances on the absorption and distribution of cadmium in mice. *Pharmacol Toxicol.* 1999 Jun;84(6):267-73. [PMID: 10401728]
6. Gondar D, Lopez R, Fiol S, et al. Cadmium, lead, and copper binding to humic acid and fulvic acid extracted from an ombrotrophic peat bog. *Geoderma.* 2006 Nov;135:196-203. doi:10.1016/j.geoderma.2005.12.003.
7. Sharma P, Jha J, Shrinivas V, et al. Shilajit: evaluation of its effects on blood chemistry of normal human subjects. *Anc Sci Life.* 2003 Oct;23(2):114-9. [PMID: 22557121]
8. Hudák A, Náray M, Nagy I, et al. Effect of the consumption of humic acid with bound complex micro elements in cases of occupational cadmium exposure. National Institute of Occupational Health, Budapest, Hungary. <http://www.omfi.hu/cejoem/Volume3/Vol3No3/ce973-2.HTM>. Accessed July 31, 2014.
9. Foreman H, Trujillo TT. The metabolism of C14 labeled ethylenediaminetetraacetic acid in human beings. *J Lab Clin Med.* 1954 Apr;43(4):566-71. [PMID: 13163555]
10. Shiels DO, Thomas DL, Kearley E. Treatment of lead poisoning by edathamil calcium-disodium. *AMA Arch Ind Health.* 1956 May;13(5):489-98. [PMID: 13312679]
11. Besunder JB, Super DM, Anderson RL. Comparison of dimercaptosuccinic acid and calcium disodium ethylenediaminetetraacetic acid versus dimercaptopropanol and ethylenediaminetetraacetic acid in children with lead poisoning. *J Pediatr.* 1997 Jun;130(6):966-71. [PMID: 9202621]
12. Aga M, Iwaki K, Ueda Y, et al. Preventive effect of Coriandrum sativum (Chinese parsley) on localized lead deposition in ICR mice. *J Ethnopharmacol.* 2001 Oct;77(2-3):203-08. [PMID: 11535365]
13. Gaur N, Kukreja A, Yadav M, et al. Assessment of phytoremediation ability of Coriander sativum for soil and water co-contaminated with lead and arsenic; a small-scale study. *J Biotech.* 2017 Jul;7(3):196. [PMID: 28667636]
14. Sharma V, Kansal L, Sharma A. Prophylactic efficacy of Coriandrum sativum (Coriander) on testis of lead-exposed mice. *Biol Trace Elem Res.* 2010 Sep;136(3):337-54. [PMID: 19902160]
15. Velaga MK, Yallapragada PR, Williams D, et al. Hydroalcoholic seed extract of Coriandrum sativum (Coriander) alleviates lead-induced oxidative stress in different regions of rat brain. *Bio Trace Elem Res.* 2014 Jun;159(1-3):351-63. [PMID: 24793421]
16. Aslani MR, Najarneshad V, Mohri M. Individual and combined effect of meso-2,3-dimercaptosuccinic acid and allicin on blood and tissue lead content in mice. *Planta Med.* 2010 Feb;76(3):241-44. [PMID: 19764011]
17. Senapati SK, Dey S, Dwivedi SK, et al. Effect of garlic (*Allium sativum* L.) extract on tissue lead level in rats. *J Ethnopharmacol.* 2001 Aug;76(3):229-32. [PMID: 11448543]
18. Shahsavani D, Baghshani H, Alishahi E. Efficacy of allicin in decreasing lead (Pb) accumulation in selected tissues of lead-exposed common carp (*Cyprinus carpio*). *Biol Trace Elem Res.* 2011 Sep;142(3):572-80. [PMID: 20711682]
19. Najjar-Nezhad V, Aslani MR, Balali-Mood M. Evaluation of allicin for the treatment of experimentally induced subacute lead poisoning in sheep. *Biol Trace Elem Res.* 2008 Winter;126(1-3):141-7. [PMID: 18719860]
20. Jiang W, Liu D, Hou W. Hyperaccumulation of cadmium by roots, bulbs and shoots of garlic (*Allium sativum* L.). *Bioresour Technol.* 2001 Jan;76(1):9-13. [PMID: 11315815]
21. Lee JH, Kang HS, Roh J. Protective effects of garlic juice against embryotoxicity of methylmercuric chloride administered to pregnant Fischer 344 rats. *Yonsei Med J.* 1999 Oct;40(5):483-9. [PMID: 10565261]
22. Melino S, Sabelli R, Paci M. Allyl sulfur compounds and cellular detoxification system: effects and perspectives in cancer therapy. *Amino Acids.* 2011 Jun;41(1):103-12. [PMID: 20213447]
23. Queiroz ML, Rodrigues AP, Bincioletto C, et al. Protective effects of Chlorella vulgaris in lead-exposed mice infected with *Listeria monocytogenes*. *Int Immunopharmacol.* 2003 Jun;3(6):889-900. [PMID: 12781705]
24. Uchikawa T, Maruyama I, Kumamoto S, et al. Chlorella suppresses methylmercury transfer to the fetus in pregnant mice. *J Toxicol Sci.* 2011 Oct;36(5):675-80. [PMID: 22008543]
25. Vassallo DV, Simões MR, Furiere LB, et al. Toxic effects of mercury, lead and gadolinium on vascular reactivity. *Braz J Med Biol Res.* 2011 Sep;44(9):939-46. [PMID: 21845340]
26. Flora SJ, Pande M, Mehta A. Beneficial effect of combined administration of some naturally occurring antioxidants (vitamins) and thiol chelators in the treatment of chronic lead intoxication. *Chem Biol Interact.* 2003 Jun 15;145(3):267-80. [PMID: 12732454]
27. James SJ, Slikker W 3rd, Melnyk S, et al. Thimerosal neurotoxicity is associated with glutathione depletion: protection with glutathione precursors. *Neurotoxicology.* 2005 Jan;26(1):1-8. [PMID: 15527868]
28. Gaetke LM, Chow CK. Copper toxicity, oxidative stress, and antioxidant nutrients. *Toxicology.* 2003 Jul 15;189(1-2):147-63. [PMID: 12821289]
29. das Neves RN, Carvalho F, Carvalho M, et al. Protective activity of hesperidin and lipoic acid against sodium arsenite acute toxicity in mice. *Toxicol Pathol.* 2004 Sep-Oct;32(5):527-35. [PMID: 15603538]
30. Bludovska M, Kotyzova D, Koutensky J, et al. The influence of alpha-lipoic acid on the toxicity of cadmium. *Gen Physiol Biophys.* 1999 Oct;18 Spec No:28-32. [PMID: 10703716]
31. Keith RL, Setiarahardjo I, Fernando Q, et al. Utilization of renal slices to evaluate the efficacy of chelating agents for removing mercury from the kidney. *Toxicology.* 1997 Jan 15;116(1-3):67-75. [PMID: 9020508]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

CholeRex™

Policosanol with OptiMag® 125



Available in 60 capsules

Discussion

CholeRex™ is an exclusive formula that features MagniSol™, a proprietary blend of policosanol from sugar cane extract and a revolutionary magnesium amino acid chelate and mineral complex produced by an innovative patented process and designed to give maximum absorption. Each capsule provides 10 mg of policosanol and 100 mg of elemental magnesium.*

An impressive body of research suggests that both policosanol and magnesium may provide significant cardioprotective benefits. CholeRex™ with MagniSol™, along with regular exercise and a nutritious diet may be an effective way to help to maintain healthy blood lipid levels and good cardiovascular function.*

Powerful, Natural Support for Blood Lipids

The powerful, beneficial effect of policosanol on blood lipids has been extensively studied in both humans and animals, and its effectiveness has been compared to several commonly prescribed lipid-modifying agents. Policosanol appears to have a modulating effect on hydroxymethylglutaryl co-enzyme A (HMG-CoA) reductase activity, a rate-limiting enzyme for endogenous cholesterol synthesis. This enzyme catalyzes the reduction of HMG-CoA to mevalonate, the key metabolite of cholesterol biosynthesis. Policosanol is believed to affect HMG-CoA reductase activity by depressing its synthesis and/or via stimulation of its degradation. Additionally, policosanol has been shown to promote binding, uptake, and degradation of low-density lipoproteins (LDL).*

Studies suggests that policosanol at a dose range of 5 to 20 mg per day is effective for promoting healthy blood lipid synthesis and metabolism. Policosanol has an excellent safety profile with reports of only mild or no side effects. Furthermore, animal toxicity data indicates that policosanol demonstrates no toxic effects, even at doses many hundred times greater than the maximum dose recommended for humans.*

Clinical Applications

- » Provides natural support for maintaining healthy blood lipid levels*
- » Promotes overall vascular health by helping to maintain blood vessel integrity and function*
- » Prevents peroxidation of low-density lipoproteins (LDL) – helps to protect arterial walls from the damaging effects of oxidized LDL*
- » Inhibits smooth muscle cell proliferation, an important factor in maintaining healthy arterial function*
- » Supports healthy blood flow by helping to maintain healthy platelet function*
- » Supports muscle relaxation and nerve transmission*

Additional Cardiovascular Benefits of Policosanol

In addition to its effect on blood lipid levels, policosanol has demonstrated positive effects on several other risk factors associated with cardiovascular disease. For instance, studies have shown that it may prevent lipid peroxidation of LDL, inhibit smooth muscle cell proliferation, exert a protective effect on vascular endothelium, and promote healthy platelet function, possibly through a decrease in the production of thromboxane A2 and B2. These additional actions can have a beneficial effect on blood vessel integrity and function and thus promote overall cardiovascular health.*

Magnesium and Cardiovascular Health

Magnesium is a vital nutrient that is essential to the proper functioning of the entire cardiovascular system. It is necessary for nearly every major physiologic process in the body and plays an important role in the regulation of muscle contraction, heartbeat, nerve transmission, and vascular tone.*

Magnesium deficiency is widely recognized as a contributing factor in the etiology of heart disease and commonly occurs with conditions such as arrhythmia, hypertension, myocardial infarction, and mitral valve prolapse. In experimental studies, low plasma levels of magnesium have been shown to accelerate atherogenesis by increasing concentrations of LDL and peroxidized lipoproteins, and by promoting inflammation. Additionally, magnesium deficiency is known to contribute to an imbalance of electrolytes, such as Na+, K+, and Ca2+, which can negatively affect myocardial function.*

Magnesium supplementation has been shown to benefit patients with cardiac arrhythmia and hypertension, improve endothelial function in patients with coronary artery disease, and increase the survival rate of patients with congestive heart failure.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

CholeRex™ Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Magnesium (as Albion® di-magnesium malate and TRAACS® magnesium lysinate glycinate chelate)	100 mg	24%
Malic Acid (as Albion® di-magnesium malate)	325 mg	**
Policosanol (from <i>Saccharum officinarum</i>) (sugarcane wax)	10 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, silica, and medium-chain triglyceride oil.

DIRECTIONS: Take one capsule one to two times daily with food, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.



TRAACS and the Albion Medallion design are registered trademarks of Albion Laboratories, Inc. Malate covered by U.S. Patent 6,706,904 and patents pending.

**References**

1. Arruzazabala ML, Mas R, Molina V, et al. Effect of policosanol on platelet aggregation in type II hypercholesterolemic patients. *Int J Tissue React* 1998;20(4):119-24
2. Arruzazabala ML, Molina V, Carbajal D, et al. Effect of policosanol on cerebral ischemia in Mongolian gerbils: role of prostacyclin and thromboxane A2. *Prostaglandins Leukot Essent Fatty Acids* 1993;49:695-97
3. Arruzazabala ML, Molina V, Mas R, Fernandez L, et al. Antiplatelet effects of policosanol (20 and 40 mg/day) in healthy volunteers and dyslipidaemic patients. *Clin Exp Pharmacol Physiol* 2002 Oct;29(10):891-7
4. Arruzazabala ML, Noa M, Menendez R, et al. Protective effect of policosanol on atherosclerotic lesions in rabbits with exogenous hypercholesterolemia. *Braz J Med Biol Res* 2000;33:835-40
5. Batista J, Stusser R, Saez F, et al. Effect of policosanol on hyperlipidemia and coronary heart disease in middle-aged patients. A 14-month study. *Int J Clin Pharmacol Ther* 1996;34(3):134-37
6. Castano G, Mas R, Fernandez L, Gamez, Illnait J. Effects of policosanol and lovastatin in patients with intermittent claudication: a double-blind comparative pilot study. *Angiology* 2003 Jan;54(1):25-38
7. Chakraborti S, Chakraborti T, Mandal M, Mandal A, Das S, Ghosh S. Protective role of magnesium in cardiovascular diseases: a review. *Mol Cell Biochem* 2002 Sep;238(1-2):163-79
8. Gouni-Berhold I, Berthold HK. Policosanol: clinical pharmacology and therapeutic significance of a new lipid-lowering agent. *Am Heart J* 2002 Feb;143(2):356-65
9. Maier JA. Low magnesium and atherosclerosis: an evidence-based link. *Mol Aspects Med* 2003 Feb 6;24(1-3):137-46
10. Menendez R, Arnor AM, Rodeiro I, et al. Policosanol modulates HMG-CoA reductase activity in cultured fibroblasts. *Archives Med Res* 2001;32:8-12
11. Menendez R, Mas, R, Arnor AM, et al. Effect of policosanol on the susceptibility of low density lipoprotein (LDL) isolated from healthy volunteers to oxidative modification in vitro. *Br J Clin Pharmacol* 2000;50:255-62
12. Mesa AR, Mas R, Noa M, et al. Toxicity of policosanol in beagle dogs: one-year study. *Toxicol Lett* 1994;73(2):81-90
13. Zhang Y, Davies LR, Martin SM, Bawaney Im, Buettner GR, Kerber RE. Magnesium reduces free radical concentration and preserves left ventricular function after direct current shocks. *Resuscitation* 2003 Feb;56(2):199-206

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

CinnDromeX™

Glucose Metabolism Support*



Available in 120 capsules

Discussion

CinSulin® is a clinically proven, patented water extract of cinnamon (*Cinnamomum cassia*) shown to powerfully influence glucose metabolism. The unique, proprietary extraction and dehydration process for manufacturing CinSulin results in a concentrated (10:1) extract that minimizes undesirable substances, while retaining those that are health-promoting, such as type-A polyphenolic polymers. Cinnamon has been studied extensively for its roles in glucose uptake, glycogen synthesis, insulin action, and support for healthy blood lipids.^[1,2] Anderson et al. demonstrated a 20-fold increase in glucose uptake in fat cells treated with water-soluble type-A polymers.^[3]

American Ginseng (*Panax quinquefolius*) exhibits activities that support blood sugar levels already in the normal range.^[4,5] The American ginseng in CinnDromeX™ is a standardized 12% (ginsenosides) extract.

Gymnema Leaf Extract (*Gymnema sylvestre*) is a water-soluble extract made from the leaves of *Gymnema sylvestre* and standardized to 25% gymnemic acid. This form does not decrease iron absorption as other forms may.^[6] *Gymnema* can enhance the effects of insulin and oral hypoglycemic agents by reducing glucose absorption in the intestine, stimulating pancreatic beta cell growth, and possibly supporting endogenous insulin secretion. *Gymnema* may also support serum lipid levels already in the normal range.^[7]

Green Tea Polyphenols (*Camellia sinensis*) protect erythrocytes from oxidative stress, possibly supporting the health of tissues that could otherwise be affected by too high levels of blood glucose.^[8] In research studies EGCG enhanced insulin activity,^[9] protected the pancreatic cells by reducing undesirable cytokines (e.g. IL-1beta), and reduced IFN-gamma-induced nitric oxide production. It affected genes that inhibit activation of NF-kappaB^[10] and reduced the level of messenger RNA for the hepatic gluconeogenic enzymes.^[11]

Alpha Lipoic Acid is a potent antioxidant that acts by multiple mechanisms, both physiologically and pharmacologically, to support

Clinical Applications

- » Supports Healthy Glucose Metabolism*
- » Supports Healthy Blood Lipid Levels Already in the Normal Range*
- » Improves/Maintains Healthy Nerve Function*

CinnDromeX™ features significant quantities of key ingredients that support insulin utilization and glucose metabolism. *CinSulin®* is a safe, patented, 100% water-soluble, 10:1 concentrated form of cinnamon that provides polyphenol polymers. Standardized American ginseng, green tea, gymnema, and alpha-lipoic acid help protect pancreatic cells, support insulin sensitivity, and provide antioxidant activity. Albion®'s TRAACS® patented chromium is added for its role in enhancing insulin activity.*

healthy peripheral nerves and maintain blood pressure already in the normal range.^[12,13] In higher doses, alpha lipoic acid supports blood sugar levels already in the normal range.

Chromium: The Albion® TRAACS® patented process that combines chromium with glycinate and niacin increases its bioavailability and supports healthy glucose metabolism.^[14] Individuals with poor glucose metabolism tend to have lower blood chromium levels. Chromium enhances the metabolic action of insulin and may support heart health, especially in overweight individuals.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

CinnDromeX™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Chromium (as TRAACS® chromium nicotinate glycinate chelate)	200 mcg	571%
American Ginseng Extract (<i>Panax quinquefolius</i>)(root and leaf) (15% ginsenosides)	375 mg	**
Alpha-Lipoic Acid	200 mg	**
Green Tea Aqueous Extract (<i>Camellia sinensis</i>)(leaf) (80% polyphenols, 60% catechins, 30% EGCG, 6% caffeine)	200 mg	**
Gymnema Extract (<i>Gymnema sylvestre</i>)(leaf)(25% gymnemic acids)	200 mg	**
Cinnamon 10:1 Aqueous Extract (<i>Cinnamomum cassia</i>)(bark)(3% type-A polymers)(CinSulin®)	200 mg	**

**Daily Value not established.

Other Ingredients: HPMC (capsule), microcrystalline cellulose, stearic acid, magnesium stearate, silica, and medium-chain triglyceride oil.**DIRECTIONS:** Take two capsules daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

CAUTIONS: Do not use if you are pregnant or lactating.**STORAGE:** Keep closed in a cool, dry place out of reach of children.**DOES NOT CONTAIN:** Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

TRAACS and the Albion Medallion design are registered trademarks of Albion Laboratories, Inc.



CinSulin® is registered trademark of Tang-An Medical Co., Ltd. US patent 6,200,569.

References

- Kim SH, Choung SY. Antihyperglycemic and antihyperlipidemic action of *Cinnamomi Cassiae* (Cinnamon bark) extract in C57BL/Ks db/db mice. *Arch Pharm Res.* 2010 Feb;33(2):325-33. [PMID: 20195835]
- Ziegenfuss TN, Hofheins JE, Mendel RW, et al. Effects of a water-soluble cinnamon extract on body composition and features of the metabolic syndrome in pre-diabetic men and women. *J Int Soc Sports Nutr.* 2006 Dec 28;3:45-53. [PMID: 18500972]
- Anderson RA, Broadhurst CL, Polansky MM, et al. Isolation and characterization of polyphenol type-A polymers from cinnamon with insulin-like biological activity. *J Agric Food Chem.* 2004 Jan 14;52(1):65-70. [PMID: 14709014]
- Rotshtyen Y, Zito SW. Application of modified in vitro screening procedure for identifying herbals possessing sulfonylurea-like activity. *J Ethnopharmacol.* 2004 Aug;93 (2-3):337-44 [PMID: 15234774]
- Sievenpiper JL, Arnason JT, Leiter LA, Vuksan V. Variable effects of American Ginseng: a batch of American ginseng (*Panax quinquefolius* L.) with a depressed ginsenoside profile does not affect postprandial glycemia. *Eur J Clin Nutr.* 2003 Feb; 57 (2):243-8 [PMID: 12571655]
- Natural Medicines Comprehensive Database. <http://www.naturaldatabase.com>. [accessed 1.29.07]
- Shanmugasundaram, E.R.B., et.al. Use of gymnema sylvestre leaf extract in the control of blood glucose in insulin-dependent diabetes mellitus. *J of Ethnopharmacol* 1990;30:228-94 [PMID: 2259216]
- Rizvi SI, Zaid MA, Anis R, Mishra N. Protective role of tea catechins against oxidation-induced damage of type 2 diabetic erythrocytes. *Clin Exp Pharmacol Physiol.* 2005 Jan-Feb; 32 (1-2): 70-5 [PMID: 15730438]
- Anderson RA, Polansky MM. Tea enhances insulin activity. *J Agric Food Chem.* 2002 Nov 20; 50(24): 7182-6. [PMID: 12428980]
- Koyama Y et.al. Effects of green tea on gene expression of hepatic gluconeogenic enzymes in vivo. *Planta Med.* 2004 Nov; 70(11):1100-2 [PMID: 15549673]
- Han MK. Epigallocatechin gallate, a constituent of green tea, suppresses cytokine-induced pancreatic beta-cell damage. *Exp Mol Med.* 2003 Apr 30;35(2):136-9 [PMID:12754418]
- Negrisanu G, Rosu M, Bolte B, Lefter D, Dabelea D. Effects of 3-month treatment with the antioxidant alpha-lipoic acid in diabetic peripheral neuropathy. *Rom J Intern Med.* 1999 Jul-Sep;37(3):297-306 [PMID: 15532308]
- de Champlain J. et.al. Oxidative stress in hypertension. *Clin Exp Hypertens.* 2004 Oct-Nov; 26 (7-8): 593-601 [PMID: 15702613]
- Preuss HG, Bagchi M. Protective effects of novel niacin-bound chromium complex and a grape seed proanthocyanidin extract on advancing age and various aspects of syndrome X. *Ann NY Acad Sci.* 2002 May; 957:250-9. [PMID: 12074977]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Cogniquil®

Support for Clarity and Motivation*



Available in 60 capsules

Discussion

Cognition, including learning and memory, is dependent upon neurons in the human brain communicating with each other through synaptic connections. Age, genetics, diet, exercise, and environment may affect how efficiently neurons communicate and, thus, overall cognitive health. Individuals who desire improvement in focus and motivation often look for formulas that target cognitive health, and these often contain ingredients that promote brain stimulation. Cogniquil® contains a targeted blend of key ingredients designed to promote mental and physical energy and fuel motivation and clarity without overstimulation.*

Magtein™ (Patented Magnesium L-Threonate)

Magnesium is involved in more than 300 essential metabolic reactions, justifying the necessity of adequate magnesium levels to support overall health, including that of the brain. In the United States, dietary intakes of this mineral are consistently below age-specific minimum recommended levels.*^[1]

More than ten years of research at MIT went into the development of Magtein, a highly bioavailable compound comprised of magnesium and L-threonate. When brain magnesium levels are not optimal, synapse function deteriorates, suggesting that magnesium plays a significant role in promoting synaptic plasticity in the brain. Ingesting conventional magnesium compounds does not appear to elevate brain magnesium, but animal studies have shown that Magtein crosses the blood-brain barrier, resulting in increased deposits in neural synapses, increased neural synaptic density, and improved brain function.^[2-4] One particular study demonstrated that Magtein enhanced magnesium bioavailability and produced a significant increase (7%-15%) in rat cerebrospinal fluid when compared to other magnesium compounds.^[2] These small but significant increases in brain magnesium levels produced profound effects on neurological function.*

Maintaining extracellular magnesium in the brain has been observed to help preserve synaptic density and synapse function.^[2,5] Early research on Magtein suggested that increasing magnesium concentration in the extracellular fluid permanently enhanced synaptic plasticity in networks of cultured hippocampal neurons.^[5] More recent studies have shown that magnesium increased signaling of the receptors in the hippocampus that play a pivotal role in memory processes. A 2016 study that explored magnesium L-threonate's mechanism of action demonstrated that L-threonate is the only ligand to efficiently transport magnesium into the cerebrospinal fluid and then into neurons.^[6] Data from these studies showed that Magtein enhances both short-term synaptic facilitation and long-term potentiation and thereby supports synaptic plasticity and learning and memory functions.^[2,3,6,7]

Clinical Applications

- » Supports Healthy Brain Magnesium Levels*
- » Promotes Concentration, Mental Clarity, and Focus*
- » Supports Cognitive Health*
- » Promotes Mental and Physical Energy and Motivation to Exercise*

*Cogniquil® provides a unique blend of patented, stimulant-free, non-habit forming ingredients. Methylcobalamin supports cognition and contributes to healthy energy metabolism; magnesium L-threonate supplies highly bioavailable magnesium to the brain, which is vital to cognitive function; and theacrine promotes mental and physical energy, focus, and motivation.**

By delivering magnesium into synapses, Magtein supports cognitive function by helping brain cells respond to signals with clarity and vigor without being overactivated.*

The effects of Magtein were studied in a randomized, double-blind, placebo-controlled trial on human cognition (n = 51). Patients 50–70 years of age who were administered a dose of 1.5 g/d to 2 g/d (25 mg/kg/d) of Magtein for 12 weeks demonstrated reduced cognitive declines compared to age-matched controls. Furthermore, the researchers calculated a particularly compelling impact of Magtein using normative TMT-B data from age-matched subjects. After six weeks of treatment, the average brain age of the Magtein group decreased from 69.6 ± 4.2 years to 60.6 ± 5.6 years, an improvement of 9.0 ± 3.5 years, and persisted after 12 weeks of treatment with 9.4 ± 3.5 years of improvement.^[8] Although future larger trials studying the effects of Magtein on the human brain would be ideal, it is clear from the research to date that Magtein has a significant effect on cognitive well-being.*

TeaCrine® (Theacrine)

Theacrine is a purine alkaloid found in certain coffee and tea species that has a similar chemical structure to caffeine yet with very different physiological effects. Both caffeine and theacrine inhibit adenosine activity via the A1 and A2A receptors, but caffeine is known to act as an orthosteric inhibitor whereas theacrine is likely to act as an indirect, allosteric modulator of these receptors and contribute to differences in habituation. Inhibitory action of the adenosine receptors plays a role in the biochemical processes that prevent fatigue. Additionally, theacrine is a dopamine D1 and D2 receptor agonist, and its actions help increase dopamine signaling associated with attention, movement, task initiation and completion, mood, learning, and the brain's "reward center."^{*}

Whereas habituation typically occurs with caffeine in as little as five days of consumption, a significant attribute of theacrine is the lack of habituation or tachyphylaxis (decrease in response). Following an eight-week study with subjects (N = 60) receiving either 200 mg or 300 mg of Teacrine or placebo, participants demonstrated no signs of the rapid tachyphylaxis typically associated with caffeine and other stimulants. Baseline values for energy, focus, concentration, anxiety, motivation to exercise, and a Profile of Mood States (POMS) questionnaire remained stable across the entire eight-week study period. Additionally, all values for clinical safety markers were within normal limits.^{*[9]}

Continued on next page

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XyMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

In a randomized, double-blind, placebo-controlled, crossover pilot study, subjects (n = 15) ingested 200 mg of Teacrine over a three-hour post-dosing period using a 100 mm visual analogue scale (VAS) to detect change in various aspects of physical and mental energy and performance. Side-effect profiles, hemodynamics, and biochemical markers of safety were also collected. The 200 mg dose was found to significantly improve concentration and energy and reduce fatigue. No changes were noted in systemic hemodynamics and no side effects were observed. A subset of subjects underwent a separate seven-day, open-label, repeated-dose study comparing 100 mg, 200 mg, and 400 mg of Teacrine. The seven-day assessment demonstrated improved subjective measurements for energy, fatigue, concentration, anxiety, motivation to exercise, and libido in the 200 mg dose group.*^[10]

In a small double-blind, placebo-controlled, crossover study, subjects (n = 8) received 25 or 125 mg of theacrine, 150 mg of caffeine, or a combination of theacrine (125 mg) and caffeine (150 mg). Results suggested that while theacrine had no impact on caffeine pharmacokinetics, the combination of caffeine and theacrine led to enhanced bioavailability. Additionally, a broad spectrum of clinical safety markers, including heart rate and blood pressure, were unaffected by concomitant use indicating a strong safety profile at the doses administered.*^[11]

Methylcobalamin (B12)

Cogniquil contains high-potency MecobalActive™, a patented pure form of methylcobalamin that is the physiologically active form of vitamin B12. Vitamin B12 plays a role in the maintenance of a healthy nervous system; chronic insufficiency affects peripheral nerves, the optic nerve, and the brain. Methylcobalamin is a cofactor in myelin synthesis; in the methylation of homocysteine, a substance thought to damage neurons; and in the synthesis of monoamine neurotransmitters.^[12-14] Studies have suggested supplemental B12 alone or in combination with folate supports healthy homocysteine levels already within the normal range.^[15] Increased homocysteine levels have been associated with declining cognitive function.*

B12 is also integral to the complex biochemical processes involved in energy metabolism. It is involved in the conversion of lipids, proteins, and carbohydrates into glucose to fuel energy production and ATP for cellular energy.*^[16]

Cogniquil® Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Vitamin B12 (as MecobalActive™ methylcobalamin)	2000 mcg	83,333%
Magnesium (as Magtein™ magnesium L-threonate)	70 mg	17%
Magtein™ Magnesium L-Threonate	1 g	**
TeaCrine® Theacrine	200 mg	**

** Daily Value not established.

Other Ingredients: Capsule (hypromellose and water), microcrystalline cellulose, ascorbyl palmitate, silica, medium-chain triglyceride oil, and calcium silicate.

DIRECTIONS: Begin with two capsules daily to determine response. Increase to a maximum of two capsules twice daily, or take as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, corn, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

MecobalActive™ is a trademark of Ferrer Health Tech.
The active form of B₁₂



TEACRINE® is a registered trademark and is protected by Patents Pending, Serial No. 61/903,362, under exclusive global distribution by Compound Solutions, Inc.

Magtein.
Think clearly™

Magtein is protected under US patents 8,178,118; 8,142,803; 8,163,301; and other pending patents.

References

1. What We Eat in America: Mean Energy and Mean Nutrient Amounts per 1000 kcal Consumed per Individual, by Gender and Age. U.S. Department of Agriculture, Agricultural Research Service. https://www.ars.usda.gov/ARSSUserFiles/80400530/pdf/1314/Table_41_DEN_GEN_13.pdf. 2013-2014. Accessed November 18, 2017.
2. Slutsky I, Abumaria N, Wu LJ, et al. Enhancement of learning and memory by elevating brain magnesium. *Neuron*. 2010 Jan 28;65(2):165-77. [PMID: 20152124]
3. Li W, Yu J, Liu Y, et al. Elevation of brain magnesium prevents synaptic loss and reverses cognitive deficits in Alzheimer's disease mouse model. *Mol Brain*. 2014 Sep 13;7(1):65. [PMID: 25213836]
4. Abumaria N, Yin B, Zhang L, et al. Effects of elevation of brain magnesium on fear conditioning, fear extinction, and synaptic plasticity in the infralimbic prefrontal cortex and lateral amygdala. *J Neurosci*. 2011 Oct 19;31(42):14871-81. [PMID: 22016520]
5. Slutsky I, Sadeghpour S, Li B, et al. Enhancement of synaptic plasticity through chronically reduced Ca²⁺ flux during uncorrelated activity. *Neuron*. 2004 Dec 2;44(5):835-49. [PMID: 15572114]
6. Sun Q, Weinger JG, Mao F, et al. Regulation of structural and functional synapse density by L-threonate through modulation of intraneuronal magnesium concentration. *Neuropharmacology*. 2016 Sep;108:426-39. [PMID: 27178134]
7. Wang D, Jacobs SA, Tsien JZ. Targeting the NMDA receptor subunit NR2B for treating or preventing age-related memory decline. *Expert Opin Ther Targets*. 2014 Oct;18(10):1121-30. [PMID: 25152202]
8. Liu G, Weinger JG, Lu ZL, et al. Efficacy and safety of mms-01, a synapse density enhancer, for treating cognitive impairment in older adults: a randomized, double blind, placebo-controlled trial. *J Alzheimers Dis*. 2015 Oct 27;49(4):971-90. [PMID: 26519439]
9. Taylor L, Mumford P, Roberts M, et al. Safety of TeaCrine®, a non-habituating, naturally occurring purine alkaloid over eight weeks of continuous use. *J Int Soc Sports Nutr*. 2016 Jan 13;13:2. [PMID: 26766930]
10. Habowski S, Sandrock J, Kedia A, et al. The effects of Teacrine™, a nature-identical purine alkaloid, on subjective measures of cognitive function, psychometric and hemodynamic indices in healthy humans: a randomized, double-blinded crossover pilot trial. *J Int Soc Sports Nutr*. 2014;11(Suppl 1):P49. doi:10.1186/1550-2783-11-S1-P49.
11. He H, Ma D, Crone LB, et al. Assessment of the drug-drug interaction potential between theacrine and caffeine in humans. *J Caffeine Res*. 2017 Sep 1;7(3):95-102. [PMID: 28875060]
12. Ansari Z. Homocysteine and mild cognitive impairment: are these the tools for early intervention in the dementia spectrum? *J Nutr Health Aging*. 2016 Feb;20(2):155-60. [PMID: 26812511]
13. Garcia A, Zanibbi K. Homocysteine and cognitive function in elderly people. *CMAJ*. 2004 Oct 12;171(8):897-904. [PMID: 15477631]
14. Puri V, Chaudhry N, Goel S, et al. Vitamin B12 deficiency: a clinical and electrophysiological profile. *Electromyogr Clin Neurophysiol*. 2005 Jul/Aug;45(5):273-84. [PMID: 16218195]
15. Clarke R. Lowering blood homocysteine with folic acid based supplements: meta-analysis of randomised trials. *Indian Heart J*. 2000 Nov-Dec;52(7 Suppl):S59-64. [PMID: 11339443]
16. Shane B. Folic acid, vitamin B-12, and vitamin B-6. In: Stipanuk M, ed. *Biochemical and Physiological Aspects of Human Nutrition*. Philadelphia: W.B. Saunders Co.; 2000:483-518.

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.



Available in 60 and 120 capsules

Discussion

ColonX™ addresses an issue of universal importance: gastrointestinal (GI) health. GI regularity and function is vital to physiological balance and overall well-being. How well the body digests, assimilates, and eliminates metabolic fuel and metabolic waste determines health at the cellular level. Toxins that enter the body must be detoxified and their metabolites must exit the body. Gastrointestinal elimination plays a major role in detoxification by expelling the remnants of toxic molecules. If these harmful remnants are not eliminated, they can recirculate throughout the body.*

Magnesium Magnesium citrate, the type of magnesium in ColonX, is used for colonoscopy preparation. Chosen for its promotion of muscle relaxation and effective elimination of feces through the bowel, magnesium citrate is also highly bioavailable.^[1] It should be noted that particular forms of magnesium may be absorbed differently. Please note that while magnesium citrate is best suited to support gastrointestinal elimination, the patented amino acid chelates such as the lysyl glycinate and dimagnesium malate chelates in XYMOGEN's OptiMag 125™ formula are designed to be bioavailable and easily absorbed.*

As a macromineral, magnesium supports cell, tissue, and organ function and participates in over 300 metabolic reactions in the body. This essential mineral plays a pivotal role in energy-producing reactions, detoxification, muscle and nerve function, and skeletal structure.^[2,3] Magnesium can readily become depleted due to inadequate intake, poor absorption, excessive losses, and drug-induced nutrient depletions.*

Cape Aloe (*Aloe ferox*) Cape Aloe has a long history of use in South Africa and continues to be closely studied for its valuable attributes,^[4] specifically how it supports GI regularity. The herb is ideally used in the short term to support the elimination of feces and subsequently the elimination of toxins. Recent research suggests that Cape Aloe supports gastrointestinal regularity and is well tolerated. Administration of the herb in animals showed no negative toxicological

Clinical Applications

- » Supports Digestion, Assimilation, and Elimination*
- » Promotes Gastrointestinal Motility and Stool Bulk*
- » Supports Final Phases of Detoxification*

*ColonX™ is designed to support gastrointestinal (GI) regularity and complement dietary fiber intake. Magnesium citrate is present to support muscle relaxation and bowel elimination. Cape Aloe is added to support normal GI transit time and stool bulk. Triphala, a balanced blend of astringent fruits used extensively in Ayurveda, is present to support all phases of digestion, assimilation, and elimination. Gastrointestinal regularity in turn plays a fundamental role in detoxification, providing a major route for elimination of toxins.**

effects at doses of up to 200 mg/kg body weight over a seven-day period.*^[5]

Triphala Triphala comprises three sour, astringent fruits: *Emblia officinalis* (amla), *Terminalia bellerica* (behada), and *Terminalia chebula* (harada). This tannin-rich herbal compound has been used traditionally for supporting digestion, assimilation, and elimination.^[6] Triphala is considered to be a cornerstone of the art and practice of Ayurveda, and it is used throughout India in herbal products. Modern-day clinical trials have confirmed the benefits of traditional uses of triphala, especially gastrointestinal support. Researchers indicated that triphala positively supports appetite, GI health, and rejuvenation.*^[7]

ColonX is intended for short-term use only and should never be consumed during pregnancy. Follow directions and label cautions carefully.*

ColonX™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Magnesium (as magnesium citrate)	200 mg	48%
Triphala Extract (Emblca officinalis)(fruit), (Terminalia chebula)(fruit), (Terminalia bclerica)(fruit)(45% tannins)	250 mg	**
Cape Aloe (<i>Aloe ferox</i>)(leaf)	50 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, silica, and medium-chain triglyceride oil.**DIRECTIONS:** Take one to two capsules at bedtime with 8 oz of water, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.**CAUTIONS: DO NOT USE IF YOU ARE PREGNANT OR NURSING.** Discontinue use if diarrhea or abdominal pain develops. Intended for occasional support of bowel movements.**STORAGE:** Keep tightly closed in a cool, dry place out of reach of children**References:**

1. Walker AF, Marakis G, Christie S, et al. Mg citrate found more bioavailable than other Mg preparations in a randomised, double-blind study. *Magnes Res.* 2003 Sep; 16(3):183-91. [PMID: 14596323]
2. Laires MJ, Monteiro CP, Bicho M. Role of cellular magnesium in health and human disease. *Front Biosci.* 2004 Jan 1;9:262-76. [PMID: 14766364]
3. Krinsky DL, LaValle JB, Hawkins EB, et al. *Natural Therapeutics Pocket Guide*, 2nd ed. Hudson, OH: Lexi-Comp; 2003.
4. Magwa ML, Gundidza M, Coopoosamy RM, et al. Chemical composition of volatile constituents from the leaves of *Aloe ferox*. *Afr J Biotechnol.* 2006 Sept;5(18):1652-1654.
5. Wintola OA, Sunmonu TO, Afolayan AJ. Toxicological evaluation of aqueous extract of *Aloe ferox* Mill. in loperamide-induced constipated rats. *Hum Exp Toxicol.* 2011 May;30(5):425-31. [PMID: 20498033]
6. Jagetia GC, Baliga MS, Malagi KJ, et al. The evaluation of the radioprotective effect of Triphala (an ayurvedic rejuvenating drug) in the mice exposed to gamma-radiation. *Phytomedicine.* 2002 Mar;9(2):99-108. [PMID: 11995956]
7. Mukherjee PK, Rai S, Bhattacharyya S, et al. Clinical study of "triphala" – a well-known phytomedicine from India. *Iranian J Pharmacol Ther.* 2006 Jan;5(1):51-54. <http://www.bioline.org.br/request?pt06008>. Accessed June 18, 2012.

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration.
This product is not intended to diagnose, treat, cure, or prevent any disease.

ConjuLean 1000™

Patented Conjugated Linoleic Acid in a Pure 78% Form



Available in 120 softgels

Discussion

Conjugated linoleic acid (CLA) is a fatty acid found in small amounts in the human diet and can amount to an estimated average intake of 0.35-0.43 g CLA per day.^[1] Research using higher doses of CLA (via supplementation) suggests that it reduces body fat in a dose-related manner. A 2007 meta-analysis of randomized, double-blind, placebo-controlled (RDBPC) human trials revealed that a mean dose of 3.2 g CLA per day produced modest fat loss in human subjects.^[2] Four capsules of ConjuLean 1000 provides 3.12 g of CLA in a 50:50 ratio of cis-9,trans-11 (c9,t11) and trans-10,cis-12 (t10,c12) isomers, the composition commonly used in clinical studies. Though c9,t11 is the principal CLA isomer found in food, t10,c12 appears to specifically affect fat cells by inhibiting lipoprotein lipase and stearoyl-CoA desaturase, resulting in reduced uptake of lipids into adipocytes.^{*[3]}

A three-month RDBPC study of 60 overweight or obese volunteers was conducted utilizing various doses of CLA. A significantly higher reduction in body fat mass (BFM) was seen in all CLA groups compared to placebo. However, no further reduction in BFM occurred with doses >3.4 g/day.^[4] A six-month clinical trial suggested that fat loss from CLA supplementation occurred primarily in the abdominal area and legs of females and in the abdomen of males without specific diet or exercise efforts. No adverse effects on blood parameters or insulin sensitivity were observed.^[5] In 2004, a long-term RDBPC study was performed in healthy, overweight subjects. After 12 months, BFM was significantly reduced in subjects receiving CLA (50:50 ratio of c9,t11 and t10,c12) in both triacylglycerol and free fatty acid form when compared to placebo. Statistical significance was observed as early as six months and increased as the study progressed. Lean body mass (LBM) was significantly higher in the free fatty acid form of CLA (the form in ConjuLean 1000) when compared to placebo; LBM in the triacylglycerol CLA supplemented group did not differ from placebo.^[6] A 12-month extension study suggested that long-term CLA supplementation decreased BFM, was well tolerated, and helped maintain reductions in body fat and weight over time.^{*[7]}

Interestingly, CLA supplementation was found to decrease body fat percentage even in normal weight subjects. Without changing diet, calorie intake, or lifestyle, the group consuming 2.4 g CLA in

Clinical Applications

- » Supports Healthy Body Composition*
- » Helps Decrease Catabolic Effect of Training on Muscle Protein*
- » Affects the Production of Cytokines and Arachidonic Acid-Derived Eicosanoids*

*ConjuLean 1000™ is a patented form of conjugated linoleic acid (CLA). The yield of CLA is at least 78%, providing 1.56 g of pure CLA per serving. Animal and human studies suggest that CLA may reduce body fat and help maintain healthy body composition and lean muscle mass. ConjuLean 1000 is guaranteed to provide the highest levels of pure CLA and contains those isomers that are most commonly associated with positive health benefits. While CLA in the diet is found primarily in dairy products and beef fat, ConjuLean 1000 is derived from pure, non-GMO safflower oil.**

an RDBPC study experienced a decrease in body fat from 21.3 to 17% (representative of a 15-20% reduction in fat but no change in weight) while the placebo group experienced an increase in body fat.^[8,9] In fact, when calories are restricted by more than 200 per day, hypocaloric intake appears to negate the effects of CLA on fat loss.^[10] Although the mechanism of action of CLA is not completely understood in humans, animal studies suggest that CLA upregulates gene expression of mitochondrial uncoupling proteins and lipid metabolizing proteins. These modifications ultimately contribute to reduced fat mass and increased LBM. CLA affects peroxisome proliferator-activated receptors as well. These nuclear receptors are found to regulate metabolic processes in the cell.^{*[11]}

A seven-week, randomized, placebo-controlled, crossover study addressing the effects of 5 g/day of CLA on muscle resistance training suggested that the CLA group had a significant increase in lean tissue mass, a significant decrease in fat mass, and a “lessening of the catabolic effect of training on muscle protein.”^[12] A study of 44 healthy young women suggested that supplementing with 3.6 g of CLA alone or with exercise helped maintain healthy glucose metabolism.^{*[13]}

Research in vivo and in vitro suggested that CLA affected the production and balance of arachidonic acid-derived eicosanoids, NF-kappaB, COX-2 enzymes, and cytokines.^[14,15] A double-blind, randomized study of 28 healthy subjects revealed that levels of TNF-alpha and IL-1beta were significantly decreased ($P < 0.05$) and levels of IL-10 were significantly increased ($P < 0.05$) following supplementation with 3 g/d CLA (50:50 ratio of c9,t11 and t10,c12 CLA).^[15] Supplementation with 2.5 g/d of CLA (equivalent to 2 g/d 50:50 ratio of c9,t11 and t10,c12 CLA) produced statistically significant test results that reflected a decrease in joint discomfort and stiffness in a randomized, double-blind placebo controlled three-month study. When combined with alpha-tocopherol, supplementation with CLA produced a significant decrease in erythrocyte sedimentation rate (ESR).^{*[16]}

ConjuLean 1000™ Supplement Facts

Serving Size: 2 Softgels

	Amount Per Serving	%Daily Value
Calories	20	
Total Fat	2 g	3%†
Conjugated Linoleic Acid (CLA)	1.56 g	**

†Percent Daily Values are based on a 2,000 calorie diet.
** Daily Value not established.

Other ingredients: Softgel (bovine gelatin, glycerin, and natural caramel color), and mixed natural tocopherols.

DIRECTIONS: Take one to two softgels twice daily with food, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy protein, dairy products, fish, shellfish, peanuts, tree nuts, egg, artificial colors, artificial sweeteners, or artificial preservatives.

References

1. Natural Standard Database. Conjugated Linoleic Acid. <http://naturalstandard.com/databases/herbssupplements/patient-conjugatedlinoleicacid.asp#undefined>. Accessed August 13, 2012.
2. Whigham LD, Watras AC, Schoeller DA. Efficacy of conjugated linoleic acid for reducing fat mass: a meta-analysis in humans. *Am J Clin Nutr*. 2007 May;85(5):1203-11. [PMID: 17490954]
3. Pariza MW, Park Y, Cook ME. The biologically active isomers of conjugated linoleic acid. *Prog Lipid Res*. 2001 Jul;40(4):283-98. [PMID: 11412893]
4. Blankson H, Stakkestad JA, Fagertun H, et al. Conjugated linoleic acid reduces body fat mass in overweight and obese humans. *J Nutr*. 2000 Dec;130(12):2943-8. [PMID: 11110851]
5. Clarinol. <http://www.clarinol.com/HealthBenefits/ResearchResults/>. Accessed August 16, 2012.
6. Gaullier JM, Halse J, Høye K, et al. Conjugated linoleic acid supplementation for 1 y reduces body fat mass in healthy overweight humans. *Am J Clin Nutr*. 2004 Jun;79(6):1118-25. [PMID: 15159244]
7. Gaullier JM, Halse J, Høye K, et al. Supplementation with conjugated linoleic acid for 24 months is well tolerated by and reduces body fat mass in healthy, overweight humans. *J Nutr*. 2005 Apr;135(4):778-84. [PMID: 15795434]
8. Pizzorno, LU, Pizzorno, JE, Murray MT. *Natural Medicine Instructions for Patients*. Churchill Livingstone; 2002.
9. Thom E, Wadstein J, Gudmundsen O. Conjugated linoleic acid reduces body fat in healthy exercising humans. *J Int Med Res*. 2001 Sep-Oct;29(5):392-6. [PMID: 11725826]
10. Park Y. Conjugated linoleic acid (CLA): Good or bad trans fat? *Journal of Food Composition and Analysis*. Dec 2009;22(Suppl):S4-S12. <http://dx.doi.org/10.1016/j.jfca.2008.12.002>.
11. Peters JM, Park Y, Gonzalez FJ, et al. Influence of conjugated linoleic acid on body composition and target gene expression in peroxisome proliferator-activated receptor alpha-null mice. *Biochim Biophys Acta*. 2001 Oct 31;1533(3):233-42. [PMID: 11731333]
12. Pinkoski C, Chilibeck PD, Candow DG, et al. The effects of conjugated linoleic acid supplementation during resistance training. *Med Sci Sports Exerc*. 2006 Feb;38(2):339-48. [PMID: 16531905]
13. Colakoglu S, Colakoglu M, Tanelli F, et al. Cumulative effects of conjugated linoleic acid and exercise on endurance development, body composition, serum leptin and insulin levels. *J Sports Med Phys Fitness*. 2006 Dec;46(4):570-7. [PMID: 17119522]
14. Li G, Barnes D, Butz D, et al. 10t,12c-conjugated linoleic acid inhibits lipopolysaccharide-induced cyclooxygenase expression in vitro and in vivo. *J Lipid Res*. 2005 Oct;46(10):2134-42. [PMID: 16061956]
15. Song HJ, Grant I, Rotondo D, et al. Effect of CLA supplementation on immune function in young healthy volunteers. *Eur J Clin Nutr*. 2005 Apr;59(4):508-17. [PMID: 15674307]
16. Aryaeian N, Shahram F, Djalali M, et al. Effect of conjugated linoleic acids, vitamin E and their combination on the clinical outcome of Iranian adults with active rheumatoid arthritis. *Int J Rheum Dis*. 2009 Apr;12(1):20-8. [PMID: 20374312]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

CoQmax™ ME and CoQmax™-100 ME

Proprietary Micro-Emulsified CoQ10



CoQmax™ ME is available in 30 softgels & 120 softgels
CoQmax™-100 ME is available in 60 softgels

Discussion

Coenzyme Q10 (CoQ10) is a fat-soluble substance that plays a major role in energy production and antioxidant protection in the body. It is found in the body primarily in its interchangeable ubiquinone and ubiquinol forms. In general, CoQ10 supports mitochondrial energy production, antioxidant activity, cell membrane stabilization, gene expression and apoptosis, and neurological and cardiovascular health.^[1,2] Levels of CoQ10 in the body can be affected by a number of factors. Dietary contribution of CoQ10 is minimal and serum levels tend to decline with age or can be reduced due to drug-induced nutrient depletion.^{*(3-5)}

Synthesis of CoQ10 in the body is regulated by the enzyme HMG-CoA reductase. A variety of factors can inhibit HMG-CoA reductase and hinder CoQ10 production and availability, resulting in a potential increase in oxidative stress and a decrease in energy generation. In the event of reduced production, or drug-induced nutrient depletion, physicians recommend supplementation with CoQ10 to help maintain normal levels in the body.^[6,7] Supplementation with CoQ10 has been found to promote favorable outcomes for a targeted group of patients^[8] and to improve quality of life, energy levels, neurological health maintenance, exercise tolerance, and muscle comfort for a wide range of individuals.^[1,9] A research study utilizing functional intracellular assay (FIA) suggested that CoQ10 may be a potential peripheral biomarker of antioxidant status in neurological health maintenance.^{*(10)}

Cardiovascular health is particularly dependent upon CoQ10 because of the heart muscle's exceedingly high energy demand.^[9] The value of CoQ10 supplementation on cardiovascular health has been confirmed by ongoing human research studies.^[6,11-13] A randomized, double-blind, placebo-controlled study utilizing the same bioidentical, naturally yeast-fermented CoQ10 found in CoQmax formulas was conducted in a select group of 49 patients. Researchers observed that supplementation with 100 mg/d of CoQ10 successfully restored plasma levels and significantly increased total CoQ10 levels by 127%.^{*(14)}

Results from the highly anticipated Q-SYMBIO research study were reported in May 2013. Prior to the Q-SYMBIO study, researchers had observed

Clinical Applications

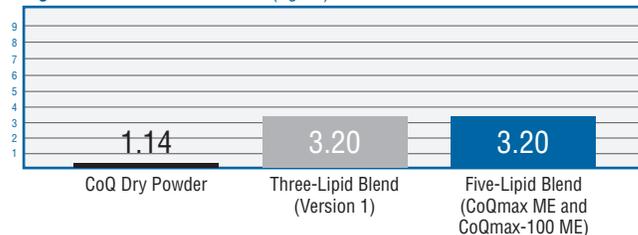
- » Innovative, Soy-Free, Five-Lipid Blend for Enhanced Absorption*
- » Support Natural Energy Generation and Mitochondrial Function*
- » Support Plasma/Tissue CoQ10 Levels*
- » Support Health/Functioning of the Cardiovascular System*
- » Support Neuromuscular and Central Nervous System Health*

*CoQmax™ ME and CoQmax™-100 ME are XYMOGEN's proprietary, micro-emulsified CoQ10 formulas that offer unparalleled absorption and bioavailability. These formulations have been shown in clinical trials to be over eight times more absorbable than powdered CoQ10 and more than twice as bioavailable as oil-based or so-called "nano"-dispersed formulas on the market. The proprietary multilipid carrier employed in CoQmax ME and CoQmax-100 ME is unmatched for optimal utilization in the support of cardiovascular and energy-based health needs.**

that myocardial CoQ10 levels were inversely related to heart health and function.^[15] The Q-SYMBIO results, in fact, supported this association. In the randomized, double-blind, placebo controlled Q-SYMBIO study, 420 patients were assigned to parallel groups to receive either the CoQ10 found in CoQmax (100 mg three times per day) or placebo. Within three months, researchers observed a reduction in N-terminal pro-brain natriuretic peptide (NT-proBNP), an important marker of heart health, in the CoQ10 supplemented patients. After two years, patients who were supplemented with CoQ10 had significant cardiovascular improvement overall compared to placebo.^{*(16,17)}

CoQmax™ ME and CoQmax™-100 ME contain a unique, micro-emulsified, and highly bioavailable form of ubiquinone delivered by a five-lipid-blend carrier system. The two formulas feature US-manufactured Kaneka Q10, a pure form of bioidentical CoQ10 fermented from natural yeast, and do not contain the impurities found in synthetically processed CoQ10. The quality and reliability of this non-GMO and self-affirmed GRAS CoQ10 is supported by 30 years of manufacturing, safety, and clinical studies.*

Figure 1. Plasma CoQ10 Cmax (ug/ml)



Continued on next page

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

CoQmax™ ME Supplement Facts

Serving Size: 1 Softgel

	Amount Per Serving	%Daily Value
Calories	10	
Total Fat	1 g	1%†
Coenzyme Q10 (as ubiquinone)(KanekaQ10®)	50 mg	**

†Percent Daily Values are based on a 2,000 calorie diet.
** Daily Value not established.

Other Ingredients: Proprietary blend of palmitic acid, oleic acid, and linoleic acid, safflower oil (non-GMO), medium-chain triglycerides, gelatin, vegetable glycerin, and annatto. Kaneka Q10® is a registered trademark of Kaneka Corp.

DIRECTIONS: Take one softgel one to two times daily, or as directed by your healthcare practitioner. Optimal results may be achieved by consuming with meals that contain fat.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children. Variations in temperature may cloud the softgels. This does not affect the formula's efficacy or safety. Do not refrigerate.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, dairy products, fish, shellfish, peanuts, tree nuts, egg, artificial colors, artificial sweeteners, or artificial preservatives.

CoQmax™-100 ME Supplement Facts

Serving Size: 1 Softgel

	Amount Per Serving	%Daily Value
Calories	15	
Total Fat	1.5 g	2%†
Coenzyme Q10 (as ubiquinone)(KanekaQ10®)	100 mg	**

†Percent Daily Values are based on a 2,000 calorie diet.
** Daily Value not established.

Other Ingredients: Proprietary blend of palmitic acid, oleic acid, and linoleic acid, safflower oil (non-GMO), medium-chain triglycerides, gelatin, vegetable glycerin, and annatto. Kaneka Q10® is a registered trademark of Kaneka Corp.

DIRECTIONS: Take one softgel one to two times daily, or as directed by your healthcare practitioner. Optimal results may be achieved by consuming with meals that contain fat.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children. Variations in temperature may cloud the softgels. This does not affect the formula's efficacy or safety. Do not refrigerate.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, dairy products, fish, shellfish, peanuts, tree nuts, egg, artificial colors, artificial sweeteners, or artificial preservatives.

Figure 2. Cmax % Dose Absorbed

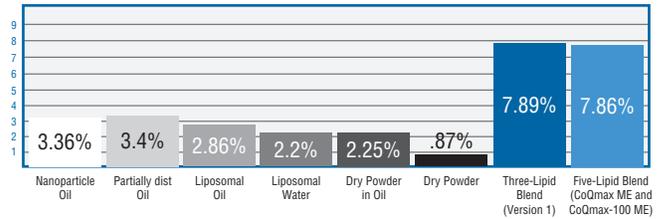
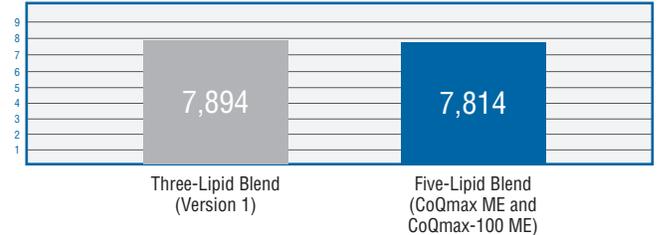


Figure 3. 12-Hour Total Absorption (ug)



References

- Morris G, Anderson G, Berk M, et al. Coenzyme Q10 Depletion in Medical and Neuropsychiatric Disorders: Potential Repercussions and Therapeutic Implications. *Mol Neurobiol*. 2013 Jun 13. [Epub ahead of print] [PMID: 23761046]
- Higdon J. CoQ10. Linus Pauling Institute. <http://lpi.oregonstate.edu/infocenter/othernuts/coq10/>. February 2003. Updated March 2012. Accessed July 25, 2013.
- Pelton R, LaValle JB, Hawkins EB, et al. *Drug-Induced Nutrient Depletion Handbook*. 2nd ed. Hudson, OH: LexiComp, Inc.; 2001.
- Berthold HK, Naini A, Di Mauro S, et al. Effect of ezetimibe and/or simvastatin on coenzyme Q10 levels in plasma: a randomised trial. *Drug Saf*. 2006;29(8):703-12. [PMID: 16872244]
- Rundek T, Naini A, Sacco R, et al. Atorvastatin decreases the coenzyme Q10 level in the blood of patients at risk for cardiovascular disease and stroke. *Arch Neurol*. 2004 Jun;61(6):889-92. [PMID: 15210526]
- Langsjoen PH, Langsjoen AM. The clinical use of HMG CoA-reductase inhibitors and the associated depletion of coenzyme Q10. A review of animal and human publications. *Biofactors*. 2003;18(1-4):101-11. Review. [PMID: 14695925]
- Crane FL. Biochemical functions of coenzyme Q10. *J Am Coll Nutr*. 2001 Dec;20(6):591-8. Review. [PMID: 11771674]
- Potgieter M, Pretorius E, Pepper MS. Primary and secondary coenzyme Q10 deficiency: the role of therapeutic supplementation. *Nutr Rev*. 2013 Mar;71(3):180-8. [PMID: 23452285]
- Zlatohlavek L, Vrablik M, Grauova B, et al. The effect of coenzyme Q10 in statin myopathy. *Neuro Endocrinol Lett*. 2012;33 Suppl 2:98-101. [PMID: 23183519]
- Mischley LK, Allen J, Bradley R. Coenzyme Q10 deficiency in patients with Parkinson's disease. *J Neurol Sci*. 2012 Jul 15;318(1-2):72-5. [PMID: 22542608]
- Littarru GP, Tian L. Clinical aspects of coenzyme Q10: an update. *Curr Opin Clin Nutr Metab Care*. 2005 Nov;8(6):641-6. Review. [PMID: 16205466]
- Munkholm H, Hansen HH, Rasmussen K. Coenzyme Q10 treatment in serious heart failure. *Biofactors*. 1999;9(2-4):285-9. [PMID: 10416042]
- Fotino AD, Thompson-Paul AM, Bazzano LA. Effect of coenzyme Q10 supplementation on heart failure: a meta-analysis. *Am J Clin Nutr*. 2013 Feb;97(2):268-75. [PMID: 23221577]
- Mabuchi H, Nohara A, Kobayashi J, et al. Effects of CoQ10 supplementation on plasma lipoprotein lipid, CoQ10 and liver and muscle enzyme levels in hypercholesterolemic patients treated with atorvastatin: a randomized double-blind study. *Atherosclerosis*. 2007 Dec;195(2):e182-89. [PMID: 17681347]
- Folkers K, Vadhanavikit S, Mortensen SA. Biochemical rationale and myocardial tissue data on the effective therapy of cardiomyopathy with coenzyme Q10. *Proc Natl Acad Sci U S A*. 1985 Feb;82(3):901-4. [PMID: 3856239]
- Mortensen SA, Kumar A, Dolliner P, et al. The effect of Coenzyme Q10 on morbidity and mortality in chronic heart failure. Results from the Q-SYMBIO study. [ESCARTIO abstract 440]. *European Journal of Heart Failure*. 2013 15(S1):S20. <http://spo.escardio.org/SessionDetails.aspx?eventid=61&fp=440&doc=abstract#UfQgDI2TjSg>. Accessed July 25, 2013.
- European Society of Cardiology. Important new data shows CoQ10 improves survival in heart failure patients. <http://www.escardio.org/congresses/hf2013/congress-to-you/Pages/new-data-CoQ10-improves-survival-heart-failure-patients.aspx>. Accessed July 28, 2013.

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

CoQmax™ Omega

Dual-Action Cardiovascular Support*



CoQmax™ Omega 50 mg available in 30 softgels and 120 softgels
CoQmax™ Omega 100 mg available in 60 softgels

Discussion

CoQMax™ Omega combines micro-emulsified coenzyme Q10 (CoQ10) with enzymatically enhanced MaxSimil® fish oil to deliver a highly absorbable formulation designed to promote optimal cardiovascular health.*

Kaneka CoQ10® (Ubiquinone)

CoQ10 is a fat-soluble compound utilized on a cellular level to generate energy in the form of adenosine triphosphate (ATP) and protect tissues from the burden of oxidative stress, particularly on the heart. CoQ10 is found in the body primarily in its interchangeable ubiquinone and ubiquinol forms.*

In general, CoQ10 supports mitochondrial energy production, antioxidant activity, cell membrane stabilization, gene expression and apoptosis, and neurological and cardiovascular health.^[1,2] Levels of CoQ10 in the body can be affected by a number of factors; dietary contribution is minimal, and serum levels tend to decline with age or can be reduced due to drug-induced depletion.^{*[3-5]}

Synthesis of CoQ10 in the body is regulated by the enzyme HMG-CoA reductase. A variety of factors can inhibit HMG-CoA reductase and hinder CoQ10 production and availability resulting in a potential increase in oxidative stress and a decrease in energy generation. In the event of reduced production or drug-induced depletion, supplementation with CoQ10 is recommended to help maintain normal levels in the body.^{*[6,7]}

The contribution of CoQ10 supplementation to cardiovascular health has been supported in human research studies.^[2,6,8-10] A randomized, double-blind, placebo-controlled study utilizing Kaneka CoQ10 ubiquinone was conducted in a select group of 49 patients. Researchers observed that supplementation with 100 mg/day successfully restored plasma levels and significantly increased total CoQ10 levels by 127%.^{*[11]}

In the randomized, double-blind, placebo-controlled Q-SYMBIO study, 420 patients were assigned to parallel groups to receive CoQ10 (100 mg three times per day) or placebo. Within three months, researchers observed in the CoQ10-supplemented patients a reduction in N-terminal pro-B-type natriuretic peptide (NT-proBNP), an important marker of heart health. After two years, patients who were supplemented with CoQ10 had significant cardiovascular improvement overall compared to placebo.^{*[12]}

In addition to the studies above that explored restoring drug-induced plasma CoQ10 production, research into restoring plasma levels that naturally decline with aging has also been conducted. In a study of older adults (N = 24) supplemented with 300 mg/day of CoQ10 for seven days prior to cardiac surgery, the CoQ10 content of

Clinical Applications

- » Supports Health/Function of the Cardiovascular System*
- » Helps Maintain Natural Plasma/Tissue CoQ10 Levels*
- » Patented Enhanced Absorption of EPA and DHA*

*CoQmax™ Omega formulations provide dual-action cardiovascular support with patented ingredients selected for their individual roles in promoting heart health. MaxSimil® highly absorbable monoglyceride fish oil is International Fish Oil Standards (IFOS) five-star certified. Kaneka Q10®, a naturally pure form of bioidentical CoQ10 (available in 50 mg and 100 mg), is well-researched for boosting energy production in the heart and protecting the cardiovascular system from oxidative stress.**

atrial tissue was significantly increased in those taking the supplement, especially in patients older than 70 years.^{*[13]}

MaxSimil® Fish Oil Concentrate

The two most well-researched omega-3 fatty acids are the biologically activated oils eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). EPA plays a role in supporting healthy cardiac and circulatory systems while DHA is an essential structural component of the central nervous system. In addition to other physiological effects, research has established that omega-3 fatty acids antagonize arachidonic acid-induced eicosanoid formation. They also help generate resolvins and protectins (EPA and DHA metabolites naturally produced in vivo through enzymatic conversion of EPA and DHA) to aid the body's "clean-up" response to the arachidonic acid cascade, and they promote cardiovascular health.^{*[14-21]}

CoQMax Omega features MaxSimil, a novel monoglyceride concentrated fish oil developed using a unique delivery system that enhances absorption of lipid-based and lipid-soluble nutraceutical and food ingredients. Its patented lipid absorption enhancement technology (PLATform) is a unique vehicle by which to deliver EPA and DHA. Due to the fact that monoglyceride oils are intrinsically emulsifiers and are, by nature, in a readily absorbable form, they can bypass the body's normal fat digestion process. Studies conducted by the manufacturer of MaxSimil provide promising results that show MaxSimil oil may be better absorbed than other fish oils. Rather than supplying a single molecule or metabolite, which would mirror the pharmaceutical model, MaxSimil provides all the benefits of EPA and DHA as well as the expected and desirable benefits of their metabolites. From a quality perspective, every batch of fish oil is IFOS five-star certified to ensure the highest standards for purity, potency, and freshness. The fish oil is also non-GMO, certified sustainable from Scandinavia, and antibiotic-free.^{*[22-25]}

An unpublished phase 1, double-blind, randomized, crossover, pharmacokinetic study was performed in healthy adults (n = 20) aged between 19 and 71 years who were administered 6 g (containing 1800 mg EPA and 1200 mg DHA) per day of ethyl ester (EE) fish oil or MaxSimil. Parameters studied were plasma EPA and DHA concentration (as percent of total fatty acids), Cmax, and AUC. Compared to EE EPA+DHA, the results indicated that at peak concentration, MaxSimil EPA and DHA forms were three times higher, they reached maximum concentration faster, and maintained their plasma levels longer demonstrating enhanced clinical bioavailability.^[25] While there is no conclusive published evidence at this time, the results from studies conducted by the makers of MaxSimil provide a promising indication of enhanced absorption rates, and additional peer-reviewed research is warranted.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

CoQmax™ Omega 50 mg Supplement Facts

Serving Size: 1 Softgel

	Amount Per Serving	%Daily Value
MaxSimil® Fish Oil Concentrate	250 mg	**
Total Omega-3 Fatty Acids	174 mg	**
EPA (eicosapentaenoic acid)	115 mg	**
DHA (docosahexaenoic acid)	50 mg	**
Kaneka Q10® Coenzyme Q10 (as ubiquinone)	50 mg	**

** Daily Value not established.

Other Ingredients: Softgel (bovine gelatin, glycerin, purified water, roasted carob powder), yellow beeswax, and mixed natural tocopherols.**Contains:** Fish (anchovy and/or sardine and/or mackerel).**DIRECTIONS:** Take one softgel twice per day, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.**DOES NOT CONTAIN:** Wheat, gluten, corn, yeast, soy protein, dairy products, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

IFOS™ Certification Mark is a registered trademark of Nutrasource Diagnostics Inc.

Manufactured using MaxSimil® fish oil. MaxSimil® is a registered trademark of Ingenutra Inc. Protected under US patents 8,119,690 and 8,198,324; Canadian patents 2672513 and 2677670.

Kaneka Q10® is a registered trademark of Kaneka Corp.

CoQmax™ Omega 100 mg Supplement Facts

Serving Size: 1 Softgel

	Amount Per Serving	%Daily Value
Calories	5	
Total Fat	0.5 g	1%†
MaxSimil® Fish Oil Concentrate	500 mg	**
Total Omega-3 Fatty Acids	348 mg	**
EPA (eicosapentaenoic acid)	230 mg	**
DHA (docosahexaenoic acid)	100 mg	**
Kaneka Q10® Coenzyme Q10 (as ubiquinone)	100 mg	**

† Percent Daily Values are based on a 2,000 calorie diet.

** Daily Value not established.

Other Ingredients: Softgel (bovine gelatin, glycerin, purified water, roasted carob powder), yellow beeswax, and mixed natural tocopherols.**Contains:** Fish (anchovy and/or sardine and/or mackerel).**DIRECTIONS:** Take one softgel twice per day, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.**DOES NOT CONTAIN:** Wheat, gluten, corn, yeast, soy protein, dairy products, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

IFOS™ Certification Mark is a registered trademark of Nutrasource Diagnostics Inc.

Manufactured using MaxSimil® fish oil. MaxSimil® is a registered trademark of Ingenutra Inc. Protected under US patents 8,119,690 and 8,198,324; Canadian patents 2672513 and 2677670.

Kaneka Q10® is a registered trademark of Kaneka Corp.

References

- Morris G, Anderson G, Berk M, et al. Coenzyme Q10 depletion in medical and neuropsychiatric disorders: potential repercussions and therapeutic implications. *Mol Neurobiol.* 2013 Dec;48(3):883-903. [PMID: 23761046]
- Higdon J. CoQ10. Linus Pauling Institute. <https://lpi.oregonstate.edu/mic/dietary-factors/coenzyme-Q10> February 2003. Updated April 2018. Accessed September 5, 2018.
- Pelton R, LaValle JB, Hawkins EB, et al. *Drug-Induced Nutrient Depletion Handbook*. 2nd ed. Hudson, OH: LexiComp, Inc.; 2001.
- Berthold HK, Naini A, Di Mauro S, et al. Effect of ezetimibe and/or simvastatin on coenzyme Q10 levels in plasma: a randomised trial. *Drug Saf.* 2006;29(8):703-12. [PMID: 16872244]
- Rundek T, Naini A, Sacco R, et al. Atorvastatin decreases the coenzyme Q10 level in the blood of patients at risk for cardiovascular disease and stroke. *Arch Neurol.* 2004 Jun;61(6):889-92. [PMID: 15210526]
- Langsjoen PH, Langsjoen AM. The clinical use of HMG CoA-reductase inhibitors and the associated depletion of coenzyme Q10. A review of animal and human publications. *Biofactors.* 2003;18(1-4):101-11. [PMID: 14695925]
- Crane FL. Biochemical functions of coenzyme Q10. *J Am Coll Nutr.* 2001 Dec;20(6):591-8. Review. [PMID: 11771674]
- Littarru GP, Tiano L. Clinical aspects of coenzyme Q10: an update. *Nutrition.* 2010 Mar;26(3):250-4. [PMID: 19932599]
- Munkholm H, Hansen HH, Rasmussen K. Coenzyme Q10 treatment in serious heart failure. *Biofactors.* 1999;9(2-4):285-9. [PMID: 10416042]
- Fotino AD, Thompson-Paul AM, Bazzano LA. Effect of coenzyme Q10 supplementation on heart failure: a meta-analysis. *Am J Clin Nutr.* 2013 Feb;97(2):268-75. [PMID: 23221577]
- Mabuchi H, Nohara A, Kobayashi J, et al. Effects of CoQ10 supplementation on plasma lipoprotein lipid, CoQ10 and liver and muscle enzyme levels in hypercholesterolemic patients treated with atorvastatin: a randomized double-blind study. *Atherosclerosis.* 2007 Dec;195(2):e182-89. [PMID: 17681347]
- Mortensen SA, Rosenfeldt F, Kumar A, et al. The effect of coenzyme Q10 on morbidity and mortality in chronic heart failure: results from Q-SYMBIO: a randomized double-blind trial. *JACC Heart Fail.* 2014 Dec;2(6):641-9. [PMID: 25282031]
- Rosenfeldt FL, Pepe S, Linnane A, et al. The effects of ageing on the response to cardiac surgery: protective strategies for the ageing myocardium. *Biogerontology.* 2002;3(1-2):37-40. [PMID: 12014839]
- Kim YJ, Kim HJ, No JK, et al. Anti-inflammatory action of dietary fish oil and calorie restriction. *Life Sci.* 2006 Apr 18;78(21):2523-32. [PMID: 16438990]
- Maroon JC, Bost JW. Omega-3 fatty acids (fish oil) as an anti-inflammatory: an alternative to nonsteroidal anti-inflammatory drugs for discogenic pain. *Surg Neurol.* 2006 Apr;65(4):326-31. [PMID: 16531187]
- Weylandt KH, Chiu CY, Gomolka B, et al. Omega-3 fatty acids and their lipid mediators: towards an understanding of resolvin and protectin formation. *Prostaglandins Other Lipid Mediat.* 2012 Mar;97(3-4):73-82. [PMID: 22326554]
- Kremmyda LS, Tvrzicka E, Stankova B, et al. Fatty acids as biocompounds: their role in human metabolism, health and disease: a review. part 2: fatty acid physiological roles and applications in human health and disease. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub.* 2011 Sep;155(3):195-218. [PMID: 22286806]
- Weitz D, Weintraub H, Fisher E, et al. Fish oil for the treatment of cardiovascular disease. *Cardiol Rev.* 2010 Sep-Oct;18(5):258-63. [PMID: 20699674]
- Psota TL, Gebauer SK, Kris-Etherton P. Dietary omega-3 fatty acid intake and cardiovascular risk. *Am J Cardiol.* 2006 Aug 21;98(4A):3i-18i. [PMID: 16919512]
- Sasaki J, Yokoyama M, Matsuzaki M, et al. Relationship between coronary artery disease and non-HDL-C, and effect of highly purified EPA on the risk of coronary artery disease in hypercholesterolemic patients treated with statins: sub-analysis of the Japan EPA Lipid Intervention Study (JELIS). *J Atheroscler Thromb.* 2012;19(2):194-204. [PMID: 22186099]
- Zhang J, Wang C, Li L, et al. Inclusion of Atlantic salmon in the Chinese diet reduces cardiovascular disease risk markers in dyslipidemic adult men. *Nutr Res.* 2010 Jul;30(7):447-54. [PMID: 20797476]
- Marik PE, Varon J. Omega-3 dietary supplements and the risk of cardiovascular events: a systematic review. *Clin Cardiol.* 2009 Jul;32(7):365-72. [PMID: 19609891]
- Unpublished, internal data. Ingenutra.
- Fortin S, inventor; Centre de Recherche sur les Biotechnologies Marines, assignee. Compositions comprising polyunsaturated fatty acid monoglycerides or derivatives thereof and uses thereof. US patent 8,198,324. June 12, 2012.
- MaxSimil Patented Lipid Absorption Technology Clinical Study Report: MaxSimil® 3020 Omega-3. Sherbrooke (Québec), Canada: Ingenutra; 2015. [Unpublished, internal data]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

CoQmax™ Ubiquinol

Bioactive Antioxidant Support*



CoQmax™ Ubiquinol available in 60 softgels
CoQmax™ Ubiquinol 200 mg available in 30 softgels

Discussion

CoQ10 and the CoQ10 cycle play fundamental roles in the antioxidant and energy systems of the body. The ubiquinone form of CoQ10 is produced in the mitochondria, where it directly participates in energy production by accepting electrons in the electron transport chain. Through the action of an oxidoreductase enzyme, ubiquinone is rapidly converted to ubiquinol, the lipid-soluble form that supports antioxidant activity throughout the body. Conversion of ubiquinone to ubiquinol declines with age, particularly after age 40. Supplementation may help maintain normal levels of ubiquinol in the body as well as address drug-induced nutrient depletion of CoQ10. Until recently, the ubiquinol form had not been effective as a supplement because it was chemically unstable and easily oxidized. CoQmax Ubiquinol™ contains a patented, absorbable form of ubiquinol that maintains its structure and stability in the gastrointestinal environment.*

Antioxidant Status Oxidative stress is detrimental to the integrity and function of cell membranes and tissues, and ultimately to DNA itself. Antioxidant status must be maintained throughout the body in order to protect vulnerable cells. Research indicates that ubiquinol supports antioxidant activity, including the regeneration of vitamins C and E, helping to maintain normal levels of free radical activity in the body. Researchers also suggest a possible role for CoQ10 in redox control of cell signaling and gene expression.*^[1]

Cholesterol Antioxidant protection is vital to maintaining the integrity of cholesterol and its role as a precursor to vitamin D, hormones, cell membranes, and brain tissue. Reactive oxygen species, including superoxide released by immune cells, cause the oxidation of cholesterol and can turn a vital biochemical precursor into a toxin.*^[2]

CoQ10 Depletion Serum CoQ10 levels decline with age but are also reduced with inhibition of the HMG-CoA reductase enzyme, an enzyme essential to CoQ10 production. In the event of reduced production, or drug-induced nutrient depletion, physicians recommend

Clinical Applications

- » Supports Antioxidant Activity in Lymph, Blood, and Cell Membranes*
- » Provides Fully Reduced Form of CoQ10*
- » Neutralizes Superoxide and Other Free Radicals*
- » Patented, Stabilized Form of Ubiquinol*

*Ubiquinol, the bioactive form of CoQ10, supports antioxidant activity by neutralizing free radicals and toxic superoxides. It supports cytoprotection by minimizing membrane lipid peroxidation as well. The patented, lipid-stabilized form of ubiquinol in CoQmax™ Ubiquinol is present for enhanced bioavailability. Ubiquinol, representing over 90% of total body CoQ10, is efficiently converted to the energy-generating ubiquinone form as the body needs it.**

supplementation with CoQ10 to help maintain normal levels in the body.^[3] Related depletion of vitamin E in lymphocytes may raise further concerns about patients' vulnerability to oxidative stress.*^[4]

Heart Health Research suggests that patients experienced significant support of cardiac function after receiving supplemental ubiquinol (an average 450-580 mg per day). These patients achieved more desirable levels of serum CoQ10 when switched from ubiquinone to ubiquinol.^[5] Researchers suggest that ubiquinol had dramatically improved absorption. Research on the elderly also appears to indicate that supplemental CoQ10 can increase tolerance to aerobic stress in cardiac tissue.*^[6]

Aging The role of CoQ10 in aging has become a topic of great interest. Supplementation with both forms of CoQ10—ubiquinone and ubiquinol—was studied in a SAMP1 mouse model. Results suggest that the ubiquinol form more effectively raised CoQ10 levels in the liver (the main target tissue), followed by kidney, heart, and brain. Ubiquinol also appeared to have a more positive effect on maintenance of healthy function than did ubiquinone.*^[7,8]

Kaneka QH™ Stabilized ubiquinol was developed by Kaneka Corporation^[9] (the world's largest manufacturer of CoQ10) and was found to be safe and bioavailable following single and multiple doses.*^[10]

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

CoQmax™ Ubiquinol Supplement Facts

Serving Size: 2 Softgels

	Amount Per Serving	%Daily Value
Calories	15	
Total Fat	1.5 g	2%†
Kaneka Ubiquinol® Coenzyme Q10 (as ubiquinol)	200 mg	**

† Percent Daily Values are based on a 2,000 calorie diet.
 ** Daily Value not established.

Other Ingredients: Medium-chain triglycerides, softgel (bovine gelatin, glycerin, purified water, and annatto in sunflower oil), ascorbyl palmitate, white beeswax, and sunflower lecithin.

DIRECTIONS: Take one to two softgels daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



Q+®, Kaneka Ubiquinol®, and the quality seal® are registered or pending trademarks of Kaneka Corp.

The use of Ascorbyl Palmitate in the formulation is covered by US patent 6,740,338.

CoQmax™ Ubiquinol 200 mg Supplement Facts

Serving Size: 1 Softgel

	Amount Per Serving	%Daily Value
Calories	10	
Total Fat	1 g	1%†
Kaneka Ubiquinol® Coenzyme Q10 (as ubiquinol)	200 mg	**

† Percent Daily Values are based on a 2,000 calorie diet.
 ** Daily Value not established.

Other Ingredients: Medium-chain triglycerides, softgel (bovine gelatin, glycerin, purified water, and annatto in sunflower oil), ascorbyl palmitate, sunflower lecithin, and white beeswax.

DIRECTIONS: Take one softgel daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



Q+®, Kaneka Ubiquinol®, and the quality seal® are registered or pending trademarks of Kaneka Corp.

The use of Ascorbyl Palmitate in the formulation is covered by US patent 6,740,338.

References

1. Crane FL. Biochemical functions of coenzyme Q10. *J Am Coll Nutr.* 2001 Dec;20(6):591-8. Review. [PMID: 11771674]
2. Cathcart MK, McNally AK, Morel DW, et al. Superoxide anion participation in human monocyte-mediated oxidation of low-density lipoprotein and conversion of low-density lipoprotein to a cytotoxin. *J Immunol.* 1989 Mar 15;142(6):1963-9. [PMID: 2537865]
3. Langsjoen PH, Langsjoen AM. The clinical use of HMG CoA-reductase inhibitors and the associated depletion of coenzyme Q10. A review of animal and human publications. *Biofactors.* 2003;18(1-4):101-11. Review. [PMID: 14695925]
4. Passi S, Stancato A, Aleo E, et al. Statins lower plasma and lymphocyte ubiquinol/ubiquinone without affecting other antioxidants and PUFA. *Biofactors.* 2003;18(1-4):113-24. [PMID: 14695926]
5. Langsjoen PH, Langsjoen AM. Supplemental ubiquinol in patients with advanced congestive heart failure. *Biofactors.* 2008;32(1-4):119-28. [PMID: 19096107]
6. Rosenfeldt FL, Pepe S, Ou R, et al. Coenzyme Q10 improves the tolerance of the senescent myocardium to aerobic and ischemic stress: studies in rats and in human atrial tissue. *Biofactors.* 1999;9(2-4):291-9. [PMID: 10416043]
7. Schmelzer C, Kubo H, Mori M, et al. Supplementation with the reduced form of Coenzyme Q10 decelerates phenotypic characteristics of senescence and induces a peroxisome proliferator-activated receptor-alpha gene expression signature in SAMP1 mice. *Mol Nutr Food Res.* 2010 Jun;54(6):805-15. [PMID: 19960455]
8. Yan J, Fujii K, Yao J, et al. Reduced coenzyme Q10 supplementation decelerates senescence in SAMP1 mice. *Exp Gerontol.* 2006 Feb;41(2):130-40. [PMID: 16387461]
9. Kaneka QH™ Ubiquinol. <http://www.kanekaqh.com>. Accessed December 15, 2011.
10. Hosoe K, Kitano M, Kishida H, et al. Study on safety and bioavailability of ubiquinol (Kaneka QH) after single and 4-week multiple oral administration to healthy volunteers. *Regul Toxicol Pharmacol.* 2007 Feb;47(1):19-28. [PMID: 16919858]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Corticare B™

Enhanced Support for Coenzyme A Production*



Available in 120 capsules and 240 capsules

Discussion

Pantothenic Acid (as d-calcium pantothenate) Pantothenic acid, a B complex vitamin also known as vitamin B5, occurs as an unstable oil. Its water-soluble salt, d-calcium pantothenate, is the form most commonly used in supplements. D-calcium pantothenate is composed of 91.5% pantothenic acid and 7.5% calcium. Among its many physiological functions, pantothenic acid is a precursor to the synthesis of coenzyme A (CoA), is an essential cofactor for ATP production, and is essential to the adrenal cortex for production of glucocorticoids.*

Vitamin B6 (as pyridoxal 5'-phosphate and pyridoxine HCl)

Corticare B™ provides vitamin B6 as both pyridoxine HCl and activated pyridoxal 5'-phosphate, the form in which B6 is transported in the blood. Physiologically, vitamin B6 influences the adrenal glucocorticoid receptor, stimulates the secretion of adrenal catecholamines, and aids in sodium and potassium balance.*

Vitamin C (as magnesium ascorbate) The release of adrenocorticotrophic hormone (ACTH) from the pituitary gland in tandem with the body's physiological response to stress will deplete the relatively large amount of vitamin C typically stored in the adrenal cortex.^[1] This vitamin is essential for the synthesis of epinephrine, the hormone secreted by the adrenal medulla in response to stress. Epinephrine, in turn, plays a role in the synthesis of aldosterone, the hormone that regulates blood pressure, volume, and pH.*

Folate (as calcium folinate and 5-MTHF) Corticare B provides the activated form of folic acid—5-MTHF as Quatrefolic^[2]—to ensure superior bioavailability. Folic acid is important for building and repairing protein that may be broken down by stress hormones. It is also key to the synthesis of serotonin, a neurotransmitter that affects mood, appetite, and sleep,^[3, 4] all of which are often negatively affected by stress.*

Clinical Applications

- » Supports Adrenal Hormone Synthesis*
- » Supports Adrenal Physiological Functions*
- » Supports Energy Production*

*Corticare B™ is formulated to support the body's efforts in adrenal hormone production and energy generation. It provides activated B vitamins, vitamin C, and L-carnitine, as well as BioPerine® to support nutrient absorption. The Quatrefolic®† form of 5-methyltetrahydrofolate (5-MTHF) is present for optimal folate bioavailability. L-carnitine enhances activation of pantothenate kinase—the first, most critical enzyme involved in the metabolic conversion of pantothenic acid to coenzyme A.**

L- Carnitine (as tartrate) This conditionally essential nutrient derived from lysine is needed for the “carnitine shuttle.” It transports long-chain fatty acyl CoA from the outside to the inside of the mitochondria, making it a key nutrient in the production of energy.*

BioPerine® This patented extract of black pepper (*Piper nigrum*) has been shown to significantly enhance the availability of vitamin C and vitamin B6.*^[5]

Corticare B™ Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Vitamin C (as magnesium ascorbate)	37.5 mg	42%
Vitamin B6 (as pyridoxine HCl and pyridoxal 5'-phosphate)	37.5 mg	2206%
Folate (100 mcg DFE as calcium folinate and 100 mcg DFE as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt)	200 mcg DFE	50%
Pantothenic Acid (as d-calcium pantothenate)	375 mg	7500%
Calcium (as d-calcium pantothenate)	30 mg	2%
L-Carnitine (as L-carnitine L-tartrate)	75 mg	**
BioPerine® Black Pepper Extract (<i>Piper nigrum</i>)(fruit)(95% piperine)	1.5 mg	**

** Daily Value not established.
Other Ingredients: HPMC (capsule), microcrystalline cellulose, stearic acid, magnesium stearate, and silica.

DIRECTIONS: Take one capsule twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

BioPerine is a registered trademark of Sabinsa Corp. BioPerine is protected by US patents 5,536,506; 5,744,161; 5,972,382; and 6,054,585.

 **Quatrefolic**® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,662.

**References**

1. Murray RK, Granner DK, Mayes PA, et al. *Harper's Biochemistry*. 25 ed. Stamford, CT: Appleton & Lange; 2000.
2. Quatrefolic® - The fourth generation folate. www.quatrefolic.com. Accessed July 12, 2011.
3. Miller AL. The methylation, neurotransmitter, and antioxidant connections between folate and depression. *Altern Med Rev*. 2008 Sep;13(3):216-26. [PMID: 18950248]
4. Trivedi MH. The link between depression and physical symptoms. *Prim Care Companion J Clin Psychiatry*. 2004;6(Suppl 1):12-6. [PMID: 16001092]
5. BioPerine® - An Ingredient of Sabinsa. www.bioperine.com. Updated April 20, 2010. Accessed July 12, 2011.

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Cortisolv[®]

Natural Stress Buster*



Available in 60 and 120 capsules

Discussion

Cortisolv is a multifunctional herbal supplement that has far-reaching and complementary benefits for individuals seeking help in dealing with everyday stress. It features a unique combination of clinically tested and patented ingredients, including Relora[®], Sensoril[®], and Suntheanine[®], along with banaba leaf and maral extracts. Together, these herbs help the overstressed body and mind work toward their normal state of balance and resolve many of the biochemical changes that occur as a result of repeated, frequent exposure to stressors and cortisol.*

Relora[®] is a patented and proprietary blend of *Magnolia officinalis* and *Phellodendron amurense* bark extracts standardized to honokiol and berberine, respectively. These herbs have a history of traditional use in treating stress and occasional feelings of anxiousness. In modern times, they and their actives (honokiol and berberine) are used to support relaxation and reduce the perception of stress and stress-related eating. Rodent stress studies demonstrate a reduction in induced feelings of anxiousness.^[1,2] Human studies demonstrate positive changes in DHEA (dehydroepiandrosterone) and cortisol levels, less weight gain (compared to controls), and reductions in perceived stress and transitory feelings of anxiousness in subjects taking Relora (500 mg to 750 mg for four to six weeks).^[2-5] As an example, cortisol exposure and psychological mood states were studied in 56 subjects (35 men and 21 women) taking Relora (250 mg twice daily) or placebo. After four weeks of supplementation, salivary cortisol exposure was significantly ($p < 0.05$) lower (-18%) in the Relora group compared to placebo. The Relora group also had significantly better ($p < 0.05$) mood state parameters, including lower indices of overall stress (-11%), tension (-13%), anger (-42%), occasional fatigue (-31%), and confusion (-27%), and higher indices of global mood state (+11%) and vigor (+18%).^{*[3]}

Sensoril[®] is an optimized ashwagandha (*Withania somnifera*) root and leaf extract that represents a major advancement in ashwagandha preparations. Sensoril's proprietary and patented extraction process produces very high, powerful levels of stress-fighting, cognition-enhancing ashwagandha bioactive constituents. In fact, Sensoril is standardized to a minimum of 10% glycowithanolides. Sensoril's excellent safety record is one of the most comprehensive of any ashwagandha ingredient sold.*

Clinical Applications

- » Helps the Body Cope with the Physiological Effects of Stress*
- » Supports Healthy Cortisol Levels*
- » Supports Relaxation and Restful Sleep*
- » Promotes Mental Clarity*
- » Helps Alleviate Occasional Fatigue*

*Cortisolv[®] helps your body resist and recover from the effects of everyday stress. Components of this multifunctional formula have been shown to support healthy cortisol levels, help alleviate occasional fatigue, promote mental clarity, and support relaxation and restful sleep.**

Ashwagandha has been revered as an adaptogen for thousands of years. It is used to balance, energize, and revitalize the body and for its value as a cognition enhancer. Sensoril possesses multiple health benefits, and its superior efficacy has been demonstrated in randomized, double-blind, placebo-controlled human clinical trials.^[6-10] The results of these trials revealed that Sensoril, taken in doses of 500 to 1000 mg/d, supported healthy cortisol and DHEA levels; enhanced working memory, reaction time, and cognitive capacity; improved auditory-verbal working memory; ameliorated negative changes in cardiovascular parameters associated with mental stress; and improved endothelial function and glucose and lipid metabolism.*

Suntheanine[®] is a pure form of L-theanine that is produced via a patented fermentation process, resulting in a 100% pure L-isomer-theanine. Clinical research suggests that 50 to 200 mg/d of Suntheanine naturally stimulates activity in the brain known as alpha waves, which are associated with a relaxed but alert mental state.^[11] L-theanine had significant anti-stress effects on experimental animals under psychosocial stress.^[12] In humans, similar results were observed wherein L-theanine helped the body resist biochemical changes associated with stress.^[13,14] In a randomized, double-blind, placebo-controlled trial, a high dose of Suntheanine (400 mg/d) given to boys, aged 8-12 years, improved aspects of sleep quality, including significantly higher sleep percentage and sleep efficiency scores as well as a non-significant trend for less activity during sleep.^{*[15]}

Banaba Leaf (1% Corosolic Acid) and Maral Extracts Banaba leaf (*Lagerstroemia speciosa*) has a long history of use in folk medicine, particularly in Southeast Asia, as a glucose modulator. More recently, animal and human research on banaba leaf and its actives, including corosolic acid, suggest multiple mechanisms that influence glucose and lipid metabolism.^[16,17] Furthermore, corosolic acid inhibits the enzyme that facilitates the conversion of cortisone to cortisol.^[18] Maral extract (*Rhaponticum carthamoides*) has been widely used in traditional Siberian medicine, mainly to treat overstrain and common weakness resulting from illness. It has also been used historically as a stimulant and a remedy to support male sexual function.^{*[19]}

Continued on next page

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XyMOGEN[®] Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

Cortisol® Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Relora® (a proprietary blend of a patented†1 extract from <i>Magnolia officinalis</i> bark and a proprietary extract from <i>Phellodendron amurense</i> bark)	250 mg	**
Sensoril® Ashwagandha (<i>Withania somnifera</i>) Root and Leaf Extract (10% withanolides)	150 mg	**
Suntheanine® L-Theanine	100 mg	**
Banaba Leaf Extract (<i>Lagerstroemia speciosa</i>) (1% corosolic acid)	50 mg	**
Maral 4-6:1 Extract (<i>Rhaponticum carthamoides</i>) (root)	50 mg	**
** Daily Value not established		

Other Ingredients: HPMC (capsule), L-leucine, ascorbyl palmitate, medium-chain triglyceride oil, silica, and microcrystalline cellulose.

DIRECTIONS: Take one capsule twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, dairy products, fish, shellfish, peanuts, tree nuts, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

Sensoril® is a trademark of Natreon, Inc. and is protected under US patents 6,153,198 and 7,318,938.



Suntheanine®

Suntheanine® is a registered trademark of Taiyo International, Inc. U.S. and International Patents Pending. U.S. Patent Nos. 6831103, 6589566, 6297280.

RELORA

†Relora® is a registered trademark of NPI, LLC
††U.S. Patent No. US 6,582,735

The principal bioactive constituents of this plant are ecdysteroids, flavonoids, and phenolic acids.^[20] A review of maral chemistry and pharmacology calls it an “adaptogenic herbal remedy.”^[20] Furthermore, preliminary animal research suggests that maral lowers corticosterone levels and positively influences glucose and fat metabolism.*^[19]

References

1. Sufka KJ, Roach JT, Chambliss WG Jr, et al. Anxiolytic properties of botanical extracts in the chick social separation-stress procedure. *Psychopharmacology* (Berl). 2001 Jan 1;153(2):219-24. [PMID: 11205422]
2. LaValle JB, Hawkins EB. Botanicals in dietary supplements: Stress and anxiety: the potential benefit of a proprietary combination of magnolia and phellodendron extracts. Dana Point, CA: Integrative Health Resources; 2013:1-15. <http://www.nextpharmaceuticals.com/stage/pdfs/Relora%20Article-2013-LaValle.pdf>. Accessed February 22, 2015.
3. Talbott SM, Talbott JA, Pugh M. Effect of *Magnolia officinalis* and *Phellodendron amurense* (Relora®) on cortisol and psychological mood state in moderately stressed subjects. *J Int Soc Sports Nutr*. 2013 Aug 7;10(1):37. [PMID: 23924268]
4. Garrison R, Chambliss WG. Effect of a proprietary Magnolia and Phellodendron extract on weight management: a pilot, double-blind, placebo-controlled clinical trial. *Altern Ther Health Med*. 2006 Jan-Feb;12(1):50-54. [PMID: 16454147]
5. Kalman DS, Feldman S, Feldman R, et al. Effect of a proprietary Magnolia and Phellodendron extract on stress levels in healthy women: a pilot, double-blind, placebo-controlled clinical trial. *Nutr J*. 2008 Apr 21;7:11. [PMID: 18426577]
6. Pingali U, Pilli R, Fatima N. Effect of standardized aqueous extract of *Withania somnifera* on tests of cognitive and psychomotor performance in healthy human participants. *Pharmacognosy Res*. 2014 Jan;6(1):12-18. [PMID: 24497737]
7. Chengappa KN, Bowie CR, Schlicht PJ, et al. Randomized placebo-controlled adjunctive study of an extract of *withania somnifera* for cognitive dysfunction in bipolar disorder. *J Clin Psychiatry*. 2013 Nov;74(11):1076-83. [PMID: 24330893]
8. Auddy B, Hazra J, Mitra A, et al. A standardized *Withania somnifera* extract significantly reduces stress-related parameters in chronically stressed humans; a double-blind, randomized, placebo-controlled study. *JANA*. 2008;11(1):50-56. http://www.lifeforce.net/pdfs/withania_review.pdf. Accessed February 23, 2015.
9. Pingali U, Pilli R, Fatima N. Effect of *Withania somnifera* extract on mental stress induced changes in hemodynamic properties and arterial wave reflections in healthy subjects. *Curr Top Nutraceutical Res*. 2013;11(4):151-158. [on file]
10. Pingali U, Fatima N, Kumar CU, et al. Evaluation of a highly standardized *Withania somnifera* extract on endothelial dysfunction and biomarkers of oxidative stress in patients with type 2 diabetes mellitus: a randomized, double blind, placebo controlled study. *Int J Ayur Pharma Research*. 2014;2(3):22-32. <http://ijapr.in/articles/research/231482.pdf>. Accessed February 23, 2015.
11. Nobre AC, Rao A, Owen GN. L-theanine, a natural constituent in tea, and its effect on mental state. *Asia Pac J Clin Nutr*. 2008;17 Suppl 1:167-8. [PMID: 18296328]
12. Tian X, Sun L, Gou L, et al. Protective effect of L-theanine on chronic restraint stress-induced cognitive impairments in mice. *Brain Res*. 2013 Mar 29;1503:24-32. [PMID: 23395732]
13. Unno K, Tanida N, Ishii N, et al. Anti-stress effect of theanine on students during pharmacy practice: positive correlation among salivary α-amylase activity, trait anxiety and subjective stress. *Pharmacol Biochem Behav*. 2013 Oct;111:128-35. [PMID: 24051231]
14. Yoto A, Motoki M, Murao S, et al. Effects of L-theanine or caffeine intake on changes in blood pressure under physical and psychological stresses. *J Physiol Anthropol*. 2012 Oct 29;31:28. [PMID: 23107346]
15. Lyon MR, Kapoor MP, Juneja LR. The effects of L-theanine (Suntheanine®) on objective sleep quality in boys with attention deficit hyperactivity disorder (ADHD): a randomized, double-blind, placebo-controlled clinical trial. *Altern Med Rev*. 2011 Dec;16(4):348-54. [PMID: 22214254]
16. Miura T, Takagi S, Ishida T. Management of diabetes and its complications with banaba (*lagerstroemia speciosa* l.) and corosolic acid. *Evid Based Complement Alternat Med*. 2012;2012:871495. [PMID: 23082086]
17. Miura T, Itoh Y, Kaneko T, et al. Corosolic acid induces GLUT4 translocation in genetically type 2 diabetic mice. *Biol Pharm Bull*. 2004 Jul;27(7):1103-05. [PMID: 15256748]
18. Rollinger JM, Kratschmar DV, Schuster D, et al. 11β-Hydroxysteroid dehydrogenase 1 inhibiting constituents from *Eriobotrya japonica* revealed by bioactivity-guided isolation and computational approaches. *Bioorg Med Chem*. 2010 Feb 15;18(4):1507-15. [PMID: 20100662]
19. Dushkin M, Khrapova M, Kovshik G, et al. Effects of *rhaponticum carthamoides* versus *glycyrrhiza glabra* and *punica granatum* extracts on metabolic syndrome signs in rats. *BMC Complement Altern Med*. 2014 Jan 20;14:33. [PMID: 24444255]
20. Kokoska L, Janovska D. Chemistry and pharmacology of *Rhaponticum carthamoides*: a review. *Phytochemistry*. 2009 May;70(7):842-55. [PMID: 19457517]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

CurcuPlex CR™

Curcumin with Enhanced Bioavailability*



Available in 60 tablets and 120 tablets

Discussion

The therapeutic effectiveness of curcumin is limited due to its poor absorption from the gastrointestinal (GI) tract, rapid metabolism, and rapid systemic elimination. Instead of increasing the dose, CurcuPlex CR is formulated to increase the amount of curcumin absorbed and bioavailable. It combines turmeric rhizome extract (95% curcuminoids) with BioPerine, a patented extract of piperine from black pepper fruit. BioPerine has GRAS (generally recognized as safe) status and is a clinically validated bio-absorption enhancer. It works by optimizing the body's natural thermogenic activity, thereby selectively providing a more efficient mode of nutrient transportation into the blood. Piperine improves the bioavailability of curcumin both in preclinical studies and in studies on human volunteers. At a dose of 2 g curcumin alone, serum levels were either undetectable or very low in human volunteers. But, curcumin administered with piperine produced much higher serum concentrations from 0.25 – one hour after ingestion with a 2000% increase in bioavailability.^[1] In animals, co-administration with piperine significantly increased time to maximum serum concentration, while elimination half-life and clearance were significantly decreased.*^[1]

Combining BioPerine with curcumin results in *significantly increased utilization of smaller quantities* for optimal clinical outcomes. But CurcuPlex CR doesn't stop there. It also employs a patented, controlled-release delivery technology that prolongs GI transit time and increases curcumin's bioavailability up to 30% over standard delivery systems.*

Curcumin is a phenolic phytochemical purified from turmeric (*Curcuma longa*)—an herb extensively used in both Chinese and Ayurvedic herbology to relieve a variety of complaints. Historically, turmeric has been used for its effect on smooth muscle function and its ability to improve digestion. More recently, the cell-protecting and immunomodulatory properties of curcumin have become areas of great interest to the scientific community.*

Clinical Applications

- » Supports Brain and Neuronal Health*
- » Supports a Normal Immune Response*
- » Provides Antioxidant and Cell-Protective Activity*
- » Supports Healthy Microbial Environment*

*CurcuPlex CR™ provides curcumin, a phenolic phytochemical obtained from turmeric (Curcuma longa). To significantly enhance curcumin's naturally poor bioavailability, XYMOGEN combined turmeric extract (95% curcuminoids) with BioPerine®, a patented black pepper extract and natural bio-enhancer, and added a time-release delivery method. The antioxidant, cell-protective, and immunomodulatory properties of curcumin have interested researchers for years.**

Immune Support and Antioxidant Activity Research has demonstrated that curcumin has antioxidant activity, is an immune cell modulator, and has inhibitory effects on COX-2, iNOS enzymes, TNF- α , IL, and NF- κ B^[2,3], making it applicable to a wide array of clinical presentations. Various animal and human studies support its use in promoting health in joints, gastrointestinal mucosa, and the eye's uveal tract.^[2-8] Other research suggests curcumin may support balanced immune response in the nervous, cardiovascular, GI, and respiratory systems.^[2,3,9] Neurological tissue is particularly susceptible to oxidative stress due to its high demand for oxygen, high levels of polyunsaturated fatty acids in neural membrane phospholipids, and low antioxidant defenses.^[10] Exciting new research in the field of brain and neurological health points to the protective effects of curcumin.^[10-12] Interest in curcumin in this regard is related to its oxidant/immune modulating activity and positive effect on brain amyloid plaques.^[10] Typical doses in human studies ranged from 375 mg -1,200 mg curcumin per day.*

Cell-Protective In animal models, curcumin has demonstrated desirable activity in promoting normal cell proliferation in many, but not all, cell lines.^[2,3] Mechanisms appear to include curcumin's ability to modulate certain types of cytokines (especially transcription factor NF- κ B), support detoxification, scavenge free radicals, and to support induction of cell cycle arrest and apoptosis.^[2,3,13,14] Animal studies, and Phase I and Phase II clinical trials are encouraging; more clinical trials are needed and underway.^[2] Typical doses in human studies ranged from 450 mg – 3,600 mg curcumin per day for up to four months.*

Healthy Microbial Environment Curcumin has long been used to support a healthy microbial balance; this historical use has been supported by more recent in vitro studies.*^[2,3,15,16]

CurcuPlex CR™ Supplement Facts

Serving Size: 4 Tablets

	Amount Per Serving	%DV
Turmeric Extract (<i>Curcuma longa</i>)(root)(95% curcuminoids)	1.4 g	**
Black Pepper Extract (<i>Piper nigrum</i>)(fruit)(95% piperine)(BioPerine®)	14 mg	**

** Daily Value not established.

Other Ingredients: Dicalcium phosphate dihydrate, guar gum (high viscosity), microcrystalline cellulose, hydroxypropyl methyl cellulose (high viscosity), stearic acid, silica, coating (tapioca maltodextrin, sunflower lecithin, palm oil, guar gum), and magnesium stearate. BioPerine is a registered trademark of Sabinsa Corp. BioPerine is protected by US patents 5,536,506; 5,744,161; 5,972,382; and 6,054,585.

DIRECTIONS: Take one to four tablets daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication, especially blood thinners or cancer treatment, should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.

References

1. Shoba G, Joy D, Joseph T, et al. Influence of piperine on the pharmacokinetics of curcumin in animals and human volunteers. *Planta Med* 1998 May;64(4):353-56. [PMID: 9619120]
2. Jurenka JS. Anti-inflammatory properties of curcumin, a major constituent of *Curcuma longa*: a review of preclinical and clinical research. *Altern Med Rev*. 2009 Jun;14(2):141-53. [PMID: 19594223]
3. Jagetia GC, Aggarwal BB. "Spicing up" of the immune system by curcumin. *J Clin Immunol*. 2007 Jan;27(1):19-35. [PMID: 17211725]
4. Ukil A, Maity S, Karmakar S, et al. Curcumin, the major component of food flavour turmeric, reduces mucosal injury in trinitrobenzene sulphonic acid-induced colitis. *Br J Pharmacol*. 2003 May;139(2):209-18. [PMID: 12770926]
5. Epstein J, Docena G, MacDonald TT, et al. Curcumin suppresses p38 mitogen-activated protein kinase activation, reduces IL-1beta and matrix metalloproteinase-3 and enhances IL-10 in the mucosa of children and adults with inflammatory bowel disease. *Br J Nutr*. 2010 Mar;103(6):824-32. [PMID: 19878610]
6. Funk JL, Oyarzo JN, Frye JB, et al. Turmeric extracts containing curcuminoids prevent experimental rheumatoid arthritis. *J Nat Prod*. 2006 Mar;69(3):351-55. [PMID: 16562833]
7. Holt PR, Katz S, Kirshoff R. Curcumin therapy in inflammatory bowel disease: a pilot study. *Dig Dis Sci*. 2005 Nov;50(11):2191-93. [PMID:16240238]
8. Lal B, Kapoor AK, Asthana OP, et al. Efficacy of curcumin in the management of chronic anterior uveitis. *Phytother Res*. 1999 Jun;13(4):318-22. [PMID: 10404539]
9. Dhillon N, Aggarwal BB, Newman RA, et al. Phase II trial of curcumin in patients with advanced pancreatic cancer. *Clin Cancer Res*. 2008 Jul;14(14):4491-99. [PMID: 18628464]
10. Sun AY, Wang Q, Simonyi A, et al. Botanical phenolics and brain health. *Neuromolecular Med*. 2008;10(4):259-74. [PMID: 19191039]
11. Xie L, Li XK, Takahara S. Curcumin has bright prospects for the treatment of multiple sclerosis. *Int Immunopharmacol*. 2011 Mar;11(3):323-30. [20828641]
12. Mythri RB, Harish G, Dubey SK, et al. Glutamoyl diester of the dietary polyphenol curcumin offers improved protection against peroxynitrite-mediated nitrosative stress and damage of brain mitochondria in vitro: implications for Parkinson's disease. *Mol Cell Biochem*. 2011 Jan;347(1-2):135-43. [PMID: 20972609]
13. Ravindran J, Prasad S, Aggarwal BB. Curcumin and cancer cells: how many ways can curry kill tumor cells selectively? *AAPS J*. 2009 Sep;11(3):495-510. [PMID: 9619120]
14. Goel A, Aggarwal BB. Curcumin, the golden spice from Indian saffron, is a chemosensitizer and radiosensitizer for tumors and chemoprotector and radioprotector for normal organs. *Nutr Cancer*. 2010 Oct;62(7):919-30. [PMID: 20924967]
15. Neelofar K, Shreaz S, Rimple B, et al. Curcumin as a promising anticandidal of clinical interest. *Can J Microbiol*. 2011 Mar;57(3):204-10. [PMID: 21358761]
16. Martins CV, da Silva DL, Neres AT, et al. Curcumin as a promising antifungal of clinical interest. *J Antimicrob Chemother*. 2009 Feb;63(2):337-39. [PMID: 19038979]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

CurcuPlex-95™

BCM-95® Curcumin Complex



Available in 60 capsules and 120 capsules

Discussion

Curcumin, the principal curcuminoid in turmeric, has been the subject of vast research in recent years. The pleiotropic nature of curcumin's biological effects make it an interesting compound to researchers who study common chronic health concerns, such as those associated with joints, the cardiovascular system, glucose metabolism, brain function, mood, and cell-cycle regulation.^{*[1-6]}

The mechanisms underlying curcumin's effects are diverse and have not been fully elucidated, but it is known that curcumin has powerful antioxidant activity and that it has multiple molecular targets, including transcription factors, cell cycle proteins, cytokines, chemokines, enzymes (e.g., COX-2), receptors, and adhesion molecules.^[7] These effects make curcumin applicable to a wide array of clinical presentations.*

Patented Formulation: BCM-95®

While the beneficial effects of curcumin are hardly arguable, an area of intense research is how to make curcumin more bioavailable. Poor absorption in the gastrointestinal (GI) tract, rapid metabolism, and rapid systemic elimination are characteristics of commercially available curcumin preparations. While investigating a way to overcome these challenges, scientists discovered they could take advantage of the synergism between the curcuminoids and the sesquiterpenoids (essential oils) naturally present in turmeric.^[7] This discovery resulted in the development of BCM-95—a 100% natural whole turmeric extract composed of 86% curcuminoids (curcumin, demethoxycurcuminoid, and bisdemethoxycurcuminoid) and 7%-9% essential oils.*

Essential oils are a natural component of the turmeric rhizome. Not only do they enhance absorption of curcuminoids, but they also impart health benefits.^[8-10] The essential oils found in BCM-95 are extracted using double steam distillation. Essential oils comprise 7% to 9% of turmeric, with 50% of that being ar-turmerone, alpha-turmerone, and beta-turmerone. Some of the other essential oils present in BCM-95 include ar-curcumene, alpha-curcumene, zingiberene, beta-sesquiphellandrene, beta-atlantone, and germacrone.*

The Bioavailability of BCM-95

Animal and human studies have demonstrated the superior bioavailability of the BCM-95 curcumin composition.^[7,11,12] In a pilot crossover study, Antony et al compared the bioavailability of three forms of curcumin: BCM-95, normal

Clinical Applications

- » Provides Antioxidant and Cell-Protective Activity*
- » Supports Joint Health and Helps Relieve Minor Pain Associated With Physical Activity*
- » Supports the Health of Organs and Systems by Modulating the Production of Cytokines and Other Signaling Molecules*
- » Supports The Body's Efforts to Promote Healthy Cell Growth and Inhibit Unhealthy Cell Growth in Certain Cell Lines*
- » Supports Brain/Neuronal Health and a Healthy Mood*
- » Supports a Healthy Microbial Environment*

*CurcuPlex-95™ features BCM-95®—a 100% pure turmeric extract standardized to curcumin, demethoxycurcumin, bisdemethoxycurcumin, and essential oils of turmeric rhizome. This natural composition optimizes bioavailability and reflects true turmeric identity to deliver optimal health benefits. BCM-95 has been extensively studied and shows broad efficacy without the use of phospholipids, excipients, additives, carriers, nanotechnology, or bioenhancers.**

curcumin, and a non-controlled release curcumin-piperine-lecithin formula. The data demonstrated that the absorption of curcumin from BCM-95 was fast, peaked at 4.5 hours with a gradual decline, and that curcumin was still detectable in the blood at eight hours. The other formulas showed slower curcumin absorption with an earlier peak and rapid disappearance from the blood after 4.5 hours. The relative bioavailability of BCM-95 was approximately 6.93-fold higher than normal curcumin and 6.3-fold higher than the non-controlled release curcumin-lecithin-piperine formula. According to the researchers, the results of this study indicate that the BCM-95 curcumin is "absorbed early and retained longer" compared to other forms.^{*[7]}

Unlike other bioavailability-enhanced curcumin formulas, BCM-95 does not contain any non-turmeric compounds; no phospholipids, excipients, additives, carriers, nanotechnology, or bioenhancers are used.

BCM-95 Studies

To date, BCM-95 is backed by more than 21 published studies and over 12 years of research conducted around the world. Unlike many commercially available curcumin formulas, the bioavailability, safety, and efficacy of BCM-95 curcumin has been demonstrated in numerous preclinical and human studies. The following areas illustrate the massive body of research behind BCM-95 in relation to common health concerns: colon health^[13-17], mood and stress^[5,18-20], cognitive health^[6], joint health^[2,21], urinary health^[22], cytokine modulation^[23,24], prostate health^[25-27], breast health^[28], and cardiovascular health.^{*[29]}

As an example of the findings, in an eight-week randomized, double-blind, placebo-controlled trial (n=56), ingestion of 500 mg BCM-95 twice daily resulted in significant improvements in mood-related parameters during weeks four to eight.^[20] These findings are supported by related research into curcumin's effect on mood.^[18,19] In another study, the effects of BCM-95 on joints were evaluated. The BCM-95 group (500 mg for eight weeks) showed the highest percent of improvement in scoring related to joint health and comfort.^{*[2]}

In addition to the aforementioned published studies, eight human clinical trials using BCM-95 for periods of 21 days to one year are currently underway at prestigious institutions, including several at Baylor University Medical Center at Dallas.

Continued on next page

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

CurcuPlex-95™ Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%DV
BCM-95® Turmeric Extract (<i>Curcuma longa</i>) (rhizome) (95% total curcuminoids complex, including curcumin, curcuminoids, and volatile oils) (86% curcuminoids) (65% curcumin)	500 mg	**

** Daily Value (DV) not established.

Other Ingredients: HPMC (capsule), dicalcium phosphate, ascorbyl palmitate, silica, and carboxymethyl cellulose. BCM-95® is a registered trademark of DolCas Biotech, Ltd. Protected under US patents 7,883,728; 7,736,679; and 7,879,373.

DIRECTIONS: Take one capsule twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication, especially blood thinners or for cancer, should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.



Safety and Dosing

Turmeric has been safely consumed for thousands of years, and its medicinal compound curcumin has an outstanding safety profile. Phase I clinical trials using up to 8 g/d for four months did not result in discernable toxicities.^[30] Mild gastrointestinal distress can sometimes accompany curcumin supplementation, but this may be minimized by consuming the supplement with food. Current doses in clinical trials using BCM-95 range from 500 mg/d to 1000 mg/d.*

References

1. Yang F, Lim GP, Begum AN, et al. Curcumin inhibits formation of amyloid beta oligomers and fibrils, binds plaques, and reduces amyloid in vivo. *J Biol Chem*. 2005 Feb 18;280(7):5892-901. [PMID: 15590663]
2. Chandran B, Goel A. A randomized, pilot study to assess the efficacy and safety of curcumin in patients with active rheumatoid arthritis. *Phytother Res*. 2012 Nov;26(11):1719-25. [PMID: 22407780]
3. Garcea G, Berry DP, Jones DJ, et al. Consumption of the putative chemopreventive agent curcumin by cancer patients: assessment of curcumin levels in the colorectum and their pharmacodynamic consequences. *Cancer Epidemiol Biomarkers Prev*. 2005 Jan;14(1):120-25. [PMID: 15668484]
4. Ghosh S, Banerjee S, Sili PC. The beneficial role of curcumin on inflammation, diabetes and neurodegenerative disease: A recent update. *Food Chem Toxicol*. 2015 Sep;83:111-24. [PMID: 26066364]
5. Sanmukhani J, Satodia V, Trivedi J, et al. Efficacy and safety of curcumin in major depressive disorder: a randomized controlled trial. *Phytother Res*. 2014 Apr;28(4):579-85. [PMID: 23832433]
6. Baum L, Lam CW, Cheung SK, et al. Six-month randomized, placebo-controlled, double-blind, pilot clinical trial of curcumin in patients with Alzheimer disease. *J Clin Psychopharmacol*. 2008 Feb;28(1):110-13. [PMID: 18204357]
7. Antony B, Merina B, Iyer VS, et al. A pilot cross-over study to evaluate human oral bioavailability of BCM-95CG (Biocurcuma), a novel bioenhanced preparation of curcumin. *Indian J Pharm Sci*. 2008 Jul-Aug;70(4):445-9. [PMID: 20046768]
8. Honda S, Aoki F, Tanaka H, et al. Effects of ingested turmeric oleoresin on glucose and lipid metabolisms in obese diabetic mice: a DNA microarray study. *J Agric Food Chem*. 2006 Nov 29;54(24):9055-62. [PMID: 17117790]
9. Singh V, Jain M, Misra A, et al. Curcuma oil ameliorates insulin resistance & associated thrombotic complications in hamster & rat. *Indian J Med Res*. 2015 Jun;141(6):823-32. [PMID: 26205026]
10. Nishiyama T, Mae T, Kishida H, et al. Curcuminoids and sesquiterpenoids in turmeric (*Curcuma longa* L.) suppress an increase in blood glucose level in type 2 diabetic KK-Ay mice. *J Agric Food Chem*. 2005 Feb 23;53(4):959-63. [PMID: 15713005]
11. Shishu M. Comparative bioavailability of curcumin, turmeric and Biocurcuma™ in traditional vehicles using non-everted rat intestinal sac model. *J Funct Foods*. 2010; 2(1):60-65. [on file]
12. Benny M, Antony B. Bioavailability of Biocurcuma™ (BCM-095™). *Spice India*. 2006; Sept:11-15. http://geronova.com/wp-content/uploads/2013/06/Spice_Board.pdf. Accessed September 22, 2015.
13. Buhrmann C, Kraeche P, Lueders C, et al. Curcumin suppresses crosstalk between colon cancer stem cells and stromal fibroblasts in the tumor microenvironment: potential role of EMT. *PLoS One*. 2014 Sep 19;9(9):e107514. [PMID: 25238234]
14. Shakibaei M, Buhrmann C, Kraeche P, et al. Curcumin chemosensitizes 5-fluorouracil resistant MMR-deficient human colon cancer cells in high density cultures. *PLoS One*. 2014 Jan 3;9(1):e85397. [PMID: 24404205]
15. Toden S, Okugawa Y, Jascur T, et al. Curcumin mediates chemosensitization to 5-fluorouracil through miRNA-induced suppression of epithelial-to-mesenchymal transition in chemoresistant colorectal cancer. *Carcinogenesis*. 2015 Mar;36(3):355-67. [PMID: 25653233]
16. Toden S, Okugawa Y, Buhrmann C, et al. Novel evidence for curcumin and boswellic acid-induced chemoprevention through regulation of mir-34a and mir-27a in colorectal cancer. *Cancer Prev Res (Phila)*. 2015 May;8(5):431-43. [PMID: 25712055]
17. Shakibaei M, Buhrmann C, Kraeche P, et al. Curcumin chemosensitizes 5-fluorouracil resistant MMR-deficient human colon cancer cells in high density cultures. *PLoS One*. 2014 Jan 3;9(1):e85397. [PMID: 24404205]
18. Sanmukhani J, Anovadiya A, Tripathi CB. Evaluation of antidepressant like activity of curcumin and its combination with fluoxetine and imipramine: an acute and chronic study. *Acta Pol Pharm*. 2011 Sep-Oct;68(5):769-75. [PMID: 21928724]
19. Lopresti AL, Maes M, Meddens MJ, et al. Curcumin and major depression: a randomised, double-blind, placebo-controlled trial investigating the potential of peripheral biomarkers to predict treatment response and antidepressant mechanisms of change. *Eur Neuropsychopharmacol*. 2015 Jan;25(1):38-50. [PMID: 25523883]
20. Lopresti AL, Maes M, Maker GL, et al. Curcumin for the treatment of major depression: a randomised, double-blind, placebo controlled study. *J Affect Disord*. 2014;167:368-75. [PMID: 25046624]
21. Kizhakkedath R. Clinical evaluation of a formulation containing *Curcuma longa* and *Boswellia serrata* extracts in the management of knee osteoarthritis. *Mol Med Rep*. 2013 Nov;8(5):1542-48. [PMID: 24002213]
22. Hejazi J, Rastmanesh R, Forough-Azam T, et al. A pilot clinical trial of radioprotective effects of curcumin supplementation in patients with prostate cancer. *J Cancer Sci Ther*. 2013;5(10):320-24. <http://www.omicsonline.org/a-pilot-clinical-trial-of-radioprotective-effects-of-curcumin-supplementation-in-patients-with-prostate-cancer-1948-5956.1000222.php?aid=19259>. Accessed September 22, 2015.
23. Leray V, Freuchet B, Le Bloc'h J, et al. Effect of citrus polyphenol- and curcumin-supplemented diet on inflammatory state in obese cats. *Br J Nutr*. 2011 Oct;106 Suppl 1:S198-201. [PMID: 22005428]
24. Horohov D, Sinatra S, Chopra R, et al. The effect of exercise and nutritional supplementation on proinflammatory cytokine expression in young racehorses during training. *J Equine Vet Sci*. 2012; 32:805-15. <http://www.equinenutricentials.com/pdf/Exercise-inflammation-paper-with-back.pdf>. Accessed September 22, 2015.
25. Yan J, Katz AE. ProstaCaid induces G2/M cell cycle arrest and apoptosis in human and mouse androgen-dependent and -independent prostate cancer cells. *Integr Cancer Ther*. 2010 Jun;9(2):186-96. [PMID: 20587444]
26. Jiang J, Eliaz I, Sliva D. Suppression of growth and invasive behavior of human prostate cancer cells by ProstaCaid™: mechanism of activity. *Int J Oncol*. 2011 Jun;38(6):1675-82. [PMID: 21468543]
27. Jiang J, Loganathan J, Eliaz I, et al. ProstaCaid inhibits tumor growth in a xenograft model of human prostate cancer. *Int J Oncol*. 2012 May;40(5):1339-44. [PMID: 22293856]
28. Jiang J, Wojnowski R, Jedinak A, et al. Suppression of proliferation and invasive behavior of human metastatic breast cancer cells by dietary supplement BreastDefend. *Integr Cancer Ther*. 2011 Jun;10(2):192-200. [PMID: 20926736]
29. Baum L, Cheung SK, Mok VC, et al. Curcumin effects on blood lipid profile in a 6-month human study. *Pharmacol Res*. 2007 Dec;56(6):509-14. [PMID: 17951067]
30. Cheng AL, Hsu CH, Lin JK, et al. Phase I clinical trial of curcumin, a chemopreventive agent, in patients with high-risk or pre-malignant lesions. *Anticancer Res*. 2001 Jul-Aug;21(4B):2895-900. [PMID: 11712783]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

D3

Concentrated D3 in Softgel and Liquid Forms



D3 Liquid is available in 1 fluid ounce (30 mL) and 2 fluid ounces (60 mL)
D3 2000 is available in 120 softgels and 240 softgels
D3 5000 is available in 60 softgels, 90 softgels, and 180 softgels

Discussion

While vitamin D3 (cholecalciferol) is made in the skin when 7-dehydrocholesterol reacts with sunlight, many things affect the degree to which this biosynthesis occurs, including time of day, seasons, location, smog/pollution, clothing, shade of skin (darker skin requires more sun), and sunscreen use. Low-cholesterol diets and certain cholesterol therapies can also affect vitamin D formation. By some estimates, one billion people worldwide have vitamin D deficiency or insufficiency.^[1] Reversing deficiency and maintaining optimal serum vitamin D levels beneficially impacts biochemistry and numerous body systems; this is largely because calcitriol—the metabolic product of vitamin D—is a secosteroid hormone that targets over 200 genes in a wide variety of tissues.^[2,3] As the research demonstrates, vitamin D is clearly imperative for the development, growth, and maintenance of a healthy body from gestation to senescence.*

Bone Health The body needs vitamin D to absorb calcium, and the importance of vitamin D in skeletal health and bone density is well established. Although bone density is most often associated with calcium intakes, insufficient vitamin D negatively affects calcium absorption.^[3] Without adequate absorption, the body must take calcium from its stores in the skeleton, which weakens existing bone and prevents the formation of strong, new bone. Clinical research shows that taking vitamin D orally with calcium supplements can support healthy bone turnover^[4-6], and adequate calcium and vitamin D throughout life—as part of a well-balanced diet—may reduce the risk of osteoporosis.*

The Expanding Roles of Vitamin D The role of vitamin D in good health continues to expand as the knowledge of this vitamin's effects on different body systems grows. Research now suggests that optimal serum levels of vitamin D support normal cell differentiation,^[3,7] cardiovascular health,^[2,3] normal immune function,^[8] good balance,^[2] healthy mood,^[9] normal fetal development,^[10] neuronal growth

Clinical Applications

- » Supports Bone Strength and Dental Health*
- » Supports Modulation of Immune Function*
- » Supports Healthy Cell Differentiation*
- » Supports Neurologic and Cognitive Health*
- » Supports Musculoskeletal Comfort*
- » Supports Cardiovascular Health and Healthy Blood Sugar Metabolism*
- » Supports Vitamin D Repletion in Cases of Dietary Deficiency, Limited Sunlight Exposure, or Use of Depleting Therapies*

*D3 2000/5000 is cholecalciferol provided in convenient softgels. D3 Liquid is cholecalciferol derived from lanolin and provided in a liquid base of sunflower oil and purified water. In this liquid formula, vitamin D and sunflower oil are combined using a special micro-emulsification process designed to create a natural micellized matrix which, when coated by the stomach bile, will encourage absorption.**

and neurodevelopment,^[2,3,10,11] healthy glucose metabolism,^[2,3] musculoskeletal comfort,^[2,3] periodontal health,^[12] and normal intestinal immune responses.^[8] Areas of research that have gained momentum over the past several years concern the relationship of vitamin D deficiency or insufficiency to changes in cellular proliferation, changes in fetal brain development, and mental health.^[7,10,13-15] Evidence is also mounting that vitamin D supplementation may provide key immune support.*^[16-19]

D2, D3, and Metabolites As previously stated, D3 is the form of vitamin D produced in the skin. D2 (ergocalciferol) is derived from fungal sources by activating ergosterol with ultraviolet light. It is not naturally present in the human body. After vitamin D is formed in the skin or taken orally, it is metabolized into two different substances within the body: calcidiol (25-hydroxyvitamin D) and calcitriol (1,25-dihydroxyvitamin D). Calcidiol is the body's main storage form of vitamin D, while calcitriol (made from calcidiol) is "activated" vitamin D. Although D2 and D3 are similar biochemically, a recent study reported D3 to be approximately 87% more potent in raising and maintaining serum calcidiol concentrations and in producing two- to threefold greater storage of vitamin D than did equimolar D2.*^[20]

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

D3 2000 Supplement Facts

Serving Size: 1 Softgel

	Amount Per Serving	%Daily Value
Vitamin D3 (cholecalciferol)	50 mcg (2000 IU)	250%

Other Ingredients: Organic, extra virgin olive oil and softgel (bovine gelatin, vegetable glycerin, and purified water).

DIRECTIONS: Take one softgel daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

D3 5000 Supplement Facts

Serving Size: 1 Softgel

	Amount Per Serving	%Daily Value
Vitamin D3 (cholecalciferol)	125 mcg (5000 IU)	625%

Other Ingredients: Organic, extra virgin olive oil and softgel (bovine gelatin, vegetable glycerin, and purified water).

DIRECTIONS: Take one softgel daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

D3 Liquid Supplement Facts

Serving Size: 1 Drop (about 0.0394 mL)

	Amount Per Serving	%Daily Value
Vitamin D3 (cholecalciferol)	25 mcg (1000 IU)	125%

Other Ingredients: Sunflower oil.

DIRECTIONS: Shake well before using. Take one drop, one to five times daily (plain or in liquid), or as directed by your healthcare practitioner.

STORAGE: Refrigerate after opening.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

References

1. Tsiaras WG, Weinstock MA. Factors influencing vitamin d status. *Acta Derm Venereol.* 2011 Mar;91(2):115-24. [PMID: 21384086]
2. Cannell JJ, Hollis BW. Use of vitamin D in clinical practice. *Altern Med Rev.* 2008 Mar;13(1):6-20. [PMID: 18377099]
3. Heany RP. Vitamin D in health and disease. *Clin J Am Soc Nephrol.* 2008 Sep;3(5):1535-41. [PMID: 18525006]
4. Dawson-Hughes B, Harris SS, Krall EA, et al. Effect of calcium and vitamin D supplementation on bone density in men and women 65 years of age or older. *N Engl J Med.* 1997;337:670-76. [PMID: 9278463]
5. Papadimitropoulos E, Wells G, Shea B, et al. Meta-analyses of therapies for postmenopausal osteoporosis. VIII: Meta-analysis of the efficacy of vitamin D treatment in preventing osteoporosis in postmenopausal women. *Endocr Rev.* 2002;23:560-69. [PMID: 12202471]
6. Lips P, Bouillon R, van Schoor NM, et al. Reducing fracture risk with calcium and vitamin D. *Clin Endocrinol (Oxf).* 2010 Sep;73(3):277-85. [PMID: 20796001]
7. Garland CF, French CB, Baggerly LL, et al. Vitamin d supplement doses and serum 25-hydroxyvitamin d in the range associated with cancer prevention. *Anticancer Res.* 2011 Feb;31(2):607-11. [PMID: 21378345]
8. Raman M, Milestone AN, Walters JR, et al. Vitamin D and gastrointestinal diseases: inflammatory bowel disease and colorectal cancer. *Therap Adv Gastroenterol.* 2011 Jan;4(1):49-62. [PMID: 21317994]
9. Humble MB. Vitamin D, light and mental health. *J Photochem Photobiol B.* 2010 Nov;101(2):142-49. [PMID: 18445674]
10. Grant WB, Soles CM. Epidemiologic evidence supporting the role of maternal vitamin D deficiency as a risk factor for the development of infantile autism. *Dermatoendocrinol.* 2009 Jul;1(4):223-28. [PMID: 20592795]
11. Currenti SA. Understanding and determining the etiology of autism. *Cell Mol Neurobiol.* 2010 Mar;30(2):161-71. [PMID: 19774457]
12. Naito M, Miyaki K, Naito T, et al. Association between vitamin D receptor gene haplotypes and chronic periodontitis among Japanese men. *Int J Med Sci.* 2007 Aug;4(4):216-22. [PMID: 17848979]
13. McGrath JJ, Burne TH, Féron F, et al. Developmental vitamin D deficiency and risk of schizophrenia: a 10-year update. *Schizophr Bull.* 2010 Nov;36(6):1073-78. [PMID: 20833696]
14. Gandini S, Boniol M, Haukka J, et al. Meta-analysis of observational studies of serum 25-hydroxyvitamin D levels and colorectal, breast and prostate cancer and colorectal adenoma. *Int J Cancer.* 2011 Mar;128(6):1414-24. doi: 10.1002/ijc.25439. [PMID: 20473927]
15. Yin L, Grandi N, Raum E, et al. Meta-analysis: circulating vitamin D and ovarian cancer risk. *Gynecol Oncol.* 2011 Feb 14. [Epub ahead of print] [PMID: 21324518]
16. Grant WB, Goldstein M, Mascitelli L. Ample evidence exists from human studies that vitamin D reduces the risk of selected bacterial and viral infections. *Exp Biol Med (Maywood).* 2010 Dec;235(12):1395-96; discussion 1397. [PMID: 21171208]
17. Beard JA, Bearden A, Striker R. Vitamin D and the anti-viral state. *J Clin Virol.* 2011 Mar;50(3):194-200. [PMID: 21242105]
18. Hertting O, Holm Å, Lütthje P, et al. Vitamin D induction of the human antimicrobial peptide cathelicidin in the urinary bladder. *PLoS One.* 2010 Dec;5(12):e15580. [PMID: 21179490]
19. Grant WB, Boucher BJ. Requirements for vitamin D across the life span. *Biol Res Nurs.* 2011 Jan 17. [Epub ahead of print] [PMID: 21242196]
20. Heaney RP, Recker RR, Grote J, et al. Vitamin d3 is more potent than vitamin d2 in humans. *J Clin Endocrinol Metab.* 2011 Mar;96(3):E447-52. [PMID: 21177785]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

DHA from Algae

Supports Brain, Eye, and Immune Health*



DHA from Algae is available in 60 vegetarian softgels
DHA from Algae for Kids is available in 90 vegetarian softgels

Discussion

Algae are the original source of EPA/DHA in aquatic ecosystems. Certain microalgae produce high levels of EPA or DHA. Dr. Perlmutter's DHA from Algae is organically produced from a DHA-rich microalgae fermented broth. Clinical trials with DHA-rich oil indicate a favorable comparison to fish oil.*

Omega-3 polyunsaturated fatty acids (PUFAs) play a critical role in the normal development and functioning of the brain and central nervous system, with the conditionally essential fatty acid docosahexaenoic acid (DHA) believed to be vital to pre- and post-natal brain development. DHA is transferred directly to the fetus during pregnancy, especially during the last trimester, and is supplied to the infant in mother's breast milk after birth. Functioning exclusively via cell membranes and anchored by phospholipid molecules, PUFAs such as DHA are involved in numerous processes affecting membrane fluidity and gene regulation. DHA is the primary structural fatty acid in the brain's gray matter (~60%) and the eye's retina, optimizing signal transmission in these organs and the overall nervous system. Approximately 50% of a neuronal membrane's weight is DHA. Adequate levels of DHA are believed to support healthy memory, cognition, night vision, and mood. DHA also has immune-modulating properties and supports a healthy prostaglandin production profile. Studies using algal DHA suggest it may play a role in cardiovascular health, especially with respect to maintaining healthy lipid levels already within the normal range and supporting normal resistance to oxidative stress.*

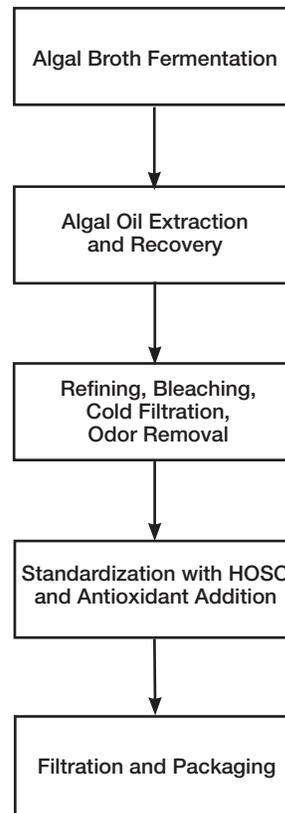
Eco-friendly, XYMOGEN's DHA from Algae and DHA from Algae for Kids meet high standards, including AIB International Consolidated Standards for Inspection of Prerequisites and Food Safety Programs, Proposition 65, and the American National Standards Institute (ANSI)/International Organization for Standardization (ISO). The DHA is extracted from a fermented algal broth and processed without any heat exposure.* (See diagram for details)

Clinical Applications

- » Provides Supplemental Omega-3 DHA from a Non-Fish Source*
- » Provides DHA for Use in Brain, Eye, and Cell Membrane Development and Function*
- » Supports Immune Health and Healthy Eicosanoid Metabolism*
- » Supports Healthy Blood Lipid Levels Already Within the Normal Range*

DHA from Algae contains docosahexaenoic acid (DHA), a conditionally essential omega-3 fatty acid. DHA is highly concentrated in brain synaptosomes, the cerebral cortex, mitochondria, and retina. It plays an important role in the fluidity and permeability of cell membranes and cellular communication, and supports optimal function of the brain, eyes, and immune system. This patented, processed formula is derived from marine algae.*

Manufacturing Process Flow Diagram:



DHA from Algae Supplement Facts

Serving Size: 1 Vegetarian Softgel

	Amount Per Serving	%Daily Value
Calories	5	
Total Fat	0.5 g	1%†
life'sDHA® DHA (docosahexaenoic acid from algal oil)	200 mg	**

†Percent Daily Values are based on a 2,000 calorie diet.
 **Daily Value not established.

Other Ingredients: Softgel (water, modified corn starch, glycerin, carrageenan, sorbitol, caramel, and beta-carotene), high oleic sunflower oil, tocopherols, natural flavor, sunflower lecithin, and ascorbyl palmitate.
 Protected by U.S. Patent: 5,407,957 and 5,492,938

DIRECTIONS: Take one vegetarian softgel daily with a meal, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, soy protein, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



life'sDHA® is a trademark of DSM.

DHA from Algae for Kids Supplement Facts

Serving Size: 1 Vegetarian Softgel

	Amount Per Serving	%Daily Value
DHA (docosahexaenoic acid from algal oil)(life'sDHA®)	100 mg	**

** Daily Value (DV) not established.

Other Ingredients: Softgel (water, modified corn starch, glycerin, carrageenan, sorbitol, caramel, and beta-carotene), high oleic sunflower oil, tocopherols, natural flavor, sunflower lecithin, and ascorbyl palmitate.
 Protected by U.S. Patent: 5,407,957 and 5,492,938

DIRECTIONS: Take one vegetarian softgel daily with a meal, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, soy protein, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



life'sDHA® is a trademark of DSM.

References

1. Doughman SD, et al. Omega-3 fatty acids for nutrition and medicine: considering microalgae oil as a vegetarian source of EPA and DHA. *Curr Diabetes Rev.* 2007 Aug;3(3):198-203. [PMID: 18220672]
2. Schuchardt JP, et al. Significance of long-chain polyunsaturated fatty acids (PUFAs) for the development and behaviour of children. *Eur J Pediatr.* 2010 Feb;169(2):149-64. Epub 2009 Aug 12 [PMID: 19672626]
3. Cole, GM, et al. Dietary fatty acids and the aging brain. *Nutr Rev.* 68(Suppl. 2):S102-S111 doi:10.1111/j.1753-4887.2010.00345.x
4. Uauy R, Dangour AD. Nutrition in brain development and aging: role of essential fatty acids. *Nutr Rev.* 2006 May;64(5 Pt 2):S24-33; discussion S72-91. [PMID: 16770950]
5. Wurtman RJ, et al. Nutritional modifiers of aging brain function: use of uridine and other phosphatide precursors to increase formation of brain synapses. *Nutr Rev.* 2010 Dec;68 Suppl 2:S88-101. doi: 10.1111/j.1753-4887.2010.00344.x. [PMID: 21091953]
6. Lindmark L, Clough P. A 5-month open study with long-chain polyunsaturated fatty acids in dyslexia. *J Med Food.* 2007 Dec;10(4):662-6. [PMID: 18158838]
7. Micronutrients and their Relevance for the Eye - Function of Lutein, Zeaxanthin and Omega-3 Fatty Acids. *Klin Monbl Augenheilkd.* 2010 Aug 25 e published ahead of print [PMID: 20740395]
8. Martins JG. EPA but not DHA appears to be responsible for the efficacy of omega-3 long chain polyunsaturated fatty acid supplementation in depression: evidence from a meta-analysis of randomized controlled trials. *J Am Coll Nutr.* 2009 Oct;28(5):525-42. Review [PMID: 20439549]
9. Ryan AS, et al. Clinical overview of algal-docosahexaenoic acid: effects on triglyceride levels and other cardiovascular risk factors. *Am J Ther.* 2009 Mar-Apr;16(2):183-92. [PMID:19145206]

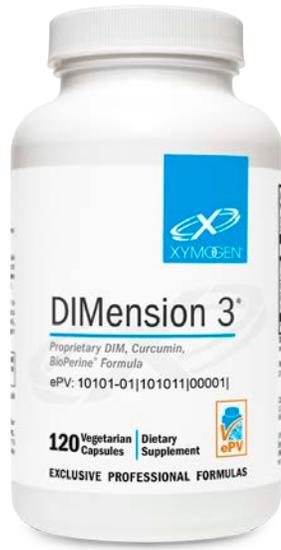
Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

DIMension 3[®]

Proprietary DIM, Curcumin, BioPerine[®] Formula



Available in 120 and 240 capsules

Discussion

DIM (3,3'-diindolylmethane) is the stable, bioactive metabolite formed when stomach acid breaks down indole-3-carbinol (I3C), a sulfur-containing glucosinolate present in cruciferous vegetables.^[1] Supplementation with DIM is preferred over I3C due to I3C's undesirable breakdown products, including the dioxin-like molecule indolo[3,2-b]carbazole (ICZ).^[2] DIM has been found to support hormone metabolism and immune activity, and stimulate antioxidant and detoxification systems.^[3] Curcumin and BioPerine[®] provide complementary support for DIM's role in healthy cell function.*

Support of Hormone Metabolism Healthy metabolism of exogenous and endogenous estrogens can be pivotal for hormonal balance.^[4] DIM promotes metabolism of estrogen into the favorable and protective 2-hydroxyestrone (2-OHE) metabolite versus production of 4-hydroxyestrone (4-OHE) and 16-alpha-hydroxyestrone (16-alpha-OHE) metabolites.^[5] DIM's influence on 2-OHE production creates a more desirable ratio of 2-OHE to 16-alpha-OHE. Assessment of 2:16-alpha-OHE ratio appears to be useful in evaluating breast health.^[6] DIM has been studied for its role in supporting prostate health as well, by reducing dihydrotestosterone binding to androgen receptors.*^[7,8]

Support of Cell Function and Metabolism Orchestration of metabolism by the thyroid gland is dependent on hormone balance. DIM was found to target proteolytic enzymes (MMP-2 and MMP-9), thus supporting the normal function and activity of thyroid cells in vitro.^[9] Ongoing research reveals DIM's positive role in regulation of gene expression, protein production, and cell function. Downregulation of certain proteins (survivin, Bcl-2, and cdc25A) and upregulation of protective proteins (NRF2 and cyclin-dependent kinase inhibitor p21waf1) promoted healthy cell growth.*^[10,11]

Antioxidant and Detoxification Support DIMension 3 provides support for both antioxidant and detoxification systems which, in turn, support cellular function and integrity. Antioxidant activity is crucial to counteracting oxidative molecules normally produced during phase I

Clinical Applications

- » Supports Healthy Estrogen Metabolism in Females and Males*
- » Supports Detoxification of Xenoestrogens*
- » Provides Support for Antioxidant Mechanisms*

*DIMension 3[®] represents a three-dimensional approach to supporting healthy estrogen metabolism. Research suggests that diindolylmethane (DIM), curcumin (from turmeric extract), and the patented black pepper extract BioPerine[®] support balanced estrogen metabolism.**

detoxification. Research on DIM suggests that it plays an important role in activating detoxification enzymes in human hepatocytes, further supporting biotransformation at a primary site in the body.*^[12]

Curcumin As the major curcuminoid found in turmeric, curcumin is valued for its promotion of antioxidant activity, support of metabolic detoxification, and modulation of cytokine production.^[13] Research studying genotoxic estrogen metabolites suggests that curcumin's inhibitory effect on anchorage-independent growth and on CYP enzymes following dioxin exposure helps support healthy cell-life regulation in human embryonic kidney cells and normal prostate cells.*^[14]

BioPerine is a patented form of piperine, the main alkaloid from black and long pepper plants that has been found to effectively support the absorption of nutrients. After a dose of 2 g of curcumin, human serum levels of curcumin were either undetectable or very low. When the same dose was given along with 20 mg of piperine (4:1 ratio), there was a 2000% increase in the bioavailability of the curcumin without adverse effects.*^[15]

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

DIMension 3® Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Turmeric Extract (<i>Curcuma longa</i>)(rhizome)(95% curcuminoids)	250 mg	**
DIM (diindolylmethane)	150 mg	**
Black Pepper Extract (<i>Piper nigrum</i>)(fruit)(BioPerine®)	2.5 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, microcrystalline cellulose, silica, and medium-chain triglyceride oil.

DIRECTIONS: Take two capsules daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication, especially blood thinners or cancer treatment, should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

BioPerine is a registered trademark of Sabinsa Corp. BioPerine is protected by US patents 5,536,506; 5,744,161; 5,972,382; and 6,054,585.



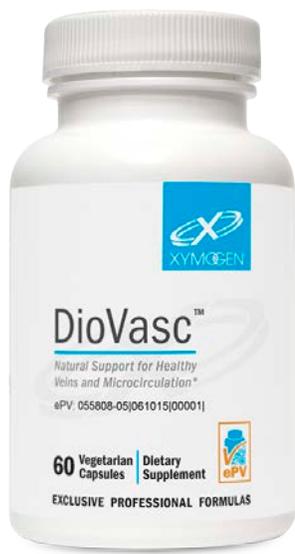
References

1. Bradlow HL. Review. Indole-3-carbinol as a chemoprotective agent in breast and prostate cancer. *In Vivo*. 2008 Jul-Aug;22(4):441-5. [PMID: 18712169]
2. Herrmann S, Seidelin M, Bisgaard HC, et al. Indolo[3,2-b]carbazole inhibits gap junctional intercellular communication in rat primary hepatocytes and acts as a potential tumor promoter. *Carcinogenesis*. 2002 Nov;23(11):1861-8. [PMID: 12419834]
3. Riby JE, Xue L, Chatterji U, et al. Activation and potentiation of interferon-gamma signaling by 3,3'-diindolylmethane in MCF-7 breast cancer cells. *Mol Pharmacol*. 2006 Feb;69(2):430-9. [PMID: 16267208]
4. Lord RS, Bongiovanni B, Bralley JA. Estrogen metabolism and the diet-cancer connection: rationale for assessing the ratio of urinary hydroxylated estrogen metabolites. *Altern Med Rev*. 2002 Apr;7(2):112-29. [PMID: 11991791]
5. Cavalieri E, Frenkel K, Liehr JG, et al. Estrogens as endogenous genotoxic agents--DNA adducts and mutations. *J Natl Cancer Inst Monogr*. 2000;(27):75-93. [PMID: 10963621]
6. Im A, Vogel VG, Ahrendt G, et al. Urinary estrogen metabolites in women at high risk for breast cancer. *Carcinogenesis*. 2009 Sep;30(9):1532-5. [PMID: 19502596]
7. Fares F, Zazzam N, Appel B, et al. The potential efficacy of 3,3'-diindolylmethane in prevention of prostate cancer development. *Eur J Cancer Prev*. 2010 May;19(3):199-203. [PMID: 20010430]
8. Le HT, Schaldach CM, Firestone GL, et al. Plant-derived 3,3'-Diindolylmethane is a strong androgen antagonist in human prostate cancer cells. *J Biol Chem*. 2003 Jun 6;278 (23): 21136-45. [PMID: 12665522]
9. Rajoria S, Suriano R, George A, et al. Estrogen induced metastatic modulators MMP-2 and MMP-9 are targets of 3,3'-diindolylmethane in thyroid cancer. *PLoS One*. 2011 Jan 18;6(1):e15879. [PMID: 21267453]
10. Ahmad A, Sakr WA, Rahman KM. Anticancer properties of indole compounds: mechanism of apoptosis induction and role in chemotherapy. *Curr Drug Targets*. 2010 Jun;11(6):652-66. [PMID: 20298156]
11. Rahman KW, Li Y, Wang Z, et al. Gene expression profiling revealed survivin as a target of 3,3'-diindolylmethane-induced cell growth inhibition and apoptosis in breast cancer cells. *Cancer Res*. 2006 May 1;66(9):4952-60. [PMID: 16651453]
12. Gross-Steinmeyer K, Stapleton PL, Liu F, et al. Phytochemical-induced changes in gene expression of carcinogen-metabolizing enzymes in cultured human primary hepatocytes. *Xenobiotica*. 2004 Jul;34(7):619-32. [PMID: 15672752]
13. Jurenka JS. Anti-inflammatory properties of curcumin, a major constituent of *Curcuma longa*: a review of preclinical and clinical research. *Altern Med Rev*. 2009 Jun;14(2):141-53. [PMID: 19594223]
14. Choi H, Chun YS, Shin YJ, et al. Curcumin attenuates cytochrome P450 induction in response to 2,3,7,8-tetrachlorodibenzo-p-dioxin by ROS-dependently degrading AhR and ARNT. *Cancer Sci*. 2008 Dec;99(12):2518-24. [PMID: 19018768]
15. Shoba G, Joy D, Joseph T, et al. Influence of piperine on the pharmacokinetics of curcumin in animals and human volunteers. *Planta Med*. 1998 May; 64 (4):353-6. [PMID: 9619120]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.



Available in 60 vegetable capsules

Discussion

Diosmin is a well-researched citrus flavonoid that has been utilized for decades to support healthy capillary and vein function as well as healthy microcirculation throughout the body. Diosmin fundamentally helps maintain the structure and function of the circulatory system, especially vein strength and competence.^[1] The most promising research results come from a micronized purified flavonoid fraction comprising 450 mg of diosmin and 50 mg of hesperidin (hesperidin is a precursor to diosmin). This is the same ratio and dose found in each DioVasc capsule. The process of micronization (reducing particle size to less than two micrometers in diameter) improves diosmin absorption.^{*[2]}

Micronized purified flavonoid fraction (MPFF) appears to support vein health by prolonging the normal effect that the catecholamine norepinephrine has on the vessel wall; and this, therefore, promotes venous tone.^[3] Research also suggests that MPFF affects the synthesis of prostaglandins and free radicals, as well as leukocyte activation, trapping, and migration. Ultimately, MPFF supports antioxidant systems and eicosanoid balance.^{*[4-7]}

Pharmacological and clinical studies suggest that MPFF—on its own and in conjunction with standard therapy—promotes normal lymph drainage, healthy capillary permeability, and favorable microcirculation. Multicenter, prospective, randomized, controlled studies document the effect of MPFF on maintaining healthy venous sufficiency.^[8] Two randomized, double-blind, placebo-controlled studies conducted over a two-month period demonstrated the venotropic nature of DioVasc's main component. Significant support of organic and functional parameters occurred along with significant support of venous hemodynamics.^[9] Some studies indicate that favorable results can be achieved within two hours of administration.^{*[10]}

A review of the literature suggests that health-related quality-of-life parameters were found to improve with the use of MPFF and were associated with the formula's support of microcirculation and vein function.^[2] A single-center, double-blind, placebo-controlled study suggested that MPFF had a positive and protective effect on five study variables (red blood cell aggregation, red blood count, microcirculatory blood flux, and amplitude and frequency of vasomotion).^[11] A double-blind placebo-controlled trial of MPFF

Clinical Applications

- » Supports Veins, Capillaries, and Circulation*
- » Helps Promote Normal Lymphatic Drainage*
- » Supports Antioxidant Activity*
- » Supports Blood Glucose Metabolism*
- » Supports Healthy Eicosanoid Metabolism*

*DioVasc™ contains well-researched, citrus-based flavonoids in a unique micronized form for enhanced absorption and bioavailability. Research suggests that these compounds support healthy veins, capillaries, and blood flow; promote healthy lymphatic drainage; and enhance antioxidant activity; and support healthy eicosanoid metabolism. More recent research suggests that the components in DioVasc also support blood glucose metabolism.**

over a six-week period suggested that the formula, administered twice daily, significantly ($p < 0.001$) supported capillary structure and health and was well tolerated throughout the study.^[12] A double-blind randomized study of 104 subjects over a three-month period revealed that MPFF at various doses (500 mg, 1000 mg, or 2000 mg per day) significantly supported transcutaneous oxygen pressure and venous competence.^{*[13]}

A meta-analysis of five prospective, randomized, controlled studies employing a total of 723 subjects suggested that MPFF promoted healthy tissue integrity when combined with conventional therapy (compression and local care).^[14,15] Similar results were obtained in a multicenter, double-blind, randomized, controlled study of 107 individuals.^{*[16]}

The worldwide RELIEF program (Reflux assessment and quality of life improvement with micronized flavonoids) studied the effects of MPFF on more than 5000 participants in 23 countries. A variety of subjects taking MPFF over a six-month period showed clinically significant improvements that indicated MPFF's supportive effect on microcirculation and vein health and function. These improvements continued throughout the study.^{*[17]}

Placebo-controlled human trials support the use of MPFF for the maintenance of healthy metabolic parameters, microcirculation, fluid balance, lymph system function, and albumin retention.^[18-20] Results suggest that MPFF specifically supports normal capillary filtration, lymphatic albumin resorption, and fluid balance at the cellular level. Research on MPFF suggests that its positive effects may be extended to various parts of the body.^{*[21,22]}

Ongoing animal studies suggest that diosmin, the major component found in MPFF, significantly supports blood glucose and insulin levels already within the normal range and exerts favorable effects on maintaining healthy serum hemoglobin.^[23,24] Results from a double-blind placebo-controlled study support the use of MPFF for maintaining healthy glucose metabolism in humans as well.^{*[25]}

DioVasc™ Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
DioVasc Proprietary Blend	500 mg	**
Micronized diosmin (<4 microns) (from <i>Citrus sinensis</i>)(fruit) and hesperidin (from <i>Citrus sinensis</i>)(fruit)		
** Daily Value not established.		

Other Ingredients: HPMC, dicalcium phosphate dihydrate, stearic acid, magnesium stearate, and silica.**DIRECTIONS:** Take one capsule twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tampo seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.**STORAGE:** Keep closed in a cool, dry place out of reach of children.**References**

1. Monograph. Diosmin. *Altern Med Rev.* 2004 Sep;9(3):308-11. [PMID: 15387721]
2. Lyseng-Williamson KA, Perry CM. Micronised purified flavonoid fraction: a review of its use in chronic venous insufficiency, venous ulcers and haemorrhoids. *Drugs.* 2003;63(1):71-100. [PMID: 12487623]
3. Pitsch F. Recent guidelines in chronic venous disease: the place of Daflon 500 mg. *Phlebolympology.* 2011;18:24-29. <http://www.phlebolympology.org/2011/01/recent-guidelines-in-chronic-venous-disease-the-place-of-daflon-500-mg/>. Accessed October 12, 2012.
4. Bergan JJ, Schmid-Schönbein GW, Takase S. Therapeutic approach to chronic venous insufficiency and its complications: place of Daflon 500 mg. *Angiology.* 2001 Aug;52 Suppl 1:S43-7. [PMID: 11510596]
5. Smith PD. Neutrophil activation and mediators of inflammation in chronic venous insufficiency. *J Vasc Res.* 1999;36 Suppl 1:24-36. [PMID: 10474048]
6. Korthui RJ, Gute DC. Anti-inflammatory actions of a micronized, purified flavonoid fraction in ischemia/reperfusion. *Adv Exp Med Biol.* 2002;505:181-90. [PMID: 12083462]
7. Jean T, Bodinier MC. Mediators involved in inflammation: effects of Daflon 500 mg on their release. *Angiology.* 1994 Jun;45(6 Pt 2):554-9. [PMID: 8203787]
8. Ramelet AA. Clinical benefits of Daflon 500 mg in the most severe stages of chronic venous insufficiency. *Angiology.* 2001 Aug;52 Suppl 1:S49-56. [PMID: 11510597]
9. Laurent R, Gilly R, Frileux C. Clinical evaluation of a venotropic drug in man. Example of Daflon 500 mg. *Int Angiol.* 1988 Apr-Jun;7(2 Suppl):39-43. [PMID: 3053942]
10. Tsouderos Y. Are the phlebotonic properties shown in clinical pharmacology predictive of a therapeutic benefit in chronic venous insufficiency? Our experience with Daflon 500 mg. *Int Angiol.* 1989 Oct-Dec;8(4 Suppl):53-9. [PMID: 2698902]
11. Le Dévéhat C, Khodabandehlou T, Vimeux M, et al. Evaluation of haemorheological and microcirculatory disturbances in chronic venous insufficiency: activity of Daflon 500 mg. *Int J Microcirc Clin Exp.* 1997;17 Suppl 1:27-33. [PMID: 9477042]
12. Galley P, Thiollot M. A double-blind, placebo-controlled trial of a new veno-active flavonoid fraction (S 5682) in the treatment of symptomatic capillary fragility. *Int Angiol.* 1993 Mar;12(1):69-72. [PMID: 8376915]
13. Belcaro G, Cesarone MR, de Sanctis MT, et al. Laser Doppler and transcutaneous oximetry: modern investigations to assess drug efficacy in chronic venous insufficiency. *Int J Microcirc Clin Exp.* 1995;15 Suppl 1:45-9. [PMID: 8748889]
14. Coleridge-Smith P, Lok C, Ramelet AA. Venous leg ulcer: a meta-analysis of adjunctive therapy with micronized purified flavonoid fraction. *Eur J Vasc Endovasc Surg.* 2005 Aug;30(2):198-208. [PMID: 15936227]
15. Smith PC. Daflon 500 mg and venous leg ulcer: new results from a meta-analysis. *Angiology.* 2005 Sep-Oct;56 Suppl 1:S33-9. [PMID: 16193225]
16. Guilhou JJ, Dereure O, Marzin L, et al. Efficacy of Daflon 500 mg in venous leg ulcer healing: a double-blind, randomized, controlled versus placebo trial in 107 patients. *Angiology.* 1997 Jan;48(1):77-85. [PMID: 8995348]
17. Jantet G. Chronic venous insufficiency: worldwide results of the RELIEF study. Reflux assessment and quality of life improvement with micronized flavonoids. *Angiology.* 2002 May-Jun;53(3):245-56. [PMID: 12025911]
18. Valensi PE, Behar A, de Champvallins MM, et al. Effects of a purified micronized flavonoid fraction on capillary filtration in diabetic patients. *Diabet Med.* 1996 Oct;13(10):882-8. [PMID: 8911782]
19. Valensi P, Behar A. Clinical implications of impaired microcirculation. *Int Angiol.* 1995 Sep;14(3 Suppl 1):26-31. [PMID: 8919261]
20. Behar A, Valensi P, de Champvallins M, et al. Capillary filtration and lymphatic resorption in diabetes. Application to the pharmacodynamic activity of Daflon 500 mg. *Int Angiol.* 1989 Oct-Dec;8(4 Suppl):27-9. [PMID: 2632646]
21. Buckshee K, Takkar D, Aggarwal N. Micronized flavonoid therapy in internal hemorrhoids of pregnancy. *Int J Gynaecol Obstet.* 1997 May;57(2):145-51. [PMID: 9184951]
22. Cospite M. Double-blind, placebo-controlled evaluation of clinical activity and safety of Daflon 500 mg in the treatment of acute hemorrhoids. *Angiology.* 1994 Jun;45(6 Pt 2):566-73. [PMID: 8203789]
23. Pari L, Srinivasan S. Antihyperglycemic effect of diosmin on hepatic key enzymes of carbohydrate metabolism in streptozotocin-nicotinamide-induced diabetic rats. *Biomed Pharmacother.* 2010 Sep;64(7):477-81. [PMID: 20362409]
24. Srinivasan S, Pari L. Ameliorative effect of diosmin, a citrus flavonoid against streptozotocin-nicotinamide generated oxidative stress induced diabetic rats. *Chem Biol Interact.* 2012 Jan 5;195(1):43-51. [PMID: 22056647]
25. Manuel y Keenoy B, Vertommen J, De Leeuw I. The effect of flavonoid treatment on the glycation and antioxidant status in Type 1 diabetic patients. *Diabetes Nutr Metab.* 1999 Aug;12(4):256-63. [PMID: 10782751]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Drainage

Formulated for symptoms associated with toxicity such as fatigue, headaches and sluggish elimination



Available in 1 fl oz bottle

Detailed Description

Drainage combines homeopathic liver “drainers” with homeopathic remedies that are known to support excretory function. Drainage focuses on the liver, kidney, and colon functions while addressing symptoms associated with toxicity.

According to the Materia Medica, the following remedies in Drainage may be administered for the following conditions:

Benzoicum acidum: Marked action on metabolism; kidney insufficiency; excess of uric acid.

Berberis vulgaris: Inflammation of kidneys; radiating pains; burning soreness in kidney region; affects liver, promotes flow of bile; cases where renal or vesicle symptoms are prominent.

Bryonia: Mucous membranes are all dry; liver region swollen, sore, tense; biliousness; irritability, nausea, and faintness; polycrest (commonly used) remedy; liver disorders.

Cantharis: Violent inflammations; raw, burning pain; dysuria (painful urination); difficulty swallowing liquids; tenacious mucous.

Carduus benedictus: Sensation of contraction which occurs in many parts; gastrointestinal disturbances; affections (maladies) of the eyes.

Carduus marianus: Liver and spleen disorders; swelling of gallbladder with tenderness; hyperemia of liver with jaundice; cirrhosis; cloudy urine, golden colored; despondency, forgetfulness; apathy.

Ceanothus americanus: Affinity for spleen; splenitis (enlarged spleen); deep-seated or cutting pains; pain in liver and back; dull pain in liver immediately after dinner.

Chelidonium majus: Liver remedy; pain under right scapula; liver enlarged, tender; lethargy; headache; fermentation and sluggish bowels.

Chionanthus virginica: Prominent liver remedy; periodic sick headaches; jaundice; pancreatic diseases; enlarged spleen.

Cinchona officinalis: Circulation; liver and spleen swollen, enlarged; jaundice; gas and bloating of abdomen; irritable, sensitive, and touchy; capricious appetite.

Cynara scolymus: Hepatic and bile drainage in all cases of hepatic insufficiency with stones or rheumatic disorders.

Dioscorea villosa: Acts on nerves, abdominal organs, sciatic nerve, and spinal cord; pains are unbearable, sharp, cutting, twisting, gripping, and grinding; gallstones; kidney stones; colic; abdomen distended; atypical body odors.

Dolichos pruriens: Intense itching without eruption; bloated abdomen; a right-sided remedy (i.e., addresses symptoms that may be worse on the right side of the body) for pronounced liver and skin symptoms.

Iris versicolor: Disorders of the pancreas; migraine and sick headaches; increases flow of bile; bilious attacks.

Juniperus communis: Allergies; coughs; catarrhal inflammation of kidneys; dropsy with suppression of urine; older persons with poor digestion; kidney hyperemia.

Nux vomica: Toxic liver; irritable nervous system; digestive disturbances; biliousness; liver engorged, with stitching pains and soreness; irritable bladder.

Ptelea trifoliata: Stomach and liver symptoms associated with pain in the limbs; edema of feet and legs; stomach pain.

Solidago virgaurea: Kidneys sensitive to pressure; urinary disturbances; feelings of weakness.

Taraxacum officinale: Bitter, sour taste; impatient and irritable; copious and frequent urination; headaches from liver disturbances; gallstones.

Uricum acidum: Most useful in cases where deposits persist, it stirs them up and helps to eliminate them; gout; lipoma.

Drainage

DIRECTIONS: Ages 12 and up, take 6 drops by mouth (ages 0 to 11, give 3 drops) at bedtime or as directed by a healthcare professional.

ACTIVE INGREDIENTS: Equal parts of Cynara 6x, Solidago 6x, Taraxacum 6x, Benzoicum ac. 15x, Berber. vulg. 15x, Bryonia 15x, Cantharis 15x, Carduus ben. 15x, Carduus mar. 15x, Ceanothus 15x, Chelidonium maj. 15x, Chionanthus 15x, Cinchona 15x, Dioscorea 15x, Dolichos 15x, Iris vers. 15x, Juniperus com. 15x, Nux vom. 15x, Ptelea 15x, Taraxacum 15x, Uricum ac. 15x.

INACTIVE INGREDIENTS: USP Purified water; USP Gluten-free, non-GMO, organic cane alcohol 20%.

WARNING: Keep out of reach of children. Do not use if tamper-evident seal is broken or missing. If symptoms worsen or persist for more than a few days, consult a doctor. If pregnant or breast-feeding, ask a doctor before use.

Detoxification

Gastrointestinal Support

Liver Support

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.



Available in 60 vegetarian capsules

Discussion

Effektiv® is an alternative for individuals seeking support for sustained energy, alertness, and motivation but commonly turn to caffeine, a widely consumed central nervous system stimulant. In small quantities, caffeine may boost energy, alertness, and even athletic performance; however, larger amounts of caffeine can cause jitteriness and even more serious problems, such as arrhythmias and changes in blood pressure.^[1] Effektiv contains less caffeine than an average cup of coffee and is combined with a targeted blend of key ingredients designed to promote lasting mental and physical energy and fuel motivation without the undesirable effects of ordinary caffeine.*

PUREENERGY™

Pureenergy is an innovative patent-protected ingredient that combines caffeine with pTeroPure® pterostilbene—a highly bioavailable analog of resveratrol—to form a unique cocrystal structure. Initial reports suggest that the caffeine in Pureenergy may be absorbed more slowly and stay in the body longer than regular caffeine, which may help sustain energy longer. In a preliminary four-week, single-blind, crossover human study (n = 12) that compared 232 mg of Pureenergy (providing 99.76 mg of caffeine) to 100 mg of ordinary caffeine, the absorption of caffeine from Pureenergy was approximately 30% slower and Pureenergy delivered 30% more caffeine to the bloodstream. Furthermore, at six hours, 51% more caffeine from Pureenergy was detected in serum compared to ordinary caffeine.^[2,3] These data point to a potential for reducing total caffeine intake. Additionally, the extended half-life and slower absorption rate of caffeine from Pureenergy may produce a more moderated and gradual finish, thereby preventing the “crash” associated with regular caffeinated energy products. While the results of these studies are promising, larger studies are needed to validate the findings and determine if these findings translate into a lengthened energy effect.*

Taurine

Taurine is a cysteine-derived amino acid that is synthesized in the body and has various functions. It is a major constituent of bile. Studies suggest it is cardioprotective, and it seems to prevent exercise-induced oxidative stress.*^[4-6]

Although clinical studies evaluating its effects are limited, taurine appears to inhibit the potential adverse effects of caffeine. In a double-blind study in college students (N = 14) that investigated the combined effects of the co-administration of caffeine and taurine, researchers observed no effect on short-term memory but did observe a significant decline in heart rate and an increase in mean arterial blood pressure.^[7] Another study explored the impact

Clinical Applications

- » Promotes Mental and Physical Energy and Motivation to Exercise*
- » Promotes Concentration and Focus*
- » Supports Sustained Energy Level and Alertness*
- » Provides an Alternative to Ordinary Caffeine*

*Effektiv® features ingredients selected for their role in promoting energy, alertness, and enjoyment whether support is needed in the classroom, the gym, or the work world. Theacrine promotes mental and physical energy, stamina, focus, and motivation; taurine calms the sympathetic nervous system and may moderate the effect of caffeine; and Pureenergy™ supports sustained energy levels and alertness.**

of an energy drink containing caffeine and taurine on myocardial contractility in healthy volunteers (N = 32) using cardiac magnetic resonance-based strain analysis. Peak systolic strain was measured at baseline and one hour after consumption of the energy drink; later, a subset (n = 10) consumed a caffeine-only drink. While the caffeine-only drink did not seem to produce any significant cardiovascular effects, individuals who consumed the drink with caffeine and taurine registered a significant increase in peak systolic strain.^[8] Additionally, a review of the literature on the effect that taurine and caffeine have on cardiovascular function concluded that taurine can neutralize several untoward effects of caffeine excess.*^[9]

TeaCrine® (Theacrine)

Theacrine is a purine alkaloid found in certain coffee and tea species. Its chemical structure is similar to caffeine, yet it has very different physiological effects. Both caffeine and theacrine inhibit adenosine activity via the A1 and A2A receptors, but caffeine is known to act as an orthosteric inhibitor whereas theacrine is likely to act as an indirect, allosteric modulator of these receptors and contribute to differences in habituation. Inhibitory action of the adenosine receptors plays a role in the biochemical processes that prevent fatigue. Additionally, theacrine is a dopamine D1 and D2 receptor agonist, and its actions help increase dopamine signaling associated with attention, movement, task initiation and completion, mood, learning, and the brain’s “reward center.”*

Whereas caffeine habituation typically occurs within as few as five days of consumption, a significant attribute of theacrine is the lack of habituation or tachyphylaxis (decrease in response). Following an eight-week study with subjects (N = 60) receiving either 200 mg or 300 mg of Teacrine or placebo, participants demonstrated no signs of the rapid tachyphylaxis typically associated with caffeine and other stimulants. Baseline values for energy, focus, concentration, anxiety, motivation to exercise, and a Profile of Mood States (POMS) questionnaire remained stable across the entire eight-week study period. Additionally, all values for clinical safety markers were within normal limits.*^[10]

In a randomized, double-blind, placebo-controlled, crossover pilot study, subjects (n = 15) ingested 200 mg of Teacrine. Over a three-hour post-dosing period, a visual analogue scale (VAS) was used to detect change in various aspects of physical and mental energy and performance. The 200 mg dose was found to significantly improve concentration and energy and reduce fatigue. No changes were noted in systemic hemodynamics and no side effects were observed. A subset of subjects underwent a separate open-label,

Continued on next page

repeated-dose study comparing 100 mg, 200 mg, and 400 mg of Teacrine. This seven-day assessment demonstrated moderate-to-large effect sizes (0.50 to 0.71) in the 200 mg dose group for the following subjective measures: energy, fatigue, concentration, anxiety, motivation to exercise, and libido.*^[1]

In a small, double-blind, placebo-controlled, crossover study, subjects (n = 8) received 25 or 125 mg of theacrine, 150 mg of caffeine, or a combination of theacrine (125 mg) and caffeine (150 mg). Results suggested that while theacrine had no impact on caffeine pharmacokinetics, the combination of caffeine and theacrine led to enhanced theacrine bioavailability. Additionally, a broad spectrum of clinical safety markers, including heart rate and blood pressure, were unaffected by concomitant use indicating a strong safety profile at the doses administered.*^[1,2]

NOTE: Calcium must be declared on a label when present at greater than 2% daily value. Calcium carbonate is an excipient used in Effektiv to distribute particles evenly and improve flow into the capsule; it does not contribute to the formula's intended function.

Effektiv® Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Calcium (as calcium carbonate)	200 mg	15%
Taurine	250 mg	**
TeaCrine® Theacrine	150 mg	**
PUREENERGY™ Caffeine Pterostilbene Cocrystal (50% pterostilbene)	120 mg	**
Caffeine (from PUREENERGY™ caffeine pterostilbene cocrystal and caffeine anhydrous)	80 mg	**
** Daily Value not established.		

Other Ingredients: Capsule (hypromellose and water), ascorbyl palmitate, microcrystalline cellulose, silica, maltodextrin, and calcium silicate.

DIRECTIONS: Take one to two capsules in the morning, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Caffeine should not be combined with synephrine or ephedrine. Use cautiously if you have a history of abnormal heart rhythm. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

TEACRINE is a registered trademark and is protected by Patents Pending, Serial No. 61/903,362, under exclusive global distribution by Compound Solutions, Inc.



PUREENERGY™ is a trademark of ChromaDex, Inc. Patents: See www.ChromaDexPatents.com

References

- Seifert SM, Schaechter JL, Hershoin ER, et al. Health effects of energy drinks on children, adolescents, and young adults. *Pediatrics*. 2011;127(3):511-528. [PMID: 21321035]
- A crossover, clinical evaluation to determine the relative bioavailability, pharmacokinetics and safety of PUREENERGY™ and pTeroPure® in healthy adult males. PK study summary. Miami, FL/Irvine, CA: Miami Research Associates/ChromaDex Inc.; 2013:1-34. [on file]
- Purenergy™: A novel next-generation caffeine alternative. Irvine, CA: ChromaDex Inc.; September 10, 2014:1-5.
- Zhang M, Izumi I, Kagamimori S, et al. Role of taurine supplementation to prevent exercise-induced oxidative stress in healthy young men. *Amino Acids*. 2004 Mar;26(2):203-7. [PMID: 15042451]
- Xu YJ, Arneja AS, Tappia PS, et al. The potential health benefits of taurine in cardiovascular disease. *Exp Clin Cardiol*. 2008 Summer;13(2):57-65. [PMID: 19343117]
- Ito T, Azuma J. Taurine is a possible anti-atherosclerotic agent [in Japanese]. *Nihon Yakurigaku Zasshi*. 2004 May;123(5):311-17. [PMID: 15118255]
- Bichler A, Swenson A, Harris MA. A combination of caffeine and taurine has no effect on short term memory but induces changes in heart rate and mean arterial blood pressure. *Amino Acids*. 2006 Nov;31(4):471-6. [PMID: 16699827]
- Doerner JM, Kuetting DL, Luetkens JA, et al. Caffeine and taurine containing energy drink increases left ventricular contractility in healthy volunteers. *Int J Cardiovasc Imaging*. 2015 Mar;31(3):595-601. [PMID: 25425431]
- Schaffer SW, Shimada K, Jong CJ, et al. Effect of taurine and potential interactions with caffeine on cardiovascular function. *Amino Acids*. 2014;46:1147-1157. [PMID: 24615238]
- Taylor L, Mumford P, Roberts M, et al. Safety of TeaCrine®, a non-habituating, naturally occurring purine alkaloid over eight weeks of continuous use. *J Int Soc Sports Nutr*. 2016 Jan 13;13:2. [PMID: 26766930]
- Habowski S, Sandrock J, Kedia A, et al. The effects of Teacrine™, a nature identical purine alkaloid, on subjective measures of cognitive function, psychometric and hemodynamic indices in healthy humans: a randomized, double-blinded crossover pilot trial. *J Int Soc Sports Nutr*. 2014;11(Suppl 1):P49. doi:10.1186/1550-2783-11-S1-P49.
- He H, Ma D, Crone LB, et al. Assessment of the drug-drug interaction potential between theacrine and caffeine in humans. *J Caffeine Res*. 2017 Sep 1;7(3):95-102. [PMID: 28875060]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Femquil®

Healthy Hormone Support for Women*



Available in 120 vegetarian capsules

Discussion

Whether it be during menstruation, ovulation, or menopause, the hormones in the female cycle fluctuate throughout a woman's lifetime. Hormonal imbalances contribute to the irritability and cramping commonly associated with premenstrual syndrome (PMS) and the hot flashes, sleep problems, and vaginal dryness associated with menopause. Hormonal imbalances may be exacerbated by xenoestrogens, a subcategory of endocrine disruptors that specifically have estrogen-like effects. Xenoestrogens have the capability to alter hormonal function in tissues, including breast, uterus, and cervix. Xenoestrogens may disrupt neurotransmitter balance, glucose homeostasis, normal reproduction, and healthy metabolism.^[1,2] Additionally, improper aromatase conversion of excess estrogens has been associated with certain forms of hormone-dependent cancers. Femquil® provides supplemental ingredients that have been traditionally and clinically used to support healthy hormone balance and promote detoxification of excess estrogens.*

Chaste Tree Berry Extract

Chasteberry (*Vitex agnus-castus*) has been used for centuries to support women with hormone-related gynecologic complaints. Chasteberry is well-known for its balancing effect on female hormones, prompting more regular cycles. Modern research has validated this traditional use by showing that various preparations of chasteberry demonstrate positive effects in women with PMS.^[3,4] The German Commission E approves the use of chasteberry to support menstrual cycle regularity, breast tenderness, and PMS; and it is widely recommended by family physicians and gynecologists in Germany for these issues.^[5] Chasteberry iridoids and flavonoids are thought to exert benefits through indirect effects on various hormones, especially prolactin and progesterone.^[5,6] Chasteberry also supports a normal, healthy attitude during the perimenopausal transition. It appears to significantly compete for binding at the estrogen receptors. Chasteberry has normalized short luteal phases and progesterone synthesis. The popular herb may help ease the common, transient symptom of mild breast tenderness possibly by inhibiting prolactin secretion.*^[7]

Black Cohosh Extract

Black cohosh (*Cimicifuga racemosa*) is an herb traditionally used by American Indians for support of gynecological issues, including menstrual cramping and related low-back discomfort. It is commonly used to address menopausal symptoms, which can be attributed to its gentle phytoestrogenic activity and ability to decrease the production of luteinizing hormone. Simply put, phytoestrogens are naturally occurring compounds in plants that have the ability to block estrogen receptor sites. Research suggests that black cohosh

Clinical Applications

- » Supports Balance of the Female Hormone Cycle*
- » May Ease Common Symptoms Associated with PMS and Menopause*
- » Promotes Estrogen Detoxification*
- » Provides Antioxidant Activity and Cellular Support*

*Femquil® delivers biologically active folate and other key methylation vitamins in combination with a targeted blend of ingredients to encourage hormone balance, help modify xenoestrogen activity, and restore tranquility. Vitex and black cohosh provide traditional hormone-balancing support; DIM, calcium D-glucarate, and 8-prenylnaringenin (from hops extract) promote estrogen detoxification; and rosemary, resveratrol, grape seed extract, and green tea extract provide antioxidant activity.**

effectively maintains a sense of calmness and healthy outlook, and it may help address menopause-associated vasomotor symptoms.^[8,9] According to Ruhlen et al, black cohosh may exert its benefits through selective estrogen receptor modulation, serotonergic pathways, antioxidant activity, or inflammatory pathways.^[10] Various studies demonstrate that black cohosh may also reduce hot flashes, night sweats, vaginal dryness and thinning, sleep disturbances, and emotional symptoms.*^[11,12]

8-prenylnaringenin (8-PN)

Hops are the female seed cones of the hop species *Humulus lupulus*. The prenylflavonoid 8-PN, obtained from the lupulin glands of hop cones, appears to provide greater phytoestrogenic activity than other commonly used isoflavone phytoestrogens, such as daidzein and genistein.^[13] In vitro and in vivo studies indicate a potential role for 8-PN in easing common menopausal concerns.^[14,15] In pilot and prospective studies that were randomized and placebo-controlled, postmenopausal women who took 100-250 mcg/day of 8-PN experienced reductions in vasomotor symptoms and other common menopausal discomforts.^[15,16] 8-PN has also been observed to affect aromatase, a cytochrome P450 isoenzyme responsible for the conversion of circulating androgens into estrogens. Aromatase is expressed in several tissues, such as breast tissue, where estrogens exert physiological activity.^[17] Research has suggested that prenylflavonoids interact with aromatase in a manner that positively affects endogenous estradiol biosynthesis.*^[18]

Diindolylmethane (DIM) and Glucoraphanin

Healthy metabolism of exogenous and endogenous estrogens can be pivotal for hormonal balance.^[19] DIM (3,3'-diindolylmethane) is the stable, bioactive metabolite formed when stomach acid breaks down indole-3-carbinol (I3C), a sulfur-containing glucosinolate present in cruciferous vegetables.^[20] DIM has been found to support hormone metabolism and immune activity and stimulate antioxidant and detoxification systems.^[21] DIM helps maintain safe estrogen levels by aiding the conversion of dangerous estrogen fractions to more favorable metabolites and by promoting restoration of healthy hormone ratios. It promotes metabolism of estrogen into the favorable and protective 2-hydroxyestrone (2-OHE) metabolite versus production of 4-hydroxyestrone (4-OHE) and 16-alpha-hydroxyestrone (16-alphaOHE) metabolites.*^[22]

The action of DIM is complemented by glucoraphanin, a compound isolated from broccoli seed that breaks down into sulforaphane glucosinolate (SGS). Researchers have shown that when SGS is broken down to sulforaphane (its active form), it safely and effectively upregulates the Nrf2 system,

Continued on next page

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

activates the antioxidant response element (ARE), enhances the production of important antioxidants, and activates vital phase II detoxification enzymes.^[23] These mechanisms provide protection from toxins, xenoestrogens, and reactive intermediates formed after phase I detoxification.*

Additional Antioxidant Activity and Detoxification Support

Femquil provides additional ingredients that provide antioxidant activity and support detoxification. Calcium D-glucarate (CGT), produced naturally in very small amounts in the body and found in many fruits and vegetables, is included for its support of glucuronidation (phase II oxidation). Green tea catechins have been found to assist in free radical scavenging and support detoxification through modification of phase I and phase II enzymes. Turmeric extract provides curcumin, a phytonutrient valued for its promotion of antioxidant activity and support of metabolic detoxification. While resveratrol (*Polygonum cuspidatum*) may be best known for its antioxidant activity, it also provides phytoestrogenic activity. Both rosemary and grape seed extracts also provide antioxidant activity.*

Folate, Methylcobalamin (B12), Vitamin B6, Calcium, and Magnesium

Readily available forms of B vitamins, including 5-methyltetrahydrofolate (folate), methylcobalamin (B12), and pyridoxal 5'-phosphate (B6) are included for their role in supporting methylation. Highly bioavailable forms of calcium and magnesium are included for their role in muscle contraction and relaxation.*

Femquil® Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Vitamin B6 (as pyridoxine HCl and pyridoxal 5'-phosphate)	15 mg	882%
Folate (as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt)	200 mcg DFE	50%
Vitamin B12 (as MecobalActive™ methylcobalamin)	200 mcg	8333%
Calcium (as DimaCal® dicalcium malate, calcium D-glucarate, and TRAACS® calcium bisglycinate chelate)	60 mg	5%
Magnesium (as Albion® dimagnesium malate)	25 mg	6%
Calcium D-Glucarate	100 mg	**
Diindolylmethane (DIM)	50 mg	**
Green Tea Extract (<i>Camellia sinensis</i>)(leaf)(98% polyphenols, 75% catechins, and 45% EGCG)	50 mg	**
Black Cohosh Extract (<i>Cimicifuga racemosa</i>)(root and rhizome) (2.5% triterpene glycosides)	50 mg	**
Chaste Tree Extract (<i>Vitex agnus-castus</i>)(berry)(0.6% aucubin and 0.5% agnuside)	50 mg	**
Turmeric Extract (<i>Curcuma longa</i>)(root)(95% curcuminoids)	25 mg	**
Rosemary Extract (<i>Rosmarinus officinalis</i>)(leaf)(5% rosmarinic acid)	25 mg	**
<i>trans</i> -Resveratrol (from <i>Polygonum cuspidatum</i>)(root)	20 mg	**
Grape Seed Extract (<i>Vitis vinifera</i>)(seeds)(95% proanthocyanidins)	12.5 mg	**
truebroc® Glucoraphanin (from broccoli extract)(<i>Brassica oleracea italica</i>)(seed)	4.5 mg	**
8-prenylnaringenin (from hops extract)(<i>Humulus lupulus</i>)(cones)	100 mcg	**

** Daily Value not established.

Other Ingredients: Capsule (hypromellose and water), maltodextrin, ascorbyl palmitate, microcrystalline cellulose, silica, L-leucine, tricalcium phosphate, and hydroxypropyl cellulose.

DIRECTIONS: Take two capsules twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

 Quatrefolic is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,662.

 Albion, DimaCal, TRAACS and the Albion Gold Medallion design are registered trademarks of Albion Laboratories, Inc. Malates covered by U.S. Patent 6,706,904.

 Produced under US patent 6,521,818 licensed from Brassica Protection Products LLC. truebroc is a registered trademark of Brassica Protection Products LLC.

 MecobalActive™ is a trademark of Ferrer Health Tech. The color form of.

Calcium D-glucarate is licensed from Applied Food Sciences, Inc. and is protected by US patent 7,662,863.

References

- Singleton DW, Khan SA. Xenoestrogen exposure and mechanisms of endocrine disruption. *Front Biosci*. 2003 Jan 1;8:s110-8. Review. [PMID: 12456297]
- Nadal A, Ropero AB, Laribi O, et al. Nongenomic actions of estrogens and xenoestrogens by binding at a plasma membrane receptor unrelated to estrogen receptor alpha and estrogen receptor beta. *Proc Natl Acad Sci U S A*. 2000 Oct 10;97(21):11603-8. [PMID: 11027358]
- Schellenberg R, Zimmermann C, Drewe J, et al. Dose-dependent efficacy of the Vitex agnus castus extract Ze 440 in patients suffering from premenstrual syndrome. *Phytomedicine*. 2012 Nov 15;19(14):1325-31. [PMID: 23022391]
- Zamani M, Neghab N, Torabian S. Therapeutic effect of Vitex agnus castus in patients with premenstrual syndrome. *Acta Med Iran*. 2012;50(2):101-06. [PMID: 22359078]
- Roemheld-Hamm B. Chasteberry. *Am Fam Physician*. 2005 Sep 1;72(5):821-24. [PMID: 16156340]
- Schellenberg R. Treatment for the premenstrual syndrome with agnus castus fruit extract: prospective, randomised, placebo controlled study. *BMJ*. 2001 Jan 20;322(7279):134-37. [PMID: 11159568]
- Chopin LB. Vitex agnus castus essential oil and menopausal balance: a research update. *Complement Ther Nurs Midwifery*. 2003 Aug;9(3):157-60. [PMID: 12852933]
- Geller SE, Studee L. Botanical and dietary supplements for menopausal symptoms: what works, what does not. *J Womens Health (Larchmt)*. 2005 Sep;14(7):634-49. [PMID: 16181020]
- Nappi RE, Malavasi B, Brundu B, et al. Efficacy of Cimicifuga racemosa on climacteric complaints: a randomized study versus low-dose transdermal estradiol. *Gynecol Endocrinol*. 2005 Jan;20(1):30-5. [PMID: 15969244]
- Ruhlen RL, Sun GY, Sauter ER. Black cohosh: insights into its mechanism(s) of action. *Integr Med Insights*. 2008;3:21-32. [PMID: 21614156]
- Lieberman S. A review of the effectiveness of Cimicifuga racemosa (black cohosh) for the symptoms of menopause. *J Women's Health*. 1998 June;7(5):525-9. [PMID: 9650153]
- Mohammad-Alizadeh-Charandabi S, Shahnaizi M, Nahaee J, et al. Efficacy of black cohosh (*Cimicifuga racemosa* L.) in treating early symptoms of menopause: a randomized clinical trial. *Chin Med*. 2013 Nov 1;8(1):20. [PMID: 24499633]
- Overk CR, Yao P, Chadwick LR, et al. Comparison of the in vitro estrogenic activities of compounds from hops (*Humulus lupulus*) and red clover (*Trifolium pratense*). *J Agric Food Chem*. 2005 Aug 10;53(16):6246-53. [PMID: 16076101]
- Bowe J, Li XF, Kinsey-Jones J, et al. The hop phytoestrogen, 8-prenylnaringenin, reverses the ovariectomy-induced rise in skin temperature in an animal model of menopausal hot flushes. *J Endocrinol*. 2006 Nov;191(2):399-405. [PMID: 17088409]
- Heyerick A, Vervarcke S, Depypere H, et al. A first prospective, randomized, double-blind, placebo-controlled study on the use of a standardized hop extract to alleviate menopausal discomforts. *Maturitas*. 2006 May 20;54(2):164-75. [PMID: 16321485]
- Erkkola R, Vervarcke S, Vansteelandt S, et al. A randomized, double-blind, placebo controlled, cross-over pilot study on the use of a standardized hop extract to alleviate menopausal discomforts. *Phytomedicine*. 2010 May;17(6):389-96. [PMID: 20167461]
- Monteiro R, Faria A, Azevedo I, et al. Modulation of breast cancer cell survival by aromatase inhibiting hop (*Humulus lupulus* L.) flavonoids. *J Steroid Biochem Mol Biol*. 2007 Jun-Jul;105(1-5):124-30. [PMID: 17643984]
- van Meeuwen JA, Nijmeijer S, Mutarapat T, et al. Aromatase inhibition by synthetic lactones and flavonoids in human placental microsomes and breast fibroblasts—a comparative study. *Toxicol Appl Pharmacol*. 2008 May 1;228(3):269-76. [PMID: 18201740]
- Lord RS, Bongiovanni B, Bralley JA. Estrogen metabolism and the diet-cancer connection: rationale for assessing the ratio of urinary hydroxylated estrogen metabolites. *Altern Med Rev*. 2002 Apr;7(2):112-29. [PMID: 11991791]
- Bradlow HL. Review. Indole-3-carbinol as a chemoprotective agent in breast and prostate cancer. *In Vivo*. 2008 Jul-Aug;22(4):441-5. [PMID: 18712169]
- Riby JE, Xue L, Chatterji U, et al. Activation and potentiation of interferon-gamma signaling by 3,3'-diindolylmethane in MCF-7 breast cancer cells. *Mol Pharmacol*. 2006 Feb;69(2):430-9. [PMID: 16267208]
- Cavalieri E, Frenkel K, Liehr JG, et al. Estrogens as endogenous genotoxic agents—DNA adducts and mutations. *J Natl Cancer Inst Monogr*. 2000;(27):75-93. [PMID: 10963621]
- Keum YS. Regulation of the Keap1/Nrf2 system by chemopreventive sulforaphane: implications of posttranslational modifications. *Ann N Y Acad Sci*. 2011 Jul;1229:184-89. [PMID: 21793854]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

FIT Food™ Lean



Available in Vanilla Delight and Creamy Chocolate

Discussion

VegaPro™ is XYMOGEN's proprietary blend of pea protein isolate and rice protein concentrate, L-glutamine, glycine, and taurine. Also added is Aminogen™—a patented, natural, plant-derived enzyme system clinically proven to increase protein digestibility and amino acid absorption.^[1] Its action boosts nitrogen retention, aids in the synthesis of muscle mass and strength, and promotes deep muscle recovery.*

The non-genetically modified (non-GMO), highly digestible pea protein isolate in VegaPro is naturally obtained by simple water extraction, keeping all the nutritional qualities intact. Its 90% protein content features a well-balanced amino acid profile, including a high content of lysine, arginine, and branched-chain amino acids to help maintain lean body mass and reduce body fat.^[2] Pea protein has the highest lysine concentration (7.2%) of all vegetable-based proteins and the highest arginine concentration (8.7%) among all commercially available proteins. The combination of pea protein and rice protein achieves an amino acid score of 100%.*

Fructose Free FIT Food Lean contains evaporated cane juice and stevia in place of fructose. Animal and human research suggests that consuming fructose-containing beverages increases visceral adiposity.*^[3,4]

Glutamine, crucial in nitrogen metabolism, is important for replenishing amino acid stores, especially after exercise or stress.^[5] This amino acid aids in intestinal cell proliferation, thereby preserving gut barrier function and intestinal health.*

Glycine, an inhibitory (calming) neurotransmitter, is vital as a constituent of collagen and a building block for other substances, such as coenzyme-A, nucleic acids, creatine phosphate, purines, bile, and other amino acids.*

Taurine, a derivative of sulfur-containing cysteine, has many healthful clinical applications, including the support of stable cell membranes,

Clinical Applications

- » Supports Healthy Body Composition*
- » Supports Immune Health*
- » Supports Post-Exercise Recovery*
- » Supports Healthy Glucose Metabolism*
- » Supports Gastrointestinal Health*
- » Contributes to Macro-Nutrition*

FIT Food™ Lean is an easy-to-mix functional food for vegans, individuals sensitive or allergic to soy and/or dairy, or anyone seeking an alternative source of quality protein. FIT Food Lean features VegaPro™, an all-natural rice and pea protein blend.

cardiovascular health, glucose tolerance, detoxification, and bile salt synthesis.*^[6]

Fiber Blend (inulin from non-GMO chicory, beta glucans, oat fiber, and corn bran) FIT Food Lean provides 6 g of fiber per serving. These fibers favorably affect serum lipids, healthy intestinal flora, the formation of short-chain fatty acids, and glucose tolerance.^[7] Beta glucans and lignins impact the binding of bile acids and support the maintenance of healthy cholesterol levels already within the normal range.^[8] Beta glucans may also offset stress to the immune system caused by intense exercise.*^[9]

Satisfaction: An Added Benefit of Increasing Protein Intake Signals that originate from the gut—in response to mechanical (gastric distention) and chemical changes that occur after the ingestion of food—let us know when we've had enough to eat. Among the macronutrients in food, proteins have been identified as having the greatest impact in this regard. Thus, the effect of consuming high-protein foods has been observed not only to yield a strong feeling of satisfaction immediately after intake but also to support a lower food intake during a subsequent meal.*^[10]

It is possible that not all proteins afford the same degree of satiety. A study on human and rat duodenal biopsies demonstrated that exposure to pea protein resulted in the release of the greatest amount of cholecystokinin (CCK) and glucagon-like peptide 1.^[11] These gastrointestinal hormones modulate appetite sensations.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

FIT Food™ Lean Vanilla Delight Nutrition Facts

14 servings per container

Serving size	2 scoops (about 40g)
Amount per serving	150
Calories	
	% Daily Value*
Total Fat 2.5g	3%
Saturated Fat 1g	5%
<i>Trans Fat</i> 0g	
Cholesterol 0mg	0%
Sodium 370mg	16%
Total Carbohydrate 14g	5%
Dietary Fiber 5g	18%
Total Sugars 5g	
Includes 5g Added Sugars	10%
Protein 17g	
Vitamin D 0mcg	0%
Calcium 17mg	2%
Iron 3mg	15%
Potassium 350mg	8%

* The % Daily Value tells you how much a nutrient in a serving of food contributes to a daily diet. 2,000 calories a day is used for general nutrition advice.

INGREDIENTS: VegaPro™ (XYMOGEN's proprietary blend of pea protein isolate, glycine, taurine, rice protein concentrate, and L-glutamine), organic dried cane syrup, fiber complex (inulin (from chicory) and oat fiber), natural flavors (no MSG), sunflower oil, tripotassium citrate, cellulose gum, xanthan gum, medium-chain triglyceride oil, Aminogen® (proprietary plant enzyme blend), guar gum, silica, and stevia leaf extract.

DIRECTIONS: Mix two scoops (40 g) in 8-12 oz cold water and consume. Adjust amount of water according to thickness desired. May be used as a snack, a "rescue" food, an occasional meal replacement, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep tightly closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

 AMINOGEN® is a registered trademark of Innophos Nutrition, Inc. AMINOGEN® is protected under US patent 5,387,422.



Typical Amino Acid Profile Per Serving:

Alanine	900 mg	Methionine	230 mg
Arginine	1,820 mg	Phenylalanine	1,150 mg
Aspartic Acid	2,400 mg	Proline	940 mg
Cysteine	210 mg	Serine	1,110 mg
Glutamic Acid	3,520 mg	Taurine	500 mg
Glycine	2,860 mg	Threonine	820 mg
Histidine	520 mg	Tryptophan	210 mg
Isoleucine	940 mg	Tyrosine	800 mg
Leucine	1,760 mg	Valine	1,050 mg
Lysine	1,500 mg		

References

- Oben J, Kothari SC, Anderson ML. An open-label study to determine the effects of an oral proteolytic enzyme system on whey protein concentrate metabolism in healthy males. *J Int Soc Sports Nutr.* 2008 Jul 24;5:10. [PMID: 18652668]
- Rigamonti E, Parolini C, Marchesi M, et al. Hypolipidemic effect of dietary pea proteins: Impact on genes regulating hepatic lipid metabolism. *Mol Nutr Food Res.* 2010 May;54 Suppl 1:S24-30. [PMID: 20077421]
- Jürgens H, Haass W, Castañeda TR, et al. Consuming fructose-sweetened beverages increases body adiposity in mice. *Obes Res.* 2005 Jul;13(7):1146-56. [PMID: 16076983]
- Stanhope KL, Schwarz JM, Keim NL, et al. Consuming fructose-sweetened, not glucose-sweetened, beverages increases visceral adiposity and lipids and decreases insulin sensitivity in overweight/obese humans. *J Clin Invest.* 2009 May;119(5):1322-34. doi: 10.1172/JCI37385. [PMID: 19381015]
- Castell L. Glutamine supplementation in vitro and in vivo, in exercise and in immunodepression. *Sports Med.* 2003;33(5):323-45. [PMID: 12696982]
- Yatabe Y, Miyakawa S, Ohmori H, et al. Effects of taurine administration on exercise. *Adv Exp Med Biol.* 2009;643:245-52. [PMID: 19239155]
- de Luis DA, de la Fuente B, Izaola O, et al. Randomized clinical trial with a inulin enriched cookie on risk cardiovascular factor in obese patients [in Spanish]. *Nutr Hosp.* 2010 Jan-Feb;25(1):53-59. [PMID: 20204256]
- Queenan KM, Stewart ML, Smith KN, et al. Concentrated oat beta-glucan, a fermentable fiber, lowers serum cholesterol in hypercholesterolemic adults in a randomized controlled trial. *Nutr J.* 2007 Mar 26;6:6. [PMID: 17386092]
- Vetvicka V, Vancikova Z. Anti-stress action of several orally-given β-glucans. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub.* 2010 Sep;154(3):235-38. [PMID: 21048809]
- Johnstone AM, Stubbs RJ, Harbron CG. Effect of overfeeding macronutrients on day-to-day food intake in man. *Eur J Clin Nutr.* 1996 Jul;50(7):418-30. [PMID: 8862477]
- Geraedts MC, Troost FJ, Tinnemans R, et al. Release of satiety proteins in response to specific dietary proteins is different between human and murine small intestinal mucosa. *Ann Nutr Metab.* 2010;56(4):308-313. [PMID: 20530962]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

FIT Food™ Lean Complete Sugar- & Stevia-Free‡



Available in French Vanilla and Dutch Chocolate

‡This formula is not a low-calorie dietary supplement. Please see the Supplement Facts panel for more details.

Discussion

VegaPro™, XYMOGEN's proprietary blend of highly digestible pea protein isolate, glycine, taurine, rice protein concentrate, and L-glutamine, is the cornerstone of FIT Food Lean Complete Sugar- & Stevia-Free. Aminogen is added to enhance protein digestion and absorption.^[1] The combination of pea protein and rice protein achieves an amino acid score of 100% and supports protein metabolism and healthy body composition.*^[2]

Protein is required for cell and tissue repair, hormone and enzyme synthesis, and a variety of metabolic functions. It is especially important for maintaining lean body mass during increased physical activity. Protein supplementation has been found to be a determining factor in increasing fat-free mass and exercise-stimulated fat oxidation. Subjects who consumed a significantly higher protein intake (~80 g/d versus ~59 g/d) experienced a significant increase in fat oxidation and fat-free mass with a significant decrease in fat mass and body fat percentage.^[3] Studies have indicated that increased protein intake enhances satiety^[2,4-6] and supports diminished food intake during subsequent meals.^[7] One randomized crossover study suggested that pea protein was superior to milk protein with respect to satiety and intermeal interval.^[8] Research has also demonstrated that pea protein stimulates release of cholecystokinin and glucagon-like peptide 1, gastrointestinal hormones that modulate appetite sensations.*^[9]

While pea-based protein provides a satisfying and versatile source of protein, it also supports cardiovascular health. Animal studies have suggested that it positively affects lipid homeostasis by modulating gene expression; that is, upregulating genes that affect hepatic cholesterol uptake and downregulating genes that affect fatty acid synthesis.*^[10,11]

Artinia® Chitin-Glucan is incorporated into FIT Food Lean Complete Sugar- & Stevia-Free to support antioxidant activity and cardiovascular health. Artinia is a purified, insoluble, gluten-free fiber ingredient composed of chitin (N-acetyl-D-glucosamine) and beta(1,3)-glucan chains.^[12] Artinia has been researched for its effects on maintaining oxidative balance and artery health, key components of cardiovascular health. A 12-week animal study indicated that chitin-glucan supports cardiovascular health by maintaining healthy arteries,

Clinical Applications

- » Supports Protein Metabolism and Healthy Body Composition*
- » Supports Cardiovascular Health*
- » Supports Gastrointestinal Health*
- » Supports Antioxidant Systems*
- » Provides Essential Micronutrients*

***FIT Food™ Lean Complete Sugar- & Stevia-Free‡** is a nutrient-rich shake mix ideal for vegans, individuals sensitive or allergic to soy and/or dairy, or those seeking an alternative source of quality protein. FIT Food Lean Complete Sugar- & Stevia-Free features VegaPro™, an all-natural pea and rice protein blend; Aminogen®, a plant enzyme that enhances protein digestibility and absorption; and Artinia® chitin-glucan, a novel fiber that supports antioxidant systems in the body. This sugar- and stevia- free formula provides an array of micronutrients, including high-potency B12, activated B vitamins, and Albion® TRAACS® chelated minerals (the real amino acid chelate system).**

reducing cardiac superoxide anion and liver malondialdehyde (markers of oxidation), and enhancing superoxide dismutase and glutathione peroxidase activity.*^[13]

Human trials have revealed significantly positive results as well. A six-week, multicenter, randomized, double-blind, placebo-controlled study (n = 130) of Artinia revealed that 1.5 g/d significantly supported subjects' LDL cholesterol at levels already within normal range, and 4.5 g/d significantly supported subjects' natural antioxidant systems and oxidative balance of LDL cholesterol.^[14,15] A 28-day pilot study found Artinia to be safe and well-tolerated at a dose of 4.5 g/d.^[15] FIT Food Lean Complete Sugar- & Stevia-Free provides 2.25 g of Artinia per serving. Artinia is a healthy alternative to phytosterol supplementation and has not been observed to interfere with absorption of fat-soluble vitamins or antioxidants.*

Micronutrient Support FIT Food Lean Complete Sugar- & Stevia-Free delivers a balanced profile of vitamins, minerals, and antioxidants, nutrients vital to supporting the vast array of metabolic processes in the body.^[16] B vitamins are present in their bioactive forms, including riboflavin 5'-phosphate, pyridoxal 5'-phosphate, methylcobalamin, and 5-methyltetrahydrofolate as Quatrefolic®.*^[17]

Sugar- and Stevia-Free This formula is sweetened with monk fruit extract in place of sugar or stevia. Animal and human research suggests that superfluous consumption of added sugars increases adiposity, disrupts lipid regulation, and elevates cardiometabolic risk.*^[18-22]

Glutamine The conditionally essential amino acid glutamine is important for replenishing amino acid stores, especially after exercise or stress.^[23] Glutamine also supports intestinal cell proliferation and thereby preserves gut barrier function and intestinal health.*^[24-26]

Inulin This soluble fiber is fermented by colonic bacteria into short-chain fatty acids that exert a positive effect on lipid metabolism and support healthy colon transit time.*^[27,28]

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

FIT Food™ Lean Complete Sugar- & Stevia-Free French Vanilla Supplement Facts

Serving Size: 2 Scoops (about 38 g)
Servings Per Container: About 14

	Amount Per Serving	%DV
Calories	150	
Total Fat	5 g	6% [†]
Saturated Fat	2.5 g	13% [†]
Total Carbohydrate	11 g	4% [†]
Dietary Fiber	7 g	25%
Protein	15 g	
Vitamin A (75% as natural beta-carotene and 25% as retinyl palmitate)	560 mcg	62%
Vitamin C (as sodium ascorbate, potassium ascorbate, zinc ascorbate, and calcium ascorbate)	125 mg	139%
Vitamin E (as d-alpha tocopheryl succinate)	33.5 mg	223%
Thiamin (as thiamine mononitrate)	5 mg	417%
Riboflavin (as riboflavin 5'-phosphate sodium)	5 mg	385%
Niacin (as niacinamide and niacin)	16 mg	100%
Vitamin B6 (as pyridoxal 5'-phosphate)	5 mg	294%
Folate (as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt)	100 mcg DFE	25%
Vitamin B12 (as methylcobalamin)	125 mcg	5208%
Biotin	250 mcg	833%
Pantothenic Acid (as d-calcium pantothenate)	50 mg	1000%
Choline (as choline dihydrogen citrate)	9 mg	2%
Calcium (as DimaCal® dicalcium malate and ingredients with naturally occurring calcium)	45 mg	3%
Iron (naturally occurring)	3 mg	17%
Iodine (as potassium iodide)	25 mcg	17%
Magnesium (as Albion® dimagnesium malate)	25 mg	6%
Zinc (as TRAACS® zinc bisglycinate chelate)	3.25 mg	30%
Selenium (as Albion® selenium glycinate complex)	25 mcg	45%
Manganese (as TRAACS® manganese bisglycinate chelate)	0.125 mg	5%
Chromium (as TRAACS® chromium nicotinate glycinate chelate)	125 mcg	357%
Molybdenum (as TRAACS® molybdenum glycinate chelate)	12.5 mcg	28%
Sodium (naturally occurring)	340 mg	15%
Potassium (from tripotassium citrate, Albion® potassium glycinate complex, and ingredients with naturally occurring potassium)	510 mg	11%
Artinia® (chitin-glucan from <i>Aspergillus niger</i>)	2.25 g	**
Mixed Tocopherols	18 mg	**
Inositol	9 mg	**
PABA (para-aminobenzoic acid)	3.25 mg	**
Vanadium (as TRAACS® vanadium nicotinate glycinate chelate)	187.5 mcg	**

[†] Percent Daily Values (DV) are based on a 2,000 calorie diet.
^{**} Daily Value (DV) not established.

Other Ingredients: VegaPro™ (XYMOGEN's proprietary blend of pea protein isolate, glycine, taurine, rice protein concentrate, and L-glutamine), inulin (from chicory), natural flavors (no MSG), sunflower oil, medium-chain triglyceride oil, cellulose gum, xanthan gum, Aminogen® fungal proteases, guar gum, and monk fruit extract.

DIRECTIONS: Mix two scoops (38 g) in 6-8 oz of cold water and consume. Adjust amount of water according to thickness desired. May be used as a snack or meal supplement, or taken as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, artificial colors, artificial sweeteners, or artificial preservatives.

‡This formula is not a low-calorie dietary supplement. Please see the Supplement Facts panel for more details.



AMINOGEN is a registered trademark of Inophos Nutrition, Inc. AMINOGEN is protected under US patent 5,387,422.



Albion®, DimaCal®, TRAACS® and the Gold Medallion® are registered trademarks of Albion Laboratories, Inc. Malates covered by US patent 6,706,904.



Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,662.

ARTINIA® is a registered trademark of Novus Nutrition Brands, LLC. Protected by US patent 7,556,946.



Typical Amino Acid Profile Per Serving:

Alanine	800 mg	Methionine	210 mg
Arginine	1,610 mg	Phenylalanine	1,020 mg
Aspartic Acid	2,120 mg	Proline	830 mg
Cysteine	190 mg	Serine	980 mg
Glutamic Acid	3,110 mg	Threonine	500 mg
Glycine	2,760 mg	Taurine	720 mg
Histidine	460 mg	Tryptophan	190 mg
Isoleucine	830 mg	Tyrosine	710 mg
Leucine	1,550 mg	Valine	930 mg
Lysine	1,320 mg		

References

- Oben J, Kothari SC, Anderson ML. An open label study to determine the effects of an oral proteolytic enzyme system on whey protein concentrate metabolism in healthy males. *J Int Soc Sports Nutr.* 2008 Jul 24;5:10. [PMID: 18652668]
- Westerterp-Plantenga MS, Lemmens SG, Westerterp KR. Dietary protein - its role in satiety, energetics, weight loss and health. *Br J Nutr.* 2012 Aug;108 Suppl 2:S105-12. Review. [PMID: 23107521]
- Soenen S, Plasqui G, Smeets AJ, et al. Protein intake induced an increase in exercise stimulated fat oxidation during stable body weight. *Physiol Behav.* 2010 Dec 2;101(5):770-4. [PMID: 20826169]
- Halton TL, Hu FB. The effects of high protein diets on thermogenesis, satiety and weight loss: a critical review. *J Am Coll Nutr.* 2004 Oct;23(5):373-85. Review. [PMID: 15466943]
- Anderson GH, Moore SE. Dietary proteins in the regulation of food intake and body weight in humans. *J Nutr.* 2004 Apr;134(4):974S-9S. Review. [PMID: 15051857]
- Veldhorst M, Smeets A, Soenen S, et al. Protein-induced satiety: effects and mechanisms of different proteins. *Physiol Behav.* 2008 May 23;94(2):300-7. Review. [PMID: 18282589]
- Johnstone AM, Stubbs RJ, Harbron CG. Effect of overfeeding macronutrients on day-to-day food intake in man. *Eur J Clin Nutr.* 1996 Jul;50(7):418-30. [PMID: 8862477]
- Diepvens K, Häberer D, Westerterp-Plantenga M. Different proteins and biopeptides differently affect satiety and anorexigenic/orexigenic hormones in healthy humans. *Int J Obes (Lond).* 2008 Mar;32(3):510-8. [PMID: 18345020]
- Geraedts MC, Troost FJ, Tinnemans R, et al. Release of satiety hormones in response to specific dietary proteins is different between human and murine small intestinal mucosa. *Ann Nutr Metab.* 2010;56(4):308-13. [PMID: 20530962]
- Rigamonti E, Parolini C, Marchesi M, et al. Hypolipidemic effect of dietary pea proteins: impact on genes regulating hepatic lipid metabolism. *Mol Nutr Food Res.* 2010 May;54 Suppl 1:S24-30. [PMID: 20077421]
- Parolini C, Manzini S, Busnelli M, et al. Effect of the combinations between pea proteins and soluble fibres on cholesterolaemia and cholesterol metabolism in rats. *Br J Nutr.* 2013 Oct;110(8):1394-401. [PMID: 23458494]
- Stratum Nutrition. Artinia™ technical data. <http://ckingredients.com/pdf/Products-Artinia.pdf>. Accessed January 24, 2017.
- Berecochea-Lopez A, Decordé K, Ventura E, et al. Fungal chitin-glucan from *Aspergillus niger* efficiently reduces aortic fatty streak accumulation in the high-fat fed hamster, an animal model of nutritionally induced atherosclerosis. *J Agric Food Chem.* 2009 Feb 11;57(3):1093-8. [PMID: 19154104]
- Bays HE, Evans JL, Maki KC, et al. Chitin-glucan fiber effects on oxidized low-density lipoprotein: a randomized controlled trial. *Eur J Clin Nutr.* 2013 Jan;67(1):2-7. [PMID: 22948945]
- Deschamps A, Nollevaux G, Gautier S, et al. Managing oxidative stress with a vegetal ingredient, chitin-glucan. *Agrofood.* 2009;20(4):12-14. [on file]
- Ames BN. A role for supplements in optimizing health: the metabolic tune-up. *Arch Biochem Biophys.* 2004 Mar 1;423(1):227-34. [PMID: 14989256]
- Quatrefolic. <http://www.quatrefolic.com/>. Accessed January 24, 2017.
- Stanhope KL, Schwarz JM, Keim NL, et al. Consuming fructose-sweetened, not glucose-sweetened, beverages increases visceral adiposity and lipids and decreases insulin sensitivity in overweight/obese humans. *J Clin Invest.* 2009 May;119(5):1322-34. [PMID: 19381015]
- Pollock NK, Bundy V, Kanto W, et al. Greater fructose consumption is associated with cardiometabolic risk markers and visceral adiposity in adolescents. *J Nutr.* 2012 Feb;142(2):251-57. [PMID: 22190023]
- Stanhope KL, Havel PJ. Fructose consumption: recent results and their potential implications. *Ann N Y Acad Sci.* 2010 Mar;1190:15-24. Review. [PMID: 20388133]
- Stanhope KL, Havel PJ. Fructose consumption: considerations for future research on its effects on adipose distribution, lipid metabolism, and insulin sensitivity in humans. *J Nutr.* 2009 Jun;139(6):1236S-1241S. [PMID: 19403712]
- DiNicolantonio JJ, Berger A. Added sugars drive nutrient and energy deficit in obesity: a new paradigm. *Open Heart.* 2016 Aug 2;3(2):e000469. [PMID: 27547437]
- Castell L. Glutamine supplementation in vitro and in vivo, in exercise and in immunodepression. *Sports Med.* 2003;33(5):323-45. Review. [PMID: 12696982]
- Chwals WJ. Regulation of the cellular and physiological effects of glutamine. *Mini Rev Med Chem.* 2004 Oct;4(8):833-8. Review. [PMID: 15544544]
- McAnena OJ, Moore FA, Moore EE, et al. Selective uptake of glutamine in the gastrointestinal tract: confirmation in a human study. *Br J Surg.* 1991 Apr;78(4):480-82. [PMID: 1903318]
- Souba WW, Klimberg VS, Plumley DA, et al. The role of glutamine in maintaining a healthy gut and supporting the metabolic response to injury and infection. *J Surg Res.* 1990 Apr;48(4):383-91. Review. [PMID: 2187115]
- Roberfroid M. Dietary fiber, inulin, and oligofructose: a review comparing their physiological effects. *Crit Rev Food Sci Nutr.* 1993;33(2):103-48. Review. [PMID: 8257475]
- Flamm G, Glinsmann W, Kritchevsky D, et al. Inulin and oligofructose as dietary fiber: a review of the evidence. *Crit Rev Food Sci Nutr.* 2001 Jul;41(5):353-62. Review. [PMID: 11497328]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

FIT Food™ Lean Whey

Whey Protein Shake Mix



Available in Creamy Chocolate No Added Sugar, No Stevia & Vanilla Delight No Added Sugar, No Stevia

Discussion

New Zealand Biosciences™ Proprietary Whey Protein Blend (NZ whey protein concentrate, L-glutamine, glycine, and taurine) is sourced from New Zealand, which is known for its highly strict dairy processing standards. Guaranteed 100% pure (hormone free), this high-biological-value whey protein concentrate contains a rich array of essential and non-essential amino acids. Whey protein is considered the “gold standard” of protein for serious athletes. Research suggests that it supports healthy body composition, retention of lean muscle mass, glucose metabolism, satiety, and gastrointestinal health.^[1-5] Its roles in the maintenance of blood pressure and blood lipid levels already within the normal range are also areas of interest.^[3,5] As a rich source of the sulfur-containing amino acids cysteine and methionine, whey protein can enhance immune function through intracellular conversion to glutathione.^[3] Whey protein also delivers high levels of naturally occurring bioactive immunoglobulins that are resistant to peptic digestion. Immunoglobulins from whey have been observed to support intestinal immunity and a healthy response to inflammation.^[3,4] Furthermore, whey protein has displayed lower allergenicity than casein.*^[6]

Glutamine and Glycine, in combination with the cysteine-rich whey protein, promote glutathione synthesis and combat free radicals. Glutamine, crucial in nitrogen metabolism, is important for replenishing amino acid stores, especially after exercise or stress.^[7,8] This amino acid aids in intestinal cell proliferation, thereby helping to preserve gut barrier function and intestinal health.^[8] Glycine, an inhibitory (calming) neurotransmitter, is vital as a constituent of collagen and a building block for other substances such as coenzyme-A, nucleic acids, creatine phosphate, purines, bile, and other amino acids.*

Taurine, as a derivative of sulfur-containing cysteine, has many healthful clinical applications, including the support of stable cell membranes, cardiovascular health, glucose tolerance, detoxification, and bile salt synthesis.*^[9]

Clinical Applications

- » Supports Healthy Body Composition*
- » Supports Immune Health*
- » Supports Normal Muscle Recovery Following Exercise*
- » Supports Gastrointestinal Health*
- » Contributes to Macro-Nutrition*

*FIT Food™ Lean Whey represents an extraordinary breakthrough in body composition/weight management functional food formulas. Our medical board of advisors' primary objective in researching and developing FIT Food Lean Whey was to find a pure source of quality whey protein that is free of genetically-engineered hormones (rBST and rBGH) which, though banned in other countries, are used in the United States dairy industry. There are growing concerns regarding the effects of these hormones, especially in early puberty. After a thorough review, our researchers determined that the stringent standards imposed by the New Zealand Ministry of Agriculture and Forestry (MAF) upon New Zealand dairy farmers results in the purest and most bioactive whey protein available. In addition to prohibiting the use of synthetic hormones in New Zealand's dairy industry, MAF-mandated feeding, climate, and calf-birthing practices further contribute to the superior quality of New Zealand's whey protein. Although importing New Zealand whey protein into the United States is more costly, our board of advisors recommended that FIT Food Lean Whey must contain 100% pure New Zealand whey protein.**

Aminogen® is a patented, natural, plant-derived enzyme system. It promotes protein digestibility and amino acid absorption, thereby boosting nitrogen retention and aiding in the synthesis of muscle mass and strength, as well as promoting deep muscle recovery.*^[10]

Medium-Chain Triglycerides provide a rapidly absorbed, easily metabolized, and quick form of energy.

Beneficial Macronutrient Ratio In every serving, FIT Food Lean Whey provides 21 g of high-quality whey protein; 3 g of fat, including 0.5 g from medium-chain triglycerides; and 11-13 g of carbohydrate, including 6-8 g of fiber. This composition supports a healthy balance of macronutrients and fiber. High-fiber foods tend to slow the absorption of glucose into the bloodstream.^[14] Furthermore, both fiber and protein tend to increase feelings of satiety.*^[14,15]

Added Sugar- and Stevia-Free FIT Food Lean Whey is free of both added sugar (including fructose) and stevia, and is sweetened only with monk fruit extract. Animal and human research suggests that consuming fructose-containing beverages increases visceral adiposity.^[16,17]

FIT Food™ Lean Whey Creamy Chocolate No Added Sugar, No Stevia Nutrition Facts

14 Servings per container

Serving size	1 Packet (about 42g)
Amount per serving	
Calories	140
	%Daily Value*
Total Fat 3.5g	4%
Saturated Fat 2g	10%
Trans Fat 0g	
Cholesterol 50mg	17%
Sodium 230mg	10%
Total Carbohydrate 13g	5%
Dietary Fiber 8g	29%
Total Sugars 2g	
Includes 0g Added Sugars	0%
Protein 21g	
Vitamin D 0mcg	0%
Calcium 100mg	8%
Iron 1mg	6%
Potassium 330mg	7%

* The % Daily Value (DV) tells you how much a nutrient in a serving of food contributes to a daily diet. 2,000 calories a day is used for general nutrition advice.

INGREDIENTS: New Zealand Biosciences™ proprietary whey protein blend (whey protein concentrate, taurine, L-glutamine, glycine), inulin (from chicory), cocoa powder, natural flavors (no MSG), sunflower oil, medium-chain triglyceride oil, cellulose gum, xanthan gum, guar gum, Aminogen® fungal proteases, sea salt, and monk fruit extract.

CONTAINS: Milk (whey protein concentrate).

DIRECTIONS: Mix the contents of one packet (42 g) in 8-12 oz cold water and consume. Adjust amount of water according to thickness desired.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner.

WARNING: Very low calorie protein diets (below 400 Calories per day) may cause serious illness or death. Do Not Use for Weight Reduction in Such Diets Without Medical Supervision. Not for use by infants, children, or pregnant or nursing women.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, fish, shellfish, peanuts, tree nuts, egg, artificial colors, artificial sweeteners, or artificial preservatives.

Typical Amino Acid Profile Per Serving:

Alanine	1,110 mg	Methionine	530 mg
Arginine	570 mg	Phenylalanine	710 mg
Aspartic Acid	2,330 mg	Proline	1,340 mg
Cysteine	590 mg	Serine	1,110 mg
Glutamic Acid	3,800 mg	Taurine	500 mg
Glycine	470 mg	Threonine	1,530 mg
Histidine	400 mg	Tryptophan	500 mg
Isoleucine	1,450 mg	Tyrosine	730 mg
Leucine	2,350 mg	Valine	1,320 mg
Lysine	1,910 mg		

AMINOGEN® is a registered trademark of Innophos Nutrition, Inc. AMINOGEN® is protected under U.S. patent 5,387,422.

**References**

- Hayes A, Cribb PJ. Effect of whey protein isolate on strength, body composition and muscle hypertrophy during resistance training. *Curr Opin Clin Nutr Metab Care*. 2008 Jan;11(1):40-44. [PMID: 18090657]
- Luhovyy BL, Akhavan T, Anderson GH. Whey proteins in the regulation of food intake and satiety. *J Am Coll Nutr*. 2007 Dec;26(6):704S-12S. [PMID: 18187437]
- Marshall K. Therapeutic applications of whey protein. *Altern Med Rev*. 2004 Jun;9(2):136-56. [PMID: 15253675]
- Souza GT, Lira FS, Rosa Neto JC, et al. Dietary whey protein lessens several risk factors for metabolic diseases: a review. *Lipids Health Dis*. 2012 Jun 7;11(1):67. [PMID: 22676328]
- Pal S, Ellis V. The chronic effects of whey proteins on blood pressure, vascular function, and inflammatory markers in overweight individuals. *Obesity (Silver Spring)*. 2010 Jul;18(7):1354-59. [PMID: 19893505]
- Lara-Villoslada F, Olivares M, Xaus J. The balance between caseins and whey proteins in cow's milk determines its allergenicity. *J Dairy Sci*. 2005 May;88(5):1654-60. [PMID: 15829656]
- Castell L. Glutamine supplementation in vitro and in vivo, in exercise and in immunodepression. *Sports Med*. 2003;33(5):323-45. [PMID: 12696982]
- Walsh NP, Blannin AK, Robson PJ, et al. Glutamine, exercise and immune function. Links and possible mechanisms. *Sports Med*. 1998 Sep;26(3):177-91. [PMID: 9802174]
- Yatabe Y, Miyakawa S, Ohmori H, et al. Effects of taurine administration on exercise. *Adv Exp Med Biol*. 2009;643:245-52. [PMID: 19239155]
- Aminogen. Triarco Industries. <http://www.triarco.com/consumercenter/aminogen/>. Accessed July 3, 2012.
- El Khoury D, Cuda C, Luhovyy BL, et al. Beta glucan: health benefits in obesity and metabolic syndrome. *J Nutr Metab*. 2012;2012:851362. [PMID: 22187640]
- de Luis DA, de la Fuente B, Izaola O, et al. Randomized clinical trial with an inulin enriched cookie on risk cardiovascular factor in obese patients [in Spanish]. *Nutr Hosp*. 2010 Jan-Feb;25(1):53-59. [PMID: 20204256]
- Queenan KM, Stewart ML, Smith KN, et al. Concentrated oat beta-glucan, a fermentable fiber, lowers serum cholesterol in hypercholesterolemic adults in a randomized controlled trial. *Nutr J*. 2007 Mar 26;6:6. [PMID: 17386092]
- Nilsson AC, Ostman EM, Holst JJ, et al. Including indigestible carbohydrates in the evening meal of healthy subjects improves glucose tolerance, lowers inflammatory markers, and increases satiety after a subsequent standardized breakfast. *J Nutr*. 2008 Apr;138(4):732-39. [PMID: 18356328]
- Paddon-Jones D, Westman E, Mattes RD, et al. Protein, weight management, and satiety. *Am J Clin Nutr*. 2008 May;87(5):1558S-1561S. Review. [PMID: 18469287]
- Jürgens H, Haass W, Castañeda TR, et al. Consuming fructose-sweetened beverages increases body adiposity in mice. *Obes Res*. 2005 Jul;13(7):1146-56. [PMID: 16076983]
- Stanhope KL, Schwarz JM, Keim NL, et al. Consuming fructose-sweetened, not glucose-sweetened, beverages increases visceral adiposity and lipids and decreases insulin sensitivity in overweight/obese humans. *J Clin Invest*. 2009 May;119(5):1322-34. doi:10.1172/JCI37385. [PMID: 19381015]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

FlashArrest®

Targeting Estrogen Activity for Men and Women*



Available in 60 capsules

Discussion

As scientific knowledge advances, it is becoming more evident that a balance of estrogenic and antiestrogenic activities within the body is normal and optimal, has important effects on the health of estrogen-sensitive tissues, and can help relieve normal menopausal symptoms. Reducing abundant estrogenic activity is one way to support balance. Another approach is to offer the body a “weak” estrogen that can support estrogenic activity when it is low or can replace more potent endogenous or exogenous estrogens.^[1] Research suggests that the ingredients in FlashArrest do both.*

8-prenylaringenin (8-PN) Hops are the female seed cones of the hop species *Humulus lupulus*, a medicinal plant that offers a wide range of biologically active components that are used for a variety of purposes. More recently, prenylflavonoids obtained from the lupulin glands of hop cones have become the focus of research. The prenylflavonoid 8-PN has been identified as one of the most potent phytoestrogens because it provides greater activity than other commonly used isoflavone phytoestrogens, such as daidzein and genistein.*^[2]

In vitro and in vivo studies conducted in recent years indicate a potential role for 8-PN in relieving common menopausal concerns.^[3,4] In pilot and prospective studies that were randomized and placebo-controlled, postmenopausal women who took 100-250 mcg/day of 8-PN experienced reductions in vasomotor symptoms and other common menopausal discomforts.^[4,5] Furthermore, research in ovariectomized rats indicated that 8-PN produced mild estrogenic effects in vaginal and uterine epithelial tissues.^[6] Although further studies are needed, animal and in vitro work show promising effects of 8-PN in cardiovascular,^[7,8] bone,^[9,10] prostate,^[11] and breast health.^[12,13] In one study, ovariectomized rats treated with 8-PN or 17 beta-estradiol displayed complete suppression of ovariectomy-induced bone and uterine changes in a qualitatively similar manner.*^[9]

Not only does 8-PN offer phytoestrogenic activity, but it has also been observed to affect aromatase—a cytochrome P450 isoenzyme responsible for the conversion of circulating androgens into estrogens. Aromatase is expressed in several tissues, such as breast tissue, where estrogens exert physiological activity.^[12] New research suggests that prenylflavonoids interact with aromatase in a manner that positively affects endogenous estradiol

Clinical Applications

- » Supports the Body's Natural Process of Healthy Aromatase Activity*
- » May Support Bone, Breast, and Prostate Tissue Health*
- » Helps to Relieve Normal Menopausal Symptoms, Such as Hot Flashes*
- » Supports Cardiovascular Health*

*FlashArrest® delivers a unique, proprietary blend of 8-prenylaringenin (8-PN) from hops and plant-lignan extract at clinically relevant levels. Research suggests lignans and 8-PN can support the body's natural process of healthy aromatase activity and exert phytoestrogen (e.g., enterolactone) and antioxidant activity. This all-natural formula may support cardiovascular, bone, breast, and prostate health and help relieve normal menopausal discomforts.**

biosynthesis^[11] and, therefore, the relative balance of other hormones, such as testosterone.^[14] Of the flavonoids studied, 8-PN has demonstrated the greatest impact on estrogen biosynthesis during in vitro experimentation.^[11,12] It has been postulated that providing phytoestrogens while modulating the production of potent endogenous estrogens may result in safer, more balanced estrogenic activity. Brunelli et al.^[15] investigated the influences of 8-PN on epidermal growth factor (EGF)-elicited pathways in certain breast cells and demonstrated that 8-PN interferes with EGF-induced cell proliferation in estrogen-receptor positive cells.*

HMRlignan™ Plant lignans are phytonutrients commonly found in small amounts in unrefined whole grains, seeds, nuts, vegetables, berries, and beverages, such as tea and coffee. The friendly bacteria in our intestines convert plant lignans into the “human” lignans called enterodiol and enterolactone. HMRlignan is a concentrated, naturally occurring plant lignan called 7-hydroxymatairesinol, which is derived from the Norway spruce (*Picea abies*). In humans, 7-hydroxymatairesinol is a direct metabolic precursor of enterolactone.*^[16]

Enterolactone is a phytoestrogen that binds to estrogen receptors and has both weak estrogenic and weak antiestrogenic effects. The latter accounts for much of its cell-protective capacity.^[17] Additionally, in vitro work has demonstrated that enterolactone affects aromatase and the biosynthesis of estrogen^[18] and has strong free radical scavenging and antioxidant properties.^[19,20] The protective effect of lignans and enterolactone on tissues, including those of the prostate and breast, is encouraging.^[21-23] At the same time, the estrogenicity of HMR and enterolactone, although milder than estradiol, offers promising applications for women with menopausal concerns.^[16] For instance, in a randomized, single-blind, parallel group pilot study, 20 menopausal women taking 50 mg/d of hydroxymatairesinol for eight weeks experienced half as many hot flushes as compared to pretreatment.^[24] Furthermore, high serum enterolactone has repeatedly been associated with cardiovascular health.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

FlashArrest® Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
FlashArrest® Proprietary Blend Norway spruce lignan extract (<i>Picea abies</i>) (knot wood) (90% hydroxymatairesinol potassium acetate) and 8-prenylnaringenin (from hops extract) (<i>Humulus lupulus</i>) (cones)	80 mg	**
** Daily Value not established.		

Other Ingredients: Microcrystalline cellulose, HPMC (capsule), stearic acid, magnesium stearate, and silica.

DIRECTIONS: Take one to two capsules daily, or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



References:

1. van Meeuwen JA, Nijmeijer S, Mutarapat T, et al. Aromatase inhibition by synthetic lactones and flavonoids in human placental microsomes and breast fibroblasts—a comparative study. *Toxicol Appl Pharmacol.* 2008 May 1;228(3):269-76. [PMID: 18201740]
2. Overk CR, Yao P, Chadwick LR, et al. Comparison of the in vitro estrogenic activities of compounds from hops (*Humulus lupulus*) and red clover (*Trifolium pratense*). *J Agric Food Chem.* 2005 Aug 10;53(16):6246-53. [PMID: 16076101]
3. Bowe J, Li XF, Kinsey-Jones J, et al. The hop phytoestrogen, 8-prenylnaringenin, reverses the ovariectomy-induced rise in skin temperature in an animal model of menopausal hot flashes. *J Endocrinol.* 2006 Nov;191(2):399-405. [PMID: 17088409]
4. Heyerick A, Vervarcke S, Depypere H, et al. A first prospective, randomized, double-blind, placebo-controlled study on the use of a standardized hop extract to alleviate menopausal discomforts. *Maturitas.* 2006 May 20;54(2):164-75. [PMID: 16321485]
5. Erkkola R, Vervarcke S, Vansteelandt S, et al. A randomized, double-blind, placebo-controlled, cross-over pilot study on the use of a standardized hop extract to alleviate menopausal discomforts. *Phytomedicine.* 2010 May;17(6):389-96. [PMID: 20167461]
6. Rimoldi G, Christoffel J, Wuttke W. Morphologic changes induced by oral long-term treatment with 8-prenylnaringenin in the uterus, vagina, and mammary gland of castrated rats. *Menopause.* 2006 Jul-Aug;13(4):669-77. [PMID: 16837889]
7. Böttner M, Christoffel J, Wuttke W. Effects of long-term treatment with 8-prenylnaringenin and oral estradiol on the GH-IGF-1 axis and lipid metabolism in rats. *J Endocrinol.* 2008 Aug;198(2):395-401. [PMID: 18499805]
8. Di Vito C, Bertoni A, Nalin M, et al. The phytoestrogen 8-prenylnaringenin inhibits agonist-dependent activation of human platelets. *Biochim Biophys Acta.* 2012 Nov;1820(11):1724-33. [PMID: 22766195]
9. Miyamoto M, Matsushita Y, Kiyokawa A, et al. Prenylflavonoids: a new class of non-steroidal phytoestrogen (Part 2). Estrogenic effects of 8-isopentenylaringenin on bone metabolism. *Planta Med.* 1998 Aug;64(6):516-19. Erratum in: *Planta Med.* 1998 Dec;64(8):769. [PMID: 9741296]
10. Sehmisch S, Hammer F, Christoffel J, et al. Comparison of the phytohormones genistein, resveratrol and 8-prenylnaringenin as agents for preventing osteoporosis. *Planta Med.* 2008 Jun;74(8):794-801. [PMID: 18537073]
11. Delmulle L, Bellahcène A, Dhooge W, et al. Anti-proliferative properties of prenylated flavonoids from hops (*Humulus lupulus* L.) in human prostate cancer cell lines. *Phytomedicine.* 2006 Nov;13(9-10):732-34. [PMID: 16678392]
12. Monteiro R, Faria A, Azevedo J, et al. Modulation of breast cancer cell survival by aromatase inhibiting hop (*Humulus lupulus* L.) flavonoids. *J Steroid Biochem Mol Biol.* 2007 Jun-Jul;105(1-5):124-30. [PMID: 17643984]
13. Hemachandra LP, Madhubhani P, Chandrasena R, et al. Hops (*Humulus lupulus*) inhibits oxidative estrogen metabolism and estrogen-induced malignant transformation in human mammary epithelial cells (MCF-10A). *Cancer Prev Res (Phila).* 2012 Jan;5(1):73-81. [PMID: 21997247]
14. Burnett-Bowie SA, McKay EA, Lee H, et al. Effects of aromatase inhibition on bone mineral density and bone turnover in older men with low testosterone levels. *J Clin Endocrinol Metab.* 2009 Dec;94(12):4785-92. [PMID: 19820017]
15. Brunelli E, Pinton G, Chianale F, et al. 8-Prenylnaringenin inhibits epidermal growth factor-induced MCF-7 breast cancer cell proliferation by targeting phosphatidylinositol-3-OH kinase activity. *J Steroid Biochem Mol Biol.* 2009 Feb;113(3-5):163-70. [PMID: 19103290]
16. Cosentino M, Marino F, Ferrari M, et al. Estrogenic activity of 7-hydroxymatairesinol potassium acetate (HMR/lignan) from Norway spruce (*Picea abies*) knots and of its active metabolite enterolactone in MCF-7 cells. *Pharmacol Res.* 2007 Aug;56(2):140-47. [PMID: 17572100]
17. Barlow RN, Johnson JP. Fact sheet on the phytoestrogen enterolactone. Breast Cancer & The Environment Research Centers. 2007 Nov;31-37. http://www.zerobreastcancer.org/research/bcerc_factsheets_phytoestrogen_enl.pdf. Accessed October 19, 2012.
18. Brooks JD, Thompson LU. Mammalian lignans and genistein decrease the activities of aromatase and 17beta-hydroxysteroid dehydrogenase in MCF-7 cells. *J Steroid Biochem Mol Biol.* 2005 Apr;94(5):461-67. [PMID: 15876411]
19. HMRlignan™—Direct Enterolactone Precursor [press release]. Locarno, Switzerland and Easton, PA: Linnea SA; August 17, 2005. http://www.hmrlignan.com/images/PressRelease_Launch.pdf. Accessed October 24, 2012.
20. Kangas L, Saarinen N, Mutanen M, et al. Antioxidant and antitumor effects of hydroxymatairesinol (HM-3000, HMR), a lignan isolated from the knots of spruce. *Eur J Cancer Prev.* 2002 Aug;11 Suppl 2:S48-57. [PMID: 12570335]
21. Bylund A, Saarinen N, Zhang JX, et al. Anticancer effects of a plant lignan 7-hydroxymatairesinol on a prostate cancer model in vivo. *Exp Biol Med (Maywood).* 2005 Mar;230(3):217-23. [PMID: 15734725]
22. Olsen A, Knudsen KE, Thomsen BL, et al. Plasma enterolactone and breast cancer incidence by estrogen receptor status. *Cancer Epidemiol Biomarkers Prev.* 2004 Dec;13(12):2084-9. [PMID: 15598765]
23. Miura D, Saarinen NM, Miura Y, et al. Hydroxymatairesinol and its mammalian metabolite enterolactone reduce the growth and metastasis of subcutaneous AH109A hepatomas in rats. *Nutr Cancer.* 2007;58(1):49-59. [PMID: 17571967]
24. Udani J, Hardy M. 7-Hydroxymatairesinol (7-HMR) New pharmacokinetic data and effect on enterolactone metabolites and hot flashes in menopausal women. Scripps Integrative Medicine 5th Annual Natural Supplements Conference; January 17-20, 2008; San Diego, CA. <http://www.hmrlignan.com/images/Research.pdf>. Accessed October 19, 2012.

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Foundation Essentials

Five Formulas in a Single-Dose Packet



Available in 30 packets

Discussion

ProbioMax® Daily DF is a vegetarian, dairy- and gluten-free, four-strain probiotic totaling 30 billion CFU per capsule. ProbioMax Daily DF provides four researched strains of beneficial bacteria, including the extensively studied HNO19® strain of *Bifidobacterium lactis*.^[1] These live microorganisms have proven health benefits and well-established safety and have been tested for epithelial cell adhesion and/or resistance to low pH.^[2] To further support resistance to low pH and the delivery of microorganisms to the small intestines, XYMOGEN employs DRcaps™ gastro-resistant capsules. These specially designed, innovative capsules help minimize exposure of the actives to stomach acid and ensure more targeted release. Though the gastrointestinal and immune-supportive benefits of probiotics are the most widely studied, scientists continue to find that gut bacteria influence many other aspects of health, including brain function, weight management, detoxification, and cytokine production.*^[3-7]

ActivNutrients® without Iron is a high-quality, hypoallergenic, multivitamin/mineral blend that includes activated vitamins; folate as Quatrefolic® (5-MTHF); and patented Albion® TRAACS® chelated mineral complexes all provided in vegetarian capsules. Good nutrition is a basis for wellness, and good nutrition usually translates into a stronger immune system and better health. An important aspect of good nutrition is micronutrition (vitamins and minerals).^[8-11] According to research by the USDA and other organizations, the American diet is lacking micronutrients.^[12-14] In fact, nine out of 10 Americans are missing key micronutrients.^[14] Mass food production, storage techniques, poor food choices, and nutrient-depleting preparation methods may contribute to inadequacies. The bottom line is that children and adults are not consuming enough nutrient-rich foods to meet all their most basic vitamin and mineral needs.^[13] What's more, some scientists feel that the recommended intakes (e.g., %DV, DRIs, EARs, RDAs) may not meet the requirements of all individuals, especially the chronically ill.*

There are many reasons to select ActivNutrients without Iron. Among them are its balanced nutrient profile for foundational wellness, bioavailable micronutrient forms for optimal absorption and utilization, generous levels of B vitamins, and broad-spectrum antioxidant and phase I detoxification support.*

Omega MonoPure® 650 EC is made using a proprietary MaxSimil composition containing monoglyceride fish oil with no additional ingredients, carriers, or excipients. Each fish-gelatin softgel is enteric-coated, and every batch of fish oil is IFOS five-star certified to ensure the world's highest standards for purity, potency, and freshness. The fish oil is non-GMO, certified sustainable from

Clinical Applications

- » Provides Foundational Supplementation for Overall Health*
- » Supports Intestinal and Microbiome Health*
- » Supports Healthy Magnesium and Vitamin D Levels*
- » Promotes Healthy Immunity*
- » Provides Omega-3 Fatty Acids for Good Nutrition and Healthy Cytokine Production*

*Foundation Essentials provides 30 days of supplementation in convenient, once-a-day packets. Each packet provides a daily dose of five XYMOGEN foundational health formulas: ProbioMax® Daily DF, ActivNutrients® without Iron, Omega MonoPure® 650 EC, OptiMag® 125, and D3 2000. These formulas provide high-potency probiotics, an iron-free multiple, IFOS five-star certified omega-3 fatty acids, and extra magnesium and D3. Foundation Essentials can be used for any number of purposes, such as to serve as a kick start to your MedPax® program, basic supplementation while you wait for lab results, or a convenient way to supplement while traveling.**

Scandinavia, and antibiotic-free. Additionally, it is eco-friendly because the greater absorption of EPA and DHA ultimately means that fewer grams of fish oil need to be harvested for the same benefit. Research suggests that consumption of EPA and DHA omega-3 fatty acids may support cardiovascular health.^[15] Studies have also shown that fish oils may support healthy cytokine production, promote optimal joint function^[16], and support overall brain and nervous system function.*^[24]

OptiMag® 125 contains Albion®'s TRAACS® magnesium lysinate glycinate (mineral amino acid chelate) and Albion's chelated di-magnesium malate—both formulated for enhanced absorption. Magnesium, the fourth most abundant mineral in the body, participates in over 600 enzymatic reactions in nearly all tissues.^[17] Deficiency is common and results from poor dietary intake, poor absorption, and excessive losses through urine, stool, perspiration, or lactation. Certain drugs, certain herbs, poor kidney function, excessive alcohol intake, and drinking mostly "soft" water can contribute to magnesium depletion as well.^[18] Malic acid (from di-magnesium malate) supports energy production and lactic acid clearance via the Krebs cycle.*^[19]

D3 2000 provides 2000 IU of cholecalciferol in each convenient softgel. While vitamin D3 (cholecalciferol) is made in the skin when 7-dehydrocholesterol reacts with sunlight, many things affect the degree to which this biosynthesis occurs, including time of day, seasons, location, smog/pollution, clothing, shade of skin (darker skin requires more sun), and sunscreen use. Low-cholesterol diets and certain cholesterol therapies can also affect vitamin D formation. By some estimates, one billion people worldwide have vitamin D deficiency or insufficiency.^[20] Reversing deficiency and maintaining optimal serum vitamin D levels beneficially impacts biochemistry and numerous body systems; this is largely because calcitriol—the physiologically active product of vitamin D—is a secosteroid hormone that targets over 200 genes in a wide variety of tissues.^[21,22] As the research demonstrates, vitamin D is clearly imperative for the development, growth, and maintenance of a healthy body from gestation to old age.*^[22]

Although D2 and D3 are similar biochemically, D3 was reported to be approximately 87% more potent in raising and maintaining serum calcidiol (body's storage form) concentrations and in producing two- to threefold greater storage of vitamin D than the equimolar D2.*^[23]

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Foundation Essentials Supplement Facts

Serving Size: 1 Packet
Servings Per Container: 30

	Amount Per Serving	%DV
Calories	5	
Total Fat	0.5 g	1%†
Vitamin A (75% as natural beta-carotene and 25% as retinyl palmitate)	1120 mcg	124%
Vitamin C (as sodium ascorbate, potassium ascorbate, zinc ascorbate, and calcium ascorbate)	125 mg	139%
Vitamin D3 (cholecalciferol)	52.5 mcg (2100 IU)	263%
Vitamin E (as d-alpha tocopheryl succinate and mixed tocopherols)	67 mg	447%
Thiamin (as thiamine mononitrate)	10 mg	833%
Riboflavin (as riboflavin 5'-phosphate sodium)	10 mg	769%
Niacin (as niacinamide and niacin)	32 mg	200%
Vitamin B6 (as pyridoxal 5'-phosphate)	10 mg	588%
Folate (as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt)	200 mcg DFE	50%
Vitamin B12 (as MecobalActive™ methylcobalamin)	250 mcg	10417%
Biotin	500 mcg	1667%
Pantothenic Acid (as d-calcium pantothenate)	100 mg	2000%
Choline (as choline dihydrogen citrate)	18 mg	3%
Calcium (as DimaCal® di-calcium malate, d-calcium pantothenate, and calcium ascorbate)	50 mg	4%
Iodine (as potassium iodide)	50 mcg	33%
Magnesium (as Albion® di-magnesium malate and TRAACS® magnesium lysinate glycinate chelate)	175 mg	42%
Zinc (as TRAACS® zinc bisglycinate chelate)	6.5 mg	59%
Selenium (as Albion® selenium glycinate complex)	50 mcg	91%
Copper (as TRAACS® copper bisglycinate chelate)	0.5 mg	56%
Manganese (as TRAACS® manganese bisglycinate chelate)	0.25 mg	11%
Chromium (as TRAACS® chromium nicotinate glycinate chelate)	250 mcg	714%
Molybdenum (as TRAACS® molybdenum glycinate chelate)	25 mcg	56%
Potassium (as Albion® potassium glycinate complex and potassium ascorbate)	49.5 mg	1%
MaxSimil® Fish Oil Concentrate	650 mg	**
Total Omega-3 Fatty Acids	430 mg	**
EPA (eicosapentaenoic acid)	300 mg	**
DHA (docosahexaenoic acid)	130 mg	**
Proprietary Blend	174 mg (15 Billion CFU ¹)	**
<i>Lactobacillus acidophilus</i> La-14®		
<i>Bifidobacterium longum</i> BI-05™		
<i>Lactobacillus plantarum</i> Lp-115®		
HOWARU® Bifido (<i>Bifidobacterium lactis</i> HN019®)	50 mg (15 Billion CFU ¹)	**
Inositol	18 mg	**
PABA (para-aminobenzoic acid)	6.5 mg	**
Vanadium (as TRAACS® vanadium nicotinate glycinate chelate)	375 mcg	**
† Percent Daily Values are based on a 2,000 calorie diet.		
** Daily Value not established.		

Other Ingredients: HPMC (capsule & acid-resistant capsule), microcrystalline cellulose, ascorbyl palmitate, silica, medium-chain triglyceride oil, vegetable stearic acid, softgel (fish gelatin, vegetable glycerin, and purified water), GRAS enteric coating (ethylcellulose, sodium alginate, purified water, medium-chain triglycerides, oleic acid, vegetable stearic acid, and ammonium hydroxide), mixed natural tocopherols, vegetable magnesium stearate, organic extra virgin olive oil, and softgel (bovine gelatin, vegetable glycerin, and purified water).

Contains: Fish (anchovy and/or sardine [sources of fish oil]), tilapia and/or pangasius [sources of fish gelatin].
¹Colony Forming Unit

DIRECTIONS: Take the contents of one packet daily, or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking blood thinners or other medication should discuss potential interactions with their healthcare practitioner. Do not use if packet is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, dairy products, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

MecobalActive™ is a trademark of Ferrer Health Tech.
The active form of B₁₂.

Albion®, DimaCal®, TRAACS®, and the Albion Gold Medallion® are registered trademarks of Albion Laboratories, Inc. Di-Magnesium Malate covered by US patent 6,706,904.

Quatrefolic® Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,862.

HOWARU®
HOWARU® and the HOWARU® logo are registered trademarks of DuPont or its affiliates.

HN019® is a registered trademark of Fonterra™ Limited and is licensed to DuPont Nutrition Biosciences.

Manufactured using MaxSimil® fish oil. MaxSimil® is a registered trademark of Ingenutra Inc. Protected under US patents 8,119,690 and 8,198,324; Canadian patents 2672513 and 2677670.



References

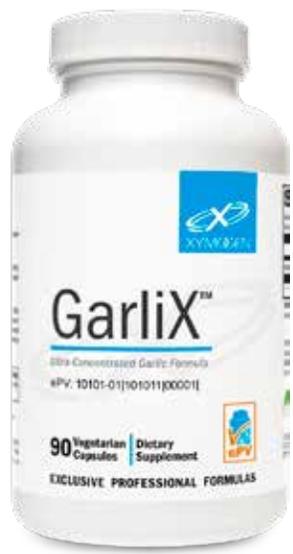
- Danisco. Strain information: Bifidobacterium lactis HN019™. http://www.danisco.com/fileadmin/user_upload/danisco/documents/products/StrainInfo_HN019_Aug_2013.pdf. Accessed May 13, 2016.
- Danisco. Strain Information Technical Sheets. Madison, WI: Dupont Nutrition and Health. [available upon request]
- Mangiola F, Ianiro G, Franceschi F, et al. Gut microbiota in autism and mood disorders. *World J Gastroenterol*. 2016 Jan 7;22(1):361-68. [PMID: 26755882]
- Masood MI, Qadir MI, Shirazi JH, et al. Beneficial effects of lactic acid bacteria on human beings. *Crit Rev Microbiol*. 2011 Feb;37(1):91-98. [PMID: 21162695]
- Drissi F, Raouf D, Merhej V. Metabolic role of lactobacilli in weight modification in humans and animals. *Microb Pathog*. 2016 Mar 23. pii: S0882-4010(15)30152-2. [Epub ahead of print] [PMID: 27033001]
- Nova E, Pérez de Heredia F, Gómez-Martínez S, et al. The role of probiotics on the microbiota: effect on obesity. *Nutr Clin Pract*. 2016 Feb 11. pii:0884533615620350. [Epub ahead of print] Review. [PMID: 26869611]
- Nowak A, Kuberski S, Libudzisz Z. Probiotic lactic acid bacteria detoxify N-nitrosodimethylamine. *Food Addit Contam Part A Chem Anal Control Expo Risk Assess*. 2014;31(10):1678-87. [PMID: 25010287]
- Ames BN. A role for supplements in optimizing health: the metabolic tune-up. *Arch Biochem Biophys*. 2004 Mar 1;423(1):227-34. [PMID: 14989256]
- Toffanello ED, Inelmen EM, Minicuci N, et al. Ten-year trends in vitamin intake in free-living healthy elderly people: the risk of subclinical malnutrition. *J Nutr Health Aging*. 2011 Feb;15(2):99-103. [PMID: 21365161]
- Block G, Jensen CD, Norkus EP, et al. Usage patterns, health, and nutritional status of long-term multiple dietary supplement users: a cross-sectional study. *Nutr J*. 2007 Oct 24;6:30. [PMID: 17958896]
- Fletcher RH, Fairfield KM. Vitamins for chronic disease prevention in adults: clinical applications. *JAMA*. 2002 Jun 19;287(23):3127-29. [PMID: 12069676]
- Moshfegh AJ, Goldman JD, Ahuja JK, et al. U.S. Department of Agriculture, Agricultural Research Service. What we eat in America, Nhanes 2005-2006. Usual nutrient intakes from food and water compared to 1997 dietary reference intakes for vitamin D, calcium, phosphorus, and magnesium. http://www.ars.usda.gov/SP2UserFiles/Place/12355000/pdf/0506/usual_nutrient_intake_vitD_ca_phos_mg_2005-06.pdf. Published July 2009. Accessed April 22, 2016.
- Sebastian RS, Cleveland LE, Goldman JD, et al. Older adults who use vitamin/mineral supplements differ from nonusers in nutrient intake adequacy and dietary attitudes. *J Am Diet Assoc*. 2007 Aug;107(8):1322-32. [PMID: 17659898]
- Milk Processor Education Program. What America's missing: a 2011 report on the nation's nutrient gap. https://milklife.com/sites/default/files/field_pdf/Nutrition/2013/08/08/what_americas_missing.pdf. Accessed April 22, 2016.
- FDA announces qualified health claims for omega-3 fatty acids. U.S. Food and Drug Administration Department of Health and Human Services. <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2004/ucm108351.htm>. Accessed February 27, 2011.
- Proudman SM, Cleland LG, James MJ. Dietary omega-3 fats for treatment of inflammatory joint disease: efficacy and utility. *Rheum Dis Clin North Am*. 2008 May;34(2):469-79. [PMID: 18638687]
- de Baaij JH, Hoenderop JG, Bindels RJ. Magnesium in man: implications for health and disease. *Physiol Rev*. 2015 Jan;95(1):1-46. [PMID: 25540137]
- Magnesium balance: can you juggle? *Albion® Research Notes*. Dec;15(4). http://www.albionhumannutrition.com/research-notes/download/doc_details/328-magnesium-balance-can-you-juggle. Accessed May 13, 2016.
- Dean W, Ward J. Krebs's cycle intermediates: maximizing your body's performance. *Nutrition Review*. <http://nutritionreview.org/2013/04/krebs-cycle-intermediates/>. Accessed April 22, 2016.
- Tsiaras WG, Weinstock MA. Factors influencing vitamin D status. *Acta Derm Venereol*. 2011 Mar;91(2):115-24. [PMID: 21384086]
- Cannell JJ, Hollis BW. Use of vitamin D in clinical practice. *Altern Med Rev*. 2008 Mar;13(1):6-20. [PMID: 18377099]
- Vitamin D council. <http://www.vitaminDcouncil.org/>. Accessed April 22, 2016.
- Heaney RP, Recker RR, Grote J, et al. Vitamin D3 is more potent than vitamin D2 in humans. *J Clin Endocrinol Metab*. 2011 Mar;96(3):E447-52. [PMID: 21177785]
- Cole GM, Ma QL, Frautschy SA. Dietary fatty acids and the aging brain. *Nutr Rev*. 2010 Dec;68(suppl 2):S102-11. [PMID:21091943]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

(RV) DRS-306
Rev. 05/02/18



Available in 90 capsules

Discussion

Well known as a venerated culinary herb, garlic (*Allium sativum*) has been used for centuries to support health and longevity. It has been found in Egyptian pyramids, ancient Greek temples, medical texts from a variety of cultures, and even on Hippocrates' list of health-promoting compounds.^[1] Garlic is used widely today to support cardiovascular health, antioxidant activity, and immune function.*^[2,3]

Organosulfur Compounds and Antioxidant Activity Many of the health-promoting benefits of garlic are attributed to its array of sulfur-containing compounds. Organosulfur compounds from whole garlic fall into two classes: gamma-glutamylcysteines and cysteine sulfoxides.^[4] Crushing, chopping, and processing garlic results in production of organosulfur compounds that fall into one of four main chemical classes—alliin, allicin, allyl cysteine, and allyl disulfide. Several of these compounds have been studied for their compelling effect on antioxidant activity. Alliin (allylcysteine sulfoxide) was found to scavenge superoxide, while allicin (a thiosulfinate) suppressed its formation. Hydroxyl radicals were scavenged by alliin, allyl cysteine, and allyl disulfide; allyl disulfide was found to be a lipid peroxidation terminator as well.^[5] GarliX contains standardized amounts of gamma-glutamylcysteines, alliin, allicin, thiosulfates, and sulfur.*

Glutathione (gamma-glutamyl-cysteinyl-glycine) is a well-researched component of vital antioxidant systems in the body. Glutathione is also recognized for its role in regulation of cellular events such as DNA and protein synthesis, gene expression, cell-life cycle regulation, signal transduction, cytokine production, and immune response.^[6] Gamma-glutamylcysteine (GGC), an endogenously produced precursor to glutathione, has been found to efficiently detoxify hydrogen peroxide and superoxide anion in the mitochondria. Research suggests that GGC may assume the neuroprotective and antioxidant functions of glutathione as needed.*^[7]

Cardiovascular Health Numerous studies suggest that garlic has a positive effect on plasma lipids, normal fibrinolytic and platelet activity, and the maintenance of blood pressure and blood glucose already

Clinical Applications

- » Supports Healthy Immune System Function*
- » Supports Cardiovascular Health*
- » Promotes Glutathione Synthesis*

*GarliX™ is a standardized extract of garlic (Allium sativum). This concentrated source provides a high yield of the sulfur-containing bioactive compound allicin. Research suggests that garlic supports immune function, antioxidant activity, and the cardiovascular system. Garlic may also support healthy blood pressure and cholesterol levels already within the normal range.**

within the normal range.^[8] A meta-analysis of 26 studies showed that garlic supported total cholesterol and triglyceride metabolism with a significance of $p = 0.001$ and $p < 0.001$ respectively.^[9] Studies suggest that garlic may play a cardioprotective role in maintaining normal levels of oxidized low-density lipoprotein (LDL), nitric oxide production, healthy cytokine balance, and normal endothelial function as well.^[10,11] Garlic-derived organosulfur compounds are converted by erythrocytes into hydrogen sulfide, which in turn supports vasodilation, vascular smooth muscle relaxation, and overall cardiovascular health.^[12] Garlic supplementation had a significant impact on cardiovascular health parameters in select subjects during a 12-week, randomized, single-blind placebo-controlled study.*^[13]

Immune Support In the mid-1900s, Louis Pasteur noted garlic's ability to support immune function, and it is known to have been used for immune support during World War I.^[12] Ongoing research reveals a broad range of immune-supportive properties associated with garlic, especially its allicin component.^[4,14] Allicin appears to react with the thiol groups of a variety of enzymes (including alcohol dehydrogenase, thioredoxin reductase, and RNA polymerase), which, in turn, supports normal microbial balance in the body.^[15] A double-blind placebo-controlled study of 146 volunteers suggests that stabilized allicin compound is significantly effective in supporting and maintaining healthy immune function.*^[16]

Modern-day research appears to confirm the health-promoting properties of garlic that ancient Egyptians, Greeks, Chinese, and Indian cultures embraced for so long. GarliX is an ultra-concentrated garlic formula with standardized levels of several organosulfur compounds designed to support antioxidant, cardiovascular, and immune systems.*

GarliX™ Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Garlic Extract (<i>Allium sativum</i>)(bulb)(1% allicin)	650 mg	**
** Daily Value not established.		

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, and silica.

DIRECTIONS: Take one capsule daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms, artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.



References

1. Rivlin RS. Historical perspective on the use of garlic. *J Nutr.* 2001 Mar;131(3s):951S-4S. [PMID: 11238795]
2. Natural Standard Garlic Monograph. <http://naturalstandard.com/databases/herbssupplements/garlic.asp>. Accessed April 17, 2012.
3. Krinsky DL, LaValle JB, Hawkins EB, et al. *Natural Therapeutics Pocket Guide*. 2nd ed. Hudson (OH): Lexi-Comp; 2003.
4. Linus Pauling Institute. <http://lpi.oregonstate.edu/infocenter/phytochemicals/garlic/>. Accessed April 18, 2012.
5. Chung LY. The antioxidant properties of garlic compounds: allyl cysteine, alliin, allicin, and allyl disulfide. *J Med Food.* 2006 Summer;9(2):205-13. [PMID: 16822206]
6. Wu G, Fang YZ, Yang S, et al. Glutathione metabolism and its implications for health. *J Nutr.* 2004 Mar;134(3):489-92. [PMID: 14988435]
7. Quintana-Cabrera R, Fernandez-Fernandez S, Bobo-Jimenez V, et al. L-glutamylcysteine detoxifies reactive oxygen species by acting as glutathione peroxidase-1 cofactor. *Nat Commun.* 2012 Mar 6;3:718. [PMID: 22395609]
8. Rahman K. Historical perspective on garlic and cardiovascular disease. *J Nutr.* 2001 Mar;131(3s):977S-9S. Review. [PMID: 11238800]
9. Zeng T, Guo FF, Zhang CL, et al. A meta-analysis of randomized, double-blind, placebo-controlled trials for the effects of garlic on serum lipid profiles. *J Sci Food Agric.* 2012 Jan 10. [Epub ahead of print] [PMID: 22234974]
10. Gorinstein S, Jastrzebski Z, Namiesnik J, et al. The atherosclerotic heart disease and protecting properties of garlic: contemporary data. *Mol Nutr Food Res.* 2007 Nov;51(11):1365-81. Review. [PMID: 17966138]
11. Siegal G, Malmsten M, Pietzsch J, et al. The effect of garlic on arteriosclerotic nanoplaque formation and size. *Phytomedicine.* 2004 Jan;11(1):24-35. [PMID: 14971718]
12. Ginter E, Simko V. Garlic (*Allium sativum* L.) and cardiovascular diseases. *Bratisl Lek Listy.* 2010;111(8):452-6. Review. [PMID: 21033626]
13. Ashraf R, Aamir K, Shaikh AR, et al. Effects of garlic on dyslipidemia in patients with type 2 diabetes mellitus. *J Ayub Med Coll Abbottabad.* 2005 Jul-Sep;17(3):60-4. [PMID: 16320801]
14. Harris JC, Cottrell SL, Plummer S, et al. Antimicrobial properties of *Allium sativum* (garlic). *Appl Microbiol Biotechnol.* 2001 Oct;57(3):282-6. Review. [PMID: 11759674]
15. Ankri S, Mirelman D. Antimicrobial properties of allicin from garlic. *Microbes Infect.* 1999 Feb;1(2):125-9. Review. [PMID: 10594976]
16. Josling P. Preventing the common cold with a garlic supplement: a double-blind, placebo-controlled survey. *Adv Ther.* 2001 Jul-Aug;18(4):189-93. [PMID: 11697022]

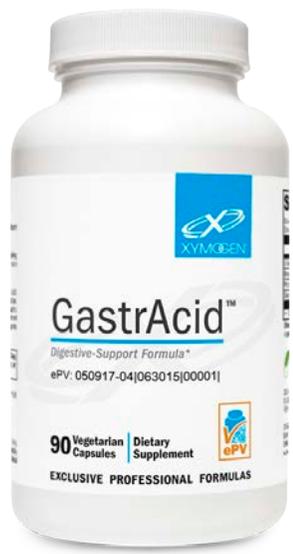
Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

GastrAcid™

Digestive-Support Formula*



Available in 90 and 180 capsules

Discussion

GastrAcid is designed to support the gastric phase of digestion directly and provide stimulus for the excretion of pancreatic digestive juices in the small intestine. Adequate hydrochloric acid is fundamental to healthy protein digestion, nutrient availability, and the maintenance of normal gastric flora.^[1-3] There is a natural decline in the ability to produce hydrochloric acid, especially after the age of 60.^[1] There appears to be an even greater decline in pepsin production related to normal aging.^[4] Support of natural gastric secretions and acidity helps support normal digestion, absorption, and immune health.^[5] Maintaining an acidic pH in the stomach helps support normal gastric and intestinal flora as well.^{*[6-8]}

L- Glutamic Acid This amino acid can be obtained from dietary protein or synthesized endogenously from other amino acids, such as glutamine. L- glutamic acid is used in GastrAcid as an acidifying agent.*

Betaine Hydrochloride (HCl) Betaine (also known as trimethylglycine) is a natural substance found in foods such as beets, spinach, and grains. Research suggests that betaine supports cell health by acting as a methyl donor, and this, in turn, supports healthy methionine, homocysteine, and hepatic fat metabolism. Betaine also functions as an osmolyte, which supports the integrity of cells and proteins during fluctuations in hydration, salinity, and temperature. Betaine HCl, the acidic form of betaine, has traditionally been used to support digestion and absorption due to its ability to lower gastric pH.^{*[9,10]}

Pepsin One of the first enzymes to initiate protein digestion, pepsin is first synthesized in the parietal cells of the gastric mucosa and secreted as the inactive zymogen precursor pepsinogen. Hydrochloric acid activates pepsinogen to convert it to pepsin once it is outside the cell. This activation sets up a chain reaction leading to the production of still more pepsin. Porcine pepsin, in addition to betaine HCl, is provided in GastrAcid with the goal of promoting more endogenous pepsin production.^{*[4,6]}

Clinical Applications

- » Provides Hydrochloric Acid to Help Maintain Gastric pH*
- » Contains Factors to Promote Healthy Digestion, Especially of Dietary Protein*
- » Supports Absorption of Certain Macro- and Micronutrients*
- » Helps Maintain Normal Gastric Flora*

*GastrAcid™ provides a variety of health-supportive factors. L-glutamic acid, betaine HCl, and pepsin, a proteolytic enzyme, which assist in protein digestion. Gentian root, an herbal bitter, promotes normal secretion of saliva and gastric acid for digestive support. HCl (hydrochloric acid) supports nutrient absorption and helps maintain a healthy gastric pH, which, in turn, supports healthy gastric ecology.**

Gentian Root (*Gentiana lutea*) Used for centuries to support healthy digestion, gentian contains the bitter glycosides gentiopicrin and amarogentin. Gentian's bitter taste can be detected even at a dilution level of 50,000:1. Gentian root appears to support digestion by stimulating secretion of saliva in the mouth, hydrochloric acid in the stomach, and digestive juices from the pancreas. Due to the stimulant effect that gentian root has on endogenous production of HCl, individuals may be able to discontinue GastrAcid™ after a period of use.^{*[11-14]}

GastrAcid is formulated with a variety of compounds and is designed to support gastric acidity, digestion, and normal gastrointestinal flora. GastrAcid should be taken with, or immediately following a meal. Do not use if there is a prior history of, or a current complaint of, a peptic or duodenal ulcer.*

GastrAcid™ Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
L-Glutamic Acid	350 mg	**
Betaine HCl	300 mg	**
Pepsin 1:10,000 (from porcine)	100 mg	**
Gentian (<i>Gentiana scabra</i>)(root)	20 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), vegetable stearic acid, silica, vegetable magnesium stearate, and medium-chain triglyceride oil.**DIRECTIONS:** Take one capsule with meals, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.**STORAGE:** Keep closed in a cool, dry place out of reach of children.**References**

1. Bland J, Liska D, Jones DS, et al. *Clinical Nutrition A Functional Approach*. 2nd ed. Gig Harbor, WA: The Institute for Functional Medicine. 2004.
2. Giannella RA, Broitman SA, Zamcheck N. Gastric acid barrier to ingested microorganisms in man: studies in vivo and in vitro. *Gut*. 1972 Apr;13(4):251-6. [PMID: 4556018]
3. Lovat LB. Age related changes in gut physiology and nutritional status. *Gut*. 1996 Mar;38(3):306-9. [PMID: 8675079]
4. Feldman M, Cryer B, McArthur KE, et al. Effects of aging and gastritis on gastric acid and pepsin secretion in humans: a prospective study. *Gastroenterology*. 1996 Apr;110(4):1043-52. [PMID: 8612992]
5. Untermayr E, Jensen-Jarolim E. The effect of gastric digestion on food allergy. *Curr Opin Allergy Clin Immunol*. 2006 Jun;6(3):214-9. Review. [PMID: 16670517]
6. Smolin LA, Grosvenor MB. *Nutrition: Science and Applications*. 2nd ed. Hoboken, NJ: John Wiley & Sons, Inc. 2010.
7. Canani RB, Terrin G. Gastric acidity inhibitors and the risk of intestinal infections. *Curr Opin Gastroenterol*. 2010 Jan;26(1):31-5. Review. [PMID: 19907324]
8. Kanno T, Matsuki T, Oka M, et al. Gastric acid reduction leads to an alteration in lower intestinal microflora. *Biochem Biophys Res Commun*. 2009 Apr 17;381(4):666-70. [PMID: 19248769]
9. Craig SA. Betaine in human nutrition. *Am J Clin Nutr*. 2004 Sep;80(3):539-49. Review. [PMID: 15321791]
10. New York University Langone Medical Center. Betaine Hydrochloride. <http://www.med.nyu.edu/content?ChunkID=21560>. Last Reviewed 2011. Accessed March 23, 2012.
11. Mowrey D. *Scientific Validation of Herbal Medicine*. New Canaan, CT: McGraw-Hill. 1999.
12. Monterey Bay Spice Company. Gentian Root. <http://www.herbco.com/p-763-gentian-root-cs-wild-crafted.aspx>. Accessed March 25, 2012.
13. Vilkin A, Levi Z, Morgenstern S, et al. Higher gastric mucin secretion and lower gastric acid output in first-degree relatives of gastric cancer patients. *J Clin Gastroenterol*. 2008 Jan;42(1):36-41. [PMID: 18097287]
14. Behrens M, Brockhoff A, Batram C, et al. The human bitter taste receptor hTAS2R50 is activated by the two natural bitter terpenoids andrographolide and amarogentin. *J Agric Food Chem*. 2009 Nov 11;57(21):9860-6. [PMID: 19817411]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

GI Protect™

Featuring IgG 2000 CWP™ and L-Glutamine

NOTICE: This formula now contains an ingredient derived from milk.



Available in Peach & Wild Cherry Flavors

Discussion

Immunoglobulins, also known as antibodies, defend the body directly through opsonization and neutralization. They also activate the complement system. A special quality about these methods by which immunoglobulins defend the body is that they allow the immune system to differentiate between antigens and the body's normal microflora.

Most antigens enter the body through mucosal tissue or stay localized on mucosal surfaces. It makes sense, then, that mucosal tissues are heavily populated with immune cells. In fact, it is estimated that the intestinal lining produces more antibodies than any other organ in the body. Aside from producing antibodies, the mucosal surface serves as a barrier that physically prevents antigens from entering circulation.

Though the body itself produces antibodies, supplementation may be beneficial in some individuals. It has been shown that the concentration of immunoglobulins in the digestive tract and on mucosal surfaces in adults is predictive of risk to immunity.^[1,2] Stress and other conditions can reduce immunoglobulin secretion and antibody production.^[3] In addition, damage to the intestinal wall resulting from stress, strenuous exercise, medications, or other causes affect gut barrier function and can make the body more vulnerable to antigens.*

IgG 2000 CWP™ is an immunoglobulin concentrate from colostrum whey peptides that delivers a minimum of 40% IgG immunoglobulin along with an array of compounds, including growth factors, sialic acid, lactoferrin, proline-rich peptides (PRPs), oligosaccharides, and gangliosides. Each of these components provides the user with different and complementary health benefits, such as fundamental support of immune function and modulation, lean body mass, brain and thymus health, microbiota modulation, and cytokine balance.*^[1]

Clinical Applications

- » Supports Immune Function (including during strenuous physical activity)*
- » Helps Maintain the Integrity of the Gut Mucosa*
- » Supports Lean Muscle Mass*

*GI Protect™ features XYMOGEN's IgG 2000 CWP™, with the added benefit of the amino acid L-glutamine. IgG 2000 CWP™ is an immunoglobulin concentrate derived from colostrum whey peptides. It delivers natural immunoglobulins (standardized to a minimum of 40% IgG), bioactive proteins, and growth factors. These components support immune function, healthy cytokine activity, gut barrier function, and gastrointestinal health and tissue repair. Advanced coagulation and filtration techniques make IgG 2000 CWP a unique, GRAS ingredient that is superior in its bioactive composition and its purity.**

*One daily dose of GI Protect provides over 2 g of IgG 2000 CWP as well as 1 g of L-glutamine, which is added to support intestinal mucosal barrier integrity. GI Protect is naturally flavored and tastes great, making it easy to consume.**

Oral consumption of immunoglobulins derived from colostrum is a means of supporting passive immunity, protecting the body, and eliminating unwanted molecules.^[4-7] The most versatile, IgG, is capable of carrying out all of the functions of immunoglobulin molecules, accounting for IgG 2000 CWP's broad range of immune-supportive effects.^[8] Review of the research confirms that bovine colostrum supplementation confers other benefits, such as the maintenance of gastrointestinal integrity.^[9-11] Oral immunoglobulins have been used in sports nutrition to support lean body mass,^[12] physical exercise, and recovery following high-intensity training.^[8,13] The 2.5 grams of immunoglobulins in each serving of GI Protect contribute to individual dosing requirements.*

L-Glutamine, the most abundant free-form amino acid in the body, is very important for maintaining gastrointestinal health and stimulated immune cell functioning. Animal and human studies also demonstrate the benefits of glutamine supplementation in gut barrier function.^[14-16] Because it is an important transporter of nitrogen (and carbon) in the body, glutamine is vital to the body's normal tissue healing processes. Although glutamine can be synthesized by the intestinal mucosa, supplementation during periods of physiological stress—when needs of the gut epithelia are increased—can be of benefit.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

GI Protect™ Peach Supplement Facts

Serving Size: 1 Scoop (about 10 g)
Servings Per Container: About 30

	Amount Per Serving	%Daily Value
Calories	35	
Total Carbohydrate	6 g	2%†
Total Sugars	6 g	**
Includes 6g Added Sugars		12%
Protein	2 g	
Calcium	20 mg	2%
IgG 2000 CWP™ (bovine-derived immunoglobulin concentrate)	2.5 g	**
Immunoglobulin G (IgG)	1 g	**
L-Glutamine	1 g	**

†Percent Daily Values are based on a 2,000 calorie diet.
**Daily Value not established.

Other Ingredients: Dried cane syrup, citric acid, natural peach flavor (no MSG), malic acid, sunflower lecithin, silica, natural red beet powder, and natural beta-carotene color.

Contains: Milk.

DIRECTIONS: Briskly stir one scoop (10 g) into at least 8 oz of water and consume twice daily, or take as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

References

- Godhia ML, Patel N. Colostrum—its composition, benefits as a nutraceutical: a review. *Curr Res Nutr Food Sci*. 2013;1(1):37-47. <http://dx.doi.org/10.12944/CRNFSJ.1.1.04>
- Cantey JR. Prevention of bacterial infections of mucosal surfaces by immune secretory IgA. *Adv Exp Med Biol*. 1978;107:461-70. [PMID: 369313]
- Jemmott JB 3rd, Borysenko JZ, Borysenko M, et al. Academic stress, power motivation, and decrease in secretion rate of salivary secretory immunoglobulin A. *Lancet*. 1983 Jun 25;1(8339):1400-02. [PMID: 6134179]
- Hurley D. Establishment of the effects of colostrally derived protein food supplements on human and animal health [dissertation]. Brookings, SD: South Dakota State University; 1994.
- Hurley WL, Theil PK. Perspectives on immunoglobulins in colostrum and milk. *Nutrients*. 2011 Apr;3(4):442-74. Review. [PMID: 22254105]
- Rump JA, Arndt R, Arnold A, et al. Treatment of diarrhoea in human immunodeficiency virus-infected patients with immunoglobulins from bovine colostrum. *Clin Invest*. 1992 Jul;70(7):588-94. [PMID: 1392428]
- Schaller JP, Saif LJ, Cordle CT, et al. Prevention of human rotavirus-induced diarrhea in gnotobiotic piglets using bovine antibody. *J Infect Dis*. 1992 Apr;165(4):623-30. [PMID: 1313067]
- Lotze MT. *Measuring Immunity: Basic Science and Clinical Practice*. London, UK: Academic Press; 2004:160.
- Davison G. Bovine colostrum and immune function after exercise. *Med Sport Sci*. 2012;59:62-9. [PMID: 23075556]
- Greenberg PD, Cello JP. Treatment of severe diarrhea caused by *Cryptosporidium parvum* with oral bovine immunoglobulin concentrate in patients with AIDS. *J Acquir Immune Defic Syndr Hum Retrovirol*. 1996 Dec 1;13(4):348-54. [PMID: 8948373]
- Kelly GS. Bovine colostrums: a review of clinical uses. *Altern Med Rev*. 2003 Nov;8(4):378-94. Review. [PMID: 14653766]
- Antonio J, Sanders MS, Van Gammeren D. The effects of bovine colostrum supplementation on body composition and exercise performance in active men and women. *Nutrition*. 2001 Mar;17(3):243-47. [PMID: 11312068]
- Shing CM, Hunter DC, Stevenson LM. Bovine colostrum supplementation and exercise performance: potential mechanisms. *Sports Med*. 2009;39(12):1033-54. [PMID: 19902984]
- Zuhl MN, Lanphere KR, Kravitz L, et al. Effects of oral glutamine supplementation on exercise-induced gastrointestinal permeability and tight junction protein expression. *J Appl Physiol* (1985). 2014 Jan 15;116(2):183-91. [PMID: 24285149]
- Beutheu S, Ouelaa W, Guérin C, et al. Glutamine supplementation, but not combined glutamine and arginine supplementation, improves gut barrier function during chemotherapy-induced intestinal mucositis in rats. *Clin Nutr*. 2013 Sep 25. pii: S0261-5614(13)00241-0. [PMID: 24095638]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

GlutAloeMine®

Enhanced Gastrointestinal Support*



Available in 30 servings and 60 servings powder

Discussion

L-Glutamine, the most abundant free form amino acid in the body, is very important for maintaining gastrointestinal and stimulated immune cell functioning. It is an important transporter of nitrogen (and carbon) in the body and therefore, is vital in wound healing. Although glutamine can be synthesized by the intestinal mucosa, during periods of physiological stress when needs can not likely be met by the body alone, gut epithelial atrophy, ulceration and even necrosis are possible.^[1] L-glutamine is metabolized to ammonia and glutamate.*

Arabinogalactan, a polysaccharide derived from the Larch tree, contributes fermentable fiber to this formula in addition to having immuno-stimulatory properties. It minimizes ammonia synthesis and absorption, enhances production of short chain fatty acids and increases the gut microflora population.*^[2]

Licorice Root Extract 10:1(deglycyrrhized) is a concentrated extract that has been processed to remove glycyrrhizin, thus eliminating any risk of licorice-associated side effects. It is anti-inflammatory, antispasmodic and has laxative and soothing effects. Aspirin-induced mucosal damage has been shown to be reduced by administration of deglycyrrhized licorice.*^[3]

Aloe Leaf Extract (standardized to 50% polysaccharides), used for thousands of years, is perhaps most well-known for healing of damaged epithelial tissue, including the bowel lining. Despite the lack of scientific published studies there is anecdotal evidence to suggest that aloe vera helps inflammatory conditions of the gastrointestinal tract. In some individuals it may increase G.I. transit time, improve protein digestion and absorption, increase stool bulk and normalize stool bacteria where high levels of yeasts previously existed.^[4] The aloe extract used in GlutAloeMine® does not have a laxative effect because the bitter principles have been removed.*

Clinical Applications

- » Gastrointestinal Support*
- » Enhanced Production of Short Chain Fatty Acids*

*GlutAloeMine® features four specialized ingredients for enhanced gastrointestinal support. This unique formula contains a concentrated extract of licorice that has been processed to remove glycyrrhizin—thus reducing risk of side effects associated with licorice. Glutamine serves as the predominant fuel and nitrogen source for the mucosal lining of the gastrointestinal (GI) tract. Arabinogalactan from the North American larch tree is a naturally occurring polysaccharide that provides excellent support for GI health. Research suggests that arabinogalactan plays a role in the promotion of gut microflora and may increase beneficial short-chain fatty acid production. The Aloe vera leaf extract in GlutAloeMine has been processed to remove the bitter principles and prevent a laxative effect.**

GlutAloeMine® Supplement Facts

Serving Size: 1 Scoop (about 5.8 g)

	Amount Per Serving	%Daily Value
Calories	5	
Total Carbohydrate	2 g	1% [†]
Dietary Fiber	1 g	4%
Sodium (naturally occurring)	5 mg	<1%
L-Glutamine	3 g	**
Arabinogalactan (from <i>Larix laricina</i>)(heartwood)	2 g	**
Deglycyrrhizinated Licorice 10:1 Aqueous Extract (<i>Glycyrrhiza glabra</i>)(root)	500 mg	**
Aloe Vera 200:1 Aqueous Extract (<i>Aloe barbadensis</i>)(leaf gel)	100 mg	**

[†]Percent Daily Values are based on a 2,000 calorie diet.

** Daily Value not established.

Other Ingredients: Stevia leaf extract.**DIRECTIONS:** Mix one scoop in 2-4 oz water once daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.**DOES NOT CONTAIN:** Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, or artificial sweeteners**References**

1. L-Glutamine. www.naturaldatabase.com {accessed 4.3.07}
2. Arabinogalactan. www.naturaldatabase.com {accessed 4.3.07}
3. Rees WD, et al. Effect of deglycyrrhizinated liquorice on gastric mucosal damage by aspirin. *Scand J Gastroenterol.* 1979;14(5):605-7. [PMID: 493863]
4. Davis K, et. al. Randomised double-blind placebo-controlled trial of aloe vera for irritable bowel syndrome. *Int J Clin Pract.* 2006 Sep;60(9):1080-6 [PMID: 16749917]

Additional References Available Upon Request.

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration.
This product is not intended to diagnose, treat, cure, or prevent any disease.

Green Tea 600™

Ultra-Pure Green Tea Extract



Available in 60 capsules

Discussion

The health benefits of the tea leaf *Camellia sinensis* are derived from a group of phytochemicals known as polyphenols. Polyphenols in fresh green tea leaves are present as a series of chemicals called catechins. The dominant and most biologically active among the catechins, (-)-epigallocatechin-3-gallate (EGCG), has been shown to induce expression of glutathione S-transferase, glutathione peroxidase, glutamate cysteine ligase, heme oxygenase-1, and other enzymes that protect a variety of cells, including cultured neurons, against oxidative stress-induced cell death. EGCG modulates the redox-sensitive transcription factor Nrf2, which plays a key role in activating detoxifying enzyme HO-1, as well as other phase II enzymes.^{[1-7]*}

Green Tea Leaf Extract Green tea polyphenols protect erythrocytes (red blood cells) from oxidative stress.^[8] In research studies, EGCG supported healthy insulin activity,^[9] protected the pancreatic cells by reducing undesirable cytokines (e.g., interleukin-1 beta), and reduced interferon-gamma-induced nitric oxide production—an excess of which may cause free radical damage. Furthermore, it was found that the polyphenols triggered genes that inhibit activation of NF-kappaB^[10] and reduced the level of messenger RNA for the hepatic gluconeogenic enzymes, which convert non-carbohydrate sources into glucose.^[11] EGCG has been shown to support healthy immune function,^[2] support the endocrine system,^[4] and promote fat oxidation beyond what would be explained by its caffeine content.^{*[3]}

Many of the wide range of health benefits derived from green tea are dose-dependent, and most Americans are not willing to consume the necessary 5-10 cups of tea a day to gain its advantages. Careful processing of the tea into an extract highly concentrates the key beneficial constituents. Each 600 mg capsule of Green Tea 600 contains 80% polyphenols, 60% catechins, and 30% EGCG. This is equivalent to approximately 10 cups of green tea. Each capsule contains 36-45 mg of caffeine per serving, roughly the equivalent of a can of cola and less than the 95-200 mg of caffeine in an 8-oz cup of brewed coffee.^[12] Naturally occurring caffeine in green tea is believed to act synergistically with the polyphenols.^{*[13]}

Clinical Applications

- » Provides Antioxidant Support*
- » Supports Healthy Immune Function*
- » Supports Healthy Endocrine Function*
- » Provides Alternative to Consumption of Multiple Cups of Green Tea*

*Green Tea 600™ is an ultra-pure, water-extracted green tea formula that is rich in polyphenols, a class of phytochemical compounds that supports antioxidant activity. Research has shown that green tea supports natural detoxifying enzymes, normal gene signaling, and the health and function of intestinal flora.**

In summary, green tea's benefits are based upon four actions: 1) it is a powerful antioxidant that protects against DNA damage; 2) it induces detoxifying enzymes; 3) it supports gene signaling, which helps regulate cellular growth, development, and apoptosis; and 4) it selectively improves the function of the intestinal bacterial flora.^{*[1,2,4-8,10,11]}

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Green Tea 600™ Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Green Tea Aqueous Extract (<i>Camellia sinensis</i>)(leaf)(80% polyphenols, 60% catechins, 30% EGCG, 6% caffeine)	600 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, and silica.**DIRECTIONS:** Take one capsule daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.

**References**

1. Weisburger JH, Chung FL. Mechanisms of chronic disease causation by nutritional factors and tobacco products and their prevention by tea polyphenols. *Food Chem Toxicol.* 2002 Aug;40(8):1145-54. [PMID: 12067577]
2. Matsunaga K, Klien TW, Friedman H, et al. Legionella pneumophila replication in macrophages inhibited by selective immunomodulatory effects on cytokine formation by epigallocatechin gallate, a major form of tea catechins. *Infect Immun.* 2001 Jun;69(6):3947-53. [PMID: 11349063]
3. Dulloo AG, Duret C, Rohrer D, et al. Efficacy of a green tea extract rich in catechin polyphenols and caffeine in increasing 24-h energy expenditure and fat oxidation in humans. *Am J Clin Nutr.* 1999 Dec;70(6):1040-45. [PMID: 10584049]
4. Kao YH, Hiipakka RA, Liao S. Modulation of endocrine systems and food intake by green tea epigallocatechin gallate. *Endocrinology.* 2000 Mar;141(3):980-7. [PMID: 10698173]
5. Wheeler DS, Catravas JD, Odoms K, et al. Epigallocatechin-3-gallate, a green tea-derived polyphenol, inhibits IL-1 beta-dependent proinflammatory signal transduction in cultured respiratory epithelial cells. *J Nutr.* 2004 May;134(5):1039-44. [PMID: 15113942]
6. Dudka J, Jodynis-Liebert J, Korobowicz E, et al. Activity of NADPH-cytochrome P-450 reductase of the human heart, liver and lungs in the presence of (-)-epigallocatechin gallate, quercetin and resveratrol: an in vitro study. *Basic Clin Pharmacol Toxicol.* 2005 Aug;97(2):74-9. [PMID: 15998352]
7. Townsend PA, Scarabelli TM, Pasini E, et al. Epigallocatechin-3-gallate inhibits STAT-1 activation and protects cardiac myocytes from ischemia/reperfusion-induced apoptosis. *FASEB J.* 2004 Oct, 18(13):1621-3. [PMID: 15319365]
8. Rizvi SI, Zaid MA, Anis R, et al. Protective role of tea catechins against oxidation-induced damage of type 2 diabetic erythrocytes. *Clin Exp Pharmacol Physiol.* 2005 Jan-Feb;32 (1-2):70-5. [PMID: 15730438]
9. Anderson RA, Polansky MM. Tea enhances insulin activity. *J Agric Food Chem.* 2002 Nov;50(24):7182-6. [PMID: 12428980]
10. Koyama Y, Abe K, Sano Y, et al. Effects of green tea on gene expression of hepatic gluconeogenic enzymes in vivo. *Planta Med.* 2004 Nov;70(11):1100-2. [PMID: 15549673]
11. Burzynski SR. Aging: gene silencing or gene activation? *Med Hypotheses.* 2005;64(1):201-8. [PMID: 15533642]
12. Mayo Clinic Staff. Nutrition and healthy eating: Caffeine content for coffee, tea, soda and more. Mayo Clinic. <http://www.mayoclinic.com/health/caffeine/AN01211>. Published October 1, 2011. Accessed August 16, 2012.
13. Dulloo AG, Seydoux J, Girardier L, et al. Green tea and thermogenesis: interactions between catechin-polyphenols, caffeine and sympathetic activity. *Int J Obes Relat Metab Disord.* 2000 Feb;24 (2):252-8. [PMID: 10702779]

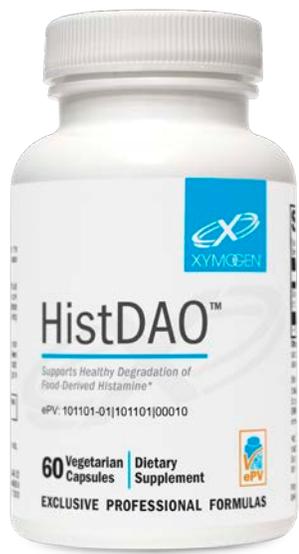
Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

HistDAO™

Supports Healthy Degradation of Food-Derived Histamine*



Available in 60 vegetarian capsules

Discussion

Histamine is a bioactive or “vasoactive” amine produced in the body in response to an injury or foreign substance. It has an array of physiological effects, including increasing blood supply to specific sites in the body. In addition, histamine is involved in the immune response, regulation of gastric acid, permeability of blood vessels, contraction of muscles, and the normal response to inflammation.^[1] The highest concentrations of histamine in the body are found in the gastrointestinal tract, lungs, and skin, with lesser amounts in the brain and heart.*

Histamine is not only produced in the body but is also present in many fermented foods, such as sauerkraut, sausage, cheese, yogurt, and alcoholic beverages. Tuna, olives, spinach, eggplant, avocados, tomatoes, cherries, and citrus fruits are other histamine-containing foods. Despite their absence of histamine, some foods, such as berries, tea, and a variety of spices, stimulate the endogenous production of the amine due to their benzoate content. In addition, microbial fermentation can convert the histidine in high-protein foods to histamine so that the histamine content of food can increase over time.*^[1]

Histamine/DAO balance Endogenous and exogenous histamine must be broken down in order to maintain homeostasis and histamine balance. The enzyme diamine oxidase (DAO) degrades histamine by converting it from 2-(4-imidazolyl)-ethylamine to the inactive metabolite imidazole acetaldehyde.^[2] The active ingredient in HistDAO is porcine-derived diamine oxidase, and research suggests that DAO derived from porcine kidney appears to have identical action to DAO derived from porcine intestine.^[3] In humans and other mammals, DAO is found in high concentrations in the gastrointestinal mucosa. Animal studies suggest that circulating DAO may be a marker for mucosal integrity and maturity.^[4] Certain drugs may affect histamine balance in the body by promoting histamine release or inhibiting DAO.*^[2]

Clinical Applications

- » Supports Healthy Degradation of Food-Derived Histamine*
- » Enhances the Presence of Diamine Oxidase in the Digestive Tract*

*HistDAO™ is a patented enzyme formula containing diamine oxidase (DAO)—the main enzyme responsible for the degradation of ingested histamine. This enzyme has been clinically tested and found to break down food-derived histamine in the digestive tract. DAO is not absorbed and does not have systemic activity. HistDAO does not manage or address antibody-related or IgE-related food allergies.**

Histamine Tolerance Histamine tolerance may not be the same for everyone. Results of a double-blind, placebo-controlled crossover study suggest that tolerance to histamine can vary from individual to individual.^[5] Total body histamine load must be considered when evaluating histamine tolerance, and a balance between histamine and DAO appears to be crucial to maintaining skin, rhinoconjunctival, and gastrointestinal health.^[2,6] Genetic and environmental factors may interact to influence DAO expression. Ongoing research addresses the role that genetic variations may play in individual differences in DAO metabolism, and serum activity was significantly associated with seven single nucleotide variations within the DAO gene.^[7,8] Histamine tolerance may be reflected in detailed questionnaires, food intake logs, trial with low-histamine diet, and measurement of DAO and histamine.*^[9,10]

Histamine tolerance and its manifestation may vary from organ to organ as well. A study of 39 patients suggested that intake of DAO produced a statistically significant reduction in symptoms associated with exogenous histamine ingestion, although single symptoms were not found to be reproducible.*^[11]

Ultimately, diminished serum DAO levels appear to be associated with changes in histamine degradation and serum histamine levels.^[10] Although the mechanism of histamine degradation is uniform throughout the body, HistDAO only addresses excess exogenous histamine found in the folds, villi, and microvilli of the small intestine. HistDAO is not absorbed and therefore does not have systemic activity. A two-capsule dose of HistDAO contains 20 mg of vitamin C and 20,000 HDU (histamine degrading units) from diamine oxidase. HistDAO is **NOT EFFECTIVE** for symptoms of immune-related food allergies, such as peanuts, shellfish, etc.*

HistDAO™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Diamine Oxidase (from porcine kidney protein concentrate)	600 mcg (20,000 HDU)	**
** Daily Value not established.		

Other Ingredients: Microcrystalline cellulose, HPMC (capsule), sucrose, ascorbic acid, rice starch, shellac, hydroxypropylcellulose, polyvinylpyrrolidone, hydrated magnesium silicate, acetylated corn starch, sodium carboxymethylcellulose, and glycerol.

DIRECTIONS: Take one to two capsules no more than 15 minutes before the consumption of histamine-rich foods, or take as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Avoid if allergic to pork or any other ingredient. HistDAO™ is NOT EFFECTIVE for symptoms of immune-related food allergies, such as peanuts, shellfish, etc., or for gluten intolerance due to sensitivity or celiac disease. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, dairy products, fish, shellfish, peanuts, tree nuts, egg, artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.

HistDAO™ is exclusively manufactured for healthcare practitioners under license of Sciotec Diagnostic Technologies GmbH, Vienna, Austria. Patented in Austria. Patent pending in the United States.

**References**

1. Histamine Intolerance. <http://www.allergynutrition.com/faq.php>. Accessed April 19, 2012.
2. Maintz L, Novak N. Histamine and histamine intolerance. *Am J Clin Nutr* 2007;85:1185-1196. [PMID: 17490952]
3. Schwelberger HG, Bodner E. Purification and characterization of diamine oxidase from porcine kidney and intestine. *Biochim Biophys Acta*. 1997 Jun 20;1340(1):152-64. [PMID: 9217025]
4. Luk GD, Bayless TM, Baylin SB. Diamine oxidase (histaminase). A circulating marker for rat intestinal mucosal maturation and integrity. *J Clin Invest*. 1980 Jul;66(1):66-70. [PMID: 6772669]
5. Wöhrl S, Hemmer W, Focke M, et al. Histamine intolerance-like symptoms in healthy volunteers after oral provocation with liquid histamine. *Allergy Asthma Proc*. 2004 Sep-Oct;25(5):305-11. [PMID: 15603203]
6. Kuefner M, Schwelberger HG, Weidenhiller M, et al. Both catabolic pathways of histamine via histamine-N-methyltransferase and diamine oxidase are diminished in the colonic mucosa of patients with food allergy. *Inflamm Res* 2004 Mar;53 Suppl 1:S31-2. [PMID: 15054605]
7. Igaz P, Fitzimons CP, Szalai C, et al. Histamine genomics in silico: polymorphisms of the human genes involved in the synthesis, action and degradation of histamine. *Am J Pharmacogenomics*. 2002;2(1):67-72. [PMID: 12083955]
8. Maintz L, Yu CF, Rodríguez E, et al. Association of single nucleotide polymorphisms in the diamine oxidase gene with diamine oxidase serum activities. *Allergy*. 2011 Jul;66(7):893-902. [PMID: 21488903]
9. Vickerstaff Joneja JM, Carmona-Silva C. Outcome of a histamine-restricted diet based on chart audit. *Journal of Nutritional & Environmental Medicine*. 2001. 2001;11:249-62. doi:10.1080/1359084012010309.
10. Maintz L, Benfadal S, Allam JP, et al. Evidence for a reduced histamine degradation capacity in a subgroup of patients with atopic eczema. *J Allergy Clin Immunol*. 2006 May;117(5):1106-12. [PMID: 16675339]
11. Komericki P, Klein G, Reider N, et al. Histamine intolerance: lack of reproducibility of single symptoms by oral provocation with histamine: a randomised, double-blind, placebo-controlled cross-over study. *Wien Klin Wochenschr*. 2011 Jan;123(1-2):15-20. [PMID: 21165702]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Hormone Protect®

Estrogen Metabolism and Detoxification Support Formula*



Available in 60 and 120 capsules

Discussion

Hormone Protect uses a dual-action approach to supporting healthy estrogen-sensitive tissues. First, it provides diindolylmethane (DIM) to promote healthy estrogen metabolism and create a better balance of estrogen metabolites (2-OH, 4-OH, 16alpha-OH) through phase I cytochrome P450 enzyme induction and promotion of 2-hydroxylation. Second, the action of DIM is complemented by providing sulforaphane glucosinolate (SGS), which protects tissues from unrestrained oxidative stress and uniquely supports phase II detoxification of harmful estrogen metabolites (e.g., estrogen quinones) and xenoestrogens. These actions may be important for the health of estrogen-sensitive tissues, such as those of the breast, uterus, cervix, and prostate.*

DIM (diindolylmethane) DIM is an advanced metabolite of indole-3-carbinol (I3C), the indole found in cruciferous vegetables. Supplementation with DIM is preferred over I3C due to I3C's undesirable breakdown products, including the dioxin-like molecule indolo[3,2-b]carbazole (ICZ).^[1] It has been established that DIM supplementation increases 2-hydroxylation of estrogen. This science has been validated in animal and human studies wherein supplementation with DIM was shown to increase the ratio of the protective, "good" 2-hydroxyestrone (2-OH) to 16alpha hydroxyestrone (16alpha-OH).^[2,3] In a study of postmenopausal women, DIM-treated subjects, relative to placebo, showed an increase of 47% in 2-OH/16alpha-OH.^[4] Studies further reveal that DIM may play a critical role in supporting normal cellular proliferation in estrogen-sensitive tissues.*^[3,5,6]

Sulforaphane Glucosinolate (SGS) Sulforaphane is the aglycone breakdown product of glucoraphanin, a glucosinolate also known as SGS. The SGS broccoli seed extract used in Hormone Protect is a super vegetable that delivers extended antioxidant support and boasts a very high level of glucoraphanin (13%). Research suggests that when SGS is broken down to sulforaphane (its active form), it safely and effectively upregulates the Nrf2 system, activates the antioxidant response element (ARE), enhances the production of important antioxidants, and activates vital phase II detoxification enzymes.^[7] These mechanisms provide protection from toxins, xenobiotics (e.g.,

Clinical Applications

- » Supports Healthy Estrogen Metabolism*
- » Supports a Healthy Ratio of 2-OH:16alpha-OH*
- » Supports Detoxification of Estrogen Metabolites/Intermediates*
- » Supports Cellular Health in Estrogen-Sensitive Tissues*
- » Helps Protect Against Damaging Reactive Oxygen Species, DNA-Damaging Electrophiles, and Cytokines
- » Supports Antioxidant Activity with SGS*

*Hormone Protect® is an ideal combination of DIM (diindolylmethane) and TrueBroc® (glucoraphanin) that helps protect estrogen-sensitive tissues by promoting healthy estrogen metabolism and supporting detoxification and neutralization of harmful estrogen metabolites and xenoestrogens.**

xenoestrogens), and reactive intermediates formed after phase I detoxification.*

Neutralizing Reactive Estrogen Quinones with SGS According to Bolton et al, the oxidation of catechol estrogens (2-OH and 4-OH) via cytochrome P450 enzymes generates reactive electrophilic estrogen quinones and reactive oxygen species (ROS) through redox cycling.^[8] Formation of quinones is largely minimized via phase II methylation, which produces methoxyestrogens. However, if methylation is suboptimal, estrogen quinones, which can cause DNA damage in estrogen-sensitive tissues, must be neutralized via other phase II enzymes such as quinone reductase. According to researchers, estrogen quinones are now recognized as a significant mechanism of estrogen-mediated cell damage.^[8,9] A promising strategy to address their deleterious effects involves the use of agents to favorably shift the balance between phase I and phase II enzymes.^[9] In fact, phase II enzymes such as quinone reductase, heme oxygenase-1 (HO-1), and glutathione S-transferase (GST) have been suggested as targets for reducing these highly reactive estrogen quinones.*

Sulforaphane has been identified as an agent that possesses the ability to potently induce phase II detoxification enzymes—including quinone reductase, HO-1, GST, and glutathione reductase—as well as to inhibit phase I enzymes involved in activation.^[10-12] In the case of estrogen quinones, quinone reductase protects cells from oxidative damage by two-electron reduction, thus suppressing oxidative cycling and reactive oxygen species generation.^[10] Sulforaphane consumption is associated with supporting cell-line health in humans, and animal research shows that sulforaphane metabolites can be found in target tissues, along with significant induction of quinone reductase and HO-1.^[10] This research has exciting implications for supporting the health of tissues as it relates to reactive estrogen quinones formed after phase I activation of catechol estrogens (2-OH, 4-OH).^{*(10)}

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Hormone Protect® Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
DIM (diindolylmethane)	300 mg	**
Glucoraphanin (from broccoli extract) (<i>Brassica oleracea italica</i>) (seed) (TrueBroc®)	60 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, silica, and microcrystalline cellulose.

DIRECTIONS: Take one to two capsules daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication or receiving cancer treatment should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep tightly closed in a cool, dry place out of reach of children.



TrueBroc® is protected by trademarks and patents of Brassica Protection Products LLC: www.brassica.com/ip



References

1. Herrmann S, Seidelin M, Bisgaard HC, et al. Indolo[3,2-b]carbazole inhibits gap junctional intercellular communication in rat primary hepatocytes and acts as a potential tumor promoter. *Carcinogenesis*. 2002 Nov;23(11):1861-68. [PMID: 12419834]
2. Rajoria S, Suriano R, Parmar PS, et al. 3,3'-diindolylmethane modulates estrogen metabolism in patients with thyroid proliferative disease: a pilot study. *Thyroid*. 2011 Mar;21(3):299-304. [PMID: 21254914]
3. Sepkovic DW, Stein J, Carlisle AD, et al. Diindolylmethane inhibits cervical dysplasia, alters estrogen metabolism, and enhances immune response in the K14-HPV16 transgenic mouse model. *Cancer Epidemiol Biomarkers Prev*. 2009 Nov;18(11):2957-64. [PMID: 19861518]
4. Dalessandri KM, Firestone GL, Fitch MD, et al. Pilot study: effect of 3,3'-diindolylmethane supplements on urinary hormone metabolites in postmenopausal women with a history of early-stage breast cancer. *Nutr Cancer*. 2004;50(2):161-67. [PMID: 15623462]
5. Del Priore G, Gudipudi DK, Montemarano N, et al. Oral diindolylmethane (DIM): pilot evaluation of a nonsurgical treatment for cervical dysplasia. *Gynecol Oncol*. 2010 Mar;116(3):464-67. [PMID: 19939441]
6. Fares F, Azzam N, Appel B, et al. The potential efficacy of 3,3'-diindolylmethane in prevention of prostate cancer development. *Eur J Cancer Prev*. 2010 May;19(3):199-203. [PMID: 20010430]
7. Keum YS. Regulation of the Keap1/Nrf2 system by chemopreventive sulforaphane: implications of posttranslational modifications. *Ann N Y Acad Sci*. 2011 Jul;1229:184-89. [PMID:21793854]
8. Bolton JL, Thatcher GR. Potential mechanisms of estrogen quinone carcinogenesis. *Chem Res Toxicol*. 2008 Jan;21(1):93-101. [PMID: 18052105]
9. Cavalieri E, Chakravarti D, Guttenplan J, et al. Catechol estrogen quinones as initiators of breast and other human cancers: implications for biomarkers of susceptibility and cancer prevention. *Biochim Biophys Acta*. 2006 Aug;1766(1):63-78. [PMID: 16675129]
10. Cornblatt BS, Ye L, Dinkova-Kostova AT, et al. Preclinical and clinical evaluation of sulforaphane for chemoprevention in the breast. *Carcinogenesis*. 2007 Jul;28(7):1485-90. [PMID: 17347138]
11. Misiewicz I, Skupińska K, Kowalska E, et al. Sulforaphane-mediated induction of a phase 2 detoxifying enzyme NAD(P)H:quinone reductase and apoptosis in human lymphoblastoid cells. *Acta Biochim Pol*. 2004;51(3):711-21. [PMID: 15448733]
12. Myzak MC, Dashwood RH. Chemoprotection by sulforaphane: keep one eye beyond Keap1. *Cancer Lett*. 2006 Feb 28;233(2):208-18. [PMID: 16520150]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

I-Sight™

Proprietary Ocular Formula*



Available in 60 capsules

Discussion

Zinc is required by superoxide dismutase and catalase for quenching free radicals in the lens and the retina. British researchers concluded that a combination of zinc and antioxidants or energy substrates rather than zinc alone should provide a safer and more effective way to preserve the health of the retina throughout the aging process. Supporting the health of the retina helps retain vision in the center of the visual field, the macula.*^[1]

Taurine and zinc interact in retinal morphology and function.^[2] This most abundant free amino acid in the retina is tissue-protective in models of oxidative damage,^[3] essential for normal visual development in infants, and may support eye health throughout life.*^[4]

N-Acetyl Cysteine (NAC), critical for maintaining the reduced state of sulfhydryl-containing proteins in the lens, may have a beneficial effect on maintaining a healthy retina later in life. A healthy retina is important for sustaining healthy vision. NAC is a free radical scavenger that boosts glutathione. NAC may have a role in the function and maintenance of the redox systems in the aging eye and in the maintenance of the lens's clarity.*^[5]

Bilberry Extract has been studied mostly in the context of multi-ingredient formulations in which it demonstrated positive effects on visual acuity and field by supporting the retina.^[6] In a study in mice, oral administration of bilberry extract standardized to 42.04% anthocyanins at doses of 50, 100, and 200 mg/kg/day for five days had a positive effect on markers of antioxidant activity.*^[7]

Alpha-Lipoic Acid (ALA) is a fat- and water-soluble nutrient with antioxidant activity. Furthermore, ALA has the ability to regenerate other antioxidants, such as vitamins C and E, as well as glutathione and coenzyme Q10 (CoQ10). Continual exposure of the lens and retina to light, oxygen, and environmental chemicals causes free radical production, oxidation, and lipid peroxidation, all of which have the potential to negatively impact vision. Free radicals appear to cause proteins in the eye to clump; they also destroy the enzymes needed

Clinical Applications

- » Helps Protect Macula, Retina, and Lens from Oxidative Damage*
- » Supports Healthy Eye Structure and Function*

*I-Sight™ is a groundbreaking supplement for the care and support of the eyes. Developed in conjunction with respected Ophthalmologists, this formula allows for the increased intake of specific ocular antioxidants in order to maintain healthy retina, lens and eyesight function during the aging years. Significant research confirms the benefits of these ingredients.**

to dispose of the damaged proteins. Oxidation in the retina leads to damage of the photoreceptor cells.^[8] ALA exerts protective effects through inhibition of the lens's epithelial cell apoptosis and activation of anti-oxidative enzymes.^[9] ALA also supports healthy blood sugar levels, an important prerequisite to optimal eye health.*^[10]

Quercetin inhibits oxidative damage in the lens and inhibits aldose reductase, the enzyme considered key to maintaining the clarity of the lens.*^[11]

Lutein is present in higher concentrations in the eye than in other human tissues. It appears to counteract light and oxygen damage, maintaining ocular cell and tissue health during the aging process. This carotenoid protects the eye from blue light damage and quenches oxygen free radicals.*^[12]

Lycopene is a carotenoid compound. Although studies of the dietary supplement (as opposed to foods that contain lycopene) appear to support a claim for antioxidant activity, the formulas used in the studies usually contain mixed ingredients. There is inadequate evidence for or against the use of lycopene for eye health. In 2003, researchers who performed in vivo and in vitro studies on rats using injectable lycopene as a single ingredient concluded that it attenuated oxidative stress and had a significant benefit in healthy vision.*^[13]

I-Sight™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Zinc (as TRAACS® zinc bisglycinate chelate)	35 mg	318%
Taurine	400 mg	**
N-Acetyl-L-Cysteine	200 mg	**
Bilberry Extract (<i>Vaccinium myrtillus</i>)(fruit)(25% anthocyanosides)	180 mg	**
Alpha-Lipoic Acid	150 mg	**
Quercetin (as quercetin dihydrate)(from <i>Sophora japonica</i>)(bud)	100 mg	**
Lutein (from marigold extract)(<i>Tagetes erecta</i>)(flowers)	30 mg	**
Lycopene (from red tomato)(<i>Lycopersicon esculentum</i>)(fruit)	6 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), stearic acid, microcrystalline cellulose, silica, magnesium stearate, and medium-chain triglyceride oil.**DIRECTIONS:** Take two capsules daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.**DOES NOT CONTAIN:** Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

TRAACS® is a registered trademark of Albion Laboratories.

**References**

- Wood JP, Osborne NN. Zinc and energy requirements in induction of oxidative stress to retinal pigmented epithelial cells. *Neurochem Res.* 2003 Oct; 28(10):1525-33. [PMID: 14570397]
- Gottschall-Pass KT, et al. Oscillatory potentials and light microscopic changes demonstrate an interaction between zinc and taurine in the developing rat retina. *J Nutr.* 1997 Jun;127(6):1206-13. [PMID: 9187637]
- Schuller-Levis GB, Park E. Taurine: new implications for an old amino acid. *FEMS Microbiol Lett.* 2003 Sep 26;226(2):195-202. [PMID: 14553911]
- Neuringer M, Sturman J. Visual acuity loss in rhesus monkey infants fed a taurine-free human infant formula. *J Neurosci Res.* 1987;18(4):597-601. [PMID: 3437473]
- Babizhayev MA. New concept in nutrition for the maintenance of the aging eye redox regulation and therapeutic treatment of cataract disease; synergism of natural antioxidant imidazole-containing amino acid-based compounds, chaperone, and glutathione boosting agents: a systemic perspective on aging and longevity emerged from studies in humans. *Am J Ther.* 2010 Jul-Aug;17(4):373-89. [PMID: 20463577]
- Egorov EA, Gvetadze AA, Vinogradova EP. Efficacy of vision correcting system "focus" for prevention and treatment of dry form of age macular degeneration [in Russian]. *Vestn Oftalmol.* 2012 Jan-Feb;128(1):44-6. [PMID: 22741296]
- Yao N, Lan F, He RR, et al. Protective effects of bilberry (*Vaccinium myrtillus* L.) extract against endotoxin-induced uveitis in mice. *J Agric Food Chem.* 2010 Apr 28;58(8):4731-6. [PMID: 20222750]
- Winkler BS, Boulton ME, Gottsch JD, et al. Oxidative damage and age-related macular degeneration. *Mol Vis.* 1999 Nov 3;5:32. [PMID: 10562656]
- Li Y, Liu YZ, Shi JM, et al. Alpha lipoic acid protects lens from H(2)O(2)-induced cataract by inhibiting apoptosis of lens epithelial cells and inducing activation of anti-oxidative enzymes. *Asian Pac J Trop Med.* 2013 Jul;6(7):548-51. [PMID: 23768827]
- Singh VP, Bali A, Singh N, et al. Advanced glycation end products and diabetic complications. *Korean J Physiol Pharmacol.* 2014 Feb;18(1):1-14. Epub 2014 Feb 13. [PMID: 24634591]
- Cornish KM, Williamson G, Sanderson J. Quercetin metabolism in the lens: role in inhibition of hydrogen peroxide induced cataract. *Free Radic Biol Med.* 2002 Jul 1;33(1):63-70. [PMID: 12086683]
- Koushan K, Rusovici R, Li W, et al. The role of lutein in eye-related disease. *Nutrients.* 2013 May 22;5(5):1823-39. Review. [PMID: 23698168]
- Gupta SK, Trivedi D, Srivastava S, et al. Lycopene attenuates oxidative stress induced experimental cataract development: an in vitro and in vivo study. *Nutrition.* 2003 Sep;19(9):794-9. [PMID: 12921892]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.



Available in Vanilla Delight & Creamy Chocolate

Discussion

VegaPro™ XYMOGEN's proprietary blend of pea protein isolate, glycine, taurine, rice protein concentrate, and L-glutamine provides 21 g of plant-based protein per serving of i5. VegaPro is easily digested, is gluten-free, and achieves an amino acid score of 100%.^[1,2] This amino acid profile supports protein metabolism and lean body mass. Aminogen® enhances protein digestibility and absorption.*

IgG 2000 CWP™ is an immunoglobulin concentrate from colostrum whey peptides that delivers a minimum of 40% IgG immunoglobulin along with an array of compounds, including growth factors, sialic acid, lactoferrin, proline-rich peptides (PRPs), oligosaccharides, and gangliosides. Each of these components provides the user with different and complementary health benefits, such as fundamental support of immune function and modulation, lean body mass, brain and thymus health, microbiota modulation, and cytokine balance.*^[3]

Oral consumption of immunoglobulins derived from colostrum is a means of supporting passive immunity, protecting the body, and eliminating unwanted molecules.^[4-7] The most versatile, IgG, is capable of carrying out all of the functions of immunoglobulin molecules, accounting for IgG 2000 CWP's broad range of immune-supportive effects.^[8] Review of the research confirms that bovine colostrum supplementation confers other benefits, such as the maintenance of gastrointestinal integrity.^[9-11] Oral immunoglobulins have been used in sports nutrition to support lean body mass,^[12] physical exercise, and recovery following high-intensity training.^[9,13] The 2.5 grams of immunoglobulins in each serving of i5 contribute to individual dosing requirements.*

OncoPLEX™ (glucoraphanin) This patented plant-based ingredient, also known as sulforaphane glucosinolate, is extracted from one of its most concentrated cruciferous sources—broccoli seeds.^[14] An abundance of research demonstrates that when glucoraphanin is broken down to its active form, sulforaphane, it safely and effectively upregulates the body's natural phase II detoxification enzymes.^[15-17] This activity in turn supports antioxidant activity and helps protect cells, cell membranes, and tissues from free-radical damage.*

Clinical Applications

- » Supports Improved Body Composition*
- » Supports Immune Function by Providing Immunoglobulins and Other Immune Factors*
- » Supports Healthy Cytokine Production*
- » Supports Intestinal Health*
- » Supports Detoxification*

*i5™ represents an innovative approach to biotransformation for individuals whose health is constantly challenged. This all-natural, fructose-free formula includes ingredients that promote overall gastrointestinal health and support detoxification mechanisms and cytokine balance in the body. i5 features patented and proprietary ingredients, including 21 g of VegaPro™, a non-GMO, vegetable-based protein, as well as IgG 2000 CWP™, OncoPLEX™ (glucoraphanin), and arabinogalactan, a prebiotic. Practitioners have reported best results when i5 is combined with a modified elimination diet.**

Arabinogalactan Sourced from the larch tree, arabinogalactan is a non-digestible, soluble dietary fiber that contains arabinose and galactose monosaccharides. It is considered an excellent source of fiber, favorably supports gut microflora as a prebiotic, and serves as a precursor to short-chain fatty acids, all elements that help support gastrointestinal health.*^[18,19]

EXCLUSIVE • PATENTED

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

i5™ Vanilla Delight Nutrition Facts

About 14 servings per container

Serving size	2 scoops (about 46g)
Amount per serving	170
Calories	
% Daily Value*	
Total Fat 3g	4%
Saturated Fat 1g	5%
Trans Fat 0g	
Cholesterol 0mg	0%
Sodium 410mg	18%
Total Carbohydrate 15g	5%
Dietary Fiber 6g	21%
Total Sugars 6g	
Includes 5g Added Sugars	10%
Protein 21g	
Vitamin D 0mcg	0%
Calcium 35mg	3%
Iron 4mg	20%
Potassium 390mg	8%

* The % Daily Value tells you how much a nutrient in a serving of food contributes to a daily diet. 2,000 calories a day is used for general nutrition advice.

INGREDIENTS: VegaPro™ (XYMOGEN's proprietary blend of pea protein isolate, glycine, taurine, rice protein concentrate, and L-glutamine), dried cane syrup, fiber complex (inulin (from chicory) and oat fiber), natural flavors (no MSG), IgG 2000 CWP™ (immunoglobulin protein concentrate), sunflower oil, arabinogalactan, tripotassium citrate, cellulose gum, xanthan gum, medium-chain triglyceride oil, Aminogen® (proprietary plant enzyme blend), OncoPLEX™ (truebroc® broccoli seed extract), guar gum, stevia leaf extract, and silica.

CONTAINS: Milk

DIRECTIONS: Blend, shake, or briskly stir 2 level scoops (46 g) into 8-12 oz chilled water and consume one to two times daily, or as directed by your healthcare practitioner. Adjust amount of water to desired sweetness and thickness.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, fish, shellfish, peanuts, tree nuts, egg, artificial colors, artificial sweeteners, or artificial preservatives.

Typical Amino Acid Profile Per Serving:

Alanine	1,130 mg	Methionine	280 mg
Arginine	2,100 mg	Phenylalanine	1,340 mg
Aspartic Acid	2,830 mg	Proline	1,180 mg
Cysteine	250 mg	Serine	1,380 mg
Glutamic Acid	4,140 mg	Taurine	500 mg
Glycine	3,010 mg	Threonine	1,050 mg
Histidine	620 mg	Tryptophan	270 mg
Isoleucine	1,110 mg	Tyrosine	950 mg
Leucine	2,090 mg	Valine	1,260 mg
Lysine	1,800 mg		

 AMINOGEN® is a registered trademark of Innophos Nutrition, Inc. AMINOGEN® is protected under US patent 5,387,422.



 Produced under US patent 6,521,818 licensed from Brassica Protection Products LLC; truebroc is a registered trademark of Brassica Protection Products LLC.

References

1. Fredrikson M, Biot P, Alminger ML, et al. Production process for high-quality pea-protein isolate with low content of oligosaccharides and phytate. *J Agric Food Chem*. 2001 Mar;49(3):1208-12. [PMID: 11312837]
2. Gausserès N, Mahé S, Benamouzig R, et al. [15N]-labeled pea flour protein nitrogen exhibits good ileal digestibility and postprandial retention in humans. *J Nutr*. 1997 Jun;127(6):1160-65. [PMID: 9187631]
3. Godhia M, Patel N. Colostrum—its composition, benefits as a nutraceutical: a review. *Curr Res Nutr Food Sci*. 2013;1(1):37-47. <http://dx.doi.org/10.12944/CRNFSJ.1.1.04>
4. Hurley D. Establishment of the effects of colostrally derived protein food supplements on human and animal health [dissertation]. Brookings, SD: South Dakota State University; 1994.
5. Hurley WL, Theil PK. Perspectives on immunoglobulins in colostrum and milk. *Nutrients*. 2011 Apr;3(4):442-74. Review. [PMID: 22254105]
6. Rump JA, Arndt R, Arnold A, et al. Treatment of diarrhoea in human immunodeficiency virus-infected patients with immunoglobulins from bovine colostrum. *Clin Investig*. 1992 Jul;70(7):588-94. [PMID: 1392428]
7. Schaller JP, Saif LJ, Cordle CT, et al. Prevention of human rotavirus-induced diarrhea in gnotobiotic piglets using bovine antibody. *J Infect Dis*. 1992 Apr;165(4):623-30. [PMID: 1313067]
8. Lotze MT. *Measuring Immunity: Basic Science and Clinical Practice*. London, UK: Academic Press; 2004:160.
9. Davison G. Bovine colostrum and immune function after exercise. *Med Sport Sci*. 2012;59:62-9. doi: 10.1159/000341966. [PMID: 23075556]
10. Greenberg PD, Cello JP. Treatment of severe diarrhea caused by *Cryptosporidium parvum* with oral bovine immunoglobulin concentrate in patients with AIDS. *J Acquir Immune Defic Syndr Hum Retrovirol*. 1996 Dec 1;13(4):348-54. [PMID: 8948373]
11. Kelly GS. Bovine colostrums: a review of clinical uses. *Altern Med Rev*. 2003 Nov;8(4):378-94. Review. [PMID: 14653766]
12. Antonio J, Sanders MS, Van Gammeren D. The effects of bovine colostrum supplementation on body composition and exercise performance in active men and women. *Nutrition*. 2001 Mar;17(3):243-7. [PMID: 11312068]
13. Shing CM, Hunter DC, Stevenson LM. Bovine colostrum supplementation and exercise performance: potential mechanisms. *Sports Med*. 2009;39(12):1033-54. [PMID: 19902984]
14. Brassica®. What is SGS? <http://sgs-broccoli.com/what-is-sgs/>. Accessed April 21, 2014.
15. Boddupalli S, Mein JR, Lakkanna S, et al. Induction of phase 2 antioxidant enzymes by broccoli sulforaphane: perspectives in maintaining the antioxidant activity of vitamins A, C, and E. *Front Genet*. 2012;3:7. [PMID: 22303412]
16. Sulforaphane glucosinolate. Monograph. *Altern Med Rev*. 2010 Dec;15(4):352-60. Review. [PMID: 21194251]
17. Fahey JW, Talalay P. Antioxidant functions of sulforaphane: a potent inducer of Phase II detoxification enzymes. *Food Chem Toxicol*. 1999 Sep-Oct;37(9-10):973-79. [PMID: 10541453]
18. Larch arabinogalactan. *Altern Med Rev*. 2000 Oct;5(5):463-66. [PMID: 11056416]
19. Kelly GS. Larch arabinogalactan: clinical relevance of a novel immune-enhancing polysaccharide. *Altern Med Rev*. 1999 Apr;4(2):96-103. Review. [PMID: 10231609]

Additional references available upon request

EXCLUSIVE • PATENTED

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

i5™ Energize

Energizing, Detoxifying Biotransformation Shake Mix*

NOTICE: This formula now contains an ingredient derived from milk.



Available in Vanilla Latte

Discussion

i5 Energize™ is an innovative and healthy way to add protein, micronutrients, immunoglobulins, and fiber to your daily routine. This nutritious and delicious shake provides antioxidant, detoxification, and energy support. It can be part of a healthy and energizing breakfast, a great pre-workout shake, or a quick pick-me-up in the afternoon. i5 Energize is a nutrient-rich alternative to common energy drinks.*

VegaPro™ XYMOGEN's proprietary blend of pea protein concentrate, pea protein isolate, taurine, rice protein concentrate, L-glutamine, and glycine provides 18 g of plant-based protein per serving of i5 Energize. VegaPro is easily digested, is gluten-free, and achieves an amino acid score of 100%.^[1,2] This amino acid profile supports protein metabolism and lean body mass. Aminogen® enhances protein digestibility and absorption.*

Coffee Fruit Extract and Green Coffee Bean Extract Blend i5 Energize contains a propriety blend of KonaRed® coffee fruit extract, green coffee bean extract, and caffeine anhydrous. Hawaiian KonaRed coffee fruit extract is a natural source of chlorogenic acids and their derivatives quinic acid and ferulic acid.^[3] Chlorogenic acids from green coffee bean extract are readily metabolized by humans and have been researched specifically for their positive effects on cytokine balance and antioxidant support.^[4,5] Animal and human studies suggest that these chlorogenic acids can be used safely and help maintain vasoreactivity and blood pressure already within the normal range.*^[6-8]

ActivNutrients® without Copper & Iron The USDA Dietary Guidelines suggest that dietary supplements can help fulfill our micronutrient needs.^[9] The balanced array of vitamins, minerals, and cofactors in i5 Energize provides a micronutrient foundation that helps support healthy energy production and metabolism.^[10] ActivNutrients without Copper & Iron delivers highly bioavailable micronutrients, such as Albion® TRAACS® minerals (the real amino acid chelate system), natural-source vitamin E as mixed tocopherols, and activated B vitamins, including 5-methyltetrahydrofolate as Quatrefolic®.*^[11]

Clinical Applications

- » Supports Healthy Energy Production and Metabolism*
- » Supports Immune Function by Providing Immunoglobulins and Other Immune Factors*
- » Supports Intestinal Health*
- » Supports Healthy Intestinal Cytokine Balance*
- » Supports Healthy Body Composition*
- » Supports Detoxification and Antioxidant Systems*

*i5™ Energize is an all-natural, nutrient-dense shake mix designed to support healthy energy production, gastrointestinal integrity, cytokine balance, and the body's natural ability to detoxify. It is a wholesome alternative for individuals seeking to maintain robust energy levels, enhance their workout, or simply maintain overall health and wellness. This unique, fructose-free formula contains the same micronutrient profile (different dosages) found in XYMOGEN's ActivNutrients® without Copper & Iron, along with supplemental methylcobalamin (activated vitamin B12) and whole coffee fruit standardized to chlorogenic acid. i5 Energize features VegaPro™, a non-GMO, pea-based protein; IgG 2000 CWP™, a bovine-derived immunoglobulin concentrate; truebroc®, glucoraphanin from broccoli seed extract; and arabinogalactan, a prebiotic. i5 Energize provides 80 mg of caffeine per serving.**

IgG 2000 CWP™ is an immunoglobulin concentrate from colostrum whey peptides that delivers a minimum of 40% IgG immunoglobulin along with an array of compounds, including growth factors, sialic acid, lactoferrin, proline-rich peptides (PRPs), oligosaccharides, and gangliosides. Each of these components provides the user with different and complementary health benefits, such as fundamental support of immune function and modulation, lean body mass, brain and thymus health, microbiota modulation, and cytokine balance.*^[12]

Oral consumption of immunoglobulins derived from colostrum is a means of supporting passive immunity, protecting the body, and eliminating unwanted molecules.^[13-16] The most versatile, IgG, is capable of carrying out all of the functions of immunoglobulin molecules, accounting for IgG 2000 CWP's broad range of immune-supportive effects.^[17] Review of the research confirms that bovine colostrum supplementation confers other benefits, such as the maintenance of gastrointestinal integrity.^[18-20] Oral immunoglobulins have been used in sports nutrition to support lean body mass,^[21] physical exercise, and recovery following high-intensity training.^[18,22] The 2.5 grams of immunoglobulins in each serving of i5 Energize contribute to individual dosing requirements.*

Oncoplex™ (glucoraphanin) This patented plant-based ingredient, also known as sulforaphane glucosinolate, is extracted from one of its most concentrated cruciferous sources—broccoli seeds.^[23] An abundance of research demonstrates that when glucoraphanin is broken down to its active form, sulforaphane, it safely and effectively upregulates the body's natural phase II detoxification enzymes.^[24-26] This activity in turn supports antioxidant activity and helps protect cells, cell membranes, and tissues from free-radical damage.*

Arabinogalactan Sourced from the larch tree, arabinogalactan is considered an excellent source of fiber, a prebiotic, and a precursor to short-chain fatty acids, all elements that help support gastrointestinal health.*^[27,28]

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

Cytokine Balance Support

Gastrointestinal Support

Immune System Support

Sports Nutrition

i5™ Energize Vanilla Latte Supplement Facts

Serving Size: 2 scoops (about 47 g)
Servings Per Container: About 14

	Amount Per Serving	%Daily Value
Calories	170	
Total Fat	4.5 g	6%†
Saturated Fat	2 g	10%†
Total Carbohydrate	19 g	7%†
Dietary Fiber	5 g	18%
Total Sugars	4 g	**
Includes 4g Added Sugars		8%
Protein	18 g	
Vitamin A (75% as natural beta-carotene and 25% as retinyl palmitate)	560 mcg	62%
Vitamin C (as sodium ascorbate, potassium ascorbate, zinc ascorbate, and calcium ascorbate)	62.5 mg	69%
Vitamin D3 (cholecalciferol)	1.25 mcg (50 IU)	6%
Vitamin E (as d-alpha tocopheryl succinate)	33.5 mg	223%
Thiamin (as thiamine mononitrate)	5 mg	417%
Riboflavin (as riboflavin 5'-phosphate sodium)	5 mg	385%
Niacin (as niacinamide and niacin)	16 mg	100%
Vitamin B6 (as pyridoxal 5'-phosphate)	5 mg	294%
Folate (as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt)	100 mcg DFE	25%
Vitamin B12 (as MecobalActive™ methylcobalamin)	2500 mcg	104167%
Biotin	250 mcg	833%
Pantothenic Acid (as d-calcium pantothenate)	50 mg	1000%
Choline (as choline dihydrogen citrate)	9 mg	2%
Calcium (as DimaCal® dicalcium malate and ingredients with naturally occurring calcium)	45 mg	3%
Iron (naturally occurring)	4 mg	22%
Iodine (as potassium iodide)	25 mcg	17%
Magnesium (as Albion® dimagnesium malate)	25 mg	6%
Zinc (as TRAACS® zinc bisglycinate chelate)	3.25 mg	30%
Selenium (as Albion® selenium glycinate complex)	25 mcg	45%
Manganese (as TRAACS® manganese bisglycinate chelate)	0.125 mg	5%
Chromium (as TRAACS® chromium nicotinate glycinate chelate)	125 mcg	357%
Molybdenum (as TRAACS® molybdenum glycinate chelate)	12.5 mcg	28%
Sodium (naturally occurring)	350 mg	15%
Potassium (from tripotassium citrate, Albion® potassium glycinate complex and ingredients with naturally occurring potassium)	345 mg	7%
IgG 2000 CWP™ (bovine-derived immunoglobulin concentrate)	2.5 g	**
Immunoglobulin G (IgG)	1 g	**
Arabinogalactan (from <i>Larix laricina</i>) (bark)	1 g	**
Proprietary Energizing Blend	585 mg	**
Whole Coffee Fruit (<i>Coffea arabica</i>) (whole fruit) (40% chlorogenic acid) and caffeine anhydrous, typically yielding a total of 80 mg of caffeine		
truebroc® Glucoraphanin (from broccoli extract) (<i>Brassica oleracea italica</i>) (seed)	30 mg	***
Mixed Tocopherols	18 mg	***
Inositol	9 mg	**
PABA (<i>para</i> -aminobenzoic acid)	3.25 mg	**
Vanadium (as TRAACS® vanadium nicotinate glycinate chelate)	187.5 mcg	**

Other Ingredients: VegaPro™ (XYMOGEN's proprietary blend of pea protein concentrate, pea protein isolate, taurine, rice protein concentrate, L-glutamine, and glycine), natural flavors (no MSG), inulin (from chicory), dried cane syrup, sunflower oil, cellulose gum, xanthan gum, medium-chain triglyceride oil, Aminogen® fungal proteases, guar gum, stevia leaf extract, and silica.

Contains: Milk

DIRECTIONS: Blend, shake, or briskly stir two level scoops (47 g) into 8-10 oz chilled water and consume once daily, or take as directed by your healthcare practitioner. Adjust amount of water to desired sweetness and thickness.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Caffeine should not be combined with synephrine or ephedrine. Use cautiously in individuals who have a history of abnormal heart rhythm. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, fish, shellfish, peanuts, tree nuts, egg, artificial colors, or artificial sweeteners.

 AMINOGEN is a registered trademark of Triarco Industries. AMINOGEN is protected under US patent 5,387,422.

 Quatrefolic is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,662.

 Albion, DimaCal, TRAACS, and the Albion Medallion design are registered trademarks of Albion Laboratories, Inc. Malates covered by US patent 6,706,904 and patents pending.

 Produced under US patent 6,521,818 licensed from Brassica Protection Products LLC. truebroc is a registered trademark of Brassica Protection Products LLC.

 MecobalActive™
The active form of B₁₂
is a trademark of Ferrer Health Tech.

References

- Fredrikson M, Biot P, Alminger ML, et al. Production process for high-quality pea-protein isolate with low content of oligosaccharides and phytate. *J Agric Food Chem*. 2001 Mar;49(3):1208-12. [PMID: 11312837]
- Gausserès N, Mahé S, Benamouzig R, et al. [15N]-labeled pea flour protein nitrogen exhibits good ileal digestibility and postprandial retention in humans. *J Nutr*. 1997 Jun;127(6):1160-65. [PMID: 9187631]
- KonaRed. Science—the most powerful antioxidant potential fruits. <http://www.konared.com/science-most-powerful-antioxidant-fruits/>. Accessed April 22, 2014.
- American Institute for Cancer Research. Foods That Fight Cancer: Coffee. <http://www.aicr.org/foods-that-fight-cancer/coffee.html>. Accessed April 22, 2014.
- Farah A, Monteiro M, Donangelo CM, et al. Chlorogenic acids from green coffee extract are highly bioavailable in humans. *J Nutr*. 2008 Dec;138(12):2309-15. [PMID: 19022950]
- Watanabe T, Arai Y, Mitsui Y, et al. The blood pressure-lowering effect and safety of chlorogenic acid from green coffee bean extract in essential hypertension. *Clin Exp Hypertens*. 2006 Jul;28(5):439-49. [PMID: 16820341]
- Ochiai R, Jokura H, Suzuki A, et al. Green coffee bean extract improves human vasoreactivity. *Hypertens Res*. 2004 Oct;27(10):731-37. [PMID: 15785008]
- Natural Standard Database. Green Coffee. <http://www.naturalstandard.com/databases/herbssupplements/greencoffee.asp?#undefined>. Accessed June 3, 2013.
- U.S. Department of Agriculture and U.S. Department of Health and Human Services. Dietary Guidelines for Americans, 2010. 7th ed. Washington, DC: U.S. Government Printing Office; December 2010:33-42. <http://www.health.gov/dietaryguidelines/dga2010/DietaryGuidelines2010.pdf>. Accessed April 2, 2013.
- Ames BN. A role for supplements in optimizing health: the metabolic tune-up. *Arch Biochem Biophys*. 2004 Mar 1;423(1):227-34. [PMID: 14989256]
- Quatrefolic. <http://www.quatrefolic.com/4thGeneration.html>. Accessed April 22, 2014.
- Godhia M, Patel N. Colostrum—its composition, benefits as a nutraceutical: a review. *Curr Res Nutr Food Sci*. 2013;1(1):37-47. <http://dx.doi.org/10.12944/CRNFSJ.1.1.04>
- Hurley D. Establishment of the effects of colostrally derived protein food supplements on human and animal health [dissertation]. Brookings, SD: South Dakota State University; 1994.
- Hurley WL, Theil PK. Perspectives on immunoglobulins in colostrum and milk. *Nutrients*. 2011 Apr;3(4):442-74. Review. [PMID: 22254105]
- Rump JA, Arndt R, Arnold A, et al. Treatment of diarrhoea in human immunodeficiency virus-infected patients with immunoglobulins from bovine colostrum. *Clin Investig*. 1992 Jul;70(7):588-94. [PMID: 1392428]
- Schaller JP, Saif LJ, Cordle CT, et al. Prevention of human rotavirus-induced diarrhea in gnotobiotic piglets using bovine antibody. *J Infect Dis*. 1992 Apr;165(4):623-30. [PMID: 1313067]
- Lozce MT. *Measuring Immunity: Basic Science and Clinical Practice*. London, UK: Academic Press; 2004:160.
- Davison G. Bovine colostrum and immune function after exercise. *Med Sport Sci*. 2012;59:62-9. doi: 10.1159/000341966. [PMID: 23075556]
- Greenberg PD, Cello JP. Treatment of severe diarrhea caused by Cryptosporidium parvum with oral bovine immunoglobulin concentrate in patients with AIDS. *J Acquir Immune Defic Syndr Hum Retrovirol*. 1996 Dec 1;13(4):348-54. [PMID: 8948373]
- Kelly GS. Bovine colostrums: a review of clinical uses. *Altern Med Rev*. 2003 Nov;8(4):378-94. Review. [PMID: 14653766]
- Antonio J, Sanders MS, Van Gammeren D. The effects of bovine colostrum supplementation on body composition and exercise performance in active men and women. *Nutrition*. 2001 Mar;17(3):243-7. [PMID: 11312068]
- Boddupalli S, Mein JR, Lakkanna S, et al. Induction of phase 2 antioxidant enzymes by broccoli sulforaphane: perspectives in maintaining the antioxidant activity of vitamins A, C, and E. *Front Genet*. 2012;3:7. [PMID: 22303412]
- Sulforaphane glucosinolate. Monograph. *Altern Med Rev*. 2010 Dec;15(4):352-60. Review. [PMID: 21194251]
- Fahey JW, Talalay P. Antioxidant functions of sulforaphane: a potent inducer of Phase II detoxification enzymes. *Food Chem Toxicol*. 1999 Sep-Oct;37(9-10):973-79. [PMID: 10541453]
- Larch arabinogalactan. *Altern Med Rev*. 2000 Oct;5(5):463-66. [PMID: 11056416]
- Kelly GS. Larch arabinogalactan: clinical relevance of a novel immune-enhancing polysaccharide. *Altern Med Rev*. 1999 Apr;4(2):96-103. Review. [PMID: 10231609]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

IG 26 DF/IG 26 Plus DF

Hyperimmune Egg/Dairy-Free Immunoglobulins and Arabinogalactan*



IG 26 Plus DF Natural Vanilla is available in 30 servings
IG 26 DF is available in 120 servings and 120 capsules

Discussion

Decades ago, immunology researchers began investigating the possible health benefits to humans that could be achieved by the consumption of products from hyperimmunized lactating cows and laying hens.^[1] Agricultural scientists soon discovered that they could simultaneously immunize a single laying hen against multiple human germs. The resulting avian immunoglobulins, known as IgY, are transferred to the egg yolk, paralleling the way human immunoglobulins (IgG) are passed to the placenta. From this discovery, a new functional food was born: the “hyperimmune egg.” IG 26 DF is the result of special hyperimmune egg harvesting and processing techniques that result in a polyvalent, immunoglobulin-rich, dried hyperimmune egg food product that can be consumed as a dietary supplement. Second generation IG 26 Plus DF is vanilla-flavored and has arabinogalactan added.

IgY Immunoglobulins and Passive Immunity

Hyperimmune egg provides a concentrated source of environmentally specific IgY antibodies and immune-supporting cofactors that can confer passive immunity to the human being who consumes it.^[1-6] There are over 100 patents associated with the production of hyperimmune egg and its use in animals and humans, and it is a self-affirmed GRAS (generally recognized as safe) product—a designation that affirms safe consumption. Furthermore, hyperimmune egg and IgY have been studied extensively.*

Oral Health In a study of healthy volunteers, the use of an oral rinse containing an aqueous IgY solution increased the presence of active antibodies in saliva.^[7] Moreover, in vitro, animal, and human research support the benefits of custom IgY solutions, IgY-supplemented diets, and IgY-containing pastes that are designed for use in the dental plaque environment and to promote gingival health.^{*[8,9]}

Intestinal Health IgY stability through the orogastrintestinal tract and its safety profile are well-documented.^[9] In vitro, animal, and human studies provide evidence that supplemental IgY from hyperimmune egg imparts passive immunity in the intestinal tract.^[1,2,4,10-13] Providing the body with an increased supply of immunoglobulins also helps maintain a healthy balance of bacteria in the intestine. Supporting passive immunity and promoting microbiome balance lead to better overall health due to the link between gut health and systemic health. Furthermore, researchers postulate that by supporting passive immunity in the gut, immune overactivation might be reduced.^{*[1]}

Immunoregulatory Factors

Hyperimmune egg not only provides IgY immunoglobulins, but it also contains bioactive immunoregulatory factors. These immunoregulatory factors act directly on gastrointestinal surfaces where they may influence effector cells and also circulate

Clinical Applications

- » Provides Immunoglobulins and Immunoregulating Factors That Promote Intestinal and Systemic Health*
- » Supports Passive Immunity in the Intestine*
- » Promotes Balanced Cytokine Production*
- » Supports Muscle Performance and Recovery*

*IG 26 DF and IG 26 Plus DF are self-affirmed GRAS supplements that provide IgY immunoglobulins and immunoregulating molecules from hyperimmune chicken egg. Research suggests that this dairy-free source of immunoglobulins and immune cofactors helps support immune function in the intestine and a healthy intestinal environment. These benefits positively impact extraintestinal health. For added support of gut microflora, the prebiotic arabinogalactan is provided in IG 26 Plus DF. Preliminary research also suggests the immunoregulating molecules in these formulas help modulate cytokines and enhance sports recovery.**

systemically where they act as intercellular communicators. As intercellular communicators, they are responsible for the regulation of a variety of immune, hormonal, and metabolic pathways that have widespread systemic effects.^[1] Preliminary studies suggest that these immunoregulatory factors in IG 26 DF benefit cytokine modulation, joint health, blood lipid metabolism, exercise performance, and overall wellness.^{*[1,5]}

Arabinogalactan IG 26 Plus DF features FiberAid™, an arabinogalactan-based, soluble fiber prebiotic derived from US-grown larch trees. The fiber is self-affirmed GRAS by the US Food and Drug Administration and other authorities. It remains pure and structurally unaltered following a multi-patented process (US 5756098, EP 866808, and other patents) that does not require harsh chemicals to free the polysaccharide from the plant matrix.

FiberAid, in doses of 4.5 g and higher, has been demonstrated to increase gut anaerobes such as lactobacilli and bifidobacteria, increase short-chain fatty acids, reduce ammonia levels in the large intestine, and support immunomodulatory activity.^{*[14-17]}

Cytokine Modulation Hyperimmune egg contains heightened levels of cytokine inhibitory factor (CIF) and cytokine activating factor (CAF).^[18,19] These bioactive molecules help balance the production of cytokines such as TNF-alpha and are believed to help the immune system recognize when to turn on and when to turn off.^{*[18,19]}

Muscle Performance and Recovery In clinical studies comparing the benefits of hyperimmune egg to an egg-protein placebo group, oral supplementation of hyperimmune egg (4.5 g to 13.5 g) for 10 days resulted in a significantly lower submaximal heart rate and higher peak power.^[20] In a double-blind, balanced, matched-pairs study, oral supplementation of hyperimmune egg (4.5 g to 13.5 g) improved strength performance and enhanced muscle recovery. The supplemented group also experienced significantly less muscle soreness.^[21] Other studies suggested that hyperimmune egg significantly increased levels of growth factors and overall bioavailability of IGF-1.^{*[22-24]}

Quality of Life HIV/AIDS patients (n=31) with varying levels of sickness were administered hyperimmune egg (4.5 g) for four to eight weeks. Research showed that supplementation appeared to improve multiple parameters of physical and mental well-being.^{*[25]}

Cardiovascular and Joint Health Studies have indicated that the consumption of hyperimmune egg may also support cardiovascular and joint health.^{*[26,27]}

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

IG 26 DF Capsule Supplement Facts

Serving Size: 4 Capsules

	Amount Per Serving	%Daily Value
Calories	10	
Total Fat	1 g	1% [†]
Cholesterol	30 mg	10% [†]
IgY Max™ Hyperimmunized Egg Powder	2 g	**

[†]Percent Daily Values are based on a 2,000 calorie diet.

** Daily Value not established

Other Ingredients: HPMC (capsule), medium-chain triglyceride oil, silica, and dicalcium phosphate.**Contains:** Egg**DIRECTIONS:** Take four capsules per day, or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner, and individuals with egg allergies should not consume this product. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, yeast, corn, soy, dairy products, fish, shellfish, peanuts, tree nuts, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

IgY Max™

IgY Max is a trademark of IgY Nutrition, LLC and is used under license.

**IG 26 Plus DF Natural Vanilla Powder Supplement Facts**

Serving Size: 1 Scoop (about 6.1 g)

Servings Per Container: About 30

	Amount Per Serving	%Daily Value
Calories	30	
Total Fat	2 g	3% [†]
Saturated Fat	0.5 g	3% [†]
Cholesterol	75 mg	25% [†]
Total Carbohydrate	1 g	<1% [†]
Dietary Fiber	1 g	4%
Protein	2 g	
IgY Max™ Hyperimmunized Egg Powder	4.5 g	**
Arabinogalactan (from <i>Larix laricina</i>) (heartwood)	1 g	**

[†]Percent Daily Values are based on a 2,000 calorie diet.

** Daily Value not established.

Other Ingredients: Natural flavor (no MSG), monk fruit extract, and silica.**Contains:** Egg**DIRECTIONS:** Blend or shake one scoop (about 6.1 g) in cold liquid or sprinkle on cold food, such as salad, or use as directed by your healthcare practitioner. Do not heat, cook, or add to hot food or liquid.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner, and individuals with egg allergies should not consume this product. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, dairy products, fish, shellfish, peanuts, tree nuts, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

IgY Max™

IgY Max is a trademark of IgY Nutrition, LLC and is used under license.

References

- Dean KL. Hyperimmune eggs capture natural immune support. *Altern Complement Ther.* June 2000;6(3):118-24. http://www.ah-gene.com.tw/pic/digi/71014101140_hug1.pdf. Accessed December 29, 2014.
- Sarker SA, Casswall TH, Juneja LR, et al. Randomized, placebo-controlled, clinical trial of hyperimmunized chicken egg yolk immunoglobulin in children with rotavirus diarrhea. *J Pediatr Gastroenterol Nutr.* 2001 Jan;32(1):19-25. [PMID: 11176319]
- Mine Y, Kovacs-Nolan J. Chicken egg yolk antibodies as therapeutics in enteric infectious disease: a review. *J Med Food.* 2002 Fall;5(3):159-69. [PMID: 12495588]
- Xie YM, Gao S, Wang LY, et al. Therapeutic effect of probiotics and oral IgY as supplementary drugs in the treatment of pediatric rotavirus enteritis: a comparative study [in Chinese]. *Zhongguo Dang Dai Er Ke Za Zhi.* 2013 Nov;15(11):1000-05. [PMID: 24229598]
- Rahman S, Van Nguyen S, Icatto FC Jr, et al. Oral passive IgY-based immunotherapeutics: a novel solution for prevention and treatment of alimentary tract diseases. *Hum Vaccin Immunother.* 2013 May;9(5):1039-48. [PMID: 23319156]
- Rahman S, Higo-Moriguchi K, Htun KW, et al. Randomized placebo-controlled clinical trial of immunoglobulin Y as adjunct to standard supportive therapy for rotavirus-associated diarrhea among pediatric patients. *Vaccine.* 2012 Jun 29;30(31):4661-69. [PMID: 22575165]
- Carlender D, Kollberg H, Larsson A. Retention of specific yolk IgY in the human oral cavity. *BioDrugs.* 2002;16(6):433-37. [PMID: 12463766]
- Hatta H, Tsuda K, Ozeki M, et al. Passive immunization against dental plaque formation in humans: effect of a mouth rinse containing egg yolk antibodies (IgY) specific to *Streptococcus mutans*. *Caries Res.* 1997;31(4):268-74. [PMID: 9197932]

IG 26 DF Powder Supplement Facts

Serving Size: 1 Scoop (about 2 g)

	Amount Per Serving	%Daily Value
Calories	10	
Total Fat	1 g	1% [†]
Cholesterol	35 mg	12%
Protein	1 g	
IgY Max™ Hyperimmunized Egg Powder	2 g	**

[†]Percent Daily Values are based on a 2,000 calorie diet.

** Daily Value not established

Other Ingredient: Silica.**Contains:** Egg**DIRECTIONS:** Blend or shake one scoop in cold liquid, or sprinkle it on cold food such as salad, or use as directed by your healthcare practitioner. Do not heat, cook, or add to hot food or liquid.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner, and individuals with egg allergies should not consume this product. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, yeast, corn, soy, dairy products, fish, shellfish, peanuts, tree nuts, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

IgY Max™

IgY Max is a trademark of IgY Nutrition, LLC and is used under license.

- Otake S, Nishihara Y, Makimura M, et al. Protection of rats against dental caries by passive immunization with hen-egg-yolk antibody (IgY). *J Dent Res.* 1991 Mar;70(3):162-66. [PMID: 1825668]
- Fujibayashi T, Nakamura M, Tomimaga A, et al. Effects of IgY against *Candida albicans* and *Candida* spp. Adherence and biofilm formation. *Jpn J Infect Dis.* 2009 Sep;62(5):337-42. [PMID: 19762981]
- Ikemori Y, Ohta M, Umeda K, et al. Passive protection of neonatal calves against bovine coronavirus-induced diarrhea by administration of egg yolk or colostrum antibody powder. *Vet Microbiol.* 1997 Nov;58(2-4):105-11. [PMID: 9453122]
- Jüdling A, Wiedemann V, Kühlmann R, et al. Chicken egg antibodies for prophylaxis and therapy of infectious intestinal diseases. IV. In vitro studies on protective effects against adhesion of enterotoxigenic *Escherichia coli* to isolated enterocytes. *Zentralbl Veterinärmed B.* 1991 Jul;38(5):373-81. [PMID: 1681635]
- Buragohain M, Dhale G, Ghalsasi G, et al. Evaluation of hyperimmune hen egg yolk derived anti-human rotavirus antibodies (anti-hrvig) against rotavirus infection. *World Journal of Vaccines.* 2012;2:73-84. <http://dx.doi.org/10.4236/wjv.2012.22010>. Accessed December 23, 2014.
- Robinson RR, Feirtag J, Slavina JL. Effects of dietary arabinogalactan on gastrointestinal and blood parameters in healthy human subjects. *J Am Coll Nutr.* 2001 Aug;20(4):279-85. [PMID: 11506055]
- Englyst HN, Hay S, Macfarlane GT. Polysaccharide breakdown by mixed populations of human faecal bacteria. *FEMS Microbiol Lett.* 1987 June;45(3):163-171. doi: 10.1016/0378-1097(87)90013-9.
- Vince AJ, McNeil NI, Wager JD, et al. The effect of lactulose, pectin, arabinogalactan, and cellulose on the production of organic acids and metabolism of ammonia by intestinal bacteria in a faecal incubation system. *Br J Nutr.* 1990 Jan;63(1):17-26. [PMID: 2317475]
- Dion C, Chappuis E, Ripoll C. Does larch arabinogalactan enhance immune function? A review of mechanistic and clinical trials. *Nutr Metab (Lond).* 2016 Apr 12;13:28. [PMID: 27073407]
- Iyer S, Johnson WL, Nguyen L, Ross SC, Xing R, inventors; Arkion Life Sciences, LLC, assignee. Purified cytokine inhibitory factor. US patent 7,083,809 B2. Aug 1, 2006.
- Iyer S, Nguyen TN, Wu DR, Xing R, inventors; Arkion Life Sciences, LLC, assignee. Protein isolated from egg whites and yolks of hyperimmunized animals; amino acid sequence seq id no: 1 and 6; upregulation of tumor necrosis factor and interleukins-6 and -1beta; downregulation of transforming growth factor-beta. US patent 6,420,337 B1. July 16, 2002.
- Scheett TP, Martin T, Carr B, et al. Hyperimmune egg protein decreases submaximal heart rate and increases peak power. Poster presented at: American College of Sports Medicine Conference; May 30-June 2, 2007; New Orleans, LA. http://igyhyperimmuneegg.org/studies/Scheett_ACSM_SubmaximalHRPeakPower.pdf. Accessed January 4, 2015.
- Scheett TP, Martin T, Carr B, et al. Increased muscular strength and enhanced muscle repair with hyperimmune egg protein supplementation. Poster presented at: National Strength and Conditioning Association Conference; July 12-15, 2007; Atlanta, GA. http://www.igyhyperimmuneegg.org/studies/Scheett_MSCA_MuscularStrengthMuscleRepair.pdf. Accessed January 4, 2015.
- Rivera LE, Boland CG, Scheett TP. Effect of the hyperimmune egg supplement on regulation of insulin-like growth factor 1. Paper presented at: Southeast American College of Sports Medicine Conference; February 14-16, 2008; Birmingham, AL. http://www.seacsm.org/SEACSM_2008_program.pdf. Accessed January 2, 2015.
- Scheett TP, Boland CG, Rivera LE, et al. Hyperimmune egg protein supplementation stimulates the GH->IGF-1 axis. Poster presented at: National Strength and Conditioning Association Conference; July 10, 2008; Las Vegas, NV. http://www.igyhyperimmuneegg.org/studies/Scheett_Boland_Rivera_GHtoIGF-1_Axis.pdf. Accessed January 2, 2015.
- Boland CG, Rivera LE, Scheett TP. Effect of the hyperimmune egg supplement on anabolic mediators of muscle repair. Paper presented at: Southeast American College of Sports Medicine Conference; February 14-16, 2008; Birmingham, AL. http://www.seacsm.org/SEACSM_2008_program.pdf. Accessed January 2, 2015.
- Kizito FB. Improvements in quality of life for HIV/AIDS patients using hyperimmune egg (Immune 26™) – The TASSO Study. Paper presented at: 3rd International AIDS Society Conference on HIV Pathogenesis and Treatment; July 24-27, 2005; Rio de Janeiro. <http://www.iasociety.org/Abstracts/A2177717.aspx>. Accessed December 29, 2014.
- Karge WH, Deluca JP, Marchitelli LJ, et al. Pilot study on the effect of hyperimmune egg protein on elevated cholesterol levels and cardiovascular risk factors. *J Med Food.* 1999;2(2):51-63. [PMID: 19281349]
- Greenblatt H, Adalsteinsson O, Kagen L. Administration to arthritis patients of a dietary supplement containing immune egg: an open-label pilot study. *J Med Food.* 1998;1(3):171-79. [on file]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

(RV) DRS-294
Rev. 03/27/17

IgG 2000 CWP™

NOTICE: This formula now contains an ingredient derived from milk.

Immunoglobulin Concentrate from Colostral Whey Peptides



Available in 120 capsules, about 25, and 75 servings powder

Clinical Applications

- » Supports Immune Function by Providing Immunoglobulins and Other Immune Factors*
- » Supports the Body's Normal Gut Repair Pathways*
- » Helps Maintain a Healthy Microbial and Cytokine Balance in the Gut*
- » Promotes Overall Health and Well-Being*

*IgG 2000 CWP™ is an immunoglobulin concentrate derived from colostrum whey peptides. It delivers natural immunoglobulins (standardized to a minimum of 40% IgG), bioactive proteins, and growth factors. These components support immune function, healthy cytokine activity, gut barrier function, and gastrointestinal health and tissue repair. Advanced coagulation and filtration techniques make IgG 2000 CWP a unique, GRAS formula that is superior in its bioactive composition and its purity.**

Discussion

Beyond Colostrum: Immunoglobulin Concentrate from Colostral Whey Peptides

IgG 2000 CWP is the result of advanced coagulation and filtration technologies that separate bioactive substances and then concentrate them. These precise systems produce a potent, pure, and generally recognized as safe (GRAS) immunoglobulin concentrate from colostrum whey peptides. IgG 2000 CWP provides immunoglobulins, including a minimum of 40% IgG; bioactive and growth factors; oligosaccharides; and gangliosides. Each of these components provides the user with different and complementary health benefits (see Chart).^{*[1]}

Immunoglobulins

Oral consumption of immunoglobulins derived from colostrum is a means of supporting passive immunity.^[2-5] Immunoglobulins flag antigens for the immune system. In doing so, immunoglobulins become key participants in protecting the body and eliminating unwanted molecules. IgG 2000 CWP delivers immunoglobulins and is particularly high (minimum of 40%) in IgG. Among immunoglobulins, IgG is said to be the most versatile, carrying out all of the functions of immunoglobulin molecules.*

Bioactive and Growth Factors

Sialic acid is an essential component of mucins, glycoproteins, oligosaccharides, and gangliosides and is therefore important to the function of cell membranes and membrane receptors. It is also important for normal brain development. Sialic acid-containing oligosaccharides in bovine colostrum can prevent certain antigens from binding to host tissues. Lactoferrin is an immune-supporting, iron-binding glycoprotein naturally found in bovine colostrum. It plays an important role in immune regulation and in the body's defense mechanisms.^[6] Studies suggest that growth factors from bovine colostrum, including IGF-1 (insulin-like growth factor) and TGF (transforming growth factor), stimulate cell growth in the gut to strengthen the gut lining, help build lean muscle mass, and slow protein catabolism.^[1] Furthermore, improvements observed in exercise performance by athletes taking colostrum have been attributed to growth factors.*

Proline-Rich Peptides

Proline-rich peptides (PRPs), which were first isolated from ovine colostrum and later from bovine colostrum, are intercellular signaling molecules. They act as regulatory

substances that have the unique ability to modulate and stabilize various biologic processes in the body, such as cytokine and immune processes.^[1] The in vitro and in vivo effects of PRPs on immunoregulation, including their effects on the maturation and differentiation of thymocytes and humoral and cellular immune responses, have been demonstrated. Also of great interest are the many studies suggesting their beneficial effects on age-associated changes in neurological health.^[7] For instance, in vivo work revealed that PRPs alleviate beta-amyloid cytotoxicity in hippocampal neuronal cells; in humans, PRPs provided an early beneficial effect on cognitive symptoms and daily functioning at a dose as low as 100 mcg/d every other day.^[8,9] Five grams of powder or eight capsules of IgG 2000 CWP provides 1% to 2% (50 to 100 mg) PRPs.*

Oligosaccharides

Bovine milk oligosaccharides, which are a component of lactose, are modulators of gut microbiota. They provide protection by acting as decoys to attract antigens and inhibit them from binding to epithelial surfaces of the intestine.^[10] Evidence also suggests that oligosaccharides act as growth promoters for a selected class of beneficial bacteria^[11] and contribute to the development and maturation of the intestinal immune response.^[12] Approximately 66 acidic and neutral oligosaccharides, including sialyloligosaccharides, which are known for their high biological activity in humans, have been detected in IgG concentrate from colostrum whey peptides.^{*[13]}

Gangliosides

Gangliosides are vital to the structure and function of cell membranes. They support neural development, and they have roles in supporting gut integrity, influencing immune cell signaling, modulating cytokine activity and production, and affecting the adherence and toxin production of antigens.^[14-17] Research has demonstrated that providing gangliosides in the diet increases ganglioside content in the intestinal mucosa. Studies have indicated that low levels of gangliosides in the intestinal mucosa are associated with increased levels of cytokines, susceptibility to antigens, and poor gut integrity.^[14] The ganglioside composition of bovine milk is predominately GM3 and GD3.^{*[15]}

IgG 2000 CWP Studies

Building on the extensive literature pointing to the health benefits associated with bovine-derived colostrum and colostrum whey, scientists performed in vitro, in vivo,

Continued on next page

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

Chart: Bioactive Compounds in IgG 2000 CWP

Active	Key Function(s)
Immunoglobulins	Immune support*
Growth Factors	Lean mass support, cell and tissue repair and rejuvenation*
Sialic Acid	Immune modulation, brain health, prebiotic*
Lactoferrin	Immune support*
Proline-Rich Peptides (PRPs)	Immune modulation, brain and thymus support*
Oligosaccharides	Microbiota modulation*
Gangliosides	Immune cell signaling*

IgG 2000 CWP™ Capsules Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%DV [†]
Calories		5
Protein	1 g	
IgG 2000 CWP™ (bovine-derived immunoglobulin concentrate)	1 g	**
Immunoglobulin G (IgG)	400 mg	**

[†]Percent Daily Values are based on a 2,000 calorie diet.
^{**} Daily Value (DV) not established.

Other Ingredients: Capsule (hypromellose and water), silica, and sunflower lecithin.
Contains: Milk

DIRECTIONS: Take two capsules twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

IgG 2000 CWP™ Powder Supplement Facts

Serving Size: 1 Tablespoon (about 5 g)

	Amount Per Serving	%DV
Calories	20	
Protein	4 g	
Calcium (from IgG 2000 CWP™)	40 mg	4%
IgG 2000 CWP™ (bovine-derived immunoglobulin concentrate)	5 g	**
Immunoglobulin G (IgG)	2 g	**

Percent Daily Values (DV) are based on a 2,000 calorie diet.
^{**} Daily Value (DV) not established.

Other Ingredients: Sunflower lecithin.
Contains: Milk

DIRECTIONS: Mix one tablespoon (about 5 g) into 2-4 oz of water and consume daily, or take as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

and human clinical studies using IgG 2000 CWP to demonstrate its bioactivity and effectiveness. In vitro, IgG 2000 CWP was shown to support the body's normal repair pathways by stimulating the migration and production of gut epithelial cells.^[18] In an in vivo model of gut integrity challenge, rats administered IgG 2000 CWP showed significant improvements in both microscopic and macroscopic mucosal health.^[18] Supplemented dogs showed a significantly higher vaccine response and higher levels of fecal IgA when compared with the control group. These results were indicative of an enhanced immune status. Researchers also observed increases in gut microbiota diversity and stability in the supplemented dogs.^[19] In humans (n = 12), 1000 mg/d of IgG 2000 CWP increased salivary IgA by 30%, improved quality of life scores, significantly increased the ability to perform activities of daily living, improved hyperimmune responses, and reduced minor health complaints by 47%.^[20]

In a randomized, crossover trial (n = 7), a five-day challenge to gut integrity caused a three-fold rise from baseline in gut permeability as measured by lactulose/rhamnose ratios. Co-administration of a 15% IgG colostrum formula inhibited this increase.^[21] When the same researchers compared the RPF[†] (repair and protection factor) of the 15% IgG colostrum formula to IgG 2000 CWP, which is a 40% IgG formula, the IgG 2000 CWP score was two times higher. This suggests that IgG 2000 CWP would offer even greater results in supporting gut integrity than did the 15% IgG colostrum formula.*

[†]RPF is a novel (patent pending) analytical method that evaluates a product's bioactive properties to determine its effectiveness in repairing damaged cells and protecting healthy cells.

References

- Godhia M, et al. *Curr Res Nutr Food Sci*. 2013;1(1):37-47. <http://dx.doi.org/10.12944/CRNFSJ.1.1.04>
- Hurley D. [Dissertation]. Brookings, SD: South Dakota State University; 1994.
- Hurley WL, et al. *Nutrients*. 2011 Apr;3(4):442-74. [PMID: 22254105]
- Rump JA, et al. *Clin Investig*. 1992 Jul;70(7):588-94. [PMID: 1392428]
- Schaller JP, et al. *J Infect Dis*. 1992 Apr;165(4):623-30. [PMID: 1313067]
- Berlutti F, et al. *Molecules*. 2011 Aug 16;16(8):6992-7018. [PMID: 21847071]
- Janusz M, et al. *Cell Mol Biol (Noisy-le-grand)*. 2013 Nov 3;59(1):4-11. [PMID: 24200016]
- Froud KE, et al. *J Alzheimers Dis*. 2010;20(2):423-26. [PMID: 20164569]
- Bilikiewicz A, et al. *J Alzheimers Dis*. 2004 Feb;6(1):17-26. [PMID: 15004324]
- Lane JA, et al. *Int J Food Microbiol*. 2012 Jul 2;157(2):182-8. [PMID: 22647676]
- Aldredge DL, et al. *Glycobiology*. 2013 Jun;23(6):664-76. [PMID: 23436288]
- Lane JA, et al. *Br J Nutr*. 2013 Dec;110(12):2127-37. [PMID: 23710626]
- Barile D. Milk oligosaccharides. Confidential Report. Brookings, SD: Sterling Technology; 2011. [on file]
- Miklavcic JJ, et al. *J Nutr Metab*. 2012;2012:280286. [PMID: 22506104]
- Lee H, et al. *J Agric Food Chem*. 2013 Oct 9;61(40):9689-96. [PMID: 24024650]
- Sánchez-Juanes F, et al. *Biol Chem*. 2009 Jan;390(1):31-40. [PMID: 18937626]
- Park EJ, et al. *J Pediatr Gastroenterol Nutr*. 2010 Mar;50(3):321-28. [PMID: 20118807]
- Playford R. [Unpublished colostrum studies]. London, UK: Hammersmith Hospital; 2007.
- Satyaraj E, et al. *Br J Nutr*. 2013 Dec;110(12):2216-21. [PMID: 23773360]
- Jensen G, et al. Interim Report 9B. Brookings, SD: Sterling Technology. September 2010. [on file]
- Playford RJ, et al. *Clin Sci (Lond)*. 2001 Jun;100(6):627-33. [PMID: 11352778]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

IgG Pure™

Pure, New Zealand-Sourced Whey Protein



Available in 15 servings powder

Discussion

Whey protein is one of the two major proteins in cow's milk. The New Zealand herds used for producing IgG Pure™ are not given hormones and are not intentionally infected with a pathogen to force them to make antibodies specific to that pathogen. IgG Pure is a whey protein, rich in immunoglobulins (antibodies) derived from very careful processing techniques under controlled temperature and pH. During a series of ultrafiltration steps, lactose and water are removed from a slurry of whey. Special care is taken to maintain the integrity of the antibodies and to optimize the protein complex. In comparison to fluid cow's milk and ordinary whey protein concentrate, IgG Pure contains significantly greater concentrations of proteins and immunoglobulins.*

IgG Pure can be used not only as a high biological value protein source for healthy individuals but also to provide immunoglobulins to those in need. The immunoglobulins it contains are almost identical to those of the mammalian species and resist peptic digestion. The immune-balancing effect of immunoglobulins supports the body's normal defense mechanisms.*^[1,2]

Each antibody in IgG Pure (IgG1, IgG2, IgM, and IgA) has a specific role in immune function. IgM responds quickly to an antigen and specifically to bacteria and viruses. Later in the response, IgG1 and IgG2 attack viruses and toxins. IgA is critical in the body's immune system. The immunoglobulins also contribute to the humoral immunity of the gut-associated lymphoid tissue (GALT).*

Among IgG Pure's ingredients is a high concentration of the branched-chain amino acids leucine, isoleucine, and valine, which can be used by skeletal muscle during stress and to support nitrogen utilization. The semi-essential amino acid arginine increases the activity of natural killer and lymphokine-activated cells as well as IGF-1.*^[1]

Cysteine and glutamate are found in higher concentrations in IgG Pure than in other high-biological-value proteins. These amino acids serve as precursors to glutathione,^[3] an endogenous antioxidant especially needed during stress, exercise, and poor nutrition. Lactoferrin, alpha-

Clinical Applications

- » Source of High-Quality Protein for Individuals Requiring Protein Supplementation*
- » Promotes/Supports Healthy Body Composition*
- » Supports Immune Response*
- » Supports Healthy Intestinal Function*
- » Improves Glutathione (GSH) Levels*

*IgG Pure™, a natural, nutritionally advanced, bioactive whey protein concentrate, contains immunoglobulins that support the delicate balance of the body's immune system. The whey is sourced from New Zealand cows where herds are free from environmental contaminants and are not subjected to hormones and antibiotics that are commonly used elsewhere. This protein is a rich source of amino acids, including those needed for the synthesis of glutathione, an important antioxidant that can be depleted by stress. This formula is resistant to stomach acid and supports intestinal health. The 80% protein content supports lean body mass**

lactalbumin, beta-lactoglobulin, and bovine serum albumin are other proteins in IgG Pure™ that contribute to glutathione synthesis and support immune function.*^[3,4]

In addition, supplementation with whey protein may support glucose metabolism and muscle protein synthesis in humans.^[5] In a group of women, whey protein improved body composition, but soy protein did not.*^[6]

IgG Pure™ Supplement Facts

Serving Size: 2 scoops (about 20 g)

	Amount Per Serving	%Daily Value
Calories	80	
Total Fat	1.5 g	2% [†]
Saturated Fat	1 g	5% [†]
Cholesterol	40 mg	13%
Total Carbohydrate	1 g	<1% [†]
Total Sugars	1 g	**
Protein	16 g	
Calcium	70 mg	5%
Sodium	55 mg	2%
Potassium	135 mg	4%
Immunoglobulins (40% IgG)	1.6 g	**

[†] Percent Daily Values are based on a 2,000 calorie diet.

** Daily Value not established.

Other Ingredients: Whey protein concentrate and sunflower lecithin.

Contains: Milk.

DIRECTIONS: Mix 2 scoops with a cold beverage or add to your favorite recipe once daily or as recommended by your healthcare practitioner. To maintain the protein activity level, do not mix in hot drinks or recipes that require baking or boiling. Also, do not mix with pineapple or papaya because their enzymes may deactivate the protein.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

Typical Amino Acid Profile Per Serving:

Alanine	1060 mg	Lysine	1820 mg
Arginine	540 mg	Methionine	500 mg
Aspartic Acid	2220 mg	Phenylalanine	680 mg
Cysteine	560 mg	Proline	1280 mg
Glutamic Acid	3620 mg	Serine	1060 mg
Glycine	400 mg	Threonine	1460 mg
Histidine	380 mg	Tryptophan	480 mg
Isoleucine	1380 mg	Tyrosine	700 mg
Leucine	2240 mg	Valine	1260 mg

References

1. Bell SJ. Whey protein concentrate enriched with immunoglobulins. Unpublished review article. [Accessible upon request]
2. Bell SJ, Forse RA. *Positive Nutrition for HIV-Infected & AIDS: A Medically Sound Take-Charge Plan to Maintain Weight and Improve Your Quality of Life*. Minneapolis, MN: Chronimed; 1996.
3. Bounous G, Gold P. The biological activity of undenatured dietary whey proteins: role of glutathione. *Clin Invest Med*. 1991 Aug;14(4):296-309. [PMID: 1782728]
4. Zimecki M, Wlaszczyk A, Cheneau P, et al. Immunoregulatory effects of a nutritional preparation containing bovine lactoferrin taken orally by healthy individuals. *Arch Immunol Ther Exp (Warsz)*. 1998;46(4):231-40. [PMID: 9779289]
5. Graf S, Egert S, Heer M. Effects of whey protein supplements on metabolism: evidence from human intervention studies. *Curr Opin Clin Nutr Metab Care*. 2011 Nov;14(6):569-80. [PMID: 21912246]
6. Baer DJ, Stote KS, Paul DR, et al. Whey protein but not soy protein supplementation alters body weight and composition in free-living overweight and obese adults. *J Nutr*. 2011 Aug;141(8):1489-94. [Epub 2011 Jun 15] [PMID: 21677076]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Immune Essentials™

Short-Term Immune Support*



Available in 45 capsules

Discussion

Every day, whether by choice or by chance, millions of people encounter physical, emotional, and physiological stress that can challenge the immune system. Immune Essentials™ is formulated to provide support for immune system function and antioxidant activity.^[1-5] Although sometimes recommended for daily use, this formula is also effective when employed at the first sign of immune challenge.*

Whole Glucan Particle (WGP), purified from *Saccharomyces cerevisiae*, is the same high-quality 1,3/1,6 beta-glucan found in Immunotix 250™. This form is considered to be the most effective^[2,6-8] because it provides immune support without the impurities that can interfere with uptake and effectiveness.^[3,6,9] Mannan, a potential trigger for cytokine-modulating reactions, has been removed.*

Research indicates that orally administered yeast beta-glucan is processed by macrophages,^[4,6,10,11] with subsequent increases in phagocytosis, selective cytokine release, and oxidative degranulation.^[12] Macrophages degrade beta-glucan into small fragments that are then bound to neutrophils (granulocytes). This action primes the neutrophils and enhances their ability to eradicate microbial challenges.^[6,9,13] Prophylactic administration of beta-glucan promotes production of antioxidant enzymes and assists in ameliorating microbial imbalance.^[5] Sustained release of beta-glucan fragments into bone marrow may affect white blood cell recovery, a unique mechanism of action exhibited by the beta-glucan found in Immune Essentials.*^[14]

A randomized, double-blind, placebo-controlled trial was conducted during the peak of seasonal immune challenge. Subjects receiving 250 mg of WGP had a significant reduction in the number of days in which signs of immune distress were experienced.^[15] A 12-week, randomized, phase II, double-blind, placebo-controlled trial of 1,3/1,6 beta-glucan from *S cerevisiae* confirmed that long-term use was well tolerated and supported immune system function.*^[3]

Clinical Applications

- » Antioxidant Support*
- » Supports Healthy Immune Function*
- » Supports the Body's Defenses Against Seasonal Immune Challenges*

*Each Immune Essentials™ capsule features the same concentrated, naturally derived beta 1,3/1,6 glucan used in XYMOGEN's Immunotix™ formulas, plus standardized olive leaf extract and vitamin C as ascorbic acid. These ingredients support the body's natural immune mechanisms to help maintain good health. This formula is designed to be taken short term.**

Olive Leaf Extract, from the traditional medicinal plant *Olea europaea*, has been shown to possess an array of healthful attributes, including antioxidant properties and effective immune support against opportunistic microbes. Olive leaf's multifaceted effects on the immune system include the ability to stimulate phagocytosis (an immune response against harmful microbes) and neutralize production of reverse transcriptase and protease enzymes that can adversely alter the ribonucleic acid (RNA) of healthy cells.*^[16-18]

Oleuropein, a bitter glycoside that was isolated from olive leaf in the late 19th century,^[19] was found to be further hydrolyzed in the body to elenolic acid, which is believed to be its most active component. Research reveals that both olive leaf extract and oleuropein exert positive immune effects, but olive leaf acts in a dose-dependent manner; that is, the greater the dose of olive leaf, the greater the inhibition of microbial replication.^[17] Immune Essentials provides concentrated olive leaf extract that is standardized to 20% oleuropein, while less concentrated formulas are standardized to as little as 6% oleuropein.*

Vitamin C (as ascorbic acid) is a well-known antioxidant and plays an important role in immune support.^[20] While most mammals are able to synthesize ascorbic acid, humans are unable to. They can quickly become depleted if intake is inadequate or requirements are increased due to exposure to stress, smoking, pollution, and temperature changes.*

Vitamin C supplementation has been studied for more than six decades with respect to moderating the severity or duration of acute immune challenges. Benefits are most notable in cases of extreme physical stress.^[20] A Cochrane Review examined 65 years of placebo-controlled studies (55 studies) in which at least 200 mg of vitamin C was administered. Within three meta-analyses, in a subgroup of six studies, vitamin C reduced signs of acute immune challenge on an average of 50% in marathon runners, skiers, and soldiers that had been physically stressed or exposed to cold temperatures.*^[21]

Immune Essentials™ Supplement Facts

Serving Size: 3 Capsules

	Amount Per Serving	%Daily Value
Vitamin C (ascorbic acid)	1000 mg	1111%
Olive Extract (<i>Olea europaea</i>)(leaf)(20% oleuropein)	1 g	**
Whole Glucan Particle (Beta-Glucan naturally derived from <i>Saccharomyces cerevisiae</i>)	250 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), stearic acid, microcrystalline cellulose, magnesium stearate, and silica.

MAY BE COVERED BY ONE OR MORE OF THE FOLLOWING PATENTS AND APPLICATIONS: US 7,981,447; US 7,022,685; US 7,566,704; US 6,369,216; US 5,702,719 and patents pending.

DIRECTIONS: For early and immediate support, take three capsules with water on an empty stomach, or use as directed by your healthcare practitioner.*

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast protein, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



References

- Kournikakis B, Mandeville R, Brousseau P, et al. Anthrax-protective effects of yeast beta 1,3 glucans. *Med Gen Med.* 2003 Mar 21;5(1):1. [PMID:12827062]
- Vetvicka V, Terayama K, Mandeville R, et al. Pilot study: orally-administered yeast B1,3-glucan prophylactically protects against anthrax infection and cancer in mice. *JANA.* 2002;5(2):5-9. Reprint. <http://www.ana-jana.org/Journal/journals/JANAVol52.pdf>. Accessed June 6, 2012.
- Feldman S, Schwartz HI, Kalman DS, et al. Randomized phase II clinical trials of Wellmune WGP® for immune support during cold and flu season. *J Appl Res.* 2009 March-June;9(1&2):30-42. <http://jrnlappliedresearch.com/articles/Vol9Iss1/FeldmanVol9No1.pdf>. Accessed June 6, 2012.
- Yan J, Allendorf DJ, Brandley B. Yeast whole glucan particle (WGP) beta-glucan in conjunction with antitumor monoclonal antibodies to treat cancer. *Expert Opin Biol Ther.* 2005 May;5 (5):691-702. [PMID: 15934844]
- Senoglu N, Yuzbasioglu MF, Aral M, et al. Protective effects of N-acetylcysteine and beta-glucan pretreatment on oxidative stress in cecal ligation and puncture model of sepsis. *J Invest Surg.* 2008 Sep-Oct;21(5):237-43. [PMID: 19160131]
- Driscoll M, Hansen R, Ding C, et al. Therapeutic potential of various beta-glucan sources in conjunction with anti-tumor monoclonal antibody in cancer therapy. *Cancer Biol Ther.* 2009 Feb;8(3):218-25. [PMID: 19106638]
- Vetvicka V. Glucan-immunostimulant, adjuvant, potential drug. *World J Clin Oncol.* 2011 Feb 10;2(2):115-9. [PMID: 21603320]
- Natural Standard Database. <http://naturalstandard.com/databases/herbssupplements/betaglucan.asp>. Accessed June 7, 2012.
- Liang J, Melican D, Caffro L, et al. Enhanced clearance of a multiple antibiotic-resistant *Staphylococcus aureus* in rats treated with PGG-glucan is associated with increased leukocyte counts and increased neutrophil oxidative burst activity. *Int J Immunopharmacol.* 1998 Nov;20(11):595-614. [PMID: 9848393]
- Tian J, Ma J, Wang S, et al. Increased expression of mGITRL on D2SC/1 cells by particulate β-glucan impairs the suppressive effect of CD4(+)/CD25(+) regulatory T cells and enhances the effector T cell proliferation. *Cell Immunol.* 2011 May 10;270(2):183-7. [PMID: 21636079]
- Qi C, Cai Y, Gunn L, et al. Differential pathways regulating innate and adaptive antitumor immune responses by particulate and soluble yeast-derived β-glucans. *Blood.* 2011 Jun 23;117(25):6825-36. [PMID: 21531981]
- Pelizon AC, Kaneno R, Soares AM, et al. Immunomodulatory activities associated with beta-glucan derived from *Saccharomyces cerevisiae*. *Physiol Res.* 2005;54(5):557-64. [PMID: 16238470]
- Tsikitis V, Albina J, Reichner J. Beta-glucan affects leukocyte navigation in a complex chemotactic ingredient. *Surgery.* 2004 Aug;136(2):384-9. [PMID: 15300205]
- Turnbull, JL, Patchen ML, Scadden DT. The polysaccharide, PGGglucan, enhances human myelopoiesis by direct action independent of and additive to early-acting cytokines. *Acta Haematol.* 1999;102(2):66-71. [PMID: 10529508]
- Fuller R, Yam T, Butt H, et al. A randomised controlled trial to assess the ability of yeast-derived 1,3/1,6 glucopolysaccharide to reduce upper respiratory tract infection symptoms. In: Programme and Abstracts of the 1st UK International Functional Food Conference; Nov 25-26; 2010; Oxford, UK. http://www.shs.brookes.ac.uk/images/pdfs/research/functional-food/conference/conference-programme_v3_nov-2010.pdf. Accessed June 7, 2012.
- Lee OH, Lee BY. Antioxidant and antimicrobial activities of individual and combined phenolics in *Olea europaea* leaf extract. *Bioresour Technol.* 2010 May; 101(10); 3751-4. [PMID: 20106659]
- Micol V, Caturla N, Pérez-Fons L, et al. The olive leaf extract exhibits antiviral activity against viral haemorrhagic septicaemia rhabdovirus (VHSV). *Antiviral Res.* 2005 Jun;66(2-3): 129-36. [PMID: 15869811]
- Markin D, Duek L, Berdicevsky I. In vitro antimicrobial activity of olive leaves. *Mycoses.* 2003 Apr;46(3-4):132-136. [PMID: 12870202]
- Ritchason J. *Olive Leaf Extract*. Salt Lake City, UT: Woodland Publishing Incorporated; 2007.
- Schlueter AK, Johnston CS. Vitamin C: Overview and Update. *J Evid-Based Comp & Alt Med (JEBCAM).* 2011 Jan;16(1):49-57. <http://chp.sagepub.com/content/16/1/49.full.pdf+html>. Accessed June 4, 2012.
- Douglas RM, Hemilä H, Chalker E, et al. Vitamin C for preventing and treating the common cold. *Cochrane Database Syst Rev.* 2007 Jul 18;(3):CD000980. [PMID: 17636648]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.



ImmunotiX 500 is available in 20 & 60 capsules
ImmunotiX 250 is available in 30 capsules

Discussion

Beta-glucan has been recognized for its support of immune system activity for centuries^[1]; and yeast-derived beta-glucan has become the subject of over 800 scientific studies to date. ImmunotiX™ contains concentrated 1,3/1,6 beta-glucan from the yeast *Saccharomyces cerevisiae*, a source known to support immune function.^[2-4] Beta-glucan is produced by fungi, grains, seaweed, and yeast, but not by mammalian cells.^[3-5] While each source of beta-glucan has its own unique structure of glucose linkages, purified yeast-derived beta-glucan from *S cerevisiae* is considered the most effective source.^[6,7] Purity of the product is vital, since protein contaminants can cause untoward immune reactions. XyMOGEN's ImmunotiX is refined to remove most impurities, including proteins and fats that can interfere with uptake and effectiveness. Mannan, a potential trigger of allergic reactions or bowel exacerbation, has been removed. ImmunotiX 250™ provides 250 mg beta-glucan per capsule, while ImmunotiX 500™ provides 500 mg beta-glucan per capsule.*

Ongoing research has unveiled a detailed mechanism of action, including activation of macrophages, neutrophils, and T-cell-mediated immunity.^[3,8,9] Orally administered yeast beta-glucan is processed by macrophages—the first line of defense in cellular immunity^[8]—with subsequent increases in phagocytosis, selective cytokine release, and oxidative degranulation.^[10] Macrophages degrade beta-glucan into small fragments that are then bound to neutrophils (granulocytes), the most abundant immune cells in the body. Neutrophils then become primed and are better able to provide support against microbial challenges.^[4] Through a process called chemotaxis, these primed neutrophils migrate to target sites with enhanced immune actions.^[3, 11] Prophylactic administration of beta-glucan was found to positively affect levels of the antioxidant enzymes catalase and superoxide dismutase, moderate tissue-damaging cytokines, and assist in ameliorating microbial imbalance.*^[12]

Research demonstrates a sustained release of soluble fragments over a multi-day period, providing a unique mechanism of action for the

Clinical Applications

- » Supports Healthy Immune Function*
- » Supports the Body's Defenses Against Seasonal Immune Challenges*
- » Supports Hematopoiesis Following Radiation and Other Bone Marrow Insults*

*ImmunotiX™'s active ingredient is beta 1,3/1,6 glucan, a unique complex carbohydrate purified from *Saccharomyces cerevisiae* (baker's yeast). It is natural, not genetically modified (non-GMO), hypoallergenic, patented, and generally recognized as safe (GRAS). Taken orally, ImmunotiX, without over-stimulating, primes and mobilizes cells in the body's first line of defense to enhance protection against harmful effects of lifestyle and physical stressors.**

beta-glucan form found in ImmunotiX. Studies also indicate that the entrance of these soluble fragments into the bone marrow may affect white-blood-cell recovery, further enhancing its health effects.^[13] Individuals at increased risk for immune challenges, those in need of immune support, or those undergoing surgery have been found to benefit from ImmunotiX.^[2,6,8,12,14] A 12-week, randomized, phase II, double-blind, placebo controlled, parallel-group trial of 1,3/1,6 beta-glucan from *S cerevisiae* was conducted. Long-term use of beta-glucan was well tolerated and resulted in a reduction in acute immune challenge discomforts.*^[2]

Immunotix 500™ Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Whole Glucan Particle (providing beta-glucan naturally derived from <i>Saccharomyces cerevisiae</i>)	500 mg	**
** Daily Value (DV) not established.		

Other Ingredients: Dicalcium phosphate anhydrous, HPMC (capsule), stearic acid, magnesium stearate, silica, and medium-chain triglyceride oil.

MAY BE COVERED BY ONE OR MORE OF THE FOLLOWING PATENTS AND APPLICATIONS: US 7,981,447; US 7,022,685; US 7,566,704; US 6,369,216; US 5,702,719 and patents pending.

DIRECTIONS: For ongoing immune support: Take one capsule daily, first thing in the morning or last thing at night (before or well after a meal), with a full 8 oz glass of water. For fast-acting immune support: Take up to two capsules per day, as above; or use as directed by your healthcare practitioner.*

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast protein, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

**Immunotix 250™ Supplement Facts**

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Whole Glucan Particle (providing beta-glucan naturally derived from <i>Saccharomyces cerevisiae</i>)	250 mg	**
** Daily Value (DV) not established.		

Other Ingredients: Dicalcium phosphate anhydrous, HPMC (capsule), stearic acid, magnesium stearate, silica, and medium-chain triglyceride oil.

MAY BE COVERED BY ONE OR MORE OF THE FOLLOWING PATENTS AND APPLICATIONS: US 7,981,447; US 7,022,685; US 7,566,704; US 6,369,216; US 5,702,719 and patents pending.

DIRECTIONS: For ongoing immune support: Take one capsule daily, first thing in the morning or last thing at night (before or well after a meal), with a full 8 oz glass of water. For fast-acting immune support: Take up to two capsules per day, as above; or use as directed by your healthcare practitioner.*

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast protein, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

**References**

- Tian J, Ma J, Wang S, et al. Increased expression of mGITRL on D2SC/1 cells by particulate β -glucan impairs the suppressive effect of CD4(+)CD25(+) regulatory T cells and enhances the effector T cell proliferation. *Cell Immunol.* 2011 May 10;270(2):183-7. [PMID: 21636079]
- Feldman S, Schwartz HI, Kalman DS, et al. Randomized phase II clinical trials of Wellmune WGP® for immune support during cold and flu season. *J Appl Res.* 2009 March-June;9(1&2):30-42. <http://jrnlappliedresearch.com/articles/Vol9Iss1/FeldmanVol9No1.pdf>. Accessed September 9, 2011.
- Driscoll M, Hansen R, Ding C, et al. Therapeutic potential of various beta-glucan sources in conjunction with anti-tumor monoclonal antibody in cancer therapy. *Cancer Biol Ther.* 2009 Feb;8(3):218-25. [PMID: 19106638]
- Liang J, D. et al. Enhanced clearance of a multiple antibiotic-resistant *Staphylococcus aureus* in rats treated with PGG-glucan is associated with increased leukocyte counts and increased neutrophil oxidative burst activity. *Int J Immunopharmacol.* 1998 Nov;20(11):595-614. [PMID: 9848393]
- Vetvicka V. Glucan-immunostimulant, adjuvant, potential drug. *World J Clin Oncol.* 2011 Feb 10;2(2):115-9. [PMID: 21603320]
- Vetvicka V, Terayama K, Mandeville R, et al. Pilot study: orally-administered yeast β 1,3-glucan prophylactically protects against anthrax infection and cancer in mice. *JANA.* 2002;5(2):5-9. Reprint. <http://www.ana-jana.org/Journal/journals/JANAVol52.pdf>. Accessed August 21.
- Natural Standard Database <http://naturalstandard.com>. Accessed July 23, 2011.
- Yan J, Allendorf DJ, Brandley B. Yeast whole glucan particle (WGP) beta-glucan in conjunction with antitumor monoclonal antibodies to treat cancer. *Expert Opin. Biol Ther.* 2005 May;5(5):691-702. [PMID: 15934844]
- Qi C, Cai Y, Gunn L, et al. Differential pathways regulating innate and adaptive antitumor immune responses by particulate and soluble yeast-derived β -glucans. *Blood.* 2011 Jun 23;117(25):6825-36. [PMID: 21531981]
- Pelizon AC, Kaneno R, Soares AM, et al. Immunomodulatory activities associated with beta-glucan derived from *Saccharomyces cerevisiae*. *Physiol Res.* 2005;54(5):557-64. [PMID: 16238470]
- Tsikitis V, Albina J, Reichner J. Beta-glucan affects leukocyte navigation in a complex chemotactic ingredient. *Surgery.* 2004 Aug;136(2):384-9. [PMID: 15300205]
- Senoglu N, Yuzbasioglu MF, Aral M, et al. Protective effects of N-acetylcysteine and beta-glucan pretreatment on oxidative stress in cecal ligation and puncture model of sepsis. *J Invest Surg.* 2008 Sep-Oct;21(5):237-43. [PMID: 19160131]
- Turnbull, JL, Patchen ML, Scadden DT. The polysaccharide, PGGlucan, enhances human myelopoiesis by direct action independent of and additive to early-acting cytokines. *Acta Haematol.* 1999;102(2):66-71. [PMID: 10529508]
- Kournikakis B, Mandeville R, Brousseau P, et al. Anthrax-protective effects of yeast beta 1,3 glucans. *Med Gen Med.* 2003 Mar 21;5(1):1. [PMID:12827062]

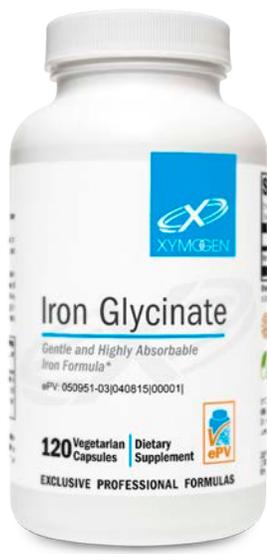
Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Iron Glycinate

Gentle and Highly Absorbable Iron Formula*



Available in 120 capsules

Discussion

Ferrous iron is reacted with glycine to form bis-glycinate chelate, a non-electrically charged compound that is totally nutritionally functional. The absence of electrical charge, uncommon for an iron supplement, makes it less likely that Iron Glycinate™ can interfere with absorption of other minerals such as calcium, vitamin E or vitamin C. Iron solubility from iron bis-glycine chelate is not affected by pH changes from 2-6. This means it travels unchanged through the stomach, into the intestine, where it is absorbed and released for transport throughout the body.*

Patient compliance with iron bis-glycinate appears to be better than that seen with inorganic forms of iron supplements for two reasons. First, the taste: In a study with 145 pregnant women (that concluded daily supplementation with iron bis-glycinate chelate was significantly more effective even at a lower dose than ferrous sulfate) the percentage of taste complaints among the women given ferrous sulfate was 29.8%, while 0% of the women on the bis-glycinate

Clinical Applications

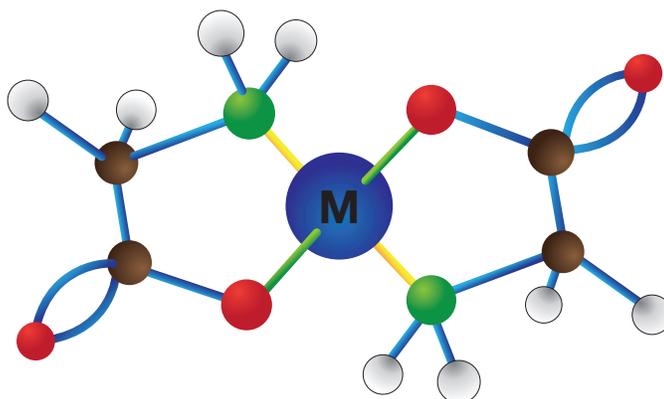
- » Supplements Inadequate Dietary Intake of Iron*
- » Supports Increased Requirement for Iron*
- » Supports Healthy Ferritin and Hemoglobin Levels*

Iron bis-glycinate is a well-studied, 100% fully-reacted, patented form of iron exclusively from Albion® Laboratories. The amino acid glycine is actually one of the two starting materials the body uses to synthesize hemoglobin. Therefore, Iron Glycinate™ contributes two key factors. This form of iron has higher bioavailability, lower toxicity, less food reactivity, less food interactions and has a longer shelf life than any other common form of iron.

chelate complained about taste. Second, iron bis-glycinate is less likely to have any of the gastrointestinal side-effects associated with standard iron supplementation.*

A published absorption study showed there was a significant correlation between iron absorption of iron bis-glycinate chelate to serum ferritin ($r = -0.60$, $p < 0.03$) (The higher the ferritin the lower the absorption and vice versa.) The amount of iron stored in the body regulates iron bis-glycinate chelate absorption. This translates into less chance of toxicity. Another benefit of the bis-glycinate chelate form of iron over other iron supplements is that it doesn't act as a pro-oxidant.*

Iron is an important component of hemoglobin, myoglobin, and ferritin. These proteins are involved in the transport, storage, and release of oxygen to the tissues.*



Iron bis-glycinate Courtesy of Albion Laboratories, Inc.®

Iron Glycinate Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Iron (as Ferrochel® ferrous bisglycinate chelate)	29 mg	161%

Other Ingredients: Microcrystalline cellulose, HPMC (capsule), stearic acid, magnesium stearate, and silica.

DIRECTIONS: Take one capsule daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

WARNING: Accidental overdose of iron-containing products is a leading cause of fatal poisoning in children under 6. Keep this product out of reach of children. In case of accidental overdose, call a doctor or poison control center immediately.

STORAGE: Keep closed in a cool, dry place, out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



Ferrochel and the Albion Medallion design are registered trademarks of Albion Laboratories, Inc.



References

1. Pineda O, Ashmead HD. Effectiveness of treatment of iron-deficiency anemia in infants and young children with ferrous bis-glycinate chelate. *Nutrition*. 2001 May;17(5):381-4. [PMID:11377130]
2. Szarfarc SC, de Cassana LM, Fujimori E, Guerra-Shinohara EM, de Oliveira IM. Relative effectiveness of iron bis-glycinate chelate (Ferrochel) and ferrous sulfate in the control of iron deficiency in pregnant women. *Arch Latinoam Nutr*. 2001 Mar;51(1 Suppl 1):42-7 [PMID: 1688081]
3. Iron, PDR: http://www.pdrhealth.com/drug_info/nmdrugprofiles/nutsupdrugs/iro_0149.shtml [accessed 11.11.05]
4. Plummer-Vinson Syndrome. <http://www.emedicine.com/med/topic3431.htm> [Accessed 11.11.05]
5. Hilal Mocan, Alisan Yildiran, Fazil Orhan, Erol Erduran. Breath holding spells in 91 children and response to treatment with iron *Arch Dis Child* 1999;81:261-262 (September) [<http://adc.bmjournals.com/cgi/content/full/81/3/261>] Accessed 11.11.05
6. Brolin RE, Gorman JH, Gorman RC, Petschenik AJ, Bradley LB, Kenler HA, Cody RP. Prophylactic iron supplementation after Roux-Y gastric bypass: a prospective, double blind, randomized study. *Arch Surg*. 1998 Jul;133 (7): 740-4. [PMID 9688002]
7. Kantor J, Kessler LJ, Brooks DG, Cotsarelis G. Decreased serum ferritin is associated with alopecia in women. *J Invest Dermatol*. 2003 Nov;121(5):985-8 [PMID:14708596]
8. Hershko C, Ronson A, Souroujon M, Maschler Z, Heyd J, Patz J. Variable hematological presentation of autoimmune gastritis: age-related progression from iron deficiency to cobalamin depletion. *Blood*. 2005 Oct 20; [Epub ahead of print] [PMID:16239424]
9. Ashmead SD. The chemistry of ferrous bis-glycinate chelate. *Arch Latinoam Nutr*. 2001 Mar; 51(1 Suppl 1):7-12 [PMID: 11688084]
10. Garcia-Casal MN, Layrisse M. The effect of change in pH on the solubility of iron bis-glycinate chelate and other iron compounds. *Arch Latinoam Nutr*. 2001 Mar;51(1 Suppl 1):35-6. [PMID: 11688079]
11. Szarfarc SC, de Cassana LM, Fujimori E, Guerra-Shinohara EM, de Oliveira IM. Relative effectiveness of iron bis-glycinate chelate (Ferrochel) and ferrous sulfate in the control of iron deficiency in pregnant women. *Arch Latinoam Nutr*. 2001 Mar;51(1 Suppl 1):42-7 [PMID: 11688081]
12. Olivares M, Pizarro F. Bioavailability of iron bis-glycinate chelate in water. *Arch Latinoam Nutr*. 2001 Mar;51 (1 Suppl 1): 22-5 [PMID: 11688077]
13. Pineda O, Ashmead HD. Effectiveness of treatment of iron-deficiency anemia in infants and young children with ferrous bis-glycinate chelate. *Nutrition*. 2001 May;17(5):381-4. [PMID: 11377130]
14. Patterson AJ, Brown WJ, Roberts DC. Dietary and supplement treatment of iron deficiency results in improvements in general health and fatigue in Australian women of childbearing age. *J Am Coll Nutr*. 2001 Aug;20(4):337-42
15. Pelton R, Lavalle JB, Hawkins EB, et al. Drug Induced Nutrient Depletion Handbook. 2nd ed . Cincinnati, OH: Lexi-Comp Inc; 2001.

Additional references available upon request.

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

K2

Natural Vitamin K2



K2-45 is available in 60 capsules
K2-D3 10,000 is available in 60 capsules and 120 capsules
K2-D3 5000 is available in 60 capsules and 120 capsules

Discussion

Naturally occurring vitamin K is found as either K1 (phyloquinone), which is derived from food sources such as green leafy vegetables, or K2 (menaquinones). Menaquinones are designated as MK-n, where n denotes the length of the molecule's aliphatic side chain. Menaquinones are synthesized by bacteria and can be obtained from animal-based and fermented foods. Structural differences between K1 and K2 impact their bioavailability and bioactivity. Furthermore, among menaquinones, menaquinone-7 (MK-7), with its longer side chain, is very hydrophobic. Compared to K1, MK-7's physiochemical properties make it highly transportable by plasma lipoproteins, increase its extrahepatic (bones, arteries, etc.) availability, and produce its long half-life.^[1-3]

Absorption of K1 from food can be limited due to its membrane-bound nature and the individual consumer's digestive and absorptive variability. Moreover, adequate consumption of foods high in K2 can be challenging. Therefore, dietary supplementation is an important option. In addition, research suggests that higher levels of menaquinones are needed than were previously thought. Supplementary vitamin K can be found in three forms: synthetic K1; MK-4, which is structurally similar to K1; and natural, long-chain MK-7. Xymogen provides MK-7 as Vitamk7™, a naturally derived and solvent-free vitamin K2 that has been obtained through a patent-granted biofermentation process of *Bacillus subtilis* natto cultures.*

MK-7 Bioavailability Increases Extrahepatic Tissue Utilization

Schurgers et al conducted human studies to compare the in vivo properties of orally administered K1 and MK-7. The results supported better bioavailability and utilization of MK-7. Expressed as AUC_{96h}, MK-7 demonstrated a six-fold better half-life, a seven- to eight-fold higher dose-response level, and a three times higher carboxylated to uncarboxylated osteocalcin ratio (cOC:ucOC[†]). Furthermore, on a molar basis, MK-7 is a three-to-four times more potent antidote for oral anticoagulation than is K1. Researchers note that, aside from sensitive individuals, "MK-7 supplements containing more than 50 mcg/d may interfere with oral anticoagulant treatment, whereas doses of at least 50 mcg are not likely to affect the INR value in a relevant way."^[2] Nonetheless, practitioners should closely monitor patients taking anticoagulants.*

While studies on the absorption and bioavailability of MK-4 at nutritional levels (i.e., doses of 500 mcg/d or lower) suggest less efficacy compared to longer-chain menaquinones at similar doses,^[4] this remains subject to debate. It is possible that rapid uptake of MK-4 could account for its observed lack of detection in serum after oral administration,^[5] but more studies are needed for clarification.*

Bone Benefits

Among the dietary factors critical to bone health, vitamin K has emerged as a key player. Vitamin K is believed to be necessary for bone mineralization. Through

Clinical Applications

- » Supports Bone Health by Promoting Carboxylation of Bone Proteins*
- » Supports Cardiovascular Health by Affecting Arterial Calcium Deposits*
- » Supports Healthy Blood Clotting*

K2-45, K2-D3 10,000, and K2-D3 5000 provide vitamin K2 as menaquinone-7 (MK-7), a highly bioavailable and bioactive form of K2. K2-D3 also features vitamin D3 (cholecalciferol), the identical form in which vitamin D is derived in the body from cholesterol and synthesized by sunlight on the skin. Historical use and numerous studies have demonstrated the efficacy of vitamin K supplements for bone and cardiovascular health.*

carboxylation, vitamin K activates osteocalcin, the protein needed to bind calcium to the mineral matrix in bone.^[6] Several studies have demonstrated the efficacy of MK-7 (e.g., doses of 45-90 mcg/d) to increase osteocalcin carboxylation and to increase the cOC:ucOC ratio. A high cOC:ucOC ratio is associated with bone health.^[1,2,4] A recent in vitro study also showed an osteogenic effect of MK-7 administration on human mesenchymal cell differentiation.^[6] In addition, the vitamin may protect bone integrity by reducing the synthesis of prostaglandin E2 or interleukin-6 by osteoclasts.^[7] Animal and human studies have demonstrated a significant beneficial effect of MK-7 supplementation on bone health.^[8-10] Vitamin K and vitamin D share some similar characteristics and are believed to act synergistically.*^[11]

Cardiovascular and Other Health Benefits

Vitamin K benefits cardiovascular health by participating in the carboxylation of matrix GLA protein (MGP), a protein regarded to be the most potent inhibitor of arterial calcification. Researchers have demonstrated that supplementation with vitamin K reduces arterial calcium deposits^[1,3,12] and that long-term intake of long-chain menaquinones is inversely correlated with calcium accumulation in arteries.*^[5]

Vitamin K has specific receptor binding sites that allow it to regulate gene activity.^[13] Besides its gene-mediating effects upon critical proteins, the vitamin can also bind with the steroid and xenobiotic receptors and influence their expression.^[14] In addition, vitamin K also demonstrates antioxidant activity^[15]; reduces levels of certain markers, such as acute phase reactants (e.g., C-reactive protein)^[16]; and participates in the induction of apoptosis.*^[17]

Vitamin D (as D3)

Although vitamin D3 (cholecalciferol) is made in the skin when 7-dehydrocholesterol reacts with sunlight, many things affect the degree to which this biosynthesis occurs, including time of day, seasons, location, smog/pollution, clothing, shade of skin (darker skin requires more sun), and sunscreen use. Low-cholesterol diets and certain cholesterol therapies can also affect vitamin D formation. By some estimates, one billion people worldwide have vitamin D deficiency or insufficiency.^[18] The body needs vitamin D to absorb calcium, and the importance of vitamin D in skeletal health and bone density is well-established. Without adequate absorption, the body must take calcium from its stores in the skeleton, which weakens existing bone and prevents the formation of strong, new bone. Researchers suggest that vitamin D supplementation may decrease bone turnover and increase bone mineral density.^[19] A pooled analysis evaluating 11 randomized, double-blind, placebo-controlled trials supported this analysis. It concluded that vitamin D supplementation (> 800 IU daily) was favorable in maintaining hip and nonvertebral bone integrity in individuals aged 65 and older.*^[20]

Continued on next page

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Although D2 and D3 are similar biochemically, one study demonstrated D3 to be approximately 87% more potent in raising and maintaining serum calcidiol (the body's storage form) concentrations and in producing two- to threefold greater storage of vitamin D than did equimolar D2.*^[21]

†The cOC:ucOC ratio can be used as a determinant of vitamin K status.

K2-45 Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Vitamin K2 (as menaquinone-7)	45 mcg	38%

Other Ingredients: Microcrystalline cellulose, HPMC (capsule), stearic acid, magnesium stearate, and silica.

DIRECTIONS: Take one capsule with a meal, one to two times daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Consider total vitamin K intake (food + supplements) if you are taking blood-thinning medication. Present studies show that 45 mcg of MK-7 from Vitamk7™ daily is not likely to interfere with blood-thinning medicines. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



K2-D3 10,000 Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Vitamin D3 (cholecalciferol)	250 mcg (10,000 IU)	1250%
Vitamin K2 (as menaquinone-7)	45 mcg	38%

Other Ingredients: Microcrystalline cellulose, HPMC (capsule), vegetable stearic acid, vegetable magnesium stearate, and silica.

DIRECTIONS: Swallow one capsule daily with water, preferably at mealtime, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Consider total vitamin K intake (food + supplements) if you are taking blood-thinning medication. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



K2-D3 5000 Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Vitamin D3 (cholecalciferol)	125 mcg (5000 IU)	625%
Vitamin K2 (as menaquinone-7)	90 mcg	75%

Other Ingredients: HPMC (capsule), microcrystalline cellulose, ascorbyl palmitate, and silica.

DIRECTIONS: Take one capsule daily, preferably at mealtime, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Consider total vitamin K intake (food + supplements) if you are taking blood-thinning medication. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



References

- Brugè F, Bacchetti T, Principi F, et al. Olive oil supplemented with menaquinone-7 significantly affects osteocalcin carboxylation. *Br J Nutr*. 2011 Oct;106(7):1058-62. [PMID: 21736837]
- Schurgers LJ, Teunissen KJ, Hamulyák K, et al. Vitamin K-containing dietary supplements: comparison of synthetic vitamin K1 and natto-derived menaquinone-7. *Blood*. 2007 Apr 15;109(8):3279-83. [PMID: 17158229]
- Beulens JW, Bots ML, Atsma F, et al. High dietary menaquinone intake is associated with reduced coronary calcification. *Atherosclerosis*. 2009 Apr;203(2):489-93. [PMID: 18722618]
- Sato T, Schurgers LJ, Uenishi K. Comparison of menaquinone-4 and menaquinone-7 bioavailability in healthy women. *Nutr J*. 2012 Nov 12;11:93. [PMID: 23140417]
- Schurgers LJ, Vermeer C. Differential lipoprotein transport pathways of K-vitamins in healthy subjects. *Biochim Biophys Acta*. 2002 Feb 15;1570(1):27-32. [PMID: 11960685]
- Gigante A, Brugè F, Cecconi S, et al. Vitamin MK-7 enhances vitamin D3-induced osteogenesis in hMSCs: modulation of key effectors in mineralization and vascularization. *J Tissue Eng Regen Med*. 2012 Oct 29. [PMID: 23109511]
- Weber P. Management of osteoporosis: is there a role for vitamin K? *Int J Vitam Nutr Res*. 1997;67(5):350-56. [PMID: 9350477]
- Yamaguchi M, Taguchi H, Gao YH, et al. Effect of vitamin K2 (menaquinone-7) in fermented soybean (natto) on bone loss in ovariectomized rats. *J Bone Miner Metab*. 1999;17(1):23-29. [PMID: 10084398]
- Knapen MH, Drummen NE, Smit E, et al. Three-year low-dose menaquinone-7 supplementation helps decrease bone loss in healthy postmenopausal women. *Osteoporos Int*. 2013 Sep;24(9):2499-507. [PMID: 23525894]
- Kanellakis S, Moschonis G, Tenta R, et al. Changes in parameters of bone metabolism in postmenopausal women following a 12-month intervention period using dairy products enriched with calcium, vitamin D, and phyloquinone (vitamin K(1)) or menaquinone-7 (vitamin K (2)): the Postmenopausal Health Study II. *Calcif Tissue Int*. 2012 Apr;90(4):251-62. [PMID: 2239252]
- Bolton-Smith C, McMurdo ME, Paterson CR, et al. Two-year randomized controlled trial of vitamin K1 (phyloquinone) and vitamin D3 plus calcium on the bone health of older women. *J Bone Miner Res*. 2007 Apr;22(4):509-19. [PMID: 17243866]
- Geleijnse JM, Vermeer C, Grobbee DE, et al. Dietary intake of menaquinone is associated with a reduced risk of coronary heart disease: the Rotterdam Study. *J Nutr*. 2004 Nov;134(11):3100-05. [PMID: 15514282]
- Igarashi M, Yogiashi Y, Mihara M, et al. Vitamin K induces osteoblast differentiation through pregnane X receptor-mediated transcriptional control of the Msx2 gene. *Mol Cell Biol*. 2007 Nov;27(22):7947-54. [PMID: 17875939]
- Azuma K, Inoue S. Vitamin K function mediated by activation of steroid and xenobiotic receptor [in Japanese]. *Clin Calcium*. 2009 Dec;19(12):1770-8. [PMID: 19949268]
- Vervoort LM, Ronden JE, Thijssen HH. The potent antioxidant activity of the vitamin K cycle in microsomal lipid peroxidation. *Biochem Pharmacol*. 1997 Oct 15;54(8):871-76. [PMID: 9354587]
- Shea MK, Booth SL, Massaro JM, et al. Vitamin K and vitamin D status: associations with inflammatory markers in the Framingham Offspring Study. *Am J Epidemiol*. 2008 Feb 1;167(3):313-20. [PMID: 18006902]
- Sada E, Abe Y, Ohba R, et al. Vitamin K2 modulates differentiation and apoptosis of both myeloid and erythroid lineages. *Eur J Haematol*. 2010 Dec;85(6):538-48. [PMID: 20887388]
- Tsiaras WG, Weinstock MA. Factors influencing vitamin d status. *Acta Derm Venereol*. 2011 Mar;91(2):115-24. [PMID: 21384086]
- Lips P, van Schoor NM. The effect of vitamin D on bone and osteoporosis. *Best Pract Res Clin Endocrinol Metab*. 2011 Aug;25(4):585-91. [PMID: 21872800]
- Bischoff-Ferrari HA, Willett WC, Orav EJ, et al. A pooled analysis of vitamin D dose requirements for fracture prevention. *N Engl J Med*. 2012 Jul 5;367(1):40-49. [PMID: 22762317]
- Heaney RP, Recker RR, Grote J, et al. Vitamin D3 is more potent than vitamin D2 in humans. *J Clin Endocrinol Metab*. 2011 Mar;96(3):E447-52. [PMID: 21177785]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

K-Mg Citrate™

Electrolyte/pH Support*



Available in 60 capsules

Discussion

Hypokalemia Causes and Concerns Hypokalemia (low blood potassium) can result from excessive sweating, vomiting, and diarrhea, or the chronic use of any of a wide variety of pharmaceuticals that cause urinary loss of potassium. Some examples of these include the use of OTCs (eg, aspirin, sodium bicarbonate, laxatives); prescription drugs, such as non-potassium-sparing diuretics and steroids; and chemotherapeutic drugs, such as cisplatin. Long-term oral supplementation with licorice extract containing glycyrrhizin can also reduce potassium levels. A host of diseases—including common conditions such as alcoholism, diabetes, and eating disorders—can also interfere with potassium homeostasis. The diversity and number of physiological processes dependent upon adequate potassium is significant. Examples such as the need for healthy muscle contraction, nerve impulse transmission, gastrointestinal and renal function, tissue synthesis, and carbohydrate metabolism clearly point to the importance of maintaining optimal blood levels of potassium. When potassium levels in the blood are too low, there is disruption in pH, enzymatic reactions, isotonicity, and the electrodynamic balance of cells. Oral administration of potassium is an effective means of maintaining healthy blood levels of potassium when risk factors are present, or for replacing the mineral when it becomes depleted.

Hypomagnesemia Causes and Concerns Hypomagnesemia (low blood magnesium), similar to hypokalemia, is often seen in alcoholism, severe or prolonged vomiting or diarrhea, as well as in type 2 diabetes where a low magnesium level is thought to cause renal impairment sooner than expected. Besides the obvious cause of malabsorption, low magnesium levels may occur due to cirrhosis of the liver, pancreatitis, inflammatory bowel disease, or renal impairment. Low blood magnesium level is often concurrent with a low potassium level in the blood, hence the combination of these minerals in XYMOGEN's formula. Not all forms of magnesium are appropriate for oral replacement. For example, the solubility, absorption, and bioavailability of magnesium carbonate is limited, and magnesium oxide is likely to cause diarrhea when used in the dose needed for replacement.

Clinical Applications

- » Maintains Healthy Cellular Function
- » Supports Healthy Kidney Function
- » Maintains Healthy Electrolyte Balance

*K-Mg Citrate™ provides two intracellular cations that are vital to maintaining healthy muscle contractility, nerve conduction, and blood pressure levels already within the normal range. These minerals help maintain healthy electrolyte and acid-base balance, and support kidney health and function.**

Calcium and the Kidneys The excretion of calcium in the urine through the kidney is a matter of concern, especially in individuals who are immobilized. A 3-year, prospective, placebo-controlled, double-blind study (n=64) demonstrated that oral supplementation of potassium-magnesium citrate provided a significant benefit in terms of calcium salt-related kidney health.^[1] Another study demonstrated that the combination of these two minerals increased urinary pH and chelated the calcium, as well as decreased undissociated uric acid concentration.^[2] These and similar studies employed larger doses of potassium/magnesium citrate than is available in a capsule of XYMOGEN's formula. Some individuals may experience bloating, gas, and loose stools when taking supplemental magnesium across a range of doses, though more so at higher doses. The symptoms are alleviated when the supplement is discontinued; but then its benefit is lost as well.

Citrate The citrate content of this formula is 398 mg (equivalent to 5.24 mEq). It is in the anhydrous form. Although the amount per capsule in this formula is not considered significant, citrate is considered protective because it forms soluble complexes with calcium ions and reduces crystallization and aggregation.^[3]

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

K-Mg Citrate™ Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Magnesium (as magnesium citrate)	70 mg	17%
Potassium (as potassium citrate)	99 mg	2%

Other Ingredients: HPMC (capsule), microcrystalline cellulose, stearic acid, magnesium stearate, medium-chain triglyceride oil, and silica.

DIRECTIONS: Take one capsule one to two times daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

**References**

1. Ettinger B, Pak CY, Citron JT, et al. Potassium-magnesium citrate is an effective prophylaxis against recurrent calcium oxalate nephrolithiasis. *J Urol.* 1997 Dec;158(6):2069-73. [PMID: 9366314]
2. Zerwekh JE, Odvina CV, Wuermsler LA, et al. Reduction of renal stone risk by potassium-magnesium citrate during 5 weeks of bed rest. *J Urol.* 2007 Jun;177(6):2179-84. [PMID: 17509313]
3. Caudarella R, Vescini F. Urinary citrate and renal stone disease: the preventive role of alkali citrate treatment. *Arch Ital Urol Androl.* 2009 Sep;81(3):182-7. [PMID: 19911682]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.



Available in Cucumber-Lime

Discussion

Glucose is the primary source of energy in the body that fuels every function from brain cognition to athletic performance. When dietary carbohydrates are consumed, they are immediately metabolized into glucose or stored in the body as glycogen, which is utilized when the body needs an energy source. When glycogen stores have been depleted, the body naturally goes into a ketogenic state. In this state, the liver uses fat stores to generate alternative fuel byproducts called ketones. The presence of ketones in the blood is known as ketosis.

Ketosis has been touted as desirable for multiple benefits, particularly for energy production, performance, and focus. Ketosis can be induced by fasting, by strictly limiting carbohydrate intake, by engaging in prolonged exercise without carbohydrate intake, or by supplementing with an exogenous source of ketones. The three primary types of ketone bodies formed in ketosis are acetate, acetoacetate, and beta-hydroxybutyrate (BHB). KetonX™ provides an exogenous source of ketones to promote a state of ketosis.*

GoBHB® (Beta-Hydroxybutyrate Salts)

Fuel/Energy Source

GoBHB is a patented and self-affirmed GRAS supplemental form of the BHB ketone body bound to mineral salts. It provides an exogenous source of ketones to help achieve ketosis without a ketogenic diet. When the body is in a natural state of ketosis, BHB is the ketone body present in the blood at the highest level;^[1] it appears to be better for energy production on a cellular level, and it is more stable than other naturally occurring ketones. Thus, most of the research on exogenous ketones utilizes either BHB salts or BHB esters.*

The first human study suggesting that exogenous ketones could rapidly increase the level of ketones in the blood was published in 2012. Healthy male and female subjects (n = 54) had elevated plasma levels of BHB and acetoacetate following the administration of a single dose of a ketone monoester delivered at 140, 357, or 714 mg/kg body weight in a meal replacement drink. The same three doses were administered three times daily over a five-day period to assess safety and tolerance. BHB levels remained elevated, but some gastrointestinal effects were reported and attributed to the large volumes of the milk-based drink, not the BHB.*^[2]

A variety of dietary strategies can be used to induce a ketogenic state; however, restriction of carbohydrates is a necessity, and higher amounts of dietary fats are typical. Some individuals may not tolerate a high fat intake and some may consider it personally undesirable. Additionally, due to a limited list of allowable

Clinical Applications

- » Provides Carbohydrate-Free Fuel for Muscles and Brain*
- » Helps Promote Ketosis*
- » Supports Energy, Performance, and Focus*

*KetonX™ is a refreshing, cucumber-lime-flavored, easy-to-use powdered drink mix featuring mineral salts of beta-hydroxybutyrate (BHB) and medium-chain triglycerides. These ingredients provide direct carbohydrate-free fuel for the brain and muscles to support energy, performance, and focus.**

foods, classic ketogenic diets may be difficult to adhere to over time. Exogenous ketones are a potentially useful adjunct to a ketogenic diet or a practical alternative to increasing circulating ketone body concentrations without having to undergo a ketogenic diet to induce ketosis.*

Performance

It has been hypothesized that during exercise, ketones essentially function as a “fourth” fuel source. They don’t necessarily provide an advantage over carbohydrates, fats, and proteins, but they possibly preserve endogenous fuel. Limiting the breakdown of carbohydrates for energy during exercise might reduce fatigue and lactate accumulation,^[3] two factors that are likely to affect athletic performance. Ketosis as a performance enhancer was introduced in the early 1980s with the idea that chronic ketosis without caloric restriction could preserve submaximal exercise capability by sparing glycogen and conserving limited carbohydrate stores. A recent review of this stated that few human studies have yielded positive results and most yielded equivocal results.*^[4]

In five separate studies (n = 39) of high-performance athletes, the effects of exogenous ketone esters on induced ketosis for physical endurance were studied. Ketosis decreased muscle glycolysis and plasma lactate concentrations while providing an alternative fuel substrate. Ketosis also increased intramuscular triacylglycerol oxidation during exercise, even in the presence of normal muscle glycogen, co-ingested carbohydrate, and elevated insulin. These findings suggest a positive effect of exogenous ketones for improvement of performance.^[5] However, other studies with varying testing protocols suggest minimal or no effect on performance.^[6,7] Further studies are needed to confirm the positive effect of exogenous ketones on performance.*

Cognitive

The body of evidence supporting a ketogenic diet and/or exogenous ketones as an effective nutrition intervention for cognitive impairment and neurodegenerative issues continues to evolve with multiple animal studies, some single case reports, and a few small human trials.*^[8-11]

Although glucose is the predominant brain fuel, ketones are utilized when glucose is not available. When an individual is fasting, strenuously exercising, or on a ketogenic diet, the brain becomes receptive to ketone bodies as an alternative fuel. This was demonstrated in a study in adult subjects (n = 4) in whom ketones were shown to rapidly cross the blood-brain barrier and provide brain neurons with energy.^[12] This efficient utilization has been suggested to play

a role in the improvement of memory, focus, and cognition when affected regions of the brain lose capacity to harness sufficient energy from glucose.^{*[11,13,14]}

Medium-Chain Triglycerides

KetonX provides a patented medium-chain triglyceride (MCT) powder with a high caprylic and capric acid content (C8/C10) that also contains acacia fiber, a prebiotic that may promote gut health and help optimize the gut-brain axis. MCTs are easily absorbed, permeate the mitochondria without the aid of enzymes, and provide a quick energy source without impacting insulin levels. Unlike other dietary fats, MCTs are not stored as body fat to any significant degree. The liver metabolizes the MCTs into ketones, which can then be used as alternative energy sources for brain cells if they are deprived of glucose.*

Both animal and human studies have explored the potential role of MCTs in increasing ketones to support brain health. In a study of adults (n = 20) with cognitive impairment who were given MCTs or placebo, significant increases in BHB were observed 90 minutes post-treatment when recall tests were administered.^[15] In a 90-day, randomized, double-blind, placebo-controlled, parallel group study, subjects (n = 152) with mild-to-moderate Alzheimer's disease were given an oral ketogenic MCT compound to determine if ketosis could affect cognitive performance. Significantly elevated levels of BHB were seen two hours after administration when compared to placebo. Correspondingly, elevated BHB levels resulted in significant differences in Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog) scores when compared to placebo.^{*[16]}

Research on MCTs as fuel for exercise also continues to emerge. A study using recreational athletes as subjects (n = 8) suggested that when consuming MCTs, blood lactate levels and rate of perceived exertion during moderate-intensity exercise were significantly reduced.^{*[17]}

Another small study suggested that endurance-trained cyclists (n = 6) who consumed MCTs during moderate-intensity exercise for two hours had significant improvements in time-trial performances during subsequent high-intensity exercise.^[18] Additional research in larger trials is ongoing to further explore these effects.*

KetonX™ Supplement Facts

Serving Size: 1 scoop (about 11.1 g)

	Amount Per Serving	%Daily Value
Calories	30	
Total Fat	1.5 g	2%†
Saturated Fat	1.5 g	8%†
Total Carbohydrate	2 g	1%†
Dietary Fiber	2 g	7%
Calcium (as goBHB® calcium beta-hydroxybutyrate)	385 mg	30%
Magnesium (as goBHB® magnesium beta-hydroxybutyrate)	50 mg	12%
Sodium (as goBHB® sodium beta-hydroxybutyrate)	385 mg	17%
goBHB® Calcium Beta-Hydroxybutyrate	2.5 g	**
goBHB® Sodium Beta-Hydroxybutyrate	2.25 g	**
Medium-Chain Triglycerides	1.5 g	**
goBHB® Magnesium Beta-Hydroxybutyrate	600 mg	**

† Percent Daily Values are based on a 2,000 calorie diet.
** Daily Value not established.

Other Ingredients: Gum acacia, citric acid, malic acid, silica, natural flavors (no MSG), stevia leaf extract, cellulose gum, xanthan gum, and sea salt.

DIRECTIONS: Dissolve the contents of one scoop (about 11.1 g) daily in 12-14 oz of water according to taste preference, or use as directed by your healthcare practitioner. When in training: Take 30 minutes before a workout or in the morning on non-training days.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, animal or dairy products, fish, shellfish, peanuts, tree nut protein, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



goBHB® is a registered trademark under exclusive global distribution by Compound Solutions, Inc.

References

1. Cahill GF Jr. Fuel metabolism in starvation. *Annu Rev Nutr.* 2006;26:1-22. Review. [PMID: 16848698]
2. Clarke K, Tchabanenko K, Pawlosky R, et al. Kinetics, safety and tolerability of (R)-3-hydroxybutyl (R)-3-hydroxybutyrate in healthy adult subjects. *Regul Toxicol Pharmacol.* 2012 Aug;63(3):401-8. [PMID: 22561291]
3. Egan B, D'Agostino DP. Fueling performance: ketones enter the mix. *Cell Metab.* 2016 Sep 13;24(3):373-375. [PMID: 27626197]
4. Scott JM, Deuster PA. Ketones and human performance. *J Spec Oper Med.* Summer 2017;17(2):112-116. [PMID: 28599043]
5. Cox PJ, Kirk T, Ashmore T, et al. Nutritional ketosis alters fuel preference and thereby endurance performance in athletes. *Cell Metab.* 2016 Aug 9;24(2):256-68. [PMID: 27475046]
6. Leckey JJ, Ross ML, Quod M, et al. Ketone diester ingestion impairs time-trial performance in professional cyclists. *Front Physiol.* 2017 Oct 23;8:806. [PMID: 29109686]
7. O'Malley T, Myette-Cote E, Durrer C, et al. Nutritional ketone salts increase fat oxidation but impair high-intensity exercise performance in healthy adult males. *Appl Physiol Nutr Metab.* 2017 Oct;42(10):1031-1035. [PMID: 28750585]
8. Murray AJ, Knight NS, Cole MA, et al. Novel ketone diet enhances physical and cognitive performance. *FASEB J.* 2016 Dec;30(12):4021-4032. [PMID: 27528626]
9. Roberts MN, Wallace MA, Tomilov AA, et al. A ketogenic diet extends longevity and health span in adult mice. *Cell Metab.* 2018 May 1;27(5):1156. [PMID: 29719228]
10. Newport MT, VanTallie TB, Kashiwaya Y, et al. A new way to produce hyperketonemia: use of ketone ester in a case of Alzheimer's disease. *Alzheimers Dement.* 2015 Jan;11(1):99-103. [PMID: 25301680]
11. Cunnane SC, Courchesne-Loyer A, Vandenbergh C, et al. Can ketones help rescue brain fuel supply in later life? Implications for cognitive health during aging and the treatment of Alzheimer's disease. *Front Mol Neurosci.* 2016 Jul 8;9:53. [PMID: 27458340]
12. Pan JW, de Graaf RA, Petersen KF, et al. [2,4-13 C2]-beta-hydroxybutyrate metabolism in human brain. *J Cereb Blood Flow Metab.* 2002 Jul;22(7):890-8. [PMID: 12142574]
13. Veech RL, Bradshaw PC, Clarke K, et al. Ketone bodies mimic the life span extending properties of caloric restriction. *IUBMB Life.* 2017 May;69(5):305-314. [PMID: 28371201]
14. Croteau E, Castellano CA, Fortier M, et al. A cross-sectional comparison of brain glucose and ketone metabolism in cognitively healthy older adults, mild cognitive impairment and early Alzheimer's disease. *Exp Gerontol.* 2018 Jul 1;107:18-26. [PMID: 28709938]
15. Reger MA, Henderson ST, Hale C, et al. Effects of beta-hydroxybutyrate on cognition in memory-impaired adults. *Neurobiol Aging.* 2004 Mar;25(3):311-4. [PMID: 15123336]
16. Henderson ST, Vogel JL, Barr LJ, et al. Study of the ketogenic agent AC-1202 in mild to moderate Alzheimer's disease: a randomized, double-blind, placebo-controlled, multicenter trial. *Nutr Metab (Lond).* 2009 Aug 10;6:31. [PMID: 19664276]
17. Nosaka N, Suzuki Y, Nagatoishi A, et al. Effect of ingestion of medium-chain triacylglycerols on moderate- and high-intensity exercise in recreational athletes. *J Nutr Sci Vitaminol (Tokyo).* 2009 Apr;55(2):120-5. [PMID: 19436137]
18. Van Zyl CG, Lambert EV, Hawley JA, et al. Effects of medium-chain triglyceride ingestion on fuel metabolism and cycling performance. *J Appl Physiol (1985).* 1996 Jun;80(6):2217-25. [PMID: 8806933]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

L-Glutamine

Cellular Support*



Available in 85 servings

Discussion

Glutamine is the most abundant free amino acid in the body and is an energy substrate for most cells—especially enterocytes (intestinal epithelial cells) and immune cells. It is also an essential component for numerous metabolic functions, including acid-base (pH) homeostasis; nitrogen supply; neurotransmitter production; and synthesis of glutathione, glucose, proteins, and nucleic acids.^[1,2] Glutamine is primarily synthesized and stored in skeletal muscle. It is considered a conditionally essential amino acid because, under normal circumstances, the body can manufacture enough to sustain physiological demands. However, under metabolic stress—such as illness/disease, injury, infection, surgery, chemotherapy, prolonged exercise, or environmental stress—glutamine is released from body stores into the bloodstream and transported to tissues in deficit. Increased demands make exogenous glutamine sources (food, supplements) a necessity.*^[2]

Support During and Recovery After Stress States During stress states, the body's glutamine requirement exceeds supply, severely reducing both plasma and skeletal muscle pools of free glutamine.^[1] Without adequate glutamine to meet the needs of the intestine, immune system, and vital organs, a negative nitrogen balance and catabolism can result.^[3] Nitrogen is necessary to repair wounds and keep the vital organs functioning; approximately one third of this nitrogen comes from glutamine. Adequate nutrition, which includes glutamine, can help spare host energy reserves and impede recovery complications.^[4] In fact, it has been recommended that patients preparing for elective surgery ready themselves nutritionally, in part through glutamine supplementation, to optimize recovery.^[5] Research also suggests glutamine may help diminish risks associated with conventional therapeutics—such as high-dose chemotherapy and radiation—by supporting mucosal integrity, immune competence, and glutathione biosynthesis.*^[4,6,7]

Intestinal Health and Barrier Function The greatest amount of glutamine is used by enterocytes. As their preferred fuel source, glutamine is necessary for their maintenance and healthy turnover.

Clinical Applications

- » Supports Glutamine Replenishment During and After Metabolic Stress*
- » Supports Intestinal Health and Barrier Integrity*
- » Supports Healthy Immune Function*
- » Supports Muscle Mass Retention*
- » Supports Increased Glutathione Synthesis*

*L-Glutamine (glutamine) is the most abundant amino acid in the body and is necessary for the maintenance of many metabolic functions. Under situations of stress, physiological demands increase, triggering a need for glutamine supplementation. For ease of dosing, XYMOGEN's L-Glutamine provides 4 grams of this amino acid per scoop to help replenish the body's stores and support glutamine's many functional roles.**

Supplementation may therefore enhance mucosal health.^[1,8] A healthy intestinal mucosa not only supports optimal nutrient absorption, but it also supports mucosal immune function and provides a barrier between bacteria and their products in the intestines and the bloodstream.^[1,9,10] Disruption of intestinal barrier function can lead to decreases in mucosal immune activity and increases in escaping toxins and bacteria, resulting in infections, illness, allergic reactions, skin conditions, and more. In various experimental models, glutamine administration has been shown to reduce epithelial cell death and preserve or improve barrier function.^[11-13] For instance, in an animal model of chemotherapy-induced intestinal damage, glutamine decreased the severity of intestinal injury perhaps through improved intestinal cell turnover and enhanced antioxidant activity.*^[14]

Muscle Tissue Preservation Of the 20 amino acids required for protein synthesis, glutamine is the most abundant. It makes up 50% of all amino acids in the blood and 60% of those in the body. Not only is glutamine necessary to maintain positive nitrogen balance and protein synthesis, but also it has recently been shown to prevent muscle loss by influencing myostatin levels.^[15] Myostatin is a protein that inhibits muscle differentiation and growth. Its increased bioactivity has been observed in glucocorticoid-induced hypercatabolism and is associated with several pathologies characterized by marked skeletal muscle depletion.*^[15]

Glutamine is thought to have ergogenic effects through its influences on fluid and electrolyte uptake, glutamine pool repletion after intense training, stimulation of muscle glycogen synthesis, and ability to increase growth hormone levels.^[16-18] While ergogenic effects are supported from a biochemical standpoint, more definitive studies are needed.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

L-Glutamine Supplement Facts

Serving Size: 1 Scoop (about 4 g)

	Amount Per Serving	%Daily Value
L-Glutamine	4 g	**
** Daily Value not established.		

Other Ingredients: None.

DIRECTIONS: Take one scoop daily, mixed with plain water, on an empty stomach, or as directed by your healthcare practitioner. Consume within 30 minutes of mixing.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.

References

- Oliveira GP, Dias CM, et al. Understanding the mechanisms of glutamine action in critically ill patients. *An Acad Bras Cienc.* 2010 Jun;82(2):417-30. [PMID: 20563423]
- Walsh NP, Blannin AK, Robson PJ, et al. Glutamine, exercise and immune function. Links and possible mechanisms. *Sports Med.* 1998 Sep;26(3):177-91. [PMID: 9802174]
- Calder PC, Yaqoob P. Glutamine and the immune system. *Amino Acids.* 1999;17(3):227-41. [PMID: 10582122]
- Kuhn KS, Muscaritoli M, Wischmeyer P, et al. Glutamine as indispensable nutrient in oncology: experimental and clinical evidence. *Eur J Nutr.* 2010 Jun;49(4):197-210. [PMID: 19936817]
- Awad S, Lobo DN. What's new in perioperative nutritional support? *Curr Opin Anaesthesiol.* 2011 Mar 30. [Epub ahead of print] [PMID: 21451404]
- Anderson PM, Schroeder G, Skubitz KM. Oral glutamine reduces the duration and severity of stomatitis after cytotoxic cancer chemotherapy. *Cancer.* 1998 Oct;83(7):1433-39. [PMID: 9762946]
- Rocha BR, Gombar FM, Barcellos LM, et al. Glutamine supplementation prevents collagen expression damage in healthy urinary bladder caused by radiotherapy. *Nutrition.* 2010 Dec 15. [Epub ahead of print] [PMID: 21167680]
- dos Santos RG, Viana ML, Generoso SV, et al. Glutamine supplementation decreases intestinal permeability and preserves gut mucosa integrity in an experimental mouse model. *JPEN J Parenter Enteral Nutr.* 2010 Jul-Aug;34(4):408-13. [PMID: 20631386]
- Nose K, Yang H, Sun X, et al. Glutamine prevents total parenteral nutrition-associated changes to intraepithelial lymphocyte phenotype and function: a potential mechanism for the preservation of epithelial barrier function. *J Interferon Cytokine Res.* 2010 Feb;30(2):67-80. [PMID: 20028208]
- Li N, Neu J. Glutamine deprivation alters intestinal tight junctions via a PI3-K/Akt mediated pathway in Caco-2 cells. *J Nutr.* 2009 Apr;139(4):710-14. [PMID: 19211824]
- Tian J, Hao L, Chandra P, et al. Dietary glutamine and oral antibiotics each improve indexes of gut barrier function in rat short bowel syndrome. *Am J Physiol Gastrointest Liver Physiol.* 2009 Feb;296(2):G348-55. [PMID: 19095767]
- Vicario M, Amat C, Rivero M, et al. Dietary glutamine affects mucosal functions in rats with mild DSS-induced colitis. *J Nutr.* 2007 Aug;137(8):1931-37. [PMID: 17634266]
- Gulgun M, Karaoglu A, Kesik V, et al. Effect of proanthocyanidin, arginine and glutamine supplementation on methotrexate-induced gastrointestinal toxicity in rats. *Methods Find Exp Clin Pharmacol.* 2010 Nov;32(9):657-61. [PMID: 21225016]
- Tazuke Y, Maeda K, Wasa M, et al. Protective mechanism of glutamine on the expression of proliferating cell nuclear antigen after cisplatin-induced intestinal mucosal injury. *Pediatr Surg Int.* 2011 Feb;27(2):151-58. [PMID: 21080177]
- Bonetto A, Penna F, Minero VG, et al. Glutamine prevents myostatin hyperexpression and protein hypercatabolism induced in C2C12 myotubes by tumor necrosis factor- α . *Amino Acids.* 2011 Feb;40(2):585-94. [PMID: 20623149]
- Hoffman JR, Ratamess NA, Kang J, et al. Examination of the efficacy of acute L-alanyl-L-glutamine ingestion during hydration stress in endurance exercise. *J Int Soc Sports Nutr.* 2010 Feb 3;7:8. [PMID: 20181080]
- Welbourne TC. Increased plasma bicarbonate and growth hormone after an oral glutamine load. *Am J Clin Nutr.* 1995 May;61(5):1058-61. [PMID: 7733028]
- Antonio J, Street C. Glutamine: a potentially useful supplement for athletes. *Can J Appl Physiol.* 1999 Feb;24(1):1-14. [PMID: 9916176]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

L-Lysine

An Essential Amino Acid



Available in 90 capsules

Discussion

An “Essential” Amino Acid Lysine, known chemically as 2,6-diaminohexanoic acid, is one of nine essential amino acids. Concentrated in muscle tissue, lysine is the amino acid that the body most highly conserves. An amino acid is a building block of protein and is considered “essential” when the body cannot manufacture it in sufficient quantities. Plants and bacteria can synthesize lysine from aspartic acid, but humans must meet their need for lysine by obtaining it directly from food and/or dietary supplementation. L-lysine is the primary limiting amino acid for protein synthesis for those who consume a cereal-based diet.*

Daily Requirement The adult recommendation for lysine intake varies according to the organization citing it. For example, the World Health Organization estimates the adult daily intake requirement to be 30 mg/kg body weight/day, while the Food and Agriculture Organization of the United Nations estimates the requirement to be only 12 mg/kg/day. Doses for short-term use range between 3000-9000 mg/day, while the general maintenance dose tends to be closer to 1000 mg per day. Additional lysine, above maintenance needs, is believed to support healthy growth in children.^[1-4] Lysine requirements may change under specific physiological circumstances as well. For example, a University of Toronto study suggested that women have an increased need for lysine during the luteal phase of their menstrual cycle due to increased protein catabolism.*^[5]

The need for lysine is mostly satisfied by an average US adult diet, which consists of 6-10 g of lysine per day. However, athletes and non-legume-consuming vegans may require more lysine. Signs of insufficient dietary intake of lysine include low energy, agitation, poor sense of balance, nausea, poor appetite, slow growth, and bloodshot eyes.*

The Importance of Lysine in Health As a building block of protein, lysine is obviously important in the growth and repair of tissue. In addition, it is essential to the body’s synthesis of carnitine, a nutrient the body uses to convert fatty acids into energy and to

Clinical Applications

- » Provides an Essential Amino Acid*
- » Provides Balance to a High Intake of Arginine*
- » Supports Synthesis of Collagen*
- » Supports Healthy Growth and Protein Synthesis*

*L-Lysine is an amino acid that is essential to human physiology. Lysine is vital for normal growth and for the manufacture of collagen, a substance important for healthy skin, bones, tendons, and cartilage. Supplemental lysine may be appropriate for individuals on a high-arginine diet.**

maintain a healthy cholesterol level. Lysine also must be available for the synthesis of collagen, a substance needed for healthy bones and connective tissue, such as skin, tendons, and cartilage. Lysine enhances calcium absorption and the incorporation of calcium into the bone matrix. It also supports renal conservation of calcium by reducing urinary loss of this mineral.^[6] In the presence of higher amounts of diet- or supplement-derived arginine in the bloodstream, additional lysine may be needed to provide balance between these two amino acids.*

Lysine and the Brain Once lysine is absorbed, a basic amino acid carrier, possibly the cationic amino acid transporter-1 (CAT-1), escorts it across the blood-brain barrier. The amino acid arginine competes with lysine for transport across the blood-brain barrier. The amount of each amino acid that actually enters the brain depends upon the relative concentration of each amino acid present. The dietary ratio of lysine to arginine is important because, unlike arginine, lysine is not synthesized by the central nervous system. It has been suggested that the relative concentration of lysine to arginine in the brain may be a factor that influences brain wellness.*^[7]

A Glance at Some Research A study in tissue culture demonstrated that the addition of lysine antagonized the viral growth-supporting nature of arginine.^[7] There is current interest in the possible benefit of lysine supplementation to support healthy cognition during the aging process.^[8] The lysine transporter could possibly decline with age, and dietary lysine intake (i.e., from meat) tends to decline with age. A three-month, randomized, double-blind, Syrian population-based study (n=93) demonstrated the negative mental health impact of consuming mostly incomplete-protein wheat as a dietary staple. As it is in most cereal grains, including wheat, lysine is the limiting amino acid. When the cereals were fortified with lysine, cortisol levels could be maintained within the normal range.*^[9]

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

L-Lysine Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
L-Lysine (as L-lysine HCl)	1 g	**
** Daily Value not established.		

Other Ingredients: HPMC (capsule), medium-chain triglyceride oil, stearic acid, magnesium stearate, and silica.

DIRECTIONS: Preferably on an empty stomach, take one to two capsules three times a day, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

**References**

- Rose WC. The amino acid requirements of adult man. *Nutr Abstr Rev Ser Hum Exp.* 1957 Jul;27(3):631-47. [PMID: 13465065]
- Kurpad AV, Raj T, El-Khoury A, et al. Lysine requirements of healthy adult Indian subjects, measured by an indicator amino acid balance technique. *Am J Clin Nutr.* 2001 May;73(5):900-7. [PMID:11333843]
- Elango R, Humayun MA, Ball RO, et al. Lysine requirement of healthy school-age children determined by the indicator amino acid oxidation method. *Am J Clin Nutr.* 2007 Aug;86(2):360-5. [PMID: 17684206]
- Food and Agriculture Organization of the United Nations (FAO). Energy and Protein Requirements: Report of a Joint FAO/WHO/UNU Expert Consultation. www.fao.org/DOCREP/003/AA040E/AA040E05.htm#ch5.6. Accessed May 31, 2012.
- Kriengsinyos W, Wykes LJ, Goonewardene LA, et al. Phase of menstrual cycle affects lysine requirement in healthy women. *Am J Physiol Endocrinol Metab.* 2004 Sep;287(3):E489-96. [PMID: 15308475]
- Fürst P. Dietary L-lysine supplementation: a promising nutritional tool in the prophylaxis and treatment of osteoporosis. *Nutrition.* 1993 Jan-Feb;9(1):71-2. [PMID: 8467115]
- Griffith RS, DeLong DC, Nelson JD. Relation of arginine-lysine antagonism to herpes simplex growth in tissue culture. *Chemotherapy.* 1981;27(3):209-13. [PMID: 6262023]
- Rubey RN. Could lysine supplementation prevent Alzheimer's dementia? A novel hypothesis. *Neuropsychiatr Dis Treat.* 2010 Oct 27;6:707-10. [PMID: 21127688]
- Smriga M, Ghosh S, Mouneimne Y, et al. Lysine fortification reduces anxiety and lessens stress in family members in economically weak communities in Northwest Syria. *Proc Natl Acad Sci U S A.* 2004 Jun 1;101(22):8285-8. [PMID: 15159538]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

L-Theanine

Patented Ingredient Supports Calm and Relaxation*



Available in 60 capsules and 120 capsules

Discussion

Green tea, prepared from the *Camellia sinensis* plant, has been consumed since ancient times for its calming influence. Modern research has looked into this “ancient wisdom” and revealed that L-theanine, an amino acid found almost exclusively in green tea, has specific and positive effects on the brain and nervous system, especially the promotion of relaxation without drowsiness.*

Neurological and Brain Support Human studies suggest that within 40 minutes of oral administration, L-theanine positively affected alpha waves in the brain, a phenomenon indicating relaxation.^[1] An eight-week, randomized, double-blind, placebo-controlled study, based on the premise that L-theanine “possesses neuroprotective, mood-enhancing, and relaxation properties,”^[2] suggested that 400 mg of L-theanine per day was found to be safe and effective. A double-blind counterbalanced study suggested that oral L-theanine positively influenced heart rate and salivary IgA levels, attenuated sympathetic nervous system activation, and positively supported individuals’ normal response to stress.^[3] In examining L-theanine’s effect on cognition, a randomized, double-blind, placebo-controlled study of 91 subjects suggested that individuals taking a combination of L-theanine and green tea extract experienced significant increases in theta waves in several areas of the brain, indicative of increased cognitive alertness.*^[4]

In cell studies, L-theanine appears to support neuronal health despite the presence of environmental toxins that ordinarily would increase the vulnerability of nigral dopaminergic neurons and negatively affect their function. L-theanine also appears to support neurological health by exerting a positive and significant impact on neurotrophic factors in the brain and assisting cell-signaling activity.*^[5]

Research into animal neurochemistry suggests that L-theanine positively supports overall nervous system health and activity due to its positive effects on serotonin, dopamine, and GABA levels, as well as its modulation of excitatory and inhibitory neurotransmission.^[6,7] L-theanine crosses the blood-brain barrier intact and may continue to

Clinical Applications

- » Promotes Relaxation Without Drowsiness*
- » Supports Nervous System Health and Function*
- » May Support Blood Pressure Already Within the Normal Range*
- » Supports Antioxidant and Detoxification Mechanisms*
- » May Support Liver Health and Function*

L-Theanine is a naturally occurring, unique amino acid found in green tea leaves. L-theanine has been found to reduce stress by promoting relaxation without drowsiness, easing nervousness due to overwork and fatigue, and reducing nervous irritability. Human studies suggest that it may also be useful in supporting concentration and in reducing negative side effects from caffeine. XYMOGEN’s L-Theanine (as Suntheanine®) is protected by several patents based on its positive effects.*

balance neurochemistry by blocking glutamate transport, significantly reducing levels of extracellular glutamate and supporting the release of dopamine and glycine from neurons.*^[6,8,9]

Hepatic, Detoxification, and Cardiovascular Support Research studying ethanol metabolism and hepatic toxicity in animals suggests that administration of L-theanine increases liver alcohol dehydrogenase and aldehyde dehydrogenase activity, reducing blood ethanol concentration within one hour compared to controls. It is also suggested that L-theanine’s effect on cytochrome P450 2E1 activity, glutathione recovery, and antioxidant mechanisms supports healthy liver tissue and function.^[10-12] L-theanine was observed to significantly inhibit hydrogen peroxide-induced cell death, and it may play an important role in the maintenance of liver health.^[13] L-theanine, along with green tea polyphenols, was found to provide antioxidant activity that supports healthy LDL and oxidation levels and may subsequently support cardiovascular health.^[14-16] Animal and human studies suggest that L-theanine supports healthy blood pressure in the normal range, in part because it moderates the negative side effects of caffeine.*^[1,17,18]

L-theanine and Suntheanine® Although theanine exists in both L- and D- forms, L-theanine is the preferred form due to its greater intestinal absorption and renal retention.^[19] An analysis of six commercial products revealed that five of them contained the poorly absorbed D-theanine along with L-theanine. Only Suntheanine, the brand in XYMOGEN’s L-Theanine, appeared to contain only the preferred L-theanine enantiomer.^[20] Suntheanine is protected by several patents that cover applications, such as reducing anxiety and promoting relaxation. The FDA has consequently approved the following structure/function claims regarding L-theanine: it reduces stress, it eases nervousness due to common everyday overwork and fatigue, and it reduces nervous irritability.^[18,21] XYMOGEN’s L-Theanine provides 400 mg of Suntheanine L-theanine per two-capsule dose.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

L-Theanine Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
L-Theanine (Suntheanine®)	400 mg	**
** Daily Value not established.		

Other Ingredients: HPMC (capsule), microcrystalline cellulose, stearic acid, magnesium stearate, silica, and medium-chain triglyceride oil.

DIRECTIONS: Take one to two capsules twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tampo seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.

Suntheanine®

Suntheanine® is a registered trademark of Taiyo International, Inc. U.S. and International Patents Pending. U.S. Patent Nos. 6831103, 6589566, 6297280.



References

1. Juneja LR, Chu D-C, Okubo T, et al. L-theanine – a unique amino acid of green tea and its relaxation effect in humans. *Trends Food Sci Technol*. 1999;10:199-204. [http://dx.doi.org/10.1016/S0924-2244\(99\)00044-8](http://dx.doi.org/10.1016/S0924-2244(99)00044-8).
2. Ritsner MS, Miodownik C, Ratner Y, et al. L-theanine relieves positive, activation, and anxiety symptoms in patients with schizophrenia and schizoaffective disorder: an 8-week, randomized, double-blind, placebo-controlled, 2-center study. *J Clin Psychiatry*. 2011 Jan;72(1):34-42. [PMID: 21208586]
3. Kimura K, Ozeki M, Juneja LR, Ohira H. L-Theanine reduces psychological and physiological stress responses. *Biol Psychol*. 2007 Jan;74(1):39-45. [PMID: 16930802]
4. Park SK, Jung IC, Lee WK, et al. A combination of green tea extract and L-theanine improves memory and attention in subjects with mild cognitive impairment: a double-blind placebo-controlled study. *J Med Food*. 2011 Apr;14(4):334-43. [PMID: 21303262]
5. Cho HS, Kim S, Lee SY, et al. Protective effect of the green tea component, L-theanine on environmental toxins-induced neuronal cell death. *Neurotoxicology*. 2008 Jul;29(4):656-62. [PMID: 18452993]
6. Yokogoshi H, Kobayashi M, Mochizuki M, et al. Effect of theanine, r-glutamylethylamide, on brain monoamines and striatal dopamine release in conscious rats. *Neurochem Res*. 1998 May;23(5):667-73. [PMID: 9566605]
7. Nathan PJ, Lu K, Gray M, et al. The neuropharmacology of L-theanine (N-ethyl-L-glutamine): a possible neuroprotective and cognitive enhancing agent. *J Herb Pharmacother*. 2006;6(2):21-30. Review. [PMID: 17182482]
8. Yamada T, Terashima T, Okubo T, et al. Effects of theanine, r-glutamylethylamide, on neurotransmitter release and its relationship with glutamic acid neurotransmission. *Nutr Neurosci*. 2005 Aug;8(4):219-26. [PMID: 16493792]
9. Kakuda T, Hinoi E, Abe A, et al. Theanine, an ingredient of green tea, inhibits [3H] glutamine transport in neurons and astroglia in rat brain. *J Neurosci Res*. 2008 Jun;86(8):1846-56. [PMID: 18293419]
10. Sadzuka Y, Inoue C, Hirooka S, et al. Effects of theanine on alcohol metabolism and hepatic toxicity. *Biol Pharm Bull*. 2005 Sep;28(9):1702-6. [PMID: 16141543]
11. Li G, Ye Y, Kang J, et al. L-Theanine prevents alcoholic liver injury through enhancing the antioxidant capability of hepatocytes. *Food Chem Toxicol*. 2012 Feb;50(2):363-72. [PMID: 22019691]
12. Sugiyama T, Sadzuka Y. Theanine, a specific glutamate derivative in green tea, reduces the adverse reactions of doxorubicin by changing the glutathione level. *Cancer Lett*. 2004 Aug 30;212(2):177-84. [PMID: 15279898]
13. Li G, Kang J, Yao X, et al. The component of green tea, L-theanine protects human hepatic L02 cells from hydrogen peroxide-induced apoptosis. *European food research & technology (Internet)*. 2011;233(3):427-35. <http://cat.inist.fr/?aModele=afficheN&cpsid=24465632>. Accessed March 28, 2012.
14. Yokozawa T, Dong E. Influence of green tea and its three major components upon low-density lipoprotein oxidation. *Exp Toxicol Pathol*. 1997 Dec;49(5):329-35. [PMID: 9455677]
15. Dufresne CJ, Farnworth ER. A review of latest research findings on the health promotion properties of tea. *J Nutr Biochem*. 2001 Jul;12(7):404-421. [PMID: 11448616]
16. NutriScience. Suntheanine® (Introduction). <http://www.l-theanine.com/intro.htm>. Accessed March 29, 2012.
17. Rogers PJ, Smith JE, Heatherley SV, et al. Time for tea: mood, blood pressure and cognitive performance effects of caffeine and theanine administered alone and together. *Psychopharmacology (Berl)*. 2008 Jan;195(4):569-77. [PMID: 17891480]
18. NutriScience Innovations. Suntheanine®. <http://www.nutriscienceusa.com/npSuntheanine.htm>. Accessed March 29, 2012.
19. Desai MJ, Gill MS, Hsu WH, et al. Pharmacokinetics of theanine enantiomers in rats. *Chirality*. 2005 Mar;17(3):154-62. [PMID: 15704209]
20. Desai MJ, Armstrong DW. Analysis of derivatized and underivatized theanine enantiomers by high-performance liquid chromatography/atmospheric pressure ionization-mass spectrometry. *Rapid Commun Mass Spectrom*. 2004;18(3):251-6. [PMID: 14755608]
21. Suntheanine®. What is Suntheanine? <http://www.suntheanine.com/WhatsSuntheanine.cfm>. Accessed March 29, 2012.

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Leptin Manager™

Targeting Fat Cells*



Available in 30 capsules

Discussion

Leptin is an adipose-derived hormone that facilitates communication between peripheral adipose tissue and the central nervous system for the control of appetite and the balance of energy. Leptin is secreted by adipocytes in proportion to their size and number. It is known to indicate satiety, to control appetite, and to participate in multiple regulatory mechanisms. These mechanisms include energy expenditure/metabolism and cell proliferation/differentiation; they also include signal interactions among other hormonal regulators of energy and metabolism, such as insulin.^[1,2]

Leptin resistance can occur when the body is overexposed to leptin (through adipose accumulation) and when pathways affecting leptin transport and signaling become disrupted, such as by a high-sugar diet or a high-fat (e.g., saturated triglyceride) diet.^[3-6] A body with leptin resistance becomes unresponsive to leptin's hormonal messages, such as satiety and reduced appetite. When leptin resistance is coupled with excess body weight, resistance to weight loss is common; furthermore, cytokine and metabolic alterations ensue,^[7] which can affect many facets of health, including joint and cardiovascular health.

Leptin Manager is a dietary supplement that provides ORALVISC®—a proprietary blend of hyaluronic acid and other glycosaminoglycans. In vitro, animal, and human studies suggest that this formula has an impact on leptin, adipogenesis, and body weight.*

In Vitro: Multipotent Cells

Mesenchymal stem cells (MSCs) are considered multipotent cells, which means that they are able to differentiate into chondrocytes, osteoblasts, and adipocytes in a competitively balanced manner. MSCs play a role in the homeostasis of adipose, bone, and joint tissues; consequently, factors influencing the differentiation of MSCs are of interest to researchers.^[8] The effect of ORALVISC on multipotent cell differentiation was tested using primary mouse embryo fibroblasts (MEFs) as a model system. The major finding was that exposure to ORALVISC suppressed spontaneous adipogenesis of MEFs, evidenced by the fact that it prevented the appearance of lipid-filled cells and the expression of adipogenic marker genes. The effect of ORALVISC on MEFs that had been hormonally-induced to differentiate into adipocytes was also tested. In this work, exposure to ORALVISC changed MEFs in the adipose state

Clinical Applications

- » Affects Adipogenesis and the Genetic Expression of Adipogenic Marker Genes in Multipotent Cells*
- » Affects Synovial Fluid and Serum Leptin Levels*
- » Supports Weight Loss*

*Leptin Manager™ represents an advanced, science-based strategy for positively affecting leptin levels. Leptin is a fat-cell derived hormone that is elevated in some individuals. Healthy leptin activity helps balance energy intake and expenditure by influencing appetite, food cravings, and metabolism.**

to a more favorable metabolic and secretory gene expression profile. The observed effects on MEFs produced by ORALVISC were not replicated by the individual ingredients in the formula, suggesting synergy among the formula's components.*^[8]

In Vivo: Mice

Obese 25-week-old C57BL6/J male mice were fed 3 mg/day of ORALVISC in order to study the formula's effect on weight loss. Animals treated with ORALVISC tended to lose more body weight more quickly than those in the control group (n = 7-8 per group). The supplemented mice also showed a higher and faster loss of body fat after switching from a high-fat, pre-study diet to the normal-fat, study diet. At sacrifice, the adiposity index was 30% lower and the circulating leptin levels were 40% lower in the treated animals. The treated animals also displayed reduced leptin gene expression in gonadal white adipose tissue and showed signs of increased insulin sensitivity.*^[9]

Human Clinical

A double-blind, randomized, controlled study tested the effects of ORALVISC on synovial fluid and serum leptin levels in overweight adults with joint discomfort. Forty patients completed the study; of these, 21 were given 80 mg of ORALVISC daily and 19 were given placebos. After 12 weeks, there was a significant (P < 0.05) decrease between initial and final—and between supplement and placebo—synovial and serum leptin levels, as measured by immunoassay. This result was accompanied by a significant (P < 0.05) reduction in synovial and serum cytokines and chemokines, including IL-1alpha, IL-1beta, and TNF-alpha.^[10,11] Significant improvements were recorded in joint comfort and function as assessed by VAS (visual analog scale) and WOMAC (Western Ontario and McMaster Universities osteoarthritis index) scores. Although participants were not told to change any lifestyle habits and their activities were monitored during the study, the supplemented group lost an average of 0.55 kilograms compared to a 0.75 kilogram weight gain in the placebo group over the 12-week period.^[10] Furthermore, as shown by post-hoc analysis, participants experienced a significant shift toward healthier blood lipid profiles; in contrast, no significant lipid-profile differences were detected in subjects treated with placebo.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

Leptin Manager™ Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Vitamin C (ascorbic acid)	15 mg	17%
ORALVISC® (proprietary, naturally occurring source of glycosaminoglycans (GAGs))	80 mg	**

** Daily Value not established

Other Ingredients: Microcrystalline cellulose, capsule (gelatin, carmine, and titanium dioxide), vegetable stearic acid, vegetable magnesium stearate, and silica.**DIRECTIONS:** Take one capsule in the morning, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep tightly closed in a cool, dry place out of reach of children.**DOES NOT CONTAIN:** Wheat, gluten, yeast, soy, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.**ORALVISC®** is a registered trademark licensed by Bioiberica, S.A.**References**

- Jéquier E. Leptin signaling, adiposity, and energy balance. *Ann N Y Acad Sci.* 2002 Jun;967:379-88. [PMID: 12079865]
- Fukuda M, Williams KW, Gautron L, et al. Induction of leptin resistance by activation of cAMP-Epac signaling. *Cell Metab.* 2011 Mar 2;13(3):331-39. [PMID: 21356522]
- Lin L, Martin R, Schaffhauser AO, et al. Acute changes in the response to peripheral leptin with alteration in the diet composition. *Am J Physiol Regul Integr Comp Physiol.* 2001 Feb;280(2):R504-09. [PMID: 11208581]
- Wang J, Obici S, Morgan K, et al. Overfeeding rapidly induces leptin and insulin resistance. *Diabetes.* 2001 Dec;50(12):2786-91. [PMID: 11723062]
- Shapiro A, Mu W, Roncal C, et al. Fructose-induced leptin resistance exacerbates weight gain in response to subsequent high-fat feeding. *Am J Physiol Regul Integr Comp Physiol.* 2008 Nov;295(5):R1370-75. [PMID: 18703413]
- Vasselli JR, Scarpace PJ, Harris RB, et al. Dietary components in the development of leptin resistance. *Adv Nutr.* 2013 Mar 1;4(2):164-75. [PMID: 23493533]
- Leon-Cabrera S, Solís-Lozano L, Suárez-Álvarez K, et al. Hyperleptinemia is associated with parameters of low-grade systemic inflammation and metabolic dysfunction in obese human beings. *Front Integr Neurosci.* 2013 Aug 23;7:62. [PMID: 23986664]
- Cross-talk between the adipogenic and the chondrogenic programs elicited by a glycosaminoglycan mixture. Barcelona, Spain: Bioiberica S.A.; 2013. [on file]
- A glycosaminoglycan-rich commercial preparation used in osteoarthritis management favors fat loss in diet-induced obese mice. Barcelona, Spain: Bioiberica S.A.; 2013. [on file]
- Wu W, Zvirbulis R, Zonca B, et al. An oral preparation containing hyaluronic acid (Oralvisc®) can significantly decrease the production of leptin levels in the serum and synovial fluid of osteoarthritic knee patients. Poster presented at: Orthopaedic Research Society (ORS) Annual Meeting. San Antonio, TX. January 26-29, 2013. [on file]
- Wu W, Pasierb M, Zonca B, et al. An oral preparation containing hyaluronic acid (Oralvisc®) can act systemically to decrease serum and synovial fluid levels of inflammatory cytokines and chemokines in osteoarthritic knee patients. Oral communication at: Orthopaedic Research Society (ORS) Annual Meeting. San Antonio, TX January 26-29, 2013. [on file]

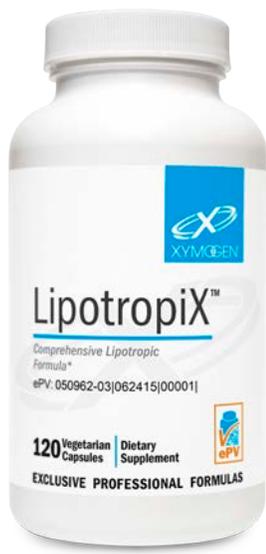
Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

LipotropiX™

Comprehensive Lipotropic Formula*



Available in 120 capsules

Discussion

LipotropiX is a specialized formula designed to target lipid metabolism and support healthy liver function.*

Inositol Hexanicotinate is a niacin derivative that consists of one molecule of inositol surrounded by six molecules of niacin. Over a period of time, the body slowly metabolizes niacin in this derived form so that the characteristic “niacin flush” is avoided. IHN is believed to work in the body in the same way as niacin: It decreases the mobilization of free fatty acids; inhibits cholesterol biosynthesis in the liver, specifically decreasing VLDL biosynthesis; and decreases the breakdown of HDL cholesterol.*^[1-3]

Greater Celandine (*Chelidonium majus*) is important in both Western phytotherapy and Traditional Chinese Medicine, as it exhibits a broad range of biological activities.^[4] Its inclusion in LipotropiX relates to in vitro and human studies that demonstrate its support of bile production and flow and its protective effect on liver cells.^[4-6] Human studies, cited in a review by Gilca et al,^[4] suggested that greater celandine helped relieve minor digestive and abdominal complaints related to the biliary system. To test the hepatotoxicity of greater celandine, researchers supplemented the diet of Wistar rats with doses that were approximately 50 to 100 times higher than those generally used in humans. The results indicated no alteration in hepatic function. Researchers caution against using greater celandine in situations (pharmacological treatments, etc.) that can compromise liver function.*^[7]

Dandelion (*Taraxacum officinale*), based on empirical findings, has been used medicinally as far back as the 10th and 11th centuries to support digestive health and kidney and liver function.^[8] Recent animal and in vitro research points to the cell-protective effects and antioxidant activity of dandelion.^[9] For instance, an in vitro study on increased lipid peroxidation in the cortex, hippocampus, and striatum of rats suggested that dandelion demonstrated protective antioxidant effects.^[10] In another study, rats that were supplemented with dandelion extract showed increased antioxidant liver enzymes,

Clinical Applications

- » May Support Bile Synthesis and Lipid Metabolism*
- » Helps Maintain Healthy Cholesterol Levels Already Within the Normal Range*
- » Supports Cardiovascular Health*
- » May Help Protect Liver Cells*

*LipotropiX™ is a specialized liver support formula that provides nutrients involved in fat metabolism, including choline, taurine, and methionine. Dandelion and celandine have been selected to support bile flow and healthy liver function. Guggul extract and inositol hexanicotinate are included to support healthy blood lipid levels already within the normal range.**

reduced lipid peroxidation, and improved blood lipid metabolism.*^[11]

Guggulsterones are the apparent bioactive compounds of guggul, an herbal extract from resin of the *Commiphora mukul* tree. Guggul is widely used in Ayurveda for its effect on blood lipids, and research suggests that guggulsterones may antagonize two nuclear hormone receptors involved in cholesterol metabolism. For example, it has been demonstrated that guggulsterone is a selective modulator of a particular bile acid receptor called a “farnesoid X receptor” (FXR). By acting as an antagonist to FXR, the guggulsterone can regulate the bile salt export pump. In other words, guggulsterone can modify the rate and amount of bile salts transported out of the liver.*^[12-14]

Choline is involved in lipid transport and metabolism. Without adequate choline, lipids accumulate in the liver. Fat and cholesterol are packaged into lipoproteins in the liver and transported in the bloodstream via very low-density lipoproteins (VLDL). The body needs choline to synthesize phosphatidylcholine, a required component of VLDL particles. Although the body can synthesize small amounts of choline, exogenous sources are needed to maintain health.*^[15]

Taurine, synthesized in the body from the amino acids methionine and cysteine, is considered a conditionally essential amino acid. It is required for efficient fat absorption and conjugation of bile acids, which solubilize cholesterol and increase its excretion. Studies suggest that taurine is important to various aspects of cardioprotection.^[16,17] A primary role of taurine in cardiovascular health relates to its ability to scavenge hypochlorous acid (HOCl), which is produced by myeloperoxidase in neutrophils and macrophages. HOCl is a major contributor to the oxidation of LDL (low-density lipoproteins).*^[17]

Methionine, a sulfur-containing essential amino acid, is one of the body’s most important methyl donors. Maintaining healthy levels of methionine is important for the downstream production of glutathione, a tripeptide that assists with the protection of the liver.*^[18]

LipotropiX™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Niacin (as inositol hexanicotinate)	375 mg	2344%
Inositol Hexanicotinate	500 mg	**
Choline Dihydrogen Citrate	200 mg	**
L-Methionine	200 mg	**
Taurine	100 mg	**
Dandelion 4:1 Extract (<i>Taraxacum officinale</i>)(root)	75 mg	**
Greater Celandine 10:1 Extract (<i>Chelidonium majus</i>)(whole herb)	50 mg	**
Guggulsterones (from guggul extract)(<i>Commiphora mukul</i>)(gum)	37.5 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), calcium silicate, silica, stearic acid, medium-chain triglyceride oil, and magnesium stearate.

DIRECTIONS: Take two capsules twice daily after meals, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

**References**

- Kruse W, Kruse W, Raetzer H, et al. Nocturnal inhibition of lipolysis in man by nicotinic acid and derivatives. *Eur J Clin Pharmacol.* 1979 Aug;16(1):11-15. [PMID: 499296]
- Yadav R, France M, Younis N, et al. Extended-release niacin with laropiprant: a review on efficacy, clinical effectiveness and safety. *Expert Opin Pharmacother.* 2012 Jun;13(9):1345-62. [PMID: 22607011]
- MacKay D, Hathcock J, Guarneri E. Niacin: chemical forms, bioavailability, and health effects. *Nutr Rev.* 2012 Jun;70(6):357-66. doi: 10.1111/j.1753-4887.2012.00479.x. [PMID: 22646128]
- Gilca M, Gaman L, Panait E, et al. Chelidonium majus—an integrative review: traditional knowledge versus modern findings. *Forsch Komplementmed.* 2010 Oct;17(5):241-48. [PMID:20980763]
- Vahlensieck U, Hahn R, Winterhoff H, et al. The effect of Chelidonium majus herb extract on choleresis in the isolated perfused rat liver. *Planta Med.* 1995 Jun;61(3):267-71. [PMID: 7617771]
- Niederer G, Göpfert E. The effect of chelidonium and turmeric root extract on upper abdominal pain due to functional disorders of the biliary system. Results from a placebo-controlled double-blind study [in German]. *Med Klin (Munich).* 1999 Aug 15;94(8):425-30. [PMID: 10495621]
- Mazzanti G, Di Sotto A, Franchitto A, et al. Chelidonium majus is not hepatotoxic in Wistar rats, in a 4 weeks feeding experiment. *J Ethnopharmacol.* 2009 Dec 10;126(3):518-24. [PMID: 19761826]
- Schütz K, Carle R, Schieber A. Taraxacum—a review on its phytochemical and pharmacological profile. *J Ethnopharmacol.* 2006 Oct 11;107(3):313-23. [PMID: 16950583]
- Mahesh A, Jeyachandran R, Cindrella L, et al. Hepatocurative potential of sesquiterpene lactones of Taraxacum officinale on carbon tetrachloride induced liver toxicity in mice. *Acta Biol Hung.* 2010 Jun;61(2):175-90. [PMID: 20519172]
- Colle D, Arantes LP, Rauber R, et al. Antioxidant properties of Taraxacum officinale fruit extract are involved in the protective effect against cellular death induced by sodium nitroprusside in brain of rats. *Pharm Biol.* 2012 Jul;50(7):883-91. [PMID: 22480378]
- Cho SY, Park JY, Park EM, et al. Alternation of hepatic antioxidant enzyme activities and lipid profile in streptozotocin-induced diabetic rats by supplementation of dandelion water extract. *Clin Chim Acta.* 2002 Mar;317(1-2):109-17. [PMID: 11814465]
- Yu BZ, Kaimal R, Bai S, et al. Effect of guggulsterone and cembranoids of Commiphora mukul on pancreatic phospholipase A(2): role in hypocholesterolemia. *J Nat Prod.* 2009 Jan;72(1):24-28. [PMID: 19102680]
- Deng R. Therapeutic effects of guggul and its constituent guggulsterone: cardiovascular benefits. *Cardiovasc Drug Rev.* 2007 Winter;25(4):375-90. [PMID: 18078436]
- Cui J, Huang L, Zhao A, et al. Guggulsterone is a farnesoid X receptor antagonist in coactivator association assays but acts to enhance transcription of bile salt export pump. *J Biol Chem.* 2003 Mar 21;278(12):10214-20. [PMID: 12525500]
- Micronutrient Information Center: Choline. Linus Pauling Institute. Micronutrient Research for Optimum Health. <http://lpi.oregonstate.edu/infocenter/othernuts/choline/>. Accessed August 20, 2012.
- Xu YJ, Arneja AS, Tappia PS, et al. The potential health benefits of taurine in cardiovascular disease. *Exp Clin Cardiol.* 2008 Summer;13(2):57-65. [PMID: 19343117]
- Ito T, Azuma J. Taurine is a possible anti-atherosclerotic agent [in Japanese]. *Nihon Yakurigaku Zasshi.* 2004 May;123(5):311-17. [PMID: 15118255]
- Methionine. Full Monograph. Natural Medicine's Comprehensive Database. <http://naturaldatabase.therapeuticresearch.com/nd/Search.aspx?cs=&s=ND&pt=100&id=42&fs=ND&searchid=36616394>. Accessed August 20, 2012.

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Liver Protect™

Hepatic Support Formula*



Available in 60 capsules & 120 capsules

Discussion

The liver is the body's major metabolic organ. It processes, packages, stores, and ships out carbohydrates, fats, proteins, and micronutrients. It is responsible for the breakdown and elimination of alcohol, toxins, hormones, and medications, as well as for the synthesis of vital proteins, such as albumin, prealbumin, and clotting factors. It may be stated that the health of the body depends on the health of the liver. Research suggests that providing targeted nutrition supplementation may help support liver function and health.*^[1]

N-Acetyl-Cysteine (NAC) An acetylated derivative of the sulfur-containing amino acid L-cysteine, NAC promotes the synthesis of glutathione—a tripeptide that is active in detoxification and antioxidant systems. Glutathione also supports a healthy defense against hepatotoxic environmental pollutants, gamma-radiation, and other potential toxins.*^[1,2]

Alpha-Lipoic Acid Sometimes referred to as thioctic acid, alpha-lipoic acid is both water- and fat-soluble. It supports glutathione, helps regenerate antioxidant vitamins C and E, helps maintain the ratio of reduced to oxidized CoQ10 in the mitochondria, and helps support healthy levels of nitric oxide in the liver and kidney.^[3] The redox couple of lipoic acid and dihydrolipoic stabilizes NF-kappaB transcription and may help support healthy immune functions in the body.*^[4,5]

Milk Thistle Seed Extract Silymarin, the active component in milk thistle, has a history of use in promoting liver health. It supports antioxidant activity, neutralizes toxins, and also may protect hepatocytes' genetic material. Like alpha-lipoic acid, silymarin supports production of cellular glutathione. Its actions in the liver include maintaining normal levels of fat peroxidation and fibrous tissue formation; supporting a healthy immune response and the natural response to inflammation; and promoting protein synthesis and normal regeneration of liver tissue.^[6] A randomized placebo-controlled study of 103 individuals suggested that silymarin yielded statistically positive results and was well tolerated.*^[7]

Clinical Applications

- » Supports Healthy Liver Function*
- » Supports Cytokine Balance*
- » Supports Glutathione Production*
- » May Protect Liver Tissue*

*Liver Protect™ contains the amino acid N-acetyl-L-cysteine, a key component of glutathione—a tripeptide that plays a significant role in detoxification and antioxidant support. Liver Protect also contains a combination of alpha-lipoic acid, silymarin from milk thistle, and selenium for support of antioxidant activity, regeneration of other antioxidants, and promotion of healthy immune function.**

Selenium (as selenomethionine) An important coenzyme for the glutathione peroxidase detoxification system, selenium also appears to support the endogenous antioxidant defenses of hepatocytes by upregulating their manganese superoxide dismutase (MnSOD) expression. At the same time, selenium appears to support healthy cytokine balance by affecting interleukin-6 (IL-6) transcription in Kupffer cells (liver-based macrophages).^[8] Kupffer cells play a crucial role in maintaining normal structure and function in the liver. Supporting their function and the body's normal inflammatory response in turn supports liver health overall.*^[9]

Upon studying targeted nutrition support for liver health, physician and researcher Dr. Burton M. Berkson chose to combine alpha-lipoic acid, silymarin, and selenium to obtain a balanced and low-cost approach to liver support.^[10] These three ingredients plus NAC are all present in Liver Protect™ to support liver health, antioxidant activity, and the body's natural immune defenses.*

Liver Protect™ Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Selenium (as L-selenomethionine)	100 mcg	182%
Milk Thistle Extract (<i>Silybum marianum</i>)(seed)(80% silymarin)	262.5 mg	**
Alpha-Lipoic Acid	200 mg	**
N-Acetyl-L-Cysteine	200 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), stearic acid, microcrystalline cellulose, magnesium stearate, and silica.**DIRECTIONS:** Take one capsule twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.**DOES NOT CONTAIN:** Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.**References**

1. Krinsky DL, LaValle JB, Hawkins EB, et al. *Natural Therapeutics Pocket Guide*. 2nd ed. Hudson (OH): Lexi-Comp; 2003.
2. Hu C, Jiang L, Geng C, et al. Possible involvement of oxidative stress in trichloroethylene-induced genotoxicity in human HepG2 cells. *Mutat Res*. 2008 Jan 18. [PMID: 18289923]
3. Abdel-Zaher AO, Abdel-Hady RH, Mahmoud MM, et al. The potential protective role of alpha-lipoic acid against acetaminophen-induced hepatic and renal damage. *Toxicology*. 2008 Jan 20;243(3):261-70. [PMID: 18068886]
4. Suzuki YJ, Aggarwal BB, Packer L. Alpha-lipoic acid is a potent inhibitor of NF-kappa B activation in human T cells. *Biochem Biophys Res Commun*. 1992 Dec 30;189(3):1709-15. [PMID: 1482376]
5. Baur A, Harter T, Peukert M, et al. Alpha-lipoic acid is an effective inhibitor of human immuno-deficiency virus (HIV-1) replication. *Klin Wochenschr*. 1991 Oct 2;69(15):722-4. [PMID: 1724477]
6. Pradhan SC, Girish C. Hepatoprotective herbal drug, silymarin from experimental pharmacology to clinical medicine. *Indian J Med Res*. 2006 Nov;124(5):491-504. [PMID: 17213517]
7. El-Kamary SS, Shardell MD, Abdel-Hamid M, et al. A randomized controlled trial to assess the safety and efficacy of silymarin on symptoms, signs and biomarkers of acute hepatitis. *Phytomedicine*. 2009 May;16(5):391-400. [PMID: 19303273]
8. Shilo S, Pardo M, Aharoni-Simon M, et al. Selenium supplementation increases liver MnSOD expression: molecular mechanism for hepato-protection. *J Inorg Biochem*. 2008 Jan;102(1):110-8. [PMID: 17804075]
9. Roberts RA, Ganey PE, Ju C, et al. Role of the Kupffer cell in mediating hepatic toxicity and carcinogenesis. *Toxicol Sci*. 2007 Mar;96(1):2-15. Review. [PMID: 17122412]
10. Berkson BM. A conservative triple antioxidant approach to the treatment of hepatitis C. Combination of alpha lipoic acid (thioctic acid), silymarin, and selenium: three case histories. *Med Klin (Munich)*. 1999 Oct 15;94 Suppl 3:84-9. [PMID: 10554539]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Magnesium Citrate



Available in 120 vegetarian capsules

Discussion

Magnesium—the fourth most abundant mineral in the body—participates in over 300 enzymatic reactions in nearly all tissues. Deficiency is common. The average American diet is thought to provide about 40% of the daily magnesium need, and reports from the World Health Organization have suggested that three quarters of Americans fall short of the daily requirement.^[1] Furthermore, because magnesium is predominantly an intracellular cation, serum magnesium remains a poor predictor of tissue magnesium content and availability; therefore, deficiency can sometimes go undetected.^[1] Magnesium deficiency can result from poor dietary intake, poor absorption, and excessive losses through urine, stool, perspiration, or lactation. Certain drugs, certain herbs, poor kidney function, excessive alcohol intake, and drinking mostly “soft” water can contribute to magnesium depletion.^[1,2] It is also important to note that physical and emotional stresses increase the need for magnesium and that hypomagnesemia and stress potentiate each other’s negative effects.^[3,4] Moreover, the adrenergic effects of psychological stress cause movement of magnesium from intracellular to extracellular space, which increases urinary excretion and depletion of body stores.*^[4,5]

Magnesium participates in the development and maintenance of bones and teeth; the metabolism of carbohydrates, proteins, and fats; the formation of cells and tissues; the modulation of cytokines; and the maintenance of muscle function, including the heart.^[1,6,7] Magnesium, in the form of magnesium citrate, is often used in the short term for bowel movement support, and some individuals find it useful for preventing calcium crystallization in the kidneys.*

Bioavailability

In vitro and in vivo research has demonstrated superior solubility and bioavailability of magnesium citrate compared to magnesium oxide.^[8] A 60-day randomized, double-blind, placebo-controlled, parallel intervention study compared a daily dose of 300 mg of elemental magnesium as magnesium citrate to the oxide and chelate forms. In this study (n=46), magnesium citrate showed the greatest increase in

Clinical Applications

- » Supports Magnesium Nutritional Adequacy*
- » Supports the Numerous Metabolic Activities of Magnesium in the Body*
- » Facilitates Bowel Movement*
- » Helps Prevent Calcium Crystallization in the Kidneys*

*Magnesium plays a vital role in hundreds of metabolic activities. The mineral particularly supports muscle and nervous system function. **Magnesium Citrate** supports healthy bowel movement by attracting water when it is in the intestine.**

magnesium concentration in the 24-hour and 60-day post-supplementation serum and saliva specimens.*^[9]

Bowel Movement Support

Magnesium citrate is a magnesium salt with citric acid in a 1:1 ratio. The bioavailability and pharmacokinetics of various magnesium salts correlate with their structure/activity relationship. Magnesium citrate is considered to be a purgative because it relaxes the bowel and pulls water into the intestine. This, in turn, softens the stool and stimulates movement of the muscles in the colon, leading to a bowel movement.*

Kidney Support

According to studies on magnesium and citrate, increased water intake and supplementation with magnesium or citrate help bind calcium and prevent its crystallization and aggregation—actions that support kidney health.^[10,11] In one study, magnesium citrate was found to inhibit the growth of stone fragments after extracorporeal shock wave lithotripsy.^[12] In other research, calcium phosphate and calcium oxalate deposits were higher in individuals with low urinary citrate levels.*^[13]

Other Research

A sampling of studies on PubMed indicates that at doses of 300-500 mg/d, magnesium citrate also has roles in supporting sleep quality,^[14] improving metabolic markers (e.g., fasting insulin and C-peptide) in overweight individuals,^[15] maintaining healthy blood pressure already within the normal range,^[16] and reducing nighttime leg cramps.^[17] These varied effects illustrate the many metabolic and physiological roles of magnesium and the usefulness of magnesium in citrate form.*

Magnesium Citrate Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Magnesium (as magnesium citrate)	100 mg	24%

Other Ingredients: Capsule (hypromellose and water), ascorbyl palmitate, and silica.

DIRECTIONS: Take one capsule daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



References

1. Long S, Romani AM. Role of cellular magnesium in human diseases. *Austin J Nutr Food Sci*. 2014 Nov 18;2(10). [PMID: 25839058]
2. Swaminathan R. Magnesium metabolism and its disorders. *Clin Biochem Rev*. 2003 May;24(2):47-66. [PMID: 18568054]
3. Seelig MS. Consequences of magnesium deficiency on the enhancement of stress reactions; preventive and therapeutic implications (a review). *J Am Coll Nutr*. 1994 Oct;13(5):429-46. [PMID: 7836621]
4. Vink R, Nechifor M, eds. *Magnesium in the Central Nervous System*. Adelaide, South Australia: University of Adelaide Press; 2011. <https://www.adelaide.edu.au/press/titles/magnesium/magnesium-ebook.pdf>. Accessed September 26, 2016.
5. Galland L. Magnesium, stress and neuropsychiatric disorders. *Magnes Trace Elem*. 1991-1992;10(2-4):287-301. [PMID: 1844561]
6. Nielsen FH. Effects of magnesium depletion on inflammation in chronic disease. *Curr Opin Clin Nutr Metab Care*. 2014 Nov;17(6):525-30. [PMID: 25023192]
7. Kramer JH, Spurney C, Iantorno M, et al. Neurogenic inflammation and cardiac dysfunction due to hypomagnesemia. *Am J Med Sci*. 2009 Jul;338(1):22-27. [PMID: 19593099]
8. Lindberg JS, Zobitz MM, Poindexter JR, et al. Magnesium bioavailability from magnesium citrate and magnesium oxide. *J Am Coll Nutr*. 1990 Feb;9(1):48-55. [PMID: 2407766]
9. Walker AF, Marakis G, Christie S, et al. Mg citrate found more bioavailable than other Mg preparations in a randomised, double-blind study. *Magnes Res*. 2003 Sep; 16(3):183-91. [PMID: 14596323]
10. Guerra A, Meschi T, Allegri F, et al. Concentrated urine and diluted urine: the effects of citrate and magnesium on the crystallization of calcium oxalate induced in vitro by an oxalate load. *Urol Res*. 2006 Dec;34(6):359-64. [PMID: 16953377]
11. Caudarella R, Vescini F. Urinary citrate and renal stone disease: the preventive role of alkali citrate treatment. *Arch Ital Urol Androl*. 2009 Sep;81(3):182-87. [PMID: 19911682]
12. Abdel-Halim RE. Urolithiasis in adults. Clinical and biochemical aspects. *Saudi Med J*. 2005 May;26 (5):705-13. [PMID: 15951854]
13. Phillips R, Hanchanale VS, Myatt A, et al. Citrate salts for preventing and treating calcium containing kidney stones in adults. *Cochrane Database Syst Rev*. 2015 Oct 6;(10):CD010057. [PMID: 26439475]
14. Nielsen FH, Johnson LK, Zeng H. Magnesium supplementation improves indicators of low magnesium status and inflammatory stress in adults older than 51 years with poor quality sleep. *Magnes Res*. 2010 Dec;23(4):158-68. [PMID: 21199787]
15. Chacko SA, Sul J, Song Y, et al. Magnesium supplementation, metabolic and inflammatory markers, and global genomic and proteomic profiling: a randomized, double-blind, controlled, crossover trial in overweight individuals. *Am J Clin Nutr*. 2011 Feb;93(2):463-73. [PMID: 21159786]
16. Bullarbo M, Ödman N, Nestler A, et al. Magnesium supplementation to prevent high blood pressure in pregnancy: a randomised placebo control trial. *Arch Gynecol Obstet*. 2013 Dec;288(6):1269-74. [PMID: 23715924]
17. Roffe C, Sills S, Crome P, et al. Randomised, cross-over, placebo controlled trial of magnesium citrate in the treatment of chronic persistent leg cramps. *Med Sci Monit*. 2002 May; 8(5):CR326-30. [PMID: 12011773]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

MCT Powder

Fuel for Brain and Muscles*



Available in 30 stick packs

Discussion

Medium-chain triglycerides (MCTs) are found in coconut oil, palm kernel oil, and dairy fat. MCTs differ from other triglycerides in that each fat molecule comprises only six to 12 carbons in length. Due to this structural uniqueness, MCTs are absorbed and utilized differently from long-chain triglycerides. They are relatively soluble in water and more readily hydrolyzed, which facilitates absorption. Once in the bloodstream, MCTs are transported through the portal system, bypassing adipose tissue. This route makes them less susceptible to hormone-sensitive lipase and deposition into adipose tissue stores.^[1] The liver metabolizes MCTs into ketones which can then be used as a quick fuel source alternative to glucose and does not appear to impact insulin levels. Furthermore, MCTs can permeate the mitochondria without the aid of enzymes.^{*[2]}

Due to the collective significance of these attributes, it has been suggested that MCTs may have a role to play in the management of healthy body weight, body composition, and exercise performance.^[1,3-5] However, other than a presumed potential benefit in supplementing MCTs to individuals who do not absorb long-chain dietary fats well, further research is needed to determine efficacy and ideal dosage.*

Additionally, although most of the clinical research has utilized the oil form of MCT, anecdotal feedback suggests that a powdered delivery form offers the same benefits as the oil but with better gut tolerability (or less GI distress) and is more convenient to the consumer. To convert the oil to a solid powder form, the MCT oil is spray-dried and micro-encapsulated with acacia fiber.*

Human studies utilizing a 3 g powdered dose of MCT are limited; however, the results of a 90-day study (2007) in moderately overweight free-living type 2 diabetic subjects in urban China (N = 40) suggested that moderate consumption of MCTs might be linked to improved risk factors in this population. The test group consumed 18 g/day of MCT oil; the controls were given corn oil. While the corn oil group had no significant changes, the MCT group showed an across-time (0, 45, 90 days) reduction in body weight and waist circumference, an increase in serum C-peptide concentration, a reduction in homeostasis model assessment of insulin resistance, and a decrease in serum cholesterol concentration (P < .05, repeated measures). The MCT group also showed a reduction in daily caloric intake,^[2] a phenomenon similar to that identified in a 1983 three-part rat study. In the study, diabetic rats that ingested MCTs reduced their food intake within two hours while diabetic rats that consumed long-chain triglycerides in the form of corn oil reduced their caloric-intake in two to four hours.^{*[6]}

Clinical Applications

- » May Support Management of Healthy Body Weight and Body Composition*
- » Ketone Body Precursor*
- » Supports Cognitive Health*
- » Provides Direct Fuel Source for Energy*
- » May Enhance Exercise Performance*
- » Promotes Gut Health*

*MCT Powder features goMCT® a patented medium-chain triglyceride (MCT) powder with high caprylic acid and capric acid content (C8/C10). MCTs are absorbed intact, are not stored as body fat, are excellent ketone body precursors, and provide a quick energy source without impacting insulin levels. goMCT® also contains acacia fiber, a prebiotic that may promote gut health.**

A 2013 systematic review and meta-analysis of randomized controlled studies on the effect of MCTs versus long-chain triacylglycerols (LCTs) on body composition in adults (11 studies, five deemed not to have any bias) demonstrated that individuals who replaced dietary LCTs with MCTs showed “significantly reduced body weight (WMD, -0.69 kg; 95% confidence interval [CI], -1.1 to -0.28; p = 0.001); body fat (-0.89 kg; 95% CI, -1.27 to -0.51; p < 0.001), and WC (waist circumference) (-1.78 cm; 95% CI, -2.4 to -1.1; P < 0.001).” However, the reviewers stated that “overall quality of the evidence was low-to-moderate” and that “trials with a crossover design were responsible for the heterogeneity.”^{*[7]}

Research into the effect of MCTs has been ongoing since 2013. Though not having human subjects limits relevancy, a 2018 study (similar to the 2007 human study noted prior) demonstrated a positive effect on serum lipids of MCTs combined with a controlled diet. This eight-week study on streptozotocin-induced type 2 diabetes (T2DM) rats given a high-fat or a low-fat diet with either soybean oil or MCT oil showed that MCT oil in conjunction with a high-fat diet lowered serum low-density lipoprotein cholesterol (LDL-C), non-esterified fatty acids, and liver total cholesterol while it increased serum high-density lipoprotein cholesterol (HDL-C) and the HDL-C/LDL-C ratio. In comparison to T2DM rats fed a high-fat soybean oil diet, the rats on the low-fat MCT oil diet had lower body weight and reproductive white adipose tissue. Also, compared to the T2DM rats given the low-fat soybean oil diet, the T2DM rats on the low-fat MCT oil diet showed higher hepatic acyl-CoA oxidase activities (an enzyme key to peroxisomal beta-oxidation).^{*[8]}

MCTs have also been suggested to be a beneficial adjunct to a ketogenic diet because of their ability to convert to ketone bodies. Concluding in a March 2018 published narrative review that the number and scope of studies related to the use of nutritional supplements to induce ketosis and reduce symptoms associated with keto induction were inadequate,^[9] the same researchers performed a randomized, double-blind, placebo-controlled trial (N = 28) in May 2018 to determine whether MCTs reduce time to nutritional ketosis. Secondly, the researchers wanted to see if MCTs reduce symptoms that commonly occur as the body transitions from a glucose-dominant fuel system to reliance on ketones and whether mood is affected. Participants were randomized into two groups and received 30 mL/day of MCT or sunflower oil for 20 days in conjunction with a ketogenic diet. Although differences between the MCT and sunflower oil groups failed to meet significance (P = 0.30), mean time to nutritional ketosis was one day shorter in the MCT group. Compared to the control group, the MCT group had comparatively lower symptoms associated

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

with keto-induction for some but not all days. The difference between groups for mood was unclear.*^[10]

Animal and human studies have explored the potential role of MCTs in increasing ketones and supporting brain health. In a study of adults (N = 20) with cognitive impairment who were given MCTs or placebo, significant increases in beta-hydroxybutyrate (BHB)—one of the three primary ketone bodies—were observed 90 minutes post-treatment when recall tests were administered.^[11] In a 90-day, randomized, double-blind, placebo-controlled, parallel group study, subjects (N = 152) with mild-to-moderate Alzheimer's disease were given an oral ketogenic MCT compound to determine if ketosis could affect cognitive performance. Significantly elevated levels of BHB were seen two hours after administration when compared to placebo. Correspondingly, elevated BHB levels resulted in significant differences in Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog) scores when compared to placebo.*^[12]

A 2018 study demonstrated increased mitochondrial biogenesis and metabolism thereby improving exercise performance in mice.^[13] Research on MCTs as fuel for exercise also continues to emerge. A small study using recreational athletes as subjects (N = 8) suggested that when consuming MCTs, blood lactate levels and rate of perceived exertion during moderate-intensity exercise were significantly reduced.^[14] Another small study suggested that endurance-trained cyclists (N = 6) who consumed MCTs during moderate-intensity exercise for two hours had significant improvements in time-trial performances during subsequent high-intensity exercise.^[15] Additional research in larger trials is necessary before any definitive conclusions can be drawn related to the effects of MCTs on exercise performance enhancement.*

XYMOGEN's MCT Powder contains a patented medium-chain triglyceride powder with a high caprylic and capric acid content plus acacia fiber. This fiber acts as a prebiotic that promotes changes in the composition and/or activity in the gastrointestinal microflora. Acacia fiber resists digestion in the small intestine; it is fermented by the gut microflora in the colon to promote overall gut health.^[16] With the knowledge of the importance of the role of gut-brain axis in health, this formula combines MCT and acacia fiber to potentially optimize this axis.*

MCT Powder Supplement Facts

Serving Size: 1 Stick Pack (about 7.8 g)

	Amount Per Serving	%Daily Value
Calories	45	
Total Fat	3.5 g	4% [†]
Saturated Fat	3.5 g	18% [†]
Total Carbohydrate	4 g	1% [†]
Dietary Fiber	4 g	14%
goMCT® Medium-Chain Triglycerides (MCTs)	3 g	**

[†] Percent Daily Values are based on a 2,000 calorie diet.
** Daily Value not established.

Other Ingredients: Gum acacia and silica.

DIRECTIONS: Mix the contents of one stick pack in 6-12 oz of water or beverage of choice, or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if stick pack is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, corn, soy, animal or dairy products, fish, shellfish, peanuts, tree nut protein, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



goMCT® is a registered trademark under exclusive global distribution by Compound Solutions, Inc.

References

- Clegg ME. Medium-chain triglycerides are advantageous in promoting weight loss although not beneficial to exercise performance. *Int J Food Sci Nutr.* 2010 Nov;61(7):653-79. [PMID: 20367215]
- Han JR, Deng B, Sun J, et al. Effects of dietary medium-chain triglyceride on weight loss and insulin sensitivity in a group of moderately overweight free-living type 2 diabetic Chinese subjects. *Metabolism.* 2007 Jul;56(7):985-91. [PMID: 17570262]
- Mumme K, Stonehouse W. Effects of medium-chain triglycerides on weight loss and body composition: a meta-analysis of randomized controlled trials. *J Acad Nutr Diet.* 2015 Feb;115(2):249-63. [PMID: 25636220]
- Babayan VK. Medium chain triglycerides and structured lipids. *Lipids.* 1987 Jun;22(6):417-20. [PMID: 3112486]
- Bach AC, Babayan VK. Medium-chain triglycerides: an update. *Am J Clin Nutr.* 1982 Nov;36(5):950-62. [PMID: 6814231]
- Friedman MI, Edens NK, Ramirez I. Differential effects of medium-and long-chain triglycerides on food intake of normal and diabetic rats. *Physiol Behav.* 1983 Dec;31(6):851-5. [PMID: 6686684]
- Bueno NB, de Melo IV, Florêncio TT, et al. Dietary medium-chain triacylglycerols versus long-chain triacylglycerols for body composition in adults: systematic review and meta-analysis of randomized controlled trials. *J Am Coll Nutr.* 2015;34(2):175-83. [PMID: 25651239]
- Sung MH, Liao FH, Chien YW. Medium-chain triglycerides lower blood lipids and body weight in streptozotocin-induced type 2 diabetes rats. *Nutrients.* 2018 Jul 26;10(8). pii: E963. [PMID: 30049949]
- Harvey CJDC, Schofield GM, Williden M. The use of nutritional supplements to induce ketosis and reduce symptoms associated with keto-induction: a narrative review. *PeerJ.* 2018 Mar 16;6:e4488. [PMID: 29576959]
- D C Harvey CJ, Schofield GM, Williden M, et al. The effect of medium chain triglycerides on time to nutritional ketosis and symptoms of keto-induction in healthy adults: a randomised controlled clinical trial. *J Nutr Metab.* 2018 May 22;2018:2630565. [PMID: 29951312]
- Reger MA, Henderson ST, Hale C, et al. Effects of beta-hydroxybutyrate on cognition in memory-impaired adults. *Neurobiol Aging.* 2004 Mar; 25 (3):311-4. [PMID: 15123336]
- Henderson ST, Vogel JL, Barr LJ, et al. Study of the ketogenic agent AC-1202 in mild to moderate Alzheimer's disease: a randomized, double-blind, placebo controlled, multicenter trial. *Nutr Metab (Lond).* 2009 Aug 10;6:31. [PMID: 19664276]
- Wang Y, Liu Z, Han Y, et al. Medium chain triglycerides enhances exercise endurance through the increased mitochondrial biogenesis and metabolism. *PLoS One.* 2018 Feb 8;13(2):e0191182. [PMID: 29420554]
- Nosaka N, Suzuki Y, Nagatoishi A, et al. Effect of ingestion of medium-chain triacylglycerols on moderate- and high-intensity exercise in recreational athletes. *J Nutr Sci Vitaminol (Tokyo).* 2009 Apr;55(2):120-5. [PMID: 19436137]
- Van Zyl CG, Lambert EV, Hawley JA, et al. Effects of medium-chain triglyceride ingestion on fuel metabolism and cycling performance. *J Appl Physiol* (1985). 1996 Jun;80(6):2217-25. [PMID: 8806933]
- Slavin J. Fiber and prebiotics: mechanisms and health benefits. *Nutrients.* 2013 Apr 22;5(4):1417-35. [PMID: 23609775]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

MedCaps DPO™

Dual-Phase Optimizers*



Available in 120 capsules

Discussion

The term “Dual-Phase Optimizers” refers to those substances with the ability to simultaneously influence and “optimize” the activity of certain phase I and phase II detoxification enzyme systems. Optimizers generally upregulate or induce phase II enzymes; however, optimizing phase I enzymes may mean downregulating them, without totally inhibiting them, when they are too high. Dual-phase optimizers may further balance the phases of detoxification by supporting antioxidant defense systems and binding free radicals formed between the two phases.*

Examples of dual-phase optimizers in MedCaps DPO™ include ellagic acid from pomegranate, catechins from green tea extract, and glucosinolates from watercress powder. Ellagic acid induces phase II enzymes at the gene level and ensures these are not over-induced by modulation of CYP1A (cytochrome P450 1A) activities.^[1,2] In addition, ellagic acid can bind directly to DNA to protect it and can also bind directly to some toxic substances to promote their excretion. The catechins in green tea support antioxidant activity and may bind directly to toxic substances as well, performing dual functions during detoxification. When toxic substances are encountered, catechins modulate detoxification by limiting phase I enzyme production.^[3] Glucosinolates are precursors to isothiocyanates. Watercress, in particular, is metabolized by gut flora into phenylethyl isothiocyanate (PEITC), which, like the other ingredients above, can selectively inhibit phase I enzymes and induce the activities of phase II enzymes.*^[4]

Liver detoxification is further supported with the inclusion of silymarin (milk thistle seed extract), artichoke leaf extract, and alpha-lipoic acid, all of which are selected for their hepatoprotective properties. These key players also promote glutathione production and assist with antioxidant protection.*^[5-7]

Additional ingredients in this formula are present to support vital phase II detoxification pathways. Key ingredients that support methylation include methylsulfonylmethane (MSM), methylcobalamin (B12), and 5-methyltetrahydrofolate (folate).^[9] 5-methyltetrahydrofolate

Clinical Applications

- » Supports Balanced Detoxification (Phases I & II)*
- » Supports Liver Health and Energy Generation*
- » Promotes a Variety of Phase II Pathways*
- » Supports Natural Antioxidant Mechanisms*

*MedCaps DPO™ is formulated to support phase I and phase II detoxification, hence the term “Dual-Phase Optimizers.” Ellagic acid, catechins, glucosinolates, silymarin, artichoke leaf, alpha-lipoic acid, methylsulfonylmethane (MSM), N-acetyl-L-cysteine (NAC), and calcium D-glucarate support critical steps in the complex process of detoxification—a function essential to overall health and vitality. This unique formula provides activated B vitamins for enhanced bioavailability, including 5-methyltetrahydrofolate (5-MTHF) as Quatrefolic® for optimal folate utilization. MedCaps DPO provides antioxidant support to minimize the damaging effects of free radicals generated between the two phases.**

(5-MTHF) is present as Quatrefolic® (a stable, bioavailable form of folate) to support methylation, energy generation, and phase I and phase II activity. Calcium D-glucarate has been added to support glucuronidation. Sulfate donors sodium sulfate and N-acetyl-cysteine (NAC) are especially important in cases of heavy-metal burden because they support glutathione production and the sulfation pathway.*^[9-13]

MedCaps DPO is designed to be part of a comprehensive detoxification protocol that includes adequate high-quality protein, carbohydrates, fats, and fiber. The resulting combination provides micronutrients to support the active phases of detoxification and macronutrients to support energy production, amino acid conjugation, and elimination.*

MedCaps DPO™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Vitamin B6 (as pyridoxal 5'-phosphate)	25 mg	1471%
Folate (as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt)	200 mcg DFE	50%
Vitamin B12 (as MecobalActive™ methylcobalamin)	100 mcg	4167%
Artichoke Aqueous Extract (<i>Cynara scolymus</i>)(leaf)(2.5% cynarin)	300 mg	**
Watercress (<i>Nasturtium officinale</i>)(aerial parts)	250 mg	**
Milk Thistle Extract (<i>Silybum marianum</i>)(seed)(80% silymarin)	118 mg	**
Pomegranate Extract (<i>Punica granatum</i>)(hull)(40% ellagic acid)	125 mg	**
Alpha-Lipoic Acid	100 mg	**
N-Acetyl-L-Cysteine	100 mg	**
Sodium Sulfate Anhydrous	100 mg	**
Green Tea Aqueous Extract (<i>Camellia sinensis</i>)(leaf)(80% polyphenols, 60% catechins, 30% EGCG, 6% caffeine)	93.75 mg	**
Methylsulfonylmethane (MSM)	50 mg	**
Calcium D-Glucarate	50 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, silica, medium-chain triglyceride oil, and microcrystalline cellulose.

DIRECTIONS: Take two capsules daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically-modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,662.



MecobalActive™ is a trademark of Ferrer Health Tech.
The active form of B₁₂

References

1. Barch DH, Rundhaugen LM, Stoner GD, et al. Structure-function relationships of the dietary anticarcinogen ellagic acid. *Carcinogenesis*. 1996 Feb;17(2):265-9. [PMID: 8625448]
2. Bala I, Bhardwaj V, Hariharan S, et al. Sustained release nanoparticulate formulation containing antioxidant ellagic acid as potential prophylaxis system for oral administration. *J Drug Target*. 2006 Jan;14(1):27-34. [PMID: 16603449]
3. Yang SP, Wilson K, Kawa A, et al. Effects of green tea extracts on gene expression in HepG2 and Cal-27 cells. *Food Chem Toxicol*. 2006 Jul;44(7):1075-81. [PMID: 16487642]
4. von Weyarn LB, Chun JA, Hollenberg PF. Effects of benzyl and phenethyl isothiocyanate on P450s 2A6 and 2A13: potential for chemoprevention in smokers. *Carcinogenesis*. 2006 Apr;27(4):782-90. [PMID: 16364922]
5. Perez-Garcia F, Adzet T, Canigual S. Activity of artichoke leaf extract on reactive oxygen species in human leukocytes. *Free Radic Res*. 2000 Nov;33(5):661-5. [PMID: 11200096]
6. Nencini C, Giorgi G, Micheli L. Protective effect of silymarin on oxidative stress in rat brain. *Phytomedicine*. 2007 Feb;14(2-3):129-35. [PMID: 16638633]
7. Abdel-Zaher AO, Abdel-Hady RH, Mahmoud MM, et al. The potential protective role of alpha-lipoic acid against acetaminophen-induced hepatic and renal damage. *Toxicology*. 2008 Jan 20;243(3):261-70. [PMID: 18068886]
8. Brosnan JT, Jacobs RL, Stead LM, et al. Methylation demand: a key determinant of homocysteine metabolism. *Acta Biochim Pol*. 2004;51(2):405-13. [PMID: 15218538]
9. Levy G. Sulfate conjugation in drug metabolism: role of inorganic sulfate. *Fed Proc*. 1986 Jul;45(8):2235-40. [PMID: 3459670]
10. Zóttaszek R, Hanausek M, Kiliańska ZM, et al. The biological role of D-glucaric acid and its derivatives: potential use in medicine [in Polish]. *Postepy Hig Med Dosw* (Online). 2008 Sep 5;62:451-62. [PMID: 18772850]
11. Zamek-Gliszczyński MJ, Hoffmaster KA, Nezasa K, et al. Integration of hepatic drug transporters and phase II metabolizing enzymes: mechanisms of hepatic excretion of sulfate, glucuronide, and glutathione metabolites. *Eur J Pharm Sci*. 2006 Apr;27(5):447-86. [PMID: 16472997]
12. Baker SM, Bennett P, Bland JS, et al. *Textbook of Functional Medicine*. Gig Harbor, WA: The Institute for Functional Medicine; 2010.
13. Shils ME, Shike MS, Ross AC, et al. *Modern Nutrition in Health and Disease*. 10th ed. Baltimore, MD: Williams & Wilkins; 2005.

Additional references available upon request

Due to the evolving nature of interactions and contraindications, it is advised that practitioners consult a current database for new information.

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

MedCaps GI™

Proprietary Gastrointestinal Support Formula*



Available in 120 capsules

Discussion

Pantothenic Acid (as calcium d-pantothenate), a component of Coenzyme A, has various essential roles that sustain life. Among these is maintenance of muscle tone of the gastrointestinal tract. Pantothenic acid supports the synthesis of serotonin and acetylcholine and therefore, may be beneficial in combating stress, often a component of gastrointestinal disorders.*

Zinc (as bis-glycinate chelate) has so many important roles in the body, including the quenching of free radicals possibly present in gastrointestinal disorders. Individuals with inflammatory bowel disorders or any diarrhea-related condition are at risk for zinc deficiency. Zinc deficiency may potentiate the effect of toxins produced by E.coli. A deficiency may also impair the absorption of water and electrolytes and perpetuate the diarrhea. Chronic low zinc impairs nitric oxide production, a substance that plays an important part in triggering diarrheal disease.*^[1]

Inulin is a prebiotic fermented by intestinal flora to produce short chain fatty acids, including butyrate. Butyrate acts as “fuel” for colonocytes and enhances expression of biotransformation genes that induce glutathione Stransferase, protecting colonocytes from carcinogens.*^[2]

L-Glutamine, a conditionally essential amino acid, is most important for intestinal energy supply; regeneration of the gastrointestinal mucosa is dependent upon its utilization. Supplementation has been shown to decrease inflammatory tissue damage in patients with conditions that generally result in low glutamine levels.^[3] L- Glutamine is considered an immunonutrient and is particularly important for the body under stress-related conditions.*

Aloe (Leaf Extract), used for thousands of years, is perhaps most well-known for healing of damaged epithelial tissue, including the bowel lining. Despite the lack of scientific published studies there is anecdotal evidence to suggest that aloe vera helps inflammatory conditions of the gastrointestinal tract. In some individuals it may

Clinical Applications

- » Support the Integrity of the G.I. Mucosa*
- » Support Optimal Function of G.I. Mucosa*

*MedCaps GI™ features L-glutamine, zinc and pantothenic acid to nutritionally support the gastrointestinal mucosa and the prebiotic inulin to provide nourishment of the gastrointestinal mucosa cells. It also features aloe leaf extract, which has traditionally been used for optimal GI function.**

increase G.I. transit time, improve protein digestion and absorption, increase stool bulk and normalize stool bacteria where high levels of yeasts previously existed.*^[4]

MedCaps GI™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Pantothenic Acid (as d-calcium pantothenate)	50 mg	1000%
Zinc (as TRAACS® zinc bisglycinate chelate)	7.5 mg	68%
Inulin (from chicory)(<i>Cichorium intybus</i>)(root)	400 mg	**
L-Glutamine	250 mg	**
<i>Aloe vera</i> 200:1 Aqueous Extract (leaf gel)	25 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), microcrystalline cellulose, stearic acid, magnesium stearate, and silica.**DIRECTIONS:** Take two capsules twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.**DOES NOT CONTAIN:** Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, or artificial sweeteners.

TRAACS is a registered trademark of Albion Laboratories, Inc.

**References**

1. Wapnir RA. J Nutr. 2000 May; 130 (5S Suppl): 1388S-92S Zinc deficiency, malnutrition and the gastrointestinal tract. [PMID: 10801949]
2. Sauer J, Richter KK, Pool-Zobel BL. Products formed during fermentation of the prebiotic inulin with human gut flora enhance expression of biotransformation genes in human primary colon cells. *Br J Nutr.* 2007 Mar 7;:1-11 [PMID: 17381985]
3. Sido B. Low intestinal glutamine level and low glutaminase activity in Crohn's disease: a rationale for glutamine supplementation? *Dig Dis Sci.* 2006 Dec;51(12):2170-9. [PMID: 17078002]
4. Davis K, et. al. Randomised double-blind placebo-controlled trial of aloe vera for irritable bowel syndrome. *Int J Clin Pract.* 2006 Sep;60(9):1080-6 [PMID: 16749917]
5. Bland, J. Ph.D. (1985), Linus Pauling Institute of Science and Medicine, Palo Alto, C.A., Prevention Magazine, Effect of Orally Consumed Aloe Vera Juice in Gastrointestinal Function in Normal Humans. [www.positivehealth.com] {accessed 3.29.07}

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration.
This product is not intended to diagnose, treat, cure, or prevent any disease.

MedCaps IS™

Proprietary Blood Glucose Formula*



Available in 60 capsules

Discussion

Thiamin activates glyceraldehyde phosphate dehydrogenase (GAPDH). Decreased availability of this enzyme has been implicated in diabetes complications such as blindness, nerve damage, kidney failure, stroke and cardiovascular disease.^[1] Thiamin repletion in the case of a six year-old girl with diabetes caused by a genetic mutation effecting thiamine transport demonstrated its benefits.^[2] Thiamin deficiency may cause diabetic neuropathy by decreasing transketolase, needed for normal myelination and thiamine monophosphatase, needed for primary sensory neuron function.^{*[3]}

Niacin is required for lipid metabolism, tissue respiration and glycogenolysis. It may preserve and protect Beta cells.^[4] Niacinamide improved insulin secretion in lean diabetics who had failed drug treatment.^{*[5]}

Chromium and Biotin synergistically improve glucose tolerance.^[6,7] Biotin, in large doses (5-15 mgs) enhances the effects of enzymes involved in glucose metabolism. One small study demonstrated reversal of diabetic neuropathy.^[8] Chromium polynicotinate, preferred for its bioavailability and biological activity may increase insulin receptor sensitivity and enhance glucose transport. Anderson, et al. showed 1000 mcgs of chromium stabilized blood sugar in two months along with insulin and cholesterol level improvement.^{*[9]}

Vanadyl Sulfate may reduce hepatic gluconeogenesis and “mimic” insulin’s effect.^[10] In rats, vanadyl sulfate was also shown to alter the expression of genes dysregulated in diabetes.^{*[11]}

Fenugreek Seed and its constituent, 4-isoleucine appear to directly stimulate insulin.^[12] The combination of fenugreek with vanadium appeared to normalize altered membrane linked functions and GLUT4 distribution.^[13] Fenugreek also lowered high serum cholesterol and triglycerides.^{*[14]}

Bitter Gourd (aka. bitter melon) contains an insulin-like polypeptide shown to exhibit hypoglycemic effects^[15] with an onset of action

Clinical Applications

- » Supports Healthy Glucose Metabolism*
- » Supports Healthy Insulin Sensitivity*
- » Supports Healthy Blood Lipid Levels Already Within The Normal Range*

*MedCaps IS™ is an extraordinary combination of herbal and nutrient support for healthy glucose metabolism. It features concentrates of fenugreek, gymnema and bitter gourd, the addition of high levels of vanadium along with select B vitamins and the mineral, chromium. This formula provides nutritional support for glucose and insulin metabolism and supports healthy blood lipid levels already within the normal range**

between 30-60 minutes and a peak effect at about 4 hours.^[16] It is approved as an antidiabetic drug in China.^{*[17]}

Gymnema sylvestre reduced fasting blood sugars, glycosylated hemoglobin (HbA1c) and glycosylated plasma protein levels and thus insulin requirements in Type 1 diabetics by reducing glucose absorption in the intestine, stimulating pancreatic beta cell growth and possibly increasing endogenous insulin secretion as suggested by an increase in C-peptide levels. Gymnema was shown to also reduce serum triglycerides, total cholesterol, VLDL and LDL.^{*[18]}

MedCaps IS™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%DV
Thiamin (as thiamine HCl)	100 mg	8333%
Niacin (as niacinamide)	100 mg	625%
Biotin	10,000 mcg	33,333%
Chromium (as TRAACS® chromium nicotinate glycinate chelate)	1000 mcg	2857%
Fenugreek Extract (<i>Trigonella foenum-graecum</i>)(seeds)(50% saponins)	300 mg	**
Bitter Gourd Extract (<i>Momordica charantia</i>)(7.5% total bitters)	150 mg	**
Gymnema Extract (<i>Gymnema sylvestre</i>)(leaf)(25% gymnemic acids)	100 mg	**
Vanadium (as TRAACS® vanadium nicotinate glycinate chelate)	5 mg	**

** Daily Value (DV) not established.

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, and silica.**DIRECTIONS:** Take two capsules daily after meals, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.**DOES NOT CONTAIN:** Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

TRAACS and the Albion Medallion design are registered trademarks of Albion Laboratories, Inc.

**References**

1. Obrenovich ME, Monnier VM. Vitamin B1 blocks damage caused by hyperglycemia. *Sci Aging Knowledge Environ*. 2003 Mar 12; 2003 (10): PE6.
2. Viana MB, Carvalho RI. Thiamine- Responsive Megaloblastic Anemia, Sensorineural Deafness, and Diabetes Mellitus: A New Syndrome?, *J Pediatrics*, August 1978; 93(2): 235-238.
3. Frydl, V., Zavadska, H. Diabetic Polyneuropathy and Vitamin B1, *Medwelt*, 1989;40:1484-6
4. Pozzilli, B. et al. Adjuvant therapy in recent onset type 1 diabetes at diagnosis and insulin requirement after 2 years. *Diabete Metab*. 1995 Feb;21(1): 4709. [PMID: 7781843]
5. Polo, V. Saibene A., Pontiroli AE. Nicotinamide improves insulin secretion and metabolic control in lean type 2 diabetic patients with secondary failure to sulfonylureas. *Acta Diabetol* 1998;35:61-4
6. McCarty MF. High dose biotin, an inducer of glutokinase expression, may synergize with chromium picolinate to enable a definitive nutritional therapy for type II diabetes. *Med Hypotheses* 1999 May;52(5):401-6
7. Singer GM, Geohas J. The effect of chromium picolinate and biotin supplementation on glycemic control in poorly controlled patients with type 2 diabetes mellitus: a placebo-controlled, double-blinded, randomized trial. *Diabetes Technol Ther*. 2006 Dec; 8(6): 636-43 [PMID:17109595]
8. Coggeshall JC, et al. Biotin status and plasma glucose in diabetes. *Annals New York Academy of Sciences* 1985; 447:389-92
9. www.naturaldatabase.com
10. Badmaev V. Vanadium: review of its potential role in the fight against diabetes; *J Altern Complement Med*, 1999; 5(3): 273-291
11. Willsky GR. Diabetes-altered gene expression in rat skeletal muscle corrected by oral administration of vanadyl sulfate: *Physiol Genomics*. 2006 Aug 16;26(3):192-201. Epub 2006 May 9. [PMID: 16684804]
12. Sauvaire Y. et al. 4-hydroxisoleucine. A novel amino acid potentiator of insulin secretion. *Diabetes* 1998; 47: 20610
13. Siddiqui MR et.al. Low doses of vanadate and Trigonella synergistically regulate Na⁺/K⁺ -ATPase activity and GLUT4 translocation in alloxan-diabetic rats. *Cell Biochem*. 2006 Apr; 285 (1-2): 17-27. Epub 2006 Apr 19 [PMID: 16622606]
14. Newall CA, Anderson LA, Philpson JD. *Herbal Medicine: A Guide for Healthcare Professionals*. London, UK The Pharmaceutical Press, 1993
15. Sarkar S, Pranava M, Marita R. Demonstration of the hypoglycemic action of *Momordica charantia* in validated animal model of diabetes. *Pharmacol Res*, 1993;33(1)1-4
16. Raman A, et al. Anti-diabetic properties and phytochemistry of *Momordica charantia* L. (Cucurbitaceae). *Phytomedicine* 1996; 26
17. Jia W, Gao W, Tang L. Antidiabetic herbal drugs officially approved in China. *Phytother Res* 2003 Dec; 17(10): 1127-1134
18. Shanmugasundaram, E.R.B., Rajeswari, G., Baskaran K., Rajesh Kumar, B.R., Radha Shanmugasundaram, K., Kizar Ahmath, B. Use of gymnema sylvestre leaf extract in the control of blood glucose in insulin-dependent diabetes mellitus. *J Ethnopharmacol* 1990;30:281-94
19. *The Review of Natural Products by Facts and Comparisons*. St. Louis, MO:Wolters Kluwer Co; 1999

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

MedCaps Menopause™

Female Herbal Nutrient Formula



Available in 120 capsules

*MedCaps Menopause™ is a unique combination blend that is formulated to provide nutritional targeted nourishment for women during menopause. It features specially selected herbs and nutrients that support the adrenal glands' adaptive response as well as support circulation, relaxation and overall well-being. Featuring a non soy derived source of isoflavones, MedCaps Menopause may also beneficially influence estrogen receptor function.**

Discussion

- » MedCaps Menopause™ is a unique combination blend that is formulated to provide targeted nourishment for women during menopause.*
- » It features specially selected herbs and nutrients that support the adrenal glands' adaptive response as well as support circulation, relaxation, and overall well-being.*
- » Featuring a non-soy derived source of isoflavones, Medcaps Menopause™ may also beneficially influence estrogen receptor function.*
- » MedCaps Menopause™ and other MedCaps formulas can be added to any of the formulas found in the XYMOGEN Modular Functional Food System™ to optimize clinical flexibility and patient compliance.*

MedCaps Menopause™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Korean Ginseng Extract (<i>Panax ginseng</i>)(whole plant)(4% ginsenosides)	200 mg	**
Hesperidin (from <i>Citrus sinensis</i>)(fruit)	100 mg	**
PABA (<i>para</i> -aminobenzoic acid)	100 mg	**
Licorice Extract (<i>Glycyrrhiza glabra</i>)(root)(20% glycyrrhizic acids)	75 mg	**
Isoflavones (from kudzu extract)(<i>Pueraria pseudo-hirsuta</i>)(root)	50 mg	**
Wild Yam 10:1 Extract (<i>Dioscorea villosa</i>)(root)	50 mg	**
Black Cohosh Extract (<i>Cimicifuga racemosa</i>)(root and rhizome) (2.5% triterpene glycosides)	50 mg	**
Dong Quai Extract (<i>Angelica sinensis</i>)(root)(1% ligustilide)	50 mg	**
<i>trans</i> -Resveratrol (from <i>Polygonum cuspidatum</i> extract)(root)	1 mg	**
Boron (as boron citrate)	50 mcg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, calcium silicate, silica, microcrystalline cellulose, and medium-chain triglyceride oil.**DIRECTIONS:** Take two capsules twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

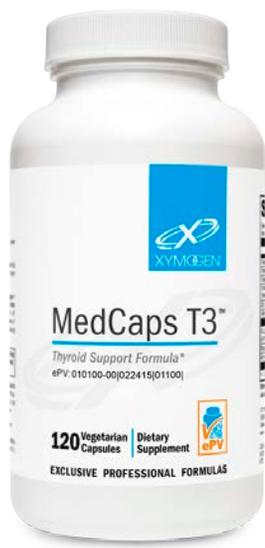
DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.**STORAGE:** Keep closed in a cool, dry place out of reach of children.

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

<p>*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.</p>
--

MedCaps T3™

Thyroid Support Formula*



Available in 120 capsules

Discussion

Iodine The thyroid gland produces two main iodine-containing hormones: thyroxine (T4) and triiodothyronine (T3). These hormones circulate in the bloodstream and work on every living tissue and cell to regulate metabolism and growth. Of the body's iodine pool (about 15 mgs in adults), 80% is contained in the thyroid gland. Iodine is primarily used as a substrate for the manufacture of T4 and T3, and healthy iodine status is imperative for normal thyroid function and thyroid hormone biosynthesis.^[1,2] Because excessive iodine intake, like inadequate iodine intake, can negatively impact thyroid function, total supplementary and dietary iodine should be considered.^[2] Medcaps T3 provides 75 mcg of iodine from Atlantic kelp in each serving.*

Selenium While the role of iodine has long been known, the mechanisms by which selenium exerts its beneficial effects on the thyroid gland have been elucidated more recently. According to Arthur et al, "Selenium is an essential component of many selenoproteins that regulate thyroid hormone synthesis, preserve thyroid integrity in conditions of marked oxidative stress, and control hormone metabolism in nonthyroidal tissues where the prohormone T4 is converted to biologically active T3 or its inactive isomer rT3."^[2] The interactive and complementary relationship between iodine and selenium has become an area of interest and research. For instance, in an animal study, it was observed that a high iodine intake in the presence of selenium deficiency may permit thyroid tissue damage as a result of low thyroidal glutathione peroxidase activity. It was further noted that even a low selenium intake helped normalize circulating T4 concentration in the presence of iodine deficiency.^[3] Evaluation of emerging data supports "selenostasis" as an important aspect of thyroid health.*^[4]

Zinc and Vitamins A and D Research suggests that inadequate intakes of zinc and vitamins A and D may impact thyroid hormone metabolism, circulating thyroid hormone concentrations, the thyroid's response to iodine prophylaxis, and antithyroid antibody levels.^[2,5-7] Researchers further propose that vitamins A and D could increase the transcriptional activity of the thyroid hormone receptor-regulated

Clinical Applications

- » Supports Healthy Thyroid Function*
- » Supports the Body's Conversion of T4 to the More Active Hormone T3*

*MedCaps T3™ features targeted nutrients and herbs that support healthy thyroid hormone biosynthesis. This combination may facilitate the expression of thyroid hormone genes. The addition of ashwagandha and guggul extract may aid in the conversion of thyroxine to triiodothyronine (T4 to T3) and may assist in maintaining healthy blood lipid levels already within the normal range.**

genes.^[8] Expression of these genes affects growth, differentiation, development, and metabolic homeostasis. More studies into the roles of zinc and vitamins A and D will help to gain a better understanding of how these nutrients interact with thyroid hormones, iodine, selenium, and each other to influence thyroid health.*

Retinyl palmitate is used in this formula rather than beta-carotene because certain individuals may lack the ability to effectively convert beta-carotene or other carotenoids into vitamin A.^[9] It is also important to note that vitamin D facilitates intestinal calcium absorption and therefore helps maintain the ratio of calcium to phosphorous, which can be affected by low thyroid function and certain thyroid therapies.*^[10,11]

Vitamin E and Rosemary "Oxidative stress" denotes an imbalance between the production of oxidants and their elimination by antioxidative systems. Studies support the concept of reducing oxidative stress in order to protect thyroid cell health and maintain normal thyroid cell growth and lifecycle.^[12] Furthermore, because active oxygen radicals can inhibit the activity of an enzyme involved in the conversion of T4 to T3, reducing oxidative stress may have a two-fold application in thyroid health.^[13] Antioxidative components in Medcaps T3, such as vitamin E and rosemary, may help protect thyroid cells/tissue and also support the enzymatic conversion of T4 to T3 by scavenging damaging free radicals.*^[13,14]

Guggulsterones and Ashwagandha Researchers have demonstrated the positive influence guggul extract can have on thyroid function and blood lipid metabolism. In one study, the gum resin of *Commiphora mukul* (guggulu) reversed induced decreases in thyroid hormone and 5'-deiodinase activity in an animal model of low thyroid function.^[15] Ashwagandha (*Withania somnifera*) is an Ayurvedic herbal tonic or adaptogen that has been used for thousands of years. Animal research suggests that ashwagandha is capable of stimulating thyroid function in mice.^[16]

MedCaps T3™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Vitamin A (as retinyl palmitate)	450 mcg RAE	50%
Vitamin D3 (cholecalciferol)	5 mcg (200 IU)	25%
Vitamin E (as d-alpha tocopheryl succinate)	33.5 mg	223%
Iodine (from organic Icelandic kelp)(<i>Laminaria digitata</i>)(stem and leaf)	75 mcg	50%
Zinc (as zinc citrate)	5 mg	45%
Selenium (as L-selenomethionine)	100 mcg	182%
Guggulsterones (from guggul extract)(<i>Commiphora mukul</i>)(gum exudate)	50 mg	**
Rosemary Extract (<i>Rosemarinus officinalis</i>)(leaf)	50 mg	**
Ashwagandha (<i>Withania somnifera</i>)(root)	50 mg	**
** Daily Value not established.		

Other Ingredients: HPMC (capsule), stearic acid, silica, magnesium stearate, calcium silicate, and medium-chain triglyceride oil.

DIRECTIONS: Take two capsules daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

CAUTIONS: Do not take if you are pregnant or lactating. Excess vitamin A intake may be toxic and may increase the risk of birth defects. Pregnant women and women who might become pregnant should not exceed 5000 IU of preformed vitamin A (retinyl palmitate) per day.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, dairy products, fish, shellfish, peanuts, tree nuts, egg, artificial colors, artificial sweeteners, or artificial preservatives.

**References**

- Mansourian AR. A review on the metabolic disorders of iodine deficiency. *Pak J Biol Sci.* 2011 Apr 1;14(7):412-24. [PMID: 21902053]
- Arthur JR, Beckett GJ. Thyroid function. *Br Med Bull.* 1999;55(3):658-68. [PMID: 10746354]
- Hotz CS, Fitzpatrick DW, Trick KD, et al. Dietary iodine and selenium interact to affect thyroid hormone metabolism of rats. *J Nutr.* 1997 Jun;127(6):1214-48. [PMID: 9187638]
- Duntas LH. Selenium and the thyroid: a close-knit connection. *J Clin Endocrinol Metab.* 2010 Dec;95(12):5180-88. [PMID: 20810577]
- Zimmermann MB. Interactions of vitamin A and iodine deficiencies: effects on the pituitary-thyroid axis. *Int J Vitam Nutr Res.* 2007 May;77(3):236-40. [PMID: 18214025]
- Ertek S, Cicero AF, Caglar O, et al. Relationship between serum zinc levels, thyroid hormones and thyroid volume following successful iodine supplementation. *Hormones (Athens).* 2010;9(3):263-68. [PMID: 20688624]
- Kivity S, Agmon-Levin N, Zisapli M, et al. Vitamin D and autoimmune thyroid diseases. *Cell Mol Immunol.* 2011;8(3):243-47. [PMID: 21278761]
- Song Y, Yao X, Ying H. Thyroid hormone action in metabolic regulation. *Protein Cell.* 2011;2(5):358-68. [PMID: 21614672]
- Aktuna D, Buchinger W, Langsteger W, et al. Beta-carotene, vitamin A and carrier proteins in thyroid diseases. *Acta Med Austriaca.* 1993;20(1-2):17-20. [PMID: 8475673]
- Al-Tonsi AA, Abdel-Gayoum AA, Saad M. The secondary dyslipidemia and deranged serum phosphate concentration in thyroid disorders. *Exp Mol Pathol.* 2004 Apr;76(2):182-87. [PMID: 15010297]
- Garton M, Reid I, Loveridge N, et al. Bone mineral density and metabolism in premenopausal women taking L-thyroxine replacement therapy. *Clin Endocrinol (Oxf).* 1994 Dec; 41(6):747-55. [PMID: 7889610]
- Xing M. Oxidative stress: a new risk factor for thyroid cancer. *Endocr Relat Cancer.* 2012 Jan 9;19(1):C7-11. [PMID: 22143496]
- Brzezinska-Slebodzinska E, Pietras B. The protective role of some antioxidants and scavengers on the free radicals-induced inhibition of the liver iodothyronine 5'-monodeiodinase activity and thiols content. *J Physiol Pharmacol.* 1997 Sep;48(3):451-59. [PMID: 9376628]
- Mano T, Iwase K, Hayashi R, et al. Vitamin E and coenzyme Q concentrations in the thyroid tissues of patients with various thyroid disorders. *Am J Med Sci.* 1998 Apr;315(4):230-32. [PMID: 9537635]
- Panda S, Kar A. Guggulu (*Commiphora mukul*) potentially ameliorates hypothyroidism in female mice. *Phytother Res.* 2005 Jan;19(1):78-80. [PMID: 15798994]
- Panda S, Kar A. *Withania somnifera* and *Bauhinia purpurea* in the regulation of circulating thyroid hormone concentrations in female mice. *J Ethnopharmacol.* 1999;67(2):233-39. [PMID: 10619390]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Melatonin

Support for Healthy Sleep Patterns*



Available in 60 tablets and 120 tablets

Discussion

Melatonin, a naturally occurring indolamine, is produced primarily in the pineal gland but also in mammalian bone marrow, platelets, gastrointestinal tract, eyes, skin, and lymphocytes.^[1] It plays a vitally important role in regulating the body's daily and annual biological rhythms and thus the sleep/wake cycle. Research suggests that melatonin supports antioxidant activity, cardiovascular health, and immune function as well.^{*[2-4]}

Normal melatonin secretion is suppressed by light and stimulated by periods of darkness. Nocturnal secretion of melatonin is at its highest during childhood, and then decreases with age. Studies, including meta-analyses, suggest that supplemental melatonin supports desirable sleep patterns in certain individuals, including the elderly and those who have unusual work hours, such as night shift workers or people traveling across time zones.^[5-10] A review of 10 trials suggests that melatonin supplementation helped support sleep patterns in individuals crossing time zones; subjects included airline passengers, airline staff, and military personnel.^[11] Daily doses between 0.5 mg to 5 mg taken at bedtime were used and found to be similarly supportive; however, the effects were greater at the higher dose. According to this review, doses higher than 5 mg do not appear to demonstrate any increased benefit.*

Human research studies suggest that melatonin supports the quality of healthy sleep as it relates to falling asleep, sleep efficiency (percent of time asleep to total time in bed), and awakening. In one study employing five experimental periods, melatonin appeared to positively support normal sleep initiation, maintenance, efficiency, and activity within one week of supplementation versus placebo.^[5] Another randomized, double-blind, placebo-controlled study of 33 individuals over a 16-day period suggested that the onset, quality, depth, and duration of sleep can be supported by melatonin supplementation without the occurrence of daytime drowsiness or adverse effects.^{*[12]}

Melatonin has been closely studied for its role in supporting antioxidant activity, especially since intracellular melatonin

Clinical Applications

- » Supports the Natural Function of the Pineal Gland*
- » Helps Support Healthy Sleep Patterns*
- » May Support Antioxidant Activity and Cardiovascular Health*
- » May Support Immune System Activity*

*Melatonin is produced naturally in the pineal gland of the brain in response to changes in light exposure; it helps maintain healthy sleep patterns as well as antioxidant and immune activities. Melatonin can be taken as a supplement to support these functions by promoting normal levels of melatonin in the body.**

is concentrated in the mitochondria, a major site of oxidative metabolism. Melatonin has been found to support extracellular antioxidant activity, support glutathione production, and stimulate production of intracellular antioxidant enzymes—including superoxide dismutases and glutathione peroxidase.^[3] Research suggests that melatonin works on a number of levels. It is able to scavenge oxygen-based and nitrogen-based free radicals, and support the natural response to inflammation by promoting cytokine balance.^[2] As a lipophilic molecule, melatonin is able to permeate the lipid portion of low-density lipoprotein (LDL) and support antioxidant activity in cells. Research suggests that melatonin supports blood pressure already in the normal range and overall cardiovascular health.^{*[3]}

Finally, research suggests that melatonin aids immune system activity by supporting T-helper cell function, immune-specific progenitor cell production, cytokine balance, and production of mediators, such as gamma-interferon and immune-supportive interleukins.^{*[1,2,4,13]} XyMOGEN offers melatonin in a convenient form that provides 3 mg per lozenge, sweetened with xylitol, mannitol, and natural peppermint flavor, to support healthy sleep patterns, antioxidant activity, cardiovascular health, and immune function.*

Melatonin Supplement Facts

Serving Size: 1 Quick-Dissolve Tablet

	Amount Per Serving	%Daily Value
Melatonin	3 mg	**
** Daily Value not established.		

Other Ingredients: Xylitol, mannitol, stearic acid, silica, magnesium stearate, and natural peppermint flavor.

DIRECTIONS: Take one quick-dissolve tablet 15 to 60 minutes before bedtime as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives. **STORAGE:** Keep tightly closed in a cool, dry place out of reach of children.

References

1. Srinivasan V, Pandi-Perumal SR, Brzezinski A, et al. Melatonin, immune function and cancer. *Recent Pat Endocr Metab Immune Drug Discov*. 2011 May;5(2):109-23. [PMID: 22074586]
2. Korkmaz A, Reiter RJ, Topal T, et al. Melatonin: an established antioxidant worthy of use in clinical trials. *Mol Med*. 2009 Jan-Feb;15(1-2):43-50. Review. [PMID: 19011689]
3. Dominguez-Rodriguez A, Abreu-Gonzalez P, Reiter RJ. Melatonin and Cardiovascular Disease: Myth or Reality? [in Spanish]. *Rev Esp Cardiol*. 2012 Mar;65(3):215-218. Epub 2012 Jan 13. [PMID: 22245066]
4. Maestroni GJ. The immunotherapeutic potential of melatonin. *Expert Opin Investig Drugs*. 2001 Mar;10(3):467-76. Review. [PMID: 11227046]
5. Haimov I, Lavie P, Laudon M, et al. Melatonin replacement therapy of elderly insomniacs. *Sleep*. 1995 Sep;18(7):598-603. [PMID: 8552931]
6. Kayumov L, Brown G, Jindal R, et al. A randomized, double-blind, placebo-controlled crossover study of the effect of exogenous melatonin on delayed sleep phase syndrome. *Psychosom Med*. 2001 Jan-Feb;63(1):40-8. [PMID: 11211063]
7. van Geijlswijk IM, Korzilius HP, Smits MG. The use of exogenous melatonin in delayed sleep phase disorder: a meta-analysis. *Sleep*. 2010 Dec;33(12):1605-14. [PMID: 21120122]
8. Olde Rikkert MG, Rigaud AS. Melatonin in elderly patients with insomnia. A systematic review. *Z Gerontol Geriatr*. 2001 Dec;34(6):491-7. Review. [PMID: 11828891]
9. Kunz D, Mahlberg R, Müller C, et al. Melatonin in patients with reduced REM sleep duration: two randomized controlled trials. *J Clin Endocrinol Metab* 2004 Jan;89(1):128-34. [PMID: 14715839]
10. Pandi-Perumal SR, Srinivasan V, Spence DW, et al. Role of the melatonin system in the control of sleep: therapeutic implications. *CNS Drugs*. 2007;21(12):995-1018. [PMID: 18020480]
11. Herxheimer A, Petrie KJ. Melatonin for the prevention and treatment of jet lag. *Cochrane Database Syst Rev*. 2002;(2):CD001520. Review. [PMID: 12076414]
12. Andrade C, Srihari BS, Reddy KP, et al. Melatonin in medically ill patients with insomnia: a double-blind, placebo-controlled study. *J Clin Psychiatry*. 2001 Jan;62(1):41-5. [PMID: 11235927]
13. Cardinali DP, Esquifino AI, Srinivasan V, et al. Melatonin and the immune system in aging. *Neuroimmunomodulation*. 2008;15(4-6):272-8. Review. [PMID: 19047804]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Melatonin CR

Biphasic Controlled-Release Melatonin Formula



Available in 90 tablets and 180 tablets

Discussion

Melatonin is a neurohormone produced from tryptophan by the pineal gland when it is stimulated by darkness. While melatonin regulates many other hormones; its primary function appears to be regulation of the body's daily and annual biological rhythms.*

Oral supplementation has been shown to have some benefit with regard to time to sleep onset, total sleep time, and sleep efficiency.^[1] Noteworthy advantages over pharmaceutical sleep aids are improved performance upon waking and the absence of memory impairment.^[2,3] According to studies, daytime melatonin supplementation by travelers crossing time zones and/or shift workers also promotes sleep.*^[4]

Research has shown that melatonin not only fights free radicals during sleep, but also stimulates the body's own antioxidant systems. For example, it reduced harmful oxidized cholesterol (LDL) in post-menopausal women.^[5] Melatonin's antioxidant capacity also accounts for its role as a neuroprotectant. By delivering antioxidant benefits and correcting the circadian rhythm, melatonin could support cognitive function.*^[6,7]

A decrease in plasma melatonin correlates with a decline in immune function in some individuals beginning around the age of sixty. Interestingly, lymphoid cells are an important physiological source of melatonin in humans. The hormone appears to stimulate production of T helper (TH) cells and their release of interleukin-2, gamma interferon and opioid peptides.^[8] Considering the decline in melatonin synthesis with age, exogenous supplementation with the hormone has long been of interest in anti-aging protocols.*^[9,10]

The addition of pyridoxine in this formula supports the biosynthesis of melatonin and may also enhance dream recall.*

The biphasic delivery system consists of 1 mg of melatonin in the coating solution and the remainder in the tablet core. The melatonin in the coating solution is immediately released upon digestion. The

Clinical Applications

- » Support Synchronization of the Body's Daily Biorhythms*
- » Support Restful Sleep*
- » Direct and Indirect Antioxidant Support*
- » Support Healthy Immune Response*
- » Support Brain Health*

*Melatonin CR is a vegetarian formula with a biphasic delivery system that releases melatonin quickly and then steadily. Melatonin is naturally produced in the pineal gland in response to changes in light exposure; it helps promote healthy sleep patterns as well as antioxidant and immune activities. Melatonin CR can support these functions by helping to maintain normal levels of melatonin in the body.**

melatonin in the tablet core is released over a 6-hour period. The tablet core contains a tableting agent, hydroxypropyl methylcellulose that works by forming a gel layer when hydrated. This gel layer acts as a diffusion barrier to control the rate of release of the melatonin in the tablet core. As the tablet travels through the intestine, the gel layer slowly erodes to release the melatonin, which then is available for absorption in the intestine.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

Melatonin CR Supplement Facts

Serving Size: 1 Tablet

	Amount Per Serving	%Daily Value
Vitamin B6 (as pyridoxine HCl)	10 mg	588%
Melatonin	5 mg	**

** Daily Value not established.

Other Ingredients: Cellulose, dibasic calcium phosphate, hypromellose, magnesium stearate, stearic acid, silica, methylcellulose, and glycerin.

DIRECTIONS: Take one tablet with water 20 minutes before bedtime, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

CAUTIONS: Not for use by children under 12 years of age. Do not take when operating machinery or driving a vehicle.

STORAGE: Keep closed in a cool, dry place.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, artificial colors, artificial sweeteners, or preservatives.

References

1. Brzezinski A, Vangel MG, Wurtman RJ, et al. Effects of exogenous melatonin on sleep: a meta-analysis. *Sleep Med Rev.*2005;9:41-50. [PMID: 15649737]
2. Paul MA, et al. Melatonin and zopiclone as pharmacologic aids to facilitate crew rest. *Aviat Space Environ Med.* 2001 Nov;72(11):974-84. [PMID: 11718517]
3. Wesensten NJ, Balkin TJ, Reichardt RM et al. Daytime sleep and performance following a zolpidem and melatonin cocktail. *Sleep.* 2005;28:93-103. [PMID: 15700725]
4. Srinivasan V, et al. Jet lag: therapeutic use of melatonin and possible application of melatonin analogs. *Travel Med Infect Dis.* 2008 Jan-Mar;6(1-2):17-28. [PMID: 18342269]
5. Wakatsuki A, et al. Melatonin inhibits oxidative modification of low-density lipoprotein particles in normolipidemic post-menopausal women. *J Pineal Res.* 2000;28:136-142 [PMID: 10739299]
6. Peck JS, et al. Cognitive effects of exogenous melatonin administration in elderly persons: a pilot study. *Am J Geriatr Psychiatry.* 2004;12:432-436. [PMID: 15249281]
7. Asayama K, Yamadera H, Ito T, et al. Double blind study of melatonin effects on the sleep-wake rhythm, cognitive and noncognitive functions in Alzheimer type dementia. *J Nippon Med Sch.* 2003;70:334-341. [PMID: 12928714]
8. Cardinali DP, et.al. Melatonin and the immune system in aging. *Neuroimmunomodulation.* 2008;15(4-6):272-8. [PMID: 19047804]
9. Armstrong SM, Redman JR. Melatonin: A chronobiotic with anti-aging properties? *Med Hypotheses* 1991;34: 300-9 [PMID: 1865836]
10. Rozencaiwig R, Grad BR, Ochoa J. The role of melatonin and serotonin in aging. *Med Hypotheses* 1987;23: 337-52 [PMID: 2889131]
11. Miyamoto A, et.al. Serum melatonin kinetics and long-term melatonin treatment for sleep disorders in Rett syndrome. *Brain Dev.* 1999 Jan;21(1):59-62 [PMID: 10082254]
12. Arendt J. Safety of melatonin in long-term use. *J Biol Rhythms* 1997;12:673-681 [PMID: 9406044]
13. Voordouw BC, et.al. Melatonin and melatonin-progestin combinations alter pituitary-ovarian function in women and can inhibit ovulation. *J Clin Endocrinol Metab.* 1992 Jan;74(1):108-17. [PMID: 1727807]
14. Abd-Allah AR, et al. Effect of melatonin on estrogen and progesterone receptors in relation to uterine contraction in rats. *Pharmacol Res.* 2003 Apr;47(4):349-54 [PMID: 12644393]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

MemorAll™

Brain Support*



Available in 60 capsules

Discussion

Vitamins B6 (as pyridoxal 5'-phosphate), B12 (as methylcobalamin), and folate (as 5-MTHF) are essential homocysteine remethylation cofactors; as such, they support the maintenance of healthy homocysteine levels. Normal blood levels of homocysteine are associated with healthy cognition in the elderly and healthy cerebrovascular function.^[1] The brain may be protected by improving methylation by providing the nutritional cofactors needed for proper functioning of the methionine cycle.*^[2]

5-MTHF (5-methyltetrahydrofolate) may better support folate nutrition in those with digestive issues and those with genetic variations in folic acid metabolism. The form of 5-MTHF in MemorAll is Quatrefolic, which is proven to have greater stability, solubility, and bioavailability over calcium salt forms of 5-MTHF.*

N-Acetyl-Cysteine is capable of crossing the blood-brain barrier and is known to combat oxidative stress, and reduced oxidative stress may support healthier nerve tissue.^[3] L-carnitine is a vital cofactor for mitochondrial oxidation of fatty acids providing the brain with an energy substrate. **Acetyl-L-carnitine**, an ester of L-carnitine, possesses properties that may be effective in supporting healthy cognition with age.^[4,5] The phospholipid **phosphatidylserine (PS)** plays an important functional role in membrane-related processes in the brain and regulates the release of acetylcholine, dopamine, and noradrenaline. PS appears to support neuronal health and healthy brain function, possibly through its effect on cytokine production and their influence on microglia.*^[6]

Ginkgo biloba leaf extract contains two main bioactive constituents—ginkgoflavonglycosides (24%) and terpene lactones (6%)—and is used in the formula because of its reported stress-alleviating and memory-supportive effects as well as its ability to support the health and integrity of neurons. The mechanisms of action may be mediated through its antioxidant, antihypoxic, and microcirculatory actions.^[7] The Ayurvedic herb **Bacopa monniera** has reported cognition-facilitating, cytokine-modulating, and anti-stress effects. These effects

Clinical Applications

- » Helps Support Normal, Healthy Cognitive Function*
- » May Support the Health of Brain Tissue*

*MemorAll™ is a unique combination of nutrients and botanicals that supports cognitive function and a healthy memory. It features select B vitamins, including Quatrefolic®, a patented form of 5-MTHF; the herbs Ginkgo biloba and Bacopa monnieri; nutrients that provide antioxidant activity; and brain-specific nutrients such as vinpocetine, acetyl-L-carnitine, and sunflower-derived phosphatidylserine. This comprehensive formula addresses the multiple pathways involved in neurological health by supporting oxidant and cytokine balance, methylation, mitochondrial function, and endocrine balance.**

are thought to be mediated through its remarkable free-radical-scavenging capacity and its protective effect on DNA cleavage.*^[8]

Vinpocetine is derived from vincamine, an alkaloid extracted from the periwinkle plant (*Vinca minor*). It has been used extensively in Eastern Europe, and more recently in the United States, to support cerebrovascular health and healthy mental function. Vinpocetine's roles in supporting brain function are multi-modal and include its influence on cerebral circulation, its antioxidant activity in the brain, and its role in affecting ion channels and cytokine production.^[9-11] Together, these varied actions support overall brain tissue health and function. The efficacy and safety of vinpocetine have been tested and validated by in vitro, animal, and human studies. Many human studies demonstrate positive results in neurologic functioning—primarily related to capillary blood flow and cellular metabolism.*^[12-15]

Huperzine A (HupA), like vinpocetine, affects ion channels. Such activity has been found to support healthy learning and memory. HupA may have a positive effect on levels of acetylcholine through its action on acetylcholinesterase (AChE). Acetylcholine is one of the chemicals that our nerves use to communicate in the brain, muscles, and other areas. HupA has been found to support healthy cognition in a broad range of animal models, and phase IV clinical trials in China demonstrated that HupA was valuable in promoting healthy recall and cognition in elderly subjects.*^[16]

MemorAll™ Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Vitamin B6 (as pyridoxal 5'-phosphate)	5 mg	294%
Folate (as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt)	100 mcg DFE	25%
Vitamin B12 (as methylcobalamin)	100 mcg	4167%
Acetyl-L-Carnitine (as acetyl-L-carnitine HCl)	250 mg	**
N-Acetyl-L-Cysteine	100 mg	**
Ginkgo Extract (<i>Ginkgo biloba</i>)(leaf)(24% ginkgolflavonglycosides and 6% terpene lactones)	60 mg	**
Bacopa Extract (<i>Bacopa monniera</i>)(leaf)(8% bacosides)	50 mg	**
Sharp•PS® GREEN Phosphatidylserine	15 mg	**
Vinpocetine	5 mg	**
<i>trans</i> -Resveratrol (from <i>Polygonum cuspidatum</i> root extract)	1 mg	**
Huperzine A (from <i>Huperzia serrata</i>)(aerial parts)	100 mcg	**
** Daily Value not established.		

Other Ingredients: HPMC (capsule), stearic acid, calcium silicate, tricalcium phosphate, silica, magnesium stearate, and microcrystalline cellulose.
 Sharp•PS® GREEN is a registered trademark of Enzymotec Ltd.
 Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US Patent 7,947,662.

DIRECTIONS: Take one capsule twice daily, or as directed by your healthcare practitioner.

CAUTIONS: Consult your healthcare practitioner before use, especially if you have low blood pressure, are taking blood-thinning agents, or are within two weeks before or after undergoing surgery. Do not take if you are pregnant or lactating. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

**References**

- Malouf R, Grimley Evans J. The effect of vitamin B6 on cognition. *Cochrane Database Syst Rev.* 2003;(4):CD004393. [PMID: 14584010]
- Miller AL. The methionine-homocysteine cycle and its effects on cognitive diseases. *Altern Med Rev.* 2003 Feb;8(1):7-19. [PMID: 12611557]
- Farr SA, Poon HF, Dogrukol-Ak D, et al. The antioxidants alpha-lipoic acid and N-acetylcysteine reverse memory impairment and brain oxidative stress in aged SAMP8 mice. *J Neurochem.* 2003 Mar;84(5):1173-83. [PMID: 12603840]
- Virmani A, Binienda Z. Role of carnitine esters in brain neuropathology. *Mol Aspects Med.* 2004 Oct-Dec;25(5-6):533-49. [PMID: 15363640]
- Milgram NW, Araujo JA, Hagen TM, et al. Acetyl-L-carnitine and alpha-lipoic acid supplementation of aged beagle dogs improves learning in two landmark discrimination tests. *FASEB J.* 2007 Nov;21(13):3756-62. [PMID: 17622567]
- Hashioka S, Han YH, Fujii S, et al. Phosphatidylserine and phosphatidylcholine-containing liposomes inhibit amyloid beta and interferon-gamma-induced microglial activation. *Free Radic Biol Med.* 2007 Apr;42(7):945-54. [PMID: 17349923]
- Mahadevan S, Park Y. Multifaceted therapeutic benefits of Ginkgo biloba L.: chemistry, efficacy, safety, and uses. *J Food Sci.* 2008 Jan;73(1):R14-19. [PMID: 18211362]
- Russo A, Izzo AA, Borrelli F, et al. Free radical scavenging capacity and protective effect of *Bacopa monniera* L. on DNA damage. *Phytother Res.* 2003 Sep;17(8):870-75. [PMID: 13680815]
- Hadjiev D. Asymptomatic ischemic cerebrovascular disorders and neuroprotection with vinpocetine. *Ideggyogy Sz.* 2003 May;56(5-6):166-72. [PMID: 12861957]
- Muravyov AV, Yakusevich VV, Chuchkanov FA, et al. Hemorheological efficiency of drugs, targeting on intracellular phosphodiesterase activity: in vitro study. *Clin Hemorheol Microcirc.* 2007;36(4):327-34. [PMID: 17502703]
- Vinpocetine. Monograph. *Altern Med Rev.* 2002 Jun;7(3):240-43. [PMID: 12126465]
- Valikovics A. Investigation of the effect of vinpocetine on cerebral blood flow and cognitive functions [in Hungarian]. *Ideggyogy Sz.* 2007 Jul;60(7-8):301-10. [PMID: 17713111]
- Chukanova EI. Efficacy of cavinton in the treatment of patients with chronic blood flow insufficiency. Russian multicenter clinical-epidemiological program "CALIPSO" [in Russian]. *Zh Nevrol Psikiatr Im S S Korsakova.* 2010;110(12):49-52. [PMID: 21311488]
- Chukanova EI. Cavinton in the complex treatment of patients with chronic cerebrovascular insufficiency [in Russian]. *Zh Nevrol Psikiatr Im S S Korsakova.* 2009;109(9):35-39. [PMID: 19770831]
- Bagoly E, Fehér G, Szapáry L. The role of vinpocetine in the treatment of cerebrovascular diseases based in human studies [in Hungarian]. *Orv Hetil.* 2007 Jul;148(29):1353-58. [PMID: 17631470]
- Wang R, Yan H, Tang XC. Progress in studies of huperzine A, a natural cholinesterase inhibitor from Chinese herbal medicine. *Acta Pharmacol Sin.* 2006 Jan;27(1):1-26. [PMID: 16364207]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

© XYMOGEN
 DRS-178
 Rev. 12/26/18



MenoFem™

Natural Herbal Support Formula*



Available in 90 capsules

Discussion

Eighty percent of American women experience common symptoms while going through the two-to-ten-year perimenopausal and menopausal transition. MenoFem™ addresses a broad spectrum of normal menopausal complaints, making it an attractive option in varied clinical settings.*

Black Cohosh (*Cimicifuga racemosa*) is an herb American Indians used for gynecological support, including relief from common, normal menstrual symptoms such as cramps and related low-back discomfort. Research shows that black cohosh effectively maintains a sense of calmness and healthy outlook, and it may help address menopause-associated vasomotor symptoms.^[1,2] According to the medical literature, black cohosh is beneficial to vaginal superficial cells and bone health without having a potentially detrimental effect upon the endometrium or follicle-stimulating hormone (FSH) levels. According to Ruhlen et al., black cohosh may exert its benefits through selective estrogen receptor modulation, serotonergic pathways, antioxidant activity, or inflammatory pathways.*^[3]

Dong Quai (*Angelica sinensis*) has its origins in China, Japan, and Korea, where it is used to balance the female cycle. Dong Quai works best in combination with other herbs to support menstrual regularity. Dong Quai can nourish dry, thin vaginal tissues.*^[4]

Licorice (*Glycyrrhiza glabra*) functions as a weak phytoestrogen and has been reputed to aid in sexual arousal. Research suggests that glabridin, an isoflavone in licorice, is an estrogen-receptor agonist and supports normal breast cell growth. Licorice has been shown to have potential for supporting healthy bone mineral density in postmenopausal women and for inhibiting serotonin re-uptake.^[5] It is used for liver and adrenal support, the latter being important as ovarian estrogen synthesis declines.*

Chasteberry (*Vitex agnus-castus*) supports symptomatic relief of common perimenopausal and menopausal symptoms. It appears to significantly compete for binding at the estrogen receptors.

Clinical Applications

- » Supports Healthy Hormone Balance During Perimenopause and Menopause*
- » Helps Relieve Bothersome Symptoms of Normal Perimenopause and Menopause, Such as Hot Flashes.*

*MenoFem™ is a unique formula integrating Native American, Chinese, and Ayurvedic herbs to provide balanced support to menopausal women.**

Chasteberry has normalized short luteal phases and progesterone synthesis. The popular herb may help relieve the common, transient symptom of mild breast tenderness possibly by inhibiting prolactin secretion. Chasteberry can help support a normal, healthy attitude during the perimenopausal transition.*^[6]

Wild Yam (*Dioscorea villosa*) has long been used to support female cycles and functions as a phytohormone. **Red Clover (*Trifolium pratense*)** is considered a phytoestrogen. Its contents include genestein and salicylic acid. While red clover is helpful in reducing flushing, it does not increase breast density or raise estradiol levels.^[7] This herb has shown a positive effect on vaginal cytology and can help maintain a healthy cellular response to hormone-induced discomfort in urinary tract tissues. Scientific evidence suggests that red clover can also support healthy blood lipids and bone health.*^[1,8]

Dandelion Root (*Taraxacum officinale*) has been commonly used for its ability to help maintain healthy fluid balance and for its cleansing effects. In vitro research suggests that the active constituents in dandelion—which include luteolin, quercetin, and inulin—suppress COX-2 and inducible nitric oxide synthase, increase antioxidant activity, upregulate phase II detoxification, and support bifidobacteria growth.*^[9-11]

Motherwort (*Leonurus cardiaca*) is a phytoestrogen especially helpful for maintaining an even heartbeat, a normal body temperature, and a healthy menstrual cycle. It has long been used to support the body's healthy response to pain, maintain healthy muscle function, and provide physical and emotional comfort and stability.*^[12]

Ashwagandha (*Withania somnifera*) Within the system of Ayurveda, ashwagandha is classified as a rasayana (rejuvenation) and is expected to promote physical and mental health, help rejuvenate the body, and increase longevity.*^[13,14]

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

MenoFem™ Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Dandelion 4:1 Extract (<i>Taraxacum officinale</i>)(root)	66.67 mg	**
Wild Yam 10:1 Extract (<i>Dioscorea villosa</i>)(root)	66.67 mg	**
Chaste Berry Extract (<i>Vitex agnus-castus</i>)(fruit)(0.5% agnuside and 0.4% aucubin)	66.67 mg	**
Black Cohosh Extract (<i>Cimicifuga racemosa</i>)(roots)(2.5% triterpene glycosides)	50 mg	**
Ashwagandha (<i>Withania somnifera</i>)(root)	33.33 mg	**
Motherwort Extract Complex (<i>Leonurus cardiaca</i>)(herb)	33.33 mg	**
Red Clover (<i>Trifolium pratense</i>)(flower tops)	33.33 mg	**
Dong Quai Extract (<i>Angelica sinensis</i>)(root)(1% ligustilide)	25 mg	**
Licorice Extract (<i>Glycyrrhiza glabra</i>)(root)(20% glycyrrhizin)	8.33 mg	**
** Daily Value not established.		

Other Ingredients: HPMC (capsule), microcrystalline cellulose, stearic acid, magnesium stearate, and silica.

DIRECTIONS: Take one capsule daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

CAUTIONS: Do not take if you are pregnant or lactating.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.

**References**

- Geller SE, Studee L. Botanical and dietary supplements for menopausal symptoms: what works, what does not. *J Womens Health(Larchmt)*. 2005 Sep;14(7):634-49. [PMID: 16181020]
- Nappi RE, Malavasi B, Brundu B, et al. Efficacy of Cimicifuga racemosa on climacteric complaints: a randomized study versus low-dose transdermal estradiol. *Gynecol Endocrinol*. 2005 Jan;20(1):30-5. [PMID: 15969244]
- Ruhlen RL, Sun GY, Sauter ER. Black cohosh: Insights into its mechanism(s) of action. *Integr Med Insights*. 2008;3:21-32. [PMID: 21614156]
- Chen JK, Chen TT. *Chinese Medical Herbology and Pharmacology*. City of Industry, CA: Art of Medicine Press, Inc; 2001:645, 919.
- Somjen D, Katzburg S, Vaya J, et al. Estrogenic activity of glabridin and glabrene from licorice roots on human osteoblasts and prepubertal rat skeletal tissues. *J Steroid Biochem Mol Biol*. 2004 Aug;91(4-5):241-6. [PMID:15336701]
- Chopin Lucks B. Vitex agnus castus essential oil and menopausal balance: a research update [Complementary Therapies in Nursing and Midwifery 8 (2003) 148-154]. *Complement Ther Nurs Midwifery*. 2003 Aug;9(3):157-60. [PMID: 12852933]
- Atkinson C, Compston JE, Day NE, et al. The effects of phytoestrogen isoflavones on bone density in women: a double-blind, randomized, placebo-controlled trial. *Am J Clin Nutr*. 2004 Feb;79(2):326-33 [PMID: 14749241].
- van de Weijer PH, Barentsen R. Isoflavones from Red clover (Promensil) significantly reduce menopausal hot flush symptoms compared with placebo. *Maturitas*. 2002 Jul 25;42(3):187-93. [PMID: 12161042]
- Schütz K, Carle R, Schieber A. Taraxacum—a review on its phytochemical and pharmacological profile. *J Ethnopharmacol*. 2006 Oct 11;107(3):313-23. [PMID: 16950583]
- Maliakal PP, Wanwimolruk S. Effect of herbal teas on hepatic drug metabolizing enzymes in rats. *J Pharm Pharmacol*. 2001 Oct;53(10):1323-29. [PMID: 11697539]
- Natural Medicines Comprehensive Database. Dandelion.[Full Monograph] <http://naturaldatabase.therapeuticresearch.com/nd/Search.aspx?cs=&s=ND&pt=100&id=706&fs=ND&searchid=34505380>. Accessed May 7, 2012.
- American Botanical Council. Motherwort herb. <http://cms.herbalgram.org/expandedE/Motherwortherb.html>. Accessed May 7, 2012.
- Kulkarni SK, Dhir A. Withania somnifera: an Indian ginseng. *Prog Neuropsychopharmacol Biol Psychiatry*. 2008 Jul 1;32(5):1093-105. [PMID: 17959291]
- Dhuley JN. Effect of ashwagandha on lipid peroxidation in stress-induced animals. *J Ethnopharmacol*. 1998 Mar;60(2):173-8. [PMID: 9582008]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Methyl Protect®

Optimal Methylation Support Formula*



Available in 60 & 120 capsules

Discussion

Methyl Protect provides 5-methyltetrahydrofolate (active folate), pyridoxal 5'-phosphate (active B6), methylcobalamin (active B12), riboflavin 5'-phosphate (active vitamin B2), and anhydrous betaine (trimethylglycine). These five nutrients promote the process of methylation. Methylation is the addition of a methyl group (a carbon atom with three hydrogen atoms attached) to proteins, enzymes, chemicals, DNA, or amino acids like homocysteine. It is a vital and fundamental process that takes place in many biochemical pathways involving detoxification, cardiovascular health, neurological health, eye health, muscle health, bone health, and redox balance. Effective methylation also has roles in the biosynthesis and breakdown of catecholamines, such as epinephrine. This is an important aspect of healthy adrenal functioning.*

Folic Acid (as calcium folinate and 5-methyltetrahydrofolate)

This B vitamin has important roles in detoxification, nervous system function, breast tissue health, prenatal development, and the conversion of homocysteine back to methionine. In its active form, folic acid serves as a donor of methyl groups. Providing the combination of calcium folinate and 5-methyltetrahydrofolate (5-MTHF) allows optimal utilization of folic acid by bypassing metabolic steps to bioactivity.^[1] In fact, 5-MTHF is the form into which the body must convert all other forms of folic acid before it can be used. In this formula, 5-MTHF is provided as calcium folinate and Quatrefolic®. Quatrefolic is proven to have greater stability, solubility, and bioavailability over the calcium salt forms of 5-MTHF.*

Despite research showing that folic acid and 5-MTHF have equivalent bioavailability and that supplementation with large doses of folic acid can "force" its conversion to the more active form, 5-MTHF may be the preferred form to support healthy folate status. This may be especially true in those with certain variations in folate metabolism or digestion that can affect conversion of folic acid to 5-MTHF.^[2-4] Folate is stored in the red blood cells, where levels have been shown to be higher after supplementation with 5-MTHF compared to folic acid and placebo. Patients given 5 mg of 5-MTHF experienced

Clinical Applications

- » Supports Cardiovascular and Neurological Health*
- » Supports the Maintenance of Healthy Homocysteine Levels Already Within Normal Range*
- » Supports Healthy Methylation of Estrogen, Dopamine, Epinephrine, Heavy Metals, and Environmental Toxins*

*Methyl Protect® is a comprehensive formula designed to support optimal methylation and help maintain healthy homocysteine levels already within normal range. It features five key nutrients that are involved in homocysteine metabolism: folate as calcium folinate and Quatrefolic® for increased bioactivity; trimethylglycine; and vitamins B12, B6, and B2. These five nutrients, provided in activated forms, support enhanced methylation and overall cardiovascular health.**

plasma levels 700% greater than patients given folic acid.^[5] In another study, authors concluded that 5-MTHF should be the primary choice of supplementation to support healthy homocysteine levels already within the normal range.*^[6]

Trimethylglycine (as anhydrous betaine) Found in several tissues in humans, trimethylglycine acts as an alternative methyl donor in homocysteine metabolism. Trimethylglycine may also be a preventive agent against the activation of NF-kappaB.*^[7]

Vitamin B12 (as methylcobalamin) Cyanocobalamin (the form of B12 present in many supplements) has to be converted in the liver to methylcobalamin, the form provided in Methyl Protect. B12 is another methyl donor, and studies suggest that it supports healthy homocysteine levels already within the normal range on its own and in combination with folate.*^[8]

Vitamin B6 (as pyridoxal 5'-phosphate) This coenzyme form of vitamin B6 is the primary bioactive form. It is a coenzyme in approximately 100 enzymatic reactions.^[9] Data from the Framingham Study showed an inverse association between homocysteine and good B6 status (as well as B12 and folate).*^[10]

Vitamin B2 (as riboflavin 5'-phosphate) As the principal coenzyme form of B2, riboflavin 5'-phosphate is used in many oxidative reactions. Folate and riboflavin interact to support healthy homocysteine levels already within the normal range, possibly by maximizing the catalytic activity of the enzyme methylenetetrahydrofolate reductase (MTHFR). The effect may be unrelated to MTHFR genotype.*^[11]

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Methyl Protect® Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Riboflavin (as riboflavin 5'-phosphate sodium)	25 mg	1923%
Vitamin B6 (as pyridoxal 5'-phosphate)	10 mg	588%
Folate (1000 mcg DFE as calcium folinate and 1000 mcg DFE as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt)	2000 mcg DFE	500%
Vitamin B12 (as methylcobalamin)	1000 mcg	41,667%
Betaine Anhydrous (trimethylglycine)	500 mg	**
** Daily Value not established.		

Other Ingredients: HPMC (capsule), stearic acid, silica, microcrystalline cellulose, magnesium stearate, and medium-chain triglyceride oil.

DIRECTIONS: Take one capsule one to two times daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,662.

**References**

- Venn BJ, Green TJ, Moser R, et al. Comparison of the effect of low-dose supplementation with L-5-methyltetrahydrofolate or folic acid on plasma homocysteine: a randomized placebo-controlled study. *Am J Clin Nutr.* 2003 Mar;77(3):658-62. [PMID: 12600857]
- Yakut M, Ustün Y, Kabaçam G, et al. Serum vitamin B(12) and folate status in patients with inflammatory bowel diseases. *Eur J Intern Med.* 2010 Aug;21(4):320-23. [PMID: 20603044]
- Halsted CH, Villanueva JA, Devlin AM, et al. Folate deficiency, methionine metabolism, and alcoholic liver disease. *Alcohol.* 2002 Jul;27(3):169-72. [PMID: 12163145]
- Kluijtmans LA, Van den Heuvel LP, Boers GH, et al. Molecular genetic analysis in mild hyperhomocysteinemia: a common mutation in the methylenetetrahydrofolate reductase gene is a genetic risk factor for cardiovascular disease. *Am J Hum Genet.* 1996 Jan;58(1):35-41. [PMID: 8554066]
- Willems FF, Boers GH, Blom HJ, et al. Pharmacokinetic study on the utilisation of 5-methyltetrahydrofolate and folic acid in patients with coronary artery disease. *Br J Pharmacol* 2004;141:825-30. [PMID: 14769778]
- Caruso R, Campolo J, Sedda V, et al. Effect of homocysteine lowering by 5-methyltetrahydrofolate on redox status in hyperhomocysteinemia. *J Cardiovasc Pharmacol.* 2006 Apr;47(4):549-55. [PMID: 16680068]
- Go EK, Jung KJ, Kim JY, et al. Betaine suppresses proinflammatory signaling during aging: the involvement of nuclear factor-kappaB via nuclear factor-inducing kinase/IkappaB kinase and mitogen-activated protein kinases. *J Gerontol A Biol Sci Med Sci.* 2005 Oct;60(10):1252-64. [PMID: 16282556]
- Lowering blood homocysteine with folic acid based supplements: meta-analysis of randomised trials. Homocysteine Lowering Trialists' Collaboration. *BMJ.* 1998 Mar;316(7135):894-98. [PMID: 9569395]
- Strain JJ, Dowey L, Ward M, et al. B-vitamins, homocysteine metabolism and CVD. *Proc Nutr Soc.* 2004 Nov;63(4):597-603. [PMID: 15831132]
- Selhub, J. 2006. The many facets of hyperhomocysteinemia: studies from the framingham cohorts. *J Nutr.* 2006 Jun;136(6 Suppl):1726S-30S. [PMID: 16702347]
- Moat SJ, Ashfield-Watt PA, Powers HJ, et al. Effect of riboflavin status on the homocysteine-lowering effect of folate in relations to the MTHFR (C677T) genotype. *Clin Chem.* 2003 Feb;49(2):295-302. [PMID: 12560354]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Methylcobalamin™

Methyl B12



Available in 60 and 120 quick-dissolve tablets

Discussion

Vitamin B12 can be obtained through its synthesis by intestinal flora, from animal-based or fortified foods, or from supplementation. Unlike most other water-soluble vitamins, vitamin B12 (4 to 6 mg) is bound to a protein and stored in the liver as methylcobalamin or 5'-deoxyadenosylcobalamin. These are the coenzyme forms of B12 that are active in human metabolism. Reserve stores of B12 can become depleted due to poor dietary intake without supplementation, lack of intrinsic factor, or poor intestinal absorption.

Many vitamin B12 supplements on the market contain cyanocobalamin. The liver is able to convert a small amount of cyanocobalamin to methylcobalamin; however, methylcobalamin is the preferred form since it is the bioactive form and therefore better utilized. In a research study, tissue retention of cobalamin was greater when using the methyl- form versus the cyano- form. This was exemplified by the fact that urinary excretion of methylcobalamin was one-third less than that of cyanocobalamin.^[1] Another point of interest regarding B12 supplementation is the commonly held belief that intramuscular injections of B12 are more effective than oral supplementation. In fact, oral supplementation is just as effective and carries the added benefits of lower cost and ease of administration.^{*[2,3]}

Methylation Methylcobalamin is required for the function of methionine synthase—the folate-dependent enzyme required for the synthesis of methionine, an amino acid, from homocysteine. Methionine, in turn, is required for the synthesis of S-adenosylmethionine (SAME), a methyl group donor used in many biological methylation reactions, including the methylation of a number of sites within DNA and RNA. As an example of its importance in homocysteine metabolism, one study showed that the addition of B12 to a folate regimen had a greater impact (7%) on homocysteine than did folate alone.^{*[4]}

Neurologic Health Methylcobalamin is necessary for the maintenance of a healthy nervous system. Chronic insufficiency can affect the

Clinical Applications

- » Supports Healthy Methylation*
- » Supports Neurological Health*
- » Supports Red Blood Cell Formation*
- » Supports Healthy Sleep Patterns*
- » Supports a Healthy Immune System*

*XYMOGEN's Methylcobalamin provides 5 mg (5,000 mcg) of vitamin B12 in each very small, pleasant-tasting tablet. Methylcobalamin, the form of B12 active in the body, appears to be better absorbed and stored in tissues in comparison to cyanocobalamin. Methylcobalamin has multiple supportive roles in the body, including red blood cell formation, nervous system health, homocysteine and folate metabolism, melatonin synthesis, and more.**

spinal cord, peripheral nerves, optic nerve, and brain. This can be explained by methylcobalamin's role as a cofactor in myelin synthesis; in methylation of the toxic byproduct homocysteine, which is thought to damage neurons; and in the synthesis of monoamine neurotransmitters, such as serotonin, dopamine, and norepinephrine.^[5-7] Methylcobalamin is the preferred form of cobalamin supplementation for neurologic health, and experimental research indicates that methylcobalamin shows better transport to organelles within nerve cells than does cyanocobalamin.^{*[8]}

Red Blood Cell Formation Like folate, erythroblasts require vitamin B12 for proliferation during their differentiation. Insufficient B12 levels will contribute to purine and thymidylate synthesis inhibition, impaired DNA synthesis, and erythroblast apoptosis, resulting in ineffective erythropoiesis.^{*[9]}

Sleep Support Methylcobalamin has been reported to affect the primary circadian rhythm associated with sleep.^[8,10] Research supports a role for methylcobalamin supplementation in modulating melatonin secretion, enhancing light-sensitivity, normalizing circadian rhythms, and improving sleep-wake cycles.^{*[1,12]}

Immune Health Research suggests an important role for B12 in immune system regulation. Human research demonstrated that methylcobalamin supplementation in patients with inadequate B12 levels improved CD4/CD8 ratio and NK cell activity, and augmented CD3-CD16+ cells, suggesting an important role in cellular immunity.^[13] In other research, among homologues studied, methylcobalamin was shown to have the strongest antibody production enhancement on an in vitro system.^{*[14]}

Methylcobalamin™ Supplement Facts

Serving Size: 1 Quick-Dissolve Tablet

	Amount Per Serving	%Daily Value
Vitamin B12 (as methylcobalamin)	5,000 mcg	208,333%

Other Ingredients: Xylitol, stearic acid, mannitol, citric acid, silica, natural orange flavor (no MSG), and magnesium stearate.

DIRECTIONS: Take one quick-dissolve tablet as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

References

1. Methylcobalamin. *Altern Med Rev.* 1998 Dec;3(6):461-3. Erratum in: *Altern Med Rev* 1999 Feb;4(1):9. [PMID: 9855571]
2. Kuzminski AM, Del Giacco EJ, Allen RH, et al. Effective treatment of cobalamin deficiency with oral cobalamin. *Blood.* 1998 Aug 15;92(4):1191-98. [PMID: 9694707]
3. Kim HI, Hyung WJ, Song KJ, et al. Oral vitamin B12 replacement: an effective treatment for vitamin B12 deficiency after total gastrectomy in gastric cancer patients. *Ann Surg Oncol.* 2011 Dec;18(13):3711-17. [PMID: 21556950]
4. Lowering blood homocysteine with folic acid based supplements: meta-analysis of randomised trials. Homocysteine Lowering Trialists' Collaboration. *BMJ.* 1998 Mar;316(7135):894-98. [PMID: 9569395]
5. Puri V, Chaudhry N, Goel S, et al. Vitamin B12 deficiency: a clinical and electrophysiological profile. *Electromyogr Clin Neurophysiol.* 2005 Jul-Aug;45(5):273-84. [PMID: 16218195]
6. Hemendinger RA, Armstrong EJ 3rd, Brooks BR. Methyl Vitamin B12 but not methylfolate rescues a motor neuron-like cell line from homocysteine-mediated cell death. *Toxicol Appl Pharmacol.* 2011 Mar 15;251(3):217-25. [PMID: 21237187]
7. Valizadeh M, Valizadeh N. Obsessive compulsive disorder as early manifestation of B12 deficiency. *Indian J Psychol Med.* 2011 Jul;33(2):203-04. [PMID: 22345852]
8. Mayer G, Kröger M, Meier-Ewert K. Effects of vitamin B12 on performance and circadian rhythm in normal subjects. *Neuropsychopharmacology.* 1996 Nov;15(5):456-64. [PMID: 8914118]
9. Koury MJ, Ponka P. New insights into erythropoiesis: the roles of folate, vitamin B12, and iron. *Annu Rev Nutr.* 2004;24:105-31. [PMID:15189115]
10. Yamadera W, Sasaki M, Itoh H, et al. Clinical features of circadian rhythm sleep disorders in outpatients. *Psychiatry Clin Neurosci.* 1998 Jun;52(3):311-16. [PMID: 9681583]
11. Kiuchi T, Sei H, Seno H, et al. Effect of vitamin B12 on the sleep-wake rhythm following an 8-hour advance of the light-dark cycle in the rat. *Physiol Behav.* 1997 Apr;61(4):551-54. [PMID: 9108574]
12. Honma K, Kohsaka M, Fukuda N, et al. Effects of vitamin B12 on plasma melatonin rhythm in humans: increased light sensitivity phase-advances the circadian clock? *Experientia.* 1992 Aug 15;48(8):716-20. [PMID: 1516676]
13. Tamura J, Kubota K, Murakami H, et al. Immunomodulation by vitamin B12: augmentation of CD8+ T lymphocytes and natural killer (NK) cell activity in vitamin B12-deficient patients by methyl-B12 treatment. *Clin Exp Immunol.* 1999 Apr;116(1):28-32. [PMID: 10209501]
14. Takimoto G, Yoshimatsu K, Isomura J, et al. The modulation of murine immune responses by methyl-B12. *Int J Tissue React.* 1982;4(2):95-101. [PMID: 6214503]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.



Available in 120 capsules

Discussion

A sufficient intake of minerals is important for the production of energy; the synthesis of blood, bone, and hormones; the immune system; enzyme function; and reproduction. Furthermore, balance—or the ratio of one mineral to another—is key to mineral utilization.*

Bioavailability is perhaps the most important consideration when selecting a formula containing minerals. The body transports minerals across the intestinal wall by bonding (or chelating) them to amino acids. To increase bioavailability of supplementary minerals, special processing is needed to create a stable bond between the minerals and the amino acids. Albion Laboratories uses patented processes to assure bond stability.^[1] The result, it has been demonstrated, is that the bioavailability of Albion's chelates is superior.^[2] Some other products on the market, which are purported to be chelates, are merely mixtures of proteins and minerals that lose stability during digestion and consequently have lower bioavailability.*

Many of the minerals in MinRex are bound to dipeptides. This combination appears to improve absorption by enhancing the minerals' transport across the intestinal wall.^[1] Three very important features of the chelated minerals in MinRex assist in absorption: (1) the absence of an electrical charge, which renders them less likely to interact with other dietary substances such as phytates, other vitamins and minerals, or medications; (2) small molecular weights that facilitate transport across the intestinal mucosa; and (3) the chelates remain intact and stable throughout the ranges of pH in the digestive tract.*

The minerals in MinRex differ from those in many formulas in that they are bound to the ligand, glycine. Unlike the ligand picolinic acid, which gets excreted unchanged in the urine, the amino acid glycine has nutritional value. This means that 100% of the mineral/amino acid compound has nutrient value.*^[3]

Another reason why MinRex stands apart from other mineral formulas on the market is because it contains malic acid, lithium, and

Clinical Applications

- » Supports Mineral Repletion*
- » Supports the Consumption of a Mineral-Rich Diet*
- » Supports Sports Nutrition*

MinRex®, XYMOGEN's highly absorbable and balanced multi-mineral formula, is composed exclusively of Albion®'s patented and fully reacted mineral amino acid chelates, malates, and mineral complexes.*

vanadium. Malic acid participates in the energy production cycle. A double-blind, placebo-controlled, cross-over pilot study using 400 mgs of malic acid three times a day (approximately the same amount as in MinRex) along with magnesium supported feelings of wellness in subjects' joints, muscles, tendons, and other soft tissues.^[4] Swedish researchers noted that a reduced content of high-energy phosphates in the muscles of some patients could be contributing to the muscle energy deficits experienced by these patients.^[5] Because of malic acid's role in energy production, NADH (which yields three ATPs) is formed and may therefore support muscle energy production. Malic acid is also thought to increase energy levels in healthy humans.*

Lithium and vanadium are known as ultra-trace elements. As yet, neither a requirement for ultra-trace elements, nor deficiency symptoms have been demonstrated in humans. Animal research suggests vanadium has important interactions with magnesium.^[6] It also appears to have positive effects on insulin and glucose metabolism.^[7] Lithium is thought to help regulate the neurotransmitter glutamate by keeping the amount of glutamate between brain cells at a stable, healthy level.^[8] Lithium doses somewhat higher than those in this formula are used by some practitioners to support healthy brain function. These ultra-trace minerals, as well as some of the others, could have very narrow margins between what are useful and what are toxic doses. According to Jeppsen et al, in their presentation at the 6th International Symposium on Chelating Agents in Pharmacology, Toxicology and Therapeutics, Albion amino acid chelates are less irritating than other forms of inorganic mineral supplements.*^[9]

Strenuous exercise is thought to increase mineral loss via urine, sweat, and metabolic demand. In addition to electrolytes, the minerals copper, iron, and especially magnesium and zinc appear to be prominent minerals that are impacted by exercise or have important roles in performance.^[10-12] Mineral supplements may therefore be beneficial for people who engage in strenuous exercise or physically demanding sports.*

Continued on next page

MinRex® Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Calcium (as DimaCal® di-calcium malate and TRAACS® calcium glycinate chelate)	150 mg	12%
Iodine (as potassium iodide)	75 mcg	50%
Magnesium (as Albion® di-magnesium malate and TRAACS® magnesium lysyl glycinate chelate)	100 mg	24%
Zinc (as TRAACS® zinc bisglycinate chelate)	15 mg	136%
Selenium (as Albion® selenium glycinate complex)	60 mcg	109%
Copper (as TRAACS® copper bisglycinate chelate)	1.5 mg	167%
Manganese (as TRAACS® manganese bisglycinate chelate)	2 mg	87%
Chromium (as TRAACS® chromium nicotinate glycinate chelate)	75 mcg	214%
Molybdenum (as TRAACS® molybdenum glycinate chelate)	50 mcg	111%
Potassium (as Albion® potassium glycinate complex)	50 mg	1%
Malic Acid (as DimaCal® di-calcium malate and Albion® di-magnesium malate)	621 mg	**
Betaine HCl	200 mg	**
Lithium (as lithium orotate)	250 mcg	**
Vanadium (as TRAACS® vanadium nicotinate glycinate chelate)	30 mcg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), microcrystalline cellulose, stearic acid, medium-chain triglyceride oil, magnesium stearate, and silica.**DIRECTIONS:** Take two capsules daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.**DOES NOT CONTAIN:** Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

 Albion, DimaCal, TRAACS and the Albion Medallion design are registered trademarks of Albion Laboratories, Inc. Malates covered by U.S. Patent 6,706,904.


Individuals who want to support their general well-being, mineral nutrition, and glucose/insulin metabolism, as well as individuals who need to replace minerals lost through intense exercise, increased excretion, or absorption challenges may benefit from MinRex.*

References

1. TRAACS FT-IR. Albion Web site. <http://www.albionminerals.com/human-nutrition/quality/traacs-ft-ir-analysis>. Published 2011. Accessed November 12, 2012.
2. Research Done on Albion Chelates. Albion Human Nutrition. <http://www.albionnutritionalfacts.com/research>. Accessed November 12, 2012.
3. Implications of the "other half" of mineral compound. *Albion® Research Notes*. http://www.albionhumannutrition.com/research-notes/download/doc_details/738-implications-of-the-qother-half-q-of-a-mineral-compound. Accessed November 5, 2012.
4. Russel IJ, Michalek JE, Flechas JD, et al. Treatment of fibromyalgia syndrome with Super Malic: a randomized, double blind, placebo controlled, crossover pilot study. *J Rheumatol*. 1995 May; 22(5):953-58. [PMID:8587088]
5. Bengtsson A, Henriksson KG. The muscle in fibromyalgia—a review of Swedish studies. *J Rheumatol Suppl*. 1989 Nov; 19: 144-49. [PMID: 2691674]
6. Sánchez C, Torres M, Bermúdez-Peña MC, et al. Bioavailability, tissue distribution and hypoglycaemic effect of vanadium in magnesium-deficient rats. *Magnes Res*. 2011 Dec;24(4):196-208. [PMID: 22068015]
7. Mehdi MZ, Pandey SK, Theberge JF, et al. Insulin signal mimicry as a mechanism for the insulin-like effects of vanadium. *Cell Biochem Biophys*. 2006;44(1):73-81. [PMID: 16456236]
8. Dixon JF, Hokin LE. Lithium acutely inhibits and chronically up-regulates and stabilizes glutamate uptake by presynaptic nerve endings in mouse cerebral cortex. *Proc Natl Acad Sci U S A*. 1998 Jul 7;95(14):8363-68. [PMID: 9653192]
9. Jeppsen RB, Bourdonnais A, Ashmead HD. The nutritional benefits and safety of minerals which have been chelated with amino acids. Paper presented at: 6th International Symposium on Chelating Agents in Pharmacology, Toxicology and Therapeutics; September 7-9, 2000; Pilsen, Czech Republic [abstract from Albion. <http://www.albionnutritionalfacts.com/research>. Accessed November 12, 2012].
10. Córdova A, Navas FJ. Effect of training on zinc metabolism: changes in serum and sweat zinc concentrations in sportsmen. *Ann Nutr Metab*. 1998;42(5):274-82. [PMID: 9812018]
11. Santos DA, Matias CN, Monteiro CP, et al. Magnesium intake is associated with strength performance in elite basketball, handball and volleyball players. *Magnes Res*. 2011 Dec;24(4):215-19. [PMID: 21983266]
12. Latunde-Dada GO. Iron metabolism in athletes - achieving a gold standard. *Eur J Haematol*. 2012 Oct 18. doi: 10.1111/ejh.12026. Epub ahead of print. [PMID: 23078160]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Mitochondrial Renewal Kit

Comprehensive Mitochondrial Biogenesis Formula



Discussion

Mitochondria are the organelles inside cells that produce energy. Representing approximately 10% of total body weight, mitochondria have a number of roles in the body. Primarily, they are cellular “fuel stations” responsible for supplying greater than 95% of the body’s energy needs.^[1] Mitochondrial biogenesis is the process by which new mitochondria are produced, and it is believed to delay the effects of aging and the onset of age-associated diseases.^[2-5] This complex process involves more than 1,000 genes^[2] and is responsible for producing 20% of total cellular protein.^[1] Aerobic exercise and caloric restriction are the two most compelling approaches to stimulate mitochondrial biogenesis,^[2-3] most notably by activating the “master regulator” of mitochondrial biogenesis and function known as PGC-1 α , a transcriptional coactivator. Dysregulation of PGC-1 α has been implicated in aging and the pathogenesis of numerous age-associated complications such as poor glucose control, increased fat mass with accompanying decrease in muscle mass, and various neurological conditions.*

PGC-1 α -deficient animals display defects in energy metabolism, glucose disposal, and insulin action. These deficient animals also display reduced resistance to oxidative stress, increased fat mass, decreased muscle mass, impaired exercise performance, and other issues suggestive of an impaired ability to adapt to metabolic and physiological stress.^[6] Conversely, PGC-1 α activation contributes to an increase in metabolic fitness in the form of an increased metabolic rate, improved glucose disposal and insulin function, enhanced fatty acid oxidation, increased resistance to oxidative stress, decreased fat mass, and increased muscle mass and exercise performance.*

The nutrients in the MRK have been clinically tested for their oral bioavailability and also for their safety and efficacy in activating PGC-1 α and upstream cellular signaling cascades. These actions mimic the protective effects of exercise and caloric restriction on mitochondrial

Clinical Applications

- » Promotes Efficient Use of Insulin and Glucose in the Body*
- » Enhances Conversion of Glucose into Usable Energy*
- » Promotes Healthy Aging*
- » Increases Exercise Performance*
- » Promotes Nitric Oxide (NO) Production*
- » Supports Cardiovascular and Endothelial Function*
- » Improves Antioxidant Status and Resistance to Oxidative Stress*

*The XYMOGEN Mitochondrial Renewal Kit (MRK) is formulated to support and promote mitochondrial biogenesis and function. MRK supplies three active, orally bioavailable formulations—N.O.max ER™, Resveratin™ Plus, and ALAMax™ CR—which function synergistically to support the critical role that mitochondria play in metabolism. The patented functional components found in the MRK are safe, well-tolerated, and have been uniquely prepared to enhance both absorption and overall bioavailability in order to maximize patient benefit and satisfaction.**

biogenesis, metabolic fitness, and aging. The key signaling cascades affected include those involving nitric oxide (N.O.max ER™), SIRT1 (Resveratin™ Plus), and AMPK (ALAMax™ CR). Ultimately, it is the stimulation of these cascades that leads to activation of PGC-1 α and subsequent upregulation of mitochondrial biogenesis and promotion of overall metabolic fitness. For optimal benefit, combine this product with a healthy diet and exercise regimen.*

N.O.max ER™ is a patented, extended-release formulation containing arginine alpha-ketoglutarate and ACTINOS^{2®}, a proprietary whey peptide fraction. This synergistic combination serves as an effective nitric oxide (NO) precursor. As a vasodilator, NO exerts a protective effect on blood vessel endothelium.^[7] Within the cell, NO plays an important role in intracellular communication, acting as a trigger for mitochondrial biogenesis.*^[8]

Resveratin™ Plus provides a distinctive bioflavonoid complex with resveratrol, quercetin, and pterostilbene (bio-optimized methylated resveratrol).^[9] These three antioxidants work together synergistically and are being extensively studied in the areas of cardiovascular health and aging.*

ALAMax™ CR is a multifunctional antioxidant that has the ability to neutralize free radicals in both the aqueous-based and lipid-based environments of cells. In addition, ALAMax CR’s patented, controlled-release formulation provides extended protection^[10] by promoting synthesis of glutathione and “recharging” other important antioxidants such as vitamin C, vitamin E, and coenzyme Q10.*

An independent study of the MRK was performed. A report of the study, written by Dr. Joseph Evans and entitled “A Three-Month, Open-Label Pilot Clinical Study Evaluating the Efficacy of the Mitochondrial Renewal Kit™ on Aerobic Conditioning and Body Composition,” is available through your XYMOGEN Functional Medicine Consultant.*

EXCLUSIVE · PATENTED

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

ALAmox™ CR Supplement Facts

Serving Size: 1 Tablet

	Amount Per Serving	%Daily Value
Biotin	450 mcg	1500%
Alpha-Lipoic Acid (thioctic acid)	600 mg	**

** Daily Value not established.

Other Ingredients: Cellulose and cellulose derivatives, silica, magnesium stearate, stearic acid, glycerin, and dicalcium phosphate.
PROTECTED BY U.S. PATENTS: 6,191,162(B1); 6,197,340(B1); 6,572,888(B2); 7,118,762(B2)

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

Resveratin™ Plus Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Quercetin (as quercetin dihydrate)(from <i>Saphora japonica</i>)(bud)	250 mg	**
<i>trans</i> -Resveratrol (as <i>Polygonum cuspidatum</i> root extract)	75 mg	**
<i>trans</i> -Pterostilbene (pTeroPure®)	62.5 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), microcrystalline cellulose, stearic acid, magnesium stearate, silica, and medium-chain triglyceride oil.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



pTeroPure™ is a trademark of ChromaDex, Inc.

N.O.max ER™ Supplement Facts

Serving Size: 3 Caplets

	Amount Per Serving	%Daily Value
Arginine <i>alpha</i> -ketoglutarate	1980 mg	**
ACTINOS® Whey Peptide Fraction†	150 mg	**

** Daily Value not established.

Other Ingredients: Cellulose and cellulose derivatives, stearic acid, magnesium stearate, silica, and glycerin.

Contains: Ingredient derived from milk (ACTINOS®).

†Controlled Delivery Formulation

PROTECTED BY U.S. PATENTS: 6,905,707 and 7,579,020.

Contains: Ingredient derived from Milk (ACTINOS®)

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, fish, shellfish, peanuts, tree nuts, egg, artificial colors, artificial sweeteners, or artificial preservatives.

UP-REGULATED WITH:



ACTINOS® is a trademark of Glanbia plc.

DIRECTIONS: Take one to two packets per day, or as directed by your healthcare practitioner. Each packet supplies three N.O.max ER, one Resveratin Plus, and one ALAmox CR. Take one packet with 8 oz. water, 30 minutes before breakfast and 30 minutes before lunch.

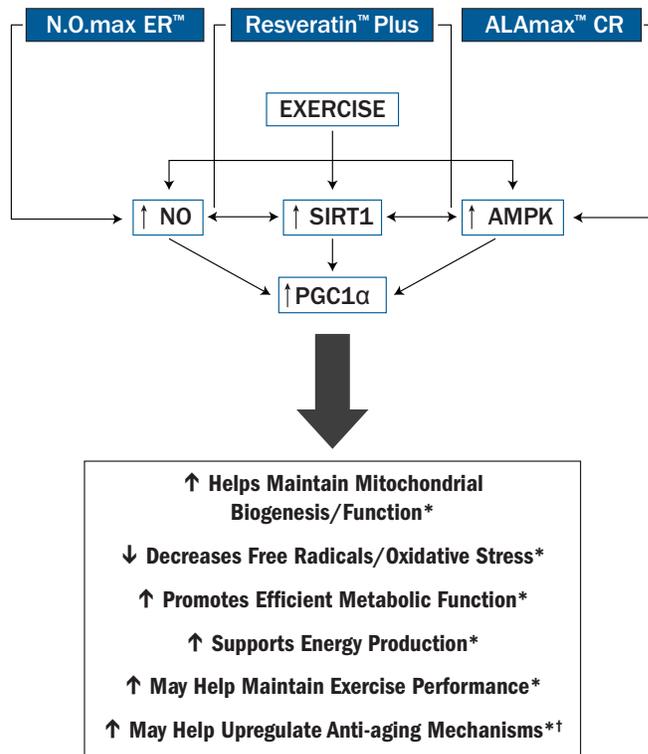
Individuals with a medical condition (including diabetes or cold sores), that are taking prescription drugs, that are pregnant or lactating, or are under the age of 18 should consult their healthcare practitioner prior to use.

STORAGE: Keep closed in a cool, dry place out of reach of children.

References

- Goffart S, Wiesner RJ. Regulation and co-ordination of nuclear gene expression during mitochondrial biogenesis. *Exp Physiol.* 2003 Jan;88(1):33-40. Review. [PMID: 12525853]
- López-Lluch G, Irujo PM, Navas P, et al. Mitochondrial biogenesis and healthy aging. *Exp Gerontol.* 2008 Sep;43(9):813-9. Review. [PMID: 18662766]
- Lanza IR, Short DK, Short KR, et al. Endurance exercise as a countermeasure for aging. *Diabetes.* 2008 Nov;57(11):2933-42. [PMID: 18716044]
- Johnston AP, De Lisio M, Parise G. Resistance training, sarcopenia, and the mitochondrial theory of aging. *Appl Physiol Nutr Metab.* 2008 Feb;33(1):191-9. Review. [PMID: 18347672]
- Wallace DC. A mitochondrial paradigm of metabolic and degenerative diseases, aging, and cancer: a dawn for evolutionary medicine. *Annu Rev Genet.* 2005;39:359-407. [PMID: 16285865]
- Leone TC, Lehman JJ, Finck BN, et al. PGC-1alpha deficiency causes multi-system energy metabolic derangements: muscle dysfunction, abnormal weight control and hepatic steatosis. *PLoS Biol.* 2005 Apr;3(4):e101. [PMID: 15760270]
- Bian K, Doursout MF, Murad F. Vascular system: role of nitric oxide in cardiovascular diseases. *J Clin Hypertens (Greenwich).* 2008 Apr;10(4):304-10. [PMID: 18401228]
- Nisoli E, Carruba MO. Nitric oxide and mitochondrial biogenesis. *J Cell Sci.* 2006 Jul 15;119(Pt 14):2855-62. [PMID: 16825426]
- Wen X, Walle T. Methylated flavonoids have greatly improved intestinal absorption and metabolic stability. *Drug Metab Dispos.* 2006 Oct;34(10):1786-92. [PMID: 16868069]
- Teichert J, Kern J, Tritschler HJ, et al. Investigations on the pharmacokinetics of alpha-lipoic acid in healthy volunteers. *Int J Clin Pharmacol Ther.* 1998 Dec;36(12):625-8. [PMID: 9876998]

Additional references available upon request



§ Based on emerging experimental research.

EXCLUSIVE • PATENTED

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Mood Food™

Nervous System Support*



Available in 60 capsules

Discussion

B Vitamins Due to their involvement in the synthesis of chemicals crucial to brain function, B vitamins are essential to mental and emotional well-being. Because B vitamins are water soluble and not stored by the body, dietary or supplementary sources are critical to maintaining optimal levels. In addition, B vitamins can be destroyed or used at a higher rate with consumption of alcohol, refined sugars, nicotine, and caffeine. Mood Food provides vitamin B6 in its principal coenzyme form, pyridoxal 5'-phosphate (P5P); vitamin B12 in its readily bioavailable form, methylcobalamin; and folate in the form of 50% calcium folinate and 50% Quatrefolic®. Quatrefolic is a form of 5-MTHF (5-methyltetrahydrofolate) that is proven to have greater stability, solubility, and bioavailability than calcium salt forms.*

Folate and vitamins B6 and B12 are needed for proper methylation, a vital and fundamental process involved in many biochemical pathways such as the conversion of homocysteine back to methionine or to cysteine. Adequate intakes of these B vitamins plus a healthy metabolic conversion of folate to 5-MTHF support the maintenance of homocysteine levels within the normal range. Moreover, healthy homocysteine levels, as well as healthy serum B-vitamin levels, have a role in nerve health and have been associated with normal psychological function, mood, and cognition.^[1-3] Because 5-MTHF can cross the blood-brain barrier and may be better utilized by those with genetic variations in folate metabolism, 5-MTHF may be particularly well-suited to supporting healthy neurotransmission and promoting healthy homocysteine levels already within the normal range.*

Pyridoxine nutritional status selectively modulates central production of both serotonin and GABA.^[4] Other neurotransmitters such as dopamine and norepinephrine are also synthesized using P5P-dependent enzymes.*

Magnesium As a cofactor for over 325 enzymes in the body, magnesium has a multitude of actions, including a calming effect on the nervous system. Laboratory, animal, and epidemiological research suggests a link between magnesium sufficiency and a healthy

Clinical Applications

- » Supports Nervous System Health*
- » Supports a Healthy Mood*
- » Supports Synthesis of Neurotransmitters, Including Serotonin*
- » May Help Reduce Carbohydrate Cravings*

*Mood Food™ combines key B vitamins, including 5-MTHF as Quatrefolic® and Albion® di-magnesium malate, with critical amino acids to support overall central nervous system health, calmness, and a positive mood.**

mood and calm demeanor.^[5,6] A suboptimal intake of magnesium could potentially cause intraneuronal magnesium deficits that affect neuronal integrity and function.*

GABA (Gamma-aminobutyric acid) GABA is an inhibitory neurotransmitter found in 30%-40% of the brain synapses. It helps calm the brain by neutralizing the excitatory effects of glutamate. It is thought that either low GABA levels or decreased GABA function in the brain may have an adverse impact on neurological health. Optimal levels of GABA support normal delta (deep) sleep and have been associated with healthy mood.*^[7]

5-HTP (5-hydroxytryptophan) 5-HTP is a precursor to serotonin, a neurotransmitter that regulates many normal brain activities, supports healthy production of norepinephrine and dopamine, and assists with supporting healthy mood and behavior. In addition, a review of studies investigating serotonergic neurotransmission suggests that increasing serotonin availability may assist in weight management as it relates to periodic carbohydrate cravings.*^[8]

In the synthesis of serotonin, tryptophan is converted into 5-HTP by the enzyme tryptophan hydroxylase. Supplementation with 5-HTP bypasses this rate-limiting conversion. Oral 5-HTP is well-absorbed in the intestine without the need for a transporter; other amino acids do not compete with it for absorption. It easily crosses the blood-brain barrier, is not degraded by the enzymes that degrade tryptophan, and it is excreted through the kidneys.*^[9,10]

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Mood Food™ Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Vitamin B6 (as pyridoxal 5'-phosphate)	4 mg	235%
Folate (400 mcg DFE as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt and 400 mcg DFE as calcium folinate)	800 mcg DFE	200%
Vitamin B12 (as methylcobalamin)	1000 mcg	41,667%
Magnesium (as Albion® di-magnesium malate)	50 mg	12%
GABA (gamma-aminobutyric acid)	250 mg	**
5-HTP (5-hydroxytryptophan)(from <i>Griffonia simplicifolia</i> (seed))	50 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, and silica.**DIRECTIONS:** Take one capsule twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication (especially those for depression, migraines, Parkinson's disease, or psychiatric disorders) should discuss potential interactions with their healthcare practitioner. Not for use by children. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

Albion is a registered trademark of Albion Laboratories, Inc.

 **Quatrefolic**® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,662.

**References**

1. Coppen A, Bolander-Gouaille C. Treatment of depression: time to consider folic acid and vitamin B12. *J Psychopharmacol.* 2005 Jan;19(1):59-65. [PMID: 15671130]
2. Lewis SJ, Lawlor DA, Davey Smith G, et al. The thermolabile variant of MTHFR is associated with depression in the British Women's Heart and Health Study and a meta-analysis. *Mol Psychiatry.* 2006 Apr;11(4):352-60. [PMID: 16402130]
3. Selhub J, Bagley LC, Miller J, et al. B vitamins, homocysteine, and neurocognitive function in the elderly. *Am J Clin Nutr.* 2000;71(2):614S-20S. [PMID: 10681269]
4. McCarty MF. High-dose pyridoxine as an 'anti-stress' strategy. *Med Hypotheses.* 2000 May;54(5):803-07. [PMID: 10859691]
5. Whittle N, Li L, Chen WQ, et al. Changes in brain protein expression are linked to magnesium restriction-induced depression-like behavior. *Amino Acids.* 2011 Apr;40(4):1231-48. [PMID: 21312047]
6. Sartori SB, Whittle N, Hetzenauer A, et al. Magnesium deficiency induces anxiety and HPA axis dysregulation: modulation by therapeutic drug treatment. *Neuropharmacology.* 2012 Jan;62(1):304-12. [PMID: 21835188]
7. Mombereau C. Genetic and pharmacological evidence of a role for GABA (B) receptors in the modulation of anxiety- and antidepressant-like behavior. *Neuropsychopharmacology.* 2004 Jun;29(6):1050-62. [PMID: 15039762]
8. Wurtman JJ. Carbohydrate craving. Relationship between carbohydrate intake and disorders of mood. *Drugs.* 1990;39 Suppl 3:49-52. [PMID: 2197075]
9. Birdsall TC. 5-Hydroxytryptophan: a clinically-effective serotonin precursor. *Altern Med Rev.* 1998 Aug;3(4):271-80. [PMID: 9727088]
10. Turner EH, Loftis JM, Blackwell AD. Serotonin a la carte: supplementation with the serotonin precursor 5-hydroxytryptophan. *Pharmacol Ther.* 2006 Mar;109(3):325-38. [PMID: 16023217]

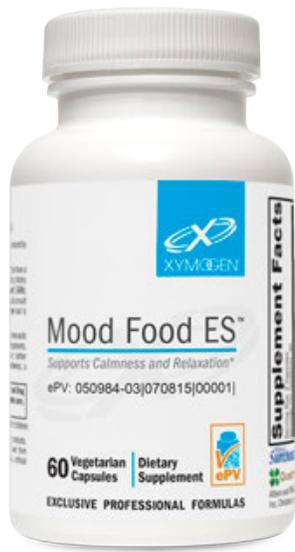
Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Mood Food ES™

Supports Calmness and Relaxation*



Available in 60 & 120 capsules

Discussion

Vitamins, minerals, amino acids, and other nutrients are necessary for the synthesis of neurotransmitters, healthy nerve transmission, healthy brain chemistry, and normal muscle contraction/relaxation. Components of Mood Food ES address each of these areas.*

Methylation is the addition of a methyl group (a carbon atom with three hydrogen atoms attached) to proteins, enzymes, chemicals, DNA, or amino acids like homocysteine. It is a vital aspect of nervous system health and is necessary for the synthesis of neurotransmitters. Mood Food ES provides key nutrients involved in the methylation pathway, such as selenomethionine; vitamin B6 as pyridoxal 5'-phosphate; vitamin B12 as the readily bioavailable form, methylcobalamin; and folate as bioactive Quatrefolic® (5-MTHF glucosamine salt) and calcium folinate.^[1] Pyridoxine nutritional status selectively modulates central production of serotonin and GABA (gamma-aminobutyric acid)—neurotransmitters that are involved in physical pain perception and mental wellness.*^[2]

Magnesium is provided as Albion® TRAACS® glycinate chelate, a specific form demonstrated to support intraneuronal magnesium sufficiency.^[3] As a cofactor for over 325 enzymes in the body, magnesium has a multitude of actions, including a calming effect on the nervous system and regulation of muscle contraction. Laboratory, animal, and epidemiological research suggests a link between magnesium sufficiency and a healthy mood and calm demeanor.*^[4,5]

Vitamin C participates in the enzyme activity of two copper-dependent monooxygenases that are important in the synthesis of norepinephrine and serotonin. In addition, vitamin C regulates the activity of some neurons within the brain that affect neurotransmitter membrane receptor synthesis and neurotransmitter dynamics.*^[6]

GABA (gamma-aminobutyric acid) is an important inhibitory neurotransmitter found in 30% to 40% of the brain synapses. It helps calm the brain by neutralizing the excitatory effects of glutamate. Research suggests that GABA supplementation or optimal GABA

Clinical Applications

- » Supports Nervous System Health*
- » Supports Inhibitory Neurotransmitters*
- » Supports Relaxation*
- » Supports a Healthy Mood*
- » Supports the Synthesis of Neurotransmitters, Including Serotonin*

*Mood Food ES™ combines the same vitamins, minerals, and amino acids as first generation Mood Food™. Modification in quantities of ingredients, plus the addition of Suntheanine®, vitamin C, and selenium, further enhance synthesis of chemical messengers that support calmness, a healthy mood, and a healthy nervous system.**

function in the brain positively affects neurological health, the body's response to stress, mood, alpha and beta brain waves, and sleep.*^[7-9]

5-HTP (5-hydroxytryptophan) is a precursor to serotonin. It is well-absorbed in the intestine and easily crosses the blood-brain barrier.^[10] Serotonin regulates many normal brain activities; influences other neurotransmitters, such as norepinephrine and dopamine; and is important in regulating mood and behavior, including food cravings. Research suggests that adequate levels of 5-HTP instill a sense of calmness and relaxation.*^[11]

L-Taurine is a conditionally essential, neuroprotective amino acid that helps maintain cell volume and stabilize cell membranes in the brain. In addition to its roles in antioxidant activity and inflammatory cytokine modulation, taurine is important in the transmission of nerve impulses and overall nerve function. Oral supplementation increases GABA.*^[12]

L-Theanine (Suntheanine®) is a naturally occurring, biologically active, free-form amino acid that provides relaxation support. Mechanisms of action appear to relate to its effects on neurotransmitters, excitatory amino acids activity, and alpha brain wave activity.^[13-15] Many practitioners utilize L-theanine to support overall relaxation without inducing drowsiness.*

Mood Food ES™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Vitamin C (ascorbic acid)	20 mg	22%
Vitamin B6 (as pyridoxal 5'-phosphate)	5 mg	294%
Folate (150 mcg DFE as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt and 150 mcg DFE as calcium folinate)	300 mcg DFE	75%
Vitamin B12 (as methylcobalamin)	30 mcg	1250%
Magnesium (as TRAACS® magnesium lysinate glycinate chelate)	70 mg	17%
Zinc (as TRAACS® zinc bisglycinate chelate)	3 mg	27%
Selenium (as Albion® selenium glycinate complex)	50 mcg	91%
Taurine	300 mg	**
5-HTP (5-hydroxytryptophan)(from <i>Griffonia simplicifolia</i> (seed))	100 mg	**
L-Theanine (Suntheanine®)	100 mg	**
GABA (gamma-aminobutyric acid)	100 mg	**

** Daily Value not established.
Other Ingredients: HPMC (capsule), microcrystalline cellulose, stearic acid, magnesium stearate, silica, and medium-chain triglyceride oil.

DIRECTIONS: Take two capsules one to two times daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner before use, especially if you have a current medical condition or take prescription drugs. Pregnant or lactating women should consult their healthcare practitioner prior to use. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

Albion and TRAACS are registered trademarks of Albion Laboratories, Inc. Chelates covered by U.S. patent 7,838,042 and patents pending.

 Suntheanine® is a registered trademark of Taiyo International, Inc. U.S. and International Patents Pending. U.S. Patent Nos. 6831103, 6598566, 6297280.



 Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,862.

References

1. Bottiglieri T, Laundry M, Crellin R, et al. Homocysteine and folate metabolism in depression. *Prog Neuropsychopharmacol Biol Psychiatry*. 2005 Sep;29(7):1103-12. [PMID: 10896698]
2. McCarty MF. High-dose pyridoxine as an 'anti-stress' strategy. *Med Hypotheses*. 2000 May;54(5):803-07. [PMID: 10859691]
3. Eby GA, Eby KL. Rapid recovery from major depression using magnesium treatment. *Med Hypotheses*. 2006;67(2):362-70. [PMID: 16542786]
4. Whittle N, Li L, Chen WQ, et al. Changes in brain protein expression are linked to magnesium restriction-induced depression-like behavior. *Amino Acids*. 2011 Apr;40(4):1231-48. [PMID: 21312047]
5. Sartori SB, Whittle N, Hetzenauer A, et al. Magnesium deficiency induces anxiety and HPA axis dysregulation: modulation by therapeutic drug treatment. *Neuropharmacology*. 2012 Jan;62(1):304-12. [PMID: 21835188]
6. Jacob, RA. Vitamin C. In: Shils M, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*. 9th ed. Baltimore, MD: Lippincott Williams & Wilkins; 1999:467-482.
7. Fatemi SH, Folsom TD, Thuras PD. Deficits in GABA(B) receptor system in schizophrenia and mood disorders: a postmortem study. *Schizophr Res*. 2011 May;128(1-3):37-43. [PMID: 21303731]
8. Mombereau C. Genetic and pharmacological evidence of a role for GABA(B) receptors in the modulation of anxiety- and antidepressant-like behavior. *Neuropsychopharmacology*. 2004 Jun;29(6):1050-62. [PMID: 15039762]
9. Shell W, Bullias D, Charuvastra E, et al. A randomized, placebo-controlled trial of an amino acid preparation on timing and quality of sleep. *Am J Ther*. 2010 Mar-Apr;17(2):133-39. [PMID: 19417589]
10. Birdsall TC. 5-Hydroxytryptophan: a clinically-effective serotonin precursor. *Altern Med Rev*. 1998 Aug;3(4):271-80. [PMID: 9727088]
11. Turner EH, Loftis JM, Blackwell AD. Serotonin a la carte: supplementation with the serotonin precursor 5-hydroxytryptophan. *Pharmacol Ther*. 2006 Mar;109(3):325-38. [PMID: 16023217]
12. Oja SS, Saransaari P. Pharmacology of taurine. *Proc West Pharmacol Soc*. 2007;50:8-15. [PMID: 18605222]
13. Di X, Yan J, Zhao Y, et al. L-theanine protects the APP (Swedish mutation) transgenic SH-SY5Y cell against glutamate-induced excitotoxicity via inhibition of the NMDA receptor pathway. *Neuroscience*. 2010 Jul 14;168(3):778-86. [PMID: 20416364]
14. Yamada T, Terashima T, Okubo T, et al. Effect of theanine, r-glutamylethylamide, on brain monoamines and striatal dopamine release in conscious rats. *Nutr Neurosci*. 2005 Aug;8(4):219-26. [PMID: 16493792]
15. Nobre AC, Rao A, Owen GN. L-theanine, a natural constituent in tea, and its effect on mental state. *Asia Pac J Clin Nutr*. 2008;17 Suppl 1:167-68. [PMID: 18296328]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

N.O.max™ ER

Extended-Release Arginine Alpha-Ketoglutarate



Available in 180 caplets

Discussion

N.O.max™ ER elevates the plasma level of L-arginine, a “semi-essential” amino acid and important nutrient whose remarkable properties are validated by a Nobel Prize in medicine (1998). More than 60,000 clinical studies have brought L-arginine to the forefront of modern medicine as a nutrient that offers a wide range of health benefits. N.O.max ER provides L-arginine in extended-release form to prolong its bioavailability.*

L-arginine is considered a direct nitric oxide (NO) precursor as it is the substrate of nitric oxide-generating enzymes called nitric oxide synthetases (NOS). Nitric oxide is an endogenously produced cellular signaling molecule involved in a variety of endothelium-mediated actions in the vasculature.^[1] The plasma concentration of L-arginine might be a rate-limiting factor for NO production. Research in humans suggests that oral supplementation with L-arginine may increase smooth muscle relaxation, inhibit platelet aggregation, and inhibit expression of adhesion molecules and endolelin-1.^[2] L-arginine drives the biosynthesis of NO in tissues, including the vascular endothelium and skeletal muscle.^[3] Acting via the cyclic guanosine monophosphate (cGMP) intracellular signaling system, NO increases blood flow without increasing blood pressure.^[4] In short, NO causes vasodilation by inhibiting smooth muscle contraction. Increased blood flow results in increased nutrient uptake and glucose utilization in muscle, especially during exercise.*^[4]

In addition to the cardiovascular/circulatory benefits, L-arginine is involved in ammonia detoxification, hormone secretion, and immune health. It supports the synthesis of protein as well.^[5] The generation of nitric oxide may act as a molecular switch that activates PGC-1 α , the master regulator of mitochondrial biogenesis and energy metabolism.^[6] Many athletes have safely and effectively used L-arginine to increase “muscle pump” during a workout and for several hours afterward. Additional desired benefits include an increase in overall workout capacity (muscular endurance) and an increase in post-exercise recovery.*^[7]

Clinical Applications

- » Supports Circulatory Health*
- » Supports Cardiovascular Health*
- » Optimizes Muscle Synthesis, Muscle Function, and Adaptation to Exercise*

***N.O.max™ ER** represents a patented, extended-release nitric oxide precursor. Scientists now refer to nitric oxide (NO) as the “foundation” of cardiovascular health. This tiny molecule is a vasodilator responsible for controlling blood flow to the entire body, which may help support healthy blood flow pressure and promote the health of the endothelium—the inside of blood vessels. With age comes diminished NO levels; that’s why since 1998, when three scientists won the Nobel Prize for their discovery of NO, researchers have been working to harness its heart-healthy activity. Today, with the application of XYMOGEN’s extended-release technology, that activity has been realized with N.O.max ER.**

ACTINOS^{2®} is a mixture of both high- and low-molecular weight fractions of proteins and peptides derived from whey through patent-pending technology. Research suggests that these fractions are NOS activators that boost NO production by factors unrelated to arginine, calcium, or bradykinin. ACTINOS² may enhance transcription of the NOS gene and supports its role in reducing the negative feedback mechanism for NO production. The synergistic activity of the size-based fractions of ACTINOS² has been shown to increase NO production in human endothelial cells in vitro from 9.5 to 12.7 times compared to a control.*^[8]

N.O.max ER is manufactured in the United States using the highest purity (>98.0%) of L-arginine alpha-ketoglutarate that is commercially available. This patented formulation is specially designed to deliver L-arginine alpha-ketoglutarate in a controlled manner over a period of approximately 4-6 hours.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

N.O.max™ ER Supplement Facts

Serving Size: 3 Caplets

	Amount Per Serving	%Daily Value
Arginine <i>alpha</i> -ketoglutarate	1.98 g	**
ACTINOS [®] Whey Peptide Fraction [‡]	150 mg	**

** Daily Value not established.

Other Ingredients: Cellulose and cellulose derivatives, stearic acid, magnesium stearate, silica, and glycerin.**Contains:** Milk**DIRECTIONS:** Take three caplets twice per day: 3 caplets 30 minutes before breakfast and 3 caplets again 30 minutes before lunch with 8 ounces of water.**CAUTIONS:** Consult your healthcare practitioner prior to use, especially if you have or suspect you have a medical condition, including diabetes or cold sores; if you take prescription drugs or are allergic to any ingredient; or if you are pregnant or lactating. Keep out of reach of children. This product is not intended for use by individuals under 18 years of age.**STORAGE:** Keep closed in a cool, dry place out of reach of children.**DOES NOT CONTAIN:** Wheat, gluten, corn, yeast, soy, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

‡Controlled Delivery Formulation

PROTECTED BY U.S. PATENTS: 6,905,707 and 7,579,020.**References**

1. Moncada S, Higgs EA. Nitric oxide and the vascular endothelium. *Handb Exp Pharmacol.* 2006;(176 Pt 1):213-54. [PMID: 16999221]
2. Tousoulis D, Böger RH, Antoniades C, et al. Mechanisms of disease: L-arginine in coronary atherosclerosis--a clinical perspective. *Nat Clin Pract Cardiovasc Med.* 2007 May;4(5):274-83. [PMID: 17457351]
3. Boger H, Bode-Boger, SM. The clinical pharmacology of L-arginine. *Annu Rev Pharmacol Toxicol.* 2001;41:79-99. [PMID: 11264451]
4. Preli RB, Klein KP, Herrington DM. Vascular effects of dietary L-arginine supplementation. *Atherosclerosis.* 2002 May;162(1):1-15. [PMID: 11947892]
5. Nisoli E, Clementi E, Tonello C, et al. Effects of nitric oxide on proliferation and differentiation of rat brown adipocytes in primary cultures. *Br J Pharmacol.* 1998 Oct;125(4):888-94. [PMID: 9831929]
6. Nisoli E, Carruba MO. Nitric oxide and mitochondrial biogenesis. *J Cell Sci.* 2006 Jul 15;119(Pt 14):2855-62. [PMID: 16825426]
7. Rassaf T, Lauer T, Heiss C, et al. Nitric oxide synthase-derived plasma nitrite predicts exercise capacity. *Br J Sports Med.* 2007 Oct;41(10):669-73: discussion 673. [PMID: 17496072]
8. Inhouse report. Glanbia Nutritionals Inc., 2006 CFMN-CSR-0506-1

Additional references available upon request**All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.**

<p>*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.</p>
--

NAC

Supports Antioxidant and Detoxification Activity*



Available in 60 capsules & 120 capsules

Discussion

NAC (N-acetyl-cysteine) NAC, a sulfur-containing derivative of the amino acid L-cysteine, supports antioxidant and detoxification mechanisms in the body. NAC supports antioxidant activity by neutralizing hydrogen peroxide, hypochlorous acid, and the highly reactive hydroxyl radical and also serves as a source of sulfhydryl groups. In addition, NAC enhances production of the tripeptide glutathione—a key component of both antioxidant and detoxification enzymes.*^[1]

NAC is recognized for its support of normal mucous production and may positively support respiratory function and eye health, especially when consumed over a prolonged period.^[1-3] Research suggests that NAC may protect cell and tissue health by supporting normal metal status in the body.*^[1,4,5]

Glutathione While the absorption of oral glutathione may be limited,^[6] supplementation with NAC may significantly increase circulating levels of glutathione in the body.^[7,8] Once NAC promotes production of glutathione, glutathione is incorporated into crucial antioxidant enzymes (e.g., glutathione peroxidase and glutathione reductase) and detoxification enzymes (glutathione S-transferases). Through the activity of these enzymes, glutathione directly supports antioxidant activity, phase II detoxification, and the normal breakdown of metabolites, toxins, and other compounds in the body. Glutathione also participates in fatty acid synthesis and amino acid transport across the cell membrane.*^[1]

A variety of factors may determine glutathione requirements, including level of exposure to toxins, increased phase I detoxification activity, and overall need for antioxidant support. Maintaining glutathione levels may be important to maintaining the health of the respiratory, hepatic, and immune systems, as well as supporting antioxidant protection of lipids and proteins and supporting the normal response to inflammation.^[7-13] Levels of endogenous antioxidants, including glutathione, may decrease

Clinical Applications

- » Supports Glutathione Synthesis*
- » Supports Detoxification of Environmental Toxins and Pollutants*
- » Supports Antioxidant Activity in all Body Cells*
- » Supports Healthy Respiratory Function*

***N-Acetyl-L-Cysteine (NAC)** is a source of the conditionally essential amino acid L-cysteine and a precursor to the tripeptide glutathione. NAC and glutathione support antioxidant and detoxification activity in the body.**

with age.^[14] It is important to maintain adequate levels of glutathione in the body to support overall health and well-being throughout the lifespan.*

NAC Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
N-Acetyl-L-Cysteine	1.2 g	**
** Daily Value not established.		

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, and silica.

DIRECTIONS: Take one to two capsules twice daily between meals, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.**STORAGE:** Keep closed in a cool, dry place out of reach of children.**References**

1. Krinsky DL, LaValle JB, Hawkins EB, et al. *Natural Therapeutics Pocket Guide*. 2nd ed. Hudson (OH): Lexi-Comp; 2003.
2. Grandjean EM, Berthet P, Ruffmann R, Leuenberger P. Efficacy of oral long-term N-acetylcysteine in chronic bronchopulmonary disease: a meta-analysis of published double-blind, placebo-controlled clinical trials. *Clin Ther*. 2000 Feb 22(2):209-21. [PMID: 10743980]
3. Yalçın E, Altın F, Cinhüseynoglu F, et al. N-acetylcysteine in chronic blepharitis. *Cornea*. 2002 Mar;21(2):164-8. [PMID: 11862087]
4. Ottenwalder H, Simon P. Differential effect of N-acetylcysteine on excretion of the metals Hg, Cd, Pb and Au. *Arch Toxicol*. 1987 Jul;60(5):401-2. [PMID: 3662815]
5. Keogh JP, Steffen B, Siegers CP. Cytotoxicity of heavy metals in the human small intestinal epithelial cell line I-407: the role of glutathione. *J Toxicol Environ Health*. 1994 Nov;43(3):351-9. [PMID: 7966443]
6. Witschi A, et al. The systemic availability of oral glutathione. *Eur J Clin Pharmacol*. 1992;43:667-9. [PMID: 1362956]
7. De Rosa SC, et al. N-acetylcysteine replenishes glutathione in HIV infection. *Eur J Clin Invest* 2000 Oct;30(10):841-2. [PMID: 11029607]
8. Atkuri KR, Mantovani JJ, Herzenberg LA, et al. N-Acetylcysteine—a safe antidote for cysteine/glutathione deficiency. *Curr Opin Pharmacol*. 2007 Aug;7(4):355-9. Review. [PMID: 17602868]
9. White AC, Thannickal VJ, Fanburg BL. Glutathione deficiency in human disease. *J Nutr Biochem*. 1994;5:218-26. <http://www.sciencedirect.com/science/article/pii/0955286394900396> Updated January 27, 2003. Accessed February 27, 2012.
10. Pace GW, Leaf CD. The role of oxidative stress in HIV Disease. *Free Rad Biol Med*. 1995;19:523-8. [PMID: 7590404]
11. Favier A, Sappey C, Leclerc P, et al. Antioxidant status and lipid peroxidation in patients infected with HIV. *Chem Biol Interact*. 1994 Jun;91(2-3):165-80. Review. [PMID: 8194133].
12. Nakamura H, Masutani H, Yodoi J. Redox imbalance and its control in HIV infection. *Antioxid Redox Signal*. 2002 Jun;4(3):455-64. [PMID: 12215212]
13. Roberts RL, Aroda VR, Ank BJ. N-acetylcysteine enhances antibody-dependent cellular toxicity in neutrophils and mononuclear cells from healthy adults and human immunodeficiency virus-infected patients. *J Infect Dis*. 1995 Dec;172(6):1492-502. [PMID: 7594708]
14. Hu HL, Forsey RJ, Blades TJ, et al. Antioxidants may contribute in the fight against ageing: an in vitro model. *Mech Ageing Dev*. 2000 Dec 20;121(1-3):217-30. [PMID: 11164475]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration.
This product is not intended to diagnose, treat, cure, or prevent any disease.

Nattokinase

Healthy Circulation Support*



Available in 60 capsules & 120 capsules

Discussion

Natto is a fermented, cheese-like food that is popular in Japan where it has been consumed safely for more than 1000 years. It is made through the fermentation of boiled soybeans by the bacterium *Bacillus subtilis* natto. In 1980, during a series of in vitro experiments at the University of Chicago Medical School, Dr. Hiroyuki Sumi discovered that natto could affect fibrin levels. Fibrin is a whitish, filamentous protein that is formed in blood after a trauma or injury to protect the body from excessive blood loss. Strands of fibrin can accumulate along the walls of blood vessels and affect blood flow.*

After Dr. Sumi discovered the effect of natto on fibrin, he proceeded to look for natto's active component. He then isolated and named this component "nattokinase," which means "enzyme in natto." According to Dr. Sumi, a 150 g portion of natto contains approximately 500 mg of nattokinase.^[1] Nattokinase is produced by *Bacillus subtilis* natto during the soybean fermentation process. While other soy foods contain enzymes, it is only the natto preparation that contains the nattokinase enzyme. Nattokinase is not a kinase enzyme, it is a serine proteinase class of enzyme.*

How Nattokinase Works Nattokinase supports healthy levels of fibrin and supports healthy blood flow through protease enzyme action (e.g., subtilisin protease, bacillopeptidase F).^[2,3] Not only does nattokinase act directly on fibrin, but as demonstrated by in vitro work, its action also causes the release of substances that trigger the body's production of other important enzymes that help regulate fibrin formation. Nattokinase can also inhibit a key enzyme that affects extracellular and arterial vasoconstriction, and it can generate tissue plasminogen activators.^[4,5] Other in vitro work revealed that nattokinase caused a significant, dose-dependent decrease of red blood cell aggregation and low-shear viscosity, and these beneficial effects were evident at concentrations similar to those achieved with in vivo animal trials.^[6] The Japanese have long believed that natto supports healthy blood flow. Now, as outlined above, modern science has uncovered mechanisms underlying this belief.*^[2-8]

Clinical Applications

- » Supports Healthy Fibrin Levels*
- » Supports the Smooth Flow of Blood*
- » Supports Healthy Blood Pressure Already Within the Normal Range*

Nattokinase is an all-natural, potent enzyme that is extracted from natto and highly purified. Natto is a fermented soybean food that has been consumed in Japan for over 1000 years. Nattokinase has been the subject of many studies, including human and animal trials. In 1980, researchers discovered that nattokinase demonstrated a positive effect on blood flow in vitro. Nattokinase may also support cardiovascular health.*

Animal and Human Studies In preliminary research performed by Dr. Sumi and his colleague Masugi Maruyama, extract of natto (equivalent to 25 mg and 200 mg respectively) showed a healthy influence on blood pressure in Wistar rats and in humans.^[9] In another animal study performed on dogs, nattokinase was tested against a placebo. Oral administration (1 g nattokinase in four capsules containing 250 mg each) supported normal circulation, as shown by angiogram.^[2] More recently, to examine the effects of nattokinase supplementation on blood pressure in humans, 86 people aged 20 to 80 years participated in an eight-week, randomized, double-blind, placebo-controlled trial. Seventy-three subjects completed the protocol. The researchers found that oral nattokinase supplementation (2000 FU/capsule) resulted in a healthy effect on blood flow.^[10] XYMOGEN's Nattokinase provides 1000 FU/capsule with a recommended dosage of two capsules per day.*

It is important to note that both natto and nattokinase have been demonstrated to have activity in humans, whereas supplementing with boiled soybeans did not.^[2] Animal research has demonstrated that nattokinase escapes the action of digestive enzymes and is absorbed from the small intestine to perform in plasma.*^[11,12]

Nattokinase Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Nattokinase (20,000 FU/g [†])	100 mg	**
** Daily Value not established.		
†Fibrinolytic Units per gram. 1000 FU/cap.		

Other Ingredients: Microcrystalline cellulose, HPMC (capsule), stearic acid, silica, magnesium stearate, and medium-chain triglyceride oil.
Contains: Soy.

DIRECTIONS: Take one to two capsules twice daily at least 30 minutes before or two hours after a meal, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

CAUTIONS: Consult your health care practitioner before taking this product if you have a bleeding disorder or are taking any drug that affects blood coagulation or blood pressure such as heparin, warfarin (Coumadin), diuretics, ACE inhibitors, or beta blockers.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

**References**

- Sumi H, Hamada H, Tsushima H, et al. A novel fibrinolytic enzyme (nattokinase) in the vegetable cheese Natto; a typical and popular soybean food in the Japanese diet. *Experientia*. 1987 Oct 15;43(10):1110-11. [PMID: 3478223]
- Sumi H, Hamada H, Nakanishi K, et al. Enhancement of the fibrinolytic activity in plasma by oral administration of nattokinase. *Acta Haematol*. 1990;84(3):139-43. [PMID: 2123064]
- Purified filtrate of *Bacillus subtilis* natto culture. JAFRA. <http://www.jafra.gr.jp/eng/natto1.html>. Accessed August 16, 2012.
- Murakami K, Yamanaka N, Ohnishi K, et al. Inhibition of angiotensin I converting enzyme by subtilisin NAT (nattokinase) in natto, a Japanese traditional fermented food. *Food Funct*. 2012 Mar 27. [Epub ahead of print] [PMID: 22453301]
- Yatagai C, Maruyama M, Kawahara T, et al. Nattokinase-promoted tissue plasminogen activator release from human cells. *Pathophysiol Haemost Thromb*. 2008;36(5):227-32. [PMID: 19996631]
- Pais E, Alexy T, Holsworth RE Jr, et al. Effects of nattokinase, a pro-fibrinolytic enzyme, on red blood cell aggregation and whole blood viscosity. *Clin Hemorheol Microcirc*. 2006;35(1-2):139-42. [PMID: 16899918]
- Fujita M, Hong K, Ito Y, et al. Thrombolytic effect of nattokinase on a chemically induced thrombosis model in rat. *Biol Pharm Bull*. 1995 Oct;18(10):1387-91. [PMID: 8593442]
- Suzuki Y, Kondo K, Ichise H, et al. Dietary supplementation with fermented soybeans suppresses intimal thickening. *Nutrition*. 2003 Mar;19(3):261-64. [PMID: 12620531]
- Maruyama M, Sumi H. Effect of natto diet on blood pressure. JAFRA. <http://www.jafra.gr.jp/eng/natto7.html>. Accessed August 14, 2012.
- Kim JY, Gum SN, Paik JK, et al. Effects of nattokinase on blood pressure: a randomized, controlled trial. *Hypertens Res*. 2008 Aug;31(8):1583-88. [PMID: 18971533]
- Fujita M, Ohnishi K, Takaoka S, et al. Antihypertensive effects of continuous oral administration of nattokinase and its fragments in spontaneously hypertensive rats. *Biol Pharm Bull*. 2011;34(11):1696-701. [PMID: 22040882]
- Fujita M, Hong K, Ito Y, et al. Transport of nattokinase across the rat intestinal tract. *Biol Pharm Bull*. 1995 Sep;18(9):1194-96. [PMID: 8845803]

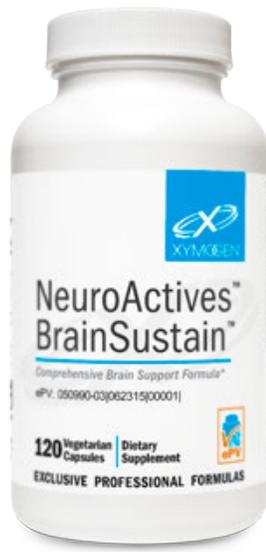
Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

NeuroActives™ BrainSustain™

Comprehensive Brain Support Formula*



Available in 120 capsules & 240 capsules

Discussion

NeuroActives™ BrainSustain™ provides an array of micronutrients and antioxidants that are essential to the structure, metabolism, and function of the brain and nervous system. This neurosupportive formula provides a foundational approach to sustaining neurological activity and integrity.*

N-Acetyl-Cysteine (NAC) As a source of the conditionally essential amino acid cysteine, NAC is a precursor to one of the brain's most important antioxidants—glutathione. NAC itself is an effective antioxidant and has been shown to reduce the formation of free radicals that can contribute to oxidative damage in the brain.*^[1]

Phosphatidylserine A phospholipid that is highly concentrated in the brain, phosphatidylserine (PS) plays a key role in neuronal energy production and communication. Since very little PS is found in food, we must synthesize or supplement the amount we need for optimal brain health. Improvements in cognitive function and memory have been observed following supplementation with PS.^[2-4] For some individuals, cognitive decline may be related to “age-related decline in nutrition,”^[5] and early nutrition intervention may be warranted. NeuroActives BrainSustain contains safe-source PS from sunflower lecithin and contains no animal products.*

Acetyl-L-Carnitine (ALCAR) The ALCAR form of the amino acid L-carnitine is found to have multifaceted roles in neuroprotection.^[6] It is able to cross the blood-brain barrier where it stabilizes cell membranes, acts as an effective antioxidant, and protects brain cells from toxic chemicals and stress-induced damage.^[7-9] In addition, ALCAR enhances neuronal energy production, facilitates transport of fuel and waste products into and out of mitochondria, and supports production of acetylcholine, a neurotransmitter essential to the processes of learning and concentration.*^[8-10]

Alpha-Lipoic Acid Acting as both a fat- and water-soluble antioxidant, alpha-lipoic acid provides intracellular and extracellular protection against oxidative stress. With its low molecular weight,

Clinical Applications

- » Supports Enhancement of Brain Function*
- » Supports Brain Health and Healthy Memory*
- » Provides Generous Antioxidant Support to the Brain*
- » Supplies Micronutrients to Support Neuronal Energy Production*

*Representing more than 30 years of neuroscience research, this unique encapsulated formula is designed to enhance brain performance and promote brain health. A key component of a complete program to ensure optimal brain function, **NeuroActives™ BrainSustain™** improves the energy production of brain mitochondria and provides generous antioxidant support to combat the damaging effects of excess free radicals in the brain.**

alpha-lipoic acid is easily absorbed in the gastrointestinal tract. It then enters circulation, crosses the blood-brain barrier, and reaches the brain where it can regenerate other important antioxidants, including glutathione, vitamin E, and vitamin C.*^[11,12]

Coenzyme Q10 (CoQ10) As a ubiquinone, CoQ10 facilitates the transfer of electrons in the electron transport chain (ETC), playing a crucial role in the formation of ATP (adenosine triphosphate) and the generation of energy within the cell. CoQ10 also donates electrons, making it an effective antioxidant. As such, CoQ10 protects cells, cell membranes, and tissues from damaging free radicals and pro-oxidants. The antioxidant activity of CoQ10 may protect the brain from the oxidative stress that is believed to be partially responsible for the degeneration of neuronal cells.*^[13]

Broccoli Seed Extract The patented form of the phytochemical in broccoli called sulforaphane glucosinolate (SGS™) is a key ingredient in NeuroActives BrainSustain. Extensive research demonstrates that when SGS is broken down to sulforaphane (its active form), it safely and effectively upregulates the Nrf2 system, enhances antioxidant production, and activates vital phase II detoxification enzymes.^[14,15] This process provides protection from common toxins and xenobiotics.*

Adequate antioxidant protection from ongoing free radical damage is crucial to maintaining the health and function of the cell and, hence, tissues and organs, especially the brain. Unbridled oxidative damage can lead to metabolic disruption and organ dysfunction over time. Antioxidant-promoting phytochemicals such as SGS are considered “lifespan essentials” because they assist in maintaining health throughout adult life.*^[16]

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

NeuroActives™ BrainSustain™ Supplement Facts

Serving Size: 4 Capsules

	Amount Per Serving	%Daily Value
Acetyl-L-Carnitine (as acetyl-L-carnitine HCl)	400 mg	**
N-Acetyl-L-Cysteine	150 mg	**
Phosphatidylserine (Sharp•PS®)	100 mg	**
Alpha-Lipoic Acid	100 mg	**
Coenzyme Q10 (as ubiquinone)	100 mg	**
Glucoraphanin (from broccoli extract) (<i>Brassica oleracea italica</i>) (seed) (TrueBroc®)	15 mg	**

** Daily Value not established.

Other Ingredients: Tricalcium phosphate, HPMC (capsule), stearic acid, magnesium stearate, silica, and calcium silicate.**DIRECTIONS:** Take two to four capsules daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication, especially cancer treatment, should discuss potential interactions with their healthcare practitioner.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.**STORAGE:** Keep closed in a cool, dry place out of reach of children.TrueBroc® is protected by trademarks and patents of Brassica Protection Products LLC: www.brassica.com/ip**References**

1. Sansone RA, Sansone LA. Getting a knack for NAC: N-acetyl-cysteine. *Innov Clin Neurosci*. 2011 Jan;8(1):10-4. [PMID: 21311702]
2. Kato-Kataoka A, Sakai M, Ebina R, et al. Soybean-derived phosphatidylserine improves memory function of the elderly Japanese subjects with memory complaints. *J Clin Biochem Nutr*. 2010 Nov;47(3):246-55. [PMID: 21103034]
3. Richter Y, Herzog Y, Cohen T, et al. The effect of phosphatidylserine-containing omega-3 fatty acids on memory abilities in subjects with subjective memory complaints: a pilot study. *Clin Interv Aging*. 2010 Nov 2;5:313-6. [PMID: 21103402]
4. Vakhapova V, Cohen T, Richter Y, et al. Phosphatidylserine containing omega-3 fatty acids may improve memory abilities in non-demented elderly with memory complaints: a double-blind placebo-controlled trial. *Dement Geriatr Cogn Disord*. 2010;29(5):467-74. [PMID: 20523044]
5. Suchy J, Chan A, Shea TB. Dietary supplementation with a combination of alpha-lipoic acid, acetyl-L-carnitine, glycerophosphocoline, docosahexaenoic acid, and phosphatidylserine reduces oxidative damage to murine brain and improves cognitive performance. *Nutr Res*. 2009 Jan;29(1):70-4. [PMID: 19185780]
6. Picconi B, Barone I, Pisani A, et al. Acetyl-L-carnitine protects striatal neurons against in vitro ischemia: the role of endogenous acetylcholine. *Neuropharmacology*. 2006 Jun;50(8):917-23. [PMID: 16500685]
7. Steffen V, Santiago M, de la Cruz CP, et al. Effect of intraventricular injection of 1-methyl-4-phenylpyridinium: protection by acetyl-L-carnitine. *Hum Exp Toxicol*. 1995 Nov;14(11):865-71. [PMID: 8588946]
8. Sorbi S, Forleo P, Fani C, et al. Double-blind, crossover, placebo-controlled clinical trial with L-acetylcarnitine in patients with degenerative cerebellar ataxia. *Clin Neuropharmacol*. 2000 Mar-Apr;23(2):114-8. [PMID: 10803803]
9. Jones LL, McDonald DA, Borum PR. Acylcarnitines: role in brain. *Prog Lipid Res*. 2010 Jan;49(1):61-75. Review. [PMID: 19720082]
10. Kobayashi S, Iwamoto M, Kon K, et al. Acetyl-L-carnitine improves aged brain function. *Geriatr Gerontol Int*. 2010 Jul;10 Suppl 1:S99-106. [PMID: 20590847]
11. Packer L, Tritschler HJ, Wessel K. Neuroprotection by the metabolic antioxidant alpha-lipoic acid. *Free Radic Biol Med*. 1997;22(1-2):359-78. Review. [PMID: 8958163]
12. Liu J. The effects and mechanisms of mitochondrial nutrient alpha-lipoic acid on improving age-associated mitochondrial and cognitive dysfunction: an overview. *Neurochem Res*. 2008 Jan;33(1):194-203. Review. [PMID: 17605107]
13. Mancuso M, Orsucci D, Volpi L, et al. Coenzyme Q10 in neuromuscular and neurodegenerative disorders. *Curr Drug Targets*. 2010 Jan;11(1):111-21. Review. [PMID: 20017723]
14. Ping Z, Liu W, Kang Z, et al. Sulforaphane protects brains against hypoxic-ischemic injury through induction of Nrf2-dependent phase 2 enzyme. *Brain Res*. 2010 Jul 9;1343:178-85. [PMID: 20417626]
15. Vauzour D, Buonfiglio M, Corona G, et al. Sulforaphane protects cortical neurons against 5-S-cysteinyldopamine-induced toxicity through the activation of ERK1/2, Nrf-2 and the upregulation of detoxification enzymes. *Mol Nutr Food Res*. 2010 Apr;54(4):532-42. [PMID: 20166144]
16. Holst B, Williamson G. Nutrients and phytochemicals: from bioavailability to bioefficacy beyond antioxidants. *Curr Opin Biotechnol*. 2008 Apr;19(2):73-82. [PMID: 18406129]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

NiaVasc™

Sustained-Release Niacin



NiaVasc™ is available in 120 tablets & 360 tablets
NiaVasc 750™ is available in 60 tablets & 120 tablets

Clinical Applications

- » Supports the Maintenance of Healthy Blood Lipids*
- » Supports Normal Carotid Intima-Media Thickness (CIMT)*

*Niacin is one of the most studied and documented nutrients for support of lipid levels already within the normal range, especially high-density lipoprotein cholesterol (HDL-C) levels. Sustained-release niacin, as found in **NiaVasc™/NiaVasc™ 750**, has a lesser flushing effect compared with instant-release niacin. Use of a proprietary, wax-coated technology permits release that is complete in seven to eight hours, the time that is considered ideal for a time-release form of niacin.**

Discussion

The cardiovascular benefits of niacin (vitamin B3) were introduced in the June 1956 issue of *Mayo Clinic Proceedings*.^[1] More than 20 years later, the Framingham Heart Study touted the benefits of niacin on lipid metabolism. A decade later, as the study continued, researchers labeled niacin “front-line” cardiovascular support.^[2] This status was further reinforced in 1988 when the National Cholesterol Education Program (NCEP) panel designated niacin a “first-line therapy” for support of specific parameters related to cardiovascular health.*^[3]

Mechanisms of Action Several mechanisms of action have been proposed for niacin. Various experimental models suggest niacin can modulate lipoprotein biosynthesis in the liver, inhibit the release of free fatty acids from adipocytes, inhibit synthesis of apo B, induce lipoprotein lipase, and help maintain the structure and function of HDL (high-density lipoprotein) by reducing the amount of apo A-1 broken down from HDL during hepatic processing.^[4,5] In addition, when niacin is used with resins, it can stimulate bile flow and may therefore affect lipid biosynthesis.*^[6]

Human Trials Since the late 1970s, studies and clinical trials, lasting from four weeks to five years with daily doses of extended-release (also known as sustained/prolonged/slow-release) niacin up to 3000 mg/day, have consistently demonstrated niacin’s efficacy and safety.^[6] In 2004, the ARBITER 6-HALTS trial clearly demonstrated that niacin offers targeted support of cardiovascular health.^[7] Final results of this trial, published in 2010, further demonstrated that niacin supports healthy carotid intima-media thickness (CIMT).^[8] While the supportive effect niacin has on blood lipids is well documented, there has been a recent focus by NCEP and other researchers on how niacin’s effect on HDL may influence cardiovascular events.^[9] More well-designed studies that address innate limitations and are carried to completion are needed.*

Why Isn’t Niacin More Widely Used? The two common concerns are cutaneous flushing and increased liver enzymes. Cutaneous flushing is

harmless, although it can be a nuisance. Flushing is most often seen with the use of immediate/instant-release forms of niacin and can occur with doses as low as 30 mg/day, but it is more likely to occur with the much higher doses used to support healthy blood lipids. Flushing may last 10 to 15 minutes and rarely, but possibly, up to two hours. The proprietary wax-coated technology used in NiaVasc tablets allows a gradual, sustained release of niacin over a seven-to-eight hour period. This delivery dramatically reduces the flushing associated with immediate-release forms. Adherence to a regimen with the special wax-coated form of niacin, as found in NiaVasc, ranged from 88-97% in four human clinical trials.^[10,11] Flushing, itching, tingling, and upper gastrointestinal side effects were minimal, but did increase when dosing was increased to 2000 mg/day. It is important to note that NiaVasc should not be confused with “no-flush” niacin, which is inositol hexanicotinate (IHN), a supplement that does not contain any free niacin and may not be as supportive of cardiovascular health as those providing nicotinic acid.*^[12,13]

The second concern with regard to liver enzyme elevation was first elucidated by the results of McKenney’s study, published in 1994 in the *Journal of the American Medical Association (JAMA)*, wherein subjects received 3000 mg/day of niacin over an extended period of time.^[14] In April 2004, McKenney retracted his earlier warnings about the harmful effects of niacin and publicly supported its unique benefits.^[15] Although they generally do not enter an unhealthy range, liver enzymes may increase when initiating niacin therapy, especially in amounts greater than 1000 mg/day. Enzyme levels return to normal promptly after cessation of niacin.*^[15]

NiaVasc™ Supplement Facts

Serving Size: 1 Tablet

	Amount Per Serving	%Daily Value
Niacin	500 mg	3125%
** Daily Value not established.		

Other Ingredients: Vegetable waxes (rice bran and/or carnauba), stearic acid, magnesium stearate, and silica.

DIRECTIONS: Take one tablet one to two times daily with food, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

CAUTIONS: Take under ongoing supervision with regular monitoring of blood chemistry, especially liver function. Do not take if you are pregnant or lactating.

STORAGE: Keep closed in a cool, dry place out of reach of children.

NiaVasc™ 750 Supplement Facts

Serving Size: 1 Tablet

	Amount Per Serving	%Daily Value
Niacin	750 mg	4688%
** Daily Value not established.		

Other Ingredients: Vegetable waxes (rice bran and/or carnauba), stearic acid, magnesium stearate, and silica.

DIRECTIONS: Take one tablet one to two times daily with food, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

CAUTIONS: Take under ongoing supervision with regular monitoring of blood chemistry, especially liver function. Do not take if you are pregnant or lactating.

STORAGE: Keep closed in a cool, dry place out of reach of children.

References:

- Parsons WB Jr, Achor RW, Berge KG, et al. Changes in concentration of blood lipids following prolonged administration of large doses of nicotinic acid to persons with hypercholesterolemia: preliminary observations. *Mayo Clin Proc.* 1956 Jun 27;31(13):377-90. [PMID: 13336128]
- Kannel WB. Recent findings from the Framingham study—I. *Med Times.* 1978 Apr;106(4):23-27. [PMID: 642745]
- Hulley SB. The US National Cholesterol Education Program. Adult treatment guidelines. *Drugs.* 1988;36 Suppl 3:100-04. [PMID: 3254822]
- Morgan JM, Carey CM, Lincoff A, et al. The effects of niacin on lipoprotein subclass distribution. *Prev Cardiol.* 2004 Fall;7(4):182-7; quiz 188. [PMID: 8424822]
- Holland RE, Rahman K, Morris AI, et al. Effect of niacin on biliary lipid output in the rat. *Biochem Pharmacol.* 1993 Jan 7;45(1):43-49. [PMID: 8424822]
- Niacin. <http://www.naturalstandard.com/naturalstandard/monographs/monoframeset.asp?monograph=/monographs/herbssupplements/aux2-niacin.asp&patientVersion=/monographs/herbssupplements/patient-niacin>. Accessed August 19, 2010.
- Taylor AJ, Sullenberger LE, Lee HJ, et al. Biology for the investigation of the treatment effects of reducing cholesterol (ARBITER) 2: a double-blind, placebo-controlled study of extended-release niacin on atherosclerosis progression in secondary prevention patients treated with statins. *Circulation.* 2004 Dec 7;110(23):3512-17. [PMID: 15537681]
- Villines TC, Stanek EJ, Devine PJ, et al. The ARBITER 6-HALTS Trial (Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol 6-HDL and LDL Treatment Strategies in Atherosclerosis): final results and the impact of medication adherence, dose, and treatment duration. *J Am Coll Cardiol.* 2010 Jun 15;55(24):2721-67. [PMID: 20399059]
- Michos ED, Sibley CT, Baer JT, et al. Niacin and statin combination therapy for atherosclerosis regression and prevention of cardiovascular disease events: reconciling the AIM-HIGH (Atherothrombosis intervention in metabolic syndrome with low hdl/high triglycerides: Impact on global health outcomes) trial with previous surrogate endpoint trials. *J Am Coll Cardiol.* 2012 Apr 4. [Epub ahead of print] [PMID: 22520249]
- Keenan JM, Fontaine PL, Wenz JB, et al. Niacin revisited. A randomized, controlled trial of wax-matrix sustained-release niacin in hypercholesterolemia. *Arch Intern Med.* 1991 Jul;151(7):1424-32. [PMID: 2064495]
- Aronov DM, Keenan JM, Akhmedzhanov NM, et al. Clinical trial of wax-matrix sustained-release niacin in a Russian population with hypercholesterolemia. *Arch Fam Med.* 1996 Nov-Dec;5(10):567-75. [PMID: 8930228]
- Backes JM, Padley RJ, Moriarty PM. Important considerations for treatment with dietary supplement versus prescription niacin products. *Postgrad Med.* 2011 Mar;123(2):70-83. Review. [PMID: 21474895]
- Norris RB. "Flush-free niacin": dietary supplement may be "benefit-free". *Prev Cardiol.* 2006 Winter;9(1):64-65. [PMID: 16407706]
- McKenney JM. A comparison of the efficacy and toxic effects of sustained- vs immediate-release niacin in hypercholesterolemic patients. *JAMA.* 1994 Mar 2;271(9):672-77. [PMID: 8309029]
- McKenney JM. Pharmacologic options for aggressive low-density lipoprotein cholesterol lowering: benefits versus risks. *Am J Cardiol.* 2005 Aug 22;96(4A):60E-66E. Review. [PMID: 16098846]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Nrf2 Activator™

Antioxidant & Detoxification Support Formula*



Available in 30 capsules & 60 capsules

Discussion

Nrf2 (NF-E2-related factor 2), a transcription factor in humans that is encoded by the NFE2L2 gene, regulates the expression of a set of antioxidant and detoxifying genes, protecting the body from the ravages of oxidative stress-related conditions, including (but not limited to) those affecting the brain and nervous system. In an unstressed state, Nrf2 is anchored in the cytoplasm by its specific inhibitor Keap1 (kelch-like ECH-associated protein 1). Keap1 functions as a sensor for oxidants and electrophilic xenobiotics. In the presence of any of these substances, Keap1 gives up its inhibition of Nrf2. This action stabilizes Nrf2, allowing it to accumulate in the nucleus and bind to the antioxidant response element (ARE) located in the enhancers of its target genes. Under this circumstance, Nrf2 then upregulates a variety of antioxidant enzymes and detoxifying proteins.*

A variety of natural substances have been shown to activate Nrf2:

Sulforaphane (SGS), a naturally occurring isothiocyanate derived from cruciferous vegetables, induces phase 2 cytoprotective enzymes, supporting the body's response to cellular insult. SGS may modify critical cysteine residues of Keap1, leading to Nrf2 stabilization and activation of the ARE and thereby inducing phase 2 enzymes. Research demonstrates that sulforaphane, through induction of Nrf2-dependent phase 2 enzymes, protects the brain against hypoxic-ischemic injury and may improve cognitive function when administered following traumatic brain injury.*

Pterostilbene, a naturally occurring phenolic compound/analog of resveratrol that has comparatively better oral bioavailability, has been shown to possess cytotoxic, cytokine-inhibiting, and antioxidant properties. Resveratrol has also been shown to increase the protein and mRNA expression of Nrf2. There is evidence that Nrf2-mediated attenuation of oxidative stress and cytokine induction could be partially responsible for resveratrol's potential effect on cell-life regulation. In rat and animal studies, resveratrol/pterostilbene have been shown to upregulate a significant number of genes

Clinical Applications

- » Antioxidant Support*
- » Attenuates the Expression and Release of Damaging Cytokines, Such as NF-κB*
- » Supports the Body's Natural Detoxification Pathways*

*Nrf2 Activator™ is an exclusive formula designed to activate the Nrf2 genetic pathway. This pathway regulates the production of important molecules that impart antioxidant activity, such as glutathione and superoxide dismutase (SOD). It also regulates the production of detoxification enzymes, including glutathione S-transferase, and downregulates signaling factors such as NF-κB. Each ingredient in this formula is backed by extensive research in peer-reviewed journals.**

involved in mitochondrial function as well as to modulate cholinergic neurotransmission and improve cognition.*

Curcumin's array of biological activities stems from its cytokine-balancing activity, antioxidant properties, and induction of phase 2 detoxifying enzymes such as heme oxygenase-1 (HO-1). Purification of curcumin yields the curcuminoids demethoxy curcumin (DMC) and bisdemethoxy curcumin (BDMC). DMC has been shown to induce HO-1 more effectively than curcumin. The ability of DMC and BDMC to induce the expression of HO-1 and to translocate Nrf2 to the nucleus of pancreatic beta cells in mice suggests that they may play a role in cellular defense. Human studies showed a significant increase in curcumin absorption when co-administered with BioPerine®, a patented black pepper extract.*

Green Tea's major polyphenol, (-)-epigallocatechin-3-gallate (EGCG), has been shown to induce expression of glutathione S-transferase, glutathione peroxidase, glutamate cysteine ligase, HO-1, and other enzymes, thereby protecting a variety of cells, including cultured neurons, against oxidative stress-induced cell death. EGCG modulates the redox-sensitive transcription factor Nrf2, which plays a key role in activating detoxifying enzyme HO-1 as well as other phase 2 enzymes.*

In summary, Nrf2 Activator is a promising approach to increasing antioxidant defenses by transcriptionally increasing the activity of the Nrf2/ARE pathway and positively affecting the transcription of damaging cytokine and antioxidant genes. Green tea, curcumin, and resveratrol (pterostilbene) have also been shown to influence amyloid formation; this influence further increases the potential of this innovative formula.*

EXCLUSIVE • PATENTED

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

Nrf2 Activator™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%DV
Turmeric Extract (<i>Curcuma longa</i>)(rhizome)(95% curcuminoids)	400 mg	**
Green Tea Aqueous Extract (<i>Camellia sinensis</i>)(leaf)(80% polyphenols, 60% catechins, 30% EGCG, 6% caffeine)	400 mg	**
<i>trans</i> -Pterostilbene (pTeroPure®)	100 mg	**
Glucoraphanin (from broccoli extract)(<i>Brassica oleracea italica</i>)(seed (truebroc™))	60 mg	**
Black Pepper Extract (<i>Piper nigrum</i>)(fruit)(BioPerine®)	4 mg	**

** Daily Value (DV) not established.

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, silica, and medium-chain triglyceride oil. BioPerine is a registered trademark of Sabinsa Corp. BioPerine is protected by US patents 5,536,506; 5,744,161; 5,972,382; and 6,054,585. pTeroPure is a trademark of ChromaDex, Inc.

DIRECTIONS: Take one to two capsules daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication, especially blood thinners or cancer treatment, should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep tightly closed in a cool, dry place out of reach of children.



Produced under US patent 5,725,895; 5,968,505; 5,968,567; 6,177,122; and 6,242,018 licensed from Brassica Protection Products LLC; truebroc is a trademark of Brassica Protection Products LLC.



Antioxidant Activity

Cell-Life Regulation

Cytokine Balance

Detoxification

Neurologic & Cognitive

References

1. Kim J, et al. Naturally occurring phytochemicals for the prevention of Alzheimer's disease. *J Neurochem*. 2010 Mar;112(6):1415-30 [PMID: 20050972]
2. Ping Z, et al. Sulforaphane protects brains against hypoxic-ischemic injury through induction of Nrf2-dependent phase 2 enzyme. *Brain Res*. 2010 Apr 24. [PMID: 20417626]
3. Dash PK, et al. Sulforaphane improves cognitive function administered following traumatic brain injury. *Neurosci Lett*. 2009 Aug 28;460(2):103-7 [PMID: 19515491]
4. Ahn YH. Electrophilic tuning of the chemoprotective natural product sulforaphane. *Proc Natl Acad Sci U S A*. 2010 May 25;107(21):9590-5. [PMID: 20439747]
5. Beal MF. Therapeutic approaches to mitochondrial dysfunction in Parkinson's disease. *Parkinsonism Relat Disord*. 2009 Dec;15 Suppl 3:S189-94 [PMID: 20082988]
6. Bishayee A, et al. Resveratrol suppresses oxidative stress and inflammatory response in diethylnitrosamine-initiated rat hepatocarcinogenesis. *Cancer Prev Res (Phila Pa)*. 2010 Jun;3(6):753-63. Epub 2010 May 25. [PMID: 20501860]
7. Schmatz R, et al. Resveratrol prevents memory deficits and the increase in acetylcholinesterase activity in streptozotocin-induced diabetic rats. *Eur J Pharmacol*. 2009 May 21;610(1-3):42-8 [PMID: 19303406]
8. Yang C, et al. Curcumin upregulates transcription factor Nrf2, HO-1 expression and protects rat brains against focal ischemia. *Brain Res*. 2009 Jul 28;1282:133-41. [PMID: 19445907]
9. Pugazhenth S, et al. Regulation of heme oxygenase-1 expression by demethoxy curcuminoids through Nrf2 by a PI3-kinase/Akt-mediated pathway in mouse beta-cells. *Am J Physiol Endocrinol Metab*. 2007 Sep;293(3):E645-55. [PMID: 17535857]
10. Romeo L, et al. The major green tea polyphenol, (-)-epigallocatechin-3-gallate, induces heme oxygenase in rat neurons and acts as an effective neuroprotective agent against oxidative stress. *J Am Coll Nutr*. 2009 Aug;28 Suppl:492S-499S. [PMID: 20234037]
11. Zhang ZM, et al. Modulation of NRF2 and UGT1A expression by epigallocatechin-3-gallate in colon cancer cells and BALB/c mice. *Chin Med J (Engl)*. 2009 Jul 20;122(14):1660-5. [PMID: 19719968]
12. Na HK, et al. (-)-Epigallocatechin gallate induces Nrf2-mediated antioxidant enzyme expression via activation of PI3K and ERK in human mammary epithelial cells. *Arch Biochem Biophys*. 2008 Aug 15;476(2):171-7. [PMID: 18424257]
13. Artali R. Green tea catechins in chemoprevention of cancer: a molecular docking investigation into their interaction with glutathione S-transferase (GST P1-1). *J Enzyme Inhib Med Chem*. 2009 Feb;24(1):287-95. [PMID: 18825537]
14. Hu L, et al. Putative chemopreventive molecules can increase Nrf2-regulated cell defense in some human cancer cell lines, resulting in resistance to common cytotoxic therapies. *Cancer Chemother Pharmacol*. 2010 Aug;66(3):467-74. [PMID: 19940992]
15. Sabinsa. BioPerine® and Curcumin. <http://www.bioperine.com/curcumin.html>. Accessed October 10, 2010.

Additional references available upon request

EXCLUSIVE • PATENTED

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.



Available in 20 vegetarian capsules

Discussion

Immune Guard®

Immune Guard is a patented blend of decaffeinated compounds from green tea standardized to 20% epigallocatechin-3-gallate (EGCG) and L-theanine, a combination that has been demonstrated to support immune system health. A randomized, double-blind, placebo-controlled study followed healthy adult subjects (n = 120) for a twelve-week period during the winter and into the spring months. Each subject recorded in a daily log any symptoms that indicated reduced immune health. Blood samples were analyzed for assessment of immune function parameters, including gamma delta T cell proliferation and gamma interferon secretion. Immune Guard resulted in a 28% increase in gamma delta T cell proliferation and secreted 26% more interferon gamma in response to gamma delta T cell antigens when compared to placebo. This increase in immune health markers corresponded with a decreased incidence of immune-related symptoms recorded by 30% of the study group.*^[1]

An additional study of the effect of Immune Guard on immune health was conducted with healthcare workers as subjects (n = 197) over a five-month period during the winter months. Volunteers were given either placebo or six capsules/day (378 mg/day of green tea catechins and 210 mg/day of theanine). The occurrence of clinically confirmed diagnoses was significantly reduced in the treatment group when compared to placebo.*^[2]

Green Tea Extract (Camellia sinensis)

Many of the beneficial effects of green tea are dose-dependent, and most Americans are not willing to consume the necessary 5-10 cups of the tea daily to gain its advantages. The health benefits of green tea are derived from a group of phytochemicals known as polyphenols. Polyphenols in fresh green tea leaves are present as catechins, which can be isolated to yield the key beneficial constituents. The dominant and most biologically active among the catechins, (-)-epigallocatechin-3-gallate (EGCG), has been shown to induce expression of the enzymes that protect a wide variety of cells against oxidative stress and to exhibit an immunomodulatory effect in addition to other benefits.*^[3-7]

L-theanine

L-theanine, an amino acid found in green tea, is catabolized to ethylamine, a molecule that specifically activates human gamma delta T-lymphocytes to proliferate and make interferon gamma, a powerful antimicrobial cytokine. There is ample evidence that supports the role of gamma delta T cells as a first-line immune defense mechanism.*^[8-10]

Clinical Applications

- » Promotes Healthy Immune Function*
- » Provides Antioxidant Activity*
- » Supports the Body's Defenses Against Immune Challenges*

*OlivDefense® features science-based, patented Immune Guard® plus extracts of elderberry and olive to support the body's natural immune defense mechanisms.**

Elderberry (Sambucus nigra)

Elderberry has a long history of traditional use in promoting immune and respiratory health. Additionally, the antioxidant activity of elderberry extracts has been evaluated in a number of studies, all suggesting a meaningful level of activity.^[11-13] Elderberry fruit and leaves contain numerous compounds thought to have immune-priming effects and provide support against opportunistic microbes.^[13,14] Several double-blind placebo-controlled studies using standardized elderberry extracts in the test groups have yielded positive results, including lessened duration and severity of immune-related symptoms.*^[15-17]

Arthricor® Olive Extract (Olea europaea)

The immune health benefits of extracts from the leaf or fruit of the olive tree date back hundreds of years, including documented use during the Spanish/Latin American wars of independence in the early 1800s, for promoting the health of soldiers returning from tropical colonies. The bitter phenolic compound oleuropein was identified decades later as one of the key health-promoting components. Hydroxytyrosol and tyrosol, along with other polyphenols with beneficial activity, have also been identified. Since then, *Olea europaea* has been studied for an array of healthful attributes including antioxidant properties and effective immune support against opportunistic microbes.*^[18-23]

In a randomized, controlled, double-blind, crossover human trial, investigators studied the effect of olive oil on mucosal immune status over a three-week period. Hypercholesterolemic subjects (n = 10) were given three different samples that varied in amount and type of phenolic compounds. Ingestion of the sample with the highest amount of hydroxytyrosol derivatives (8.49 PC/kg) yielded increased intestinal immunity markers (fecal immunoglobulin A (IgA) and IgA-coated bacteria) and increased plasma levels of C-reactive protein (CRP), yet lower levels did not show a significant effect. These results indicate that immune system stimulation occurred with very high doses of olive oil phenolic compounds.*^[24]

NOTE: Calcium must be declared on a label when present at greater than 2% Daily Value. Calcium carbonate is an excipient used in OlivDefense as a densifier; it does not contribute to the formula's intended function.

OlivDefense® Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Calories	5	
Total Carbohydrate	1 g	<1%†
Calcium (as calcium carbonate)	100 mg	8%
Immune Guard® Green Tea Extract & L-Theanine Blend (<i>Camellia sinensis</i>) (leaves) (20% EGCG) (20% L-theanine)	600 mg	**
Elderberry (<i>Sambucus nigra</i>) (fruit) (4% phenolics, 1% anthocyanins)	300 mg	**
Arthricor® Olive Extract (<i>Olea europaea</i>) (fruit) (9% hydroxytyrosol, 4% oleuropein, 1% tyrosol)	150 mg	**

† Percent Daily Values are based on a 2,000 calorie diet.

** Daily Value not established.

Other Ingredients: Ascorbyl palmitate, capsule (hypromellose and water), and silica.

DIRECTIONS: Take two capsules at first sign of immune discomfort. On the next day and until no longer needed, take 2 capsules daily, which may be taken together or as one capsule twice a day; or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if foil is punctured.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

Immune Guard® US patent 8,465,782.

Arthricor® is a registered trademark of Eight-IP.

**References**

- Rowe CA, Nantz MP, Bukowski JF, et al. Specific formulation of *Camellia sinensis* prevents cold and flu symptoms and enhances gamma, delta T cell function: a randomized, double-blind, placebo-controlled study. *J Am Coll Nutr*. 2007 Oct;26(5):445-52. [PMID: 17914132]
- Matsumoto K, Yamada H, Takuma N, et al. Effects of green tea catechins and theanine on preventing influenza infection among healthcare workers: a randomized controlled trial. *BMC Complement Altern Med*. 2011 Feb 21;11:15. [PMID: 21338496]
- Weisburger JH, Chung FL. Mechanisms of chronic disease causation by nutritional factors and tobacco products and their prevention by tea polyphenols. *Food Chem Toxicol*. 2002 Aug;40(8):1145-54. [PMID: 12067577]
- Matsunaga K, Klien TW, Friedman H, et al. Legionella pneumophila replication in macrophages inhibited by selective immunomodulatory effects on cytokine formation by epigallocatechin gallate, a major form of tea catechins. *Infect Immun*. 2001 Jun;69(6):3947-53. [PMID: 11349063]
- Pae M, Wu D. Immunomodulating effects of epigallocatechin-3-gallate from green tea: mechanisms and applications. *Food Funct*. 2013 Sep;4(9):1287-303. [PMID: 23835657]
- Serafini M, Del Rio D, Yao DN, et al. Health benefits of tea. In: Benzie IFF, Wachtel-Galor S, eds. *Herbal Medicine: Biomolecular and Clinical Aspects*. 2nd ed. Boca Raton, FL: CRC Press/Taylor & Francis; 2011:239-262. [PMID: 22593935]
- Butt MS, Sultan MT. Green tea: nature's defense against malignancies. *Crit Rev Food Sci Nutr*. 2009 May;49(5):463-73. [PMID: 19399671]
- Bukowski JF, Morita CT, Brenner MB. Human gamma delta T cells recognize alkylamines derived from microbes, edible plants, and tea: implications for innate immunity. *Immunity*. 1999 Jul;11(1):57-65. [PMID: 10435579]
- Kamath AB, Wang L, Das H, et al. Antigeny in tea-beverage prime human Vgamma 2/delta 2 T cells in vitro and in vivo for memory and nonmemory antibacterial cytokine responses. *Proc Natl Acad Sci USA*. 2003 May 13;100(10):6009-6014. [PMID: 12719524]
- Vuong QV, Bowyer MC, Roach PD. L-Theanine: properties, synthesis and isolation from tea. *J Sci Food Agric*. 2011 Aug 30;91(11):1931-9. [PMID: 21735448]
- Duymuş HG, Göger F, Başer KH. In vitro antioxidant properties and anthocyanin compositions of elderberry extracts. *Food Chem*. 2014 Jul 15;155:112-9. [PMID: 24594162]
- Mandrone M, Lorenzi B, Maggio A, et al. Polyphenols pattern and correlation with antioxidant activities of berries extracts from four different populations of Sicilian *Sambucus nigra* L. *Nat Prod Res*. 2014;28(16):1246-53. [PMID: 24666289]
- Vlachojannis JE, Cameron M, Chrubasik S. A systematic review on the sambuci fructus effect and efficacy profiles. *Phytother Res*. 2010 Jan;24(1):1-8. [PMID: 19548290]
- Porter RS, Bode RF. A review of the antiviral properties of black elder (*Sambucus nigra* L.) products. *Phytother Res*. 2017 Apr;31(4):533-554. [PMID: 28198157]
- Zakay-Rones Z, Varsano N, Zlotnik M, et al. Inhibition of several strains of influenza virus in vitro and reduction of symptoms by an elderberry extract (*Sambucus nigra* L.) during an outbreak of influenza B Panama. *J Altern Complement Med*. 1995 Winter;1(4):361-9. [PMID: 9395631]
- Zakay-Rones Z, Thom E, Wollan T, et al. Randomized study of the efficacy and safety of oral elderberry extract in the treatment of influenza A and B virus infections. *J Int Med Res*. 2004 Mar-Apr;32(2):132-40. [PMID: 15080016]
- Tiralongo E, Wee SS, Lea RA. Elderberry supplementation reduces cold duration and symptoms in air-travellers: a randomized, double-blind placebo-controlled clinical trial. *Nutrients*. 2016 Mar 24;8(4):182. [PMID: 27023596]
- Gorzynik-Debicka M, Przychodzen P, Cappello F, et al. Potential health benefits of olive oil and plant polyphenols. *Int J Mol Sci*. 2018 Feb 28;19(3). [PMID: 29495598]
- Bisignano G, Tomaino A, Lo Cascio R, et al. On the in-vitro antimicrobial activity of oleuropein and hydroxytyrosol. *J Pharm Pharmacol*. 1999 Aug;51(8):971-4. [PMID: 10504039]
- Visioli F, Bellomo G, Galli C. Free radical-scavenging properties of olive oil polyphenols. *Biochem Biophys Res Commun*. 1998 Jun 9;247(1):60-4. [PMID: 9636654]
- Visioli F, Wolfram R, Richard D, et al. Olive phenolics increase glutathione levels in healthy volunteers. *J Agric Food Chem*. 2009 Mar 11;57(5):1793-6. [PMID: 19219997]
- Paradiso VM, Di Mattia C, Giannetti M, et al. Antioxidant behavior of olive phenolics in oil-in-water emulsions. *J Agric Food Chem*. 2016 Jul 27;64(29):5877-86. [PMID: 27380032]
- Yamada K, Ogawa H, Hara A, et al. Mechanism of the antiviral effect of hydroxytyrosol on influenza virus appears to involve morphological change of the virus. *Antiviral Res*. 2009 Jul;83(1):35-44. [PMID: 19501255]
- Martín-Peláez S, Castañer O, Solà R, et al. Influence of phenol-enriched olive oils on human intestinal immune function. *Nutrients*. 2016 Apr 11;8(4):213. [PMID: 27077879]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Omega MonoPure[®] Curcumin EC

Highly Bioavailable Omega-3 & Curcumin*



Available in 30 fish gelatin softgels

Discussion

Omega MonoPure[®] Curcumin EC features highly absorbable, patented forms of both monoglyceride fish oil and standardized turmeric extract to offer combined support for cellular health and the modulation of cytokine production.*

The two most well-researched omega-3 fatty acids are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). EPA plays a role in supporting healthy cardiac and circulatory systems while DHA is an essential structural component of the central nervous system. In addition to other physiological effects, research has established that omega-3 fatty acids antagonize arachidonic acid-induced eicosanoid formation. They also help generate resolvins and protectins (EPA and DHA metabolites, called specialized proresolving mediators (SPMs), that are naturally produced in vivo through enzymatic conversion of EPA and DHA) to aid the body's "cleanup" response to the arachidonic acid cascade, and they promote cardiovascular health.*^[1-7]

Curcumin, the principal curcuminoid in turmeric, has been the subject of vast research in recent years. The pleiotropic nature of curcumin's biological effects makes it an interesting compound to researchers who study common chronic health concerns, such as those associated with joints, the cardiovascular system, glucose metabolism, brain function, mood, and cell-cycle regulation. These effects make curcumin applicable to a wide array of clinical presentations.*^[8-13]

MaxSimil[®] Fish Oil Concentrate

MaxSimil is a novel monoglyceride concentrated fish oil developed using patented lipid absorption enhancement technology (PLATform), a unique vehicle by which to deliver EPA and DHA. Due to the fact that monoglyceride oils are intrinsically emulsifiers and are, by nature, in a readily absorbable form, they can bypass the body's normal fat digestion process. Studies conducted by the manufacturer of MaxSimil provide promising results that show MaxSimil fish oil may be better absorbed than other fish oils. Rather than supplying a single molecule or metabolite, which would mirror the pharmaceutical model, MaxSimil provides all the benefits of EPA and DHA as well as the expected and desirable benefits of their metabolites. From a quality perspective, every batch of fish oil is IFOS five-star certified to ensure the highest standards for purity, potency, and freshness. The fish oil is also non-GMO, certified sustainable from Scandinavia, and antibiotic-free.*^[14-16]

An unpublished single dose, double-blind, crossover, pharmacokinetic study was performed in healthy overnight fasted male and female subjects (n = 20) aged between 19 and 60 years. Each participant was administered six softgels (containing 2000 mg EPA and 1500 mg DHA) of ethyl ester (EE) fish oil or MaxSimil. Parameters studied were plasma EPA and DHA concentration (as percent of total fatty acids), maximum concentration (C_{max}), time to concentration (T_{max}) and area under the curve (AUC). The results indicated that at peak concentration, the

Clinical Applications

- » Patented Enhanced Absorption of EPA and DHA*
- » Highly Bioavailable Curcuminoid and Turmeric Essential Oil Extract*
- » Provides Antioxidant Activity and Cytokine Balance Support*
- » Promotes Healthy Cell-Life Regulation*

*Omega MonoPure[®] Curcumin EC features complementary ingredients to help promote cellular health and modulate the production of cytokines. MaxSimil[®] highly absorbable monoglyceride fish oil is International Fish Oil Standards (IFOS) five-star certified. BCM-95[®] is an optimally absorbed turmeric extract composed of a 95% standardized curcuminoid-essential oil complex.**

MaxSimil EPA and DHA were three times higher, reached maximum concentration faster, and maintained plasma levels longer than the EE EPA+DHA demonstrating enhanced bioavailability of the MaxSimil form.^[16] While there is no conclusive published evidence at this time, the results from studies conducted by the makers of MaxSimil provide a promising indication of enhanced absorption rates, and additional peer-reviewed research is warranted.*

In a placebo-controlled, study in healthy volunteers (n = 21) investigators examined the effect of omega-3 fatty acid (2.4g/day) supplementation on increasing biologically active SPMs over a seven-day period. After five days, concentrations of SPMs were effectively increased.^[7] This study and others contribute to the body of research supporting a role for omega-3 supplementation and may help explain their role in cardiovascular health.*^[2,3,6,7]

BCM-95[®] (Turmeric Extract)

While the beneficial effects of curcumin are hardly arguable, an area of intense research in recent years has been how to make curcumin more bioavailable. Poor absorption in the gastrointestinal (GI) tract, rapid metabolism, and rapid systemic elimination are typically characteristic of commercially available curcumin preparations. During the course of investigating a way to overcome these challenges, scientists discovered they could take advantage of the synergism between the curcuminoids and the sesquiterpenoids (essential oils) naturally present in turmeric.^[9] This discovery resulted in the development of BCM-95[®]—a 100% natural whole turmeric extract composed of curcuminoids (curcumin, demethoxycurcuminoid, and bisdemethoxycurcuminoid) and essential oils.*

In a pilot crossover study, Antony et al compared the bioavailability of three forms of curcumin: BCM-95, normal curcumin, and a non-controlled release curcumin-piperine-lecithin formula. The data demonstrated that the absorption of curcumin from BCM-95 was fast, it peaked at 4.5 hours with a gradual decline, and curcumin was still detectable in the blood at eight hours. The other formulas showed slower curcumin absorption with an earlier peak and rapid disappearance from the blood after 4.5 hours. The relative bioavailability of BCM-95 was approximately 6.93-fold higher than normal curcumin and 6.3-fold higher than the non-controlled release curcumin-lecithin-piperine formula. According to the researchers, the results of this study indicated that the BCM-95 curcumin was "absorbed early and retained longer" compared to other forms.*^[8]

The safety and efficacy of curcumin has been demonstrated in numerous animal, preclinical, and human studies. The mechanisms have not been fully elucidated, but it is known that curcumin has powerful antioxidant activity and that it has multiple molecular targets, including transcription factors, cell cycle proteins, cytokines, chemokines, enzymes (e.g., COX-2), receptors, and adhesion molecules.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

The authors of a meta-analysis of eight randomized clinical trials (RCTs) examining the efficacy of turmeric extract in reducing discomfort in subjects with osteoarthritis suggested that although more rigorous and larger studies are needed for confirmation, the RCTs provided scientific evidence to support the efficacy of turmeric extract (approximately 1000 mg/day of curcumin) for easing occasional discomfort and supporting overall joint health.*^[17]

There is also growing evidence for the role of curcumin products in the management of functional GI disorders. A review of studies in patients with Crohn's disease suggests curcumin is complementary to support a reduction in C-reactive protein, interleukin-1, and tumor necrosis factor-alpha, all symptomatic markers.*^[18,19]

Regarding cardiovascular health, a meta-analysis of 20 randomized controlled trials (n = 1427) revealed a significant decrease in serum triglycerides and elevation of HDL cholesterol.^[20] Additionally, it is well-established that type 2 diabetes is a risk factor for cardiovascular health. In a 12-week randomized placebo-controlled trial in type 2 subjects (n = 118), supplemental curcumin (1000 mg/day) led to significant reduction in serum total cholesterol, non-HDL cholesterol, and lipoprotein(a).*^[21]

Omega MonoPure® Curcumin EC Supplement Facts

Serving Size: 1 Softgel

	Amount Per Serving	%DV
Calories	5	
Total Fat	0.5 g	1%†
MaxSimil® Fish Oil Concentrate	600 mg	**
Total Omega-3 Fatty Acids	417 mg	**
EPA (eicosapentaenoic acid)	276 mg	**
DHA (docosahexaenoic acid)	120 mg	**
BCM-95® Turmeric Extract (<i>Curcuma longa</i>)(rhizome)(95% total curcuminoids complex, including curcumin, curcuminoids, and volatile oils)(86% curcuminoids)(65% curcumin)	125 mg	**

† Percent Daily Values are based on a 2,000 calorie diet.
** Daily Value (DV) not established.

Other Ingredients: Softgel (fish gelatin, vegetable glycerin, purified water, and carob extract), yellow beeswax, sunflower lecithin, GRAS enteric coating (ethylcellulose, sodium alginate, ammonium hydroxide, purified water, medium-chain triglycerides, oleic acid, and vegetable stearic acid) and mixed natural tocopherols.

Contains: Fish (anchovy and/or sardine and/or mackerel [sources of fish oil] and tilapia [source of fish gelatin]).

DIRECTIONS: Take one softgel twice per day, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy protein, dairy products, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

BCM-95® is a registered trademark of Dolcas Biotech LLC.

Manufactured using MaxSimil® fish oil. MaxSimil® is a registered trademark of Ingenutra Inc. Protected under US patents 8,119,690 and 8,198,324; Canadian patents 2672513 and 2677670.

IFOS™ certification mark is a trademark of Nutrasource Diagnostics Inc.

References

- Weylandt KH, Chiu CY, Gomolka B, et al. Omega-3 fatty acids and their lipid mediators: towards an understanding of resolvin and protectin formation. *Prostaglandins Other Lipid Mediat.* 2012 Mar;97(3-4):73-82. [PMID: 22326554]
- Kremmyda LS, Tvrzicka E, Stankova B, et al. Fatty acids as biocompounds: their role in human metabolism, health and disease: a review. part 2: fatty acid physiological roles and applications in human health and disease. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub.* 2011 Sep;155(3):195-218. [PMID: 22286806]
- Manik PE, Varon J. Omega-3 dietary supplements and the risk of cardiovascular events: a systematic review. *Clin Cardiol.* 2009 Jul;32(7):365-72. [PMID: 19609891]
- Lands B. Omega-3 PUFAs lower the propensity for arachidonic acid cascade overreactions. *Biomed Res Int.* 2015;2015:285135. [PMID: 26301244]
- Tang S, Wan M, Huang W, et al. Maresins: Specialized proresolving lipid mediators and their potential role in inflammatory-related diseases. *Mediators Inflamm.* 2018 Feb 20;2018:2380319. [PMID: 29674943]
- Calder PC. Omega-3 fatty acids and inflammatory processes: from molecules to man. *Biochem Soc Trans.* 2017 Oct 15;45(5):1105-1115. [PMID: 28900017]
- Barden A, Mas E, Croft KD, et al. Short-term n-3 fatty acid supplementation but not aspirin increases plasma proresolving mediators of inflammation. *J Lipid Res.* 2014 Nov;55(11):2401-7. [PMID: 25187667]
- Antony B, Merina B, Iyer VS, et al. A pilot cross-over study to evaluate human oral bioavailability of BCM-95CG (Biocurcmax), a novel bioenhanced preparation of curcumin. *Indian J Pharm Sci.* 2008 Jul-Aug;70(4):445-9. [PMID: 20046768]
- Chandran B, Goel A. A randomized, pilot study to assess the efficacy and safety of curcumin in patients with active rheumatoid arthritis. *Phytother Res.* 2012 Nov;26(11):1719-25. [PMID: 22407780]
- Tasneem S, Liu B, Li B, et al. Molecular pharmacology of inflammation: medicinal plants as anti-inflammatory agents. *Pharmacol Res.* 2018 Nov 3;139:126-140. [PMID: 30395947]
- Ghosh S, Banerjee S, Sil PC. The beneficial role of curcumin on inflammation, diabetes and neurodegenerative disease: A recent update. *Food Chem Toxicol.* 2015 Sep;83:111-24. [PMID: 26066364]
- Kunnumakkara AB, Bordoloi D, Harsha C, et al. Curcumin mediates anticancer effects by modulating multiple cell signaling pathways. *Clin Sci (Lond).* 2017 Jul 5;131(15):1781-1799. [PMID: 28679846]
- Ghandadi M, Sahebkar A. Curcumin: an effective inhibitor of interleukin-6. *Curr Pharm Des.* 2017;23(6):921-931. [PMID: 27719643]
- Unpublished, internal data. Ingenutra.
- Fortin S, inventor; Centre de Recherche sur les Biotechnologies Marines, assignee. Compositions comprising polyunsaturated fatty acid monoglycerides or derivatives thereof and uses thereof. US patent 8,198,324. June 12, 2012.
- Brunet S, Chamoun R, Fortin S, et al. MaxSimil®: A novel, patented natural platform for enhanced absorption of omega-3s. Single dose, double-blind, 2-way crossover pilot pharmacokinetic study on healthy subjects under normal diet. Sherbrooke (Québec), Canada: Ingenutra; 2018. [Unpublished]
- Daily JW, Yang M, Park S. Efficacy of turmeric extracts and curcumin for alleviating the symptoms of joint arthritis: A systematic review and meta-analysis of randomized clinical trials. *J Med Food.* 2016 Aug;19(8):717-29. [PMID: 27533649]
- Patcharatrakul T, Gonlachanvit S. Chili peppers, curcumins, and prebiotics in gastrointestinal health and disease. *Curr Gastroenterol Rep.* 2016 Apr;18(4):19. [PMID: 26973345]
- Schneider A, Hossain I, VanderMolen J, et al. Comparison of remicade to curcumin for the treatment of Crohn's disease: a systematic review. *Complement Ther Med.* 2017 Aug;33:32-38. [PMID: 28735823]
- Simental-Mendia LE, Pirro M, Gotto AM Jr, et al. Lipid-modifying activity of curcuminoids: a systematic review and meta-analysis of randomized controlled trials. *Crit Rev Food Sci Nutr.* 2017 Nov 29;1-10. [PMID: 29185808]
- Panahi Y, Khalili N, Sahebi E, et al. Curcuminoids modify lipid profile in type 2 diabetes mellitus: a randomized controlled trial. *Complement Ther Med.* 2017 Aug;33:1-5. [PMID: 28735818]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Omega MonoPure[®] DHA EC

With Highly Concentrated DHA



Available in 30 fish gelatin softgels

Discussion

The two most well-researched omega-3 polyunsaturated fatty acids (PUFAs) are docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). DHA is an essential structural component of the central nervous system, and EPA plays a role in supporting healthy cardiac and circulatory systems. Omega MonoPure DHA EC features MaxSimil DHA. This particular form of the highly absorbable, patented MaxSimil monoglyceride fish oil contains 1,350 mg of concentrated DHA and 236 mg of EPA.*

Absorption

Studies conducted by the manufacturer of MaxSimil provide promising results suggesting better absorption than other fish oils. An unpublished, double-blind, crossover, pharmacokinetic study was performed in healthy overnight-fasted male and female subjects (N = 20) ages 19 to 60. Each subject was administered a single dose of six softgels (containing ~2000 mg EPA and ~1500 mg DHA) of either ethyl ester (EE) fish oil or MaxSimil. Compared to the EE form, MaxSimil EPA and DHA reached a peak concentration more than three times higher than that reached by EE fish oil. Moreover, MaxSimil not only reached maximum concentration faster but also maintained plasma levels longer. Additional peer-reviewed research related to bioavailability is warranted.*^[1-3]

Early Brain and Eye Development

Polyunsaturated fatty acids (PUFAs) play a critical role in the normal development of the eye, brain, and central nervous system, and DHA is the most abundant structural fatty acid in these tissues. DHA is transferred directly from mother to fetus during pregnancy, especially during the last trimester, and is available to infants through breast milk. This fatty acid plays a vital role in both prenatal and postnatal brain development. Based on recommendations made by various organizations, pregnant and nursing women should consume 100-300 mg of DHA daily to meet basic fetal and infant needs.*^[4,5]

Research indicates that DHA-supplemented and breastfed infants score significantly better on mental and psychomotor development tests and that PUFAs may support normal activity levels and learning capacity during preschool years.^[4,6] A study of infants (N = 229) enrolled in three randomized controlled trials suggested that a dose of 0.36% of total fatty acids as DHA (a concentration representative of human breast milk) contributed to favorable problem-solving performance, a parameter found to correlate with later IQ and vocabulary development.^[7] However, the outcome of a systematic review and meta-analysis showed that although omega-3 supplementation does appear to improve childhood psychomotor and visual development, more studies are needed to confirm these conclusions and to explore the significance of IQ later in childhood.*^[8]

Clinical Applications

- » Supports Early Brain Development*
- » Promotes Brain, Eye, Heart, and Cell Membrane Function Throughout the Lifespan*
- » Supports Immune Health and Eicosanoid Metabolism*

*Omega MonoPure[®] DHA EC features patented, International Fish Oil Standards (IFOS) five-star certified MaxSimil[®] DHA monoglyceride fish oil. This readily absorbed omega-3 fatty acid formula provides concentrated docosahexaenoic acid (DHA) plus eicosapentaenoic acid (EPA). DHA is often recommended during pregnancy to support healthy fetal brain development. Throughout the life span, both DHA and EPA support healthy brain, heart, immune, and eye function as well as healthy eicosanoid metabolism.**

DHA has also been researched for its role in developing and maintaining eye health and function during early life. A randomized trial of healthy formula-fed infants (N = 244) suggested that infants who were not given DHA had poorer visual acuity than those who were supplemented with DHA amounting to 0.32% of total fatty acids.^[9] Optimal retinal and visual cortex maturation was understood to depend upon dietary DHA during development, and visual acuity and mental development were “seemingly improved by extra DHA.”*^[6]

Nervous System, Brain, Eye, and Cell Membrane Function

Functioning via cell membranes and anchored by phospholipid molecules, DHA helps to optimize signal transmission in the tissues of the brain, eyes, and the overall nervous system.^[10] Levels of this fatty acid decline with aging. DHA supplementation may play a role in maintaining myelin and neuronal health, supporting healthy eicosanoid metabolism in the brain, and exerting pleiotropic effects to support healthy metabolism and aging throughout the lifespan.*^[6,11,12]

A study of healthy community volunteers (N = 280), ages 35-54, showed that higher DHA levels were significantly associated with performance improvement in the areas of nonverbal reasoning, mental flexibility, working memory, and vocabulary.^[13] Other research has focused on neuroprotectin D1 (NPD1), an important mediator derived from DHA through the action of 15-lipoxygenase-1. This mediator appears to have a positive effect on neurotrophic cell signaling, normal cell-life cycles, beta-amyloid neurobiology, and prostaglandin formation. A systematic review and meta-analysis suggested that omega-3 supplements play a role in improving cognitive development in infants. Although the research summarized in those studies indicated a functional role of DHA in brain health and an effect on attention domain, additional research is needed to further define DHA's role in cognitive function for groups other than infants.*^[14,15]

DHA is also required for the functional integrity of retinal pigment epithelium (RPE) cells and may play an ongoing role in eye health and function throughout life.^[10,16] Studies on human RPE cells suggest that NPD1 orchestrates cell-protective mechanisms (including inhibition of caspase-3 activation and COX-2 expression) and thus promotes a healthy response after cellular insult.*^[16,17]

Eicosanoid Metabolism, Heart Health, and Immune Health

In addition to the functional effects discussed above, research has established that omega-3 fatty acids antagonize arachidonic acid-induced eicosanoid formation. They also help generate resolvins and protectins known as specialized pro-resolving mediators (SPMs)—EPA and DHA metabolites that are naturally produced in vivo through enzymatic conversion of EPA and DHA—to promote a healthy response to the arachidonic acid cascade. Omega-3s have also

Continued on next page

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XyMOGEN[®] Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

been widely researched for their promotion of cardiovascular health, including maintaining healthy lipid levels already within the normal range and supporting normal resistance to oxidative stress.^[10] Although not excluding similar benefits of EPA and docosapentaenoic acid (DPA), DHA may have a direct or indirect benefit of keeping the heart rhythm healthy and consistent. In multivariable-adjusted cross-sectional analyses among older adults (N = ~3000), plasma phospholipid DHA—but not EPA or DPA—was inversely associated with resting heart rate and a trend toward lower blood pressure (BP).^[18] In one short trial, DHA reduced 24-hour ambulatory BP and heart rate^[19]; in another small trial (n = 59), the effect was not seen. Researchers speculated that statistical power may have been limited by the size of the latter study.^[20] This may have been the case since in another, larger study (N = 224) in healthy men receiving 4 g/day each of EPA and DHA, lower heart rate and blood pressure was achieved. In this study, plasma phospholipid analysis revealed that only DHA was responsible for lowering heart rate.^[21] Additionally, due to the preponderance of findings that EPA and DHA can help moderate blood pressure, the FDA has approved a qualified health claim with regard to this function.^[22] Specifically for Omega MonoPure DHA EC: Research shows that consuming EPA and DHA combined may be beneficial for moderating blood pressure, a risk factor for CHD (coronary heart disease). However, the FDA has concluded that the evidence is inconsistent and inconclusive. One serving (2 softgels) of Omega MonoPure DHA EC provides 1.58 grams of EPA and DHA.*

Omega-3 fatty acids may also have immunomodulatory effects.^[10] It has been suggested in several human studies that supplementing with a DHA-rich oil appears to decrease the activation of T lymphocytes and mononuclear cells and decrease levels of inflammatory mediators.^[23,24] The immune-altering effects may be due to the composition of the cell membrane as well as to the activity of the DHA-derived resolvins.^[25]

Omega MonoPure® DHA EC Supplement Facts

Serving Size: 2 Softgels

	Amount Per Serving	%Daily Value
Calories	25	
Total Fat	2.5 g	3%†
Cholesterol	15 mg	5%†
MaxSimil® DHA Fish Oil Concentrate	2.6 g	**
Total Omega-3 Fatty Acids	1.58 g	**
DHA (docosahexaenoic acid)	1.35 g	**
EPA (eicosapentaenoic acid)	236 mg	**

† Percent Daily Values are based on a 2,000 calorie diet.

** Daily Value not established.

Other Ingredients: Softgel (fish gelatin, vegetable glycerin, and purified water), GRAS enteric coating (ethylcellulose, sodium alginate, purified water, medium-chain triglycerides, oleic acid, vegetable stearic acid, and ammonium hydroxide), and natural mixed tocopherols.

Contains: Fish (anchovy and/or sardine and/or mackerel [sources of fish oil] and tilapia [source of fish gelatin]).

DIRECTIONS: Take one to two softgels daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy protein, dairy products, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

Manufactured using MaxSimil® fish oil. MaxSimil® is a registered trademark of Ingenutra Inc. Protected under US patents 8,119,690 and 8,198,324; Canadian patents 2672513 and 2677670.



IFOS™ Certification Mark is a registered trademark of Nutrasource Diagnostics Inc.

References

1. Unpublished, internal data. Ingenutra.
2. Fortin S, inventor; Centre de Recherche sur les Biotechnologies Marines, assignee. Compositions comprising polyunsaturated fatty acid monoglycerides or derivatives thereof and uses thereof. US patent 8,198,324. June 12, 2012.
3. Brunet S, Chamoun R, Fortin S, et al. MaxSimil®: A novel, patented natural platform for enhanced absorption of omega-3s. Single dose, double-blind, 2-way crossover pilot pharmacokinetic study on healthy subjects under normal diet. Sherbrooke (Québec), Canada: Ingenutra; 2018. [Unpublished]
4. Singh M. Essential fatty acids, DHA and human brain. *Indian J Pediatr*. 2005 Mar;72(3):239-42. [PMID: 15812120]
5. Guesnet P, Alessandri JM. Docosahexaenoic acid (DHA) and the developing central nervous system (CNS) - Implications for dietary recommendations. *Biochimie*. 2011 Jan;93(1):7-12. [PMID: 20478353]
6. Uauy R, Dangour AD. Nutrition in brain development and aging: role of essential fatty acids. *Nutr Rev*. 2006 May;64(5 Pt 2):S24-33; discussion S72-91. [PMID: 16770950]
7. Drower J, Hoffman DR, Castañeda YS, et al. Three randomized controlled trials of early long-chain polyunsaturated fatty acid supplementation on means-end problem solving in 9-month-olds. *Child Dev*. 2009 Sep-Oct;80(5):1376-84. [PMID: 19765006]
8. Shulkin M, Pimpin L, Bellinger D, et al. n-3 fatty acid supplementation in mothers, preterm infants, and term infants and childhood psychomotor and visual development: a systematic review and meta-analysis. *J Nutr*. 2018 Mar 1;148(3):409-418. [PMID: 29546296]
9. Birch EE, Carlson SE, Hoffman DR, et al. The DIAMOND (DHA intake and measurement of neural development) study: a double-masked, randomized controlled clinical trial of the maturation of infant visual acuity as a function of the dietary level of docosahexaenoic acid. *Am J Clin Nutr*. 2010 Apr;91(4):848-59. [PMID: 20130095]
10. Ghasemi Fard S, Wang F, Sinclair AJ, et al. How does high DHA fish oil affect health? A systematic review of evidence. *Crit Rev Food Sci Nutr*. 2018 Mar 1:1-44. [PMID: 29494205]
11. Bazan NG, Rodriguez de Turco EB, Gordon WC. Pathways for the uptake and conservation of docosahexaenoic acid in photoreceptors and synapses: biochemical and autoradiographic studies. *Can J Physiol Pharmacol*. 1993 Sep;71(9):690-8. [PMID: 8313233]
12. Cole GM, Ma QL, Frautschy SA. Dietary fatty acids and the aging brain. *Nutr Rev*. 2010 Dec;68 Suppl 2:S102-11. [PMID: 21091943]
13. Muldoon MF, Ryan CM, Sheu L, et al. Serum phospholipid docosahexaenoic acid is associated with cognitive functioning during middle adulthood. *J Nutr*. 2010 Apr;140(4):848-53. [PMID: 20181791]
14. Jiao J, Li Q, Chu J, et al. Effect of n-3 PUFA supplementation on cognitive function throughout the life span from infancy to old age: a systematic review and meta-analysis of randomized controlled trials. *Am J Clin Nutr*. 2014 Dec;100(6):1422-36. [PMID: 25411277]
15. Lukiw WJ, Bazan NG. Docosahexaenoic acid and the aging brain. *J Nutr*. 2008 Dec;138(12):2510-4. [PMID: 19022980]
16. Bazan NG. Neuroprotectin D1 (NPD1): a DHA-derived mediator that protects brain and retina against cell injury-induced oxidative stress. *Brain Pathol*. 2005 Apr;15(2):159-66. [PMID: 15912889]
17. Bazan NG, Calandria JM, Serhan CN. Rescue and repair during photoreceptor cell renewal mediated by docosahexaenoic acid-derived neuroprotectin D1. *J Lipid Res*. 2010 Aug;51(8):2018-31. [PMID: 20382842]
18. Mozaffarian D, Lemaitre RN, King IB, et al. Circulating long-chain ω -3 fatty acids and incidence of congestive heart failure in older adults: the cardiovascular health study: a cohort study. *Ann Intern Med*. 2011 Aug;155(3):160-70. [PMID: 21810709]
19. Mori TA, Bao DQ, Burke V, et al. Docosahexaenoic acid but not eicosapentaenoic acid lowers ambulatory blood pressure and heart rate in humans. *Hypertension*. 1999 Aug;34(2):253-60. [PMID: 10454450]
20. Woodman RJ, Mori TA, Burke V, et al. Effects of purified eicosapentaenoic and docosahexaenoic acids on glycemic control, blood pressure, and serum lipids in type 2 diabetic patients with treated hypertension. *Am J Clin Nutr*. 2002 Nov;76(5):1007-15. [PMID: 12399272]
21. Grimsgaard S, Bønaa KH, Hansen JB, et al. Effects of highly purified eicosapentaenoic acid and docosahexaenoic acid on hemodynamics in humans. *Am J Clin Nutr*. 1998 Jul;68(1):52-9. [PMID: 9665096]
22. FDA Announces New Qualified Health Claims for EPA and DHA Omega-3 Consumption and the Risk of Hypertension and Coronary Heart Disease [update]. Silver Spring, MD: Center for Food Safety and Applied Nutrition Constituent Update, US Food and Drug Administration; June 19, 2019. <https://www.fda.gov/food/cfsan-constituent-updates/fda-announces-new-qualified-health-claims-epa-and-dha-omega-3-consumption-and-risk-hypertension-and>. Accessed July 18, 2019.
23. Kew S, Mesa MD, Tricon S, et al. Effects of oils rich in eicosapentaenoic and docosahexaenoic acids on immune cell composition and function in healthy humans. *Am J Clin Nutr*. 2004 Apr;79(4):674-81. [PMID: 15051614]
24. Vedin I, Cederholm T, Freund Levi Y, et al. Effects of docosahexaenoic acid-rich n-3 fatty acid supplementation on cytokine release from blood mononuclear leukocytes: the OmegaAD study. *Am J Clin Nutr*. 2008 Jun;87(6):1616-22. [PMID: 18541548]
25. Calder PC. The relationship between the fatty acid composition of immune cells and their function. *Prostaglandins Leukot Essent Fatty Acids*. 2008 Sep-Nov;79(3-5):101-8. [PMID: 18951005]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

© XYMOGEN
DRS-231
Rev. 05/03/19



7 22537150984 8

Omega MonoPure[®] Formulas

3X Greater Absorption*



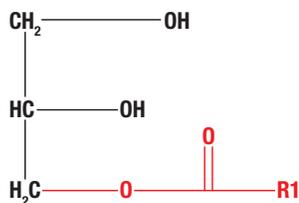
Omega MonoPure[®] 1300 EC is available in 60 softgels and 120 softgels
Omega MonoPure[®] 650 EC is available in 60 softgels and 120 softgels

Discussion

MaxSimil[®] Patented Lipid Absorption Enhancement Technology (PLATform)

The MaxSimil PLATform is a novel monoglyceride delivery system that enhances absorption of lipid-based and lipid-soluble nutraceutical and food ingredients. This technology has been applied to XYMOGEN's Omega MonoPure formulas in order to create a unique vehicle by which to deliver EPA and DHA. Due to the fact that monoglyceride oils are intrinsically emulsifiers and are, by nature, in a readily absorbable form (Figure 1), they can bypass the body's normal fat digestion process. These qualities make Omega MonoPure an excellent method for delivering omega-3 fatty acids, especially to individuals with digestive, pancreatic, or gall bladder challenges. Studies show that MaxSimil fish oils (FO) have three times (300%) greater absorption of EPA and DHA compared to other leading fish oils.*^[1-3]

Figure 1. Monoglyceride Chemical Representation in MaxSimil Fish Oils (R1 = fatty acid)



Unique structure: One fatty acid attached to a glycerol backbone provides two polar ends that attract water and a non-polar tail end (R1) that attracts fat, thus enabling self-emulsification of the Omega MonoPure formulas.

Reprinted with permission from Ingenutra, Inc.

Quality

Omega MonoPure formulas are made using proprietary MaxSimil compositions containing monoglyceride FO with no additional ingredients, carriers, or excipients. Each fish-gelatin softgel is enteric-coated, and every batch of fish oil is IFOS five-star certified to ensure the world's highest standards for purity, potency, and freshness. The fish oil is non-GMO, certified sustainable from Scandinavia, and antibiotic-free. Additionally, it is eco-friendly because the greater absorption of EPA and DHA ultimately means that fewer grams of fish oil need to be harvested for the same benefit.*

In Vitro and In Vivo Animal Studies

The ability of MaxSimil-enhanced EPA and DHA to positively influence growth inhibition and apoptosis in colorectal, breast, lung, and prostate diseased cell lines was first demonstrated in a series of in vitro studies.^[4-6] Researchers

Clinical Applications

- » Positively Affects the Production of Arachidonic Acid-Derived Eicosanoids*
- » Supports Cardiovascular Health*
- » Supports Healthy Mental Functioning*
- » Supports Healthy Glucose and Insulin Metabolism*
- » By Supplying the Precursors EPA and DHA, Helps the Body Generate Specialized Proresolving Lipid Mediators, Such as Resolvins and Protectins*

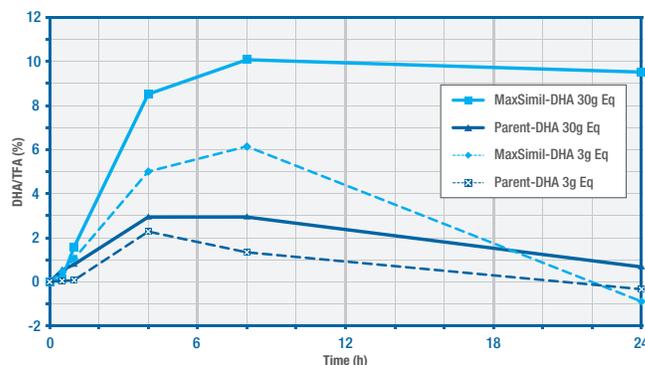
The *Omega MonoPure* family of formulas feature IFOS five-star certified MaxSimil[®] monoglyceride fish oil that has a three times greater EPA+DHA absorption rate than an equivalent dose of other leading fish oils. Through the use of MaxSimil patented lipid absorption enhancement technology (PLATform), the fish oil is absorption-ready and can be directly assimilated in the intestinal tract for maximum benefit.*

subsequently set out to demonstrate efficacy in animal models after oral administration. In three separate animal models, MaxSimil EPA and DHA forms showed superior activity on diseased cell-line growth inhibition and cytokine production when compared to control, corn oil, krill oil, or the parent forms ethyl ester (EE) EPA and ethyl ester (EE) DHA.^[4,7,8] These in vivo animal studies proved that orally supplemented MaxSimil EPA and DHA were well-absorbed and bioactive. Researchers postulated that the observed superior effects of MaxSimil EPA and DHA forms were the result of enhanced absorption, and they set out to prove this hypothesis.*

Preclinical Bioavailability Studies

The in vivo pharmacokinetic studies in rodents involved a comparison between MaxSimil DHA FO and its parent EE DHA FO and an analysis of blood concentrations of DHA over time. The doses used were equivalent to human doses of 3 g/day and 30 g/day; the latter was included primarily to investigate toxicity at high doses. Researchers found that MaxSimil DHA FO had a three times (3x) higher peak concentration (6% versus 2%, Figure 2), a 3x higher saturation potential at the high dose (10% versus 3%), and a 3x higher absorption rate (at a 3 g/day equivalent human dose) than its parent DHA FO. No toxicity was observed at either dose level.^[1,2] This research demonstrated superior bioavailability and presumably better exposure of cells to DHA.*

Figure 2. Preclinical Bioavailability Study in Rodents Demonstrates Superior Peak Concentration, Saturation, and Absorption of MaxSimil DHA FO Versus Its Parent DHA FO
Data were derived from Ingenutra, Inc.^[1,2]



Continued on next page

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN[®] Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

Blood Sugar Support

Cardiovascular Support

Cytokine Balance Support

Essential Fatty Acids

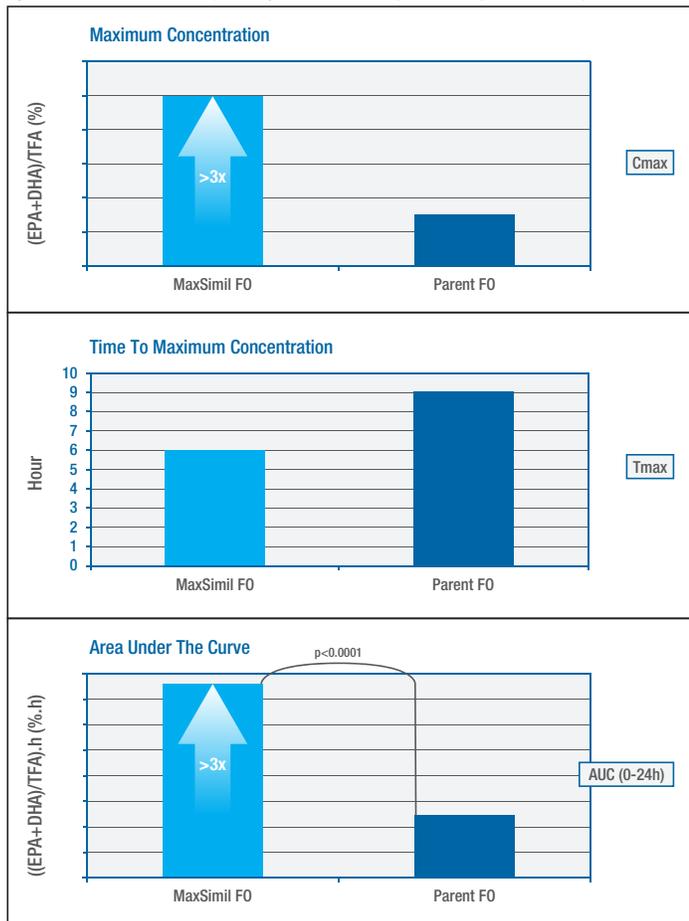
Neurologic & Cognitive

Clinical Bioavailability Study

A phase 1, double-blind, randomized, crossover, pharmacokinetic study was performed in 20 healthy adults aged between 19 and 71 years who were administered 6 g (containing 1800 mg EPA and 1200 mg DHA) per day of EE FO or MaxSimil FO.^[3] Parameters studied were plasma EPA and DHA concentration (as percent of total fatty acids), Cmax, and AUC. Compared to EE EPA+DHA, the results indicated that at peak concentration, MaxSimil EPA and DHA forms were 3x higher, they reached maximum concentration faster, and maintained their plasma levels longer (Figure 3). The finding in the animal study was validated: the MaxSimil FO instantaneous absorption was 3x greater than the EE form. Likewise, the AUC over 24 hours was also more than 3x higher (P<.0001) for MaxSimil EPA and DHA (MaxSimil FO).*

Not only did this study confirm the bioavailability findings in the animal study, but it also demonstrated that after 24 hours, the MaxSimil FO maintained 2-3x higher blood levels of EPA and DHA than the EE FO. This means that, given a daily dose, circulating EPA and DHA levels can be expected to ramp up over time and remain high with steadily increasing exposure of cells to EPA, DHA, and their metabolites. Based on the results of the bioavailability studies, an individual would get more EPA and DHA from MaxSimil FO than from EE FO gram for gram. Furthermore, as shown in the animal studies, one could anticipate enhanced effects. It is noteworthy that all 20 adults who completed the study saw their omega-3 absorption enhanced when taking the MaxSimil enhanced FO.*

Figure 3. Human Clinical Study Findings Demonstrate Superior Absorption of and Exposure to EPA



and DHA as Indicated by Cmax, Tmax, and AUC

Reprinted with permission from Ingenutra, Inc.

Expanding Research

In vitro and animal studies have demonstrated the positive effects of MaxSimil FO on airway immune response (e.g., IgE, leukocytes); the expression of COX-2, NF-kB, cytokines (e.g., IL-6, IL-8), MUC5AC, and mucin; and Ca(2+) hypersensitivity in lung tissues.^[8-11] In other research, rats subjected to eight weeks of a high-fat, high-carbohydrate diet were either not

supplemented or provided 3 g/day of MaxSimil DHA. Compared to the data from the non-supplemented group, the data from the MaxSimil DHA supplemented group clearly showed a positive impact on cardiovascular health parameters. Measures included blood pressure, heart rate, serum lipid levels, cytokine production, aortic wall thickness, and a DHA:AA ratio in aortic tissue, which correlated with the production of resolvin D2 and D3 metabolites.*^[12]

A Note About Resolvins and Other EPA and DHA Metabolites

Specialized proresolving lipid mediators, such as resolvins, protectins, and maresins, are EPA and DHA metabolites naturally produced in vivo through enzymatic conversion of EPA and DHA. These mediators aid the body's "clean-up" response to the arachidonic acid cascade.^[13] Rather than supplying a single molecule or metabolite, which would mirror the pharmaceutical model, Omega MonoPure fish oils provide all the benefits of EPA and DHA as well as the expected and desirable benefits of their metabolites.*

Omega MonoPure® 1300 EC Supplement Facts

Serving Size: 1 Softgel

	Amount Per Serving	%Daily Value
Calories	10	
Total Fat	1 g	1%†
MaxSimil® Fish Oil Concentrate	1.3 g	**
Total Omega-3 Fatty Acids	860 mg	**
EPA (eicosapentaenoic acid)	600 mg	**
DHA (docosahexaenoic acid)	260 mg	*

† Percent Daily Value based on a 2,000 calorie diet.

** Daily Value not established.

Other Ingredients: Softgel (fish gelatin, vegetable glycerin, and purified water), GRAS enteric coating (ethylcellulose, sodium alginate, purified water, medium-chain triglycerides, oleic acid, vegetable stearic acid, and ammonium hydroxide), and mixed natural tocopherols.

Contains: Fish (anchovy and/or sardine [sources of fish oil], tilapia and/or pangasius [sources of fish gelatin]).

DIRECTIONS: Take one softgel daily, or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking blood thinners or other medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep tightly closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy protein, dairy products, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



Third-Party Certificate of Analysis (COA) can be found by visiting:
<http://www.ifosprogram.com/consumer-reports.aspx>

Manufactured using MaxSimil® fish oil. MaxSimil® is a registered trademark of Ingenutra Inc. Protected under US patents 8,119,690 and 8,198,324; Canadian patents 2672513 and 2677670.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Omega MonoPure® 650 EC Supplement Facts

Serving Size: 1 Softgel

	Amount Per Serving	%Daily Value
Calories	5	
Total Fat	0.5 g	1%†
MaxSimil® Fish Oil Concentrate	650 mg	**
Total Omega-3 Fatty Acids	430 mg	**
EPA (eicosapentaenoic acid)	300 mg	**
DHA (docosahexaenoic acid)	130 mg	*

† Percent Daily Value based on a 2,000 calorie diet.

** Daily Value not established.

Other Ingredients: Softgel (fish gelatin, vegetable glycerin, and purified water), GRAS enteric coating (ethylcellulose, sodium alginate, purified water, medium-chain triglycerides, oleic acid, vegetable stearic acid, and ammonium hydroxide), and mixed natural tocopherols.

Contains: Fish (anchovy and/or sardine [sources of fish oil], tilapia and/or pangasius [sources of fish gelatin]).

DIRECTIONS: Take one softgel daily, or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking blood thinners or other medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep tightly closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy protein, dairy products, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



Third-Party Certificate of Analysis (COA) can be found by visiting:
<http://www.ifosprogram.com/consumer-reports.aspx>

Manufactured using MaxSimil® fish oil. MaxSimil® is a registered trademark of Ingenutra Inc. Protected under US patents 8,119,690 and 8,198,324; Canadian patents 2672513 and 2677670.

References

1. Unpublished, internal data. Ingenutra.
2. Fortin S, inventor; Centre de Recherche sur les Biotechnologies Marines, assignee. Compositions comprising polyunsaturated fatty acid monoglycerides or derivatives thereof and uses thereof. US patent 8,198,324. June 12, 2012.
3. MaxSimil Patented Lipid Absorption Technology Clinical Study Report: MaxSimil® 3020 Omega-3. Sherbrooke (Québec), Canada: Ingenutra; 2015. [Unpublished, internal data]
4. Morin C, Rousseau É, Fortin S. Anti-proliferative effects of a new docosapentaenoic acid monoacylglyceride in colorectal carcinoma cells. *Prostaglandins Leukot Essent Fatty Acids*. 2013 Sep;89(4):203-13. [PMID: 23932824]
5. Fortin S, inventor; Centre de Recherche sur les Biotechnologies Marines, assignee. Polyunsaturated fatty acid monoglycerides, derivatives, and uses thereof. US patent 8,119,690. February 21, 2012.
6. Fortin S, inventor; Centre de Recherche sur les Biotechnologies Marines, assignee. Polyunsaturated fatty acid monoglycerides, derivatives, and uses thereof. US patent 8,329,747. December 11, 2012.
7. Morin C, Blier PU, Fortin S. Eicosapentaenoic acid and docosapentaenoic acid monoglycerides are more potent than docosahexaenoic acid monoglyceride to resolve inflammation in a rheumatoid arthritis model. *Arthritis Res Ther*. 2015 May 29;17:142. [PMID: 26022389]
8. Morin C, Fortin S, Cantin AM, et al. Docosahexaenoic acid derivative prevents inflammation and hyperreactivity in lung: implication of PKC-Potentiated inhibitory protein for heterotrimeric myosin light chain phosphatase of 17 kD in asthma. *Am J Respir Cell Mol Biol*. 2011 Aug;45(2):366-75. [PMID: 21057106]
9. Morin C, Fortin S, Cantin AM, et al. MAG-EPA resolves lung inflammation in an allergic model of asthma. *Clin Exp Allergy*. 2013 Sep;43(9):1071-82. [PMID: 23957343]
10. Morin C, Cantin AM, Rousseau É, et al. Pro-resolving action of MAG-DHA in lung inflammatory models related to cystic fibrosis. *Am J Respir Cell Mol Biol*. 2015 Oct;53(4):574-83. [PMID: 25781052]
11. Morin C, Fortin S, Rousseau É. New omega-3 derivatives reduce airway inflammation and prevent rho-kinase activation in an allergic model of asthma. *J Aller Ther*. 2012;3(S1):003. doi:10.4172/2155-6121.S1-003.
12. Morin C, Rousseau E, Blier PU, et al. Effect of docosahexaenoic acid monoacylglyceride on systemic hypertension and cardiovascular dysfunction. *Am J Physiol Heart Circ Physiol*. 2015 Jul 1;309(1):H93-H102. [PMID: 25910811]
13. Weylandt KH, Chiu CY, Gomolka B, et al. Omega-3 fatty acids and their lipid mediators: towards an understanding of resolvins and protectin formation. *Prostaglandins Other Lipid Mediat*. 2012 Mar;97(3-4):73-82. [PMID: 22326554]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

© XYMOGEN
DRS-308
Rev. 08/29/18



OmegaPure™

Alaskan IFOS Five-Star Certified Fish Oil



OmegaPure 600 EC™ is available in 60 softgels & 120 softgels
OmegaPure 780 EC™ is available in 120 softgels
OmegaPure 820™ is available in 120 softgels
OmegaPure 900 EC™ is available in 90 softgels & 120 softgels

Discussion

IFOS Five-Star Certified Purity and quality are paramount when selecting fish oil supplements. This is precisely why XYMOGEN chose an Alaskan fish oil that is IFOS (international fish oil standards) five-star certified. IFOS is the only third-party testing and certification program for omega-3 fish oil products; it sets the gold standard for analyzing products for comparison to the highest industry standards with regard to contaminants, stability, heavy metals, and potency. Furthermore, IFOS provides detailed results for all testing categories for each individual lot tested. These assays are displayed on the IFOS website.^[1] IFOS is exclusively focused on omega-3 fish oil products, and it has long-standing experience with testing fish oil at all points along the supply chain. Five-star certification means:

- Product complies with all CRN[†]/GOED^{††}/WHO^{†††} testing categories
- Quantity of active ingredients matches the label claim
- Oxidation level is below the CRN/GOED standard by at least 75%
- PCB levels are below the CRN/GOED standard by at least 50%
- Dioxin levels are below the WHO standard by at least 50%

Source and Processing The omega-3 concentrate used in XYMOGEN's OmegaPure line of fish oils is exclusively sourced from US-caught fish, namely certified sustainable wild Alaskan walleye pollock and Pacific whiting obtained from the cold, clear waters off Alaska. Freshly caught fish are processed within hours to make quick-frozen fish fillets. The result is exceptionally fresh raw fish oil. To achieve the level of quality found in OmegaPure fish oils, a series of critical steps are undertaken: (1) raw fish oil triglycerides are broken down into ethyl esters; (2) EPA and DHA are separated from other fats and concentrated through flash distillation; (3) cold extraction further concentrates the oil, resulting in up to 85% omega-3; (4) molecular distillation removes fishy odor and taste, resulting in extremely fresh oil; (5) PCBs, chlorinated organopollutants, and toxic heavy metals are removed through filtration; and (6) high purity products are packaged in 190 kg drums or 900 kg totes under inert gas.

Clinical Applications

- » Affects the Production of Arachidonic Acid-Derived Eicosanoids*
- » Helps the Body Generate Specialized Proresolving Lipid Mediators, Such as Resolvins and Protectins*
- » Supports Cardiovascular Health*
- » Supports Healthy Mental Functioning*
- » Supports Healthy Glucose and Insulin Metabolism*

*OmegaPure Fish Oils are International Fish Oil Standards (IFOS) five-star certified, which assures the highest level of purity, stability, and potency in fish oils. Each dose of these concentrated fish oils provides 600-900 mg of EPA and DHA and is delivered in a small, fish-gelatin-based softgel. With the exception of OmegaPure 820, the softgels are covered with a GRAS-certified enteric coating so that they are easy to swallow and the EPA/DHA content is optimally absorbed. EPA and DHA from fish oil promote wellness by supporting cardiovascular health, cytokine balance, joint health, and brain and nervous system function.**

GRAS-Certified Enteric Coating OmegaPure fish oils employ a fish-gelatin—not a bovine-gelatin—softgel that is enteric-coated (except for OmegaPure 820) and GRAS-certified to further guarantee quality. The enteric coating helps ensure that the fish oils reach the small intestine before being metabolized, resulting in better delivery of actives to the intestines for absorption. This delivery may also reduce the occurrence of a fishy aftertaste.*

Ethyl Ester Form Despite aggressive marketing claims to the contrary, a recent publication by Oelrich et al found that no significant difference in the effect on serum triglycerides was detected in patients taking triglyceride (TG) or ethyl ester forms of omega-3 supplements.^[2] In the study, three fish oil supplementation forms were examined. The active therapy was 4 g/day of combined EPA and DHA provided as: a 90% TG formulation, a 60% TG formulation, or ethyl esters (i.e., 0% TG). In addition to the main finding, researchers also noted that the omega-3 fish oils provided in the ethyl ester form tended to have less impact on increasing LDL-cholesterol levels compared to the omega-3 fish oils delivered in the triglyceride form.*

Health Benefits of EPA/DHA Research and studies have shown that omega-3 fatty acids antagonize arachidonic acid-induced eicosanoid formation; help generate resolvins and protectins to aid the body's "cleanup" response to the arachidonic acid cascade; promote neurological health and mental functioning; and promote cardiovascular health, a balanced immune response, and healthy glucose and insulin metabolism.^[3-15] Research suggests that it takes 2 g/day of DHA supplementation over a period of a month to saturate the plasma and three to six months of supplementation to saturate the tissues.^[16] Concentrations of DHA increased in breast milk within less than a week of supplementation.*^[16]

[†] Council for Responsible Nutrition

^{††} Global Organization for EPA and DHA Omega-3

^{†††} World Health Organization

OmegaPure 600 EC™ Supplement Facts

Serving Size: 2 Softgels

	Amount Per Serving	%Daily Value
Calories	20	
Calories from Fat	20	
Total Fat	2 g	3%†
Fish Oil Concentrate	2 g	**
Total Omega-3 Fatty Acids	1.3 g	**
EPA (eicosapentaenoic acid)	720 mg	**
DHA (docosahexaenoic acid)	480 mg	**

† Percent Daily Value based on a 2,000 calorie diet.
 ** Daily Value not established.

Other Ingredients: Softgel (tilapia fish gelatin, vegetable glycerin, and purified water), GRAS enteric coating (purified water, ethylcellulose, sodium alginate, ammonium hydroxide, medium-chain triglycerides, oleic acid, and vegetable stearic acid), and mixed natural tocopherols.

Contains: Fish (Alaska pollock, Pacific whiting [sources of fish oil], tilapia [source of fish gelatin]) from certified sustainable sources.

DIRECTIONS: Take two softgels daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking blood thinners or other medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy protein, dairy products, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.



Third-Party Certificate of Analysis (COA) can be found by visiting:
<http://www.ifosprogram.com/consumer-reports.aspx>

OmegaPure 780 EC™ Supplement Facts

Serving Size: 2 Softgels

	Amount Per Serving	%Daily Value
Calories	20	
Calories from Fat	20	
Total Fat	2 g	3%†
Fish Oil Concentrate	2.8 g	**
Total Omega-3 Fatty Acids	1.82 g	**
EPA (eicosapentaenoic acid)	900 mg	**
DHA (docosahexaenoic acid)	660 mg	**

† Percent Daily Value based on a 2,000 calorie diet.
 ** Daily Value not established.

Other Ingredients: Softgel (tilapia fish gelatin, vegetable glycerin, and purified water), GRAS enteric coating (purified water, ethylcellulose, sodium alginate, ammonium hydroxide, medium-chain triglycerides, oleic acid, and vegetable stearic acid), and mixed natural tocopherols.

Contains: Fish (Alaska pollock, Pacific whiting [sources of fish oil], tilapia [source of fish gelatin]) from certified sustainable sources.

DIRECTIONS: Take one or two softgels one to three times daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking blood thinners or other medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy protein, dairy products, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep tightly closed in a cool, dry place out of reach of children.



Third-Party Certificate of Analysis (COA) can be found by visiting:
<http://www.ifosprogram.com/consumer-reports.aspx>

OmegaPure 820™ Supplement Facts

Serving Size: 2 Softgels

	Amount Per Serving	%Daily Value
Calories	20	
Calories from Fat	20	
Total Fat	2 g	3%†
Fish Oil Concentrate	2.5 g	**
Total Omega-3 Fatty Acids	1.875 g	**
EPA (eicosapentaenoic acid)	1 g	**
DHA (docosahexaenoic acid)	640 mg	**

† Percent Daily Value based on a 2,000 calorie diet.
 ** Daily Value not established.

Other Ingredients: Softgel (tilapia fish gelatin, vegetable glycerin, and purified water), and mixed natural tocopherols

Contains: Fish (Alaska pollock, Pacific whiting [sources of fish oil], tilapia [source of fish gelatin]) from certified sustainable sources.

DIRECTIONS: Take one or two softgels one to three times daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking blood thinners or other medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy protein, dairy products, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep tightly closed in a cool, dry place out of reach of children.



Third-Party Certificate of Analysis (COA) can be found by visiting:
<http://www.ifosprogram.com/consumer-reports.aspx>

OmegaPure 900 EC™ Supplement Facts

Serving Size: 1 Softgel

	Amount Per Serving	%Daily Value
Calories	10	
Calories from Fat	10	
Total Fat	1 g	2%†
Fish Oil Concentrate	1.29 g	**
Total Omega-3 Fatty Acids	967 mg	**
EPA (eicosapentaenoic acid)	515 mg	**
DHA (docosahexaenoic acid)	385 mg	*

† Percent Daily Value based on a 2,000 calorie diet.
 ** Daily Value not established.

Other Ingredients: Softgel (tilapia fish gelatin, vegetable glycerin, and purified water), GRAS enteric coating (ethylcellulose, sodium alginate, purified water, ammonium hydroxide, medium-chain triglycerides, oleic acid, and vegetable stearic acid), and mixed natural tocopherols.

Contains: Fish (Alaska pollock, Pacific whiting [sources of fish oil], tilapia [source of fish gelatin]) from certified sustainable sources.

DIRECTIONS: Take one softgel daily, or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking blood thinners or other medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy protein, dairy products, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep tightly closed in a cool, dry place out of reach of children.



Third-Party Certificate of Analysis (COA) can be found by visiting:
<http://www.ifosprogram.com/consumer-reports.aspx>

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

References

1. IFOS Consumer Reports. <http://www.ifosprogram.com/consumer-reports.aspx>. Accessed August 16, 2013.
2. Oelrich B, Dewell A, Gardner CD. Effect of fish oil supplementation on serum triglycerides, LDL cholesterol and LDL subfractions in hypertriglyceridemic adults. *Nutr Metab Cardiovasc Dis*. 2011 Sep 15. Epub ahead of print. [PMID: 21924882]
3. Storey A, McArdle F, Friedmann PS, et al. Eicosapentaenoic acid and docosahexaenoic acid reduce UVB- and TNF alpha-induced IL-8 secretion in keratinocytes and UVB-induced IL-8 in fibroblasts. *J Invest Dermatol*. 2005 Jan;124(1):248-55. [PMID: 15654981]
4. Kim YJ, Kim HJ, No JK, et al. Anti-inflammatory action of dietary fish oil and calorie restriction. *Life Sci*. 2006 Apr 18;78(21):2523-32. [PMID: 16438990]
5. Maroon JC, Bost JW. Omega-3 fatty acids (fish oil) as an anti-inflammatory: an alternative to nonsteroidal anti-inflammatory drugs for discogenic pain. *Surg Neurol*. 2006 Apr;65(4):326-31. [PMID: 16531187]
6. Weylandt KH, Chiu CY, Gomolka B, et al. Omega-3 fatty acids and their lipid mediators: towards an understanding of resolvin and protectin formation. *Prostaglandins Other Lipid Mediat*. 2012 Mar;97(3-4):73-82. [PMID: 22326554]
7. Kremmyda LS, Tvrzicka E, Stankova B, et al. Fatty acids as biocompounds: their role in human metabolism, health and disease: a review. part 2: fatty acid physiological roles and applications in human health and disease. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub*. 2011 Sep;155(3):195-218. [PMID: 22286806]
8. Frangou S, Lewis M, McCrone P. Efficacy of ethyl-eicosapentaenoic acid in bipolar depression: randomized double-blind placebo-controlled study. *Br J Psychiatry*. 2006 Jan;188:46-50. [PMID: 16388069]
9. Kankaanpaa P, Sutas Y, Salminen S, et al. Dietary fatty acids and allergy. *Ann Med*. 1999 Aug;31(4):282-87. [PMID: 10480759]
10. Ebbesson SO, Risica PM, Ebbesson LO, et al. Omega-3 fatty acids improve glucose tolerance and components of the metabolic syndrome in Alaskan Eskimos: the Alaska Siberia project. *Int J Circumpolar Health*. 2005 Sep;64(4):396-408. [PMID:16277123]
11. Nettleton JA, Katz R. n-3 long-chain polyunsaturated fatty acids in type 2 diabetes: a review. *J Am Diet Assoc*. 2005 Mar;105(3):428-40. [PMID:15746832]
12. Weitz D, Weintraub H, Fisher E, et al. Fish oil for the treatment of cardiovascular disease. *Cardiol Rev*. 2010 Sep-Oct;18(5):258-63. [PMID: 20699674]
13. Psota TL, Gebauer SK, Kris-Etherton P. Dietary omega-3 fatty acid intake and cardiovascular risk. *Am J Cardiol*. 2006 Aug 21;98(4A):3i-18i. [PMID: 16919512]
14. Sasaki J, Yokoyama M, Matsuzaki M, et al. Relationship between coronary artery disease and non-HDL-C, and effect of highly purified EPA on the risk of coronary artery disease in hypercholesterolemic patients treated with statins: sub-analysis of the Japan EPA Lipid Intervention Study (JELIS). *J Atheroscler Thromb*. 2012;19(2):194-204. [PMID: 22186099]
15. Zhang J, Wang C, Li L, et al. Inclusion of Atlantic salmon in the Chinese diet reduces cardiovascular disease risk markers in dyslipidemic adult men. *Nutr Res*. 2010 Jul;30(7):447-54. [PMID: 20797476]
16. Arterburn LM, Hall EB, Oken H. Distribution, interconversion, and dose response of n-3 fatty acids in humans. *Am J Clin Nutr*. 2006 Jun;83(Suppl):1467S-1476S. Review. [PMID: 16841856]

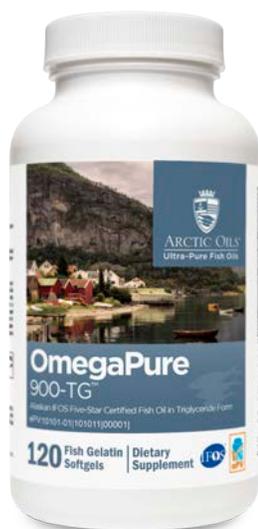
Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

OmegaPure 900-TG™

Alaskan IFOS Five-Star Certified Fish Oil in Triglyceride Form



Available in 120 fish gelatin softgels

Discussion

OmegaPure 900-TG offers you the best in omega-3 triglyceride-based supplementation. No other professional brand has this potency level: 900 mg EPA and DHA in a single softgel or capsule. In addition, OmegaPure 900-TG™ is IFOS five-star certified, which assures the highest and purest quality oil.

Processing for Purity and Quality

The fish oil used in OmegaPure 900-TG is produced under state-of-the-art GMP guidelines approved by international regulatory authorities, including the FDA. To arrive at a high-quality, pure fish oil supplement, several aspects must be considered during the processing of the crude oil:

Contaminants

Heavy metals and persistent organic pollutants (POPs), such as dioxins, dichlorodiphenyltrichloroethane (DDT), polychlorinated biphenyls (PCBs), and brominated flame retardants (BFRs) accumulate in the marine food chain. Proprietary manufacturing procedures, including triple distillation or stripping of the starter oil, reduce these aforementioned contaminants and other POPs to extremely low levels. Every batch is controlled to be less than half of the limits set in the current guidelines (e.g., European Pharmacopoeia, Global Organization for EPA and DHA (GOED), United States Pharmacopeia), and actual POP levels typically show values close to or below detection limits.

Oxidation

Fish oil is highly susceptible to oxidation. If the oil becomes oxidized during processing, the oil's health benefits may be diminished. Closed production under nitrogen or low pressure from first refining to finished drumming ensures low oxidation, which is indicated by anisidine values that fall well below other oils on the market. Every batch is tested for oxidation products before release.

Potency

Crude fish oil contains approximately 30% of the active omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). This means that 70% is made up of various fatty acids with different properties. By concentrating the amount of EPA and DHA to high levels, we assure optimal delivery of the fatty acids that are associated with clinical benefits.*

Clinical Applications

- » Affects the Production of Arachidonic Acid-Derived Eicosanoids*
- » Helps the Body Generate Specialized Proresolving Lipid Mediators, Such as Resolvins and Protectins*
- » Supports Cardiovascular Health*
- » Supports Healthy Mental Functioning*
- » Supports Healthy Glucose and Insulin Metabolism*

*OmegaPure 900-TG™ is International Fish Oil Standards (IFOS) five-star certified, which assures the highest level of purity, stability, and potency in fish oils. Each fish gelatin softgel contains concentrated Alaskan fish oil that provides 900 mg of EPA and DHA omega-3 fatty acids in triglyceride form. To assure maximum purity and freshness, the oil is stabilized with mixed natural tocopherols. EPA and DHA from fish oil have been extensively researched for their health benefits. They promote wellness by supporting cardiovascular health, normal platelet aggregation, cytokine balance, joint health, and brain and nervous system function.**

When these aspects are treated with exacting standards during processing, the product can be awarded third-party IFOS (International Fish Oil Standards) certification.

IFOS Five-Star Certification

OmegaPure 900-TG is sourced from Norwegian fish oil that is IFOS five-star certified. IFOS is the only third-party testing and certification program for omega-3 fish oil products; it sets the gold standard for analyzing products for comparison to the highest industry standards with regard to contaminants, heavy metals, stability, and potency. Furthermore, IFOS provides detailed results for all testing categories on each individual lot tested. These assays are displayed on the IFOS website.^[1] IFOS is exclusively focused on omega-3 fish oil products, and it has long-standing experience with testing fish oil at all points along the supply chain. Five-star certification means:

- Product complies with all CRN⁺/GOED⁺⁺/WHO⁺⁺⁺ testing categories
- Quantity of active ingredients matches the label claim
- Oxidation level is below the CRN/GOED standard by at least 75%
- PCB levels are below the CRN/GOED standard by at least 50%
- Dioxin levels are below the WHO standard by at least 50%

Triglyceride Form

A triglyceride (or triacylglycerol) consists of three fatty acids bound to a glycerol backbone. Unrefined fish oils naturally contain triglycerides with varying amounts of DHA and EPA attached to glycerol. During the production of concentrated fish oils, the fatty acids are liberated into free ethyl ester (EE) form. The EE form can be maintained or the free fatty acids can be re-esterified to produce the triglyceride (TG) form. Both TG and EE forms, as found in *concentrated* fish oils, are classified as esters. OmegaPure 900-TG delivers 900 mg of EPA and DHA as a 70% TG formula.

Fish Gelatin Capsules—No Enteric Coating

By using 100% fish-derived gelatin softgels, OmegaPure 900-TG is appropriate for pescetarians. To allow for natural digestion of the TG molecule, no enteric coating is used to cover the fish-gelatin softgel. Furthermore, the oil is stabilized with natural vitamin E (as d-alpha tocopherol) to help ensure maximum purity and freshness.

Continued on next page

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

Blood Sugar Support

Cardiovascular Support

Cytokine Balance Support

Essential Fatty Acids

Neurologic & Cognitive

OmegaPure 900-TG™ Supplement Facts

Serving Size: 1 Softgel

	Amount Per Serving	%Daily Value
Calories	10	
Total Fat	1 g	1%†
Fish Oil Concentrate	1.286 g	**
Total Omega-3 Fatty Acids	964 mg	**
EPA (eicosapentaenoic acid)	634 mg	**
DHA (docosahexaenoic acid)	257 mg	**

† Percent Daily Value based on a 2,000 calorie diet.

** Daily Value not established.

Other Ingredients: Softgel (tilapia fish gelatin, vegetable glycerin, and purified water) and mixed natural tocopherols.

Contains: Fish (Alaska pollock [source of fish oil], tilapia [source of fish gelatin]) from certified sustainable sources.

DIRECTIONS: Take one softgel daily, or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking blood thinners or other medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy protein, dairy products, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

Third-Party Certificate of Analysis (COA) for this specific lot can be found by scanning the QR code.



IFOS™ Certification Mark is a registered trademark of Nutrasource Diagnostics Inc.

Health Benefits of EPA/DHA

Research and studies have shown that omega-3 fatty acids antagonize arachidonic acid-induced eicosanoid formation and help generate resolvins and protectins to aid the body's "cleanup" response to the arachidonic acid cascade.^[2-6] EPA and DHA also support neurological health, a balanced immune response, and healthy glucose and insulin metabolism.^[7-12]

Supportive but not conclusive research shows that consumption of EPA and DHA omega-3 fatty acids may reduce the risk of coronary heart disease.^[13-17] One serving of OmegaPure 900-TG provides 900 mg of EPA and DHA omega-3 fatty acids.*

Research suggests that it takes 2 g/day of DHA supplementation over a period of a month to saturate the plasma and three to six months of supplementation to saturate the tissues. Concentrations of DHA increase in breast milk within less than a week of supplementation.^{*[17]}

† Council for Responsible Nutrition

†† Global Organization for EPA and DHA Omega-3

††† World Health Organization

References

1. IFOS Consumer Reports. <http://www.ifosprogram.com/consumer-reports.aspx>. Accessed August 18, 2014.
2. Storey A, McArdle F, Friedmann PS, et al. Eicosapentaenoic acid and docosahexaenoic acid reduce UVB- and TNF alpha-induced IL-8 secretion in keratinocytes and UVB-induced IL-8 in fibroblasts. *J Invest Dermatol*. 2005 Jan;124(1):248-55. [PMID: 15654981]
3. Oh da Y, Walenta E. Omega-3 fatty acids and FFAR4. *Front Endocrinol (Lausanne)*. 2014 Jul 16;5:115. [PMID: 25076939]
4. Maroon JC, Bost JW. Omega-3 fatty acids (fish oil) as an anti-inflammatory: an alternative to nonsteroidal anti-inflammatory drugs for discogenic pain. *Surg Neurol*. 2006 Apr;65(4):326-31. [PMID: 16531187]
5. Weylandt KH, Chiu CY, Gomolka B, et al. Omega-3 fatty acids and their lipid mediators: towards an understanding of resolvins and protectin formation. *Prostaglandins Other Lipid Mediat*. 2012 Mar;97(3-4):73-82. [PMID: 22326554]
6. Kremmyda LS, Tvřizicka E, Stankova B, et al. Fatty acids as biocompounds: their role in human metabolism, health and disease: a review. part 2: fatty acid physiological roles and applications in human health and disease. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub*. 2011 Sep;155(3):195-218. [PMID: 22286806]
7. Frangou S, Lewis M, McCrone P. Efficacy of ethyl-eicosapentaenoic acid in bipolar depression: randomized double-blind placebo-controlled study. *Br J Psychiatry*. 2006 Jan;188:46-50. [PMID: 16388069]
8. Kankaanpaa P, Sutas Y, Salminen S, et al. Dietary fatty acids and allergy. *Ann Med*. 1999 Aug;31(4):282-87. [PMID: 10480759]
9. Stonehouse W. Does consumption of LC omega-3 PUFA enhance cognitive performance in healthy school-aged children and throughout adulthood? Evidence from clinical trials. *Nutrients*. 2014 Jul 22;6(7):2730-58. [PMID: 25054550]
10. Gow RV, Hibbeln JR. Omega-3 fatty acid and nutrient deficits in adverse neurodevelopment and childhood behaviors. *Child Adolesc Psychiatr Clin N Am*. 2014 Jul;23(3):555-90. [PMID: 24975625]
11. Ebbesson SO, Risica PM, Ebbesson LO, et al. Omega-3 fatty acids improve glucose tolerance and components of the metabolic syndrome in Alaskan Eskimos: the Alaska Siberia project. *Int J Circumpolar Health*. 2005 Sep;64(4):396-408. [PMID: 16277123]
12. Nettleton JA, Katz R. n-3 long-chain polyunsaturated fatty acids in type 2 diabetes: a review. *J Am Diet Assoc*. 2005 Mar;105(3):428-40. [PMID: 15746832]
13. Weitz D, Weintraub H, Fisher E, et al. Fish oil for the treatment of cardiovascular disease. *Cardiol Rev*. 2010 Sep-Oct;18(5):258-63. [PMID: 20699674]
14. Psota TL, Gebauer SK, Kris-Etherton P. Dietary omega-3 fatty acid intake and cardiovascular risk. *Am J Cardiol*. 2006 Aug 21;98(4A):3i-18i. [PMID: 16919512]
15. Sasaki J, Yokoyama M, Matsuzaki M, et al. Relationship between coronary artery disease and non-HDL-C, and effect of highly purified EPA on the risk of coronary artery disease in hypercholesterolemic patients treated with statins: sub-analysis of the Japan EPA Lipid Intervention Study (JELIS). *J Atheroscler Thromb*. 2012;19(2):194-204. [PMID: 22186099]
16. Zhang J, Wang C, Li L, et al. Inclusion of Atlantic salmon in the Chinese diet reduces cardiovascular disease risk markers in dyslipidemic adult men. *Nutr Res*. 2010 Jul;30(7):447-54. [PMID: 20797476]
17. Arterburn LM, Hall EB, Oken H. Distribution, interconversion, and dose response of n-3 fatty acids in humans. *Am J Clin Nutr*. 2006 Jun;83(6 Suppl):1467S-1476S. Review. [PMID: 16841856]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

© XYMOGEN
DRS-287
Rev. 03/26/19



OmegaPure DHA™

Essential Fatty Acids from Coldwater Fish



Available in 60 softgels

Discussion

DHA (docosahexaenoic acid), a conditionally essential omega-3 fatty acid, is highly concentrated in mitochondria, synaptosomes of the brain, the cerebral cortex, and the photoreceptors of the retina. It plays an important role in the fluidity and permeability of cell membranes and cellular communication, and is vital to the optimal function of the brain, eyes, heart, and immune system.^[1,2] Conversion of the essential omega-3 alpha-linolenic acid (ALA) to EPA (eicosapentaenoic acid) and then to DHA can be inefficient, making EPA and DHA conditionally essential. It is estimated that only a small percentage of ALA ultimately gets converted to DHA.^[3]

Neurological and Brain Health DHA is the most abundant structural fatty acid in the brain and nervous system and plays a vital role in prenatal and postnatal brain development. The fetus and developing infant are dependent on exogenous sources due to a limited ability to convert ALA into long-chain omega-3 EPA and DHA.^[4] Preformed DHA is transferred directly from mother to fetus and is passed to infants via mother's milk. Pregnant and nursing women are advised to consume at least 2.6 g of omega-3 fatty acids and 100-300 mg of DHA per day in order to meet the needs of fetus or infant.^[4] Research suggests that DHA-supplemented and breast-fed infants score significantly better on mental and psychomotor development tests, and that essential fatty acids and DHA may support normal activity levels and learning capacity during preschool years.^[4,5] A study of 229 infants in three randomized controlled trials suggested that a dose of 0.36% of total fatty acids as DHA (a concentration representative of human breast milk) contributed to favorable problem-solving performance, a parameter found to correlate with later IQ and vocabulary development.^[6]

It is purported that aging is associated with decreased brain levels of DHA,^[5] and supplementation may be beneficial throughout the lifespan. Researchers propose that DHA may play a role in maintaining myelin and neuronal health, supporting healthy eicosanoid metabolism (especially in the brain), and exerting pleiotropic effects to support healthy metabolism and aging.^[7] A study of 280 healthy

Clinical Applications

- » Supports Early Brain Development*
- » Supports Brain Structure and Function Throughout the Lifespan*
- » Supports Healthy Eicosanoid Metabolism*
- » Supports Eye Health*
- » Third-Party Tested for Freshness, Purity, and Safety

*OmegaPure DHA™, a coldwater fish-derived oil containing highly concentrated docosahexaenoic acid (DHA), is a molecularly distilled, antioxidant-stabilized, third-party tested formula. DHA is an omega-3 fatty acid that physicians often recommend to support healthy pregnancy and lactation, and to support brain development and function in the fetus and infant. Throughout the life span, DHA supports healthy brain structure and function, immune and eye health, and healthy eicosanoid metabolism.**

middle-aged community volunteers (ages 35-54) investigated the association between omega-3 fatty acids (ALA, EPA, and DHA) in serum phospholipids and five major dimensions of cognitive functioning. Higher DHA levels were significantly associated with better performance in the areas of nonverbal reasoning, mental flexibility, working memory, and vocabulary. Neither ALA nor EPA was related to any of the five dimensions tested.^[8] DHA may also play a role in memory formation throughout a person's lifetime.^[9] Current research has focused on the DHA-derived neuroprotectin D1 (NPD1) and its role in the health and maintenance of brain cells. NPD1—an important mediator produced from DHA through the action of 15-lipoxygenase-1—appears to have a positive effect on neurotrophic cell signaling, normal cell-life cycles, and prostaglandin formation. DHA and NPD1 appear to play a regulatory role in beta-amyloid neurobiology as well.^[10]

Eye Health and Immune Health DHA is recognized for developing and maintaining eye health and function during early life. Optimal retinal and visual cortex maturation were understood to depend upon dietary DHA during development, and visual acuity and mental development were “seemingly improved by extra DHA.”^[5] A double-masked randomized trial of 244 healthy formula-fed infants suggests that visual acuity is significantly improved with DHA supplementation at 0.32% of total fatty acids.^[11] DHA is concentrated in the photoreceptors of the retina, is required for the functional integrity of retinal pigment epithelium (RPE) cells, and may play an ongoing role in eye health and function throughout life.^[1,9] Studies on human RPE cells suggest that NPD1 orchestrates cell-protective mechanisms (including inhibition of caspase-3 activation and COX-2 expression) and thus promotes a healthy “cleanup” response after cellular insult.^[9,12] Research suggests that DHA's effects play a role in immune system balance and health as well.^[13,14]

OmegaPure DHA is a highly concentrated, pure form of DHA designed to support brain, eye, and overall health and well-being.*

OmegaPure DHA™ Supplement Facts

Serving Size: 2 Softgels

	Amount Per Serving	%Daily Value
Calories	20	
Total Fat	2 g	3%†
Fish Oil Concentrate	2 g	**
DHA (docosahexaenoic acid)	1.16 g	**
EPA (eicosapentaenoic acid)	120 mg	**

† Percent Daily Values are based on a 2,000 calorie diet.
 ** Daily Value not established.

Other Ingredients: Softgel (bovine gelatin, vegetable glycerin, purified water) and mixed tocopherols.
Contains: Fish (anchovy, and/or sardine).

DIRECTIONS: Take one to two softgels with water daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy protein, dairy products, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

References

1. Krinsky DL, LaValle JB, Hawkins EB, et al. *Natural Therapeutics Pocket Guide*. 2nd ed. Hudson, OH: Lexi-Comp; 2003.
2. Swanson D, Block R, Mousa SA. Omega-3 fatty acids EPA and DHA: health benefits throughout life. *Adv Nutr*. 2012 Jan;3(1):1-7. [PMID: 22332096]
3. Gerster H. Can adults adequately convert alpha-linolenic acid (18:3n-3) to eicosapentaenoic acid (20:5n-3) and docosahexaenoic acid (22:6n-3)? *Int J Vitam Nutr Res*. 1998;68(3):159-73. Review. [PMID: 9637947]
4. Singh M. Essential fatty acids, DHA and human brain. *Indian J Pediatr*. 2005 Mar;72(3):239-42. Review. [PMID: 15812120]
5. Uauy R, Dangour AD. Nutrition in brain development and aging: role of essential fatty acids. *Nutr Rev*. 2006 May;64(5 Pt 2):S24-33; discussion S72-91. [PMID: 16770950]
6. Drover J, Hoffman DR, Castañeda YS, et al. Three randomized controlled trials of early long-chain polyunsaturated Fatty Acid supplementation on means-end problem solving in 9-month-olds. *Child Dev*. 2009 Sep-Oct;80(5):1376-84. [PMID: 19765006]
7. Cole GM, Ma QL, Frautschy SA. Dietary fatty acids and the aging brain. *Nutr Rev*. 2010 Dec;68 Suppl 2:S102-11. Review. [PMID: 21091943]
8. Muldoon MF, Ryan CM, Sheu L, et al. Serum phospholipids docosahexaenoic acid is associated with cognitive functioning during middle adulthood. *J Nutr*. 2010 Apr;140(4):848-53. [PMID: 20181791]
9. Bazan NG. Neuroprotectin D1 (NPD1): a DHA-derived mediator that protects brain and retina against cell injury-induced oxidative stress. *Brain Pathol*. 2005 Apr;15(2):159-66. Review. [PMID: 15912889]
10. Lukiw WJ, Bazan NG. Docosahexaenoic acid and the aging brain. *J Nutr*. 2008 Dec;138(12):2510-4. Review. [PMID: 19022980]
11. Birch EE, Carlson SE, Hoffman DR, et al. The DIAMOND (DHA Intake and Measurement of Neural Development) Study: a double-masked, randomized controlled clinical trial of the maturation of infant visual acuity as a function of the dietary level of docosahexaenoic acid. *Am J Clin Nutr*. 2010 Apr;91(4):848-59. [PMID: 20130095]
12. Bazan NG, Calandria JM, Serhan CN. Rescue and repair during photoreceptor cell renewal mediated by docosahexaenoic acid-derived neuroprotectin D1. *J Lipid Res*. 2010 Aug;51(8):2018-31. Review. [PMID: 20382842]
13. van den Elsen L, Garssen J, Willemsen L. Long Chain n-3 Polyunsaturated Fatty Acids in the Prevention of Allergic and Cardiovascular Disease. *Curr Pharm Des*. 2012;18(16):2375-92. [PMID: 22390701]
14. Oliver E, McGillicuddy FC, Harford KA, et al. Docosahexaenoic acid attenuates macrophage-induced inflammation and improves insulin sensitivity in adipocytes-specific differential effects between LC n-3 PUFA. *J Nutr Biochem*. 2011 Nov 30. [Epub ahead of print] [PMID: 22137266]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

© XYMOGEN
 DRS-236
 Rev. 07/15/19



OmegaPure EPA™

Essential Fatty Acids from Coldwater Fish



Available in 60 softgels

Discussion

Eicosapentaenoic acid (EPA) is a long chain omega-3 fatty acid. Although EPA does not significantly affect clotting factors, it does reduce blood viscosity^[1] and blood triglycerides.^[2] The finding of a low incidence of acute myocardial infarction among native Greenland Eskimos launched interest in EPA in the 1970's.^[3] EPA is a precursor for the platelet aggregation inhibitor, prostaglandin-3, and for the eicosanoids, thromboxane-3 and leukotriene-5. It competes with arachadonic acid for inclusion in the lipoxxygenase and cyclooxygenase pathways.*^[4]

There is some evidence that EPA supplementation benefits mental health, perhaps due to its healthful effect upon membrane fluidity. Studies showing improvement in mood and behavior have not only demonstrated the effectiveness of 1-2 grams of EPA alone or with standard treatment, but have demonstrated superiority in the effectiveness of the ethyl form, which is identical to the form contained in OmegaPure EPA.*^[5]

An eight-week placebo-controlled study with 500mg three times daily of ethyl-EPA showed a modest reduction in the number of daily menopausal hot flashes.^[6] A similarly designed study showed improvement in menopausal-related poor mood.^[7] Whether or not supplementation with EPA inhibits lipolysis is not clear; yet, it has been shown to reduce weight loss in cachectic patients. However, this is possibly due to attenuation of the degradation of skeletal muscle.*^[8]

Besides its presence in breast milk, algae, and the vegetable, purslane, this polyunsaturated fatty acid (PUFA) is mostly available through consumption of fatty fish (such as sardines and anchovies) and/or their oils, the sources for OmegaPure EPA. This fatty acid may also be obtained by the conversion of alpha linolenic acid (ALA), although conversion is generally inefficient.*

XYMOGEN's OmegaPure EPA is processed under strictly controlled conditions according to the acceptable published standards of the Council for Responsible Nutrition (CRN) and the World Health

Clinical Applications

- » Support for manufacture of prostaglandins*
- » Support for healthy cell membranes*
- » Support for cardiovascular system*
- » Support for healthy cognition/mood/behavior*

*This ultra-pure, molecularly distilled oil from anchovies and sardines contains one of the highest concentrations of Eicosapentaenoic Acid (EPA) available, with one softgel meeting the ISSFAL recommendation of 650mg omega-3 per day. EPA is a conditionally essential fatty acid. OmegaPure EPA, like all of XYMOGEN's OmegaPure oils, is third-party tested for purity and freshness.**

Organization (WHO), as well as the most stringent current standard, the International Fish Oils Standard (IFOS). The oil is molecularly distilled under vacuum. Independent third party testing confirms freshness, purity, and safety.*

OmegaPure EPA™ Supplement Facts

Serving Size: 2 Softgels

	Amount Per Serving	%Daily Value
Calories	20	
Total Fat	2 g	3%†
Fish Oil Concentrate	2 g	**
EPA (eicosapentaenoic acid)	1.32 g	**
DHA (docosahexaenoic acid)	60 mg	**

†Percent Daily Value based on a 2,000 calorie diet.
 ** Daily value not established.

Other Ingredients: Softgel (bovine gelatin, vegetable glycerin, purified water), and mixed tocopherols.

Contains: Fish (anchovy and/or sardine).

DIRECTIONS: Take one to two softgels with water daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy protein, dairy products, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

References

1. Terano T, et al. Effect of oral administration of highly purified eicosapentaenoic acid on platelet function, blood viscosity and red cell deformability in healthy human subjects. *Atherosclerosis*. 1983 Mar;46(3):321-31. [PMID: 6303363]
2. Oya J, Nakagami T, et al. Intake of n-3 polyunsaturated fatty acids and non-alcoholic fatty liver disease: a cross-sectional study in Japanese men and women. *Eur J Clin Nutr*. 2010 Oct;64(10):1179-85. Epub 2010 Aug 4 [PMID: 20683463]
3. Ponte E, Cafagna D, Balbi M. [Cardiovascular disease and omega-3 fatty acids]. *Minerva Med*. 1997 Sep;88(9):343-53. [PMID: 9411311]
4. Sakamoto Y, Node K. [Anti-atherosclerotic effect of fibrates and eicosapentaenoic acid]. *Nippon Rinsho*. 2011 Jan;69(1):87-91. [PMID: 21226266]
5. Colin A, [Lipids, depression and suicide]. *Encephale*. 2003 Jan-Feb;29(1):49-58. [PMID: 12640327]
6. Lucas M, et al. Effects of ethyl-eicosapentaenoic acid omega-3 fatty acid supplementation on hot flashes and quality of life among middle-aged women: a double-blind, placebo-controlled, randomized clinical trial. *Menopause*. 2009 Mar-Apr;16(2):357-66 [PMID: 19034052]
7. Lucas M, et al. Ethyl-eicosapentaenoic acid for the treatment of psychological distress and depressive symptoms in middle-aged women: a double-blind, placebo-controlled, randomized clinical trial. *Am J Clin Nutr*. 2009 Feb;89(2):641-51. Epub 2008 Dec 30 [PMID: 19116322]
8. Tisdale MJ. Cancer cachexia. *Langenbecks Arch Surg*. 2004 Aug;389(4):299-305. Epub 2004 May 28. [PMID: 15168125]

Additional references available upon request



All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

© XYMOGEN
 DRS-243
 Rev. 07/15/19

OmegaPure Krill™

Omega-3 Oil from Sustainable Antarctic Krill



Available in 60 fish gelatin softgels

Discussion

OmegaPure Krill™ contains K•REAL® krill oil. Krill oil's uniqueness lies in its composition. Unlike fish oil, krill oil is rich in phospholipids. Research suggests that this special composition allows the omega-3s to be better absorbed into red blood cells and by target organs—such as the heart, brain, and liver—compared to fish oil. K•Real krill oil is produced using a multi-stage oil (MSO®) extraction process that preserves the natural nutrient profile of krill oil while removing spoilage components, such as trimethylamine, total volatile nitrogen, and other oxidative elements and derivatives. The purity of K•Real combined with its phospholipid composition prevents the “fishy burps” associated with some fish oils.*

Antarctic Krill (*Euphausia superba*)

Krill, a coldwater marine crustacean, is a rich source of omega-3 EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid). Krill is considered to be stable and relatively resistant to oxidation, unlike other sources of polyunsaturated fatty acids (PUFAs). Krill's stability is attributed to its antioxidant content, which includes vitamin E and astaxanthin.^[1] K•Real krill oil is extracted from krill biomass supplied only from vessels and facilities monitored by members of the Convention for the Conservation of Antarctic Marine Living Resources (CCAMLR), and OmegaPure Krill is five-star IKOS (International Krill Oil Standards) certified, which ensures the highest quality.

Omega-3 Fatty Acids

EPA and DHA, conditionally essential omega-3 fatty acids, have been extensively studied for their positive effects on cardiovascular health, cognitive integrity, immune function, and the body's production of arachidonic acid-derived eicosanoids.^[2,3] Research suggests that serum levels of EPA and DHA are inversely associated with cardiovascular health. In this regard, it is appropriate to note that the omega-3 index (a measurement of EPA and DHA in erythrocyte membranes) has become recognized as a biomarker of cardiovascular health.*^[4,5]

Phospholipids

Considered the building blocks of healthy cells, phospholipids help maintain cell membrane fluidity and function. The phospholipid form of EPA and DHA is easily recognized, integrated, and utilized by the body's cells. The major phospholipid in OmegaPure Krill is phosphatidylcholine, which is highly concentrated in the heart, brain, liver, and kidneys.*^[6]

Clinical Applications

- » Provides a Highly Absorbable, Phospholipid Form of Omega-3 EPA and DHA*
- » Promotes a Healthy Cytokine Balance in the Body*
- » Helps Maintain a Healthy Omega-3 Index*
- » Supports Healthy Cell Membrane Fluidity*
- » Supports Normal Blood Lipid Metabolism*
- » Supports Cardiovascular Health*
- » Supports a Healthy, Comfortable Response to Menstrual Cycle Fluctuations*

*OmegaPure Krill™ features K•REAL® Antarctic krill oil, which provides the omega-3 fatty acids (EPA and DHA) attached to phospholipids as well as to triglycerides. Clinical testing suggests that this molecular composition absorbs into red blood cells, reduces the n-6:n-3 PUFA ratio, and increases the omega-3 index more effectively than fish oil. Krill oil is also naturally complexed with astaxanthin, which provides powerful antioxidant activity and helps stabilize the oil.**

Astaxanthin

Both animal and clinical research suggest that astaxanthin, a red-orange member of the carotenoid family, supports antioxidant mechanisms and helps promote a healthy cytokine balance in the body.^[7] Krill is recognized as a rich source of astaxanthin, which not only provides health benefits, but also serves to stabilize the krill oil.*^[1,8]

Krill Oil Research

In addition to a plethora of animal studies, krill oil has been used in several human clinical trials, and research consistently suggests that it has higher bioavailability than fish oil, supports cardiovascular health, and positively influences the production of arachidonic acid-derived eicosanoids.^[8-14] For instance, a double-blind crossover trial compared uptake of EPA/DHA from krill (in phospholipid form) to uptake of two forms of fish oil (ethyl esters and reesterified triacylglycerides). Results suggested that krill oil had superior bioavailability and promoted the highest incorporation of EPA and DHA into plasma phospholipids.^[13] A randomized, double-blind, parallel-arm trial of 76 subjects indicated that 2 g/day of krill oil significantly increased plasma EPA and DHA levels and was well-tolerated.*^[10]

K•REAL Research

In a double-blind, placebo-controlled, crossover design, the effects of krill oil (3g/d) on plasma and red blood cell fatty acid profile was studied in healthy volunteers. Results indicated that K•Real krill oil more effectively increased plasma and red blood cell EPA and DHA concentrations, decreased the total n-6:n-3 PUFA ratio, and increased the omega-3 index compared to fish oil. These findings suggest that the bioavailability of krill oil omega-3 PUFA might be more pronounced than that of fish oil, which is likely due to the structural differences between these two marine oils. Krill oil was well tolerated with no adverse events.*^[14]

In a randomized, double-blind controlled crossover trial involving 47 participants, krill oil supplementation was shown to support cardiovascular health by improving endothelial function and supporting healthy blood lipid metabolism. Participants presented improved endothelial function after taking krill oil daily for four weeks compared to participants taking olive oil. During the additional 17-week supplementation period, 34 of the participants showed a statistically significant improvement in endothelial function and lipid metabolism when compared with their respective baseline measures.*^[15]

OmegaPure Krill™ Supplement Facts

Serving Size: 2 Softgels

	Amount Per Serving	%Daily Value
Calories	10	
Total Fat	1 g	2%†
K-REAL® Krill Oil	1.65 g	**
Phospholipids	540 mg	**
Total Omega-3 Fatty Acids	363 mg	**
EPA (eicosapentaenoic acid)	165 mg	**
DHA (docosahexaenoic acid)	99 mg	**
Astaxanthin (from microalgae)(<i>Haematococcus pluvialis</i>)	2 mg	**

†Percent Daily Values are based on a 2,000 calorie diet.

** Daily Value not established.

Other Ingredients: Softgel (tilapia fish gelatin, vegetable glycerin, and purified water), sorbitol, natural mixed tocopherols, and ascorbyl palmitate.

Contains: Crustacean shellfish (krill) and fish (tilapia [source of fish gelatin])

K-REAL® is a registered trademark of Enzymotec Ltd.

DIRECTIONS: Take two softgels in the morning, preferably after breakfast, or as recommended by your healthcare practitioner. Do not crush or chew softgels.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner, especially if you have coagulopathy or are taking an anticoagulant. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, dairy products, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



IKOS™ certification mark is a registered trademark of Nutrasource Diagnostics Inc.

References

1. Tou JC, Jaczynski J, Chen YC. Krill for human consumption: nutritional value and potential health benefits. *Nutr Rev*. 2007 Feb;65(2):63-77. [PMID: 17345959]
2. Linus Pauling Institute. <http://lpi.oregonstate.edu/infocenter/othernuts/omega3fa/#metabolism>. Accessed April 20, 2012.
3. DHA, EPA, Omega-3 Institute: The Source for Objective Science-based DHA/ EPA Omega-3 Information. <http://www.dhaomega3.org/Updates-On-Omega-3-Research>. Accessed October 6, 2015.
4. Pottala JV, Garg S, Cohen BE, et al. Blood eicosapentaenoic and docosahexaenoic acids predict all-cause mortality in patients with stable coronary heart disease: the Heart and Soul study. *Circ Cardiovasc Qual Outcomes*. 2010 Jul;3(4):406-12. [PMID: 20551373]
5. Harris WS. The omega-3 index as a risk factor for coronary heart disease. *Am J Clin Nutr*. 2008 Jun;87(6):1997S-2002S. [PMID: 18541601]
6. Phosphatidylcholine. Natural Standard Database. <http://naturalstandard.com/databases/herbssupplements/phosphatidylcholine.asp>. Accessed April 16, 2012.
7. Hussein G, Sankawa U, Goto et al. Astaxanthin, a carotenoid with potential in human health and nutrition. *J Nat Prod*. 2006 Mar;69(3):443-9. Review. [PMID: 16562856]
8. Kidd PM. Omega-3 DHA and EPA for cognition, behavior, and mood: clinical findings and structural-functional synergies with cell membrane phospholipids. *Altern Med Rev*. 2007 Sep;12(3):207-27. [PMID: 18072818]
9. Konagai C, Yanagimoto K, Hayamizu K, et al. Effects of krill oil containing n-3 polyunsaturated fatty acids in phospholipid form on human brain function: a randomized controlled trial in healthy elderly volunteers. *Clin Interv Aging*. 2013;8:1247-57. [PMID: 24098072]
10. Maki KC, Reeves MS, Farmer M, et al. Krill oil supplementation increases plasma concentrations of eicosapentaenoic and docosahexaenoic acids in overweight and obese men and women. *Nutr Res*. 2009 Sep;29(9):609-15. [PMID: 19854375]
11. Banni S, Carta G, Murru E, et al. Krill oil significantly decreases 2-arachidonoylglycerol plasma levels in obese subjects. *Nutr Metab (Lond)*. 2011 Jan 30;8(1):7. [PMID: 21276269]
12. Ulven SM, Holven KB. Comparison of bioavailability of krill oil versus fish oil and health effect. *Vasc Health Risk Manag*. 2015 Aug 28;11:511-24. [PMID: 26357480]
13. Schuchardt JP, Schneider I, Meyer H, et al. Incorporation of EPA and DHA into plasma phospholipids in response to different omega-3 fatty acid formulations—a comparative bioavailability study of fish oil vs. krill oil. *Lipids Health Dis*. 2011 Aug 22;10:145. [PMID: 21854650]
14. Ramprasath VR, Eyal I, Zchut S, et al. Enhanced increase of omega-3 index in healthy individuals with response to 4-week n-3 fatty acid supplementation from krill oil versus fish oil. *Lipids Health Dis*. 2013 Dec 5;12:178. [PMID: 24304605]
15. Lobraico JM, DiLello LC, Butler AD, et al. Effects of krill oil on endothelial function and other cardiovascular risk factors in participants with type 2 diabetes, a randomized controlled trial. *BMJ Open Diabetes Res Care*. 2015 Oct 14;3(1):e000107. [PMID: 26504524]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

OncoPLEX™

Glucoraphanin



OncoPLEX™ is available in 30 capsules & 120 capsules
OncoPLEX ES™ is available in 60 capsules

Discussion

Glucoraphanin (also known as sulforaphane glucosinolate or “sgs”) is a naturally occurring phytochemical found in cruciferous vegetables and in **OncoPLEX™** formulas. Glucoraphanin, which is heat stable and water soluble, is metabolized in the body to the biologically active isothiocyanate sulforaphane (SFN). Scientists at Johns Hopkins University School of Medicine isolated sulforaphane in 1992 and identified glucoraphanin as its precursor. Since their discovery, over 500 scientific studies have been conducted on SFN and glucoraphanin, documenting their positive effects on antioxidant activity, detoxification, cellular metabolism, and cell-life regulation.^[1-3] Glucoraphanin and SFN appear to be the “missing link” that correlates a diet rich in cruciferous vegetables (from the *Brassicaceae* family) with good health. Glucoraphanin from food is enzymatically converted to SFN via the action of the myrosinase enzyme during chewing and food preparation (cutting/slicing). Gastrointestinal microorganisms are able to produce SFN from glucoraphanin as well. Microorganism conversion is an important contribution to SFN production as the myrosinase enzyme is easily inactivated by heat.*^[4]

Early research identified broccoli sprouts as a concentrated source of glucoraphanin.^[5] It is present in much higher concentrations in broccoli seeds and three-day-old broccoli sprouts than in the mature vegetable.^[6,7] One capsule of OncoPLEX provides 30 g of glucoraphanin, which equates to approximately 0.33 oz of broccoli sprouts or 8 oz of broccoli. One capsule of OncoPLEX ES equates to 1.3 oz of broccoli sprouts or 27 oz of broccoli.^[5]

Antioxidant and Detoxification Support Sulforaphane, upon conversion from glucoraphanin, is found to be an effective long-acting indirect antioxidant and significant inducer of phase II detoxification enzymes.^[3,4] Research suggests that SFN strongly induces expression of key enzymes (via the KEAP1/Nrf2/ARE pathway), which in turn supports antioxidant activity, redox cycling, and phase II detoxification. The antioxidant enzymes generated are believed to participate in the recycling and maintenance of vitamins A, C, and E as well.^[4] After

Clinical Applications

- » Provides Concentrated Glucoraphanin from Broccoli Seed Extract
- » Supports Healthy Cell-Life Cycles*
- » Supports Phase II Detoxification Enzymes*
- » Supports Extended Antioxidant Activity*

*truebroc™ broccoli seed extract is obtained using a patented process to extract glucoraphanin (also known as sulforaphane glucosinolate or “sgs”) from its most concentrated cruciferous source—broccoli seeds. Glucoraphanin is enzymatically converted to the extensively researched isothiocyanate known as sulforaphane (SFN). Research suggests that SFN supports long-lasting antioxidant activity and the production of detoxification enzymes. It also extends support to the immune, nervous, and cardiovascular systems, addressing the maintenance of good health throughout adult life. OncoPLEX™ provides 30 mg of glucoraphanin per capsule and OncoPLEX ES™ provides 100 mg of glucoraphanin per capsule.**

studying the effects of various doses of glucoraphanin administered to study subjects, researchers suggest that there may be a dose-dependent association between glucoraphanin and antioxidant enzyme induction. Accordingly, a metabolically effective dose may vary from tissue to tissue (e.g., upper airway, gastric mucosa, mammary, etc.).^[4,8]

Activation of transcription factor Nrf2 induces increased output of specialized enzymes, an output that can extend antioxidant activity 72 hours or more. This is a significantly longer activity phase than direct antioxidants, such as vitamin C, vitamin E, and beta-carotene, are able to promote.^[2,6,9-11] Adequate antioxidant protection is crucial to maintaining the health and function of cells, tissues, and organs. Because they assist in maintaining health throughout adult life, phytonutrients, such as glucoraphanin and SFN, are considered “lifespan essentials.”^[12]

Support for Cellular Health and Cell-Life Cycles Glucoraphanin and SFN are believed to play an important role in maintaining healthy gastrointestinal flora; healthy cellular life cycles; immune, eye, and cardiovascular health; and a normal response to inflammation. Sulforaphane’s induction of phase II enzymes, coupled with an inhibitory effect on certain phase I enzymes, is considered to have a protective effect on cells. Research suggests that SFN plays a multidimensional role in maintaining normal cellular life cycles, inhibiting tubulin polymerization, activating checkpoint 2 kinase, and inhibiting histone deacetylase activity.^[2,13,14] These actions assist in gene regulation, normal cell growth, and cytokine balance.*

Research suggests that sulforaphane’s effect on Nrf2 pathways, macrophage activation, and NF-kappa B may support a normal, healthy response to inflammation and promote cardiovascular and eye health.^[2,15-18] Sulforaphane is also studied for its role in maintaining immune health and a healthy gastrointestinal microflora.*^[19,20]

EXCLUSIVE • PATENTED

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

Antioxidant Activity

Cell-Life Regulation

Cytokine Balance Support

Detoxification

Immune System Support

OncoPLEX™ Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Glucoraphanin (from broccoli extract)(<i>Brassica oleracea italica</i>) (seed)(truebroc™)	30 mg	**

** Daily Value not established.

Other Ingredients: Microcrystalline cellulose, HPMC (capsule), stearic acid, magnesium stearate, and silica.**DIRECTIONS:** Take one capsule daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.**STORAGE:** Keep closed in a cool, dry place out of reach of children.

Produced under US patent 5,725,895; 5,968,505; 5,968,567; 6,177,122; and 6,242,018 licensed from Brassica Protection Products LLC; truebroc is a trademark of Brassica Protection Products LLC.

**OncoPLEX™ ES Supplement Facts**

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Glucoraphanin (from broccoli extract)(<i>Brassica oleracea italica</i>) (seed)(truebroc™)	100 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, medium-chain triglyceride oil, and silica.**DIRECTIONS:** Take one capsule twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.**STORAGE:** Keep tightly closed in a cool, dry place out of reach of children.

Produced under US patent 5,725,895; 5,968,505; 5,968,567; 6,177,122; and 6,242,018 licensed from Brassica Protection Products LLC; truebroc is a trademark of Brassica Protection Products LLC.

**References**

- Zhang Y, Talalay P, Cho CG, et al. A major inducer of anticarcinogenic protective enzymes from broccoli: isolation and elucidation of structure. *Proc. Natl. Acad. Sci USA*. 1992 Mar 15;89(6):2399-403. [PMID: 1549603]
- Cheung KL, Kong AN. Molecular targets of dietary phenethyl isothiocyanate and sulforaphane for cancer chemoprevention. *AAPS J*. 2010 Mar;12(1):87-97. [PMID: 20013083]
- Sulforaphane glucosinolate. Monograph. *Altern Med Rev*. 2010 Dec;15(4):352-60. Review. [PMID: 21194251]
- Boddupalli S, Mein JR, Lakkanna S, et al. Induction of phase 2 antioxidant enzymes by broccoli sulforaphane: perspectives in maintaining the antioxidant activity of vitamins a, C, and e. *Front Genet*. 2012;3:7. Epub 2012 Jan 24. [PMID: 22303412]
- Brassica®. <http://www.brassica.com>. Accessed May 5, 2012.
- Fahey JW, Zhang Y, Talalay P. Broccoli sprouts: an exceptionally rich source of inducers of enzymes that protect against chemical carcinogens. *Proc Natl Acad Sci USA*. 1997 Sep 16;94(19):10367-72. [PMID: 9294217]
- West LG, Meyer KA, Balch BA, et al. Glucoraphanin and 4-hydroxyglucobrassicin contents in seeds of 59 cultivars of broccoli, raab, kohlrabi, radish, cauliflower, Brussels sprouts, kale, and cabbage. *J Agric Food Chem*. 2004 Feb 25;52(4):916-26. [PMID: 14969551]
- Riedl MA, Saxon A, Diaz-Sanchez D. Oral sulforaphane increases Phase II antioxidant enzymes in the human upper airway. *Clin Immunol*. 2009 Mar;130(3):244-51. [PMID: 19028145]
- Shapiro TA, Fahey JW, Wade KL, et al. Chemoprotective glucosinolates and isothiocyanates of broccoli sprouts: metabolism and excretion in humans. *Cancer Epidemiol Biomarkers Prev*. 2001 May;10(5):501-8. [PMID: 11352861]
- Nestle M. Broccoli sprouts as inducers of carcinogen-detoxifying enzyme systems: clinical, dietary, and policy implications. *Proc Natl Acad Sci USA*. 1997 Oct 14;94(21):11149-51. [PMID: 9326574]
- Wagner AE, Ernst I, Iori R, et al. Sulforaphane but not ascorbigen, indole-3-carbinole and ascorbic acid activates the transcription factor Nrf2 and induces phase-2 and antioxidant enzymes in human keratinocytes in culture. *Exp Dermatol*. 2010 Feb;19(2):137-44. [PMID: 19558496]
- Holst B, Williamson G. Nutrients and phytochemicals: from bioavailability to bioefficacy beyond antioxidants. *Curr Opin Biotechnol*. 2008 Apr;19(2):73-82. [PMID: 18406129]
- Myzak MC, Dashwood RH. Chemoprotection by sulforaphane: keep one eye beyond Keap1. *Cancer Lett*. 2006 Feb 28;233(2):208-18. Review. [PMID: 16520150]
- Ho E, Clarke JD, Dashwood RH. Dietary sulforaphane, a histone deacetylase inhibitor for cancer prevention. *J Nutr*. 2009 Dec;139(12):2393-6. [PMID: 19812222]
- Zakkar M, et al. Activation of Nrf2 in endothelial cells protects arteries from exhibiting a proinflammatory state. *Arterioscler Thromb Vasc Biol*. 2009 Nov;29(11):1851-7. [PMID: 19729611]
- Wu L, Noyan-Ashraf MH, Facci M, et al. Dietary approach to attenuate oxidative stress, hypertension, and inflammation in the cardiovascular system. *Proc Natl Acad Sci U S A*. 2004 May 4;101(18):7094-9. [PMID: 15103025]
- Noyan-Ashraf MH, Sadeghinejad Z, Juurlink BH. Dietary approach to decrease aging-related CNS inflammation. *Nutr Neurosci*. 2005 Apr;8(2):101-10. [PMID: 16053242]
- Gao X, Talalay P. Induction of phase 2 genes by sulforaphane protects retinal pigment epithelial cells against photooxidative damage. *Proc Natl Acad Sci USA*. 2004 Jul 13;101(28):10446-51. [PMID: 15229324]
- Yanaka A, Fahey JW, Fukumoto A, et al. Dietary sulforaphane-rich broccoli sprouts reduce colonization and attenuate gastritis in Helicobacter pylori-infected mice and humans. *Cancer Prev Res (Phila)*. 2009 Apr;2(4):353-60. [PMID: 19349290]
- Kim HJ, Barajas B, Wang M, et al. Nrf2 activation by sulforaphane restores the age-related decrease of T(H)1 immunity: role of dendritic cells. *J Allergy Clin Immunol*. 2008 May;121(5):1255-1261. [PMID: 18325578]

Additional references available upon request

EXCLUSIVE • PATENTED

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

(RV) DRS-132
Rev. 09/29/15

OptiCleanse® GHI

Support for Gastrointestinal System, Hepatic Function, and Cytokine Balance*



Available in Vanilla Delight, Creamy Chocolate, & Chai

Discussion

OptiCleanse® GHI contains macro- and micronutrients, as well as a host of ingredients (some patented or proprietary) that support fatty acid metabolism, gastrointestinal health, and healthy eicosanoid and cytokine metabolism. Activated cofactors support mitochondrial energy production needed for biotransformation and detoxification. This formula's ingredients help moderate phase I detoxification, upregulate and support phase II pathways, and provide antioxidant support as well.*

Protein Metabolism

VegaPro is XYMOGEN's proprietary blend of pea protein isolate and rice protein concentrate, L-glutamine, glycine, and taurine. Generation of glutathione and sulfation cofactors—vital for phase II conjugation—requires an array of amino acids. The combination of pea protein and rice protein, containing a complement of amino acids, achieves an amino acid score of 100%. Glutamine, a conditionally essential and versatile amino acid with two nitrogen moieties, is crucial to nitrogen metabolism and helps maintain healthy liver tissue and function.^[1,2] The amino acid glycine is needed for bile synthesis, phase II detoxification, and glutathione production. Taurine, a derivative of the sulfur-containing amino acid cysteine, is also important for synthesis of bile salts and helps stabilize cell membranes.*

Gastrointestinal Support

Ginger root, included to support healthy digestion including the release of bile from the gallbladder, acts at several sites to moderate PGE(2) production and support the normal response to inflammation.^[3] Fiber (from inulin and flaxseeds) supports production of short-chain fatty acids as well as a healthy intestinal flora. **MeadowPure™**, an organic flaxseed complex, possesses excellent oxidative stability, supports antioxidant activity, and provides lignins, soluble fiber, and omega-3 and omega-6 essential fatty acids.^[4] **Glutamine** plays a key role in healthy intestinal cell proliferation and gut barrier integrity, immune function, and normal tissue healing.*^[1,2]

Detoxification Support

Ellagic acid (from pomegranate extract) prevents over-induction of CYP1A enzymes, works at the gene level to induce synthesis of glutathione-S-transferases and other phase II activities, binds directly to toxins, and protects DNA and hepatocytes.^[5,6] **Watercress** is a rich source of beta-phenylethyl isothiocyanate (PEITC)—a versatile compound found to inhibit phase I enzymes

Clinical Applications

- » Supports Natural Detoxification Mechanisms*
- » Supports Gastrointestinal Health*
- » Supports a Balanced Cytokine Profile*
- » Lactose-Free Vegan Protein Source*

***OptiCleanse® GHI** is a comprehensive, fructose-free, low-allergy-potential dietary supplement designed to support gastrointestinal (GI) function and balanced detoxification. It features VegaPro™, XYMOGEN's proprietary amino acid and pea/rice protein blend; Aminogen®, to facilitate protein absorption; phytonutrients; mineral amino acid chelates; and activated B vitamins, including Quatrefolic® and methylcobalamin. In conjunction with a modified elimination diet, OptiCleanse GHI addresses GI and hepatic function as well as eicosanoid balance and cytokine metabolism. This formula is suitable for vegans.**

and induce the phase II enzymes associated with biotransformation and excretion of toxins. Watercress was found to contain even stronger phase II inducers known as 7-methylsulfinylheptyl and 8-methylsulfinyloctyl isothiocyanates as well.^[7,8]

Green tea catechins not only support antioxidant activity but also appear to act as modulators of phase I and phase II detoxification.^[9] **Choline** is present to support lipid metabolism in the liver and can be converted to betaine, a methyl donor.*^[10]

The active, bioavailable form of **B vitamins** (pyridoxal-5'-phosphate (B6), 5-methyltetrahydrofolate (folate), methylcobalamin (B12)) and glycine all support amino acid conjugation and are vital for the detoxification of xenobiotics and xenoestrogens. 5-methyltetrahydrofolate (5-MTHF), methylcobalamin, betaine, and **methylsulfonylmethane (MSM)** are present to support methylation and detoxification. 5-MTHF supports healthy folate nutrition, especially in those with variations in folate metabolism. In OptiCleanse GHI, 5-MTHF is provided as Quatrefolic® for enhanced stability, solubility, and bioavailability.*^[11]

Preventium®, a patented form of potassium hydrogen d-glucarate, supports glucuronidation. Sulfation is supported by **MSM** and **sodium sulfate**. Acetylation is supported by **d-calcium pantothenate**, pyridoxal-5'-phosphate, and magnesium. Several minerals in OptiCleanse GHI are provided as Albion® mineral chelates and TRAACS® mineral amino acid chelates for enhanced gastrointestinal absorption and bioavailability.*^[12]

Antioxidant Support and Cytokine Balance

Bioflavonoids, quercetin, rutin, and curcumin support antioxidant activity, counter free radicals, and support healthy eicosanoid and cytokine metabolism.^[13,14] Curcumin has a long history of use for its support of a normal, healthy response to inflammation.^[15] **N-acetyl-cysteine (NAC)** stimulates glutathione synthesis, enhances glutathione-S-transferase activity, and promotes detoxification.^[16] **Selenium glycinate** provides support for glutathione metabolism and antioxidant protection.*

OptiCleanse GHI provides an array of nutrients that supports gastrointestinal health; detoxification and antioxidant mechanisms; and a normal, healthy response to inflammation and cytokine balance. This formula is designed to be used as part of a step-approach cleanse in conjunction with a modified elimination plan.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

Antioxidant Activity

Cytokine Balance Support

Detoxification

Gastrointestinal Support

Liver Support

OptiCleanse® GHI Vanilla Delight Supplement Facts

Serving Size: 2 Scoops (about 57 g)

	Amount Per Serving	%DV
Calories	230	
Total Fat	7 g	9%*
Saturated Fat	1.5 g	8%*
Total Carbohydrate	15 g	5%*
Dietary Fiber	3 g	11%
Total Sugars	5 g	**
Includes 5g Added Sugars		10%
Protein	26 g	
Vitamin A (as natural beta-carotene)	750 mcg	83%
Vitamin C (as sodium ascorbate)	250 mg	278%
Thiamin (as thiamine HCl)	15 mg	1250%
Riboflavin (as riboflavin 5'-phosphate sodium)	5 mg	385%
Niacin (as niacinamide and niacin)	40 mg	250%
Vitamin B6 (as pyridoxal 5'-phosphate)	5 mg	294%
Folate (as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt)	200 mcg DFE	50%
Vitamin B12 (as methylcobalamin)	50 mcg	2083%
Biotin	150 mcg	500%
Pantothenic Acid (as d-calcium pantothenate)	35 mg	700%
Choline (as choline bitartrate)	100 mg	18%
Calcium (as DimaCal® di-calcium malate and ingredients with naturally occurring calcium)	220 mg	17%
Iron (naturally occurring)	5 mg	28%
Iodine (as potassium iodide)	60 mcg	40%
Magnesium (as Albion® di-magnesium malate)	140 mg	33%
Zinc (as TRAACS® zinc bisglycinate chelate)	10 mg	91%
Selenium (as Albion® selenium glycinate complex)	100 mcg	182%
Manganese (as TRAACS® manganese bisglycinate chelate)	2 mg	87%
Chromium (as TRAACS® chromium nicotinate glycinate chelate)	60 mcg	171%
Molybdenum (as TRAACS® molybdenum glycinate chelate)	35 mcg	78%
Sodium (from ingredients with naturally occurring sodium, sodium sulfate anhydrous, and sodium ascorbate)	560 mg	24%
Potassium (from tripotassium citrate and ingredients with naturally occurring potassium)	455 mg	10%
Stabilized Flaxseed	5.6 g	**
Typical Alpha-Linolenic Acid Content	1.28 g	**
Typical Linoleic Acid Content	392 mg	**
Pomegranate Extract (<i>Punica granatum</i>) (hull) (40% ellagic acid)	400 mg	**
Betaine Anhydrous (trimethylglycine)	250 mg	**
Lemon Bioflavonoid Complex (<i>Citrus x limon</i>) (fruit peel) (25% bioflavonoids)	250 mg	**
Quercetin (as quercetin dihydrate from <i>Dimorphandra mollis</i>) (pod)	250 mg	**
Preventium® (potassium d-glucarate)	250 mg	**
Rutin (from <i>Sophora japonica</i>) (bud)	200 mg	**
BCM-95® Turmeric Extract (<i>Curcuma longa</i>) (rhizome) (95% total curcuminoids complex, including curcumin, curcuminoids, and volatile oils) (86% curcuminoids) (65% curcumin)	200 mg	**
N-Acetyl-L-Cysteine	150 mg	**
Ginger (<i>Zingiber officinale</i>) (rhizome)	150 mg	**
Methylsulfonylmethane (MSM)	120 mg	**
Sodium Sulfate Anhydrous	100 mg	**
Watercress (<i>Nasturtium officinale</i>) (herb)	100 mg	**
Green Tea Aqueous Extract (<i>Camellia sinensis</i>) (leaf) (80% polyphenols, 60% catechins, 30% EGCG, 6% caffeine)	82 mg	**

* Percent Daily Values (DV) are based on a 2,000 calorie diet.
** Daily Value not established.

Other Ingredients: VegaPro™ (XYMOGEN's proprietary blend of pea protein isolate, taurine, glycine, rice protein concentrate, and L-glutamine), dried cane syrup, sunflower oil, natural flavors (no MSG), medium-chain triglyceride oil, cellulose gum, xanthan gum, Aminogen® fungal proteases, stevia leaf extract, guar gum, and silica.

DIRECTIONS: Blend, shake, or briskly stir 2 level scoops (57 g) into 10-12 ounces chilled, pure water (or mix amount for desired thickness) and consume once daily, or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

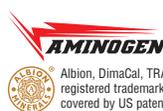
DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

Also available in Creamy Chocolate, & Chai.

 Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,662.

Preventium® is a registered trademark of Applied Food Sciences, LLC. (US patents 4,845,123, 5,364,644, 5,561,160).

BCM-95® is a registered trademark of DolCas Biotech, Ltd. Protected under US patents 7,883,728; 7,736,679; and 7,879,373.



AMINOGEN® is a registered trademark of Innophos Nutrition, Inc. AMINOGEN® is protected under US patent 5,387,422.

Albion, DimaCal, TRAACS and the Albion Medallion design are registered trademarks of Albion Laboratories, Inc. Malates covered by US patent 6,706,904.

References

- Smith RJ, Wilmore DW. Glutamine nutrition and requirements. *JPEN J Parenter Enteral Nutr.* 1990 Jul-Aug;14(4 Suppl):94S-99S. Review. [PMID: 2119461]
- Lacey JM, Wilmore DW. Is glutamine a conditionally essential amino acid? *Nutr Rev.* 1990 Aug;48(8):297-309. Review. [PMID: 2080048]
- Lantz RC, Chen GJ, Sarihan M, et al. The effect of extracts from ginger rhizome on inflammatory mediator production. *Phytomedicine.* 2007 Feb;14(2-3):123-28. [PMID: 16709450]
- Adolphe JL, Whiting SJ, Juurlink BH, Thorpe LU, Alcorn J. Health effects with consumption of the flax lignan secoisolariciresinol diglucoside. *Br J Nutr.* 2010 Apr;103(7):929-38. Review. [PMID: 20003621]
- Barch DH, Rundhaugen LM, Stoner GD, et al. Structure-function relationships of the dietary anticarcinogen ellagic acid. *Carcinogenesis.* 1996 Feb;17(2):265-9. [PMID: 8625448]
- Girish C, Koner BC, Jayanthi S, et al. Hepatoprotective activity of picroliv, curcumin and ellagic acid compared to silymarin on paracetamol induced liver toxicity in mice. *Fundam Clin Pharmacol.* 2009 Dec;23(6):735-45. [PMID: 19656205]
- Rose P, Faulkner K, Williamson G, et al. 7-Methylsulfinylheptyl and 8-methylsulfinyloctyl isothiocyanates from watercress are potent inducers of phase II enzymes. *Carcinogenesis.* 2000 Nov;21(11):1983-8. [PMID: 11062158]
- Hofmann T, Kuhnt A, Schubert A, et al. Modulation of detoxification enzymes by watercress: in vitro and in vivo investigations in human peripheral blood cells. *Eur J Nutr.* 2009 Dec;48(8):483-91. [PMID: 19636603]
- Akhlaghi M, Bandy B. Dietary green tea extract increases phase 2 enzyme activities in protecting against myocardial ischemia-reperfusion. *Nutr Res.* 2010 Jan;30(1):32-39. [PMID: 20116658]
- Linus Pauling Institute. <http://lpi.oregonstate.edu/infocenter/othernuts/choline/>. Accessed May 8, 2012.
- Quatrefolic. <http://www.quatrefolic.com/>. Accessed May 8, 2012.
- Albion. <http://www.albionminerals.com/>. Accessed May 8, 2012.
- Garg R, Gupta S, Maru GB. Dietary curcumin modulates transcriptional regulators of phase I and phase II enzymes in benzo[a]pyrene-treated mice: mechanism of its anti-initiating action. *Carcinogenesis.* 2008 May;29(5):1022-32. [PMID: 18321868]
- Amália PM, Possa MN, Augusto MC, et al. Quercetin prevents oxidative stress in cirrhotic rats. *Dig Dis Sci.* 2007 Oct;52(10):2616-21. [PMID: 17431769]
- Jurenka JS. Anti-inflammatory properties of curcumin, a major constituent of *Curcuma longa*: a review of preclinical and clinical research. *Altern Med Rev.* 2009 Jun;14(2):141-53. Review. Erratum in: *Altern Med Rev.* 2009 Sep;14(3):277. [PMID: 19594223]
- Kelly GS. Clinical applications of N-acetylcysteine. *Altern Med Rev.* 1998 Apr;3(2):114-27. Review. [PMID: 9577247]

Additional references available upon request.

Due to the evolving nature of interactions and contraindications, it is advised that practitioners consult a current database for new information.

Typical Amino Acid Profile Per Serving:

Alanine	1,280 mg
Arginine	2,580 mg
Aspartic Acid	3,400 mg
Cysteine	300 mg
Glutamic Acid	4,990 mg
Glycine	1,720 mg
Histidine	740 mg
Isoleucine	1,330 mg
Leucine	2,490 mg
Lysine	2,120 mg
Methionine	330 mg
Phenylalanine	1,630 mg
Proline	1,340 mg
Serine	1,570 mg
Taurine	1,160 mg
Threonine	500 mg
Tryptophan	300 mg
Tyrosine	1,130 mg
Valine	1,490 mg

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

OptiCleanse® GHI Sugar- & Stevia-Free[†]

Support for Gastrointestinal System, Hepatic Function, and Cytokine Balance[†]



Available in Vanilla Delight and Creamy Chocolate

†This formula is not a low-calorie dietary supplement. Please see the Supplement Facts panel for more details.

Discussion

OptiCleanse® GHI Sugar- & Stevia-Free[†] is now sweetened with a natural, high-potency sweetener extracted from monk fruit. This generally recognized as safe (GRAS) monk-fruit extract offers a high-quality sweetness and flavor without the bitter aftertaste associated with some natural sweeteners.

Like XYMOGEN's other OptiCleanse GHI formulas, OptiCleanse™ GHI Sugar- & Stevia-Free[†] contains macro- and micronutrients, as well as a host of ingredients (some patented or proprietary) that support fatty acid metabolism, gastrointestinal health, and healthy eicosanoid and cytokine metabolism. Activated cofactors support mitochondrial energy production needed for biotransformation and detoxification. This formula's ingredients help moderate phase I detoxification, upregulate and support phase II pathways, and provide antioxidant support as well.[†]

Protein Metabolism

VegaPro is XYMOGEN's proprietary blend of pea protein isolate and rice protein concentrate, L-glutamine, glycine, and taurine. Generation of glutathione and sulfation cofactors—vital for phase II conjugation—requires an array of amino acids. The combination of pea protein and rice protein, containing a complement of amino acids, achieves an amino acid score of 100%. Glutamine, a conditionally essential and versatile amino acid with two nitrogen moieties, is crucial to nitrogen metabolism and helps maintain healthy liver tissue and function.^[1,2] The amino acid glycine is needed for bile synthesis, phase II detoxification, and glutathione production. Taurine, a derivative of the sulfur-containing amino acid cysteine, is also important for synthesis of bile salts and helps stabilize cell membranes.[†]

Gastrointestinal Support

Ginger root, included to support healthy digestion such as the release of bile from the gallbladder, acts at several sites to moderate PGE(2) production and support the normal response to inflammation.^[3] Fiber (from inulin and flaxseeds) supports production of short-chain fatty acids as well as a healthy intestinal flora. **MeadowPure™**, an organic flaxseed complex, possesses excellent oxidative stability, supports antioxidant activity, and provides lignins, soluble fiber, and omega-3 and omega-6 essential fatty acids.^[4] The flaxseed is extensively milled, which provides a smoother mouthfeel and less grit than earlier versions of OptiCleanse formulas. **Glutamine** plays a key role in healthy intestinal cell proliferation and gut barrier integrity, immune function, and normal tissue healing.^[11,2]

Clinical Applications

- » Supports Natural Detoxification Mechanisms[†]
- » Supports Gastrointestinal Health[†]
- » Supports a Balanced Cytokine Profile[†]
- » Lactose-Free Vegan Protein Source[†]

***OptiCleanse® GHI Sugar- & Stevia-Free[†]** is a comprehensive, monk-fruit-extract-sweetened, low-allergy-potential dietary supplement designed to support gastrointestinal (GI) function and balanced detoxification. It features VegaPro™, XYMOGEN's proprietary amino acid and pea/rice protein blend; Aminogen®, to facilitate protein absorption; phytonutrients; mineral amino acid chelates; and activated B vitamins, including Quatrefolic® and methylcobalamin. In conjunction with a modified elimination diet, OptiCleanse GHI Sugar- and Stevia-Free[†] addresses GI and hepatic function as well as eicosanoid balance and cytokine metabolism. This formula is suitable for vegans.[†]*

Detoxification Support

Ellagic acid (from pomegranate extract) prevents over-induction of CYP1A enzymes, works at the gene level to induce synthesis of glutathione-S-transferases and other phase II activities, binds directly to toxins, and protects DNA and hepatocytes.^[5,6] **Watercress** is a rich source of beta-phenylethyl isothiocyanate (PEITC)—a versatile compound found to inhibit phase I enzymes and induce the phase II enzymes associated with biotransformation and excretion of toxins. Watercress has been found to contain even stronger phase II inducers known as 7-methylsulfinylheptyl and 8-methylsulfinyloctyl isothiocyanates as well.^[7,8] **Green tea catechins** not only support antioxidant activity but also appear to act as modulators of phase I and phase II detoxification.^[9] **Choline** is present to support lipid metabolism in the liver and can be converted to betaine, a methyl donor.^[10]

The active, bioavailable form of **B vitamins** (pyridoxal-5'-phosphate (B6), 5-methyltetrahydrofolate (folate), methylcobalamin (B12)) and glycine all support amino acid conjugation and are vital for the detoxification of xenobiotics and xenoestrogens. 5-methyltetrahydrofolate (5-MTHF), methylcobalamin, betaine, and **methylsulfonylmethane (MSM)** are present to support methylation and detoxification. 5-MTHF supports healthy folate nutrition, especially in individuals with variations in folate metabolism. In OptiCleanse GHI, 5-MTHF is provided as Quatrefolic® for enhanced stability, solubility, and bioavailability.^[11]

Preventium®, a patented form of potassium hydrogen d-glucarate, supports glucuronidation. Sulfation is supported by **MSM** and **sodium sulfate**. Acetylation is supported by **d-calcium pantothenate**, pyridoxal-5'-phosphate, and magnesium. Several minerals in OptiCleanse GHI are provided as Albion® mineral chelates and TRAACS® mineral amino acid chelates for enhanced gastrointestinal absorption and bioavailability.^[12]

Antioxidant Support and Cytokine Balance

Bioflavonoids, quercetin, rutin, and curcumin support antioxidant activity, counter free radicals, and support healthy eicosanoid and cytokine metabolism.^[13,14] Curcumin has a long history of use for its support of a normal, healthy response to inflammation.^[15] **N-acetyl-cysteine (NAC)** stimulates glutathione synthesis, enhances glutathione-S-transferase activity, and promotes detoxification.^[16] **Selenium glycinate** provides support for glutathione metabolism and antioxidant protection.[†]

†These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

Antioxidant Activity

Cytokine Balance Support

Detoxification

Gastrointestinal Support

Liver Support

Antioxidant Activity

Cytokine Balance Support

Detoxification

Gastrointestinal Support

Liver Support

OptiCleanse® GHI Sugar- & Stevia-Free Vanilla Delight Supplement Facts

Serving Size: 2 Scoops (about 53 g)

Servings Per Container: About 14

	Amount Per Serving	%DV
Calories	210	
Total Fat	8 g	10%*
Saturated Fat	2 g	10%*
Total Carbohydrate	10 g	4%*
Dietary Fiber	4 g	14%
Protein	26 g	
Vitamin A (as natural beta-carotene)	750 mcg	83%
Vitamin C (as sodium ascorbate)	250 mg	278%
Thiamin (as thiamine HCl)	15 mg	1250%
Riboflavin (as riboflavin 5'-phosphate sodium)	5 mg	385%
Niacin (as niacinamide and niacin)	40 mg	250%
Vitamin B6 (as pyridoxal 5'-phosphate)	5 mg	294%
Folate (as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt)	200 mcg DFE	50%
Vitamin B12 (as methylcobalamin)	50 mcg	2083%
Biotin	150 mcg	500%
Pantothenic Acid (as d-calcium pantothenate)	35 mg	700%
Choline (as choline bitartrate)	100 mg	18%
Calcium (as DimaCal® di-calcium malate and ingredients with naturally occurring calcium)	225 mg	17%
Iron (naturally occurring)	5 mg	28%
Iodine (as potassium iodide)	60 mcg	40%
Magnesium (as Albion® di-magnesium malate)	140 mg	33%
Zinc (as TRAACS® zinc bisglycinate chelate)	10 mg	91%
Selenium (as Albion® selenium glycinate complex)	100 mcg	182%
Manganese (as TRAACS® manganese bisglycinate chelate)	2 mg	87%
Chromium (as TRAACS® chromium nicotinate glycinate chelate)	60 mcg	171%
Molybdenum (as TRAACS® molybdenum glycinate chelate)	35 mcg	78%
Sodium (from ingredients with naturally occurring sodium, sodium sulfate anhydrous, and sodium ascorbate)	560 mg	24%
Potassium (from tripotassium citrate and ingredients with naturally occurring potassium)	455 mg	10%
Stabilized Flaxseed	5.6 g	**
Typical Alpha-Linolenic Acid Content	1.28 g	**
Typical Linoleic Acid Content*	392 mg	**
Pomegranate Extract (<i>Punica granatum</i>)(hull)(40% ellagic acid)	400 mg	**
Betaine Anhydrous (trimethylglycine)	250 mg	**
Lemon Bioflavonoid Complex (<i>Citrus x limon</i>)(fruit peel)(25% bioflavonoids)	250 mg	**
Quercetin (as quercetin dihydrate from <i>Dimorphandra mollis</i>)(pod)	250 mg	**
Preventium® (potassium d-glucarate)	250 mg	**
Rutin (from <i>Sophora japonica</i>)(bud)	200 mg	**
BCM-95® Turmeric Extract (<i>Curcuma longa</i>)(rhizome)(95% total curcuminoids complex, including curcumin, curcuminoids, and volatile oils)(86% curcuminoids)(65% curcumin)	200 mg	**
N-Acetyl-L-Cysteine	150 mg	**
Ginger (<i>Zingiber officinale</i>)(rhizome)	150 mg	**
Methylsulfonylmethane (MSM)	120 mg	**
Sodium Sulfate Anhydrous	100 mg	**
Watercress (<i>Nasturtium officinale</i>)(herb)	100 mg	**
Green Tea Aqueous Extract (<i>Camellia sinensis</i>)(leaf)(80% polyphenols, 60% catechins, 30% EGCG, 6% caffeine)	82 mg	**

* Percent Daily Values (DV) are based on a 2,000 calorie diet.
** Daily Value not established.

Other Ingredients: VegaPro™ (XYMOGEN's proprietary blend of pea protein isolate, taurine, glycine, rice protein concentrate, and L-glutamine), sunflower oil, natural flavors (no MSG), medium-chain triglyceride oil, cellulose gum, xanthan gum, Aminogen® fungal proteases, monk fruit extract, guar gum, and silica.

DIRECTIONS: Blend, shake, or briskly stir 2 level scoops (53 g) into 10-12 ounces of chilled, pure water (or mix amount for desired thickness) and consume once daily, or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

*This formula is not a low-calorie dietary supplement. Please see the Supplement Facts panel for more details.

Also available in Creamy Chocolate.

Preventium® is a registered trademark of Applied Food Sciences, LLC. (US patents 4,845,123; 5,364,644; 5,561,160).

BCM-95® is a registered trademark of DolCas Biotech, Ltd. Protected under US patents 7,883,728; 7,736,679; and 7,879,373.



References

- Smith RJ, Wilmore DW. Glutamine nutrition and requirements. *JPEN J Parenter Enteral Nutr.* 1990 Jul-Aug;14(4 Suppl):94S-99S. Review. [PMID: 2119461]
- Lacey JM, Wilmore DW. Is glutamine a conditionally essential amino acid? *Nutr Rev.* 1990 Aug;48(8):297-309. Review. [PMID: 2080048]
- Lantz RC, Chen GJ, Sarihan M, et al. The effect of extracts from ginger rhizome on inflammatory mediator production. *Phytomedicine.* 2007 Feb;14(2-3):123-28. [PMID: 16709450]
- Adolphe JL, Whiting SJ, Juurlink BH, Thorpe LU, Alcorn J. Health effects with consumption of the flax lignan secoisolariciresinol diglucoside. *Br J Nutr.* 2010 Apr;103(7):929-38. Review. [PMID: 20003621]
- Barch DH, Rundhaugen LM, Stoner GD, et al. Structure-function relationships of the dietary anticarcinogen ellagic acid. *Carcinogenesis.* 1996 Feb;17(2):265-9. [PMID: 8625448]
- Girish C, Koner BC, Jayanthi S, et al. Hepatoprotective activity of picroliv, curcumin and ellagic acid compared to silymarin on paracetamol induced liver toxicity in mice. *Fundam Clin Pharmacol.* 2009 Dec;23(6):735-45. [PMID: 19656205]
- Rose P, Faulkner K, Williamson G, et al. 7-Methylsulfinylheptyl and 8-methylsulfinylheptyl isothiocyanates from watercress are potent inducers of phase II enzymes. *Carcinogenesis.* 2000 Nov;21(11):1983-8. [PMID: 11062158]
- Hofmann T, Kuhnert A, Schubert A, et al. Modulation of detoxification enzymes by watercress: in vitro and in vivo investigations in human peripheral blood cells. *Eur J Nutr.* 2009 Dec;48(8):483-91. [PMID: 19636603]
- Akhlaghi M, Bandy B. Dietary green tea extract increases phase 2 enzyme activities in protecting against myocardial ischemia-reperfusion. *Nutr Res.* 2010 Jan;30(1):32-39. [PMID: 20116658]
- Linus Pauling Institute. <http://lpi.oregonstate.edu/infocenter/othernuts/choline/>. Accessed May 8, 2012.
- Quatrefolic. <http://www.quatrefolic.com/>. Accessed May 8, 2012.
- Albion. <http://www.albionminerals.com/>. Accessed May 8, 2012.
- Garg R, Gupta S, Maru GB. Dietary curcumin modulates transcriptional regulators of phase I and phase II enzymes in benzo[a]pyrene-treated mice: mechanism of its anti-initiating action. *Carcinogenesis.* 2008 May;29(5):1022-32. [PMID: 18321868]
- Amália PM, Possa MN, Augusto MC, et al. Quercetin prevents oxidative stress in cirrhotic rats. *Dig Dis Sci.* 2007 Oct;52(10):2616-21. [PMID: 17431769]
- Jurenka JS. Anti-inflammatory properties of curcumin, a major constituent of *Curcuma longa*: a review of preclinical and clinical research. *Altern Med Rev.* 2009 Jun;14(2):141-53. [PMID: 19594223]
- Kelly GS. Clinical applications of N-acetylcysteine. *Altern Med Rev.* 1998 Apr;3(2):114-27. Review. [PMID: 9577247]

Additional references available upon request

Typical Amino Acid Profile Per Serving:

Alanine	1,280 mg
Arginine	2,580 mg
Aspartic Acid	3,400 mg
Cysteine	300 mg
Glutamic Acid	4,990 mg
Glycine	1,720 mg
Histidine	740 mg
Isoleucine	1,330 mg
Leucine	2,490 mg
Lysine	2,120 mg
Methionine	330 mg
Phenylalanine	1,630 mg
Proline	1,340 mg
Serine	1,570 mg
Taurine	1,160 mg
Threonine	500 mg
Tryptophan	300 mg
Tyrosine	1,130 mg
Valine	1,490 mg



AMINOGEN® is a registered trademark of Innophos Nutrition, Inc. AMINOGEN® is protected under US patent 5,387,422.



Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,662.



Albion, DimaCal, TRAACS and the Albion Medallion design are registered trademarks of Albion Laboratories, Inc. Malates covered by US patent 6,706,964.

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

†These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

OptiCleanse® Plus



Available in Vanilla Delight and Creamy Chocolate

Discussion

OptiCleanse® Plus represents an advanced, comprehensive approach to supporting the body's detoxification processes. Provision of high-quality, easy-to-digest protein with the addition of amino acids, micronutrients, essential fatty acids, and metabolic cofactors makes OptiCleanse Plus an indispensable adjunct to an effective detoxification program.*

VegaPro™ is XYMOGEN's proprietary blend of pea protein isolate and rice protein concentrate plus L-glutamine, L-glycine, and taurine. Generation of glutathione and sulfation cofactors necessary for phase II conjugation requires an array of amino acids. The combination of pea protein and rice protein provides a non-GMO protein source that is easily digested and achieves an amino acid score of 100% (a measure of how efficiently a protein meets the protein synthesis needs of children and adults). VegaPro does not contain milk, soy, wheat, corn, or animal-based protein.*

OptiCleanse Plus contains 24 grams of protein per serving—the equivalent of approximately three-and-a-half ounces of dietary protein derived from sources such as poultry or fish. Dietary protein is essential for building and maintaining lean body mass, hormones, and neurotransmitters. Protein is also essential for the biosynthesis of metabolically active tripeptides such as glutathione, a key factor in detoxification of exogenous and endogenous toxins. Overall protein-energy metabolism affects phase II detoxification reactions as well as the activity of cytochrome P450 enzymes, the enzymes which detoxify environmental chemicals and drugs.*^[1]

Vitamins and Minerals Adequate biotransformation depends upon the mitochondrial generation of ATP, which requires several nutrient cofactors including thiamin, riboflavin, niacin, pantothenic acid, and magnesium. Minerals such as selenium, copper, zinc, and manganese, along with vitamins A, C, and E support antioxidant mechanisms that counteract the reactive oxygen species (intermediary metabolites) that occur between phase I and phase II detoxification. N-acetyl-cysteine

Clinical Applications

- » Supports Natural Detoxification Mechanisms*
- » Supports Healthy Hormone Metabolism*
- » Provides High-Quality Macro- and Micronutrients*

*OptiCleanse® Plus provides macro- and micronutrients that support all phases of biotransformation and detoxification; these nutrients also support the mitochondrial energy production necessary to complete this vital function. OptiCleanse Plus is easy to digest and has a low-allergy potential, a pleasant taste, and no added fructose. OptiCleanse Plus features VegaPro™, XYMOGEN's proprietary pea/rice protein blend; Aminogen®, to facilitate protein absorption; activated B vitamins, such as riboflavin 5'-phosphate (B2), pyridoxal 5'-phosphate (B6), 5-methyltetrahydrofolate (folate), and methylcobalamin (B12); and Albion's patented TRAACS® mineral amino acid chelates. 5-methyltetrahydrofolate (5-MTHF) is provided as Quatrefolic®†, a stable, bioavailable form of folate. In conjunction with a modified elimination diet, OptiCleanse Plus not only addresses healthy detoxification, but also supports energy generation. This formula is suitable for vegans.**

and alpha-lipoic acid are present to support production of glutathione, which is also provided intact in OptiCleanse Plus.*

Specific ingredients that support phase II pathways comprise the activated, readily available form of B vitamins, including 5-methyltetrahydrofolate (folate), methylcobalamin (B12), and pyridoxal 5'-phosphate (B6) for methylation; Preventium® (a patented form of potassium hydrogen d-glucarate) for glucuronidation; alpha-lipoic acid (for antioxidant and liver support); N-acetyl-cysteine for sulfation; and d-calcium pantothenate, pyridoxal 5'-phosphate, and magnesium for acetylation.^[2-7] 5-methyltetrahydrofolate (5-MTHF) is provided as Quatrefolic®, which has greater stability, solubility, and bioavailability than calcium salt forms. Using science and patented technology, the formula's pharmaceutical-grade inorganic minerals have been transformed into mineral amino acid chelates for enhanced absorption by the body. XYMOGEN has earned, and OptiCleanse Plus proudly bears, the Albion Gold Seal.*

MeadowPure™ provides organic, full-fat, non-GMO, milled golden flax seeds that have been selected and processed under U.S. patent. Flaxseed is found to be the most abundant source of the lignan SDG (secoisolariciresinol diglucoside). Metabolites of SDG are closely studied for their roles in supporting healthy hormone metabolism, detoxification, antioxidant mechanisms, and maintenance of normal lipid and glucose levels.^[8] MeadowPure is also a source of the essential omega-3 fatty acid alpha-linolenic acid, as well as soluble fiber, vitamins, minerals, and the essential omega-6 fatty acid, linoleic acid.*

Designed for comprehensive detoxification with additional gastrointestinal support, OptiCleanse Plus also provides inulin (from non-GMO chicory), a valuable prebiotic and source of dietary fiber, as well as glutamine,^[9-11] a conditionally essential amino acid.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

OptiCleanse® PLUS Vanilla Delight Supplement Facts

Serving Size: 2 Scoops (about 57 g)
Servings Per Container: About 14

	Amount Per Serving	%Daily Value
Calories	240	
Total Fat	9 g	12%†
Saturated Fat	2 g	10%†
Total Carbohydrate	15 g	5%†
Dietary Fiber	4 g	14%
Total Sugars	5 g	**
Includes 5g Added Sugars		10%
Protein	24 g	
Vitamin A (as natural beta-carotene)	1500 mcg	167%
Vitamin C (ascorbic acid)	220 mg	244%
Vitamin E (as d-alpha tocopherol and mixed tocopherols)	70 mg	467%
Thiamin (as thiamine HCl)	5 mg	417%
Riboflavin (as riboflavin 5'-phosphate sodium)	2.2 mg	169%
Niacin (as niacinamide)	10 mg	63%
Vitamin B6 (as pyridoxal 5'-phosphate)	5 mg	294%
Folate (as Quatrefolic® (6S)-5-methyltetrahydrofolate, glucosamine salt)	200 mcg DFE	50%
Vitamin B12 (as methylcobalamin)	22 mcg	917%
Biotin	320 mcg	1067%
Pantothenic Acid (as d-calcium pantothenate)	6 mg	120%
Calcium (as DimaCal® di-calcium malate and ingredients with naturally occurring calcium)	200 mg	15%
Iron (naturally occurring)	5 mg	28%
Phosphorus (as dipotassium phosphate)	120 mg	10%
Iodine (as potassium iodide)	55 mcg	37%
Magnesium (as Albion® di-magnesium malate)	140 mg	33%
Zinc (as TRAACS® zinc bisglycinate chelate)	12 mg	109%
Selenium (as Albion® selenium glycinate complex)	55 mcg	100%
Manganese (as TRAACS® manganese bisglycinate chelate)	1.8 mg	78%
Chromium (as TRAACS® chromium nicotinate glycinate chelate)	55 mcg	157%
Molybdenum (as TRAACS® molybdenum glycinate chelate)	150 mcg	333%
Sodium (naturally occurring)	470 mg	20%
Potassium (as dipotassium phosphate, tripotassium citrate, and ingredients with naturally occurring potassium)	860 mg	18%
Stabilized Flaxseed	9 g	**
Typical Alpha-Linolenic Acid Content	2.07 g	**
Typical Linoleic Acid Content	630 mg	**
Preventium® (potassium d-glucarate)	250 mg	**
N-Acetyl-L-Cysteine	55 mg	**
L-Glutathione	29 mg	**

† Percent Daily Values are based on a 2,000 calorie diet.

** Daily Value not established.

Other Ingredients: VegaPro™ (XYMOGEN's proprietary blend of pea protein isolate, taurine, glycine, rice protein concentrate, and L-glutamine), sunflower oil, dried cane syrup, natural flavors (no MSG), medium-chain triglyceride oil, cellulose gum, xanthan gum, Aminogen® fungal proteases, guar gum, stevia leaf extract, and silica.

DIRECTIONS: Blend, shake, or briskly stir two level scoops (57 g) into 10-12 oz chilled water and consume once daily, or as directed by your healthcare practitioner. Adjust amount of water to desired sweetness and thickness.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



Albion, DimaCal, TRAACS and the Albion Medallion design are registered trademarks of Albion Laboratories, Inc. Malates covered by US patent 6,706,904.



AMINOGEN® is a registered trademark of Triarco Industries
AMINOGEN® is protected under U.S. patent 5,387,422.



Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US Patent 7,947,662.

Preventium® is a registered trademark of Applied Food Sciences, LLC. (US patents 4,845,123, 5,364,644, 5,561,160).

References:

1. Wu G, Fang YZ, Yang S, et al. Glutathione metabolism and its implications for health. *J Nutr.* 2004 Mar;134(3):489-92. [PMID: 14988435]
2. Brosnan JT, et al. Methylation demand: a key determinant of homocysteine metabolism. *Acta Biochim Pol.* 2004;51(2):405-13. [PMID: 15218538]
3. Levy G. Sulfate conjugation in drug metabolism: role of inorganic sulfate. *Fed Proc.* 1986 Jul;45(8):2235-40. [PMID: 3459670]
4. Zóttaszek R. The biological role of D-glucaric acid and its derivatives: potential use in medicine [in Polish]. *Postepy Hig Med Dosw (Online).* 2008 Sep 5;62:451-62. [PMID: 18772850]
5. Zamek-Gliszczyński MJ, Hoffmaster KA, Nezasa K, et al. Integration of hepatic drug transporters and phase II metabolizing enzymes: mechanisms of hepatic excretion of sulfate, glucuronide, and glutathione metabolites. *Eur J Pharm Sci.* 2006 Apr;27(5):447-86. [PMID: 16472997]
6. Baker SM, Bennett P, Bland JS, et al. *Textbook of Functional Medicine.* Gig Harbor, WA: The Institute for Functional Medicine; 2010.
7. Shils ME, Shike MS, Ross AC, et al. *Modern Nutrition in Health and Disease.* 10th ed. Baltimore, MD: Williams & Wilkins; 2005.
8. Adolphe JL, Whiting SJ, Juurlink BH, et al. Health effects with consumption of the flax lignan secoisolariciresinol diglucoside. *Br J Nutr.* 2010 Apr;103(7):929-38. [PMID: 20003621]
9. Turczynowski W, Szczepanik AM, Garlicki J, et al. Glutamine--its metabolic role and possibilities for clinical use [in Polish]. *Przegl Lek.* 1998;55(12):659-62. Review. [PMID: 10354717]
10. Wang WW, Qiao SY, Li DF. Amino acids and gut function. *Amino Acids.* 2009 May;37(1):105-10. Review. [PMID: 18670730]
11. Wischmeyer PE. Glutamine: role in critical illness and ongoing clinical trials. *Curr Opin Gastroenterol.* 2008 Mar;24(2):190-7. Review. [PMID: 18301270]

Additional references available upon request

Due to the evolving nature of interactions and contraindications, it is advised that practitioners consult a current database for new information.

Typical Amino Acid Profile Per Serving:

Alanine	1,170 mg
Arginine	2,360 mg
Aspartic Acid	3,120 mg
Cysteine	280 mg
Glutamic Acid	4,570 mg
Glycine	1,620 mg
Histidine	680 mg
Isoleucine	1,220 mg
Leucine	2,280 mg
Lysine	1,940 mg
Methionine	300 mg
Phenylalanine	1,500 mg
Proline	1,220 mg
Serine	1,440 mg
Taurine	500 mg
Threonine	1,060 mg
Tryptophan	270 mg
Tyrosine	1,040 mg
Valine	1,360 mg

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

OptiFiber® Lean

100% Natural and Soluble Propolmannan Fiber



Available in 30 servings powder and 180 capsules

Discussion

While a healthy diet and exercise are paramount to good health and maintaining healthy body composition, adding supplementary soluble fiber offers additional benefits. When selecting fiber, there are many aspects to review. Each fiber is unique in origin, purity, viscosity, and overall stability once ingested. In fact, even one type of fiber can vary greatly in quality. *Amorphophallus konjac*, a tuberous plant, is a rich source of the soluble fiber glucomannan. This fiber has an exceptional ability to absorb water and is one of the most viscous dietary fibers known.^[1]

Not All Glucomannans Are Created Equal

There are many aspects of glucomannan that affect end-product quality: the species of konjac used, the harvesting location, the time of harvesting, the production process, impurities (e.g., sulfites), viscosity, the response of the viscosity to different pH levels and temperatures, and hydration speed. For these reasons, finding the material with the most manufacturing and processing experience and scientific research behind it is important.^[1]

Propol® A Propolmannan

Shimizu Chemical Corporation is a pioneer in the world of dietary fiber and its health benefits. Using its vast knowledge—over 300 years of processing raw material (Japanese *Amorphophallus konjac* species) and extracting glucomannan—it has developed Propol A propolmannan, a highly purified glucomannan. Shimizu's unique and proprietary three-stage purification process is carried out in large-scale extraction plants and involves pulverizing the *Amorphophallus* tubers, collecting mannan-glucose particles, and polishing the particles in order to dislodge and extract noxious materials that adhere to them. With the use of cutting-edge technology, Propol A has been reduced to a special particle size that maximizes density while remaining in desirable viscous form. This process yields a pure, refined, high-performance *Amorphophallus* propolmannan that improves product solubility, stability, and overall functionality.^[1]

Viscosity, Stability Through the Digestive Tract

Viscosity is a physicochemical property of soluble fiber that reflects the fiber's ability to thicken as it mixes with fluid. Viscosity is a recognized factor affecting physiological responses to soluble fiber.^[2] Propol A features an extremely high viscosity (100,000 mPa·s), which is thought to contribute to its health benefits.^[1] Furthermore, as a benefit of its unique processing, Propol A remains intact in the digestive tract—another key factor in fiber functionality. Viscosity and stability, taken together, produce a highly effective material that, once in the digestive tract, attracts water and forms a viscous gel-like substance that slows digestion, delays the emptying of food from the stomach into the small intestine, slows down the influx of carbohydrates and fats into the bloodstream, binds to bile acids, and impedes dietary fat absorption.^{*[3,4]}

Satiety and Weight Control

Soluble fiber is known to act as a bulking agent in the stomach and intestine, which creates the signals of fullness and causes individuals to eat less.^[2,3,5,6] Studies suggest that glucomannan supplementation significantly reduces weight at doses of 3 g/d to 4 g/d

Clinical Applications

- » Supports Satiety*
- » Supports Weight Control*
- » Supports Glucose Metabolism*
- » Supports Cholesterol Metabolism*
- » Supports Healthy Bowel Movements*
- » Serves as a Prebiotic for Intestinal Bacteria*

OptiFiber® Lean features Shimizu Propol® A propolmannan—a highly pure, natural soluble fiber. Propol A is created from *Amorphophallus konjac*-derived glucomannan using proprietary processing techniques. This fiber has been studied for its viscosity and for its stability through the digestive tract; and studies support its health effects, such as on satiety, weight control, glucose and lipid metabolism, and bowel regularity.*

when compared to placebo.^[3,4,7-11] In a randomized, double-blind, placebo-controlled study, the effects of 3 g/d of Propol (1 g 30-60 minutes prior to each meal) combined with 300 mg/d of calcium were studied. When dosing compliant and non-complaint subgroups were analyzed, the results indicated that compliant subjects experienced a significant reduction in scale weight, body fat percentage, and fat mass without a loss of fat-free mass or bone density.^[7] In another study, the mean weight loss for the glucomannan group was 5.5 lbs in eight weeks, while subjects in the placebo group gained 1.5 lbs.^{*[3]}

Glucose and Lipid Metabolism

Soluble fiber slows the absorption of carbohydrates, which influences the release of insulin and the rate of fat storage. Glucomannan studies have not only demonstrated a positive impact on postprandial glucose handling and glucose metabolism but also on cholesterol metabolism.^[3,4,7,10-13] This latter effect is thought to result from the fact that soluble fiber reduces fat and cholesterol absorption and carries bile out of the intestines.^[3,4] When fewer bile acids are available, the body draws cholesterol from the bloodstream to make more.*

Healthy Bowel Function, Prebiotic

Glucomannan not only allows more water to remain in the stool, thereby making waste softer, larger, and easier to pass through the intestines, but it is also an excellent prebiotic.^[15-17] In a placebo-controlled, randomized, parallel, double-blind, crossover trial, doses of 3 g/d and 4 g/d of glucomannan had a positive impact on intestinal habit (i.e., daily and weekly evacuations) and stool characteristics when compared to placebo.^[18] Glucomannan has also been shown to reduce mouth-to-cecum transit time compared to placebo.^[19] In other research, glucomannan improved defecation frequency, eased bowel movement, increased the fecal concentration of lactobacilli as well as the daily output of bifidobacteria, lactobacilli, and total bacteria. In addition, fermentation of glucomannan resulted in greater fecal acetate, propionate, and i-butyrate concentrations and lower fecal pH.^{*[17]}

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

OptiFiber® Lean Capsule Supplement Facts

Serving Size: 6 Capsules

	Amount Per Serving	%Daily Value
Dietary Fiber (from Propol® A propolmannan)(<i>Amorphophallus konjac</i>)(tuber)	3 g	11%†

†Percent Daily Values are based on a 2,000 calorie diet.

Other Ingredients: Microcrystalline cellulose, HPMC (capsule), ascorbyl palmitate, and silica. Propol® is a registered trademark of Shimizu Chemical Corporation.

DIRECTIONS: Take three to six capsules once per day, or take three capsules 30 to 60 minutes before each of your two biggest meals, or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication, especially hypoglycemic agents, should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



OptiFiber® Lean Powder Supplement Facts

Serving Size: 2 Scoops (about 3.2 g)

	Amount Per Serving	%Daily Value
Dietary Fiber (from Propol® A propolmannan)(<i>Amorphophallus konjac</i>)(tuber)	3 g	11%†

†Percent Daily Values are based on a 2,000 calorie diet.

Other Ingredients: None. Propol® is a registered trademark of Shimizu Chemical Corporation.

DIRECTIONS: Mix one to two scoops (1.6-3.2 g) in 8-12 oz of water or other non-alcoholic beverage and consume once per day, or mix one scoop as directed and consume 30 to 60 minutes before each of your two biggest meals, or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication, especially hypoglycemic agents, should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

References

1. Fiber Research International LLC. <http://www.fiberresearchinternational.com>. Web pages: Propol comparison to different glucomannans, manufacturing, and Propol comparison to other fibers. Published June 2015. Accessed November 20, 2015.
2. Kristensen M, Jensen MG. Dietary fibres in the regulation of appetite and food intake. Importance of viscosity. *Appetite*. 2011 Feb;56(1):65-70. [PMID: 21115081]
3. Walsh DE, Yaghoubian V, Behrooz A. Effect of glucomannan on obese patients: a clinical study. *Int J Obes*. 1984;8(4):289-93. [PMID: 6096282]
4. Doi K, Nakamura T, Aoyama N, et al. Metabolic and nutritional effects of long-term use of glucomannan in the treatment of obese diabetics. In: Oomura Y, Tarue S, Inoue S, Shimazu T, eds. *Progress in Obesity Research 1990*. London: John Libbey; 1991:507-14. [on file]
5. Keithley J, Swanson B. Glucomannan and obesity: a critical review. *Altern Ther Health Med*. 2005 Nov-Dec;11(6):30-34. [PMID: 16320857]
6. Burton-Freeman B. Dietary fiber and energy regulation. *J Nutr*. 2000 Feb;130(2S Suppl):272S-75S. [PMID: 10721886]
7. Kaats GR, Bagchi D, Preuss HG. Konjac glucomannan dietary supplementation causes significant fat loss in compliant overweight adults. *J Am Coll Nutr*. 2015 Oct 22:1-7. [PMID: 26492494]
8. Biancardi G, Palmiero L, Ghirardi PE. Glucomannan in the treatment of overweight patients with osteoarthritis. *Curr Ther Res*. 1989;46:908-12. [on file]
9. Reffo GC, Ghirardi PE, Forantini C. Glucomannan in hypertensive outpatients: pilot clinical trial. *Curr Ther Res*. 1988;44(1):22-27. [on file]
10. Salvatoni A, Bosetti G, Gambarini G. Lipid profile and excess body weight in obese children: effect of a dietary drug supplement (glucomannan vs detsastranum). *Ped Oggi*. 1991;11:243-45. [on file]
11. Kraemer WJ, Vingren JL, Silvestre R, et al. Effect of adding exercise to a diet containing glucomannan. *Metabolism*. 2007 Aug; 56(8):1149-58. [PMID: 17618964]
12. Hopman WP, Houben PG, Speth PA, et al. Glucomannan prevents postprandial hypoglycaemia in patients with previous gastric surgery. *Gut*. 1988;29(7):930-34. [PMID: 2840365]
13. Vita PM, Restelli A, Caspani P, et al. Chronic use of glucomannan in the dietary treatment of severe obesity [in Italian]. *Minerva Med*. 1992 Mar;83(3):135-39. [PMID: 1313163]
14. Vuksan V, Jenkins DJ, Spadafora P, et al. Konjac-mannan (glucomannan) improves glycemia and other associated risk factors for coronary heart disease in type 2 diabetes. A randomized controlled metabolic trial. *Diabetes Care*. 1999 Jun;22(6):913-19. [PMID: 10372241]
15. Marzio L, Del Bianco R, Donne MD, et al. Mouth-to-cecum transit time in patients affected by chronic constipation: effect of glucomannan. *Am J Gastroenterol*. 1989 Aug;84(8):888-91. [PMID: 2547312]
16. Passaretti S, Franzoni M, Comin U, et al. Action of glucomannans on complaints in patients affected with chronic constipation: a multicentric clinical evaluation. *Ital J Gastroenterol*. 1991 Sep-Oct;23(7):421-25. [PMID: 1742540]
17. Chen HL, Cheng HC, Wu WT, et al. Supplementation of konjac glucomannan into a low-fiber Chinese diet promoted bowel movement and improved colonic ecology in constipated adults: a placebo-controlled, diet-controlled trial. *J Am Coll Nutr*. 2008 Feb;27(1):102-08. [PMID: 18460488]
18. Marsicano LJ, Berrizbeitia ML, Mondelo A. Use of glucomannan dietary fiber in changes in intestinal habit [in Spanish]. *G E N*. 1995 Jan-Mar;49(1):7-14. [PMID: 8566676]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

© XYMOGEN
DRS-302
Rev. 07/15/19



OptiMag® 125

Proprietary Blend of Patented Magnesium



Available in 120 & 240 capsules

Discussion

Magnesium Lysinate Glycinate Chelate, a mineral amino acid chelate in which magnesium is bound to two amino acids, creates a complex that is more readily absorbed across the intestinal wall. Since the body can efficiently absorb dipeptides (two amino acids linked together), Albion's TRAACS® magnesium lysinate glycinate is an excellent delivery system for magnesium. In general, Albion TRAACS patented mineral amino acid chelates are resistant to competitive minerals, do not weaken the action of vitamins, and pose a smaller risk of overdosing.*^[1]

Di-Magnesium Malate, the other chelate in OptiMag 125, contains 69% malate (malic acid). Each capsule of OptiMag 125 supplies approximately 400 mg of malic acid. Malic acid was chosen because it forms complexes with magnesium.^[2] Magnesium and malate play critical roles in energy production under aerobic conditions or when oxygen is lacking.^[3] Malic acid also appears to exert a protective effect by binding aluminum.*^[4]

Magnesium, the fourth most abundant mineral in the body, participates in about 300-350 enzymatic reactions in nearly all tissues. Deficiency is common and results from poor dietary intake, poor absorption, and excessive losses through urine, stool, perspiration, or lactation. Certain drugs, certain herbs, poor kidney function, excessive alcohol intake, and drinking mostly "soft" water can contribute to magnesium depletion as well.*^[5]

Magnesium's role in the clinical applications cited above is quite well established. Beyond these commonly recognized applications, researchers have demonstrated that magnesium can support cytokine balance and decrease sensitivity to oxidative stress.^[6] An analysis of the results of a National Health and Nutrition Examination Survey (NHANES) suggested that children who consumed less than 75% of the recommended dietary allowance (RDA) for magnesium were 58% more likely to have elevated C-reactive protein (CRP) levels.^[7] Magnesium's role in modulating CRP and supporting the body's normal response to inflammation may be significant. In addition,

Clinical Applications

- » Supports Cardiovascular Health*
- » Supports Healthy Muscle Function/Healthy Nerve Conduction*
- » Supports Bone Health*
- » Supports Energy Production*
- » May Support Healthy Glucose Metabolism*

*Magnesium, the fourth most abundant mineral in the human body, plays a role in over 300 metabolic processes. It participates in the development and maintenance of bones and teeth; the metabolism of carbohydrates, blood glucose, fats, and proteins; the formation of cells and tissues; and the maintenance of muscle function, including cardiac muscle. OptiMag® 125 contains Albion®'s TRAACS® magnesium lysinate glycinate (mineral amino acid chelate) and Albion's chelated dimagnesium malate—both formulated for enhanced absorption. Malic acid (from di-magnesium malate) supports energy production and lactic acid clearance via the Krebs cycle. Malic acid may also support antioxidant systems by enhancing glutathione and antioxidant enzymes.**

although underlying mechanisms remain unclear, it appears that men who consume diets rich in magnesium are able to maintain healthy gallbladder function.^[8] Adequate magnesium intake indeed has strong, far-reaching health benefits.*^[9]

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

OptiMag® 125 Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Magnesium (as Albion® di-magnesium malate and TRAACS® magnesium lysinate glycinate chelate)	250 mg	60%
Malic Acid (as Albion® di-magnesium malate)	828 mg	**

** Daily value not established.

Other Ingredients: HPMC (capsule), stearic acid, medium-chain triglyceride oil, magnesium stearate, and silica.**DIRECTIONS:** Take one to two capsules twice daily at or between meals, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.**DOES NOT CONTAIN:** Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

Albion, TRAACS and the Albion Medallion design are registered trademarks of Albion Laboratories, Inc. Malate covered by U.S. Patent 6,706,904 and patents pending.

**References**

1. Albion Minerals. <http://www.albionminerals.com/human-nutrition/>. Accessed May 23, 2012.
2. Schell J. Interdependence of pH, malate concentration, and calcium and magnesium concentrations in the xylem sap of beech roots. *Tree Physiol.* 1997 Jul;17(7):479-83. [PMID: 14759841]
3. Krinsky DL, LaValle JB, Hawkins EB, et al. *Natural Therapeutics Pocket Guide*. 2nd ed. Hudson, OH: Lexi-Comp; 2003.
4. Suzuki T, Tamura S, Nakanishi H, et al. Reduction of aluminum toxicity by 2-isopropylmalic acid in the budding yeast *Saccharomyces cerevisiae*. *Biol Trace Elem Res.* 2007 Winter;120(1-3):257-63. [PMID: 17916978]
5. Magnesium Balance: Can You Juggle? Albion Human Nutrition Research Notes. 2006 Dec;15(4). http://www.albionhumannutrition.com/research-notes/download/doc_details/328-magnesium-balance-can-you-juggle. Accessed May 29, 2012.
6. Scanlan BJ, Tuft B, Elfrey JE, et al. Intestinal inflammation caused by magnesium deficiency alters basal and oxidative stress-induced intestinal function. *Mol Cell Biochem.* 2007 Dec; 306(1-2):59-69. [PMID: 17657590]
7. King DE, Mainous AG 3rd, Geesey ME, et al. Magnesium intake and serum C-reactive protein levels in children. *Magnes Res.* 2007 Mar;20(1):32-6. [PMID: 17536486]
8. Tsai CJ, Leitzmann MF, Willett WC, et al. Long-term effect of magnesium consumption on the risk of symptomatic gallstone disease among men. *Am J Gastroenterol.* 2008 Feb;103(2):375-82. [PMID: 18076730]
9. Lares MJ, Monteiro CP, Bicho M. Role of cellular magnesium in health and human disease. *Front Biosci.* 2004 Jan 1;9:262-76. [PMID: 14766364]

Additional references available upon request



All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

© XYMOGEN
DRS-177
Rev. 07/15/19

OptiMag[®] Neuro

Patented Magnesium for the Brain*



OptiMag[®] Neuro is available in Natural Mixed Berry, Natural Lemon-Lime, and Unflavored

Discussion

OptiMag Neuro – Optimizes Magnesium Delivery to Body and Brain

Dietary intakes of magnesium are consistently below minimum recommended levels, and an insufficiency of magnesium is implicated in a wide range of health concerns, including those that affect the brain.^[1] Because many forms of magnesium have low bioavailability, XMOGEN carefully selected magnesium compounds backed by research and studies to formulate OptiMag Neuro. Built upon the long-term clinical success of OptiMag 125, OptiMag Neuro features a unique combination of OptiMag 125's highly absorbable, organic Albion minerals—dimagnesium malate and TRAACS[®] magnesium lysinate glycinate chelate—and Magtein[™]. Magtein is a groundbreaking organic magnesium compound that was developed by MIT (Massachusetts Institute of Technology) researchers to support “brain power.”*

Magtein – Patented Magnesium L-Threonate

Magtein is the result of 10 years of research at MIT. This novel form of magnesium is changing the way we support brain health. Unlike other brain products on the market that work via brain stimulation (often overstimulation), Magtein works via a completely different mechanism. When brain magnesium levels are not optimal, synapse function deteriorates. By delivering magnesium into synapses, Magtein helps brain cells stay healthy, without being overactivated; consequently, brain cells respond to signals with clarity and robustness.*

Magtein Raises Brain Magnesium Levels

Studies show that Magtein crosses the blood-brain barrier and raises the brain's magnesium levels, which result in increased magnesium deposits in neural synapses, increased neural synaptic density, and improved brain function.^[2-4] One animal study showed that when the bioavailability of several magnesium compounds was compared to controls, only Magtein significantly enhanced magnesium bioavailability and produced a significant increase (7% to 15%) in rat cerebrospinal fluid.^[2] These small but significant increases in brain magnesium levels produced profound effects on neurological function.*

Magtein Supports Healthy Synaptic Number and Function

Maintaining extracellular magnesium in the brain helps preserve synaptic density and keeps the synapses working properly.*^[2,5]

By increasing magnesium concentration in the extracellular fluid, researchers observed permanent enhancement of synaptic plasticity in networks of cultured hippocampal neurons.^[5] Delving deeper into the mechanisms involved, later animal research showed that magnesium increased receptor signaling; specifically, the signaling of the NR2B-containing N-methyl-D-aspartate (NMDA)

Clinical Applications

- » Supports Healthy Brain Magnesium Levels*
- » Supports Healthy Synapse Number and Function*
- » Supports Cognitive Health*
- » Supports Stress Management, Sleep Quality, and a Healthy Mood*
- » Helps Ensure an Optimal Magnesium Intake for Overall Health*

*OptiMag[®] Neuro features the same Albion forms of magnesium found in OptiMag 125 plus Magtein[™] (magnesium L-threonate), the only form of magnesium proven in animal studies to cross the blood-brain barrier. Boosting the brain's magnesium level is vital to healthy cognition, which includes long- and short-term memory, learning, stress management, and sleep.**

receptor. NMDA receptors are rich in the hippocampus and play a pivotal role in memory processes.*

Data from these studies suggest that increasing brain magnesium with Magtein “enhances both short-term synaptic facilitation and long-term potentiation and thereby supports synaptic plasticity and learning and memory functions in rats.”*^[2,3,6]

Magtein Supports Cognitive Health

The cognitive effects of Magtein were studied by Liu et al in a randomized, double-blind, placebo-controlled trial (n = 51). At a dose of 1.5 g/d to 2 g/d (25 mg/kg/d) for 12 weeks, patients 50-70 years of age taking Magtein demonstrated reduced cognitive declines compared to age-matched controls.^[7] Furthermore, the researchers calculated a particularly compelling impact of Magtein using normative TMT-B⁺ data from age-matched subjects: After six weeks of treatment, the average brain age of the Magtein group decreased from 69.6 ± 4.2 years to 60.6 ± 5.6 years, an improvement of 9.0 ± 3.5 years, and persisted after 12 weeks of treatment with 9.4 ± 3.5 years of improvement. These clinical benefits have been supported by the data of several animal studies.*

Several pre-clinical animal studies that used assessments such as the NORT (novel object recognition test), T-maze, Morris water maze, conditioned fear memory, and conditioned taste aversion have also validated Magtein's effectiveness.*

In these studies, researchers demonstrated that when brain magnesium levels were increased, significant benefits were detected in multiple aspects of learning and memory in young and aged rodents.^[2-4,8] For instance, NORT tests performed by Slutsky et al revealed that short-term memory improved approximately 135% and long-term memory improved approximately 85% in aged rats treated with Magtein compared to control (untreated) rats.*

One study examined the effects of Magtein in test mice (genetically altered mice that model age-related cognitive changes). Li et al found that the test mice not given Magtein exhibited “unequivocal learning deficits,” while the test mice given Magtein performed similarly to normal mice.^[9] In short, Magtein helped preserve normal brain function. When magnesium levels in the brain tissue were quantified, the relationship became even clearer: According to researchers, brain magnesium levels positively correlated with cognitive function; that is, the lower a mouse's brain magnesium level, the poorer its memory function in the NORT task. Furthermore, histological analysis of brain tissue showed that Magtein administration preserved synapse density and NMDA receptor signaling and also had positive effects on the expression of certain proteins associated with changes in memory.*^[9]

[†]The Trail Making Test – Part B (TMT-B) assesses executive function as well as impulsivity, visual search, visual attention, and motor speed.

Continued on next page

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XMOGEN[®] Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

OptiMag® Neuro Supplement Facts

Serving Size: 1 Scoop (about 2.5 g)

	Amount Per Serving	%Daily Value
Calories	5	
Total Carbohydrate	2 g	1% [†]
Magnesium (as Albion® di-magnesium malate, Magtein™ magnesium L-threonate, and TRAACS® magnesium lysinate glycinate chelate)	200 mg	48%
Magtein™ (magnesium L-threonate)	1 g	**

[†] Percent Daily Values are based on a 2,000 calorie diet.^{**} Daily Value not established.**Other Ingredients:** Citric acid, malic acid, natural flavors (no MSG), stevia leaf extract, and anthocyanin extract (color).

DIRECTIONS: Dissolve one level scoop in 4 oz water or adjust amount of water to desired sweetness. First week: one serving per day immediately before dinner or one hour before bedtime. Thereafter: one serving during the day, preferably mid-afternoon, and a second serving before bedtime; or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep tightly closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

Albion and TRAACS are registered trademarks of Albion Laboratories, Inc. Malate covered by US patent 6,706,904 and patents pending.



Magtein is protected under US patents 8,178,118; 8,142,803; 8,163,301; and other pending patents.

Magnesium in Stress Management, Sleep Quality, and Mood

Magnesium is known to benefit the body in ways that counter stress, promote restful sleep, and support a healthy mood. In rats, magnesium administration attenuated neurologic changes brought on by chronic mild stress.^[9] Additionally, by increasing fear memory extinction, Magtein showed promise as a modulator of worry.^[4,10] In human studies, magnesium supplementation partially reversed sleep changes associated with aging and improved objective and subjective measures of sleep.^[11-13] Improving sleep quality and countering the effects of chronic stress positively impact mood—another area that is beneficially influenced by optimal magnesium status.^{*[9,10,14,15]}

References

1. Moshfegh AJ, Goldman JD, Ahuja JK, et al. U.S. Department of Agriculture, Agricultural Research Service. What we eat in America, Nhanes 2005-2006. Usual nutrient intakes from food and water compared to 1997 dietary reference intakes for vitamin D, calcium, phosphorus, and magnesium. http://www.ars.usda.gov/SP2UserFiles/Place/80400530/pdf/0506/usual_nutrient_intake_vitD_ca_phos_mg_2005-06.pdf. Published July 2009. Accessed November 21, 2014.
2. Slutsky I, Abumaria N, Wu LJ, et al. Enhancement of learning and memory by elevating brain magnesium. *Neuron*. 2010 Jan 28;65(2):165-77. [PMID: 20152124]
3. Li W, Yu J, Liu Y, et al. Elevation of brain magnesium prevents synaptic loss and reverses cognitive deficits in Alzheimer's disease mouse model. *Mol Brain*. 2014 Sep 13;7(1):65. [PMID: 25213836]
4. Abumaria N, Yin B, Zhang L, et al. Effects of elevation of brain magnesium on fear conditioning, fear extinction, and synaptic plasticity in the infralimbic prefrontal cortex and lateral amygdala. *J Neurosci*. 2011 Oct 19;31(42):14871-81. [PMID: 22016520]
5. Slutsky I, Sadeghpour S, Li B, et al. Enhancement of synaptic plasticity through chronically reduced Ca²⁺ flux during uncorrelated activity. *Neuron*. 2004 Dec 2;44(5):835-49. [PMID: 15572114]
6. Wang D, Jacobs SA, Tsien JZ. Targeting the NMDA receptor subunit NR2B for treating or preventing age-related memory decline. *Expert Opin Ther Targets*. 2014 Oct;18(10):1121-30. [PMID: 25152202]
7. Liu G, Weinger JG, Lu ZL, et al. Efficacy and safety of mmfs-01, a synapse density enhancer, for treating cognitive impairment in older adults: a randomized, double-blind, placebo-controlled trial. *J Alzheimers Dis*. 2015 Oct 27;49(4):971-90. [PMID: 26519439]
8. Mickley GA, Hoxha N, Luchsinger JL, et al. Chronic dietary magnesium-L-threonate speeds extinction and reduces spontaneous recovery of a conditioned taste aversion. *Pharmacol Biochem Behav*. 2013 May;106:16-26. [PMID: 23474371]
9. Pochwat B, Szewczyk B, Sowa-Kucma M, et al. Antidepressant-like activity of magnesium in the chronic mild stress model in rats: alterations in the NMDA receptor subunits. *Int J Neuropsychopharmacol*. 2014 Mar;17(3):393-405. [PMID: 24067405]
10. Abumaria N, Luo L, Ahn M, et al. Magnesium supplement enhances spatial-context pattern separation and prevents fear overgeneralization. *Behav Pharmacol*. 2013 Aug;24(4):255-63. [PMID: 23764903]
11. Held K, Antonijevic IA, Künzel H, et al. Oral Mg(2+) supplementation reverses age-related neuroendocrine and sleep EEG changes in humans. *Pharmacopsychiatry*. 2002 Jul;35(4):135-43. [PMID: 12163983]
12. Abbasi B, Kimiagar M, Sadeghniai K, et al. The effect of magnesium supplementation on primary insomnia in elderly: A double-blind placebo-controlled clinical trial. *J Res Med Sci*. 201 Dec;17(12):1161-69. [PMID: 23853635]
13. Hornyak M, Voderholzer U, Hohagen F, et al. Magnesium therapy for periodic leg movements-related insomnia and restless legs syndrome: an open pilot study. *Sleep*. 1998 Aug 1;21(5):501-05. [PMID: 9703590]
14. Fromm L, Heath DL, Vink R, et al. Magnesium attenuates post-traumatic depression/anxiety following diffuse traumatic brain injury in rats. *J Am Coll Nutr*. 2004 Oct;23(5):529S-533S. [PMID: 15466958]
15. Eby GA, Eby KL. Rapid recovery from major depression using magnesium treatment. *Med Hypotheses*. 2006;67(2):362-70. [PMID: 16542786]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

© XYMOGEN
DRS-292
Rev. 08/05/19



OptiMag® Plus Calcium

Great Tasting, Flexible Dosing



Available in Natural Pear

Discussion

Calcium and magnesium are critical minerals involved in a plethora of biochemical and structural functions within the body. Insufficient intake of these minerals, due to the modern Western diet, is not unusual. Adding to this, functional medicine practitioners find that individuals, including children, who consume restricted or specialized diets due to food intolerances or health challenges may be at greater risk for deficiency.*

Magnesium

Magnesium, the fourth most abundant mineral in the body, participates in over 300 enzymatic reactions in nearly all tissues. Deficiency is common. The average American diet is thought to provide about 40% of the daily magnesium need, and reports from the World Health Organization have suggested that three quarters of American diets fall short of this amount.^[1] Deficiency can result from poor dietary intake, poor absorption, and excessive losses through urine, stool, perspiration, or lactation. Because magnesium is predominantly an intracellular cation, serum magnesium levels remain a poor predictor of tissue magnesium content and availability.^[1] Particular drugs, certain herbs, poor kidney function, excessive alcohol intake, and drinking mostly “soft” water can contribute to magnesium depletion.^[1,2] It is also important to note that physical and emotional stress can increase the need for magnesium and that hypomagnesemia and stress potentiate each other’s negative effects.^[3,4] Furthermore, the adrenergic effects of psychological stress cause movement of magnesium from intracellular to extracellular space, which increases urinary excretion and depletion of body stores.^{*(4,5)}

Magnesium participates in the development and maintenance of bones and teeth; the metabolism of carbohydrates, blood glucose, fats, and proteins; the formation of cells and tissues; the modulation of cytokines; and the maintenance of muscle function.^[1,6,7] In addition, magnesium is often used to support normal, healthy bowel movements. Of particular interest are the associations between levels of magnesium and neurological health, behavior, and brain function.^{*(8)}

Magnesium and Neurological Health

Magnesium is an integral part of nervous system function—from biosynthesis of neurotransmitters to neurotransmission. Magnesium affects permeability of excitable membranes and thereby acts as a “gatekeeper” to excitatory neurotransmitters (e.g., glutamate).^[1] According to researchers, the most common clinical manifestations of magnesium deficiency are produced by neural and neuromuscular hyperexcitability.^[2,5] Animal and human studies suggest that magnesium supports relaxation, successful sleep, comfort with surroundings and situations, attentiveness, and a healthy mood.^[1,9-12] Low intracellular magnesium is associated with increased defensive behaviors in animals.^[12] As an example, mice

Clinical Applications

- » Supports Neurologic Health*
- » Supports Healthy Muscle Function/Healthy Nerve Conduction*
- » Supports Calm Behaviors and Healthy Mood*
- » Supports Bone Health*
- » Supports Energy Production*
- » Provides Magnesium and Calcium for Optimum Nutrition*

*OptiMag® Plus Calcium is a delicious, pear-flavored powdered supplement that provides high-quality, patented Albion® minerals in a state-of-the-art calcium/magnesium formulation. This supplement is easy to take for all ages, and the special forms of the minerals promote optimal absorption and utilization, while being gentle on the gastrointestinal tract.**

with low magnesium erythrocyte levels displayed restless and aggressive behaviors when under stress.^[12,13] Several animal studies show the positive impact of magnesium administration on stress-related behaviors.^[12] Low levels of magnesium have been observed in children who have difficulty focusing and magnesium supplementation has been observed to influence attention behavior positively.^[8,11,14] In *Magnesium in the Central Nervous System*, the authors state that high doses of magnesium are associated with “decreased physical aggression and improved social responsiveness” in children.^[4]

Magnesium Quality and Absorbability

Magnesium lysinate glycinate comprises magnesium bound to two amino acids to create a chelate that is more readily absorbed through the mucosa than other mineral forms. Since the body can efficiently absorb dipeptides (two amino acids linked together), Albion’s TRAACS® magnesium lysinate glycinate is an excellent delivery system for magnesium.*

Di-magnesium malate consists of magnesium complexed in a 2:1 ratio of magnesium to malic acid. As a naturally occurring organic compound, malic acid is found in apples, watermelon, plums, lychees, and cherries in high concentration. It is more soluble than citric acid, and it forms mineral complexes.^[15] Magnesium and malate play critical roles in the Krebs and glyoxylate energy producing cycles.^[16] Malic acid also appears to exert a protective effect by binding aluminum.^{*(17)}

Calcium

During childhood and adolescence, the body uses calcium to build strong bones. Calcium is required for vascular contraction and vasodilation and intracellular signaling and hormonal secretion. It also plays an important part in making sure that muscles and nerves work properly. Children and adults that adhere to a dairy-free diet are often at greater risk of an insufficient intake of calcium.^{*(18)}

OptiMag Plus Calcium provides 600 mg of elemental calcium as DimaCal in every scoop. Many calcium forms have low elemental calcium content when compared to DimaCal, which is 29% elemental calcium and 64% malic acid. Additional factors such as bioavailability and gastric tolerance should be evaluated when comparing DimaCal to calcium carbonate. Unlike calcium carbonate and other alkali forms of calcium, DimaCal does not cause the formation of gas when subjected to stomach acid. With malic acid acting as a natural buffering agent, DimaCal does not give rise to the acid rebound that can result from the use of other forms of calcium.^{*(16)}

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

OptiMag® Plus Calcium Supplement Facts

Serving Size: 1 Scoop (about 6.8g)
Servings Per Container: About 30

	Amount Per Serving	% Daily Value
Calories	20	
Total Carbohydrate	3 g	1%†
Dietary Fiber	1 g	4%
Calcium (as DimaCal® di-calcium malate)	600 mg	46%
Magnesium (as Albion® di-magnesium malate and TRAACS® magnesium lysinate glycinate chelate)	300 mg	71%

† Percent Daily Values are based on a 2,000 calorie diet.

Other Ingredients: Citric acid, malic acid, guar gum, natural flavors (no MSG), stevia extract, and riboflavin (for color).

DIRECTIONS: Dissolve one scoop in 6 oz of cool, pure water. Drink once daily, or use as directed by your healthcare practitioner.

Consult a healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.



Albion, DimaCal, TRAACS and the Albion Medallion design are registered trademarks of Albion Laboratories, Inc. Malates covered by U.S. Patent 6,706,904 and patents pending.

References

- Long S, Romani AM. Role of cellular magnesium in human diseases. *Austin J Nutr Food Sci*. 2014 Nov 18;2(10). [PMID: 25839058]
- Swaminathan R. Magnesium metabolism and its disorders. *Clin Biochem Rev*. 2003 May;24(2):47-66. [PMID: 18568054]
- Seelig MS. Consequences of magnesium deficiency on the enhancement of stress reactions; preventive and therapeutic implications (a review). *J Am Coll Nutr*. 1994 Oct;13(5):429-46. [PMID: 7836621]
- Vink R, Nechifor M, eds. *Magnesium in the Central Nervous System*. Adelaide, South Australia: University of Adelaide Press;2011.
- Galland L. Magnesium, stress and neuropsychiatric disorders. *Magnes Trace Elem*. 1991-1992;10(2-4):287-301. [PMID: 1844561]
- Nielsen FH. Effects of magnesium depletion on inflammation in chronic disease. *Curr Opin Clin Nutr Metab Care*. 2014 Nov;17(6):525-30. [PMID: 25023192]
- Kramer JH, Spurney C, Iantorno M, et al. Neurogenic inflammation and cardiac dysfunction due to hypomagnesemia. *Am J Med Sci*. 2009 Jul;338(1):22-27. [PMID: 19593099]
- Magnesium. Somerville, MA: Natural Medicines. <https://naturalmedicines.therapeuticresearch.com/databases/food,-herbs-supplements/professional.aspx?productid=998>. Updated February 24, 2016. Accessed June 22, 2016.
- Eby GA, Eby KL. Rapid recovery from major depression using magnesium treatment. *Med Hypotheses*. 2006;67(2):362-70. [PMID: 16542786]
- Jacka FN, Overland S, Stewart R, et al. Association between magnesium intake and depression and anxiety in community-dwelling adults: the Hordaland Health Study. *Aust N Z J Psychiatry*. 2009 Jan;43(1):45-52. [PMID: 19085527]
- Kozielec T, Starobrat-Hermelin B. Assessment of magnesium levels in children with attention deficit hyperactivity disorder (ADHD). *Magnes Res*. 1997 Jun;10(2):143-48. [PMID: 9368235]
- Henrotte JG, Franck G, Santarromana M, et al. Mice selected for low and high blood magnesium levels: a new model for stress studies. *Physiol Behav*. 1997 May;61(5):653-58. [PMID: 9145932]
- Szewczyk B, Poleszak E, Sowa-Kučma M, et al. Antidepressant activity of zinc and magnesium in view of the current hypotheses of antidepressant action. *Pharmacol Rep*. 2008 Sep-Oct;60(5):588-89. [PMID: 19066406]
- Starobrat-Hermelin B, Kozielec T. The effects of magnesium physiological supplementation on hyperactivity in children with attention deficit hyperactivity disorder (ADHD). Positive response to magnesium oral loading test. *Magnes Res*. 1997 Jun;10(2):149-56. [PMID: 9368236]
- Schell J. Interdependence of pH, malate concentration, and calcium and magnesium concentrations in the xylem sap of beech roots. *Tree Physiol*. 1997 Jul;17(7):479-83. [PMID: 14759841]
- DimaCal. Albion Minerals. <http://www.albionminerals.com/calcium/dimacal>. Accessed June 22, 2016.
- Suzuki T, Tamura S, Nakanishi H, et al. Reduction of aluminum toxicity by 2-isopropylmalic acid in the budding yeast *Saccharomyces cerevisiae*. *Biol Trace Elem Res*. 2007 Winter;120(1-3):257-63. [PMID: 17916978]
- Calcium. National Institutes of Health, Office of Dietary Supplements. <https://ods.od.nih.gov/factsheets/Calcium-HealthProfessional/>. Updated June 01, 2016. Accessed June 22, 2016.

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

OptiMetaboliX™ and OptiMetaboliX™ 2:1

For Support of Healthy Glucose and Insulin Metabolism*
Featuring InSea²®—Next Generation Carbohydrate Control*



OptiMetaboliX is available in Vanilla Delight No Added Sugar, No Stevia
OptiMetaboliX 2:1 is available in Vanilla Delight

Discussion

InSea² is a clinically tested blend of purified polyphenols sourced from *Ascophyllum nodosum* and *Fucus vesiculosus*, two species of wild-crafted brown seaweed. It is the only product on the market that targets enzymes involved in carbohydrate digestion and assimilation with a dual mechanism of action. InSea² inhibits alpha-amylase (a starch-degrading enzyme) and alpha-glucosidase (a sucrose-degrading enzyme) and reduces the after-meal impact of ingested high-glycemic-index foods. In humans, InSea² (500 mg/d) attenuated by 48% the rise in blood glucose normally produced by ingesting white bread, reduced insulin secretion by 12%, and improved insulin sensitivity by 8% compared to placebo.^[1] Lowering postprandial blood glucose may support glucose/insulin regulation, improve insulin sensitivity, and support healthy lipid profiles, leptin levels, and appetite control. In another human trial, treatment with a formulation containing InSea² resulted in a 33% increase in feelings of satiety, a decrease in next-meal caloric intake, and a significant impact on weight reduction compared to placebo.^[2] InSea² has been evaluated in clinical trials, animal safety and efficacy studies, and in vitro tests. It has an excellent safety profile and is friendly to the gastrointestinal tract.*

CinSulin[®] is a clinically proven, patented water extract of cinnamon (*Cinnamomum cassia*) shown to influence glucose metabolism. The unique proprietary extraction and dehydration process for manufacturing CinSulin results in a concentrated (10:1) extract that minimizes undesirable substances while retaining those substances that are health-promoting, such as type-A polyphenolic polymers. Cinnamon has been studied extensively for its roles in glucose uptake, glycogen synthesis, insulin action, and support for healthy blood lipid metabolism.^[3,4] Anderson et al demonstrated a 20-fold increase in glucose uptake in fat cells treated with water-soluble type-A polymers.^[5] In human studies, water-extracted cinnamon supplementation (500 mg/d) helped the body maintain healthy blood sugar levels,^[6] improved antioxidant status,^[7] and supported healthy blood pressure and body composition changes.*^[4]

VegaPro™ is a pure, sweetener-free, vegetable protein blend sourced from non-GMO pea protein isolate, and rice protein concentrate. This proprietary blend achieves an amino acid score of 100% and has excellent digestibility. Moderately high-protein, low-glycemic foods help increase feelings of satiety and support healthy body composition, healthy blood lipid metabolism, and postprandial glucose levels.^[8-10] In an animal study comparing the effects of pea protein and casein on blood lipids, rats fed pea proteins showed a significant improvement in blood lipid levels compared to rats that were fed

Clinical Applications

- » Supports Healthy Glucose and Insulin Metabolism*
- » Helps Reduce Glycemic Impact of Meals*
- » Supports Healthy Body Composition*
- » Supports Healthy Blood Lipid Metabolism*
- » Provides Antioxidant Support*
- » Supports the Maintenance of Healthy Peripheral Nerves*

OptiMetaboliX™ and OptiMetaboliX™ 2:1 exclusive combination of well-researched, clinically validated, and highly bioavailable ingredients that provides multimodal support for healthy insulin and glucose metabolism and related pathways. It features InSea²®—an optimized blend of purified polyphenols from wild-crafted brown seaweed. InSea² uniquely slows carbohydrate digestion and assimilation and can reduce the impact of high-glycemic foods. This newly developed, next generation dual carb controller is 100% natural, has an excellent safety profile, and is friendly to the gastrointestinal tract. OptiMetaboliX 2:1 provides the same active ingredients as OptiMetaboliX but with fewer grams of carbohydrate (13 g versus 21 g per serving), yielding approximately a 2:1 protein to carbohydrate ratio.**

casein. The researchers also found that the pea proteins appeared to “affect cellular lipid homeostasis by upregulating genes involved in hepatic cholesterol uptake and by downregulating fatty acid synthesis genes.”^[10] These findings were echoed in a 2013 study performed in rats that tested the effects of a combination of pea protein and soluble fibers on cholesterol homeostasis and metabolism.*^[11]

Inulin, a soluble fiber from chicory root, is utilized in the OptiMetaboliX formulas (8 g/ serving) as a low-glycemic-index carbohydrate that supports glucose management and gastrointestinal health. In a randomized, triple-blind, controlled trial, 49 females received either 10 g/d of inulin (intervention, n = 24) or maltodextrin (control, n = 25) for two months. At the end of the study period, significant positive effects were recorded on several glycemic and antioxidant indices (e.g., glucose metabolism, glycosylated hemoglobin, malondialdehyde, and total antioxidant capacity) in the inulin group when compared to the maltodextrin group (P < 0.05).^[12] As a prebiotic, inulin promotes the growth of beneficial intestinal bacteria.*

Benfotiamine is a lipid-soluble, highly bioavailable form of thiamin (vitamin B1) that enhances the activity of transketolase, an enzyme that catalyzes the conversion of harmful glucose intermediate metabolites in the pentose phosphate pathway.^[13] In vitro research showed treatment with benfotiamine had an impressive effect on transketolase activity (454% increase from control). Researchers further demonstrated that increasing transketolase activity diverts harmful intermediate metabolites away from three of the major pathways (including advanced glycation end-product formation) implicated in hyperglycemia-induced vascular damage.^[14] In addition to benfotiamine, OptiMetaboliX and OptiMetaboliX 2:1 provide a full spectrum of highly bioavailable B vitamins, including folate, as Quatrefolic, and high-dose biotin to support carbohydrate/ glucose metabolism, insulin action, and nerve health.*

Alpha-Lipoic Acid (ALA) and Green Tea Leaf Extract are included in OptiMetaboliX and OptiMetaboliX 2:1 for their well-known protective antioxidant effects as well as for their roles in glucose metabolism and insulin action and sensitivity.^[15,16] Additionally, green tea leaf extract has been shown to support a healthy body mass index, and ALA has important roles in protecting peripheral nerves.^[17] AMP-activated protein kinase (AMPK) and adiponectin, an adipokine, are targets of cardiometabolic health research due to their roles in cellular energy homeostasis and insulin sensitizing, respectively. The effects of ALA on these targets were studied in rats fed a high-fat or low-fat

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

OptiMetaboliX™ Vanilla Delight No Added Sugar, No Stevia Supplement Facts

Serving Size: 2 Scoops (about 46 g)
Servings Per Container: About 14

	Amount Per Serving	% Daily Value
Calories	160	
Total Fat	5 g	6% [†]
Saturated Fat	1.5 g	8% [†]
Total Carbohydrate	15 g	5% [†]
Dietary Fiber	10 g	36%
Total Sugars	1 g	**
Protein 21 g	21 g	
Niacin (as niacinamide)	40 mg	250%
Vitamin B6 (as pyridoxal 5'-phosphate)	5 mg	294%
Folate (as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt)	200 mcg DFE	50%
Vitamin B12 (as methylcobalamin)	50 mcg	2083%
Biotin	5000 mcg	16,667%
Pantothenic Acid (as d-calcium pantothenate)	35 mg	700%
Calcium (naturally occurring)	25 mg	2%
Iron (naturally occurring)	4 mg	22%
Zinc (as TRAACS® zinc bisglycinate chelate)	15 mg	136%
Chromium (as TRAACS® chromium nicotinate glycinate chelate)	500 mcg	1429%
Sodium (naturally occurring)	430 mg	19%
Potassium (from tripotassium citrate and ingredients with naturally occurring potassium)	410 mg	9%
InSea® Brown Seaweed Blend (<i>Ascophyllum nodosum</i> and <i>Fucus vesiculosus</i>) (20% polyphenols)	500 mg	**
CinSulin® Cinnamon 10:1 Aqueous Extract (<i>Cinnamomum cassia</i>) (bark) (3% Type-A polymers)	200 mg	**
Organic Green Tea Aqueous Extract (<i>Camellia sinensis</i>) (leaf) (25% polyphenols, 15% catechins, <10% caffeine)	200 mg	**
Alpha-Lipoic Acid	200 mg	**
Benfotiamine	50 mg	**
Vanadium (as TRAACS® vanadium nicotinate glycinate chelate)	2.5 mg	**

[†] Percent Daily Values are based on a 2,000 calorie diet.
^{**} Daily Value not established.

Other Ingredients: VegaPro™ (XYMOGEN's proprietary blend of pea protein isolate, taurine, glycine, rice protein concentrate, and L-glutamine), inulin (from chicory), natural flavors (no MSG), sunflower oil, cellulose gum, xanthan gum, medium-chain triglyceride oil, Aminogen® fungal proteases, guar gum, and monk fruit extract.

DIRECTIONS: Blend, shake, or briskly stir two level scoops (46 g) into 8-10 oz chilled water and consume one to two times daily; or take one to two scoops approximately 20-30 minutes before each main meal; or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Not intended for use by pregnant or lactating women or children under 12. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, artificial colors, artificial sweeteners, or artificial preservatives.

 Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,862.

 AMINOGEN® is a registered trademark of Innophos Nutrition, Inc. AMINOGEN® is protected under US patent 5,387,422.

InSea® is a registered trademark of innoVactiv Inc.

Albion® and TRAACS® are registered trademarks of Albion Laboratories, Inc. Chelates covered by US patent 7,838,042 and patents pending.

CinSulin® is a registered trademark of Tang-An Medical Ltd., manufactured under US patents 8,304,000 and 8,329,232.

OptiMetaboliX is also Available in Chocolate Mint
OptiMetaboliX 2:1 is available in Vanilla Delight.

OptiMetaboliX 2:1 contains all of the same active ingredients found in OptiMetaboliX. However, it contains significantly fewer grams of carbohydrate (13 g/serving).

(control) diet. The researchers found ALA supplementation reduced body weight and adiposity in both groups. In the high-fat diet group, ALA supported insulin homeostasis and stimulated AMPK and adiponectin in white adipose tissue.*^[18]

Chromium, Vanadium, and Zinc are provided as Albion® TRAACS® amino acid chelates for optimal absorption and utilization. Chromium supports the metabolic action of insulin and may work synergistically with biotin to improve glucose tolerance. Vanadium may reduce hepatic gluconeogenesis and mimic insulin's effect while zinc plays a major role in the stabilization of insulin hexamers and the pancreatic storage of the hormone.*^[19]

References

- Paradis ME, Couture P, Lamarche B. A randomised crossover placebo-controlled trial investigating the effect of brown seaweed (*Ascophyllum nodosum* and *Fucus vesiculosus*) on postchallenge plasma glucose and insulin levels in men and women. *Appl Physiol Nutr Metab*. 2011 Dec;36(6):913-9. Epub 2011 Nov 16. [PMID: 22087795]
- Tremblay A, Jobin M, Pérusse F, et al. Effects of gly-sea-max on glycemia and the control of food intake. Research report. Centre de Recherche, Institut Universitaire de Cardiologie et de Pneumologie; Hôpital Laval, Québec, Canada: innoVactiv Inc.; 2011:1-19. (data on file)
- Kim SH, Choung SY. Antihyperglycemic and antihyperlipidemic action of Cinnamomi Cassiae (Cinnamon bark) extract in C57BL/Ks db/db mice. *Arch Pharm Res*. 2010 Feb;33(2):325-33. [PMID: 20195835]
- Ziegenfuss TN, Hofheins JE, Mendel RW, et al. Effects of a water-soluble cinnamon extract on body composition and features of the metabolic syndrome in pre-diabetic men and women. *J Int Soc Sports Nutr*. 2006 Dec 28;3:45-53. [PMID: 18500972]
- Anderson RA, Broadhurst CL, Polansky MM, et al. Isolation and characterization of polyphenol type-A polymers from cinnamon with insulin-like biological activity. *J Agric Food Chem*. 2004 Jan 14;52(1):65-70. [PMID: 14709014]
- Mang B, Wolters M, Schmitt B, et al. Effects of a cinnamon extract on plasma glucose, HbA_{1c} and serum lipids in diabetes mellitus type 2. *Eur J Clin Invest*. 2006 May;36(5):340-44. [PMID: 16634838]
- Roussel AM, Hininger I, Benaraba R, et al. Antioxidant effects of a cinnamon extract in people with impaired fasting glucose that are overweight or obese. *J Am Coll Nutr*. 2009 Feb;28(1):16-21. [PMID: 19571155]
- Navas-Carretero S, Abete I, Zulet MA, et al. Chronologically scheduled snacking with high-protein products within the habitual diet in type-2 diabetes patients leads to a fat mass loss: a longitudinal study. *Nutr J*. 2011 Jul 14;10:74. [PMID: 21756320]
- Johnstone AM, Stubbs RJ, Harbron CG. Effect of overfeeding macronutrients on day-to-day food intake in man. *Eur J Clin Nutr*. 1996 Jul;50(7):418-30. [PMID: 8862477]
- Rigamonti E, Parolini C, Marchesi M, et al. Hypolipidemic effect of dietary pea proteins: Impact on genes regulating hepatic lipid metabolism. *Mol Nutr Food Res*. 2010 May;54 Suppl 1:S24-30. [PMID: 20077421]
- Parolini C, Manzini S, Busnelli M, et al. Effect of the combinations between pea proteins and soluble fibres on cholesterolaemia and cholesterol metabolism in rats. *Br J Nutr*. 2013 Oct;110(8):1394-401. [PMID: 23458494]
- Pourghassem Gargari B, Dehghan P, et al. Effects of high performance inulin supplementation on glycemic control and antioxidant status in women with type 2 diabetes. *Diabetes Metab J*. 2013 Apr;37(2):140-8. [PMID: 23641355]
- Balakumar P, Rohilla A, Krishan P, et al. The multifaceted therapeutic potential of benfotiamine. *Pharmacol Res*. 2010 Jun;61(6):482-88. [PMID: 20188835]
- Hammes HP, Du X, Edelstein D, et al. Benfotiamine blocks three major pathways of hyperglycemic damage and prevents experimental diabetic retinopathy. *Nat Med*. 2003 Mar;9(3):294-99. [PMID: 12592403]
- Tsuneki H, Ishizuka M, Terasawa M, et al. Effect of green tea on blood glucose levels and serum proteomic patterns in diabetic (db/db) mice and on glucose metabolism in healthy humans. *BMC Pharmacol*. 2004 Aug 26;4:18. [PMID: 15331020]
- Hininger-Favier I, Benaraba R, Coves S, et al. Green tea extract decreases oxidative stress and improves insulin sensitivity in an animal model of insulin resistance, the fructose-fed rat. *J Am Coll Nutr*. 2009 Aug;28(4):355-61. [PMID: 20368373]
- McCluff CE, Rutkove SB. Critical appraisal of the use of alpha lipoic acid (thioctic acid) in the treatment of symptomatic diabetic polyneuropathy. *Ther Clin Risk Manag*. 2011;7:377-85. [PMID: 21941444]
- Prieto-Hontoria PL, Pérez-Matute P, Fernández-Galilea M, et al. Effects of lipoic acid on AMPK and adiponectin in adipose tissue of low- and high-fat-fed rats. *Eur J Nutr*. 2013 Mar;52(2):779-87. [PMID: 22664981]
- Wiernsperger N, Rapin J. Trace elements in glucometabolic disorders: an update. *Diabetol Metab Syndr*. 2010 Dec 19;2:70. [PMID: 21167072]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Oraxinol™

Antioxidant Support from Fruits and Berries*



Available in 60 capsules

Discussion

Fruit and vegetable intake has a profound and well-recognized correlation with health, and increased intake has been found to increase plasma antioxidant capacity in humans.^[1] Fruits contain a wide range of bioactive compounds; they not only contribute to antioxidant protection but also support cellular health in a variety of ways. Isolation of these beneficial compounds and investigations into their specific effects on human health is ongoing. The hope is that concentrated sources of these bioactive phytonutrients will become a convenient way to augment intake of fruits and vegetables.*

Oraxinol™ has a new and improved profile of concentrated extracts from the following nutrient-dense fruits: grape, pomegranate, blueberry, chokeberry, mangosteen, cranberry, goji berry, apple, and bilberry. These fruits are featured in the Oraxinol formula because of their phytonutrient content, antioxidant-supportive properties, and polyphenol concentration. Polyphenols (phenolic acids, flavonoids, stilbenes, and lignans) are produced by plants and often play a defensive role, protecting the plant from UV radiation, oxidation, and pathogens. In many cases, it is the polyphenol component of medicinal plants that exerts activity, such as modulating enzymes and cell receptors, in the body.^[2] Research strongly supports a role for polyphenols in promoting and maintaining health.*^[3,4]

Berries are an especially rich source of polyphenols and other health-promoting elements.^[5,6] Blueberries, cranberries, and chokeberries have been found to contain relatively high concentrations of compounds with highly effective radical scavenging structures, contributing to total antioxidant capacity.^[7] The consumption of bilberry and chokeberry has been shown to significantly increase the concentration of health-supportive polyphenols in plasma.^[8] Goji berries have been consumed for their health-promoting benefits for over 2000 years. Contemporary research suggests that goji juice supplementation significantly increased antioxidant markers in human subjects.*^[9]

Alongside Oraxinol's berry concentrates are extracts from a variety of

Clinical Applications

- » Supports Antioxidant Activity*
- » Supports Cardiovascular Health*
- » Contains Health-Supportive Polyphenols*

*Oraxinol™ is a proprietary fruit extract blend containing fruits and berries rich in polyphenols and antioxidant-supportive elements. This high-quality extract goes through a multiple-stage quality assurance program to ensure potency, safety, integrity, and purity from field to finished product.**

other “super” fruits. Mangosteen is a “berry-type” fruit; its pericarp (peel, rind, hull) has a long history of use as a traditional medicine and recently has been studied for its role in antioxidant and immune support.^[10,11] Pomegranate juice supplementation was found to have an inhibitory effect on lipid peroxidation in plasma, lipoproteins, and macrophages; researchers suggest this is important to the support of cardiovascular and cellular health.^[12] Oraxinol contains grape skin, seed, and pulp in a concentrated extract. Research on grape polyphenols suggests that they may have direct effects on vasorelaxation and may promote cardiovascular health and function.^[13] The apple has long been understood to be a pillar in the foundation of a healthy diet, and this has been underscored by the old adage we learned as children: “an apple a day keeps the doctor away.” Research supports this traditional wisdom and reveals that even the skin of the apple contains polyphenols that appear to play a protective role in oxidative stress.*^[14]

The role of polyphenols appears to extend beyond their antioxidant capacity. Research suggests that polyphenol-rich extracts may exert positive effects on cardiovascular health.^[6] Mechanisms of action appear to include the promotion of endothelial function and healthy platelet aggregation.^[3,15-17] In order to more accurately highlight the health effects of specific polyphenols, researchers have called for the compilation of a comprehensive polyphenol database.^[2] Ongoing research promises to reveal even more detailed and intriguing facts about the role that these complex phytonutrients play in human health.*^[18]

Oraxinol features concentrated whole fruit and berry extracts with a total polyphenol content of no less than 40% and an oxygen radical absorbance capacity (ORAC) of not less than 6000 TE/gram. Oraxinol ingredients undergo stringent quality assurance testing through the Adulterant Screening Program. This program screens for economic adulterants, pesticide residues, solvent residues, ETO (ethylene oxide), irradiation, and GMOs (genetically modified organisms).^[19]

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Oraxinol™ Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Oraxinol™ (proprietary blend of grape (<i>Vitis vinifera</i>)(seed, skin, and pulp), pomegranate (<i>Punica granatum</i>)(whole fruit), blueberry (<i>Vaccinium uliginosum</i>)(whole berry), chokeberry (<i>Aronia arbutifolia</i>)(whole berry), mangosteen (<i>Garcinia mangostana</i>)(skin), cranberry (<i>Vaccinium macrocarpon</i>)(whole berry), goji berry (<i>Lycium barbarum</i>)(whole berry), apple (<i>Malus pumila</i> Mill)(skin), bilberry (<i>Vaccinium myrtillus</i>)(whole berry))(6,000 µmol TE/g)	500 mg	**
** Daily Value not established.		

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, and silica.

DIRECTIONS: Take one capsule twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep tightly closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



References

1. Cao G, Booth SL, Sadowski JA, et al. Increases in human plasma antioxidant capacity after consumption of controlled diets high in fruit and vegetables. *Am J Clin Nutr.* 1998 Nov;68(5):1081-7. [PMID: 9808226]
2. Manach C, Scalbert A, Morand C, et al. Polyphenols: food sources and bioavailability. *Am J Clin Nutr.* 2004 May;79(5):727-47. Review. [PMID: 15113710]
3. Scalbert A, Johnson IT, Saltmarsh M. Polyphenols: antioxidants and beyond. *Am J Clin Nutr.* 2005 Jan;81(1 Suppl):215S-217S. Review. [PMID: 15640483]
4. American Institute for Cancer Research. Cancer Fighters in Your Food. <http://www.aicr.org/assets/docs/pdf/brochures/US11FactsonPreventingCancerTheCancerFightersinYourFood.pdf>. Accessed July 28, 2013.
5. Seeram NP, Adams LS, Zhang Y, et al. Blackberry, black raspberry, blueberry, cranberry, red raspberry, and strawberry extracts inhibit growth and stimulate apoptosis of human cancer cells in vitro. *J Agric Food Chem.* 2006 Dec 13;54(25):9329-39. [PMID: 17147415]
6. Seeram NP. Berry fruits: compositional elements, biochemical activities, and the impact of their intake on human health, performance, and disease. *J Agric Food Chem.* 2008 Feb 13;56(3):627-9. [PMID: 18211023]
7. Zheng W, Wang SY. Oxygen radical absorbing capacity of phenolics in blueberries, cranberries, chokeberries, and lingonberries. *J Agric Food Chem.* 2003 Jan 15;51(2):502-9. [PMID: 12517117]
8. Erlund I, Koli R, Alfthan G, et al. Favorable effects of berry consumption on platelet function, blood pressure, and HDL cholesterol. *Am J Clin Nutr.* 2008 Feb;87(2):323-31. [PMID: 18258621]
9. Amagase H, Sun B, Borek C. Lycium barbarum (goji) juice improves in vivo antioxidant biomarkers in serum of healthy adults. *Nutr Res.* 2009 Jan;29(1):19-25. [PMID: 19185773]
10. Sukatta U, Takenaka M, Ono H, et al. Distribution of major xanthones in the pericarp, aril, and yellow gum of mangosteen (*Garcinia mangostana* linn.) fruit and their contribution to antioxidative activity. *Biosci Biotechnol Biochem.* 2013 May 23;77(5):984-7. [PMID: 23649258]
11. Pedraza-Chaverri J, Cárdenas-Rodríguez N, Orozco-Ibarra M, et al. Medicinal properties of mangosteen (*Garcinia mangostana*). *Food Chem Toxicol.* 2008 Oct;46(10):3227-39. Review. [PMID: 18725264]
12. Aviram M, Dornfeld L, Rosenblat M, et al. Pomegranate juice consumption reduces oxidative stress, atherogenic modifications to LDL, and platelet aggregation: studies in humans and in atherosclerotic apolipoprotein E-deficient mice. *Am J Clin Nutr.* 2000 May;71(5):1062-76. [PMID: 10799367]
13. Barona J, Aristizabal JC, Blesso CN, et al. Grape polyphenols reduce blood pressure and increase flow-mediated vasodilation in men with metabolic syndrome. *J Nutr.* 2012 Sep;142(9):1626-32. [PMID: 22810991]
14. Denis MC, Furtos A, Dudonné S, et al. Apple peel polyphenols and their beneficial actions on oxidative stress and inflammation. *PLoS One.* 2013;8(1):e53725. [PMID: 23372666]
15. Manach C, Mazur A, Scalbert A. Polyphenols and prevention of cardiovascular diseases. *Curr Opin Lipidol.* 2005 Feb;16(1):77-84. Review. [PMID: 15650567]
16. Vita JA. Polyphenols and cardiovascular disease: effects on endothelial and platelet function. *Am J Clin Nutr.* 2005 Jan;81(1 Suppl):292S-297S. Review. [PMID: 15640493]
17. Arts IC, Hollman PC. Polyphenols and disease risk in epidemiologic studies. *Am J Clin Nutr.* 2005 Jan;81(1 Suppl):317S-325S. Review. [PMID: 15640497]
18. World Congress on Polyphenols Applications. <http://www.polyphenols-site.com/>. Accessed July 28, 2013.
19. Ethical Naturals. http://www.ethicalnaturals.com/index.php?option=com_content&view=article&id=21&Itemid=11. Accessed July 28, 2013.

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.



Available in Greens and Spice

Discussion

Utilizing the great taste and high protein of organic cashew butter, living organic foods with active enzymes, and sprouted whole grains, OrganiX™ food bars represent the perfect healthy blend of taste and nutrition. Each of the three varieties of the 50 gram OrganiX raw food bars represents a perfect on-the-go, healthy, between-meals snack or occasional meal accompaniment for children and adults alike. Each bar is nutritionally fortified with phytonutrients, fiber, and omega-3 rich Organic Bio Flax Sprouts™, making these bars dramatically more nutritious compared to other products that contain flax oil, flax flour, or flaxseeds.*

OrganiX food bars acquire their natural sweetness from agave nectar, date paste, and raisins. Healthy fats come not only from the flax but also from cashew and sesame nut butters. The naturally occurring sugars are balanced by the presence of the equivalents of approximately: the amount of protein in an ounce of chicken (7 g), slightly less than the amount of fat in a teaspoon and a half of oil (7 g), the amount of saturated fat in less than ½ teaspoon of butter (2 g), and the fiber in a slice of whole wheat bread (2 g).*

Organic Bio Flax Sprouts are produced using a technology that creates a living, enzyme-active food and blends the health benefits of omega-3 fatty acids, (α-linolenic acid), lignans, soluble and insoluble fiber, vitamins, minerals, and enzymes. Flax seeds have a high amount of secoisolariciresinol diglucoside which is metabolized into mammalian lignans by the gut microflora. Both plant and mammalian lignans modulate hormone metabolism and act as antioxidants.*^[1-3]

Many of the ingredients in each variety of the bars are in sprouted form. Sprouting not only increases enzyme activity but also biologically activates the seed, thus increasing the bioavailability of the plant proteins, essential fats, carbohydrates, vitamins, minerals, and phytonutrients.*

OrganiX bars are appropriate for individuals who are food-sensitive/ allergic to gluten (including wheat), soy, or dairy as none of these

Clinical Applications

- » Healthy On-the-Go Snack or Meal Accompaniment*
- » Suitable for a Vegetarian Diet*
- » Healthy Food for Individuals on Sodium-Restricted Diets*

*These three varieties of delicious, vegan-certified, kosher, non-GMO, USDA organic, all-natural, raw food bars are free of dairy, soy, wheat, and gluten as well as refined sugars, salt, additives, and preservatives. Each bar makes a great, portable, quick-energy snack for those on the go or in need of a nutritious, 200-calorie meal accompaniment. The whole food ingredients are alkalizing, enzyme active, and rich in antioxidants.**

ingredients are present. OrganiX bars are manufactured in a facility that processes tree nuts, peanuts, seeds, soy, wheat, and dairy (milk).*

The chart below shows the ORAC (high oxygen radical absorbance capacity) scores for ingredients similar to those contained in the OrganiX 100% whole food bars. The general aim is to consume adequate fruits and vegetables to average approximately 3000 ORAC per day.*

Ingredient (Depending Upon Variety)	ORAC Score (per 100 g)
Raisins	2,830
Blueberries	2,400
Raspberries	1,220
Broccoli	890

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

OrganiX™ Greens Bar Nutrition Facts

Serving Size 1 Bar (50 g)

	Calories from Fat 70	
	Amount Per Serving	%Daily Value*
Calories: 210		
Total Fat	8 g	12%
Saturated Fat	1.5 g	8%
Trans Fat	0 g	
Cholesterol	0 mg	0%
Sodium	5 mg	0%
Total Carbohydrates	27 g	9%
Total Dietary Fiber	2 g	8%
Sugars	18 g	
Protein	8 g	
Vitamin A		6%
Vitamin C		4%
Calcium		2%
Iron		10%

* Percent Daily Value (DV) are based on a 2,000 calorie diet.

INGREDIENTS: Organic Cashew Butter, Organic Date Paste, Organic Agave, Organic Rice Protein, Organic Raisins, Organic Flax, Organic Quinoa, Organic Wheat Grass, Organic Barley Grass, Organic Spirulina, Organic Blueberry Powder, Organic Raspberry Powder, Organic Broccoli Powder, Organic Beet Powder, and Organic Carrot Juice Powder.

ALLERGEN INFORMATION: Contains Wheat and Tree Nuts (cashews). Made in a facility that processes peanuts, soy, dairy (milk), and eggs.

Do not use if wrapper is tampered with or damaged.

The labeling on this product does not comply with California's Proposition 65. Therefore, this product may not be sold in California.



Certified Organic By ECOCERT ICO

**References**

1. Saarinen NM, Wärrä A, Airio M, et al. Role of dietary lignans in the reduction of breast cancer risk. *Mol Nutr Food Res.* 2007 Jul;51(7):857-66. [PMID: 17576639]
2. Bergman Jungeström M, Thompson LU, Dabrosin C. Flaxseed and its lignans inhibit estradiol-induced growth, angiogenesis, and secretion of vascular endothelial growth factor in human breast cancer xenografts in vivo. *Clin Cancer Res.* 2007 Feb 1;13(3):1061-7. [PMID: 17289903]
3. Hu C, Yuan YV, Kitts DD. Antioxidant activities of the flaxseed lignan secoisolariciresinol diglucoside, its aglycone secoisolariciresinol and the mammalian lignans enterodiol and enterolactone in vitro. *Food Chem Toxicol.* 2007 Nov;45(11):2219-27. [PMID: 17624649]

Additional references available upon request

OrganiX™ Spice Bar Nutrition Facts

Serving Size 1 Bar (50 g)

	Calories from Fat 90	
	Amount Per Serving	%Daily Value*
Calories: 220		
Total Fat	10 g	15%
Saturated Fat	2 g	10%
Trans Fat	0 g	
Cholesterol	0 mg	0%
Sodium	0 mg	0%
Total Carbohydrates	26 g	9%
Total Dietary Fiber	3 g	12%
Sugars	17 g	
Protein	7 g	
Vitamin A		0%
Vitamin C		0%
Calcium		2%
Iron		10%

* Percent Daily Value (DV) are based on a 2,000 calorie diet.

INGREDIENTS: Organic Cashew Butter, Organic Date Paste, Organic Agave, Organic Raisins, Organic Brown Rice Protein, Organic Flax, Organic Cinnamon, and Organic Quinoa.

ALLERGEN INFORMATION: Contains Tree Nuts (cashews). Made in a facility that processes wheat, peanuts, soy, dairy (milk), and eggs.

Do not use if wrapper is tampered with or damaged.

The labeling on this product does not comply with California's Proposition 65. Therefore, this product may not be sold in California.



Certified Organic By ECOCERT ICO

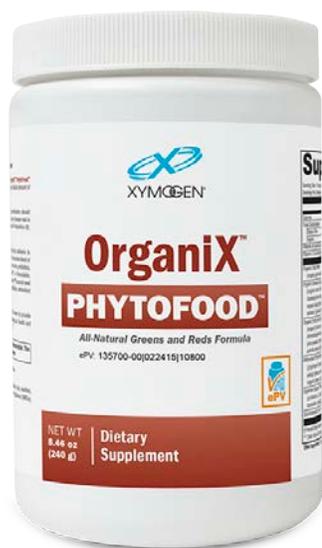


All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

OrganiX™ PhytoFood™

All-Natural Greens and Reds Formula



Available in 30 servings powder

Discussion

XYMOGEN's OrganiX PhytoFood is formulated to provide a convenient source of indispensable phytonutrients, antioxidants, fiber, and digestive enzymes to complement a healthy diet and lifestyle.^[1-5] A colorful blend of organic health-promoting "superfoods" have been incorporated into this all-natural greens and reds drink for their phytonutrient content and support of antioxidant activity.^[6] truebroc™ from broccoli seed extract is added for long-lasting antioxidant and detoxification support. Probiotics, fiber, and digestive enzymes augment gastrointestinal health, absorption, and utilization of nutrients in this comprehensive superfood blend. Organic flavoring and natural sweeteners (stevia and Luo Han Guo) make OrganiX PhytoFood not only healthful but great tasting, as well.*

Organic Fiber Blend Organic gum acacia, inulin, and flaxseeds provide a total of 3 g of dietary fiber per scoop of OrganiX PhytoFood to support gastrointestinal function and probiotic activity as well as to assure multiple health benefits from increased dietary fiber intake.*^[7]

Organic Greens and Veggies Blend Organic carrots, green cabbage, broccoli, beets, chlorella, and spinach provide concentrated sources of folate, chlorophyll, carotenoids, and a multitude of phytonutrients that promote health and fight disease.^[8,9] The greens in OrganiX PhytoFood are naturally alkalizing. An alkaline pH is needed for optimal metabolic, enzymatic, repair, and immune functions in the body.*

Antioxidant Support Ascorbic acid, organic astragalus root, organic ginger root, and organic lycium berry extract provide an antioxidant-rich foundation to protect tissues from free-radical damage and promote cellular health. OxyPhyte® Ultra Blend (white tea leaf extract, apple fruit extract, and rosemary leaf extract) provides antioxidant support. In fact, in a preclinical bioavailability trial, results suggested that this blend increased serum antioxidant levels in human subjects.*^[10]

Organic Fruits and Berries Blend Organic apple juice powder, strawberry juice powder, sea buckthorn juice powder, açai, acerola

Clinical Applications

- » Provides Nutrient-Dense Superfoods, Fiber, Probiotics, and Digestive Enzymes*
- » Provides a Concentrated Source of Antioxidant-Rich Phytonutrients*
- » Contains Standardized truebroc™ From Broccoli Seeds for Antioxidant and Detoxification Support*
- » Promotes Optimal pH Levels in the Body*

*OrganiX PhytoFood is a convenient powdered formulation providing key nutrients to support a healthy lifestyle. This comprehensive formula incorporates an innovative blend of organic greens, vegetables, fruits, berries, phytonutrients, organic fiber sources, probiotics, and digestive enzymes. OrganiX PhytoFood also features OxyPhyte®, a bioavailable, antioxidant-rich blend of green tea and apple extracts. In addition, truebroc® broccoli seed extract with standardized glucoraphanin content is present to provide long-lasting antioxidant support. This nutrient-dense formula features concentrates from "superfoods" known to provide phytonutrients and antioxidants that play important roles in maintaining our health and well-being. OrganiX PhytoFood is lactose-free and suitable for vegans.**

fruit extract, plum fruit extract, and blueberry concentrates provide additional antioxidant capacity and health-promoting phytonutrients.*

truebroc® Broccoli Seed Extract truebroc provides a concentrated source of sulforaphane glucosinolate, also known as glucoraphanin. Glucoraphanin is a phytochemical precursor to sulforaphane, a naturally occurring isothiocyanate in broccoli that supports and promotes antioxidant and detoxification activity.^[11,12] Scientists at Johns Hopkins University School of Medicine identified glucoraphanin (GR) and sulforaphane (SFN) as the "missing links" that correlate a diet rich in cruciferous vegetables with the maintenance of good health. Broccoli sprouts and seeds provide higher concentrations of GR than the mature vegetable.^[13,14] Glucoraphanin is converted to SFN via the action of myrosinase, an enzyme in broccoli that is released during chewing, cutting, or slicing. Microorganisms can also convert GR to SFN; the presence of probiotics and broccoli in OrganiX PhytoFood may enhance this conversion in the body. Research suggests that GR and SFN provide long-lasting antioxidant and detoxification support that may improve overall health and well-being.*

Digestive Support Blend Probiotic organisms *L acidophilus*, *B longum*, *L casei*, and *L rhamnosus* are present to maintain a healthy gastrointestinal microflora. A healthy microflora provides gastrointestinal and immune support and helps to moderate and eliminate pathogenic bacteria. Digestive enzymes (protease, amylase, bromelain, cellulase, lactase, papain, and lipase) in OrganiX PhytoFood assist in the breakdown of carbohydrates, fats, proteins, and lactose to enhance nutrient digestion and availability.*

OrganiX PhytoFood can be consumed by itself or as an accompaniment to any smoothie or protein drink. The inclusion of phytonutrient-rich superfoods, OxyPhyte Ultra Blend, and truebroc creates an innovative and ideal formula for antioxidant support.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

OrganiX™ PhytoFood™ Supplement Facts

Serving Size: 1 Scoop (about 8 g)
Servings Per Container: About 30

	Amount Per Serving	%DV
Calories	30	
Total Carbohydrate	7 g	3%†
Dietary Fiber	4 g	14%
Total Sugars	1 g	**
Vitamin C (as ascorbic acid and ingredients with naturally occurring vitamin C)	300 mg	333%
Organic Fiber Blend (organic gum acacia, organic inulin, organic flaxseed)	4.275 g	**
Organic Greens and Veggies Blend (organic carrot (<i>Daucus carota</i>)(whole carrot), organic green cabbage (<i>Brassica oleracea L. var. Capitata</i>)(whole cabbage), organic broccoli (<i>Brassica oleracea Botrytis cymosa</i>)(whole plant), organic beet (<i>Beta vulgaris</i>)(root), organic chlorella (<i>Chlorella vulgaris</i>)(whole plant), organic spinach (<i>Spinacia oleracea</i>)(whole plant))	1.28 g	**
Organic Fruits and Berries Blend (organic blueberry (<i>Vaccinium corymbosum</i>)(whole berry), organic apple (<i>Malus domestica</i>)(whole apple), organic strawberry (<i>Fragaria Spp.</i>)(whole fruit), organic sea-buckthorn juice powder (<i>Hippophae rhamnoides</i>)(fruit), organic acai (<i>Euterpe oleracea</i>)(berry), organic acerola cherry extract (<i>Malpighia glabra</i>)(fruit), organic plum extract (<i>Prunus salicina</i>)(fruit))	875 mg	**
Antioxidant Phytonutrients Blend (OxyPhyte® Ultrablend (organic green tea extract (<i>Camellia sinensis</i>)(leaf) and organic apple extract (<i>Malus sieversii</i>)(whole fruit)), organic astragalus (<i>Astragalus membranaceus</i>)(root), organic ginger (<i>Zingiber officinale</i>)(root), organic goji berry extract (<i>Lycium sp.</i>)(fruit))	710 mg	**
Digestive Support* Blend (probiotics (<i>L. acidophilus</i> , <i>B. longum</i> , <i>L. casei</i> , <i>L. rhamnosus</i>) and enzymes (protease, amylase, bromelain, cellulase, lactase, papain, lipase))	20 mg	**
truebroc® Glucoraphanin (from broccoli extract)(<i>Brassica oleracea italica</i>)(seed)	5 mg	**
† Percent Daily Values are based on a 2,000 calorie diet. ** Daily Value (DV) not established.		

Other Ingredients: Organic flavors, organic stevia extract, and organic Luo Han Guo extract.

DIRECTIONS: Blend, shake, or briskly stir one level scoop (8 g) of OrganiX™ PhytoFood™ into 6-8 fl oz chilled water, or as directed by your healthcare practitioner. Adjust amount of water to desired sweetness and/or thickness.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner.

STORAGE: Keep tightly closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



Produced under US patent 6,521,818 licensed from Brassica Protection Products LLC; TrueBroc is a registered trademark of Brassica Protection Products LLC.

References

- Murphy MM, Barraj LM, Herman D, et al. Phytonutrient intake by adults in the United States in relation to fruit and vegetable consumption. *J Am Diet Assoc.* 2011 Nov 9. [PMID: 22078816]
- Valko M, Leibfritz D, Moncol J, et al. Free radicals and antioxidants in normal physiological functions and human disease. *Int J Biochem Cell Biol.* 2007;39(1):44-84. [PMID: 16978905]
- Block G. Dietary guidelines and the results of food consumption surveys. *Am J Clin Nutr.* 1991 Jan;53(1 Suppl):356S-357S. [PMID: 1985410]
- Wallace TC, Guarner F, Madsen K, et al. Human gut microbiota and its relationship to health and disease. *Nutr Rev.* 2011 Jul;69(7):392-403. [PMID: 21729093]
- Willcox DC, Willcox BJ, Todoriki H, et al. The Okinawan diet: health implications of a low-calorie, nutrient-dense, antioxidant-rich dietary pattern low in glycemic load. *J Am Coll Nutr.* 2009 Aug;28 Suppl:500S-516S. [PMID: 20234038]
- American Institute for Cancer Research. <http://www.aicr.org/assets/docs/pdf/brochures/US11FactsonPreventingCancerTheCancerFightersinYourFood.pdf>. Accessed July 14, 2012.
- Anderson JW, Baird P, Davis RH Jr, et al. Health benefits of dietary fiber. *Nutr Rev.* 2009 Apr;67(4):188-205. Review. [PMID: 19335713]
- American Institute for Cancer Research. www.aicr.org. Accessed July 12, 2012.
- Merchant RE, Andre CA. A review of recent clinical trials of the nutritional supplement Chlorella pyrenoidosa in the treatment of fibromyalgia, hypertension, and ulcerative colitis. *Altern Ther Health Med.* 2001 May-Jun;7(3):79-91. [PMID: 11347287]
- RFI Ingredients. <http://rfiingredients.com/clinically.asp>. Accessed July 12, 2012.
- Zhang Y, Talalay P, Cho CG, et al. A major inducer of anticarcinogenic protective enzymes from broccoli: isolation and elucidation of structure. *Proc Natl Acad Sci U S A.* 1992 Mar 15;89(6):2399-403. [PMID: 1549603]
- Riedl MA, Saxon A, Diaz-Sanchez D. Oral sulforaphane increases Phase II antioxidant enzymes in the human upper airway. *Clin Immunol.* 2009 Mar;130(3):244-51. [PMID: 19028145]
- Fahey JW, Zhang Y, Talalay P. Broccoli sprouts: an exceptionally rich source of inducers of enzymes that protect against chemical carcinogens. *Proc Natl Acad Sci USA.* 1997 Sep 16;94(19):10367-72. [PMID: 9294217]
- Brassica®. <http://www.brassica.com>. Accessed July 12, 2012.

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

© XYMOGEN
DRS-263
Rev. 08/05/19



OSAples™ Formulas

Overall Bone Health and Strength*



OSAples™ and OSAples MK-7™ are available in 60 packets
OSAples™ CF is available in 30 packets

Discussion

Bone health is dependent on a constant supply of micronutrients for maintenance and repair. Instead of adopting a single-nutrient, unbalanced approach to supplementation, XYMOGEN® utilizes an array of complementary, well-researched nutrients in its OSAples line of formulas to build and maintain bone over time.*

OSAples™ is our original formula, and it provides ch-OSA®, MCHC (microcrystalline hydroxyapatite concentrate), and vitamin D3.

ch-OSA® (Choline-Stabilized Orthosilicic Acid)

ch-OSA is a patented, stabilized, readily absorbed, and bioactive form of silicon called orthosilicic acid. Because regular orthosilicic acid is highly unstable, leading it to form polymers, and because the polymers are too large for the human body to absorb, ch-OSA features patented “choline stabilization” technology. This stabilization prevents polymers from forming, ensuring optimal absorption of orthosilicic acid.*

Decades of research suggest that there is a positive association between dietary silicon and bone mineral density (BMD).^[1] The mechanisms of action appear to be silicon's support of collagen synthesis and stabilization, extracellular matrix mineralization, and connective tissue integrity.^[2-3] Cell-line studies have shown that type I collagen synthesis is stimulated by orthosilicic acid (silicon).^[4] Type I collagen is a dense, heavily cross-linked protein that creates an extremely high tensile strength^[5] and contributes to bone strength and flexibility. These strong collagen strands are believed to create core-post “binding sites” for calcium and other bone minerals.*^[6-8] In a 12-month clinical trial conducted at St. Thomas' Hospital in London, women already taking 1000 mg of calcium and 800 IU of vitamin D, to which they added ch-OSA, saw thighbone mineral density at the hip (i.e., femoral neck) increase by 2.00% compared to placebo. This was as a result of an increase in actual bone formation, not just a decrease in loss.^[9] Furthermore, the procollagen marker P1NP (procollagen type-1 N-terminal propeptide) increased significantly after 12 months in women who took ch-OSA compared to women in the placebo group. P1NP is known as the most sensitive marker for bone collagen formation and an early marker of bone formation.^[9] Animal studies support the human clinical findings for ch-OSA with respect to collagen formation and BMD.*^[6,7,10]

Microcrystalline Hydroxyapatite Concentrate (MCHC)

XYMOGEN uses standardized, safe, bovine-sourced MCHC (Ossopan) from New Zealand. The OIE-World Organisation for Animal Health has classified New Zealand as a “negligible BSE risk country,” the most favorable official classification a country

Clinical Applications

- » Provide a Calcium-Free Option and MCHC Options for Bone Support*
- » Provide a Multifaceted Approach to Bone Maintenance and Strength*
- » Provide Foundational Bone Support with Choline-Stabilized Orthosilicic Acid (ch-OSA®)*
- » Support Bone Collagen Formation, Bone Mineral Density, and Bone Calcium Binding Sites*
- » Provide a Complementary Combination of Micronutrients*

*OSAples™ formulas offer a variety of micronutrient profiles that allow scope for individualized nutritional support of bone health and maintenance. The foundation of each of these distinct formulas is choline-stabilized orthosilicic acid (ch-OSA®), a source of the mineral silicon. Silicon has been researched for its role in collagen synthesis and bone mineral density (BMD). By adding other bone-specific nutrients to the ch-OSA foundation, each OSAples formula is tailored to meet individual needs.**

can be given.^[11] MCHC is manufactured under proprietary processes that meet FDA, USDA, and EU regulatory requirements, and frequent heavy metal assays assure purity. Proprietary techniques preserve the bioactive contents of bone and create a naturally balanced formula because whole-bone extract provides an array of nutrients found in healthy bone: calcium, phosphorus, magnesium, bioactive growth factors, type I collagen, amino acids, glycosaminoglycans, and a broad range of essential trace elements. Gentle processing retains the delicate protein matrix and organic factors, and X-ray-diffraction analysis confirms the microcrystalline structure. The MCHC is assayed for hydroxyproline content and the collagen content is greater than 22% with the majority being type I, the predominant collagen occurring in bone.*

Decades of scientific studies suggest that Ossopan/MCHC supplementation fundamentally supports BMD and bone health.^[12-15] A meta-analysis of six controlled studies suggested that hydroxyapatite was significantly more effective than calcium carbonate in supporting bone structure and BMD, and another study favorably compared its absorption to calcium gluconate.*^[16,17]

Vitamin D3

Although vitamin D3 (cholecalciferol) is made in the skin when 7-dehydrocholesterol reacts with sunlight, many things affect the degree to which this biosynthesis occurs, including time of day, seasons, location, smog/pollution, clothing, shade of skin (darker skin requires more sun), and sunscreen use. Low-cholesterol diets and certain cholesterol therapies can also affect vitamin D formation. By some estimates, one billion people worldwide have vitamin D deficiency or insufficiency.^[18] The body needs vitamin D to absorb calcium, and the importance of vitamin D in skeletal health and bone density is well-established. Without adequate absorption, the body must take calcium from its stores in the skeleton, which weakens existing bone and prevents the formation of strong, new bone. Researchers suggest that vitamin D supplementation may decrease bone turnover and increase BMD.^[19] A pooled analysis evaluating 11 randomized, double-blind, placebo-controlled trials supported this analysis. It concluded that vitamin D supplementation (> 800 IU daily) was favorable in maintaining hip and nonvertebral bone integrity in individuals aged 65 and older.*^[20]

Although D2 and D3 are similar biochemically, one study demonstrated D3 to be approximately 87% more potent in raising and maintaining serum calcidiol (the body's storage form) concentrations and in producing two- to threefold greater storage of vitamin D than did equimolar D2.*^[21]

Continued on next page

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

OSAplex™ Supplement Facts

Serving Size: 1 Packet

	(2) Ossopan 1100™ with (1) ch-OSA® Capsule vitamin D3 Capsules			
	Amount Per Serving	%DV	Amount Per Serving	%DV
Vitamin D3 (cholecalciferol)	50 mcg (2000 IU)	250%		
Choline (as choline-stabilized orthosilicic acid [†])			60 mg	11%
Calcium (as MCHC [†])	550 mg	42%		
Phosphorus (as MCHC [†])	198 mg	16%		
MCHC [†]	2.2 g	**		
Microcrystalline Hydroxyapatite (as MCHC [†])	1.32 g	**		
Silicon (as choline-stabilized orthosilicic acid [†])			3 mg	**

** Daily Value (DV) not established.

Other Ingredients for Ossopan 1100 with vitamin D3: HPMC (capsule), vegetable stearic acid, vegetable magnesium stearate, medium-chain triglyceride oil, and silica.

Other Ingredients for ch-OSA: Microcrystalline cellulose, HPMC (capsule), and purified water.

[†]Microcrystalline Hydroxyapatite Concentrate

[‡]Choline-stabilized orthosilicic acid (ch-OSA[®]) is a registered trademark of and manufactured by Bio Minerals n.v., Belgium. Produced under US patents 5,922,360; 7,968,528; and 8,771,757.

DIRECTIONS: Consume the contents of one packet with a meal, one to two times daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



OSAplex MK-7™ Supplement Facts

Serving Size: 1 Packet

	(2) Ossopan 1100™ with (1) ch-OSA® Capsule vitamins D3 and K2 Capsules			
	Amount Per Serving	%DV	Amount Per Serving	%DV
Vitamin D3 (cholecalciferol)	25 mcg (1000 IU)	125%		
Vitamin K2 (as menaquinone-7)	45 mcg	38%		
Choline (as choline-stabilized orthosilicic acid [†])			60 mg	11%
Calcium (as MCHC [†])	550 mg	42%		
Phosphorus (as MCHC [†])	198 mg	16%		
MCHC [†]	2.2 g	**		
Microcrystalline Hydroxyapatite (as MCHC [†])	1.32 g	**		
Silicon (as choline-stabilized orthosilicic acid [†])			3 mg	**

** Daily Value (DV) not established.

Other Ingredients for Ossopan 1100 with vitamins D3 and K2 capsule: HPMC (capsule), vegetable stearic acid, vegetable magnesium stearate, medium-chain triglyceride oil, and silica.

Other Ingredients for ch-OSA capsule: Microcrystalline cellulose, HPMC (capsule), and purified water.

[†]Choline-stabilized orthosilicic acid (ch-OSA) is a registered trademark of and manufactured by Bio Minerals n.v., Belgium. Produced under US patents 5,922,360; 7,968,528; and 8,771,757.

[‡]Microcrystalline Hydroxyapatite Concentrate

DIRECTIONS: Consume the contents of one packet with a meal, one to two times daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Consider total vitamin K intake (food + supplements) if you are taking blood-thinning medication. Present studies show that 45 mcg of MK-7 from VitaMK7™ daily is not likely to interfere with blood-thinning medicines. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



OSAplex™ MK-7 provides the same ingredients found in OSAplex (ch-OSA, MCHC, and D3) as well as vitamin K2 as menaquinone-7 (MK-7).

Vitamin K2

MK-7 is a bioactive, bioavailable form of vitamin K2.^[22] The biological role of vitamin K in relation to calcium and bone is to help deposit calcium into appropriate areas in the body, such as bones and teeth. Conversely, vitamin K is needed to prevent the accumulation of calcium in other areas, such as in arteries and soft tissues, through vitamin K-dependent carboxylation of Gla proteins. Vitamin K also supports bone integrity by moderating the synthesis of prostaglandin E2 (PGE-2) and interleukin-6 (IL-6) by osteoclasts.^[23,24] A three-year study utilizing 180 mcg/d of MK-7 concluded that MK-7 significantly improved vitamin K status, supported bone mineral content and BMD, and favorably supported bone strength and integrity in healthy postmenopausal women.^{*[25]}

OSAplex™ CF is our calcium/MCHC-free formula that combines Bonolive® olive leaf extract with ch-OSA, D3, and MK-7 to provide bone and cardiovascular support.*

Bonolive Olive Leaf Extract

Bonolive is a pharmaceutical-grade olive leaf extract that features a unique polyphenol complex (40% polyphenols), including oleuropein. This proprietary olive leaf extract preparation is fully water-soluble, which makes its oral bioavailability superior. Historical and traditional use as well as clinical testing and toxicological assessment confirm the safety of its oral consumption.^{*[26,27]}

Stem cell research has shown that olive polyphenol bioactivity is associated with increased osteoblast formation, increased extracellular matrix mineralization, and overall bone maintenance.^[28] Five preclinical studies in a well-established rat model for bone health demonstrated that olive polyphenols exert protective effects on the formation and maintenance of bone.^[29-33] In addition, a randomized, double-blind, placebo-controlled clinical study provided strong support for Bonolive supplementation. The results of this study revealed that 250 mg/d of Bonolive promoted a statistically significant improvement (32% increase) in levels of the bone formation marker osteocalcin over a 12-month period. Furthermore, DEXA scan results suggested that Bonolive supplementation positively supported BMD at the lumbar spine and the femur neck compared to placebo.^[26] The treatment group also experienced reduced adipocyte formation and a positive effect on lipid metabolism (i.e., cholesterol and triglycerides), confirming Bonolive's double mode of action: to positively influence bone health and cardiovascular health. Other research continues to confirm the positive cardiovascular effects of olive leaf extract and oleuropein at varying doses.^{*[34-37]}

Certain cytokines (IL-1, TNF-alpha, IL-6) are thought to be involved in bone turnover regulation by increasing bone resorption.^[30] Moreover, an excess of reactive oxygen species can impair bone metabolism and lead to bone loss.^[38] In experimental animal studies on ovariectomized rats, oleuropein and olives were shown to improve cytokine and oxidative status and thereby support bone maintenance.^[29-32] Garcia-Villalba et al demonstrated the superior oral bioavailability of Bonolive polyphenols and their positive effect on antioxidant status in pre- and postmenopausal women.^[39] Furthermore, the oxidative stress marker malondialdehyde (MDA), formed in the process of lipid oxidation, decreased by 32% after supplementation.*

As an interesting note, a synergistic effect of olive oil and vitamin D has been proposed. Tagliaferri et al demonstrated that virgin (high polyphenol content) olive oil fortified with vitamin D3 helped maintain bone density in mice challenged by estrogen deprivation.^{*[38]}

Continued on next page

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

OSAplex™ CF Supplement Facts

Serving Size: 1 Packet

	(2) OsteoBloX™ CF Capsules		(2) ch-OSA® Capsules	
	Amount Per Serving	%DV	Amount Per Serving	%DV
Vitamin D3 (cholecalciferol)	50 mcg (2000 IU)	250%		
Vitamin K2 (as menaquinone-7)	40 mcg	33%		
Choline (as choline-stabilized orthosilicic acid [†])			120 mg	22%
Bonolive® Olive Extract (<i>Olea europaea</i>) (leaves) (40% polyphenols)	500 mg	**		
Silicon (as choline-stabilized orthosilicic acid [†])			6 mg	**

Other Ingredients for OsteoBloX CF: HPMC (capsule), microcrystalline cellulose, ascorbyl palmitate, silica, and medium-chain triglyceride oil.

Other Ingredients for ch-OSA capsule: Microcrystalline cellulose, HPMC (capsule), and purified water.

[†]Choline-stabilized orthosilicic acid (ch-OSA) is a registered trademark of and manufactured by Bio Minerals n.v., Belgium. Produced under US patents 5,922,360; 7,968,528; and 8,771,757. Bonolive is a registered trademark of BioActar.

DIRECTIONS: Take one packet daily, or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Consider total vitamin K intake (food + supplements) if you are taking blood-thinning medication. Do not use if tamper seal is damaged.

STORAGE: Keep tightly closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



References

- Jugdaohsingh R. Silicon and bone health. *J Nutr Health Aging*. 2007 Mar-Apr;11(2):99-110. [PMID: 17435952]
- Silicon. Natural Medicines. <https://naturalmedicines.therapeuticresearch.com/databases/food,-herbs-supplements/professional.aspx?productid=1096>. Accessed March 3, 2016.
- Martin KR. Silicon: the health benefits of a metalloid. *Met Ions Life Sci*. 2013;13:451-73. [PMID: 24470100]
- Reffitt DM, Ogston N, Jugdaohsingh R, et al. Orthosilicic acid stimulates collagen type 1 synthesis and osteoblastic differentiation in human osteoblast-like cells in vitro. *Bone*. 2003 Feb;32(2):127-35. [PMID: 12633784]
- Blair HC, Robinson LJ, Huang CL, et al. Calcium and bone disease. *Biofactors*. 2011 May-Jun;37(3):159-67. [PMID: 21674636]
- Calomme MR, Vanden Berghe DA. Supplementation of calves with stabilized orthosilicic acid. Effect on the Si, Ca, Mg, and P concentrations in serum and the collagen concentration in skin and cartilage. *Biol Trace Elem Res*. 1997 Feb;56(2):153-65. [PMID: 9164661]
- Calomme MR, Geusens P, Demeester N, et al. Partial prevention of long-term femoral bone loss in aged ovariectomized rats supplemented with choline-stabilized orthosilicic acid. *Calcif Tissue Int*. 2006 Apr;78(4): 227-32. [PMID: 16604283]
- Viguet-Carrin S, Garnero P, Delmas PD. The role of collagen in bone strength. *Osteoporos Int*. 2006;17(3):319-36. [PMID: 16341622]
- Spector TD, Calomme MR, Anderson SH, et al. Choline-stabilized orthosilicic acid supplementation as an adjunct to calcium/vitamin D3 stimulates markers of bone formation in osteopenic females: a randomized, placebo-controlled trial. *BMC Musculoskelet Disord*. 2008 Jun 11;9:85. [PMID: 18547426]
- Calomme MR, Wijnen P, Sindambiwe JB, et al. Effect of choline-stabilized orthosilicic acid on bone density in chicks. *Calcif Tissue Int*. 2002; 70:292. Poster presented at: 29th European Symposium on Calcified Tissues; May 25-29, 2002; Zagreb, Croatia. Abstract P-139. <http://www.ectsoc.org/zagreb2002/poster3.htm>. Accessed April 26, 2016.
- Bovine Spongiform Encephalopathy (BSE). OIE-World Organization for Animal Health Web site. <http://www.oie.int/animal-health-in-the-world/official-disease-status/bse/list-of-bse-risk-status/>. Accessed April 26, 2016.
- Pelayo I, Haya J, De la Cruz JJ, et al. Raloxifene plus ossein-hydroxyapatite compound versus raloxifene plus calcium carbonate to control bone loss in postmenopausal women: a randomized trial. *Menopause*. 2008 Nov-Dec;15(6):1132-38. [PMID: 18791486]
- Castelo-Branco C, Pons F, Vicente JJ, et al. Preventing postmenopausal bone loss with ossein-hydroxyapatite compounds. Results of a two-year, prospective trial. *J Reprod Med*. 1999 Jul;44(7):601-05. [PMID: 10442322]
- Albertazzi P, Steel SA, Howarth EM, et al. Comparison of the effects of two different types of calcium supplementation on markers of bone metabolism in a postmenopausal osteopenic population with low calcium intake: a double-blind placebo-controlled trial. *Climacteric*. 2004 Mar;7(1):33-40. [PMID: 15259281]

- Rüeggsegger P, Keller A, Dambacher MA. Comparison of the treatment effects of ossein-hydroxyapatite compound and calcium carbonate in osteoporotic females. *Osteoporos Int*. 1995 Jan;5(1):30-34. [PMID: 7703621]
- Castelo-Branco C, Ciria-Recasens M, Cancelo-Hidalgo MJ, et al. Efficacy of ossein-hydroxyapatite complex compared with calcium carbonate to prevent bone loss: a meta-analysis. *Menopause*. 2009 Sep-Oct;16(5):984-91. [PMID: 19407667]
- Buclin T, Jacquet AF, Burckhardt P. Intestinal absorption of calcium gluconate and ossein-mineral complex: an evaluation by conventional analyses [in French]. *Schweiz Med Wochenschr*. 1986 Dec 13;116(50):1780-83. [PMID: 3026039]
- Tsiaras WG, Weinstein MA. Factors influencing vitamin D status. *Acta Derm Venereol*. 2011 Mar;91(2):115-24. [PMID: 21384086]
- Lips P, van Schoor NM. The effect of vitamin D on bone and osteoporosis. *Best Pract Res Clin Endocrinol Metab*. 2011 Aug;25(4):585-91. [PMID: 21872800]
- Bischoff-Ferrari HA, Willett WC, Orav EJ, et al. A pooled analysis of vitamin D dose requirements for fracture prevention. *N Engl J Med*. 2012 Jul 5;367(1):40-49. [PMID: 22762317]
- Heaney RP, Recker RR, Grote J, et al. Vitamin D3 is more potent than vitamin D2 in humans. *J Clin Endocrinol Metab*. 2011 Mar;96(3):E447-52. [PMID: 21177785]
- Schurgers LJ, Teunissen KJ, Hamulyák K, et al. Vitamin K-containing dietary supplements: comparison of synthetic vitamin K1 and natto-derived menaquinone-7. *Blood*. 2007 Apr 15;109(8):3279-83. [PMID: 17158229]
- Weber P. Management of osteoporosis: is there a role for vitamin K? *Int J Vitam Nutr Res*. 1997;67(5):350-56. [PMID: 9350477]
- Shearer MJ. The roles of vitamins D and K in bone health and osteoporosis prevention. *Proc Nutr Soc*. 1997 Nov;56(3):915-37. [PMID: 9483660]
- Knapen MH, Drummen NE, Smit E, et al. Three-year low-dose menaquinone-7 supplementation helps decrease bone loss in healthy postmenopausal women. *Osteoporos Int*. 2013 Sep;24(9):2499-507. [PMID: 23525894]
- Filip R, Possemiers S, Heyerick A, et al. Twelve-month consumption of a polyphenol extract from olive (*Olea europaea*) in a double blind, randomized trial increases serum total osteocalcin levels and improves serum lipid profiles in postmenopausal women with osteopenia. *J Nutr Health Aging*. 2015 Jan;19(1):77-86. [PMID: 25560820]
- Clewell AE, Béres E, Vértési A, et al. A comprehensive toxicological safety assessment of an extract of *Olea europaea* L. leaves (Bonolive™). *Int J Toxicol*. 2015 Dec 10. pii: 1091581815619764. Epub ahead of print. [PMID: 26658007]
- Santiago-Mora R, Casado-Díaz A, De Castro MD, et al. Oleuropein enhances osteoblastogenesis and inhibits adipogenesis: the effect on differentiation in stem cells derived from bone marrow. *Osteoporos Int*. 2011 Feb;22(2):675-84. [PMID: 20495905]
- Puel C, Mardon J, Agalias A, et al. Major phenolic compounds in olive oil modulate bone loss in an ovariectomy/inflammation experimental model. *J Agric Food Chem*. 2008 Oct 22;56(20):9417-22. [PMID: 18800805]
- Puel C, Mathey J, Agalias A, et al. Dose-response study of effect of oleuropein, an olive oil polyphenol, in an ovariectomy/inflammation experimental model of bone loss in the rat. *Clin Nutr*. 2006 Oct;25(5):859-68. [PMID: 16740345]
- Puel C, Quintin A, Agalias A, et al. Olive oil and its main phenolic micronutrient (oleuropein) prevent inflammation-induced bone loss in the ovariectomized rat. *Br J Nutr*. 2004 Jul;92(1):19-27. [PMID: 15230995]
- Puel C, Mardon J, Kati-Coulibaly S, et al. Black Lucques olives prevented bone loss caused by ovariectomy and talc granulomatosis in rats. *Br J Nutr*. 2007 May;97(5):1012-20. [PMID: 17408530]
- Hagiwara K, Goto T, Araki M, et al. Olive polyphenol hydroxytyrosol prevents bone loss. *Eur J Pharmacol*. 2011 Jul 15;662(1-3):78-84. [PMID: 21539839]
- Lockyer S, Rowland I, Spencer JP, et al. Impact of phenolic-rich olive leaf extract on blood pressure, plasma lipids and inflammatory markers: a randomised controlled trial. *Eur J Nutr*. 2016 Mar 7. ePub ahead of print. [PMID: 26951205]
- Romero M, Toral M, Gómez-Guzmán M, et al. Antihypertensive effects of oleuropein-enriched olive leaf extract in spontaneously hypertensive rats. *Food Funct*. 2016 Jan 20;7(1):584-93. [PMID: 26593388]
- Susalit E, Agus N, Effendi I, et al. Olive (*Olea europaea*) leaf extract effective in patients with stage-1 hypertension: comparison with Captopril. *Phytomedicine*. 2011 Feb 15;18(4):251-58. [PMID: 21036583]
- Perrinjaquet-Moccetti T, Busjahn A, Schmidlin C, et al. Food supplementation with an olive (*Olea europaea* L.) leaf extract reduces blood pressure in borderline hypertensive monozygotic twins. *Phytother Res*. 2008 Sep;22(9):1239-42. [PMID: 18729245]
- Tagliaferri C, Davicco MJ, Lebecque P, et al. Olive oil and vitamin D synergistically prevent bone loss in mice. *PLoS One*. 2014 Dec 31;9(12):e115817. [PMID: 25551374]
- García-Villalba R, Larrosa M, Possemiers S, et al. Bioavailability of phenolics from an oleuropein-rich olive (*Olea europaea*) leaf extract and its acute effect on plasma antioxidant status: comparison between pre- and postmenopausal women. *Eur J Nutr*. 2014 Jun;53(4):1015-27. [PMID: 24158653]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.



Ossopan

Comprehensive Bone Support*



Ossopan MD™ is available in 120 & 240 capsules
Ossopan 1100™ is available in 120 capsules

Discussion

More than 20 years of scientific research have given the name *Ossopan* worldwide recognition as a source of microcrystalline hydroxyapatite concentrate (MCHC). Numerous published studies support the safety, tolerability, and bone health-related effectiveness of MCHC supplementation.^[1,2] Studies suggest that the bioavailability of calcium from MCHC supplements may be as good as or better than the bioavailability of calcium from calcium gluconate supplements.^[3,4] XYMOGEN utilizes standardized, safe, bovine-sourced MCHC from New Zealand, a country with stringent standards. Its production features a proprietary technique that preserves the bioactive contents of bone. This process creates a naturally balanced formula because whole bone extract provides all of the nutrients found in healthy bone.*

Unlike other calcium supplements on the market, Ossopan consists of collagenous and non-collagenous proteins and peptides. These compounds include insulin-like growth factors I and II (IGF-I, IGF-II), transforming growth factor beta (TGF-beta), and osteocalcin, factors that stimulate alkaline phosphatase activity and support metabolism in human bone cells.^[5] Removal of the protein fraction appears to reduce the positive effects of the formula, highlighting the importance of its presence.*^[6]

A study suggested that the occurrence of positive and statistically significant changes in forearm bone integrity were the result of daily supplementation with 3000 mg of microcrystalline hydroxyapatite.^[7] Earlier studies compared Ossopan to other forms of calcium with regard to the support of normal bone turnover and bone mineral integrity. In one 20-month, double-blind study, women were given 1400 mg of elemental calcium (equivalent to approximately 5000 mg MCHC) as either calcium carbonate or Ossopan. At the end of the study, the presence of bone integrity was statistically significant in the Ossopan group.*^[8]

Clinical trials suggested that Ossopan supplementation was well-tolerated and yielded a positive outcome for dental status, bone

Clinical Applications

- » Supports Bone Metabolism*
- » Supports Bone Strength*
- » Provides Micronutrients for Utilization in Bone Production and Structure*

*Ossopan is a well-researched, standardized extract from one of the world's safest premium sources of bone—free-range New Zealand cattle. Ossopan contains microcrystalline hydroxyapatite concentrate (MCHC), a complex crystalline compound containing calcium, phosphorus, bioactive growth factors, type I collagen, amino acids, glycosaminoglycans, and a broad range of essential trace elements that naturally comprise healthy bone.**

***Ossopan 1100™** delivers 1100 mg of MCHC per capsule to optimally support bone strength and structure. **Ossopan MD™** delivers 500 mg of MCHC per capsule along with additional calcium and magnesium in the form of highly absorbable Albion® minerals. Vitamin D, in the form of cholecalciferol, supports intestinal calcium absorption and homeostasis in the body and completes the comprehensiveness of this bone-support formula.**

integrity, and healthy bone metabolism.^[9,10] A randomized, controlled study indicated that the addition of Ossopan to exogenously administered hormones provided statistically significant support (4.7%, P<0.1) to vertebral bone mass.^[10] Another study of 60 subjects suggested that bone mass was maintained while on Ossopan.*^[11]

Ossopan is high-quality MCHC from New Zealand. The World Organization for Animal Health (the OIE) has classified New Zealand as a “negligible BSE risk country,” the most favorable official classification a country can be given.^[12] Ossopan is manufactured under proprietary processes that meet FDA, USDA, and EU regulatory requirements. Gentle processing is used to retain the delicate protein matrix and organic factors. X-ray-diffraction analysis confirms the microcrystalline structure. The MCHC is assayed for hydroxyproline content. The collagen content is greater than 22% with the majority being type I, the predominant collagen occurring in bone. Frequent heavy metal assays assure purity.

Ossopan 1100™ delivers 1100 mg of Ossopan per capsule. Ossopan MD™ delivers 500 mg of Ossopan per capsule along with vitamin D, magnesium, and additional calcium. Vitamin D is provided as cholecalciferol, which stimulates intestinal calcium absorption and helps support calcium and phosphorus homeostasis in the body. Calcium is provided as MCHC and DimaCal® dicalcium malate, and magnesium is provided as Albion dimagnesium malate and TRACS® magnesium bisglycinate chelate. The buffering malate forms of calcium and magnesium do not react with stomach acid and are less likely than carbonates to cause discomfort and acid rebound.*^[13]

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Ossopan 1100™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Calcium (as MCHC ¹)	550 mg	42%
Phosphorus (as MCHC ¹)	198 mg	16%
MCHC ¹	2.2 g	**
Microcrystalline Hydroxyapatite (as MCHC ¹)	1.32 g	**

Other Ingredients: HPMC (capsule), vegetable stearic acid, medium-chain triglycerides, microcrystalline cellulose, vegetable magnesium stearate, and silica.

¹Microcrystalline Hydroxyapatite Concentrate.

DIRECTIONS: Take one to two capsules up to two times daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep tightly closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

Albion, DimaCal, and TRAACS are registered trademarks of Albion Laboratories, Inc. Malates covered by US patent 6,706,904 and patents pending.

**References**

1. Pines A, Raafat H, Lynn AH, et al. Clinical trial of microcrystalline hydroxyapatite compound ('Ossopan') in the prevention of osteoporosis due to corticosteroid therapy. *Curr Med Res Opin.* 1984;8(10):734-42. [PMID: 6373153]
2. Stellon A, Davies A, Webb A, et al. Microcrystalline hydroxyapatite compound in prevention of bone loss in corticosteroid-treated patients with chronic active hepatitis. *Postgrad Med J.* 1985 Sep;61(719):791-6. [PMID: 2997764]
3. Buclin T, Jacquet AF, Burckhardt P. Intestinal absorption of calcium gluconate and oseine-mineral complex: an evaluation by conventional analyses [in French]. *Schweiz Med Wochenschr.* 1986 Dec 13;116(50):1780-3. [PMID: 3026039]
4. Epstein O, Kato Y, Dick R, et al. Vitamin D, hydroxyapatite, and calcium gluconate in treatment of cortical bone thinning in postmenopausal women with primary biliary cirrhosis. *Am J Clin Nutr.* 1982 Sep;36(3):426-30. [PMID: 6287835]
5. Stepan JJ, Mohan S, Jennings JC, et al. Quantitation of growth factors in ossein-mineral-compound. *Life Sci.* 1991;49(13):PL79-84. [PMID: 1653384]
6. Anefeld M, Caviezel R, Schacht E, et al. The influence of ossein-hydroxyapatite compound ('Ossopan') on the healing of a bone defect. *Curr Med Res Opin.* 1986;10(4):241-50. [PMID: 3022988]
7. Fernández-Pareja A, Hernández-Blanco E, Pérez-Maceda JM, et al. Prevention of osteoporosis: four-year follow-up of a cohort of postmenopausal women treated with an ossein-hydroxyapatite compound. *Clin Drug Investig.* 2007;27(4):227-32. [PMID: 17358094]
8. Rüeeggsegger P, Keller A, Dambacher MA. Comparison of the treatment effects of ossein-hydroxyapatite compound and calcium carbonate in osteoporotic females. *Osteoporos Int.* 1995 Jan;5(1):30-4. [PMID: 7703621]
9. Khadzhiev A, Rachev E, Katsarova M, et al. The results of a clinical trial of the preparation Ossopan [in Bulgarian]. *Akush Ginekol (Sofia).* 1990;29(4):85-7. [PMID: 2176437]
10. Castelo-Branco C, Martínez de Osaba MJ, Pons F, et al. Ossein-hydroxyapatite compounds for preventing postmenopausal bone loss. Coadjuvant use with hormone replacement therapy. *J Reprod Med.* 1999 Mar;44(3):241-6. [PMID: 10202741]
11. Castelo-Branco C, Pons F, Vicente JJ, et al. Preventing postmenopausal bone loss with ossein-hydroxyapatite compounds. Results of a two-year, prospective trial. *J Reprod Med.* 1999 Jul;44(7):601-5. [PMID: 10442322]
12. Bovine Spongiform Encephalopathy Status of Members. OIE-World Organization for Animal Health Web site. <http://www.oie.int/animal-health-in-the-world/official-disease-status/bse/list-of-bse-risk-status/>. Accessed May 9, 2014.
13. Malic acid can be the right ligand for certain applications. *Albion® Research Notes.* April 2003;12(2). <http://www.albionhumannutrition.com/research-notes/download?start=40>. Accessed May 9, 2014.

Additional references available upon request

Ossopan MD™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Vitamin D3 (cholecalciferol)	2.5 mcg (100 IU)	13%
Calcium (as MCHC ¹ and DimaCal® di-calcium malate)	400 mg	31%
Phosphorus (as MCHC ¹)	90 mg	7%
Magnesium (as Albion® di-magnesium malate)	100 mg	24%
MCHC ¹	1 g	**
Microcrystalline Hydroxyapatite (as MCHC ¹)	600 mg	**

Other Ingredients: HPMC (capsule), microcrystalline cellulose, vegetable stearic acid, medium-chain triglyceride oil, vegetable magnesium stearate, and silica.

¹Microcrystalline Hydroxyapatite Concentrate

DIRECTIONS: Take two capsules with meals, twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

Albion, DimaCal, and TRAACS are registered trademarks of Albion Laboratories, Inc. Malates covered by US patent 6,706,904.



All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

© XYMOGEN
DRS-111
Rev. 08/05/19



OsteoBloX™ CF

Calcium-Free Bone Support*



Available in 60 vegetarian capsules

Discussion

Bone remodeling is a lifelong process that involves resorption of damaged bone by osteoclasts and novel bone matrix formation by osteoblasts. During growth years, bone formation outpaces destruction. If bone formation is not sufficiently supported after skeletal maturity has been reached, bone resorption may surpass formation, resulting in net bone loss. OsteoBloX CF features three complementary ingredients that work together to positively influence and maintain the balance of bone remodeling without using calcium.*

Bonolive® Olive Leaf Extract

Interest in the effects of olive polyphenols on bone metabolism was triggered by epidemiological data showing a lower incidence of hip fractures in people of European countries adhering to a Mediterranean diet. Indeed, in a two-year study, a Mediterranean diet enriched with virgin olive oil was shown to increase serum osteocalcin (bone formation marker) and P1NP (procollagen marker) concentrations.^[1] These beneficial effects on bone have been largely attributed to the polyphenol content of olive oil. In particular, olive leaves are a rich source of the main active olive polyphenol, oleuropein. Bonolive is a pharmaceutical-grade olive leaf extract that features a unique polyphenol complex (40% polyphenols), including oleuropein.*

Stem cell research has shown that olive polyphenol bioactivity is associated with increased osteoblast formation, increased extracellular matrix mineralization, and overall bone maintenance.^[2] A total of five preclinical studies in a well-established rat model for bone health confirmed this mode of action and demonstrated that olive polyphenols exert protective effects on the formation and maintenance of bone.^[3-7] In addition, a randomized, double-blind, placebo-controlled (RDBPC) clinical study provided strong support for Bonolive supplementation. The results of this study revealed that 250 mg/d of Bonolive promoted a statistically significant improvement (32% increase) in levels of osteocalcin over a 12-month period. Furthermore, DEXA scan results suggested that Bonolive supplementation positively supported BMD (bone mineral density) at the lumbar spine and the femur neck compared to placebo.^[8] It's worth noting that the treatment group also experienced reduced adipocyte formation and a positive effect on lipid metabolism (e.g., cholesterol and triglycerides), confirming Bonolive's double mode of action: to positively influence bone health and cardiovascular health.*

Certain cytokines (IL-1, TNF-alpha, IL-6) are thought to be involved in bone turnover regulation by increasing bone resorption.^[4] Moreover, an excess of reactive oxygen species can impair bone metabolism and lead to bone loss.^[9]

Clinical Applications

- » Supports Bone Health*
- » Promotes Healthy Bone Metabolism*
- » Supports Healthy Levels of Osteocalcin*
- » Promotes Osteoblast Activity and Bone Mineralization*
- » Supports Musculoskeletal Comfort*

*OsteoBloX™ CF features vitamin D3 as cholecalciferol, vitamin K as menaquinone-7 (MK-7), and Bonolive® olive leaf extract to give you science-based bone support without calcium. These nutrients address the multiple needs of a healthy skeletal system—from bone mineralization to stimulating bone-building cells.**

In experimental animal studies on ovariectomized rats, oleuropein and olives were shown to improve cytokine and oxidative status and thereby support bone maintenance.^[3-6] Bonolive is a fully water-soluble, proprietary olive leaf extract, which results in superior bioavailability. García-Villalba et al demonstrated the superior oral bioavailability of Bonolive polyphenols and their positive effect on antioxidant status in pre- and postmenopausal women.*^[10]

Bonolive has an excellent safety profile. Olive fruit, oil, and leaves have long histories of consumption and traditional use. Additionally, the 12-month Bonolive clinical trial by Filip et al showed no adverse effects. Most importantly, a comprehensive good laboratory practices toxicology assessment of Bonolive confirmed the safety of its oral consumption.*^[11]

Vitamin D3

Although vitamin D3 (cholecalciferol) is made in the skin when 7-dehydrocholesterol reacts with sunlight, many factors affect the degree to which this biosynthesis occurs, including time of day, season, location, smog/pollution, clothing, skin color (darker skin requires more sun), and sunscreen use. Low-cholesterol diets and certain cholesterol therapies can also affect vitamin D formation. By some estimates, one billion people worldwide have vitamin D deficiency or insufficiency.^[12] The body needs vitamin D to absorb calcium, and the importance of vitamin D in skeletal health and bone density is well-established. Insufficient vitamin D negatively affects calcium absorption.^[13] Without adequate absorption, the body must take calcium from its stores in the skeleton, which weakens existing bone and prevents the formation of strong, new bone. Vitamin D is also needed by osteoblasts and osteoclasts for bone remodeling. Researchers suggest that vitamin D supplementation may decrease bone turnover and increase BMD.^[14] A pooled analysis evaluating 11 RDBPC trials concluded that vitamin D supplementation (> 800 IU daily) was favorable in maintaining hip and nonvertebral bone integrity in individuals aged 65 and older.*^[15]

Vitamin K2

OsteoBloX CF provides vitamin K2 as menaquinone-7 (MK-7)—a bioactive, bioavailable form of vitamin K.^[16] The biological role of vitamin K in relation to calcium and bone is to help deposit calcium into appropriate areas in the

Continued on next page

OsteoBioX™ CF Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Vitamin D3 (cholecalciferol)	25 mcg (1000 IU)	125%
Vitamin K2 (as menaquinone-7)	20 mcg	17%
Olive Extract (Olea europaea)(leaves) (40% polyphenols)(Bonolive®)	250 mg	**

** Daily Value not established.
Other Ingredients: HPMC (capsule), microcrystalline cellulose, ascorbyl palmitate, silica, and medium-chain triglyceride oil.
 Bonolive is a registered trademark of BioActor.

DIRECTIONS: Take one capsule daily, or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Consider total vitamin K intake (food + supplements) if you are taking blood-thinning medication. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



body, such as bones and teeth, and to prevent its accumulation in other areas, such as in arteries and soft tissues. It accomplishes this through carboxylation of Gla-proteins (e.g., osteocalcin). Vitamin K also supports bone integrity by moderating the synthesis of prostaglandin E2 (PGE-2) and interleukin-6 (IL-6) by osteoclasts.^[17,18] A three-year study utilizing 180 mcg/d of MK-7 concluded that MK-7 significantly improved vitamin K status, supported bone mineral content and BMD, and favorably supported bone strength and integrity in healthy postmenopausal women.*^[19]

References

1. Fernández-Real JM, Bulló M, Moreno-Navarrete JM, et al. A Mediterranean diet enriched with olive oil is associated with higher serum total osteocalcin levels in elderly men at high cardiovascular risk. *J Clin Endocrinol Metab.* 2012 Oct;97(10):3792-98. [PMID: 22855341]
2. Santiago-Mora R, Casado-Díaz A, De Castro MD, et al. Oleuropein enhances osteoblastogenesis and inhibits adipogenesis: the effect on differentiation in stem cells derived from bone marrow. *Osteoporos Int.* 2011 Feb;22(2):675-84. [PMID: 20495905]
3. Puel C, Mardon J, Agalias A, et al. Major phenolic compounds in olive oil modulate bone loss in an ovariectomy/inflammation experimental model. *J Agric Food Chem.* 2008 Oct 22;56(20):9417-22. [PMID: 18800805]
4. Puel C, Mathey J, Agalias A, et al. Dose-response study of effect of oleuropein, an olive oil polyphenol, in an ovariectomy/inflammation experimental model of bone loss in the rat. *Clin Nutr.* 2006 Oct;25(5):859-68. [PMID: 16740345]
5. Puel C, Quintin A, Agalias A, et al. Olive oil and its main phenolic micronutrient (oleuropein) prevent inflammation-induced bone loss in the ovariectomised rat. *Br J Nutr.* 2004 Jul;92(1):119-27. [PMID: 15230995]
6. Puel C, Mardon J, Kati-Coulibaly S, et al. Black Lucques olives prevented bone loss caused by ovariectomy and talc granulomatosis in rats. *Br J Nutr.* 2007 May;97(5):1012-20. [PMID: 17408530]
7. Hagiwara K, Goto T, Araki M, et al. Olive polyphenol hydroxytyrosol prevents bone loss. *Eur J Pharmacol.* 2011 Jul 15;662(1-3):78-84. [PMID: 21539839]
8. Filip R, Possemiers S, Heyerick A, et al. Twelve-month consumption of a polyphenol extract from olive (*Olea europaea*) in a double blind, randomized trial increases serum total osteocalcin levels and improves serum lipid profiles in postmenopausal women with osteopenia. *J Nutr Health Aging.* 2015 Jan;19(1):77-86. [PMID: 25560820]
9. Tagliaferri C, Davicco MJ, Lebecque P, et al. Olive oil and vitamin D synergistically prevent bone loss in mice. *PLoS One.* 2014 Dec 31;9(12):e115817. [PMID: 25551374]
10. García-Villalba R, Larrosa M, Possemiers S, et al. Bioavailability of phenolics from an oleuropein-rich olive (*Olea europaea*) leaf extract and its acute effect on plasma antioxidant status: comparison between pre- and postmenopausal women. *Eur J Nutr.* 2014 Jun;53(4):1015-27. [PMID: 24158653]
11. Clewell AE, Béres E, Vértési A, et al. A comprehensive toxicological safety assessment of an extract of *Olea europaea* L. leaves (Bonolive™). *Int J Toxicol.* 2015 Dec 10. pii: 1091581815619764. Epub ahead of print. [PMID: 26658007]
12. Tsiaras WG, Weinstock MA. Factors influencing vitamin d status. *Acta Derm Venereol.* 2011 Mar;91(2):115-24. [PMID: 21384086]
13. Heany RP. Vitamin D in health and disease. *Clin J Am Soc Nephrol.* 2008 Sep;3(5):1535-41. [PMID: 18525006]
14. Lips P, van Schoor NM. The effect of vitamin D on bone and osteoporosis. *Best Pract Res Clin Endocrinol Metab.* 2011 Aug;25(4):585-91. Review. [PMID: 21872800]
15. Bischoff-Ferrari HA, Willett WC, Orav EJ, et al. A pooled analysis of vitamin D dose requirements for fracture prevention. *N Engl J Med.* 2012 Jul 5;367(1):40-49. [PMID: 22762317]
16. Schurgers LJ, Teunissen KJ, Hamulyák K, et al. Vitamin K-containing dietary supplements: comparison of synthetic vitamin K1 and natto-derived menaquinone-7. *Blood.* 2007 Apr 15;109(8):3279-83. [PMID: 17158229]
17. Weber P. Management of osteoporosis: Is there a role for vitamin K? *Int J Vitam Nutr Res.* 1997;67(5):350-56. [PMID: 9350477]
18. Shearer MJ. The roles of vitamins D and K in bone health and osteoporosis prevention. *Proc Nutr Soc.* 1997 Nov;56(3):915-37. [PMID: 9483660]
19. Knapen MH, Drummen NE, Smit E, et al. Three-year low-dose menaquinone-7 supplementation helps decrease bone loss in healthy postmenopausal women. *Osteoporos Int.* 2013 Sep;24(9):2499-507. [PMID: 23525894]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

© XYMOGEN
 DRS-305
 Rev. 08/05/19



PanXyme pH™

Acid Resistant, Non-Animal Derived Digestive Enzymes



Available in 90 capsules & 180 capsules

Clinical Applications

- » Supports Healthy Digestion of Proteins, Carbohydrates, Fats, and Vegetable Fiber*
- » Supports Assimilation of Nutrients*
- » Supports Normal Pancreatic Function*

*PanXyme pH™ is a blend of digestive enzymes derived from the fermentation action of fungi such as *Aspergillus niger* and *Rhizopus niveus*, microorganisms safely used in fermenting foods, including cheese, soy sauce, and yogurt. These non-animal derived enzymes support the assimilation of nutrients in foods and the digestion of proteins, carbohydrates, fats, and vegetable matter. Clinical trials suggest that PanXyme pH is effective across a broad spectrum of pH ranges.**

Discussion

Enzymes are functional proteins that participate in important metabolic processes throughout the body, such as the digestion of macronutrients (carbohydrates, proteins, and fats). During digestion, specific enzymes break down specific macronutrients: amylases convert carbohydrates to simple sugars (mono- and di-saccharides), proteases (also called proteolytic enzymes) convert proteins into peptides and free amino acids, and lipases break down fats into free fatty acids (monoglycerides) and glycerol. The pancreas produces these enzymes and releases them into the small intestine, where the majority of digestion takes place. Adequate production, release, and delivery of enzymes are necessary for optimal digestion.*

The use of supplemental digestive enzymes was employed in the 1940s by physician and researcher Edward Howell,^[1] and today supplemental enzymes continue to be utilized clinically to support digestion, assimilation, and gastrointestinal health.^[2] Digestive enzymes are recommended to select individuals to support normal pancreatic digestive function.*^[3,4]

PanXyme pH contains a variety of digestive enzymes to provide broad spectrum support.^[5] **Biodiastase** contains amylase for carbohydrate digestion, protease for protein digestion, and cellulase to support the breakdown of vegetable fiber. **Lipase** is present to facilitate the breakdown of fats. **Newlase** contains both protease and lipase to further support healthy and complete digestion.*

PanXyme pH maintains optimal activity throughout the digestive tract, an important factor in supporting healthy digestion and absorption. It is not denatured by gastric acid or negatively affected by the alkaline environment in the intestines. A pH range of 3.5 to 6.0 creates the optimal environment for the enzymes in PanXyme pH; however, the enzymes remain stable within a range of 3.0 to 9.0.*

In addition to improving the digestive process, the combination of biodiastase, lipase, and newlase—the enzymes found in PanXyme pH—was clinically tested in a 25-week intervention trial to see if it

improved the nutritional status of elderly individuals. Although body weight did not change significantly, individuals receiving the digestive enzyme blend were found to have a significant increase in both serum albumin and high density lipoprotein (HDL) cholesterol levels, suggesting that pancreatic enzyme administration supported markers for health and longevity.*^[6,7]

The enzymes in PanXyme pH are prepared by fermentation, extraction, purification, and standardization of enzymes produced by types of fungi such as *Aspergillus niger*, *Aspergillus* sp., and *Rhizopus niveus*. Microbes employed for the manufacture of enzymes are safe microorganisms that have been used for a long time in the manufacture of fermented foods, such as beer, cheese, soy sauce, and yogurt. XYMOGEN is proud to source this formula from Amano Enzyme Inc., a Japanese company that has been manufacturing enzymes since 1950 and is one of the top enzyme producers in the world.^[8] The company performs intensive testing to confirm the safety of the enzymes and the specific strains used. Amano also assays the individual enzymes in PanXyme pH for heavy metals and overall purity.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

PanXyme pH™ Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Amylase (from Biodiastase 2000)	45 mg (292,500 MWU)	**
Lipase	10.2 mg (510 FIP)	**
Newlase	10 mg	**
Protease	550 JF	
Lipase	40 FIP	

** Daily Value not established.

Other Ingredients: Calcium carbonate, microcrystalline cellulose, HPMC (capsule), stearic acid, magnesium stearate, and silica.**DIRECTIONS:** Take one capsule with or after each meal, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

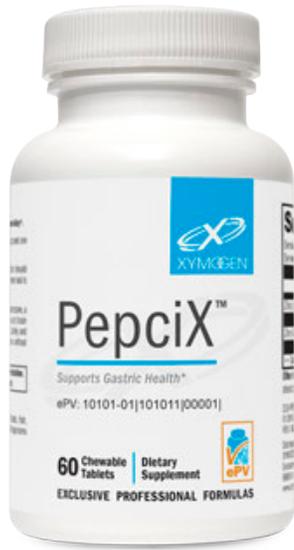
DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.**STORAGE:** Keep closed in a cool, dry place out of reach of children.**References**

1. Howell E, Murray M. *Enzyme nutrition: The food enzyme concept*. Wayne, NJ: Avery Publishing Group; 1985.
2. PeaceHealth Medical Group. <http://www.peacehealth.org/xhtml/content/cam/hn-1052003.html#hn-1052003-supplements>. Accessed January 3, 2013.
3. Halgreen H, Pedersen NT, Worning H. Symptomatic effect of pancreatic enzyme therapy in patients with chronic pancreatitis. *Scand J Gastroenterol*. 1986 Jan;21(1):104-8. [PMID: 3633631]
4. Scolapio JS, Malhi-Chowla N, Ukleja A. Nutrition supplementation in patients with acute and chronic pancreatitis. *Gastroenterol Clin North Am*. 1999 Sep;28(3):695-707. Review. [PMID: 10503145]
5. Amano Enzyme Inc. Dietary Supplement Use. <https://www.amano-enzyme.co.jp/aeu/product/dietarysupplement.html>. Accessed January 3, 2013.
6. Shibata H. Nutritional factors on longevity and quality of life in Japan. *J Nutr Health Aging*. 2001;5(2):97-102. [PMID: 11426289]
7. Amano Enzyme Inc. Digestive enzymes improve nutritional status in the elderly. *Enzyme Wave*. Newsletter. June 2004; vol 7. http://www.amano-enzyme.co.jp/pdf/wave_e/vol7/vol7_topic.pdf. Accessed January 3, 2013.
8. Amano Enzyme Inc. <https://www.amano-enzyme.co.jp/aeu/index.html>. Accessed January 3, 2013.

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration.
This product is not intended to diagnose, treat, cure, or prevent any disease.



Available in 60 chewable tablets

Discussion

Many factors impact digestion, the stomach's mucosal lining, and the overall health of the upper gastrointestinal (GI) tract. For various reasons, there may be temporary upset in the balance of flora present in the gastric environment.^[1] A wide range of treatments exist for the approximately 25-40% of Americans who suffer from occasional common upper GI discomforts. Whereas an effort is commonly made to either neutralize or block gastric acid, PepciX, a zinc L-carnosine complex, supports the stomach's natural "cytoprotective" defense mechanisms without negatively impacting stomach pH. In human studies, including four- and eight-week clinical trials among 691 subjects, zinc L-carnosine exhibited high efficacy without any serious side effects.*^[2]

Carnosine is a naturally occurring dipeptide composed of the amino acids L-histidine and beta-alanine. Carnosine can form stable complexes (ligands) with ion minerals like zinc and copper. PepciX contains a unique, proprietary zinc L-carnosine complex that has been in wide use in Japan since 1994. PepciX differs chemically and biologically from a simple combination of zinc and L-carnosine and has been shown to be approximately three times more effective than supplementing individually with either zinc sulfate or L-carnosine.*^[3]

A healthy gastric mucosal lining protects the upper gastrointestinal tract unless it is overburdened by the damaging effects of stress, bacteria, or irritating substances. Since L-carnosine and zinc each have mucosa-supportive properties, it is not surprising that the zinc L-carnosine ligand significantly protects and has been shown to enhance the integrity of the gastric lining. Thus, a healthy balance of flora may be re-established within the stomach in a relatively short time frame. In addition to its support of mucosa integrity, PepciX has been shown, in a study on rats, to enhance cellular resistance to ethanol without affecting endogenous prostaglandins.^[4,5] This is highly relevant because prostaglandins are key components of the mucosa. This zinc L-carnosine complex has also been shown to have anti-urease activity, which may indirectly support the gastric mucosa by maintaining a healthy balance of flora in the stomach.*^[6]

Clinical Applications

- » Supports the Relief of Occasional Gastric Discomforts (e.g., occasional heartburn/indigestion, upset stomach, belching, burping, bloating, mild nausea)*
- » Helps Maintain a Healthy Balance of Gastric Flora*
- » Protects and Supports the Integrity of the Gastric Mucosa*
- » Provides Antioxidant Activity in the Upper Gastrointestinal Tract*
- » Supports Healthy Cytokine Expression in Gastric Cells*

*PepciX™ is a zinc-carnosine complex consisting of elemental zinc as well as L-carnosine, a naturally occurring dipeptide (beta-alanine and L-histidine) found in muscle and brain tissue. More than 40 human and animal studies have demonstrated PepciX safely and effectively supports the stomach's own natural cell-protective mechanisms without interfering in the normal digestive process.**

Zinc L-carnosine complex does not rapidly break down in the stomach because it is a polymer. Japanese researchers found that this prolonged-release complex adheres to areas of the stomach lining and forms a new mixed ligand complex with other body components (perhaps proteins, like albumin) for extra support. At some point, a ligand exchange frees the L-carnosine and zinc from the complex and makes each available to optimize the health of the mucosal lining.^[6] In addition to the benefits these nutrients have in the GI tract, L-carnosine has antioxidant activity^[7] and zinc participates in the body's healthy natural response to inflammation.^[8] Animal studies have demonstrated that the zinc L-carnosine complex maintains the homeostasis of the gastric mucosa by its antioxidative, membrane-stabilizing capability^[6,9] and by protecting gastric cells via promotion of mucous production.^[5] The zinc L-carnosine complex also blunts genetic proinflammatory signaling and the release of proinflammatory cytokine expression in the gastric epithelial cells.^[10] A 2012 phase III clinical trial in Japan demonstrated a mechanism of action that explains why, in dietary zinc-deficient rats, zinc L-carnosine administration restored the lingual epithelium's zinc content. Interestingly, it also improved deficiency-induced delayed cell proliferation of taste bud cells.*^[11]

PepciX is a zinc L-carnosine complex that safely and effectively supports the stomach and upper GI tract's integrity.

PepciX™ Supplement Facts

Serving Size: 1 Tablet

	Amount Per Serving	%Daily Value
Zinc (as zinc-carnosine)	16 mg	145%
Zinc-Carnosine	75 mg	**

** Daily Value not established.

Other Ingredients: Isomalt, cellulose, stearic acid, magnesium stearate, and silica.**DIRECTIONS:** Swallow with liquid or chew one tablet immediately after breakfast and one tablet before bedtime, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.**DOES NOT CONTAIN:** Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.**References**

1. Sanduleanu S, Jonkers D, De Bruïne A, et al. Double gastric infection with *Helicobacter pylori* and non-*Helicobacter pylori* bacteria during acid-suppressive therapy: increase of pro-inflammatory cytokines and development of atrophic gastritis. *Aliment Pharmacol Ther*. 2001 Aug;15(8):1163-75. [PMID: 11472319]
2. Compilation of numerous studies presented in *Jpn Pharmacol Ther*. 1992;(20)1.
3. Korolkiewicz RP, Fujita A, Seto K, et al. Polaprezinc exerts a salutary effect on impaired healing of gastric lesions in diabetic rats. *Dig Dis Sci*. 2000;45(6):1200-1209. [PMID:10877238]
4. Nishiwaki H, Kato S, Sugamoto S, et al. Ulcerogenic and healing impairing actions of monochloramine in rat stomachs: effects of zinc L-carnosine, polaprezinc. *J Physiol Pharmacol* 1999;50:183-95. [PMID: 10424716]
5. Arakawa T, Satoh H, Nakamura A, et al. Effects of zinc L-carnosine on gastric mucosal and cell damage caused by ethanol in rats. Correlation with endogenous prostaglandin E2. *Dig Dis Sci*. 1990;35:559-66. [PMID: 2331952]
6. Matsukura T, Tanaka H. Applicability of zinc complex of L-carnosine for medical use. *Biochemistry (Mosc)*. 2000 Jul;65(7):817-23. [PMID: 10951100]
7. Guiotto A, Calderan A, Ruzza P, et al. Carnosine and carnosine-related antioxidants: a review. *Curr Med Chem*. 2005;12(20):2293-315. [PMID: 16181134]
8. Sempértegui F, Díaz M, Mejía R, et al. Low concentrations of zinc in gastric mucosa are associated with increased severity of *Helicobacter pylori*-induced inflammation. *Helicobacter*. 2007 Feb;12(1):43-8. [PMID: 17241300]
9. Seiki M, Aita H, Ueki S, et al. Effect of Z-103 on wound healing by dermal incision in guinea pigs [in Japanese]. *Nippon Yakurigaku Zasshi*. 1992 Aug;100(2):165-72. [PMID: 1385281]
10. Shimada T, Watanabe N, Ohtsuka Y, et al. Polaprezinc down-regulates proinflammatory cytokine-induced nuclear factor-kappaB activation and interleukin-8 expression in gastric epithelial cells. *J Pharmacol Exp Ther*. 1999 Oct;291(1): 345-52. [PMID: 10490923]
11. Takei M. The development of polaprezinc research [in Japanese]. *Yakugaku Zasshi*. 2012;132(3):271-7. [PMID: 22382829]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

© XYMOGEN
DRS-179
Rev. 08/05/19

PhosphaLine™

100% Pure Polyenylphosphatidylcholine Concentrate



Available in 100 softgels and 8 fl oz (236.5 mL)

Discussion

Phospholipids are the basic building blocks of cellular membranes. Every phospholipid contains two fatty acid tails (triglycerides contain three) linked to a group of molecules containing phosphorus. The phosphorus-containing “head” of a phospholipid is hydrophilic; the “tails” are hydrophobic and love oil. When phospholipids come in contact with water, the hydrophobic tails line up soldier-fashion next to each other with the hydrophilic head groups on either side forming a very thin, flexible (or “fluid”), and partially permeable bilayer structure—the cell membrane.*

The cell membrane is where virtually all the important metabolic reactions occur. But lowered phospholipid availability may sometimes limit these essential functions. While the body can biosynthesize phospholipids from other substances, the process requires many enzymes and a great deal of energy. Exogenous sources of phospholipids can supplement biosynthesis. Research suggests that supporting phospholipid availability is important in cellular protection and repair and in membrane fluidity.^[1,2] Furthermore, scientific understanding of the importance of phospholipids in organ and system health continues to grow. As explained by Krosnjari et al, “A healthy cell membrane leads to healthy cells and then healthy tissue and then to healthy organs or body systems and finally, healthy bodies and minds.”*^[3]

Phosphatidylcholine is a class of phospholipids that, while similar in many respects to other types of phospholipids, has some important health-promoting differences. The most distinguishable physical characteristics between simple phospholipids and phosphatidylcholine are the choline head and the unsaturated fatty acid chains that comprise the tail. Phosphatidylcholine is perhaps the most important molecule among tens of thousands of molecules that comprise a cell, accounting for nearly 50% of the cell membrane.*

Not only does phosphatidylcholine support healthy cell membrane composition and function, it also supports healthy choline levels and brain acetylcholine formation.^[4] Furthermore, areas of

Clinical Applications

- » Supports Healthy Cell Membrane Composition and Normal Membrane Repair Mechanisms*
- » Supports Cell Membrane Fluidity*
- » Supports Liver Health and Function*
- » Supports Detoxification Enzymes*
- » Supports Cardiovascular Health*
- » A Source of Choline (~130 mg/softgel)

*PhosphaLine™ provides 2.7 g of pure polyenylphosphatidylcholine (PPC) per serving plus the highest concentrated source of 1,2 DLPC (dilinoleoylphosphatidylcholine). Unlike most other phosphatidylcholine products on the market, PhosphaLine contains no other phospholipids, aside from PPC and DLPC, that may compete for absorption. Studies suggest that PPC ingestion increases choline levels in the blood and brain and supports acetylcholine synthesis for healthy neuronal and cell function. Daily supplementation of PPC may help maintain healthy brain and liver function, healthy cholesterol levels already within the normal range, and gastric mucosal protection. PPC is widely used to support healthy aging.**

research suggesting the health benefits that may be gained from phosphatidylcholine supplementation include liver function,^[2,5] detoxification,^[2,5] lipid metabolism and lipoprotein biosynthesis,^[6,7] cytoprotection (gastric, beta cells),^[8,9] and cytokine formation.*^[10,11]

Polyenylphosphatidylcholine (PPC) is a polyunsaturated phosphatidylcholine extracted from soybeans. As an excellent source of phosphatidylcholine, PPC supplementation has been widely studied.^[2,4,7-9,12] PhosphaLine provides a patented and purified source of 100% pure PPC. PPC is thought to be functionally superior to other forms of phosphatidylcholine because of its content of 1,2-dilinoleoylphosphatidylcholine (DLPC) and linoleic acid, which binds at the c1 and c2 positions of the DLPC molecule.*^[2,3,11,12]

1,2 dilinoleoylphosphatidylcholine (DLPC) The quantitatively and qualitatively dominating molecule in PPC is DLPC, and PhosphaLine provides up to 52% DLPC. The presence of DLPC in PPC is the most important difference between PPC and typical phospholipids, such as triple lecithin and raw lecithin, and this difference is thought to be the main reason for the advantages PPC has over other phospholipids.^[11,12] Increasing the DLPC content of cell membranes increases membrane fluidity and therefore positively influences membrane-dependent functions.^[2] For instance, in vitro research suggests that DLPC can modulate the inflammatory response through nuclear erythroid 2-related factor 2 (Nrf2).^[11] Other in vitro work revealed that PPC has strong antioxidant activity and that DLPC is mainly responsible for its protective effect.*^[12]

Fatty Acids As stated earlier, the fatty acid tails of soy-derived PPC provide polyunsaturated fatty acids. Each of our cells can produce many of the lipid tails, such as saturated (palmitic and stearic) fatty acids and monounsaturated (oleic and nervonic) fatty acids, but not essential polyunsaturated fatty acids.*

PhosphaLine™ Supplement Facts

Serving Size: 3 Softgels

	Amount Per Serving	%Daily Value
Calories	30	
Total Fat	3 g	4%†
Polyenylphosphatidylcholine (PPC)(from soybean lecithin)	2.7 g	**

†Percent Daily are based on a 2,000 calorie diet.
** Daily Value not established.

Other Ingredients: Softgel (porcine gelatin, vegetable glycerin, water), glycerides and fatty acids (from safflower oil and sunflower seed oil glyceride), medium-chain triglyceride oil, and ethanol.
Contains: Soy.

DIRECTIONS: Take two to three softgels daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep tightly closed in a dry place at controlled room temperature 15°-30°C (59°-86°F), out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, dairy products, fish, shellfish, peanuts, tree nuts, egg, artificial colors, artificial sweeteners, or artificial preservatives.

PhosphaLine™ Liquid Supplement Facts

Serving Size: One Teaspoon (about 5 mL)

	Amount Per Serving	%Daily Value
Calories	30	
Total Fat	3 g	4%†
Polyenylphosphatidylcholine (PPC)(from soybean lecithin)	3 g	**

†Percent Daily are based on a 2,000 calorie diet.
** Daily Value not established.

Other Ingredients: Glycerides and fatty acids (from safflower seed oil and sunflower seed oil glyceride), medium-chain triglyceride oil, ethanol, and D-alpha-tocopherol.
Contains: Soy.

DIRECTIONS: As a dietary supplement, take one teaspoon per day or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep tightly closed in a dry place at controlled room temperature 15°-30°C (59°-86°F), out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, artificial colors, artificial sweeteners, or artificial preservatives.

References

- Cui Z, Houweling M. Phosphatidylcholine and cell death. *Biochim Biophys Acta*. 2002 Dec 30;1585(2-3):87-96. Review. [PMID: 12531541]
- Gundermann KJ, Kuenker A, Kuntz E, et al. Activity of essential phospholipids (EPL) from soybean in liver diseases. *Pharmacol Rep*. 2011;63(3):643-59. [PMID: 21857075]
- Krosnar S, Todić M, Bakić S, et al. Oral acute toxicity of polyenylphosphatidylcholine (PPC) in rats. *Bosn J Basic Med Sci*. 2005 Aug;5(3):63-68. [PMID: 16351585]
- Magil SG, Zeisel SH, Wurtman RJ. Effects of ingesting soy or egg lecithins on serum choline, brain choline and brain acetylcholine. *J Nutr*. 1981 Jan;111(1):166-70. [PMID: 7192727]
- Lieber CS. New concepts of the pathogenesis of alcoholic liver disease lead to novel treatments. *Curr Gastroenterol Rep*. 2004 Feb;6(1):60-65. [PMID: 14720455]
- Cohn JS, Kamili A, Wat E, et al. Dietary phospholipids and intestinal cholesterol absorption. *Nutrients*. 2010 Feb;2(2):116-27. [PMID: 22254012]
- Kirsten R, Heintz B, Nelson K, et al. Polyenylphosphatidylcholine improves the lipoprotein profile in diabetic patients. *Int J Clin Pharmacol Ther*. 1994 Feb;32(2):53-56. [PMID: 8004358]
- Lee SH, Han YM, Min BH, et al. Cytoprotective effects of polyenylphosphatidylcholine (PPC) on beta-cells during diabetic induction by streptozotocin. *J Histochem Cytochem*. 2003 Aug;51(8):1005-15. [PMID: 12871982]
- Demirbilek S, Ersoy MO, Demirbilek S, et al. Effects of polyenylphosphatidylcholine on cytokines, nitrite/nitrate levels, antioxidant activity and lipid peroxidation in rats with sepsis. *Intensive Care Med*. 2004 Oct;30(10):1974-78. [PMID: 15045164]
- Kovács T, Varga G, Erces D, et al. Dietary phosphatidylcholine supplementation attenuates inflammatory mucosal damage in a rat model of experimental colitis. *Shock*. 2012 Aug;38(2):177-85. [PMID: 22576006]
- Son Y, Lee JH, Kim NH, et al. Dilinoleoylphosphatidylcholine induces the expression of the anti-inflammatory heme oxygenase-1 in RAW264.7 macrophages. *Biofactors*. 2010 May-Jun;36(3):210-15. [PMID: 20336709]
- Aleynik SI, Leo MA, Takeshige U, et al. Dilinoleoylphosphatidylcholine is the active antioxidant of polyenylphosphatidylcholine. *J Invest Med*. 1999 Nov;47(9):507-12. [PMID: 10572382]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

PMS Soothe™

Menstrual Cycle Support*



Available in 60 capsules

Discussion

This tradition-based, multi-herb formula combines “female herbs” and traditional tonics that have been chosen by means of clinical observation for their complementary and compounding effects.

Chaste Berry Extract (*Vitex angus-castus*) has been used for centuries to support women with hormone-related gynecologic complaints. Modern research has validated this traditional use by showing that various preparations of chaste berry demonstrate positive effects in women with premenstrual syndrome (PMS).^[1,2] The German Commission E approves the use of chaste berry to support menstrual cycle regularity, breast tenderness, and PMS; and it is widely recommended by family physicians and gynecologists in Germany.^[3] Iridoids and flavonoids are thought to exert benefits through indirect effects on various hormones, especially prolactin and progesterone.^{*[3,4]}

Parsley (*Petroselinum crispum*) promotes fluid balance. Its effect appears to be mediated through an inhibition of the sodium-potassium pump. As an aquaretic, parsley is ascribed the benefit of increasing urine volume while supporting retention of electrolytes. Parsley is also considered to have cleansing and detoxifying properties.^{*[5,6]}

Dandelion (*Taraxacum officinale*) has been commonly used for its ability to help maintain healthy fluid balance and for its cleansing effects. In vitro research suggests that the active constituents in dandelion—which include luteolin, quercetin, and inulin—suppress cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS), increase antioxidant activity, upregulate phase II detoxification, and support bifidobacteria growth.^{*[7,8]}

Dong Quai Extract (*Angelica sinensis*) has its origins in China, Japan, and Korea, where it has been traditionally used to balance the female cycle and address common symptoms of PMS. Research suggests that dong quai affects the contractive rhythm of the uterus. Many functional medicine practitioners believe dong quai works best in combination with other herbs to support menstrual regularity.^{*[9]}

Clinical Applications

- » Offers Natural Support for Women with Common Premenstrual Complaints*
- » Provides Herbs That Have a Long History of Use in Women’s Reproductive Health*

*PMS Soothe™ is a comprehensive blend of Native American and Chinese herbs traditionally used to provide balance and support for a healthy menstrual cycle.**

Licorice Extract (*Glycyrrhiza glabra*) functions as a weak phytoestrogen and has traditionally been used to help regulate menstruation and relieve commonly experienced menstruation-related muscle cramping. In vitro research also suggests that licorice has a positive influence on inflammatory pathways.^{*[10,11]}

Peony (*Paeonia lactiflora*), also known as bai shao yao, is a Chinese herb used to help regulate menses and decrease minor pain. In traditional Chinese medicine (TCM), peony and licorice are used together and are thought to have great synergism relating to their effects on neuromuscular junctions.^{*[12]}

Tangerine (*Citrus reticulata*) is a traditional Chinese herb also known as pericarpium or chen pi. It is derived from aged tangerine peel and traditionally used to help relieve the common premenstrual complaint of breast tenderness. TCM practitioners also use chen pi to help prevent stagnation and relieve minor abdominal fullness and minor pain.^{*[13]}

Ginger Root (*Zingiber officinale*) has been studied for its effects on inflammatory mediator biosynthesis. In fact, in vitro work suggests that components of ginger can positively affect the expression of inflammatory genes. It is thought that the production of inflammatory mediators may encourage some of the common symptoms of PMS. Ginger is also thought to be good for circulation, nausea, and gas. In this formula, ginger is included for its “warming” effect which balances the “cooling” effects of other herbs.^{*[14]}

Red Raspberry (*Rubus idaeus*) has been used by women for centuries to support and balance the reproductive system, and to relax the uterus. In traditional herbalism, red raspberry has been connected to female health and is used as a remedy to support normal menstrual flow.^{*[15,16]}

Bupleurum (*Bupleurum falcatum*), also known as chai hu, is a traditional “female cycle balancer” that has uterine-calming

Continued on next page

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

PMS Soothe™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Chaste Berry Extract (<i>Vitex agnus-castus</i>)(fruit)(0.5% agnuside and 0.4% aucubin)	225 mg	**
Bupleurum (<i>Bupleurum chinense</i>)(root)	100 mg	**
Tangerine (<i>Citrus reticulata</i>)(peel)	100 mg	**
Dandelion 4:1 Extract (<i>Taraxacum officinale</i>)(root)	100 mg	**
Dong Quai Extract (<i>Angelica sinensis</i>)(root)(1% lingustilide)	100 mg	**
Peony (<i>Paeonia lactiflora</i>)(root)	100 mg	**
Ginger 10:1 Extract (<i>Zingiber officinale</i>)(root)	60 mg	**
Parsley (<i>Petroselinum crispum</i>)(leaves)	50 mg	**
Red Raspberry (<i>Rubus idaeus</i>)(leaves)	50 mg	**
Licorice Extract (<i>Glycyrrhiza glabra</i>)(root)(20% glycyrrhizin)	25 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, silica, and medium-chain triglyceride oil.**DIRECTIONS:** Take two capsules daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.**DOES NOT CONTAIN:** Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

activity. Chinese medicine practitioners use chai hu to unblock liver qi stagnation that manifests as menstrual cramping, emotional changes, and breast tenderness. An animal study suggests that chai hu supports a healthy mood through central adrenergic mechanisms.^[17] It also has been shown to regulate the neuroendocrine system by increasing beta-endorphin and decreasing epinephrine and dopamine, which probably accounts for its relaxing properties.*^[18]

References

- Schellenberg R, Zimmermann C, Drewe J, et al. Dose-dependent efficacy of the Vitex agnus castus extract Ze 440 in patients suffering from premenstrual syndrome. *Phytotherapy Research*. 2012 Sep 27. pii: S0944-7113(12)00280-2. doi: 10.1016/j.phymed.2012.08.006. Epub ahead of print. [PMID: 23022391]
- Zamani M, Neghab N, Torabian S. Therapeutic effect of Vitex agnus castus in patients with premenstrual syndrome. *Acta Med Iran*. 2012;50(2):101-06. [PMID: 22359078]
- Roemheld-Hamm B. Chasteberry. *Am Fam Physician*. 2005 Sep 1;72(5):821-24. [PMID: 16156340]
- Schellenberg R. Treatment for the premenstrual syndrome with agnus castus fruit extract: prospective, randomised, placebo controlled study. *BMJ*. 2001 Jan 20;322(7279):134-37. [PMID: 11159568]
- Wright CI, Van-Buren L, Kroner CI, et al. Herbal medicines as diuretics: a review of the scientific evidence. *J Ethnopharmacol*. 2007 Oct 8;114(1):1-31. [PMID: 17804183]
- Natural Medicines Comprehensive Database. *Parsley*. Stockton, CA: Therapeutic Research Faculty; 1995-2012. <http://naturaldatabase.therapeuticresearch.com/nd/Search.aspx?rn=4&cs=&s=ND&pt=100&id=792&ds=&name=PARSLEY&searchid=38851690>. Accessed December 13, 2012.
- Schütz K, Carle R, Schieber A. Taraxacum—a review on its phytochemical and pharmacological profile. *J Ethnopharmacol*. 2006 Oct 11;107(3):313-23. [PMID: 16950583]
- Natural Medicines Comprehensive Database. *Dandelion*. Stockton, CA: Therapeutic Research Faculty; 1995-2012. <http://naturaldatabase.therapeuticresearch.com/nd/Search.aspx?cs=&s=ND&pt=100&id=706&fs=ND&searchid=34505380>. Accessed December 14, 2012.
- Angelica sinensis [monograph]. *Altern Med Rev*. 2004 Dec;9(4):429-33. [PMID: 15656714]
- Glycyrrhiza glabra [monograph]. *Altern Med Rev*. 2005 Sep;10(3):230-37. [PMID: 16164378]
- Licorice. Medline Plus. <http://www.nlm.nih.gov/medlineplus/druginfo/natural/881.html>. Accessed December 17, 2012.
- Monograph. Peony. *Altern Med Rev*. 2001 Oct;6(5):495-99. [PMID: 11703170]
- Zhang M, Shen Y, Zhu Z, et al. Pharmacological studies on warming the middle-jiao to alleviate pain by Pericarpium Zanthoxyli [in Chinese]. *Zhongguo Zhong Yao Za Zhi*. 1991 Aug;16(8):493-97, 513. [PMID: 1804190]
- Lee HY, Park SH, Lee M, et al. 1-Dehydro-[10]-gingerdione from ginger inhibits IKK β activity for NF- κ B activation and suppresses NF- κ B-regulated expression of inflammatory genes. *Br J Pharmacol*. 2012 Sep;167(1):128-40. [PMID: 22489648]
- Rahnama P, Montazeri A, Huseini HF, et al. Effect of Zingiber officinale R. rhizomes (ginger) on pain relief in primary dysmenorrhea: a placebo randomized trial. *BMC Complement Altern Med*. 2012 Jul 10;12:92. doi:10.1186/1472-6882-12-92. [PMID: 22781186]
- Red Raspberry. University of Michigan Health System. <http://www.uofmhealth.org/health-library/hn-2154002#hn-2154002-uses>. Accessed December 14, 2012.
- Lee B, Yun HY, Shim I, et al. Bupleurum falcatum prevents depression and anxiety-like behaviors in rats exposed to repeated restraint stress. *Microbial Biotechnol*. 2012 Mar;22(3):422-30. [PMID: 22450800]
- Chen JX, Ji B, Lu ZL, et al. Effects of chai hu (radix burpleuri) containing formulation on plasma beta-endorphin, epinephrine and dopamine on patients. *Am J Chin Med*. 2005;33(5):737-45. [PMID: 16265986]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Prenatal Essentials™

Prenatal Support Packets*



Available in 30 packets

Discussion

Each component of Prenatal Essentials has an important role in maternal nutrition and a healthy pregnancy outcome.* For ease of use, all are provided together in one convenient packet:

Omega-3s, Vitamin D, and Choline The importance of these nutrients in maternal health and healthy fetal neurodevelopment cannot be overstated. Adequate intakes of omega-3 fatty acids are critically important during pregnancy because they are building blocks of fetal brain and retina.^[1] Furthermore, it is believed that during mid-to-late gestation, docosahexaenoic acid (DHA) plays an important role in the development of neurocognitive and neuromotor functions.^[1] Within the last several years, research on vitamin D and the prevalence of its insufficiency has exploded. Vitamin D is important for neuronal growth and development. Maternal vitamin D metabolism and vitamin D insufficiency are important considerations given the association made between maternal vitamin D status during pregnancy and brain function in the child.^[2-4] Maternal reserves of choline are depleted during pregnancy, yet its availability is critical because it is the starting material for important metabolites that play key roles in fetal development, particularly brain development. Current data show that most pregnant women are not achieving target intake levels and, in addition, certain common genetic variants may increase requirements.*^[5,6]

Folate Prenatal Essentials provides calcium folinate as well as 5-methyltetrahydrofolate (5-MTHF)—the most bioavailable, active form of folate. 5-MTHF is provided as Quatrefolic®, which is proven to have greater stability, solubility, and bioavailability than calcium salt forms of 5-MTHF. Adequate folate nutrition before and during pregnancy supports normal fetal neurological development and a healthy pregnancy outcome.^[7] Supplementing with bioactive 5-MTHF allows for the bypassing of steps in folate metabolism. This may be especially beneficial in those with digestive concerns and those with genetic variations in folate metabolism.*^[8,9]

Clinical Applications

- » Supports Maternal Nutrition Before and During Pregnancy*
- » Supports a Healthy Pregnancy Outcome*
- » Provides Key Ingredients to Promote Healthy Fetal Neurodevelopment*

*Prenatal Essentials™ is designed to meet the higher nutritional needs of women who are preparing for pregnancy or are pregnant. Not only does Prenatal Essentials address these needs in a comprehensive way, but it also reflects recent research with its inclusion of generous levels and active forms of key nutrients, such as OmegaPure DHA™, 5-methyltetrahydrofolate as Quatrefolic®, 2000 IU of Vitamin D3, Ferrochel® iron, and TRAACS® chelated minerals. This formula is designed to assure optimal utilization while being gentle to the digestive tract.**

B Vitamins Prenatal Essentials provides generous levels of these critical vitamins because sufficient levels are needed for energy production; cell growth and division, including that of red blood cells; and neurologic, cardiovascular, immune, dermatological, and emotional health.^[10] In addition, B6 (pyridoxal 5'-phosphate) has been studied for its ability to soothe the stomach during pregnancy.*^[11,12]

Bioavailable, yet Gentle Iron Approximately 20% of pregnant women have iron deficiency anemia^[13], and it's likely that a greater number have insufficient levels of iron. Ferrochel iron has been shown to help increase and maintain blood levels of iron while being gentle to the stomach and colon. This form of iron performs the stomach's work in advance by binding minerals to amino acids, an action which allows the iron molecules to pass easily through the intestinal wall thereby avoiding stomach upset (as seen with other forms of iron) while maximizing absorption.*^[14,15]

Other Important Nutrients Prenatal Essentials provides supportive nutrients, including vitamins A, C, D, and E; mixed carotenoids; and selenium to address the increased physiological stress of pregnancy and promote healthy tissue maintenance and growth. Research suggests that good maternal antioxidant status may positively influence birth weight.^[16] Zinc, copper, manganese, chromium, and molybdenum are provided as TRAACS® amino acid chelates for improved absorption in the gut and optimal assimilation. Calcium is provided as DimaCal®, a patented complex of calcium and malic acid that not only supports optimal calcium utilization and gastric tolerance but also supports the body's energy-producing cycles. Calcium is provided in a 2:1 ratio with magnesium, which may help support normal muscular contraction in legs and arteries.^[17,18] Vitamin K and iodine are added to help ensure maternal sufficiency.*

Prenatal Essentials™ Supplement Facts

Serving Size: 1 Packet

	5 Prenatal Multivitamin/Mineral Capsules		1 OmegaPure DHA™ Softgel	
	Amount Per Serving	%DV for Pregnant or Lactating Women	Amount Per Serving	%DV for Pregnant or Lactating Women
Calories			10	
Total Fat			1 g	1% [†]
Vitamin A (60% as natural beta-carotene and 40% as retinyl palmitate)	1500 mcg	115%		
Vitamin C (ascorbic acid)	100 mg	83%		
Vitamin D3 (cholecalciferol)	50 mcg (2000 IU)	333%		
Vitamin E (as d-alpha tocopheryl succinate and mixed tocopherols)	134 mg	705%		
Vitamin K2 (as menaquinone-7)	100 mcg	111%		
Thiamin (as thiamine HCl)	5 mg	357%		
Riboflavin (as riboflavin 5'-phosphate sodium)	5 mg	313%		
Niacin (as niacinamide)	25 mg	139%		
Vitamin B6 (as pyridoxal 5'-phosphate)	20 mg	1000%		
Folate (400 mcg DFE as Quatrefolic® (6S)-5-methyltetrahydrofolate acid, glucosamine salt and 400 mcg DFE as calcium folinate)	800 mcg DFE	133%		
Vitamin B12 (as methylcobalamin)	50 mcg	1786%		
Biotin	300 mcg	857%		
Pantothenic Acid (as d-calcium pantothenate)	25 mg	357%		
Choline (as choline dihydrogen citrate)	200 mg	36%		
Calcium (as DimaCal® di-calcium malate)	400 mg	31%		
Iron (as Ferrochel® ferrous bisglycinate chelate)	30 mg	111%		
Iodine (as potassium iodide)	225 mcg	78%		
Magnesium (as Albion® di-magnesium malate)	200 mg	50%		
Zinc (as TRAACS® zinc bisglycinate chelate)	20 mg	154%		
Selenium (as L-selenomethionine)	100 mcg	143%		
Copper (as TRAACS® copper bisglycinate chelate)	2 mg	154%		
Manganese (as TRAACS® manganese bisglycinate chelate)	5 mg	192%		
Chromium (as TRAACS® chromium nicotinate glycinate chelate)	100 mcg	222%		
Molybdenum (as TRAACS® molybdenum glycinate chelate)	100 mcg	200%		
Malic Acid (as di-calcium malate and Albion® di-magnesium malate)	1.6 g	**		
Fish Oil Concentrate			1 g	**
DHA (docosahexaenoic acid)			580 mg	**
EPA (eicosapentaenoic acid)			60 mg	**

[†] Percent Daily Values are based on a 2,000 calorie diet.

** Daily Value (DV) not established.

Other Ingredients for Prenatal Multivitamin/Mineral Capsule: HPMC (capsule), microcrystalline cellulose, ascorbyl palmitate, silica, and medium-chain triglyceride oil.**Other Ingredients for OmegaPure DHA:** Gelatin, glycerin, purified water, and mixed natural tocopherols.**Contains:** Fish (tuna, sardine, anchovy).**DIRECTIONS:** Take contents of one packet daily as directed by your healthcare practitioner.**WARNING:** Accidental overdose of iron-containing products is a leading cause of fatal poisoning in children under 6. Keep this product out of reach of children. In case of accidental overdose, call a doctor or poison control center immediately.**CAUTIONS:** Consult your healthcare practitioner before use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.**Vitamin A:** Excess vitamin A intake may be toxic and may increase the risk of birth defects. Pregnant women and women who may become pregnant should not exceed 1,500 mcg RAE (5,000 IU) of preformed vitamin A (retinyl acetate or retinyl palmitate) per day.**Vitamin K:** Consider total vitamin K intake (food and supplements) if you are taking blood-thinning medication.**STORAGE:** Keep closed in a cool, dry place out of reach of children.**DOES NOT CONTAIN:** Wheat, gluten, yeast, soy protein, dairy products, shellfish, peanuts, tree nuts, egg, artificial colors, artificial sweeteners, or artificial preservatives.

Albion, DimaCal, FerroChel, and TRAACS are registered trademarks of Albion Laboratories, Inc. Malates covered by U.S. Patent 6,706,904 and patents pending.



Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,662.

References

- Coletta JM, Bell SJ, Roman AS. Omega-3 fatty acids and pregnancy. *Rev Obstet Gynecol.* 2010;3(4):163-71. [PMID: 21364848]
- Currenti SA. Understanding and determining the etiology of autism. *Cell Mol Neurobiol.* 2010 Mar;30(2):161-71. [PMID: 19774457]
- Cannell JJ. On the aetiology of autism. *Acta Paediatr.* 2010 Aug;99(8):1128-30. [PMID: 20491697]
- Grant WB, Soles CM. Epidemiologic evidence supporting the role of maternal vitamin D deficiency as a risk factor for the development of infantile autism. *Dermatoendocrinol.* 2009 Jul;1(4):223-28. [PMID: 20592795]
- Caudill MA. Pre- and postnatal health: evidence of increased choline needs. *J Am Diet Assoc.* 2010 Aug;110(8):1198-206. [PMID: 20656095]
- Zeisel SH. Importance of methyl donors during reproduction. *Am J Clin Nutr.* 2009 Feb;89(2):673S-77S. [PMID: 19116320]
- Folic Acid Fact Sheet. U.S. Department of Health and Human Services, Office on Women's Health. <http://www.womenshealth.gov/publications/our-publications/fact-sheet/folic-acid.cfm>. Updated May 18, 2010. Accessed June 19, 2012.
- Prinz-Langenohl R, Brämswig S, Tobolski O, et al. [6S]-5-methyltetrahydrofolate increases plasma folate more effectively than folic acid in women with the homozygous or wild-type 677C->T polymorphism of methylenetetrahydrofolate reductase. *Br J Pharmacol.* 2009 Dec;158(8):2014-21. [PMID: 19917061]
- Lamers Y, Prinz-Langenohl R, Brämswig S, et al. Red blood cell folate concentrations increase more after supplementation with [6S]-5-methyltetrahydrofolate than with folic acid in women of childbearing age. *Am J Clin Nutr.* 2006 Jul;84(1):156-61. [PMID: 16825690]
- B Vitamins. Medline PLUS. <http://www.nlm.nih.gov/medlineplus/bvitamins.html>. Accessed March 28, 2011.
- Ebrahimi N, Maltepe C, Einarson A. Optimal management of nausea and vomiting of pregnancy. *Int J Womens Health.* 2010 Aug;2:241-48. [PMID: 21151729]
- Jewell D, Young G. Interventions for nausea and vomiting in early pregnancy. *Cochrane Database Syst Rev.* 2003;(4):CD000145. [PMID: 14583914]
- Anemia During Pregnancy. Utah Department of Health: Maternal and Infant Health Program. http://health.utah.gov/mihp/pregnancy/preged/duringpreg/Anemia_during_pregnancy.htm. Accessed March 29, 2011.
- Szarfarc SC, de Cassana LM, Fujimori E, et al. Relative effectiveness of iron bisglycinate chelate (Ferrochel) and ferrous sulfate in the control of iron deficiency in pregnant women. *Arch Latinoam Nutr.* 2001 Mar;51(1 Suppl 1):42-47. [PMID: 11688081]
- Ferrochel Effectiveness. Albion Human Nutrition. <http://www.albionferrochel.com/effectiveness>. Accessed March 28, 2011.
- Osorio JC, Cruz E, Milanés M, et al. Influence of maternal redox status on birth weight. *Reprod Toxicol.* 2011 Jan;31(1):35-40. [PMID: 20934506]
- Roffe C, Sils S, Crome P, et al. Randomised, cross-over, placebo controlled trial of magnesium citrate in the treatment of chronic persistent leg cramps. *Med Sci Monit.* 2002 May;8(5):CR326-30. [PMID: 12011773]
- Jain S, Sharma P, Kulshreshtha S, et al. The role of calcium, magnesium, and zinc in pre-eclampsia. *Biol Trace Elem Res.* 2010 Feb;133(2):162-70. [PMID: 19547932]

Additional references available upon request

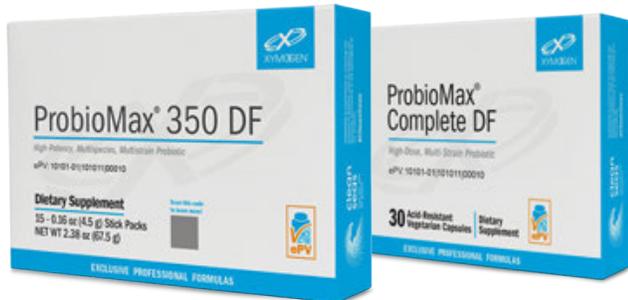
All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

© XYMOGEN
DRS-159
Rev. 08/05/19

ProbioMax[®] 350 DF & ProbioMax[®] Complete DF

High-Potency, Multispecies, Multistrain Probiotic



ProbioMax 350 DF is available in 15 stick packs
ProbioMax Complete DF is available in 30 acid-resistant vegetable capsules

Discussion

Multiplicity of microbiota species is characteristic of the GI microbiome in healthy individuals, and a loss in species has adverse effects.^[1-3] Dietary diversity and taking a variety of probiotic species and strains are methods that help support a healthy microbiome.^[1,4] ProbioMax 350 DF and ProbioMax Complete DF provide 18 different strains belonging to 13 different species of three different genera. For consumer convenience, these formulas are available as a powder at a dose of 350 CFUs per stick pack or encapsulated at a maintenance dose of 45 billion CFUs per capsule. The HOWARU and FloraFIT strains that comprise these formulas are stable, proven, and trusted worldwide.*

Featured Strains: *Bifidobacterium lactis* HN019[®] and *Lactobacillus rhamnosus* HN001[®]

B. lactis HN019[®] and *L. rhamnosus* HN001[®] have been studied extensively in vitro and in vivo (in animals and humans) to establish beneficial effects and safety.^[5-20] In human research, *B. lactis* HN019[®] significantly decreased mean whole-gut transit time in adults compared to placebo.^[6] Supplementation also had a positive effect on functional GI symptoms, as were self-reported by patient surveys. In a randomized, double-blind, placebo-controlled human dietary intervention study in subjects 60 or more years of age, supplementary HN019[®] resulted in desirable changes in the intestinal microflora, including significant increases in bifidobacteria and lactobacilli.^[1,3] HN019[®] has also shown promising effects on parameters of cardiovascular and metabolic health. Compared with baseline and control group values, individuals taking 27 billion CFU had a significant reduction in body mass index, significant improvements in cholesterol and low-density lipoprotein metabolism, and significant decreases in tumor necrosis factor-alpha and interleukin-6.^[19] In a three-week study, individuals consuming low-fat/low-lactose milk supplemented with HN019[®] or HN001[®] showed increased immune activity when compared to a milk-alone run in.^[10] These increases were significantly correlated with age; that is, subjects older than 70 years experienced significantly greater improvements than those under 70 years. Researchers suggest that these results demonstrate the ability of HN019[®] and HN001[®] to combat some of the deleterious effects of immunosenescence on cellular immunity.^[10] Animal studies demonstrate the ability of HN001[®] to support natural and acquired immunity as well as promote resistance.^[17,18] More recently, human studies have demonstrated HN001[®]'s protective effect on skin health in genetically susceptible individuals.*^[7,11]

Clinical Applications

- » Supports a Healthy Microbiome*
- » Replenishes Good Bacteria in the Gut*
- » Supports the Natural Immune Response*
- » Supports Lactose Digestion*
- » Supports Bowel Regularity*

*ProbioMax[®] 350 DF and ProbioMax[®] Complete DF feature a diverse blend of HOWARU[®] and FloraFIT[®] probiotic strains to support a healthy gut microbiome. Each strain is well-researched and identity-verified and has been genetically characterized and properly classified for your safety and assurance. These strains were not only selected for their health benefits and complementary actions but also for their viability and stability. To protect the bacteria from light and moisture, opaque and foil-lined packaging is utilized for both formulas.**

Other Strains in ProbioMax 350 DF and ProbioMax Complete DF Have Demonstrated Probiotic Effects in Either In Vitro or In Vivo Research:

- Cause the development of inhibition zones around *Clostridium difficile*, *Salmonella typhimurium*, *Staphylococcus aureus*, *Escherichia coli*, and *Listeria monocytogenes* in agar assays*^[20]
- Populate vaginal tissue*^[21]
- Induce moderate maturation and activation of dendritic cells*^[22]
- Degrade oxalates*^[23]
- Increase IgA and IgG responses*^[25]
- Reduce levels of *E. coli* and *enterococcus* after antibiotic therapy*^[26]
- Help increase and recover numbers of intestinal lactobacilli and/or bifidobacteria*^[27]
- Promote well-being in relation to intestinal cytokine production*^[28,29]
- Improve gastrointestinal health and well-being when under challenge*^[27,29]
- Help maintain upper respiratory health*^[30]
- Alter the fecal microbiota in obese subjects*^[31]
- Maintain healthy fluid balance and integrity of intestinal wall*^[32]
- Support intestinal barrier function*^[32]

Genetic Testing, Acid and Bile Tolerance, Adhesion

The lactic acid-producing strains in these formulas have a history of safe consumption and, based on testing, have excellent probiotic potential.^[20,33,34] Each bacterium has been genetically characterized and properly classified by independent labs. The organisms have demonstrated tolerance to low pH conditions (hydrochloric acid and pepsin at pH3 for one hour at 37°C), tolerance to bile at concentrations existing in the duodenum, and the ability to adhere to human epithelial cell lines (Caco-2 and HT-29). Adhesion is thought to be an important factor affecting these bacteria's length of time in the intestines, their ability to modulate immune function, and their ability to take up intestinal "real estate" in competition with other organisms.*^[34]

Many of the strains have had additional studies performed, which include testing for the following^[20]:

Continued on next page

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN[®] Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

Competitive Inhibition – The ability of probiotics to maintain a healthy microbial balance in the gut is unquestionably important to its usefulness. Probiotics produce inhibitory compounds that limit the growth of other organisms, they compete with other organisms for adhesion sites and nutrients, and they inhibit the production of toxins, among other actions.*

Cytokine and Immune Modulation – Microbiota are key elements in the body's defense system. Cytokines regulate immune system function, and the included strains have demonstrated the ability to upregulate or downregulate various cytokines.*

Antibiotic Resistance – Antibiotic susceptibility patterns are an important means of indicating the potential of an organism to be readily inactivated by antibiotics used in human therapy. Importantly, acquired antibiotic resistance or antibiotic resistance transfer have not been detected in any of these strains.*

ProbioMax® 350 DF Supplement Facts

Serving Size: 1 Stick Pack (about 4.5 g)
Servings Per Container: 15

	Amount Per Serving	%Daily Value
Calories	15	
Total Carbohydrate	3 g	1%†
Protein	1 g	
Sodium	5 mg	<1%†
<i>Lactobacillus acidophilus</i> La-14®	625 mg (125 Billion CFU)†	**
<i>Bifidobacterium lactis</i> BI-04®	200 mg (100 Billion CFU)†	**
<i>Lactobacillus bulgaricus</i> Lb-87™	100 mg (5 Billion CFU)†	**
<i>Bifidobacterium longum subsp. Infantis</i> BI-26™	100 mg (5 Billion CFU)†	**
HOWARU® Bifido (<i>Bifidobacterium lactis</i> HN019®)	83.3 mg (25 Billion CFU)†	**
<i>Lactobacillus plantarum</i> Lp-115®	50 mg (20 Billion CFU)†	**
<i>Bifidobacterium longum</i> BI-05™	50 mg (5 Billion CFU)†	**
<i>Bifidobacterium bifidum</i> Bb-06™	50 mg (5 Billion CFU)†	**
HOWARU® Rhamnosus (<i>Lactobacillus rhamnosus</i> HN001®)	33.3 mg (15 Billion CFU)†	**
<i>Lactobacillus rhamnosus</i> Lr-32®	25 mg (5 Billion CFU)†	**
<i>Lactobacillus brevis</i> Lbr-35™	25 mg (5 Billion CFU)†	**
<i>Lactobacillus gasseri</i> Lg-36™	25 mg (5 Billion CFU)†	**
<i>Lactobacillus casei</i> Lc-11®	16.67 mg (5 Billion CFU)†	**
<i>Lactobacillus salivarius</i> Ls-33®	16.67 mg (5 Billion CFU)†	**
<i>Bifidobacterium breve</i> Bb-03™	16.67 mg (5 Billion CFU)†	**
<i>Lactococcus lactis</i> LI-23™	16.67 mg (5 Billion CFU)†	**
<i>Streptococcus thermophilus</i> St-21™	12.5 mg (5 Billion CFU)†	**
<i>Bifidobacterium bifidum/Bifidobacterium lactis</i> Bb-02™	11.1 mg (5 Billion CFU)†	**

† Percent Daily Values are based on a 2,000 calorie diet.

** Daily Value not established.

Other Ingredients: Potato maltodextrin, calcium silicate, and magnesium stearate.

‡ Colony-Forming Units

†† Formulated with 650 billion CFU‡ at time of manufacture.

HN001® and HN019® are registered trademarks of Fonterra™ Limited and are licensed to DuPont Nutrition Biosciences.

DIRECTIONS: Dissolve the contents of one stick pack (350 billion CFU)†† into 2-4 oz of pure water and consume once daily, or take as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if stick pack is damaged.

STORAGE: Keep tightly closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, artificial colors, artificial sweeteners, or artificial preservatives.

HOWARU®

HOWARU®, FLORAFIT® and the HOWARU® logo are registered trademarks of DuPont or its affiliates.

ProbioMax® Complete DF Supplement Facts

Serving Size: 1 Capsule
Servings Per Container: 30

	Amount Per Serving	%Daily Value
<i>Lactobacillus acidophilus</i> La-14®	80 mg (16 Billion CFU)†	**
<i>Bifidobacterium lactis</i> BI-04®	26 mg (13 Billion CFU)†	**
<i>Lactobacillus bulgaricus</i> Lb-87™	12 mg (0.6 Billion CFU)†	**
<i>Bifidobacterium longum subsp. Infantis</i> BI-26™	12 mg (0.6 Billion CFU)†	**
HOWARU® Bifido (<i>Bifidobacterium lactis</i> HN019®)	10.66 mg (3.2 Billion CFU)†	**
<i>Lactobacillus plantarum</i> Lp-115®	7.5 mg (3 Billion CFU)†	**
<i>Bifidobacterium longum</i> BI-05™	6 mg (0.6 Billion CFU)†	**
<i>Bifidobacterium bifidum</i> Bb-06™	6 mg (0.6 Billion CFU)†	**
HOWARU® Rhamnosus (<i>Lactobacillus rhamnosus</i> HN001®)	4.44 mg (2 Billion CFU)†	**
<i>Lactobacillus rhamnosus</i> Lr-32®	3 mg (0.6 Billion CFU)†	**
<i>Lactobacillus brevis</i> Lbr-35™	3 mg (0.6 Billion CFU)†	**
<i>Lactobacillus gasseri</i> Lg-36™	3 mg (0.6 Billion CFU)†	**
<i>Lactobacillus casei</i> Lc-11®	2 mg (0.6 Billion CFU)†	**
<i>Lactobacillus salivarius</i> Ls-33®	2 mg (0.6 Billion CFU)†	**
<i>Bifidobacterium breve</i> Bb-03™	2 mg (0.6 Billion CFU)†	**
<i>Lactococcus lactis</i> LI-23™	2 mg (0.6 Billion CFU)†	**
<i>Streptococcus thermophilus</i> St-21™	1.5 mg (0.6 Billion CFU)†	**
<i>Bifidobacterium bifidum/Bifidobacterium lactis</i> Bb-02™	1.3 mg (0.6 Billion CFU)†	**

** Daily Value not established.

Other Ingredients: Potato maltodextrin, acid-resistant capsule (hypromellose, gellan gum, and water), hydroxypropyl cellulose, magnesium stearate, and calcium silicate.

† Colony-forming units

HN001® and HN019® are registered trademarks of Fonterra™ Limited and are licensed to DuPont Nutrition Biosciences.

DIRECTIONS: Take one capsule with water daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner.

STORAGE: Keep tightly closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, artificial colors, artificial sweeteners, or artificial preservatives.

HOWARU®

HOWARU® and the HOWARU® logo are registered trademarks of DuPont or its affiliates.



All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

References

- Heiman ML, Greenway FL. A healthy gastrointestinal microbiome is dependent on dietary diversity. *Mol Metab*. 2016 Mar 5;5(5):317-20. [PMID: 27110483]
- Lloyd-Price J, Abu-Ali G, Huttenhower C. The healthy human microbiome. *Genome Med*. 2016 Apr 27;8(1):51. doi: 10.1186/s13073-016-0307-y. [PMID: 27122046]
- Xu Z, Knight R. Dietary effects on human gut microbiome diversity. *Br J Nutr*. 2015 Jan;113 Suppl:S1-5. doi: 10.1017/S0007114514004127. [PMID: 25498959]
- Grimm V, Riedel CU. Manipulation of the microbiota using probiotics. *Adv Exp Med Biol*. 2016;902:109-17. doi: 10.1007/978-3-319-31248-4_8. [PMID: 27161354]
- Sanders ME. Summary of probiotic activities of Bifidobacterium lactis HN019. *J Clin Gastroenterol*. 2006 Oct;40(9):776-83. [PMID: 17016131]
- Gopal P, Prasad J, Gill H. Effects of consumption of Bifidobacterium lactis HN019 (DR-10™) and galacto-oligosaccharides on the microflora of the gastrointestinal tract in human subjects. *Nutr Res*. 2003;23:1313-28. <http://www.sciencedirect.com/science/article/pii/S0271531703001349>. Accessed May 4, 2016.
- Sistek D, Kelly R, Wickens K, et al. Is the effect of probiotics on atopic dermatitis confined to food sensitized children? *Clin Exp Allergy*. 2006 May;36(5):629-33. [PMID: 16650048]
- Waller PA, Gopal PK, Leyer GJ, et al. Dose-response effect of Bifidobacterium lactis HN019 on whole gut transit time and functional gastrointestinal symptoms in adults. *Scand J Gastroenterol*. 2011 Sep;46(9):1057-64. [PMID: 21663486]
- Sazawal S, Dhingra U, Sarkar A, et al. Efficacy of milk fortified with a probiotic Bifidobacterium lactis HN019 (DR-10™) and prebiotic galacto-oligosaccharide in prevention of morbidity—a community based double masked randomized trial. *J Pediatr Gastroenterol Hepatol Nutr*. Second World Congress; July 3-7, 2004;371-74; Paris, France. <http://apiyca.org/wp-content/uploads/2014/01/Sazawal-2004-DR10-and-prebiotic-morbidity.pdf>. Accessed May 3, 2016
- Gill HS, Rutherford KJ, Cross ML. Dietary probiotic supplementation enhances natural killer cell activity in the elderly: an investigation of age-related immunological changes. *J Clin Immunol*. 2001 Jul;21(4):264-71. [PMID: 11506196]
- Wickens K, Stanley TV, Mitchell EA, et al. Early supplementation with Lactobacillus rhamnosus HN001 reduces eczema prevalence to 6 years: does it also reduce atopic sensitization? *Clin Exp Allergy*. 2013 Sep;43(9):1048-57. [PMID: 23957340]
- Dekker J W, Wickens K, Black P, et al. Safety aspects of probiotic bacterial strains Lactobacillus rhamnosus HN001 and Bifidobacterium animalis subsp. lactis HN019 in human infants aged 0-2 years. *Int Dairy J*. March 2009;19(3): 149-154. <http://www.sciencedirect.com/science/article/pii/S0958694608001787>. Accessed May 4, 2016
- Ahmed M, Prasad J, Gill H, et al. Impact of consumption of different levels of Bifidobacterium lactis HN019 on the intestinal microflora of elderly human subjects. *J Nutr Health Aging*. 2007 Jan-Feb;11(1):26-31. [PMID: 17315077]
- Sheih YH, Chiang BL, Wang LH, et al. Systemic immunity-enhancing effects in healthy subjects following dietary consumption of the lactic acid bacterium Lactobacillus rhamnosus HN001. *J Am Coll Nutr*. 2001 Apr;20(2Suppl):149-56. [PMID: 11349938]
- Bifidobacterium lactis HN019—a probiotic with proven efficacy. Technical Memorandum 58-1e. Brabrand, Denmark: Danisco. [on file]
- HOWARU™ Rhamnosus. Technical Memorandum 2053-1e. Brabrand, Denmark: Danisco. [on file]
- Gill HS, Rutherford KJ. Immune enhancement conferred by oral delivery of Lactobacillus rhamnosus HN001 in different milk-based substrates. *J Dairy Res*. 2001 Nov;68(4):611-16. [PMID: 11928957]
- Gill HS, Shu Q, Lin H, et al. Protection against translocating Salmonella typhimurium infection in mice by feeding the immuno-enhancing probiotic Lactobacillus rhamnosus strain HN001. *Med Microbiol Immunol*. 2001 Dec;190(3):97-104. [PMID: 11827205]
- Bernini LJ, Simão AN, Alfieri DF, et al. Beneficial effects of Bifidobacterium lactis on lipid profile and cytokines in patients with metabolic syndrome: A randomized trial. Effects of probiotics on metabolic syndrome. *Nutrition*. 2016 Jun;32(6):716-9. [PMID: 27126957]
- Strain Characteristics Reports. Brabrand, Denmark: Danisco. [on file]
- De Alberti D, Russo R, Terruzzi F, et al. Lactobacilli vaginal colonisation after oral consumption of Respecta(®) complex: a randomized controlled pilot study. *Arch Gynecol Obstet*. 2015 Oct;292(4):861-67. [PMID: 25855055]
- Elawadli I, Brisbin JT, Mallard BA, et al. Differential effects of lactobacilli on activation and maturation of mouse dendritic cells. *Benef Microbes*. 2014 Sep;5(3):323-34. [PMID: 24913839]
- Giardina S, Scilironi C, Michelotti A, et al. In vitro anti-inflammatory activity of selected oxalate-degrading probiotic bacteria: potential applications in the prevention and treatment of hyperoxaluria. *J Food Sci*. 2014 Mar;79(3):M384-90. [PMID: 24471378]
- Turróni S, Vitali B, Bendazzoli C, et al. Oxalate consumption by lactobacilli: evaluation of oxalyl-CoA decarboxylase and formyl-CoA transferase activity in Lactobacillus acidophilus. *J Appl Microbiol*. 2007 Nov;103(5):1600-09. [PMID: 17953571]
- Paineau D, Carcano D, Leyer G, et al. Effects of seven potential probiotic strains on specific immune responses in healthy adults: a double-blind, randomized, controlled trial. *FEMS Immunol Med Microbiol*. 2008 Jun;53(1):107-13. [PMID: 18422632]
- Luo X, Lun Y, Gao W, et al. Effects of spent culture supernatant of Lactobacillus acidophilus on intestinal flora in mice with antibiotic-associated diarrhoea [in Chinese]. *World Chinese J Digestology*. 2006;14(19):1870-73. http://en.cnki.com.cn/Article_en/CJFDTotal-XXHB200619005.htm. Accessed May 16, 2016.
- Bartosch S, Woodmansey EJ, Paterson JC, et al. Microbiological effects of consuming a synbiotic containing Bifidobacterium bifidum, Bifidobacterium lactis, and oligofructose in elderly persons, determined by real-time polymerase chain reaction and counting of viable bacteria. *Clin Infect Dis*. 2005 Jan 1;40(1):28-37. [PMID: 15614689]
- Foligne B, Nutten S, Granette C, et al. Correlation between in vitro and in vivo immunomodulatory properties of lactic acid bacteria. *World J Gastroenterol*. 2007 Jan 14;13(2):236-43. [PMID: 17226902]
- Collado MC, Meriluoto J, Salminen S. Role of commercial probiotic strains against human pathogen adhesion to intestinal mucus. *Letf Appl Microbiol*. 2007 Oct;45(4):454-60. [PMID: 17897389]
- West NP, Horn PL, Pyne DB, et al. Probiotic supplementation for respiratory and gastrointestinal illness symptoms in healthy physically active individuals. *Clin Nutr*. 2014 Aug;33(4):581-87. [PMID: 24268677]
- Larsen N, Vogensen FK, Gøbel RJ, et al. Effect of Lactobacillus salivarius Ls-33 on fecal microbiota in obese adolescents. *Clin Nutr*. 2013 Dec;32(6):935-40. [PMID: 23510724]
- Elian SD, Souza EL, Vieira AT, et al. Bifidobacterium longum subsp. infantis BB-02 attenuates acute murine experimental model of inflammatory bowel disease. *Benef Microbes*. 2015;6(3):277-86. [PMID: 25391346]
- Kailasapathy K, Chin J. Survival and therapeutic potential of probiotic organisms with reference to Lactobacillus acidophilus and Bifidobacterium spp. *Immunol Cell Biol*. 2000 Feb;78(1):80-88. [PMID: 10651933]
- Tuomola E, Crittenden R, Playne M, et al. Quality assurance criteria for probiotic bacteria. *Am J Clin Nutr*. 2001;73(suppl):393S-98S. <http://ajcn.nutrition.org/content/73/2/393s.full.pdf+html>. Accessed May 16, 2016.

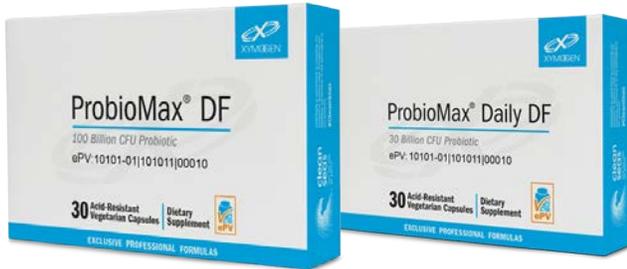
Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

ProbioMax[®] DF

30 & 100 Billion CFU Probiotics



ProbioMax[®] Daily DF is available in 30 capsules and 60 capsules
ProbioMax[®] DF is available in 30 capsules

Discussion

Supplementation with probiotics has many mechanisms of action that benefit health, including but not limited to: (1) supporting metabolic activity, such as the production of short-chain fatty acids and vitamins, nutrient absorption, and digestion of lactose; (2) adhering to intestinal epithelial cells to help maintain a healthy balance of organisms in the intestinal tract; (3) helping to establish populations of good bacteria after disruption in balance; (4) supporting immune function; (5) promoting intestinal epithelial cell survival; (6) supporting healthy bowel function; and (7) degrading oxalates.*^[1-8]

Common challenges associated with probiotic supplementation are maintaining stability of the organisms during distribution and shelf life and, once taken by a consumer, survival of the organisms as they travel through the digestive tract so that they reach the target tissue (intestines) alive. To help ensure stability, XYMOGEN packages the ProbioMax capsules in sealed, nitrogen-purged aluminum blister packs to serve as protection from factors proven to compromise the stability of probiotics, such as heat, moisture, and oxygen. Careful selection of organisms is another way XYMOGEN helps ensure stability. Careful organism selection, as performed for ProbioMax, is also a critical aspect of supporting digestive survival. To further support resistance to low pH and the delivery of microorganisms to the small intestines, XYMOGEN employs DRcaps[™] gastro-resistant capsules. These specially designed, innovative capsules help slow exposure of actives to stomach acid to promote a more targeted release.*

HOWARU[™] (*Bifidobacterium lactis* HN019[®]) Discovered in 1899, *B. lactis* play a key role in the human microflora throughout a person's life. Researchers have identified strain HN019[®] as having excellent probiotic potential based upon its ability to survive the transit through the human gastrointestinal tract, adhere to epithelial cells, and proliferate.^[6] *B. lactis* HN019[®] has been extensively studied, and its safety and effectiveness is well accepted.^[7,8] To assess the impact of *Bifidobacterium lactis* HN019[®] supplementation on whole-gut transit

Clinical Applications

- » Helps Maintain a Healthy Intestinal Microecology*
- » Supports the Natural Immune Response*
- » Supports Bowel Regularity*
- » Supports Lactose Digestion*

ProbioMax[®] DF is a vegetarian, dairy- and gluten-free, four-strain probiotic totaling 100 billion CFU per capsule. Each vegetarian capsule is sealed in nitrogen-purged aluminum blister packs to serve as protection from factors proven to compromise the stability of probiotics such as heat, moisture, and oxygen. ProbioMax DF provides four researched strains of beneficial bacteria, including the extensively studied HN019[®] strain of *Bifidobacterium lactis*. These live microorganisms have proven health benefits and well-established safety, and have been tested for epithelial cell adhesion and/or resistance to low pH.**

*To further support resistance to low pH and the delivery of microorganisms to the small intestines, XYMOGEN employs DRcaps[™] gastro-resistant capsules. These specially designed, innovative capsules help slow exposure of actives to stomach acid and ensure more targeted release.**

time in adults, 100 subjects were given daily doses for 14 days of 17.2 billion colony-forming units (CFU), 1.8 billion CFU, or placebo. Decreases in mean whole-gut transit time over the 14-day study period were statistically significant in the high-dose group and the low-dose group, but not in the placebo group.^[8] This level of dosing also supported other parameters of healthy GI function, as were self-reported by patient survey.^[9] In another study of preschool-age children, supplementing milk for one year with 1.9 x 10⁹ CFU per day *B. lactis* HN019[®] and 2.4 g/day of prebiotic oligosaccharides supported both healthy iron status and weight gain.^[9] In a randomized, double-blind, placebo-controlled human dietary intervention study in elderly subjects (>60 yrs.), supplementary *B. lactis* HN019[®] resulted in statistically significant increases in the beneficial organisms *bifidobacteria* and *lactobacilli*.^{*[10]}

***Lactobacillus acidophilus* (*Lactobacillus acidophilus* La-14)** This common inhabitant of the human mouth, intestinal tract, and vagina, is also found in some traditional fermented milks (e.g., kefir) and is widely used in probiotic foods and supplements. It has a history of safe human consumption. The *L. acidophilus* La-14 strain is of human origin and has been identified as a type A1 *L. acidophilus*. *L. acidophilus* shows excellent adhesion to human epithelial cell-lines.^{*[11,12]}

***Lactobacillus plantarum* (*Lactobacillus plantarum* Lp-115)** This bacteria was isolated from plant material and is abundantly present in lactic acid-fermented foods, such as olives and sauerkraut. In vitro studies have shown that *L. plantarum* strain Lp-115 has excellent adhesion to epithelial cell lines.^[13] In addition, *L. plantarum* is resistant to low pH conditions and survives the presence of bile at duodenal concentrations.^{*[13,14]}

***Bifidobacterium longum* (*Bifidobacterium longum* BI-05)** The *B. longum* BI-05 strain is well accepted as safe for human consumption. *B. longum* is resistant to low pH and bile salts and is well suited to the intestinal environment.^{*[14]}

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

ProbioMax® DF Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Proprietary Blend <i>Lactobacillus acidophilus</i> La-14® <i>Bifidobacterium longum</i> BI-05™ <i>Lactobacillus plantarum</i> Lp-115®	409 mg (50 Billion CFU ¹)	**
HOWARU® Bifido (<i>Bifidobacterium lactis</i> HN019®)	167 mg (50 Billion CFU ¹)	**

** Daily Value not established.

Other Ingredients: HPMC (acid-resistant capsule), microcrystalline cellulose, magnesium stearate, and silica.
¹Colony-Forming Unit

DIRECTIONS: Take one capsule with water daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner.

DOES NOT CONTAIN: Wheat, gluten, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.

HOWARU®

HOWARU® and the HOWARU® logo are registered trademarks of DuPont or its affiliates.
HN019® is a registered trademark of Fonterra™ Limited and is licensed to DuPont Nutrition Biosciences.

**ProbioMax® Daily DF Supplement Facts**

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Proprietary Blend <i>Lactobacillus acidophilus</i> La-14® <i>Bifidobacterium longum</i> BI-05™ <i>Lactobacillus plantarum</i> Lp-115®	174 mg (15 Billion CFU ¹)	**
HOWARU® Bifido (<i>Bifidobacterium lactis</i> HN019®)	50 mg (15 Billion CFU ¹)	**

** Daily Value not established.

Other Ingredients: Microcrystalline cellulose, HPMC (acid-resistant capsule), stearic acid, magnesium stearate, and silica.
¹Colony-Forming Unit

DIRECTIONS: Take one capsule with water daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner.

DOES NOT CONTAIN: Wheat, gluten, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: No refrigeration necessary. Keep closed in a cool, dry place out of reach of children.

HOWARU®

HOWARU® and the HOWARU® logo are registered trademarks of DuPont or its affiliates.
HN019® is a registered trademark of Fonterra™ Limited and is licensed to DuPont Nutrition Biosciences.

**References**

- Vanderpool C, Yan F, Polk DB. Mechanisms of probiotic action: Implications for therapeutic applications in inflammatory bowel diseases. *Inflamm Bowel Dis*. 2008 Nov;14(11):1585-96. [PMID: 18623173]
- Abratt VR, Reid SJ. Oxalate-degrading bacteria of the human gut as probiotics in the management of kidney stone disease. *Adv Appl Microbiol*. 2010;72:63-87. [PMID: 20602988]
- Masood MI, Qadir MI, Shirazi JH, et al. Beneficial effects of lactic acid bacteria on human beings. *Crit Rev Microbiol*. 2011 Feb;37(1):91-98. [PMID: 21162695]
- Turrioni S, Vitali B, Bendazzoli C, et al. Oxalate consumption by lactobacilli: evaluation of oxalyl-CoA decarboxylase and formyl-CoA transferase activity in *Lactobacillus acidophilus*. *J Appl Microbiol*. 2007 Nov;103(5):1600-09. [PMID: 17953571]
- Shu Q, Lin H, Rutherford KJ, et al. Dietary *Bifidobacterium lactis* (HN019) enhances resistance to oral *Salmonella typhimurium* infection in mice. *Microbiol Immunol*. 2000;44(4):213-22. [PMID: 10832963]
- Gopal P, et al. Effects of the consumption of *Bifidobacterium lactis* HN019 (DR10TM) and galacto-oligosaccharides on the microflora of the gastrointestinal tract in human subjects. *Nutr. Res*. 2003;23:1313-28. <http://www.daniscosupplements.com/clinical-study-bibliography.html>. Accessed June 24, 2011.
- Danisco. Clinical study bibliography & abstracts. HOWARU Bifido – Bif. lactis HN019. <http://www.daniscosupplements.com/clinical-study-bibliography.html>. Accessed June 24, 2011.
- Waller PA, Gopal PK, Leyer GJ, et al. Dose-response effect of *Bifidobacterium lactis* HN019 on whole gut transit time and functional gastrointestinal symptoms in adults. *Scand J Gastroenterol*. 2011 Sep;46(9):1057-64. [PMID: 21663486]
- Sazawal S, Dhingra U, Hiremath G, et al. Effects of *Bifidobacterium lactis* HN019 and prebiotic oligosaccharide added to milk on iron status, anemia, and growth among children 1 to 4 years old. *J Pediatr Gastroenterol Nutr*. 2010 Sep;51(3):341-46. [PMID: 20601905]
- Ahmed M, Prasad J, Gill H, et al. Impact of consumption of different levels of *Bifidobacterium lactis* HN019 on the intestinal microflora of elderly human subjects. *J Nutr Health Aging*. 2007 Jan-Feb;11(1):26-31. [17315077]
- Greene JD, Klaenhammer TR. Factors involved in adherence of lactobacilli to human Caco-2 cells. *Appl Environ Microbiol*. 1994 Dec;60(12):4487-94. [PMID: 7811085]
- Kleeman EG, Klaenhammer TR. Adherence of *Lactobacillus* species to human fetal intestinal cells. *J Dairy Sci*. 1982 Nov;65(11):2063-69. [PMID: 7153393].
- Collado MC, Meriluoto J, Salminen S. Role of commercial probiotic strains against human pathogen adhesion to intestinal mucus. *Lett Appl Microbiol*. 2007 Oct;45(4):454-60. [PMID: 17897389]
- Ding WK, Shah NP. Acid, bile, and heat tolerance of free and microencapsulated probiotic bacteria. *J Food Sci*. 2007 Nov;72(9):M446-50. [PMID: 18034741]

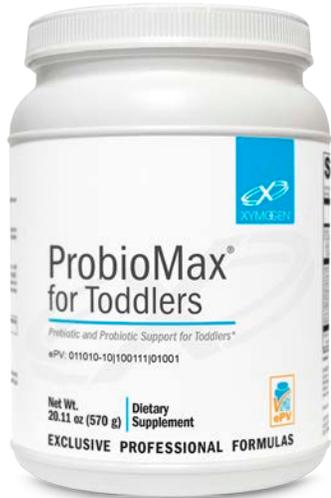
Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

ProbioMax[®] for Toddlers

Prebiotic and Probiotic Support for Toddlers*



Available in 30 servings

Discussion

The human microbiome is an individual's unique microorganism profile. It is partially imprinted when a baby travels through the mother's birth canal and is further shaped when the baby is exposed to organisms through breastfeeding and in the environment. Like a fingerprint, no two humans have the same microbiome; this unique profile is maintained throughout the individual's life and is essential to the person's biological identity. After about the age of two, humans do not adopt any more permanent "residents" in their microbiome; additional microorganisms are essentially transient though some persist more than others.

Results of clinical studies in young children have suggested that supplemental probiotics may be beneficial to the development of gut flora, digestive health, and immune health.*^[1-8]

HOWARU[®] Protect *Lactobacillus rhamnosus* HN001[®]

The immune-responsiveness of a child's digestive system is affected by genetic predisposition, diet, state of bacterial colonization, and exposure to substances such as pathogens and medications that may disrupt the microbial balance. It is thought that dysregulation or interference with the early development of the intestinal mucosal defense system may be at the root of many intestinal and systemic health issues.^[9] A review of 13 randomized controlled trials, which included seven studies in children aged six months to 12 years, adults aged 18 to 65, and older people (N = 3720), suggested that probiotics are more effective than placebo when considering that fewer upper respiratory tract events occurred and duration was reduced in subjects taking probiotics.^[10] Additionally, a systematic review based on clinical trials in healthy children (N = 2417) from birth to age 10 suggested the use of probiotics decreased the incidence of respiratory events.*^[11]

In a series of studies over a period of six years, investigators looked at the impact of 6 billion colony-forming units (CFUs) of *Lactobacillus rhamnosus* (*L. rhamnosus*) HN001 and 9 billion CFUs of *Bifidobacterium animalis* subsp. *lactis* (*B. animalis* subsp. *lactis*)

Clinical Applications

- » Helps Promote Gut Flora Development*
- » Supports Digestive Health*
- » Supports Immune Health/Function*
- » Promotes Balance of Gut Microbiota*

ProbioMax[®] for Toddlers provides a comprehensive multi-strain combination of probiotics with 10 billion colony-forming units (CFUs) to help promote gut flora development, promote digestive health, and support immune function. Galacto-oligosaccharides (GOS)—prebiotics with a similar structure to those naturally found in breast milk—are included to promote the balance of gut microbiota towards more beneficial species.*

HN019 on immune markers associated with allergic issues and atopic sensitization. In a birth cohort (N = 474) at high-risk for skin related conditions, mothers were supplemented with HN001, HN019, or placebo from 35 weeks gestation through six months of breastfeeding, and infants were supplemented from birth until two years. The results indicated that HN001 impacted the immune markers IFN- γ , IgA, and IgE in subjects supplemented until age two, but effects were seen up to age six. Higher IgE concentration in early life is associated with allergic issues, including those of the skin, so these results suggest that the specific probiotic HN001 may be an appropriate intervention for at-risk children who need immune system support. The absence of a significant outcome in the HN019 group indicated that benefits may be species-specific.*^[12-14]

In a double-blind placebo-controlled trial in children aged one to five years (N = 398) randomized to receive 10 billion CFUs of HN001 or placebo for three months, the regular intake of the probiotic suggested modulation of intestinal immune responses; however, researchers noted that the difference between placebo and HN001 supplemented groups in frequency or severity of respiratory episodes was not significant. Fecal *Lactobacillus* counts as well as IgA levels increased significantly in the HN001 group compared to control, suggesting stimulation of the secretory immune response in the gut.*^[15]

Although more evidence is needed to draw firm conclusions, this body of research puts forward that HN001 may positively impact respiratory and immune health in young children.*

Lactobacillus reuteri (*L. reuteri*)

As a natural colonizer of the gastrointestinal flora, *L. reuteri* has also been studied for use in occasional intestinal upset. In a double-blind, placebo-controlled, randomized study in children (N = 44) at least six months old with constipation, administration of *L. reuteri* had a positive effect on stool frequency.^[16] Another double-blind study with *L. reuteri* (100 million CFUs) evaluated frequency and duration of loose stools and other health outcomes in healthy children (N = 336) aged six to

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

36 months. When compared to placebo, the *L. reuteri* supplemented group exhibited less intestinal and respiratory episodes at both the three- and six-month test points.^{*[17]}

Other Strains

In a double-blind placebo-controlled study, children aged three to five years (N = 326) were assigned to receive placebo, *Lactobacillus acidophilus* (*L. acidophilus*) NCFM, or *L. acidophilus* in combination with *B. animalis* subsp *lactis*[®] Bi-07 for a six-month period. Both the single and combination test groups demonstrated less seasonal immune symptoms and number of school days missed attributable to those symptoms.^[18] In another study, an analysis was conducted at the start and after nine months of supplementation on 140 fecal samples from a larger cohort (n = 379) of children aged two to five years who were given placebo, 2 billion CFUs of *Lactobacillus paracasei* (*L. paracasei*) Lpc-37, or 5 billion CFUs of *Bifidobacterium lactis* (*B. lactis*). Following intervention, *L. paracasei* correlated positively with total *Bifidobacterium* counts and branched-chain fatty acid levels, and *B. lactis* counts were found to compare positively with total bacterial counts and negatively with short-chain fatty acid levels. Although additional research is needed to make firm conclusions, both of these findings were linked to reduced risk for loose stools in the intervention groups.^{*[19]}

Galacto-Oligosaccharides (GOS)

GOS is comprised of a short chain of galactose molecules, this type of oligosaccharide has been studied for its prebiotic effect of stimulating the development of bifidobacteria. A review of experimental and clinical data demonstrates that a prebiotic mixture of GOS modulates the intestinal flora similarly to flora modulation by human breast milk.^[20,21] Although randomized controlled trials have studied the effects of prebiotic supplementation, additional well-designed studies are warranted.*

ProbioMax[®] for Toddlers Supplement Facts

Serving Size: 2 Scoops (about 19 g)

	Amount Per Serving	%DV for Children 1 through 3 Years of Age
Calories	70	
Total Carbohydrate	19 g	13%†
Dietary Fiber	4 g	29%
Total Sugars	4 g	**
Galacto-Oligosaccharides (GOS)	5 g	**
<i>Lactobacillus reuteri</i> 1E1™	25.96 mg (1.5 Billion CFU) [‡]	**
<i>Lactobacillus acidophilus</i> NCFM [®]	8.04 mg (2 Billion CFU) [‡]	**
<i>Bifidobacterium bifidum</i> Bb-06™	5.72 mg (1 Billion CFU) [‡]	**
<i>Bifidobacterium lactis</i> Bi-04 [®]	4.18 mg (2 Billion CFU) [‡]	**
HOWARU [®] Protect <i>Lactobacillus rhamnosus</i> HN001 [®]	2.64 mg (1.5 Billion CFU) [‡]	**
<i>Lactobacillus paracasei</i> Lpc-37 [®]	2.54 mg (1 Billion CFU) [‡]	**
<i>Bifidobacterium lactis</i> Bi-07 [®]	2.24 mg (1 Billion CFU) [‡]	**

†Percent Daily Values are based on a 1,000 calorie diet.
 ** Daily Value (DV) not established.

Other Ingredients: Maltodextrin and microcrystalline cellulose.
Contains: Milk

DIRECTIONS: *Toddlers 12 months through 3 years:* 2 scoops, or take as directed by your healthcare practitioner. Mix thoroughly with food or liquid; do not mix with hot food or hot liquids.

Consult your healthcare practitioner prior to use. If the child is taking medication, potential interactions should be discussed with the child’s healthcare practitioner. This product should be given to healthy children only and not children with immune challenges.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, soy, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

HOWARU[®]

‡colony-forming unit

HOWARU[®], FLORAFIT[®] and the HOWARU[®] logo are registered trademarks of DuPont or its affiliates.

HN001[®] is a registered trademark of Fonterra™ Limited and is licensed to DuPont Nutrition Biosciences.

Safety

Each of the seven probiotic strains in ProbioMax for Toddlers has a history of safe consumption in healthy young children and, based on testing, is regarded to have excellent probiotic potential. Each bacterium has been genetically characterized and properly classified by independent labs to assure quality. It should be noted that further research will help solidify the clinical applications of probiotic species, optimal duration, and dose.*

§Bifidobacterium lactis has been reclassified as *Bifidobacterium animalis* subsp *lactis*. For ease, it still tends to be referred to as *Bifidobacterium lactis*, as it is on this label. Moreover, companies trademark their particular strains by adding a letter and number code after them.

References

- Singh VP, Sharma J, Babu S, et al. Role of probiotics in health and disease: a review. *J Pak Med Assoc.* 2013 Feb;63(2):253-7. [PMID: 23894906]
- Food and Agriculture Organization of the United Nations and World Health Organization. Guidelines for the Evaluation of Probiotics in Food. London, ON, Canada: 30 April–1 May 2002. https://www.who.int/foodsafety/fs_management/en/probiotic_guidelines.pdf. Accessed January 9, 2019.
- Wilkins T, Sequoia J. Probiotics for gastrointestinal conditions: a summary of the evidence. *Am Fam Physician.* 2017 Aug 1;96(3):170-178. [PMID: 28762696]
- Markowiak P, Śliżewska K. Effects of probiotics, prebiotics, and synbiotics on human health. *Nutrients.* 2017 Sep 15;9(9). [PMID: 28914794]
- Sanders M, Merenstein C, Merrifield C, et al. Probiotics for human use. *Nutrition Bulletin.* 2018 Sept;43(3):212–225. doi:10.1111/nbu.12334.
- Johnson CL, Versalovic J. The human microbiome and its potential importance to pediatrics. *Pediatrics.* 2012 May;129(5):950-60. [PMID: 22473366]
- Stewart CJ, Ajami NJ, O'Brien JL, et al. Temporal development of the gut microbiome in early childhood from the TEDDY study. *Nature.* 2018 Oct;562(7728):583-588. [PMID: 30356187]
- Vatanen T, Plichta DR, Somani J, et al. Genomic variation and strain-specific functional adaptation in the human gut microbiome during early life. *Nat Microbiol.* 2018 Dec 17. [PMID: 30559407]
- Thomas D, Greer F. Probiotics and prebiotics in pediatrics. 2010 Dec; 126(6):1217-31. <http://pediatrics.aappublications.org/content/126/6/1217>. Accessed January 9, 2019.
- Hao Q, Dong BR, Wu T. Probiotics for preventing acute upper respiratory tract infections. *Cochrane Database Syst Rev.* 2015 Feb 3;(2):CD006895. [PMID: 25927096]
- Araujo GV, Oliveira Junior MH, Peixoto DM, et al. Probiotics for the treatment of upper and lower respiratory-tract infections in children: systematic review based on randomized clinical trials. *J Pediatr (Rio J).* 2015 Sep-Oct;91(5):413-27. [PMID: 26054771]
- Wickens K, Black PN, Stanley TV, et al. A differential effect of 2 probiotics in the prevention of eczema and atopy: a double-blind, randomized, placebo-controlled trial. *J Allergy Clin Immunol.* 2008 Oct;122(4):788-794. [PMID: 18762327]
- Wickens K, Black P, Stanley TV, et al. A protective effect of *Lactobacillus rhamnosus* HN001 against eczema in the first 2 years of life persists to age 4 years. *Clin Exp Allergy.* 2012 Jul;42(7):1071-9. [PMID: 22702506]
- Wickens K, Stanley TV, Mitchell EA, et al. Early supplementation with *Lactobacillus rhamnosus* HN001 reduces eczema prevalence to 6 years: does it also reduce atopic sensitization? *Clin Exp Allergy.* 2013 Sep;43(9):1048-57. [PMID: 23957340]
- Cáceres P, Montes S, Vega N, et al. Effects of *Lactobacillus rhamnosus* HN001 on acute respiratory infections and intestinal secretory IgA in children. *J Pediatr Infect Dis.* 2010;5(4):353-362. doi:10.3233/JPI-2010-0267.
- Coccorullo P, Strisciuglio C, Martinelli M, et al. *Lactobacillus reuteri* (DSM 17938) in infants with functional chronic constipation: a double-blind, randomized, placebo-controlled study. *J Pediatr.* 2010 Oct;157(4):598-602. [PMID: 20542295]
- Gutiérrez-Castrellón P, López-Velázquez G, Díaz-García L, et al. Diarrhea in preschool children and *Lactobacillus reuteri*: a randomized controlled trial. *Pediatrics.* 2014 Apr;133(4):e904-9. [PMID: 24639271]
- Leyer GJ, Li S, Mubasher ME, et al. Probiotic effects on cold and influenza-like symptom incidence and duration in children. *Pediatrics.* 2009 Aug;124(2):e172-9. [PMID: 19651563]
- Hemalatha R, Ouweland AC, Saarinen MT, et al. Effect of probiotic supplementation on total lactobacilli, bifidobacteria and short chain fatty acids in 2–5-year-old children. *Microb Ecol Health Dis.* 2017 Mar 10;28(1):1298340. [PMID: 28572751]
- Fanaro S, Boehm G, Garssen J, et al. Galacto-oligosaccharides and long-chain fructo-oligosaccharides as prebiotics in infant formulas: a review. *Acta Paediatr Suppl.* 2005 Oct;94(449):22-6. [PMID: 16214761]
- Vandenplas Y, Zakharova I, Dmitrieva Y. Oligosaccharides in infant formula: more evidence to validate the role of prebiotics. *Br J Nutr.* 2015 May 14;113(9):1339-44. [PMID: 25989994]

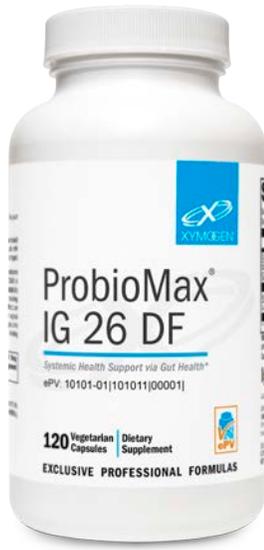
Additional references available upon request

All XYMOGEN[®] Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

ProbioMax[®] IG 26 DF

Systemic Health Support via Gut Health*



Available in 120 vegetarian capsules

Discussion

Diversity of gut microflora is characteristic of a healthy GI microbiome and contributes to overall health and vitality by promoting optimum digestion, assimilation, gut integrity, motility, and efficient removal of toxins and waste. Many internal and external influences, including stress, a poor diet, food sensitivities, medication, environmental factors, and certain disease conditions, can impact the microbial balance within this fine-tuned community. Their impact can allow for potential colonization by pathogenic organisms and disrupt a healthy balance, which can result in adverse effects ranging from GI symptoms to impaired immune response.^[1-3] Probiotics are part of the key to promoting the optimal balance of the microbiome,^[4] whether they originate from dietary sources or from supplements. Providing an increased supply of immunoglobulins also encourages a healthy balance of bacteria in the intestine. Due to the link between gut health and systemic health, supporting immunity through enhancement of a healthy GI microbiome balance promotes overall health.*

LactoSpore[®] (*Bacillus coagulans* MTCC5856)

Lactic acid-producing bacteria are suggested to play a role in GI microecology. They prevent the growth of non-beneficial microorganisms through competitive inhibition, generation of non-conducive acidic environments, and production of antibiotic-like substances.^[5] *B. coagulans* is a unique lactic acid-producing probiotic strain featuring a thermostable spore coating that enables viability throughout shelf life and the ability to survive gastric secretions intact until reaching the gut.^[6] *B. coagulans* has a well-documented safety profile.^[7] It received premarket safety approval in Canada in 2014 and has USDA GRAS status. Furthermore, since its market introduction over 20 years ago, extensive research has suggested several beneficial physiological roles for LactoSpore*:

GI Health

Studies have suggested a role for *B. coagulans* in improvement of both acute and chronic GI symptoms due to abnormalities in intestinal flora.^{*(8,9)} *B. coagulans* is indicated for reducing discomfort of intestinal gas. In a study of adults (n=61) with post-prandial abdominal pain, distention, and flatulence but no GI diagnosis, improvement on a GI symptom rating scale was noted for 10 of 12 variables with significant improvement in three of 12 GI variables.^[10] Additional studies have shown efficacy in the management of GI problems associated with infections or the use of antibiotics.^{*(11,12)}

The effect of *B. coagulans* on pain, discomfort, and bloating in patients (n=44) with irritable bowel syndrome (IBS) was evaluated over an eight-week period with statistically significant improvements noted from baseline value using a self-assessment score.^[13] Adding significance to the benefits for use in IBS, a double-blind, placebo-controlled, multicenter trial evaluating the safety and efficacy of LactoSpore in IBS patients (n=36) over a 90-day period suggested that

Clinical Applications

- » Supports a Healthy Balance of Microflora to Promote Digestive Health*
- » Provides Immunoglobulins and Immunoregulating Factors to Promote Systemic Health*
- » Enhances the Integrity of Intestinal Mucosa*

ProbioMax[®] IG 26 DF features clinically validated ingredients to support microbiome wellness and overall immune health. *LactoSpore[®]* (*Bacillus coagulans* MTCC5856) is a unique strain of shelf-stable L (+) lactic acid-producing bacteria with a naturally protective spore coating. In addition to its research-supported role in promoting healthy bacterial balance in the gut, this strain has been studied for its effects on maintaining blood lipid levels already within a healthy range and its effect on vaginal health. IG 26 DF (IgY Max™), hyperimmunized egg powder, provides immunoglobulins and immune cofactors to support the body's natural defenses by limiting non-beneficial microbial adhesion.*

daily supplementation with two billion spores significantly decreased symptoms of vomiting, bloating, diarrhea, abdominal pain, and stool frequency (P<0.01).^[14] This study ultimately resulted in licensure of a Canadian health claim for the use of LactoSpore to address IBS.*

Hyperlipidemia and Vaginal Health

While the evidence base supporting *B. coagulans* is most notable for GI health, effects on maintaining blood lipid levels already within a healthy range have been demonstrated.^[15-17] In an open-label fixed-dose trial of 17 patients with hyperlipidemia, a daily regimen of *B. coagulans* for 12 weeks suggested a significant reduction in total serum cholesterol and LDL cholesterol. The level of HDL cholesterol was marginally increased with no change in serum triglyceride concentrations noted.^[16] It has also been suggested that *B. coagulans* plays a role in the beneficial management of non-specific vaginitis.^{*(18-20)}

IgY Max™ Hyperimmunized Egg Powder

Microbial imbalance occurs when non-beneficial bacteria over-proliferate in the gut, taking up vital nutrients that beneficial flora need to survive.^[21] As an innovative approach to modifying the composition of the microbiome, ProbioMax IG 26 DF combines LactoSpore with IgY Max to help promote the attachment of beneficial flora and address non-beneficial bacteria by imparting passive immunity in the intestinal tract, thus allowing the beneficial flora to thrive.*

Decades ago, immunology researchers began investigating the possible health benefits to humans that could be achieved by the consumption of products from hyperimmunized lactating cows and laying hens.^[22] Agricultural scientists soon discovered that they could simultaneously immunize a single laying hen against multiple human germs. The resulting avian immunoglobulins, known as IgY, are transferred to the egg yolk, paralleling the way human immunoglobulins (IgG) are passed to the placenta. From this discovery, a new functional food was born: the "hyperimmune egg." IgY Max is the result of special hyperimmune egg harvesting and processing techniques that result in a polyvalent, immunoglobulin-rich, dried hyperimmune egg food product that can be consumed as a dietary supplement. Hyperimmune egg provides a concentrated source of environmentally specific IgY antibodies and immune-supporting cofactors that can confer passive immunity to those who consume it.^[22-27] There are over 100 patents associated with the production of hyperimmune egg and its use in animals and humans. Additionally, IgY Max is self-affirmed GRAS—a designation that affirms safe consumption—and it holds a Food Additive Master File number.^{*(28)}

Furthermore, in-vitro, animal, and human studies of hyperimmune egg and IgY have shown that supplemental IgY from hyperimmune egg imparts passive immunity in the intestinal tract.^{*(22,23,27,29-32)}

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN[®] Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

ProbioMax® IG 26 DF Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Calories	5	
Cholesterol	15 mg	5%
Sodium	5 mg	<1%
IgY Max™ Hyperimmunized Egg Powder	1 g	**
LactoSpore® <i>Bacillus coagulans</i> MTCC5856	10 mg (1 Billion spores)	**

Other Ingredients: HPMC (capsule), medium-chain triglyceride oil, silica, dicalcium phosphate, and sweet potato maltodextrin.

Contains: Egg

DIRECTIONS: Take two capsules twice daily with cold water, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner, and individuals with egg allergies should not consume this product. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, corn, soy, dairy products, fish, shellfish, peanuts, tree nuts, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

IgY Max™ IgY Max is a trademark of IgY Nutrition, LLC and is used under license.



LactoSpore® is a registered trademark of Sabinsa Corp.

References

- Heiman ML, Greenway FL. A healthy gastrointestinal microbiome is dependent on dietary diversity. *Mol Metab.* 2016 Mar 5;5(5):317-20. [PMID: 27110483]
- Lloyd-Price J, Abu-Ali G, Huttenhower C. The healthy human microbiome. *Genome Med.* 2016 Apr 27;8(1):51. [PMID: 27122046]
- Xu Z, Knight R. Dietary effects on human gut microbiome diversity. *Br J Nutr.* 2015 Jan;113 Suppl:S1-5. [PMID: 25498959]
- Grimm V, Riedel CJ. Manipulation of the microbiota using probiotics. *Adv Exp Med Biol.* 2016;902:109-17. [PMID: 27161354]
- Majeed M, Prakash L. Probiotics for Health and Well-Being. White Paper. East Windsor, NJ: Sabinsa Corporation; 2014.
- Majeed M, Nagabhushanam K, Natarajan S, et al. Evaluation of genetic and phenotypic consistency of *Bacillus coagulans* MTCC 5856: a commercial probiotic strain. *World J Microbiol Biotechnol.* 2016 Apr;32(4):60. [PMID: 26925622]
- Majeed M, Nagabhushanam K, Natarajan S, et al. A double-blind, placebo-controlled, parallel Study evaluating the safety of *Bacillus coagulans* MTCC 5856 in healthy individuals. *J Clin Toxicol.* 2016;6:283:2161-0495. <http://dx.doi.org/10.4172/2161-0495.1000283>.
- Hyronimus B, Le Marrec C, Urdaci MC. Coagulin, a bacteriocin-like inhibitory substances produced by *Bacillus coagulans* I4. *J Appl Microbiol.* 1998 Jul;85(1):42-50. [PMID: 9721655]
- Duc le H, Hong HA, Barbosa TM, et al. Characterization of *Bacillus* probiotics available for human use. *Appl Environ Microbiol.* 2004 Apr;70(4):2161-71. [PMID: 15066809]
- Kalman DS, Schwartz P, Alvarez S, et al. A prospective, randomized, double-blind, placebo-controlled parallel-group dual site trial to evaluate the effects of a *Bacillus coagulans*-based product on functional intestinal gas symptoms. *BMC gastroenterology.* 2009 Nov 18;9:85. [PMID: 19922649]
- Chandra RK. Effect of *Lactobacillus* on the incidence and severity of acute rotavirus diarrhoea in infants. A prospective placebo-controlled double-blind study. *Nutrition research.* 2002 Jan-Feb;22(1-2):65-69. [https://doi.org/10.1016/S0271-5317\(01\)00367-0](https://doi.org/10.1016/S0271-5317(01)00367-0).
- La Rosa M, Bottaro G, Gulino N, et al. Prevention of antibiotic-associated diarrhea with *Lactobacillus* sporegens and fructo-oligosaccharides in children. A multicentric double-blind vs placebo study [in Italian]. *Minerva pediatrica.* 2003 Oct;55(5):447-52. [PMID: 14608267]
- Hun L. *Bacillus coagulans* significantly improved abdominal pain and bloating in patients with IBS. *Postgrad Med.* 2009 Mar;121(2):119-24. [PMID: 19332970]
- Majeed M, Nagabhushanam K, Natarajan S, et al. *Bacillus coagulans* MTCC 5856 supplementation in the management of diarrhea predominant Irritable Bowel Syndrome: a double blind randomized placebo controlled pilot clinical study. *Nutr J.* 2016 Feb 27;15:21. [PMID: 26922379]
- Balliett M, Burke JR. Changes in anthropometric measurements, body composition, blood pressure, lipid profile, and testosterone in patients participating in a low-energy dietary intervention. *J Chiropr Med.* 2013 Mar;12(1):3-14. [PMID: 23997718]
- Mohan JC, Arora R, Khalilullah M. Short term hypolipidemic effects of oral *Lactobacillus* sporogenes therapy in patients with primary dyslipidemias. *Indian Heart J.* 1990 Sep-Oct;42(5):361-4. [PMID: 2086441]
- Mohan JC, Arora R, Khalilullah M. Preliminary observations on effect of *Lactobacillus* sporogenes on serum lipid levels in hypercholesterolemic patients. *Indian J Med Res.* 1990 Dec;92:431-2. [PMID: 2079358]
- Sankholkar PC, Sali M. "Myconip" (Sporlac) vaginal tablets in non-specific vaginitis. Clinical study report from B. J. Medical College, Pune, India. Unpublished. [on file]
- Kale V, Trivedi RV, Wate SP, et al. Development and evaluation of a suppository formulation containing *Lactobacillus* and its application in vaginal diseases. *Ann N Y Acad Sci.* 2005 Nov;1056:359-65. [PMID: 16387701]
- Riasi S, Dover SE, Chikindas ML. Mode of action and safety of lactosporin, a novel antimicrobial protein produced by *Bacillus coagulans* ATCC 7050. *J Appl Microbiol.* 2012 Sep;113(3):714-22. [PMID: 22737982]
- Kamada N, Chen GY, Inohara N, et al. Control of pathogens and pathobionts by the gut microbiota. *Nat Immunol.* 2013 Jul;14(7):685-90. [PMID: 23778796]
- Dean KL. Hyperimmune eggs capture natural immune support. *Altern Complemen Ther.* 2000 June;6(3):118-24. http://www.ah-gene.com.tw/pic/digi/71014101140_hug1.pdf. Accessed June 30, 2017.
- Sarker SA, Casswall TH, Juneja LR, et al. Randomized, placebo-controlled, clinical trial of hyperimmunized chicken egg yolk immunoglobulin in children with rotavirus diarrhea. *J Pediatr Gastroenterol Nutr.* 2001 Jan;32(1):19-25. [PMID: 11176319]
- Mine Y, Kovacs-Nolan J. Chicken egg yolk antibodies as therapeutics in enteric infectious disease: a review. *J Med Food.* 2002 Fall;5(3):159-69. [PMID: 12495588]
- Xie YM, Gao S, Wang LY, et al. Therapeutic effect of probiotics and oral IgY as supplementary drugs in the treatment of pediatric rotavirus enteritis: a comparative study [in Chinese]. *Zhongguo Dang Dai Er Ke Za Zhi.* 2013 Nov;15(11):1000-05. [PMID: 24229598]
- Rahman S, Van Nguyen S, Icatto FC Jr, et al. Oral passive IgY-based immunotherapeutics: a novel solution for prevention and treatment of alimentary tract diseases. *Hum Vaccin Immunother.* 2013 May;9(5):1039-48. [PMID: 23319156]
- Rahman S, Higo-Moriguchi K, Htun KW, et al. Randomized placebo-controlled clinical trial of immunoglobulin Y as adjunct to standard supportive therapy for rotavirus-associated diarrhea among pediatric patients. *Vaccine.* 2012 Jun 29;30(31):4661-69. [PMID: 22575165]
- Artis AM. Food and Drug Administration Food Additive Master File 000595. May 17, 1996.
- Fujibayashi T, Nakamura M, Tominaga A, et al. Effects of IgY against *Candida albicans* and *Candida* spp. Adherence and biofilm formation. *Jpn J Infect Dis.* 2009 Sep;62(5):337-42. [PMID: 19762981]
- Ikemori Y, Ohta M, Umeda K, et al. Passive protection of neonatal calves against bovine coronavirus induced diarrhea by administration of egg yolk or colostrum antibody powder. *Vet Microbiol.* 1997 Nov;58(2-4):105-11. [PMID: 9453122]
- Jüngling A, Wiedemann V, Kühnmann R, et al. Chicken egg antibodies for prophylaxis and therapy of infectious intestinal diseases. IV. In vitro studies on protective effects against adhesion of enterotoxigenic *Escherichia coli* to isolated enterocytes. *Zentralbl Veterinarmed B.* 1991 Jul;38(5):373-81. [PMID: 1681635]
- Buragohain M, Dhale G, Ghalsasi G, et al. Evaluation of hyperimmune hen egg yolk derived anti-human rotavirus antibodies (anti-hrvig) against rotavirus infection. *World J Vaccines.* 2012;2:73-84. <http://dx.doi.org/10.4236/wjv.2012.22010>. Accessed June 30, 2017.
- Burdette C, Heck M. IG 26 DF: Gut Health Support. Poster presented at: Xymogen Xperience Conference; June 24, 2016; Orlando, FL. <https://www.igynutrition.com/burdette>. Accessed July 1, 2017.

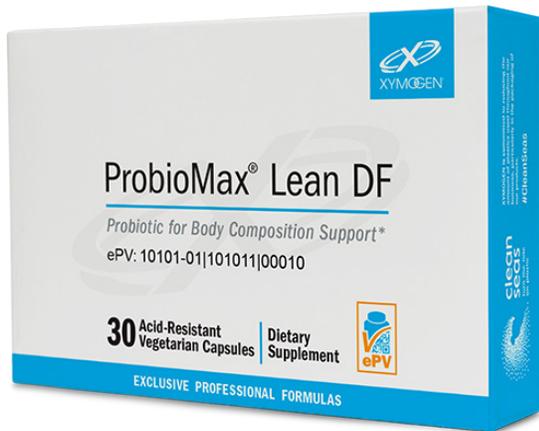
Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

ProbioMax[®] Lean DF

Probiotic for Body Composition Support*



Available in 30 acid-resistant vegetarian capsules

Discussion

At the turn of the 20th century, Nobel Prize laureate Ilya Metchnikov introduced the concept that bacteria in yogurt can support the neutralization of gut pathogens, which may, in turn, support longevity. Since then, the role of beneficial bacteria in human health has become well established in the literature and continues to evolve. In 2002, the FAO (Food and Agriculture Organization of the United Nations) and WHO (World Health Organization) working group experts established a definition of probiotics as “live strains of strictly selected microorganisms, which, when administered in adequate amounts, confer a health benefit on the host.” Results of clinical studies have suggested a positive effect of supplemental probiotics on a wide range of health concerns, including gastrointestinal issues, allergies, immune support, and weight-management.*^[1-7]

Epithelial integrity is key to the function of the gastrointestinal tract, and according to in vitro and animal research, disturbance of this integrity appears to be linked to metabolic disorders. To address the potential effects of consuming specific probiotic bacteria to protect epithelial cells from the effects of pathogenic bacteria, Caco-2 cells were treated with cell-free supernatants (CFSs) of four probiotics—*Bifidobacterium lactis* 420 (B420), *Bifidobacterium lactis* HN019, *Lactobacillus acidophilus* NCFM, and *Lactobacillus salivarius* Ls-33—and by a cell-free supernatant of a pathogenic bacteria *Escherichia coli* (EHEC) O157:H7. Tight junction integrity as well as expression of cyclooxygenases were measured with results suggesting that the B420 CFS counteracted damage done by the EHEC CFS.^[8] One cannot be certain that B420 CFS would prevent junction damage by live bacteria EHEC, but the results suggest that probiotic bacteria produce soluble metabolites that appear to protect epithelial cells and positively influence cytokine balance. Awareness of the existence and activity of soluble bacterial metabolites in vitro leads to speculation whether the same metabolites are also formed in the intestine with similar effects in vivo. However, the evidence presented does seem to suggest that oral consumption of B420 probiotic may benefit epithelial integrity.*

Clinical Applications

- » Supports Healthy Weight Management*
- » Promotes Gut Barrier Function*
- » Promotes Intake of Less Calories*
- » Supports Reduction of Body Fat Mass*

*ProbioMax[®] Lean DF features vegetarian, gluten- and dairy-free, patented HOWARU[®] Shape Bifidobacterium animalis subsp lactis B420. This probiotic strain has been proven safe, effective, and well-tolerated. It has been shown to assist with healthy body composition by improving gut barrier function, supporting the reduction of body fat mass, and promoting less calorie consumption.**

In animal research, the potential benefit of B420 in reducing high-fat, diet-induced body weight gain and diabetes was studied with results indicating a reduction of fat mass and glucose intolerance in both obese and diabetic mice. Reduced intestinal mucosal adherence and decreased levels of plasma lipopolysaccharide suggested a mechanism related to reduced translocation of gut microbes.*^[9]

HOWARU[®] Shape B420 (*Bifidobacterium animalis subsp lactis* B420)

The in vitro and experimental animal studies discussed above utilized B420 with positive results in improving epithelial integrity and potential for role in weight management. These results led to the need for a human trial to validate these effects. In a double-blind, placebo-controlled study in overweight volunteers (N = 225) aged 18-65, the effects of B420 and the combination of B420 with a prebiotic fiber on body-fat mass and other weight-related parameters were investigated. The authors speculated that the underlying mechanism for reduction of body fat mass could have been related to circulating zonulin (a potential marker of gut barrier function) and C-reactive protein (CRP), a speculation that had been supported by previous findings with experimental animals. Subjects were not required to make changes in dietary or exercise habits. Body composition was monitored with dual-energy X-ray absorptiometry, and the primary outcome was a relative change in body fat mass when treatment groups were compared to placebo. Other outcomes included anthropometric measurements, food intake, and blood and fecal biomarkers. Although results indicated that B420 in combination with the prebiotic offered the most significant benefits when compared to placebo (4.5% reduction in body fat mass), B420 alone (10¹⁰ CFU/day) resulted in reduced body fat mass of 4.0% with changes in fat mass being most pronounced in the abdominal region and in waist circumference. Significant reduced caloric intake was also shown in both groups compared to placebo, and there were no differences between groups in the incidence of adverse events.*^[7]

Continued on next page

Building on the data reported for B420 thus far, investigators looked into whether changes in the gut microbiota were associated with clinical benefits and obesity-related issues. Fecal and plasma samples obtained from a subset (n = 134) of the participants in the above mentioned clinical trial were assessed at baseline, two, four, and six months as well as one-month post-intervention. Consumption of B420 resulted in alterations of the specific gut microbiota *Lactobacillus* and *Akkermansia muciniphila*. *Akkermansia muciniphila*, often in lower amounts in obese individuals with metabolic dysfunction, is associated with improved metabolic health. This strain supports gut barrier function and improves obesity-related markers and thus supports the probiotic benefits of B420.^[10] More clinical trials are warranted to confirm these effects in larger participant populations and to further elucidate the underlying mechanisms.*

XYMOGEN packages the ProbioMax® Lean DF capsules in sealed, nitrogen-purged blister packs to serve as protection from factors known to compromise the stability of probiotics, such as heat, moisture, and oxygen. To further support resistance to low pH and the delivery of microorganisms to the small intestines, XYMOGEN utilizes DRcaps™ gastro-resistant capsules. These specially designed, innovative capsules help slow exposure of actives to stomach acid to promote a more targeted release.*

‡Also referred to in more recent literature as *Bifidobacterium animalis* subsp. *lactis*.

ProbioMax® Lean DF Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
HOWARU® Shape B420 (<i>Bifidobacterium animalis</i> subsp. <i>lactis</i> B420)	25 mg (10 Billion CFU) [†]	**

**Daily Value not established.

Other Ingredients: Microcrystalline cellulose, acid-resistant capsule (hypromellose, gellan gum, and water), ascorbyl palmitate, and silica.

DIRECTIONS: Take one capsule with water daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

†colony-forming unit

HOWARU®

HOWARU® and the HOWARU® logo are registered trademarks of DuPont or its affiliates.



References

1. Singh VP, Sharma J, Babu S, et al. Role of probiotics in health and disease: a review. *J Pak Med Assoc.* 2013 Feb;63(2):253-7. [PMID: 23894906]
2. Report of a Joint FAO/WHO Working Group on Drafting Guidelines for the Evaluation of Probiotics in Food. FAO; London, ON, Canada. 30 April–1 May 2002. https://www.who.int/foodsafety/fs_management/en/probiotic_guidelines.pdf. Accessed December 11, 2018.
3. Wilkins T, Sequoia J. Probiotics for gastrointestinal conditions: a summary of the evidence. *Am Fam Physician.* 2017 Aug 1;96(3):170-178. [PMID: 28762696]
4. Markowiak P, Śliżewska K. Effects of probiotics, prebiotics, and synbiotics on human health. *Nutrients.* 2017 Sep 15;9(9). pii: E1021. [PMID: 28914794]
5. Sanders M, Merenstein C, Merrifield C, et al. Probiotics for human use. *Nutrition Bulletin.* 2018 Sept;43(3):212–225. doi: 10.1111/nbu.12334. <https://onlinelibrary.wiley.com/doi/epdf/10.1111/nbu.12334>. Accessed December 11, 2018.
6. Kadooka Y, Sato M, Imaizumi K, et al. Regulation of abdominal adiposity by probiotics (*Lactobacillus gasseri* SBT2055) in adults with obese tendencies in a randomized controlled trial. *Eur J Clin Nutr.* 2010 Jun;64(6):636-43. [PMID: 20216555]
7. Stenman LK, Lehtinen MJ, Meland N, et al. Probiotic with or without fiber controls body fat mass, associated with serum zonulin, in overweight and obese adults—randomized controlled trial. *EBioMedicine.* 2016 Nov;13:190-200. [PMID: 27810310]
8. Putaala H, Salusjärvi T, Nordström M, et al. Effect of four probiotic strains and *Escherichia coli* O157:H7 on tight junction integrity and cyclo-oxygenase expression. *Res Microbiol.* 2008 Nov-Dec;159(9-10):692-8. [PMID: 18783733]
9. Stenman LK, Waget A, Garret C, et al. Potential probiotic *Bifidobacterium animalis* ssp. *lactis* 420 prevents weight gain and glucose intolerance in diet-induced obese mice. *Benef Microbes.* 2014 Dec;5(4):437-45. [PMID: 25062610]
10. Hibberd AA, Yde CC, Ziegler ML, et al. Probiotic or synbiotic alters the gut microbiota and metabolism in a randomised controlled trial of weight management in overweight adults. *Benef Microbes.* 2018 Dec 10:1-16. [PMID: 30525950]

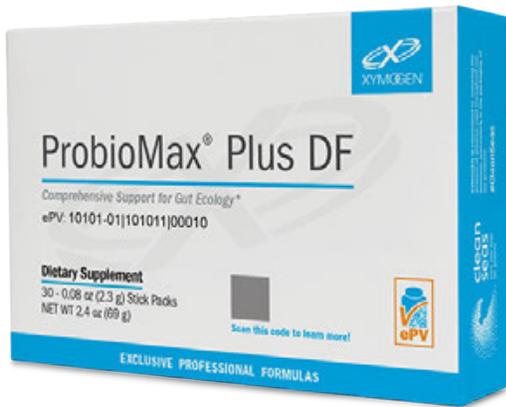
Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

ProbioMax® Plus DF

Comprehensive Support for Gut Ecology*



Available in 30 stick packs

Discussion

Supplementation with probiotics has many mechanisms of action that benefit health, including but not limited to: (1) supporting metabolic activity, such as the production of short-chain fatty acids and vitamins, nutrient absorption, and digestion of lactose; (2) adhering to intestinal epithelial cells to help maintain a healthy balance of organisms in the intestinal tract; (3) helping to establish populations of good bacteria after disruption in balance; (4) supporting immune function; (5) promoting intestinal epithelial cell survival; (6) supporting healthy bowel function; and (7) degrading oxalates.*^[1-8]

HOWARU® (*Bifidobacterium lactis* HN019) Discovered in 1899, *B. lactis* plays a key role in the human microflora throughout a person's life. Researchers have identified strain HN019 as having excellent probiotic potential based upon its ability to survive the transit through the human gastrointestinal tract, adhere to epithelial cells, and proliferate.^[6] *B. lactis* HN019 has been extensively studied, and its safety and effectiveness is well-accepted.^[7,8] To assess the impact of *B. lactis* HN019 supplementation on whole-gut transit time in adults, 100 subjects were given daily doses for 14 days of 17.2 billion colony-forming units (CFU), 1.8 billion CFU, or placebo. Decreases in mean whole-gut transit time over the 14-day study period were statistically significant in the high-dose group and the low-dose group, but not in the placebo group.^[8] This level of dosing also supported other parameters of healthy GI function, as were self-reported by patient survey.^[8] In another study of preschool-age children, supplementing milk for one year with 1.9 x 10 CFU per day *B. lactis* HN019 and 2.4 g/day of prebiotic oligosaccharides supported both healthy iron status and weight gain.^[9] In a randomized, double-blind, placebo-controlled human dietary intervention study in elderly subjects (>60 yrs.), supplementary *B. lactis* HN019 resulted in statistically significant increases in the beneficial organisms bifidobacteria and lactobacilli.*^[10]

***Lactobacillus acidophilus* (*Lactobacillus acidophilus* La-14)** This common inhabitant of the human mouth, intestinal tract, and vagina is also found in some traditional fermented milks (e.g., kefir) and is widely used in probiotic foods and supplements. It has a history of

Clinical Applications

- » Maintains Healthy Intestinal Microecology, Neutralizes Certain Bacterial Toxins*
- » Supports Balance of Healthy Intestinal Flora*
- » Supports the Natural Immune Response*
- » Supports Bowel Regularity*
- » Enhances Integrity of Mucosa and Enzymatic Activity of the Intestinal Cells*
- » Positively Affects the Production of Cytokines*

ProbioMax® Plus DF is an ideal combination of ingredients for individuals seeking a well-rounded supplement to address intestinal ecology, cellular health, and immunity. It features well-researched probiotic strains; *Saccharomyces boulardii*, a non-pathogenic yeast; and arabinogalactan, a prebiotic. By combining these ingredients, the individual benefits of each component can be complemented by the mechanisms of the others.*

safe human consumption. The *L. acidophilus* La-14 strain is of human origin and has been identified as a type A1 *L. acidophilus*. *L. acidophilus* shows excellent adhesion to human epithelial cell-lines.*^[11,12]

***Lactobacillus plantarum* (*Lactobacillus plantarum* Lp-115)** This bacteria was isolated from plant material and is abundantly present in lactic acid-fermented foods, such as olives and sauerkraut. In vitro studies have shown that *L. plantarum* strain Lp-115 has excellent adhesion to epithelial cell lines.^[13] In addition, *L. plantarum* is resistant to low pH conditions and survives the presence of bile at duodenal concentrations.*^[13,14]

***Bifidobacterium longum* (*Bifidobacterium longum* B1-05)** The *B. longum* B1-05 strain is well-accepted as safe for human consumption. *B. longum* is resistant to low pH and bile salts and is well-suited to the intestinal environment.*^[14]

Saccharomyces boulardii is a natural, non-pathogenic yeast that has been shown to maintain and restore the healthy ecology of the small and large intestines. In a 2010 systematic review and meta-analysis of 31 randomized placebo-controlled treatment arms in 27 trials (encompassing 5,029 adult study patients), *S. boulardii* was found to be significantly efficacious and safe in 84% of those treatments arms. Extensively researched and published in European and American peer-reviewed journals, *S. boulardii* has demonstrated multiple mechanisms of action. These can be found by referring to DRS-109, which details XYMOGEN's Saccharomycin DF™. The *S. boulardii* used in this formula is processed by low temperature vacuum drying for improved stability.*^[15-17]

XYMOGEN has also included the prebiotic **Arabinogalactan** in ProbioMax Plus DF. Present in many plants, arabinogalactan is a non-digestible, soluble dietary fiber that contains the monosaccharides galactose and arabinose. The generally recognized as safe (GRAS) source of arabinogalactan in this formula is the larch tree. In addition

Continued on next page

EXCLUSIVE • PATENTED

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

ProbioMax® Plus DF Supplement Facts

Serving Size: 1 Stick Pack (about 2.3 g)

	Amount Per Serving	%Daily Value
Calories	5	
Total Carbohydrate	1 g	0% [‡]
Dietary Fiber	1 g	4% [‡]
Arabinogalactan (from <i>Larix laricina</i> (heartwood)	1.5 g	**
<i>Saccharomyces boulardii</i>	500 mg (10 Billion CFU [†])	**
Proprietary Blend <i>Lactobacillus acidophilus</i> La-14® <i>Bifidobacterium longum</i> BI-05™ <i>Lactobacillus plantarum</i> Lp-115®	174 mg (15 Billion CFU [†])	**
HOWARU® Bifido (<i>Bifidobacterium lactis</i> HN019®)	50 mg (15 Billion CFU [†])	**

[‡]Percent Daily Values are based on a 2,000 calorie diet.

**Daily Value not established.

Other Ingredients: Silica.

[†]Colony-Forming Unit

DIRECTIONS: Dissolve the contents of one stick pack in 1–2 oz pure water and consume one to three times daily, or take as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use, especially if you have severe immune suppression. Individuals taking antifungal or other medication should discuss potential interactions with their healthcare practitioner. Do not use if stick pack is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

HOWARU®

HOWARU® and the HOWARU® logo are registered trademarks of DuPont or its affiliates.

HN019® is a registered trademark of Fonterra™ Limited and is licensed to DuPont Nutrition Biosciences.

to its involvement in cellular communication and possession of immune-supporting properties, arabinogalactan minimizes ammonia synthesis and absorption, enhances production of short-chain fatty acids, and favorably alters gut microflora.*

References

- Vanderpool C, Yan F, Polk DB. Mechanisms of probiotic action: Implications for therapeutic applications in inflammatory bowel diseases. *Inflamm Bowel Dis*. 2008 Nov;14(11):1585-96. [PMID: 18623173]
- Abrott VR, Reid SJ. Oxalate-degrading bacteria of the human gut as probiotics in the management of kidney stone disease. *Adv Appl Microbiol*. 2010;72:63-87. [PMID: 20602988]
- Masood MI, Qadir MI, Shirazi JH, et al. Beneficial effects of lactic acid bacteria on human beings. *Crit Rev Microbiol*. 2011 Feb;37(1):91-98. [PMID: 21162695]
- Turroni S, Vitali B, Bendazzoli C, et al. Oxalate consumption by lactobacilli: evaluation of oxalyl-CoA decarboxylase and formyl-CoA transferase activity in *Lactobacillus acidophilus*. *J Appl Microbiol*. 2007 Nov;103(5):1600-09. [PMID: 17953571]
- Shu Q, Lin H, Rutherford KJ, et al. Dietary *Bifidobacterium lactis* (HN019) enhances resistance to oral *Salmonella typhimurium* infection in mice. *Microbiol Immunol*. 2000;44(4):213-22. [PMID: 10832963]
- Gopal P, et al. Effects of the consumption of *Bifidobacterium lactis* HN019 (DR10TM) and galacto-oligosaccharides on the microflora of the gastrointestinal tract in human subjects. *Nutr Res*. 2003;23(10):1313-28. [http://www.nrjournal.com/article/S0271-5317\(03\)00134-9/abstract](http://www.nrjournal.com/article/S0271-5317(03)00134-9/abstract). Accessed June 24, 2011.
- Danisco. Clinical study bibliography and abstracts. <http://www.danisco.com/product-range/probiotics/howarur-premium-probiotics/howaru-r-bifido-probiotics/howaru-bifido-clinical-studies/>. Accessed April 14, 2014.
- Waller PA, Gopal PK, Leyer GJ, et al. Dose-response effect of *Bifidobacterium lactis* HN019 on whole gut transit time and functional gastrointestinal symptoms in adults. *Scand J Gastroenterol*. 2011 Sep;46(9):1057-64. [PMID: 21663486]
- Sazawal S, Dhingra U, Hiremath G, et al. Effects of *Bifidobacterium lactis* HN019 and prebiotic oligosaccharide added to milk on iron status, anemia, and growth among children 1 to 4 years old. *J Pediatr Gastroenterol Nutr*. 2010 Sep;51(3):341-46. [PMID: 20601905]
- Ahmed M, Prasad J, Gill H, et al. Impact of consumption of different levels of *Bifidobacterium lactis* HN019 on the intestinal microflora of elderly human subjects. *J Nutr Health Aging*. 2007 Jan-Feb;11(1):26-31. [PMID: 17315077]
- Greene JD, Klaenhammer TR. Factors involved in adherence of lactobacilli to human Caco-2 cells. *Appl Environ Microbiol*. 1994 Dec;60(12):4487-94. [PMID: 7811085]
- Kleeman EG, Klaenhammer TR. Adherence of *Lactobacillus* species to human fetal intestinal cells. *J Dairy Sci*. 1982 Nov;65(11):2063-69. [PMID: 7153393]
- Collado MC, Meriluoto J, Salminen S. Role of commercial probiotic strains against human pathogen adhesion to intestinal mucus. *Lett Appl Microbiol*. 2007 Oct;45(4):454-60. [PMID: 17897389]
- Ding WK, Shah NP. Acid, bile, and heat tolerance of free and microencapsulated probiotic bacteria. *J Food Sci*. 2007 Nov;72(9):M446-50. [PMID: 18034741]
- McFarland LV. Systematic review and meta-analysis of *Saccharomyces boulardii* in adult patients. *World J Gastroenterol*. 2010 May 14;16(18):2202-22. [PMID: 20458757]
- Vandenplas Y, Brunser O, Szajewska H, et al. *Saccharomyces boulardii* in childhood. *Eur J Pediatr*. 2009 Mar;168(3):253-65. [PMID: 19096876]
- Buts JP, De Keyser N. Effects of *Saccharomyces boulardii* on intestinal mucosa. *Dig Dis Sci*. 2006 Aug;51(8):1485-92. [PMID: 16838119]

Additional references available upon request

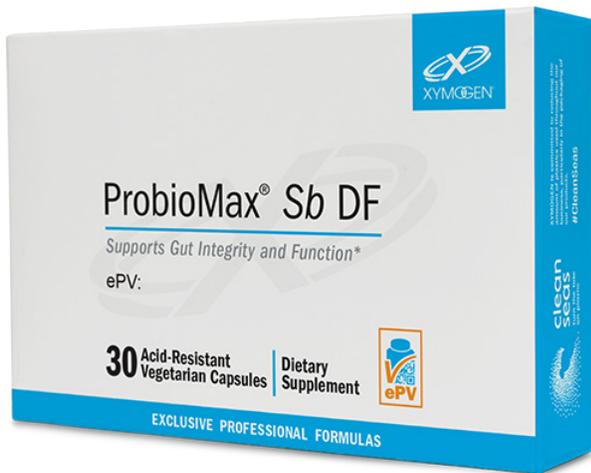
EXCLUSIVE • PATENTED

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

ProbioMax[®] Sb DF

Supports Gut Integrity and Function*



Available in 30 vegetarian capsules

Discussion

Diversity of gut microflora is characteristic of a healthy GI microbiome and contributes to overall health and vitality by promoting optimum digestion, assimilation, gut integrity, motility, and efficient removal of toxins and wastes. Many internal and external influences, including stress, a poor diet, food sensitivities, medication, environmental factors, and certain disease conditions, can impact the microbial balance within this fine-tuned community. Their impact can allow potential colonization by pathogenic organisms and disrupt a healthy balance, which can result in adverse effects ranging from GI symptoms to impaired immune response.^[1-3] Probiotics are part of the key to promoting the optimal balance of the microbiome,^[4] whether they originate from dietary sources or from supplements. Probiotic yeasts, such as *Saccharomyces boulardii*, also play a role in gut ecology by supporting intestinal barrier function and integrity.*

Common challenges associated with probiotic supplementation are maintaining the stability of the organisms during distribution and shelf life and, after they are swallowed, the survival of the organisms as they travel through the digestive tract to the targeted tissue. To help ensure stability, XYMOGEN packages ProbioMax Sb DF capsules in sealed, nitrogen-purged blister packs to serve as protection from factors proven to compromise the stability of probiotics, such as heat, moisture, and oxygen. Careful selection of organisms is another way XYMOGEN helps ensure stability and digestive survivability. To further support resistance to low pH and the delivery of microorganisms to the small intestines, XYMOGEN encapsulates the ingredients in gastro-resistant DRcaps™. These specially designed, innovative capsules help slow exposure of actives to stomach acid to promote a more targeted release.*

HOWARU[®] (*Bifidobacterium lactis* HN019) Discovered in 1899, *B. lactis* play a key role in the human microflora throughout a person's life. Researchers have identified strain HN019 as having excellent probiotic potential based on its ability to survive the transit through the human gastrointestinal tract, adhere to epithelial cells, and proliferate.^[5] *B. lactis* HN019 has been extensively studied, and its safety and effectiveness

Clinical Applications

- » Helps Maintain a Healthy Intestinal Microecology*
- » Supports Bowel Regularity*
- » Supports Gastrointestinal-Based Immunity*

*ProbioMax[®] Sb DF is ideal for individuals seeking a well-rounded supplement to support a healthy balance of intestinal flora, cellular health, and immune health. It features four probiotic strains, including the extensively studied HN019 strain of Bifidobacterium lactis, plus Saccharomyces boulardii (Sb), a non-pathogenic yeast, to further complement healthy gastrointestinal ecology. Gastro-resistant, vegetarian capsules provide an innovative solution for targeted delivery of sensitive ingredients to the small intestine, as they alleviate exposure to the low pH environment of the stomach. Additionally, each capsule is sealed in a nitrogen-purged blister pack to provide protection from heat, moisture, and oxygen, factors known to compromise probiotic stability.**

are well-accepted.^[6,7] To assess the impact of *B. lactis* HN019 supplementation on whole-gut transit time in adults, subjects (N = 100) were given daily doses of 17.2 billion colony-forming units (CFU), 1.8 billion CFU, or placebo for 14 days. Decreases in mean whole-gut transit time over the 14-day study period were statistically significant in the high-dose group and the low-dose group, but not in the placebo group.^[7] This level of dosing also supported other parameters of healthy GI function, as were self-reported by patient survey.^[7] In a randomized, double-blind, placebo-controlled human dietary intervention study, 80 subjects older than 60 years who took supplementary *B. lactis* HN019 had statistically significant increases in the beneficial organisms bifidobacteria and lactobacilli.*^[8]

***Lactobacillus acidophilus* (*Lactobacillus acidophilus* La-14)** This common inhabitant of the human microbiome is also found in some traditional fermented milks (e.g., kefir) and is widely used in probiotic foods and supplements with a history of safe human consumption. The *L. acidophilus* La-14 strain is of human origin and has been identified as a type A1 *L. acidophilus*, showing excellent adhesion to human epithelial cell-lines.*^[9,10]

***Lactobacillus plantarum* (*Lactobacillus plantarum* Lp-115)** Isolated from plant material, the *L. plantarum* strain is abundantly present in lactic acid-fermented foods, such as olives and sauerkraut. In vitro studies have shown that *L. plantarum* Lp-115 has excellent adhesion to epithelial cell lines.^[11] In addition, *L. plantarum* is resistant to low pH conditions and survives the presence of bile at duodenal concentrations.*^[11,12]

***Bifidobacterium longum* (*Bifidobacterium longum* BI-05)** The *B. longum* BI-05 strain is well-accepted as safe for human consumption. *B. longum* is resistant to low pH and bile salts and is well-suited to the intestinal environment.*^[12]

Saccharomyces boulardii* *S. boulardii might be most well-known by consumers for its role as the type of yeast used in the widely popular

Continued on next page

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

kombucha beverages. Extensive research in both European and American peer-reviewed journals has shown that this natural, non-pathogenic yeast has multiple mechanisms of action that support healthy gut ecology. In a 2010 systematic review and meta-analysis of 31 randomized placebo-controlled treatment arms in 27 trials (encompassing 5,029 adult study patients), *S. boulardii* was found to be significantly efficacious in 84% of those treatment arms.^[13] *S. boulardii* was also found to be efficacious for use in children in a double-blind, randomized, placebo-controlled study that yielded statistically significant positive results for supporting normal gastrointestinal function in children aged 3-59 months.^[14] When safety data was examined in adult subjects (n = 2,963) in a trial of patients with *Clostridium difficile* infections, the adverse reactions associated with *S. boulardii* were minimal (<0.3%): thirst in five subjects and constipation in eight subjects.^[13] Another study in children aged three months and older demonstrated that *S. boulardii* can be used safely and effectively in this population group.*^[15]

With regard to maintaining normal GI function and transit time, research suggests that *S. boulardii* secretes a protease that may assist in directly degrading bacterial toxins and stimulating antibody production against those toxins.^[16-18] *S. boulardii* is also believed to exert a trophic effect on intestinal mucosa and positively support the immune system.*^[14]

This probiotic yeast appears to support normal gastrointestinal flora and integrity^[19,20]; promote production of intestinal enzymes and secretory IgA^[21]; and support cytokine balance through its effects on IL-8, IL-6, IL-10, NF-kappaB, TNF-alpha, and PPAR-gamma.^[18,22,23] Research also suggests a role for *S. boulardii* in the production of health-promoting short-chain fatty acids including butyrate, which supports homeostasis of colonic flora and fuels intestinal epithelial cells among its other benefits.^[24,25] The *S. boulardii* used in this formula is processed by low-temperature vacuum drying for improved stability.*

ProbioMax® Sb DF Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
<i>Saccharomyces boulardii</i>	250 mg (5 Billion CFU [†])	**
Proprietary Blend	174 mg (15 Billion CFU [†])	**
<i>Lactobacillus acidophilus</i> La-14®		
<i>Bifidobacterium longum</i> BI-05™		
<i>Lactobacillus plantarum</i> Lp-115®		
HOWARU® Bifido (<i>Bifidobacterium lactis</i> HN019)	50 mg (15 Billion CFU [†])	**
** Daily Value not established.		

Other Ingredients: Capsule (hypromellose, gellan gum, and water), microcrystalline cellulose, hydroxypropyl cellulose, ascorbyl palmitate, and silica.
† Colony-Forming Unit

DIRECTIONS: Take one capsule daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

HOWARU®

HOWARU® and the HOWARU® logo are registered trademarks of DuPont or its affiliates.

HN019® is a registered trademark of Fonterra™ Limited and is licensed to DuPont Nutrition Biosciences.



References

- Heiman ML, Greenway FL. A healthy gastrointestinal microbiome is dependent on dietary diversity. *Mol Metab.* 2016 Mar 5;5(5):317-20. [PMID: 27110483]
- Lloyd-Price J, Abu-Ali G, Huttenhower C. The healthy human microbiome. *Genome Med.* 2016 Apr 27;8(1):51. [PMID: 27122046]
- Xu Z, Knight R. Dietary effects on human gut microbiome diversity. *Br J Nutr.* 2015 Jan;113 Suppl:S1-5. [PMID: 25498959]
- Grimm V, Riedel CU. Manipulation of the microbiota using probiotics. *Adv Exp Med Biol.* 2016;902:109-17. [PMID: 27161354]
- Gopal P, Prasad J, Gill HS. Effects of the consumption of *Bifidobacterium lactis* HN019 (DR10TM) and galacto-oligosaccharides on the microflora of the gastrointestinal tract in human subjects. *Nutr Res.* 2003;23:1313-28. <https://www.optibacprobiotics.co.uk/uploads/gopal-2003-effect-of-HN019-and-GOS-on-microflora-in-GIT-in-humans.pdf>. Accessed January 9, 2018.
- Danisco. Clinical study bibliography & abstracts. HOWARU® Bifido. <http://www.danisco.com/product-range/probiotics/howarur-premium-probiotics/howarur-bifido-probiotics/howarur-bifido-clinical-studies/#c21397>. Accessed January 9, 2018.
- Waller PA, Gopal PK, Leyer GJ, et al. Dose-response effect of *Bifidobacterium lactis* HN019 on whole gut transit time and functional gastrointestinal symptoms in adults. *Scand J Gastroenterol.* 2011 Sep;46(9):1057-64. [PMID: 21663486]
- Ahmed M, Prasad J, Gill H, et al. Impact of consumption of different levels of *Bifidobacterium lactis* HN019 on the intestinal microflora of elderly human subjects. *J Nutr Health Aging.* 2007 Jan-Feb;11(1):26-31. [PMID: 17315077]
- Greene JD, Klaenhammer TR. Factors involved in adherence of lactobacilli to human Caco-2 cells. *Appl Environ Microbiol.* 1994 Dec;60(12):4487-94. [PMID: 7811085]
- Kleeman EG, Klaenhammer TR. Adherence of *Lactobacillus* species to human fetal intestinal cells. *J Dairy Sci.* 1982 Nov;65(11):2063-69. [PMID: 7153393]
- Collado MC, Meriluoto J, Salminen S. Role of commercial probiotic strains against human pathogen adhesion to intestinal mucus. *Lett Appl Microbiol.* 2007 Oct;45(4):454-60. [PMID: 17897389]
- Ding WK, Shah NP. Acid, bile, and heat tolerance of free and microencapsulated probiotic bacteria. *J Food Sci.* 2007 Nov;72(9):M446-50. [PMID: 18034741]
- McFarland LV. Systematic review and meta-analysis of *Saccharomyces boulardii* in adult patients. *World J Gastroenterol.* 2010 May 14;16(18):2202-22. [PMID: 20458757]
- Riaz M, Alam S, Malik A, et al. Efficacy and safety of *Saccharomyces boulardii* in acute childhood diarrhea: a double blind randomised controlled trial. *Indian J Pediatr.* 2012 Apr;79(4):478-82. [PMID: 21997865]
- Vandenplas Y, Brunser O, Szajewska H. *Saccharomyces boulardii* in childhood. *Eur J Pediatr.* 2009 Mar;168(3):253-65. [PMID: 19096876]
- Can M, Besirbellioglu BA, Avci IY, et al. Prophylactic *Saccharomyces boulardii* in the prevention of antibiotic-associated diarrhea: a prospective study. *Med Sci Monit.* 2006 Apr;12(4):P119-22. [PMID: 16572062]
- Castagliuolo I, Riegler MF, Valenick L, et al. *Saccharomyces boulardii* protease inhibits the effects of *Clostridium difficile* toxins A and B in human colonic mucosa. *Infect Immun.* 1999 Jan;67(1):302-7. [PMID: 9864230]
- Im E, Pothoulakis C. Recent advances in *Saccharomyces boulardii* research [in French]. *Gastroenterol Clin Biol.* 2010 Sep;34 Suppl 1:S62-70. Review. [PMID: 20889007]
- Krasowska A, Murzyn A, Dyjankiewicz A, et al. The antagonistic effect of *Saccharomyces boulardii* on *Candida albicans* filamentation, adhesion and biofilm formation. *FEMS Yeast Res.* 2009 Dec;9(8):1312-21. [PMID: 19732158]
- Natural Standard Database. *Saccharomyces Boulardii* Monograph. <http://naturaldatabase.therapeuticresearch.com/nd/Search.aspx?cs=&s=ND&pt=100&id=332&ds=>. Accessed January 9, 2018.
- Buts JP, Bernasconi P, Vaerman JP, et al. Stimulation of secretory IgA and secretory component of immunoglobulins in small intestine of rats treated with *Saccharomyces boulardii*. *Dig Dis Sci.* 1990 Feb;35(2):251-6. [PMID: 2302983]
- Dahan S, Dalmaso G, Imbert V, et al. *Saccharomyces boulardii* interferes with enterohemorrhagic *Escherichia coli*-induced signaling pathways in T84 cells. *Infect Immun.* 2003 Feb;71(2):766-73. [PMID: 12540556]
- Pothoulakis C. Review article: anti-inflammatory mechanisms of action of *Saccharomyces boulardii*. *Aliment Pharmacol Ther.* 2009 Oct 15;30(8):826-33. Review. [PMID: 19706150]
- Schneider SM, Girard-Pipau F, Filippi J, et al. Effects of *Saccharomyces boulardii* on fecal short-chain fatty acids and microflora in patients on long-term total enteral nutrition. *World J Gastroenterol.* 2005 Oct 21;11(39):6165-9. [PMID: 16273644]
- Lewis K, Lutgendorff F, Phan V, et al. Enhanced translocation of bacteria across metabolically stressed epithelia is reduced by butyrate. *Inflamm Bowel Dis.* 2010 Jul;16(7):1138-48. [PMID: 20024905]

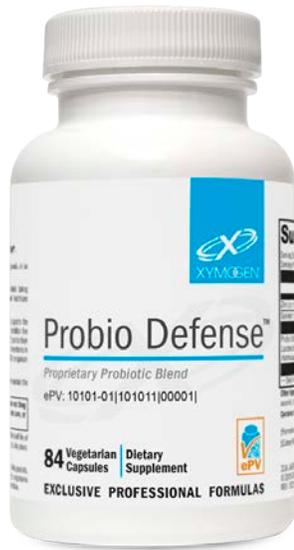
Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Probio Defense™

Proprietary Probiotic Blend



Available in 84 capsules

Discussion

Probiotics refer to the beneficial microorganisms that reside in our gastrointestinal (GI) tracts and appear to exist in a symbiotic relationship with the human body. Several probiotic bacteria, including *Lactobacilli* and *Bifidobacteria*, have been studied for their beneficial effects on health and wellness. The American Gastroenterological Society provides a comprehensive review of the uses and proposed benefits of probiotics.^[1] Research on probiotics has focused on the positive impact they appear to have on immune function, GI health, and the body's normal response to inflammation.*^[2-6]

Mechanisms of Action It is suggested that the mechanisms by which probiotics exert their beneficial health effects are manifold and include the production of inhibitory substances (e.g., lactic acid, bacteriocins) and competition for epithelial cell adhesion, both of which help good bacteria predominate; stimulation of mucus production; metabolic activities that decrease microbial toxins, break down lactose, and support host digestion; changes in corticosterone levels; and downregulation of inflammatory interleukins and cytokines.^[7-12] Additional proposed mechanisms include stimulation of immunoglobulin A, trophic influences on intestinal mucosa, and assistance in the delivery of therapeutic substances to various portions of the intestine.^[13] These varied mechanisms help preserve the health, integrity, and function of the GI tract at both the cellular and system levels. Research suggests that in some cases a mixture of strains, including *Lactobacilli* and *Bifidobacteria*, appears to be most beneficial.*^[1]

Proprietary Strains Probio Defense comprises *Lactobacillus helveticus* Rosell-52,[†] *Lactobacillus rhamnosus* Rosell-11, and *Bifidobacterium longum* Rosell-175. These strains were isolated and are produced by Institut Rosell-Lallemand (IR), a company that has made significant discoveries in the fields of microbiology and nutrition since 1934 with a focus on providing reliable, stable, and documented strains to the healthcare industry.^[15] IR uses the most advanced DNA-analysis technology to verify their strains. They then test these strains to measure gastric acid and intestinal solution resistance over various time spans and temperatures. IR also tests adhesion to the intestinal mucosa. Competitive inhibition and increased mucin expression have been documented by IR, along with stability at various temperatures and humidity.*

Clinical Applications

- » Contributes to Balanced Gastrointestinal Flora*
- » Supports a Healthy Immune System*
- » Supports Intestinal Health and Function*
- » Supports Lactose Tolerance*

Probio Defense™ is a combination of probiotic bacteria that supports the immune and gastrointestinal systems. It is formulated with ten billion live organisms per capsule and provides well-researched strains chosen for their ability to maintain viability throughout the small intestine. The three strains in Probio Defense are registered in the National Collection of Microorganism Cultures at the Institut Pasteur in France. Selenium and zinc are present to provide antioxidant support, help balance intestinal flora, and stimulate the body's natural immune defenses.**

Human Clinical Trials Numerous clinical trials employing double-blind, randomized, placebo-controlled techniques have been performed with the probiotic strains found in Probio Defense. The majority of these studies focus on host intestinal flora and GI health. For instance, studies completed on children demonstrated that the *Lactobacillus* strains in Probio Defense reduce bacterial toxin load and support gastrointestinal health.^[10,16,17] Large-scale studies support the role of these *Lactobacillus* strains as adjunct therapy in promoting GI health and healthy bowel function.^[18,19] A small-scale study also indicates that lactose tolerance was supported in 19 adult patients taking these strains daily for two weeks.^[11] A randomized, controlled, single-blind study of children aged 10-12 years suggested that *Lactobacillus* strains, such as those found in Probio Defense, positively supported lactose tolerance in those who received them.^[20] A double-blind, randomized, controlled trial utilizing *Bifidobacterium longum*, along with an inulin-based prebiotic, resulted in a significant reduction in inflammatory cytokines.*^[21]

Psychological Benefits Emerging studies (animal and human) suggest that probiotics affect the host's psychological state and normal response to stress. This may be due to the effect that beneficial bacteria have on cytokine balance, neurotransmitter production, and the support of normal glucose tolerance. A study of *Lactobacillus helveticus* and *Bifidobacterium longum* suggested that these strains positively support mood and a normal response to stress, as measured by standard testing.*^[22]

Host Defense and Digestive Transit With the provision of the essential trace minerals selenium and zinc, Probio Defense also provides antioxidant and immune support.^[23] In addition, studies indicate that the three probiotic strains found in Probio Defense remain viable as they travel through the digestive tract to the distal end of the small intestine, further supporting their positive effects on health.*^[24]

[†]New and improved genetic methods have allowed deeper insight into bacterial chromosomes. Use of these methods led to the reclassification, in 2006, of Rosell-52 from *Lactobacillus acidophilus* to *Lactobacillus helveticus*. This name change has no impact on safety or on the value of scientific and clinical documentation.

Probio Defense™ Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Zinc (as zinc yeast)	2 mg	18%
Selenium (as selenium yeast)	12.5 mcg	23%
Probio Defense Blend Lactobacillus helveticus Rosell-52, Lactobacillus rhamnosus Rosell-11, Bifidobacterium longum Rosell-175	51.553 mg (2 Billion† CFU‡)	**
** Daily Value not established.		

Other Ingredients: Potato starch, HPMC (capsule), magnesium stearate, and ascorbic acid.

Contains: Milk and Soy.

†Formulated with 10 Billion CFU‡ at time of manufacture

‡Colony-Forming Units

DIRECTIONS: Take one capsule twice daily before or during meals, or as directed by your healthcare professional.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tampo seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, animal products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Probio Defense is shipped refrigerated to preserve the shelf life of the strains. In order to maximize shelf life, keep closed in a cool, dry place. Keep out of the reach of children.



References

1. American Gastroenterological Association. Probiotics: What they are and what they can do for you. <http://www.gastro.org/patient-center/diet-medications/probiotics>. Published August 2008. Updated April 24, 2010. Accessed October 19, 2012.
2. Doron S, Gorbach SL. Probiotics: their role in the treatment and prevention of disease. *Expert Rev Anti Infect Ther*. 2006 Apr;4(2):261-75. [PMID: 16597207]
3. Perdigon G, Fuller R, Raya R. Lactic acid bacteria and their effect on the immune system. *Curr Issues Intest Microbiol*. 2001 Mar;2(1):27-42. [PMID: 11709854]
4. Cross ML. Microbes versus microbes: immune signals generated by probiotic lactobacilli and their role in protection against microbial pathogens. *FEMS Immunol Med Microbiol*. 2002 Dec 13;34(4):245-53. [PMID: 12443824]
5. Vanderhoof JA, Young RJ. The role of probiotics in the treatment of intestinal infections and inflammation. *Curr Opin Gastroenterol*. 2001 Jan;17(1):58-6. [PMID: 17031151]
6. Sanders ME. Probiotics: definition, sources, selection, and uses. *Clin Infect Dis*. 2008 Feb 1;46 Suppl 2:S58-61; discussion S144-51. [PMID: 18181724]
7. Johnson-Henry KC, Mitchell DJ, Avitzur Y, et al. Probiotics reduce bacterial colonization and gastric inflammation in H. pylori-infected mice. *Dig Dis Sci*. 2004 Aug;49(7-8):1095-102. [PMID:15387328]
8. Johnson-Henry KC, Nadjafi M, Avitzur Y, et al. Amelioration of the effects of Citrobacter rodentium infection in mice by pretreatment with probiotics. *J Infect Dis*. 2005 Jun 15;191(12):2106-17. [PMID: 15897997]
9. Zareie M, Johnson-Henry K, Jury J, et al. Probiotics prevent bacterial translocation and improve intestinal barrier function in rats following chronic psychological stress. *Gut*. 2006 Nov;55(11):1553-60. [PMID: 16638791]
10. Foster LM, Tompkins TA, Dahl WJ. A comprehensive post-market review of studies on a probiotic product containing Lactobacillus helveticus R0052 and Lactobacillus rhamnosus R0011. *Benef Microbes*. 2011 Dec 1;2(4):319-34. [PMID: 22146691]
11. Kocian J. [Further possibilities in the treatment of lactose intolerance: Lactobacilli] [in Czech]. *Praktický lékař*. 1994;74:212-14. [translation on file]
12. Kocian J. Lactobacilli in the treatment of dyspepsia in dysmicrobia in different aetiology [in Czech]. *Vnitřní Lekarství*. 1994;40:79-83. [PMID: 8140765]
13. Elmer GW. Probiotics: "living drugs". *Am J Health Syst Pharm*. 2001 Jun 15;58(12):1101-9. [PMID: 11449853]
14. Marteau P. Living drugs for gastrointestinal diseases: the case for probiotics. *Dig Dis*. 2006;24(1-2):137-47. [PMID: 16699272]
15. Institut Rosell-Lallemand. <http://www.institut-rosell-lallemand.com/index.php?langue=2>. Accessed October 19, 2012.
16. Ivanko O. Lacidofi I in the prevention of Clostridium difficile diarrhea in children. Zaporozhye State Medical University, Ukraine. Unpublished results. [summary on file]
17. Tlaskal P, Michkova H, Klayarova L, et al. Lactobacillus acidophilus in the treatment of children with gastrointestinal tract illnesses [in Czech]. *Cesko-Slovenska Pediatrie*. 1995;51:615-19. [translation on file]
18. Ziemniak W. Efficacy of Helicobacter pylori eradication taking into account its resistance to antibiotics. *J Physiol Pharmacol*. 2006 Sep;57 Suppl 3:123-41. [PMID: 17033111]
19. Song HJ, Kim JY, Jung SA, et al. Effect of probiotic Lactobacillus (Lacidofil® cap) for the prevention of antibiotic-associated diarrhea: a prospective, randomized, double-blind, multicenter study. *J Korean Med Sci*. 2010 Dec;25(12):1784-91. [PMID: 21165295]
20. Rampengan NH, Manoppo J, Warouw SM. Comparison of efficacies between live and killed probiotics in children with lactose malabsorption. *Southeast Asian J Trop Med Public Health*. 2010 Mar;41(2):474-81. [PMID: 20578532]
21. Furrie E, Macfarlane S, Kennedy A, et al. Synbiotic therapy (Bifidobacterium longum/Synergy 1) initiates resolution of inflammation in patients with active ulcerative colitis: a randomised controlled pilot trial. *Gut*. 2005 Feb;54(2):242-9. [PMID: 15647189]
22. Messaoudi M, Violle N, Bisson JF, et al. Beneficial psychological effects of a probiotic formulation (Lactobacillus helveticus R0052 and Bifidobacterium longum R0175) in healthy human volunteers. *Gut Microbes*. 2011 Jul-Aug;2(4):256-61. [PMID: 21983070]
23. Puertollano MA, Puertollano E, de Cienfuegos GÁ, et al. Dietary antioxidants: immunity and host defense. *Curr Top Med Chem*. 2011;11(14):1752-66. Review. [PMID: 21506934]
24. Firmesse O, Mogenet A, Bresson JL, et al. Lactobacillus rhamnosus R11 consumed in a food supplement survived human digestive transit without modifying microbiota equilibrium as assessed by real-time polymerase chain reaction. *J Mol Microbiol Biotechnol*. 2008;14(1-3):90-9. [PMID: 17957115]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

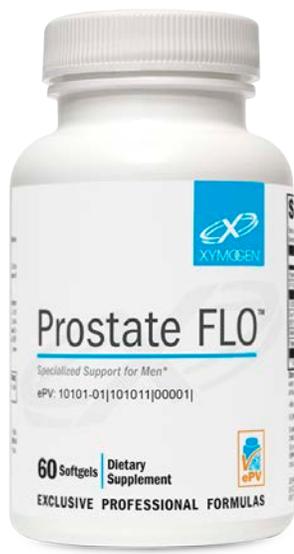
*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

© XYMOGEN
DRS-118
Rev. 08/05/19



Prostate FLO™

Specialized Support for Men*



Available in 60 softgels

Discussion

As men age, the need for maintaining or supporting normal prostate and lower urinary tract (LUT) health and function increases. Prostate FLO represents the latest in specialized formulations for men.

FLOWENS®

Cranberry fruit has a history of use among Native Americans for kidney and urinary health.^[1] Modern research supports this traditional use.^[1-4] Cranberry fruit is recognized as a rich source of oligosaccharides and phytochemicals, including proanthocyanidins, flavonols, and triterpenoids. FLOWENS is a 100% all-natural, full-spectrum cranberry powder designed and optimized for men's health. In a clinical study, FLOWENS was shown to improve quality of life and support urinary tract function with improvements noted within the first month of supplementation. In a six-month double-blind, randomized, placebo-controlled study, supplementation with 250 or 500 mg/d of FLOWENS resulted in clinically-relevant, dose-dependent improvements in primary (a clinically validated questionnaire) and secondary (e.g., uroflowmetry scores, urine storage) outcome measures related to prostate function in men older than 45 years. No side effects were reported. The researchers suggested that the observed effects may have resulted from activities on detrusor contraction and relaxation, modulation of the micturition reflex, or a reduction in certain cytokines.*^[1]

Saw Palmetto (*Serenoa repens*)

Saw palmetto extracts have been widely used in Europe and more recently in the United States as a natural way to help maintain normal prostate health and LUT function. A systematic review^[5] of 18 randomized controlled trials involving 2,939 men and another analysis of 21 clinical trials involving 3,000 men and reviewed by Cochrane^[6] support the safety and efficacy of saw palmetto extract preparations, and animal and human clinical trials continue to support a role for saw palmetto in prostate health.^[7-10] Mechanisms of action have not been fully elucidated, but there is evidence that saw palmetto inhibits 5-alpha reductase (5AR)—the enzyme that reduces testosterone to the more potent androgen dihydrotestosterone (DHT).^{*[11,12]}

Clinical Applications

- » Supports Healthy Lower Urinary Tract (LUT) Function in Men*
- » Supports Normal Urinary Flow and Nocturnal Frequency*
- » Supports Healthy Prostate-Related Hormone Metabolism*
- » Supports Prostate Health*

*Prostate FLO™ supports normal male lower urinary tract function and prostate health. Clinically meaningful levels of key ingredients target urinary flow and frequency as well as prostate-related hormone metabolism. This formula features FLOWENS®—a full-spectrum cranberry powder optimized for men's health—combined with beta-sitosterol, pyridoxal 5'-phosphate, TRAACS® zinc bisglycinate chelate, and highly concentrated, standardized extracts of saw palmetto and pygeum.**

Other effects have been proposed, including that saw palmetto prevents DHT from binding to androgen receptors, has antiestrogenic and antiproliferative effects, inhibits growth factors, affects alpha-1 adrenoceptors and 1,4-dihydropyridine receptors, and helps maintain healthy fluid balance in prostate tissues.^[7,12-15] Prostate FLO features a high-quality, standardized (85% free fatty acids) extract to assure the opportunity for the best clinical outcomes.*

Pygeum Africanum (*Pygeum africanum*)

The use of pygeum dates back approximately 300 years, and extracts are a well-known and often-used alternative for supporting prostate health in many European countries.^[16] Numerous open and placebo-controlled studies in large populations have demonstrated its efficacy and acceptability for supporting healthy urine flow and volume, reducing nocturnal voiding, and improving quality of life.^[17-21] Multiple mechanisms of action have been proposed for the genitourinary effects of pygeum, which contains numerous beneficial constituents, such as beta-sitosterol. Mechanisms are thought to include 5AR inhibition; estrogenic, antiandrogenic, and antiproliferative effects; and modulation of cell signaling molecules, including cytokines.*^[18,20]

Beta-Sitosterol

Beta-sitosterol is a plant phytosterol commonly used to promote LUT function in men. In a randomized, double-blind, placebo-controlled, multicenter study, 200 patients were supplemented with 20 mg of beta-sitosterol three times per day or placebo. Significant improvements in urinary flow parameters were observed in the beta-sitosterol group only.^[22] In a follow-up study, the beneficial effects of beta-sitosterol treatment were maintained for 18 months.^[23] In a six-month randomized, double-blind, placebo-controlled clinical trial (n = 177), 130 mg/d of beta-sitosterol resulted in significant improvements in patients' quality of life, urinary flow rate, and residual volume compared to placebo.^[24] A systematic review of clinical trials also supported the benefits of beta-sitosterol to LUT function in men.*^[25]

Continued on next page

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

Prostate FLO™ Supplement Facts

Serving Size: 2 Softgels

	Amount Per Serving	%Daily Value
Vitamin B6 (as pyridoxal 5'-phosphate)	10 mg	588%
Zinc (as TRAACS® zinc bisglycinate chelate)	30 mg	273%
FLOWENS® Cranberry Fruit Solids (<i>Vaccinium macrocarpon</i>) (fruits)	500 mg	**
Saw Palmetto Extract (<i>Serenoa repens</i>) (dried fruits) (85% free fatty acids)	320 mg	**
Beta-Sitosterol	180 mg	**
Pygeum Extract (<i>Prunus africana</i>) (bark) (2.5% beta-sitosterol)	100 mg	**

**Daily Value not established.

Other Ingredients: Organic flaxseed oil, softgel (bovine gelatin, vegetable glycerin, purified water, and natural caramel color), sunflower lecithin, tricalcium phosphate, maltodextrin, citric acid, and silica.

TRAACS® is a registered trademark of Albion Laboratories, Inc.

FLOWENS® is a trademark of Naturex.

DIRECTIONS: Take one to two softgels daily, or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

References

- Vidlar A, Student V Jr, Vostalova J, et al. Cranberry fruit powder (Flowens™) improves lower urinary tract symptoms in men: a double-blind, randomized, placebo-controlled study. *World J Urol.* 2016 Mar;34(3):419-24. [PMID: 26049866]
- Vasileiou I, Katsargyris A, Theocharis S, et al. Current clinical status on the preventive effects of cranberry consumption against urinary tract infections. *Nutr Res.* 2013 Aug;33(8):595-607. [PMID: 23890348]
- Sun J, Marais JP, Khoo C, et al. Cranberry (*Vaccinium macrocarpon*) oligosaccharides decrease biofilm formation by uropathogenic *Escherichia coli*. *J Funct Foods.* 2015 Aug;17:235-42. [PMID: 26613004]
- Blumberg JB, Camesano TA, Cassidy A, et al. Cranberries and their bioactive constituents in human health. *Adv Nutr.* 2013 Nov 6;4(6):618-32. [PMID: 24228191]
- Wilt TJ, Ishani A, Stark G, et al. Saw palmetto extracts for treatment of benign prostatic hyperplasia: a systematic review. *JAMA.* 1998 Nov 11;280(18):1604-09. Erratum in: *JAMA* 1999 Feb 10;281(6):515. [PMID: 9820264]
- Wilt T, Ishani A, MacDonald R. *Serenoa repens* for benign prostatic hyperplasia. *Cochrane Database Syst Rev.* 2002;(3):CD001423. Review. Update in: *Cochrane Database Syst Rev.* 2009;(2):CD001423. [PMID: 12137626]
- Saw palmetto: clinical overview. In: Blumenthal M, Goldberg A, Kunz T, Dinda K, eds. *The ABC Clinical Guide to Herbs.* Austin, TX: American Botanical Council; 2003:309-319. http://abc.herbalgram.org/site/DocServer/Saw_Palmetto.pdf?docID=167. Accessed May 24, 2016.
- Mantovani F. *Serenoa repens* in benign prostatic hypertrophy: analysis of 2 Italian studies. *Minerva Urol Nefrol.* 2010 Dec;62(4):335-40. [PMID: 20944533]
- lii Colado-Velázquez J, Mailloux-Salinas P, Medina-Contreras J, et al. Effect of serenoa repens on oxidative stress, inflammatory and growth factors in obese wistar rats with benign prostatic hyperplasia. *Phytother Res.* 2015 Oct;29(10):1525-31. [PMID: 26104840]
- Tacklind J, MacDonald R, Rutks I, et al. *Serenoa repens* for benign prostatic hyperplasia. *Cochrane Database Syst Rev.* 2012 Dec 12;12:CD001423. [PMID: 23235581]
- Marks LS, Hess DL, Dorey FJ, et al. Tissue effects of saw palmetto and finasteride: use of biopsy cores for in situ quantification of prostatic androgens. *Urology.* 2001 May;57(5):999-1005. [PMID: 11337315]
- Suzuki M, Ito Y, Fujino T, et al. Pharmacological effects of saw palmetto extract in the lower urinary tract. *Acta Pharmacol Sin.* 2009 Mar;30(3):227-81. [PMID: 19262550]
- Saw Palmetto. Somerville, MA: Natural Medicines; 2016. <https://naturalmedicines.therapeuticresearch.com/databases/food,-herbs-supplements/professional.aspx?productid=971>. Accessed May 24, 2016.

Zinc and Vitamin B6

Zinc is highly concentrated in the prostate gland, and a lack of zinc may be associated with a reduced DNA damage and repair response in prostate tissue.^[26] Therefore, zinc adequacy is vital for optimal prostate health, especially with advancing age.^[27] In this formula, zinc is provided as the highly absorbable Albion® TRAACS® zinc bisglycinate chelate. Pyridoxal 5'-phosphate (P5P) is the active form of vitamin B6. In a population-based prospective study of 525 men, Kasperzyk et al found that high vitamin B6 intake had an inverse association with prostate-related mortality.*^[28]

- Di Silverio F, D'Armeo G, Lubrano C, et al. Evidence that *Serenoa repens* extract displays an antiestrogenic activity in prostatic tissue of benign prostatic hypertrophy patients. *Eur Urol.* 1992;21(4):309-14. [PMID: 1281103]
- Wadsworth TL, Carroll JM, Mallinson RA, et al. Saw palmetto extract suppresses insulin-like growth factor-I signaling and induces stress-activated protein kinase/c-Jun N-terminal kinase phosphorylation in human prostate epithelial cells. *Endocrinology.* 2004 Jul;145(7):3205-14. [PMID: 15033918]
- Levin RM, Das AK. A scientific basis for the therapeutic effects of Pygeum africanum and *Serenoa repens*. *Urol Res.* 2000 Jun;28(3):201-09. [PMID: 10929430]
- Breza J, Dzuryn O, Borowka A, et al. Efficacy and acceptability of tadenan (Pygeum africanum extract) in the treatment of benign prostatic hyperplasia (BPH): a multicentre trial in central Europe. *Curr Med Res Opin.* 1998;14(3):127-39. [PMID: 9787978]
- Pygeum Africanum. Somerville, MA: Natural Medicines; 2016. <https://naturalmedicines.therapeuticresearch.com/databases/food,-herbs-supplements/professional.aspx?productid=388>. Accessed May 24, 2016.
- Ishani A, MacDonald R, Nelson D, et al. Pygeum africanum for the treatment of patients with benign prostatic hyperplasia: a systematic review and quantitative meta-analysis. *Am J Med.* 2000 Dec 1;109(8):654-64. [PMID: 11099686]
- Quiles MT, Arbós MA, Fraga A, et al. Antiproliferative and apoptotic effects of the herbal agent Pygeum africanum on cultured prostate stromal cells from patients with benign prostatic hyperplasia (BPH). *Prostate.* 2010 Jul 1;70(10):1044-53. [PMID: 20503393]
- Wilt T, Ishani A, MacDonald R, et al. Pygeum africanum for benign prostatic hyperplasia. *Cochrane Database Syst Rev.* 2002;(1):CD001044. [PMID: 11869585]
- Berges RR, Windeler J, Trampisch HJ, et al. Randomised, placebo-controlled, double-blind clinical trial of beta-sitosterol in patients with benign prostatic hyperplasia. Beta-sitosterol study group. *Lancet.* 1995 Jun 17;345(8964):1529-32. [PMID: 7540705]
- Berges RR, Kassen A, Senge T. Treatment of symptomatic benign prostatic hyperplasia with beta-sitosterol: an 18-month follow-up. *BJU Int.* 2000 May;85(7):842-46. [PMID: 10792163]
- Klippel KF, Hiltl DM, Schipp B. A multicentric, placebo-controlled, double-blind clinical trial of beta-sitosterol (phytosterol) for the treatment of benign prostatic hyperplasia. German BPH-Phyto Study group. *Br J Urol.* 1997 Sep;80(3):427-32. [PMID: 9313662]
- Wilt TJ, MacDonald R, Ishani A. Beta-sitosterol for the treatment of benign prostatic hyperplasia: a systematic review. *BJU Int.* 1999 Jun;83(9):976-83. [PMID: 10368239]
- Yan M, Song Y, Wong CP, et al. Zinc deficiency alters DNA damage response genes in normal human prostate epithelial cells. *J Nutr.* 2008 Apr;138(4):667-73. [PMID: 18356318]
- Costello LC, Franklin RB, Tan MT. A critical assessment of epidemiology studies regarding dietary/supplemental zinc and prostate cancer risk. *Open Urol Nephrol J.* 2008;1. [PMID: 24204440]
- Kasperzyk JL, Fall K, Mucci LA, et al. One-carbon metabolism-related nutrients and prostate cancer survival. *Am J Clin Nutr.* 2009 Sep;90(3):561-69. [PMID: 19571222]

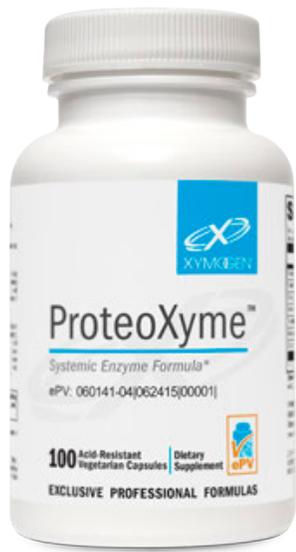
Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

ProteoXyme™

Systemic Enzyme Formula*



Available in 100 vegetable capsules

Discussion

Enzymes are complex proteins that catalyze metabolic reactions throughout the body, and sufficient levels are necessary for optimizing many bodily functions. Though the body naturally produces its own supply of enzymes, production can vary with age and biochemical individuality.*^[1]

Proteolytic enzymes, also known as proteases, specifically break down proteins into peptides and amino acids through the process of “proteolysis.” For example, proteases produced by the pancreas assist in the digestion of dietary protein. Some proteases, such as trypsin, are then resorbed, transported in the bloodstream, and resecreted by the pancreas. Enzymes in circulation are bound to antiprotease alpha-2-macroglobulin to protect them from being degraded by other serum proteases and to retain their enzymatic activity.*

ProteoXyme is a proteolytic enzyme formula designed to be absorbed across the gastrointestinal mucosa and into circulation.^[2] When distributed systemically, proteolytic enzymes can break down proteins and complexes generated during injury and tissue damage. This action supports the body’s normal recovery process.*

In vivo studies suggest that trypsin and other proteases, though normally confined to the bloodstream, are able to enter the site of injury.^[3] At this site, they are able to support immune function and affect cytokine production. Research suggests that orally administered proteolytic enzymes may exert this beneficial effect as well.^[3,4] It is thought that they function as proteinase-activated receptor (PAR) modulators, a feature which allows them to contribute to immune and cytokine balance.^[5] Proteolysis of intestinal microorganisms may contribute to the immunostimulatory effects of oral proteolytic enzymes as well.*^[6]

Proteolytic enzymes have been used worldwide for decades to support health and healing. For example, research on bromelain (an enzyme obtained from pineapple) suggests that it positively affects eicosanoid production and balance.^[7-9] Furthermore, it is suggested

Clinical Applications

- » Supports Joint Health and Mobility*
- » Supports Healthy Immune System Balance*
- » Supports the Body’s Ability to Heal and Maintain Tissue Integrity*
- » Affects Eicosanoid Production and Cytokine Balance*

*ProteoXyme™ affects cytokine and eicosanoid balance, promotes joint comfort, and supports the body’s ability to maintain tissue integrity. Proteolytic enzymes in ProteoXyme may break down proteins and complexes that can be produced as a result of injury and tissue damage. This activity is believed to aid nutrient and oxygen delivery and may help speed the body’s ability to recover and heal. Acid-resistant capsules facilitate systemic delivery of enzymes.**

that bromelain supports the body’s innate and adaptive immune function,^[10,11] signifying an effect beyond that of proteolysis in some cases.*

Serrapeptase (also known as serratiopeptidase) is an enzyme produced by microorganisms in the gastrointestinal tract of silkworms. Silkworms use it to digest their cocoons. Multicenter, double-blind studies suggest that serrapeptase significantly supports tissue integrity and comfort and is well-tolerated.^[12,13] Pancreatin in ProteoXyme is a mixture of pancreatic enzymes containing chymotrypsin, trypsin, amylase, and lipase. The papain present is a proteolytic enzyme derived from papaya fruit.*

The effect of combining various proteolytic enzymes has been studied closely for decades. For example, the combination of trypsin and chymotrypsin has a history of use in the support of tissue integrity and healing, with positive results in early double-blind trials.^[14-16] The combination of bromelain, trypsin, and rutin has been researched and found to produce positive results as well.^[17] For example, in a six-week, randomized, double-blind, parallel group trial (n=90), oral proteolytic enzymes were well-tolerated and positively affected clinical outcomes, including Western Ontario and McMaster Universities osteoarthritis index (WOMAC) and Lequesne’s index scores, as efficiently as other compounds studied.^[18] Another randomized double-blind controlled study using systemic enzyme therapy (a combination of bromelain, trypsin, and rutin) reported “remarkable differences” in tissue comfort and integrity in subjects who received the enzyme therapy.*^[19]

ProteoXyme contains a combination of pancreatin, papain, rutin, bromelain, trypsin, chymotrypsin, and serrapeptase in acid-resistant capsules that are designed to withstand gastric juices, ultimately allowing direct absorption into the bloodstream. For best results, the formula should be consumed on an empty stomach.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

ProteXyme™ Supplement Facts

Serving Size: 5 Capsules

	Amount Per Serving	%Daily Value
Pancreatin 10x (from porcine)	500 mg (125,000 USP)	**
Papain (from papaya) (<i>Carica papaya</i>) (fruit)	300 mg (4,800,000 PU)	**
Rutin (from <i>Sophora japonica</i>) (leaf)	250 mg	**
Bromelain (from pineapple) (<i>Ananas comosus</i>) (stems)	225 mg (540 GDU)	**
Trypsin (from porcine)	125 mg (288,000 USP)	**
Serrapeptase	99 mg (60,000 U)	**
Chymotrypsin (from porcine)	37.5 mg (37,500 USP)	**
** Daily Value not established.		

Other Ingredients: Inulin, HPMC (capsule), microcrystalline cellulose, vegetable stearic acid, vegetable magnesium stearate, and silica.

DIRECTIONS: Take three to five capsules daily on an empty stomach, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking blood thinners or other medication as well as those with bleeding disorders or liver damage should discuss potential interactions and contraindications with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, soy, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.



References

- Paczek L, Michalska W, Bartłomiejczyk I. Trypsin, elastase, plasmin and MMP-9 activity in the serum during the human ageing process. *Age Ageing*. 2008 May;37(3):318-23. [PMID: 18332058]
- Castell JV, Friedrich G, Kuhn CS, et al. Intestinal absorption of undegraded proteins in men: presence of bromelain in plasma after oral intake. *Am J Physiol*. 1997 Jul;273(1 Pt 1):G139-46. [PMID: 9252520]
- Lehmann PV. Immunomodulation by proteolytic enzymes. *Nephrol Dial Transplant*. 1996 Jun;11(6):952-5. [PMID: 8671947]
- Shahid S. Role of systemic enzymes in infections. *WebmedCentral COMPLEMENTARY MEDICINE* 2011;2(11):WMC002495. http://www.webmedcentral.com/article_view/2495. Accessed October 4, 2012.
- Steinhoff M, Buddenkotte J, Shpacovitch V, et al. Proteinase-activated receptors: transducers of proteinase-mediated signaling in inflammation and immune response. *Endocr Rev*. 2005 Feb;26(1):1-43. [PMID: 15689571]
- Biziulevicius GA. Where do the immunostimulatory effects of oral proteolytic enzymes ("systemic enzyme therapy") come from? Microbial proteolysis as a possible starting point. *Med Hypotheses*. 2006;67(6):1386-8. [PMID: 16870353]
- Kelly GS. Bromelain: A Literature Review and Discussion of its Therapeutic Applications. *Alt Med Rev*. 1996;1(4): 243-57. [copy on file].
- Wallace JM. Nutritional and botanical modulation of the inflammatory cascade—eicosanoids, cyclooxygenases, and lipoxygenases—as an adjunct in cancer therapy. *Integr Cancer Ther*. 2002 Mar;1(1):7-37; discussion 37. Review. [PMID: 14664746].
- Taussig SJ, Batkin S. Bromelain, the enzyme complex of pineapple (*Ananas comosus*) and its clinical application. An update. *J Ethnopharmacol*. 1988 Feb-Mar;22(2):191-203. [PMID: 3287010]
- Barth H, Guseo A, Klein R. In vitro study on the immunological effect of bromelain and trypsin on mononuclear cells from humans. *Eur J Med Res*. 2005 Aug 17;10(8):325-31. [PMID: 16131473]
- Maurer HR. Bromelain: biochemistry, pharmacology and medical use. *Cell Mol Life Sci*. 2001 Aug;58(9): 1234-45. [PMID: 11577981]
- Tachibana M, Mizukoshi O, Harada Y, et al. A multi-centre, double-blind study of serrapeptase versus placebo in post-antrotomy buccal swelling. *Pharmatherapeutica*. 1984;3(8):526-30. [PMID: 6366808]
- Mazzone A, Catalani M, Costanzo M, et al. Evaluation of Serratia peptidase in acute or chronic inflammation of otorhinolaryngology pathology: a multicentre, double-blind, randomized trial versus placebo. *J Int Med Res*. 1990 Sep-Oct;18(5):379-88. [PMID: 2257960]
- Deitrick RE. Oral proteolytic enzymes in the treatment of athletic injuries: A double-blind study. *Pa Med*. 1965 Oct;68(10):35-7. [PMID: 5318158]
- Rathgeber WF. The use of proteolytic enzymes (Chymoral) in sporting injuries. *S Afr Med J*. 1971 Feb 13;45(7):181-3. [PMID: 4928685]
- Buck JE, Phillips N. Trial of Chymoral in professional footballers. *Br J Clin Pract*. 1970 Sept;24(9):375-7. [PMID: 4918726]
- Akhtar NM, Naseer R, Farooqi AZ, et al. Oral enzyme combination versus diclofenac in the treatment of osteoarthritis of the knee—a double-blind prospective randomized study. *Clin Rheumatol*. 2004 Oct;23(5):410-5. [PMID: 15278753]
- Klein G. Efficacy and tolerance of an oral enzyme combination in painful osteoarthritis of the hip. A double-blind, randomized study comparing oral enzymes with non-steroidal anti-inflammatory drugs. *Clin Exp Rheumatol*. 2006 Jan-Feb;24(1):25-30. [PMID: 16539815]
- Kamenicek V, Holán P, Franek P. Systemic enzyme therapy in the treatment and prevention of post-traumatic and postoperative swelling [in Czech]. *Acta Chir Orthop Traumatol Cech*. 2001;68(1):45-9. [PMID: 11706714]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

RegeneMax[®] Liquid

Advanced Collagen Generator^{®*}



RegeneMax Liquid is available in 1 ounces (30 mL)

Discussion

Collagen is the body's main structural protein. Collagen makes up 70% of skin and gives skin both strength and elasticity. Collagen forms 30% of bone and gives bones the flexibility they need to withstand impact. The collagen fibers in bone are the binding sites for calcium as well as all bone minerals.^[1] Collagen is the major component of fascia, cartilage, ligaments, and tendons. But collagen production begins decreasing at age 18. By the age of 40, the decrease is about 1% per year.^[2] For women, the decline equates to a loss of 7% of skin thickness every 10 years. Following menopause, the decline in thickness accelerates to as much as 1.13% annually, while skin elasticity degrades 0.55% per year.^[3] Adequate collagen production correlates with healthy bones and strong hair and nails.^{*[2-4]}

For years, orthosilicic acid was the focus of intense research because it was viewed as a potential collagen generator. As a result of that research, the molecular complex known as choline-stabilized orthosilicic acid (ch-OSA[®]) was created. Choline not only has the positively charged nitrogen atom that forms the vital bond with OSA, but according to leading collagen researchers, choline transports the orthosilicic acid into target cells where it activates the pathways involved in collagen production. Clinical trials also suggest that beyond its ability to generate collagen, ch-OSA promotes keratin and elastin formation—two proteins that assist in skin elasticity and hair tensile strength.^{*[5-7]}

In a 20-week, randomized, double-blind, placebo-controlled study of 50 women with photo-damaged facial skin, oral intake of two ch-OSA capsules resulted in significantly improved skin, visco-elasticity properties, and a 30% reduction in micro-wrinkle depth compared to placebo.^[5] In the same clinical trial, the women's hair and nails showed significant improvements in strength. In a nine-month, randomized, double-blind, placebo-controlled trial with 48 healthy Caucasian women with fine hair (average age 43.3 years), ch-OSA (in daily capsules) significantly improved hair thickness and hair tensile strength.^[6] In a 12-month clinical trial conducted at St. Thomas' Hospital in London, women already taking 1000 mg of calcium and

Clinical Applications

- » Reduces Fine Lines and Wrinkles*
- » Thickens and Strengthens Hair*
- » Strengthens Nails*
- » Increases Hip Bone Mineral Density*
- » Adds Flexibility to Bones*
- » Promotes Healthy Joints*

*RegeneMax[®] Liquid provides ch-OSA[®] (choline-stabilized orthosilicic acid), that helps naturally nourish your body's beauty proteins. Regular orthosilicic acid is highly unstable, leading it to form polymers. These polymers are too large for the human body to absorb. But the patented "choline stabilization" technology in RegeneMax Liquid prevents the polymers from forming, ensuring optimal absorption. RegeneMax Liquid has been formulated with clinically proven ch-OSA for your assurance.**

800 IU of vitamin D to which they added ch-OSA saw thigh bone mineral density at the hip increase by 2.00% over the placebo as a result of an increase in actual bone formation, not just a decrease in loss.^[7] The procollagen marker P1NP (procollagen type-1 N-terminal propeptide) increased significantly after 12 months in women who took ch-OSA compared to women in the placebo group. P1NP is known as the most sensitive marker for bone collagen formation and an early marker of bone formation.^[7] Animal studies support the human clinical findings for ch-OSA with respect to collagen formation and bone mineral density.^{*[8-10]}

EXCLUSIVE • PATENTED

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN[®] Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

RegeneMax® Liquid Supplement Facts

Serving Size: 6 Drops (about 0.30 mL)
 Servings Per Container: About 100

	Amount Per Serving	%DV
Choline (as choline-stabilized orthosilicic acid)	120 mg	22%
Silicon (as choline-stabilized orthosilicic acid)	6 mg	**

** Daily Value (DV) not established.

Other Ingredients: Glycerol and purified water.

DIRECTIONS: For Bones: One time per day, take six drops in 2 oz (1/4 cup) liquid. Stir and drink immediately. **For Skin, Hair, Nails, and Joint benefits:** Increase dose to five drops, twice daily.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Store in a cool, dry place out of reach from children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

Produced under US patent 7,968,528.

ch-OSA and Advanced Collagen Generator are registered trademarks of Bio Minerals NV, Belgium.

MADE BY BIO MINERALS NV, BELGIUM

References

- Viguet-Carrin S, Garnero P, Delmas PD. The role of collagen in bone strength. *Osteoporos Int.* 2006;17:319-336. [PMID: 16341622]
- Shuster S. Osteoporosis, a unitary hypothesis of collagen loss in skin and bone. *Med Hypotheses.* 2005;65(3):426-432. [PMID: 15951132]
- Calleja-Agius J, Muscat-Baron Y, Brincaat MP. Skin ageing. *Menopause Int.* 2007 June;13(2):60-4. [PMID: 17540135]
- Sumino H, Ichikawa S, Abe M, et al. (2004). Effects of aging and postmenopausal hypoestrogenism on skin elasticity and bone mineral density in Japanese women. *Endocr J.* 2004 Apr;51(2):159-164. [PMID: 15118265]
- Barel A, Calomme M, Timchenko A, et al. Effect of oral intake of choline-stabilized orthosilicic acid on skin, nails and hair in women with photodamaged skin. *Arch Dermatol Res.* 2005 Oct;297(4):147-153. [PMID: 16205932]
- Wickett RR, Kossman E, Barel A, et al. Effect of oral intake of choline-stabilized orthosilicic acid on hair tensile strength and morphology in women with fine hair. *Arch Dermatol Res.* 2007 Dec;299(10):499-505. [PMID: 17960402]
- Spector TD, Calomme MR, Anderson SH, et al. Choline-stabilized orthosilicic acid supplementation as an adjunct to calcium/vitamin D3 stimulates markers of bone formation in osteopenic females: a randomized, placebo-controlled trial. *BMC Musculoskelet Disord.* 2008 Jun 11;9:85. [PMID: 18547426]
- Calomme MR, Vanden Berghe DA. Supplementation of calves with stabilized orthosilicic acid. Effect on the Si, Ca, Mg, and P concentrations in serum and the collagen concentration in skin and cartilage. *Biol Trace Elem Res.* 1997 Feb;56(2):153-165. [PMID: 9164661]
- Calomme MR, Wijnen P, Sindambiwe JB, et al. Effect of choline-stabilized orthosilicic acid on bone density in chicks. *Calcif Tissue Int.* 2002, 70:292. Presented at: 29th European Symposium on Calcified Tissues; May 25-29, 2002; Zagreb, Croatia.
- Calomme MR, Geusens P, Demeester N, et al. Partial prevention of long-term femoral bone loss in aged ovariectomized rats supplemented with choline-stabilized orthosilicic acid. *Calcif Tissue Int.* 2006, Apr;78(4): 227-232. [PMID: 16604283]

Additional references available upon request

EXCLUSIVE • PATENTED

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

RegeneMax® Plus

Advanced Collagen Generator®*
Clinically Proven ch-OSA® Plus Biotin



Available in 60 and 120 vegetarian capsules

Discussion

Silicon and Choline-Stabilized Orthosilicic Acid

Silicon is a ubiquitous element present in various tissues of the human body. It performs an important role in connective tissue health, especially in the formation of the organic matrix (e.g., collagen and glycosaminoglycan formation).^[1] Cereal/grain-based products and vegetables are the main dietary sources of silicon, but modern processing is likely to reduce intake from these sources. Soluble silicon is found as orthosilicic acid (OSA) in beverages and water.^[2] Because regular orthosilicic acid is highly unstable, leading it to form polymers, and because the polymers are too large for the human body to absorb, RegeneMax Plus features patented “choline stabilization” technology. This stabilization prevents polymers from forming, ensuring optimal absorption of orthosilicic acid. Choline-stabilized orthosilicic acid (ch-OSA®) is a bioavailable form of silicon that has been found to increase the hydroxyproline concentration in the dermis of animals.^[2] Furthermore, the ch-OSA in RegeneMax Plus is clinically proven for your assurance.*^[2-4]

“Beauty Proteins” and Orthosilicic Acid

ch-OSA helps naturally nourish the body’s beauty proteins: collagen, elastin, and keratin. Collagen is the body’s main structural protein. It makes up 70% of skin and gives skin its strength and elasticity. It forms 30% of bone to give bones the flexibility they need to withstand impact. Additionally, the collagen fibers in bone are the binding sites for calcium and other bone minerals.^[5] Collagen is also the major component of fascia, cartilage, ligaments, and tendons. Unfortunately, collagen production begins decreasing at age 18. By the age of 40, the decrease is about 1% per year.^[6] For women, the decline equates to a loss of 7% of skin thickness every 10 years. Following menopause, the decline in thickness accelerates to as much as 1.13% annually, while skin elasticity degrades 0.55% per year.^[7] Adequate collagen production correlates with healthy bones and strong hair and nails.*^[6-8]

For years, OSA was the focus of intense research because it was viewed as a potential collagen generator. As a result of that research, the molecular complex known ch-OSA was created. Choline not only has the positively charged nitrogen atom that forms the vital bond with OSA, but according to leading collagen researchers, choline transports the orthosilicic acid into target cells where it activates the pathways involved in collagen production. Clinical trials also suggest that beyond its ability to generate collagen, ch-OSA promotes keratin and elastin formation—two proteins that assist in skin elasticity and hair tensile strength.*^[2-4]

ch-OSA Clinical Studies

In a 20-week, randomized, double-blind, placebo-controlled study of 50 women with photo-damaged facial skin, oral intake of 10 mg/d silicon as ch-OSA

Clinical Applications

- » Reduces Fine Lines and Wrinkles*
- » Thickens and Strengthens Hair*
- » Strengthens Nails*
- » Supports Healthy Bone Mineral Density*
- » Supports Bone Flexibility*
- » Promotes Connective Tissue Formation for Healthy Joints*

*RegeneMax® Plus features clinically tested ch-OSA® (choline-stabilized orthosilicic acid) complemented with biotin. ch-OSA naturally helps nourish your body’s beauty proteins by supporting and activating enzymes used by collagen-generating cells to make collagen. Regular orthosilicic acid (OSA) has to be stabilized to avoid polymerization, a process that decreases bioavailability. ch-OSA’s patented choline-stabilization technology prevents polymers from forming and ensures OSA’s optimal absorption. By combining ch-OSA with biotin, RegeneMax Plus offers an even greater level of beauty support.**

resulted in significantly improved skin visco-elastic properties and a 19% reduction in roughness with a 30% reduction in micro-wrinkle depth (measured as maximum roughness) compared to placebo.^[2] In the same clinical trial, the women’s hair and nails showed significant improvements in strength. Furthermore, serum silicon was significantly higher (+72%) in subjects after 20 weeks of supplementation with ch-OSA compared to the placebo group. In a nine-month, randomized, double-blind, placebo-controlled trial with 48 healthy Caucasian women with fine hair (average age 43.3 years), 10 mg/d of silicon as ch-OSA for nine months improved hair tensile strength including elasticity and break load and resulted in thicker hair.*^[3]

In a 12-month clinical trial conducted at St. Thomas’ Hospital in London, women already taking 1000 mg of calcium and 800 IU of vitamin D, to which they added ch-OSA, saw thighbone mineral density at the hip (i.e., femoral neck) increase by 2.00% compared to placebo. This was as a result of an increase in actual bone formation, not just a decrease in loss.^[4] Furthermore, the procollagen marker P1NP (procollagen type-1 N-terminal propeptide) increased significantly after 12 months in women who took ch-OSA compared to women in the placebo group. P1NP is known as the most sensitive marker for bone collagen formation and an early marker of bone formation.^[4] Animal studies support the human clinical findings for ch-OSA with respect to collagen formation and bone mineral density.*^[9-11]

In an open clinical study, 18 subjects were given five drops of ch-OSA twice daily for six months. Hair growth and hair loss assessments were performed using a semi-quantitative rating scale, and scores were analyzed using the Friedman test. At the end of the six months, 94% of respondents had improved hair growth with 58% in the categories of moderate to marked hair growth. All respondents noted improvement in the body and texture of their hair.*^[12]

Biotin

Biotin, as an essential component of carboxylase enzymes, has diverse roles in maintaining health. While overt biotin deficiency is known to result in skin irritation and hair loss, anecdotal evidence suggests that biotin supplementation supports healthy hair growth, and supplementing with biotin is a common method for enhancing skin health and hair and nail strength. Studies testing the effects of biotin on nail health suggest that biotin supplementation improves nail thickness and reduces splitting.^[13-15] In one study, 91% of subjects showed definite improvement with firmer and harder finger nails after 5.5+/-2.3 months of 2.5 mg/d biotin.^[16] Higher doses of biotin (9 mg to 16 mg/d) are used to support healthy lipid and glucose metabolism; and more recently, doses up to 300 mg/d have been used to support muscle function related to neurologic health.*^[17,18]

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

RegeneMax® Plus Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Biotin	5000 mcg	1667%
Choline (as choline-stabilized orthosilicic acid)	100 mg	**
Silicon (as choline-stabilized orthosilicic acid)	5 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), microcrystalline cellulose, and purified water.
Produced under US patents 5,922,360; 7,968,528; and 8,771,757.
ch-OSA and Advanced Collagen Generator are registered trademarks of Bio Minerals NV, Belgium.
MADE BY BIO MINERALS NV, BELGIUM

DIRECTIONS: Take one capsule two times per day, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tampo seal is damaged.

STORAGE: Store in a cool, dry place out of reach from children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or preservatives.



References

1. Carlisle EM. Silicon as a trace nutrient. *Sci Total Environ*. 1988 Jul1;73(1-2):95-106. [PMID: 3212453]
2. Barel A, Calomme M, Timchenko A, et al. Effect of oral intake of choline-stabilized orthosilicic acid on skin, nails and hair in women with photodamaged skin. *Arch Dermatol Res*. 2005 Oct;297(4):147-153. [PMID: 16205932]
3. Wickett RR, Kossman E, Barel A, et al. Effect of oral intake of choline-stabilized orthosilicic acid on hair tensile strength and morphology in women with fine hair. *Arch Dermatol Res*. 2007 Dec;299(10):499-505. [PMID: 17960402]
4. Spector TD, Calomme MR, Anderson SH, et al. Choline-stabilized orthosilicic acid supplementation as an adjunct to calcium/vitamin D3 stimulates markers of bone formation in osteopenic females: a randomized, placebo-controlled trial. *BMC Musculoskelet Disord*. 2008 Jun 11;9:85. [PMID: 18547426]
5. Viguet-Carrin S, Garnero P, Delmas PD. The role of collagen in bone strength. *Osteoporos Int*. 2006;17:319-336. [PMID: 16341622]
6. Shuster S. Osteoporosis, a unitary hypothesis of collagen loss in skin and bone. *Med Hypotheses*. 2005;65(3):426-432. [PMID: 15951132]
7. Calleja-Agius J, Muscat-Baron Y, Brincat MP. Skin ageing. *Menopause Int*. 2007 June;13(2):60-4. [PMID: 17540135]
8. Sumino H, Ichikawa S, Abe M, et al. (2004). Effects of aging and postmenopausal hypoestrogenism on skin elasticity and bone mineral density in Japanese women. *Endocr J*. 2004 Apr;51(2):159-164. [PMID: 15118265]
9. Calomme MR, Vanden Berghe DA. Supplementation of calves with stabilized orthosilicic acid. Effect on the Si, Ca, Mg, and P concentrations in serum and the collagen concentration in skin and cartilage. *Biol Trace Elem Res*. 1997 Feb;56(2):153-165. [PMID: 9164661]
10. Calomme MR, Wijnen P, Sindambiwe JB, et al. Effect of choline-stabilized orthosilicic acid on bone density in chicks. *Calcif Tissue Int*. 2002, 70:292. Poster presented at: 29th European Symposium on Calcified Tissues; May 25-29, 2002; Zagreb, Croatia. <http://www.ectsoc.org/zagreb2002/poster3.htm>. Abstract P-139. Accessed December 16, 2015.
11. Calomme MR, Geusens P, Demeester N, et al. Partial prevention of long-term femoral bone loss in aged ovariectomized rats supplemented with choline-stabilized orthosilicic acid. *Calcif Tissue Int*. 2006, Apr;78(4): 227-232. [PMID: 16604283]
12. Chan G. An open clinical study of the efficacy of choline-stabilized orthosilicic acid in the management of hair loss. A pilot study. Paper presented at: 17th Regional Conference of Dermatology; September 13-16, 2006; Bali, Indonesia.
13. Colombo VE, Gerber F, Bronhofer M, et al. Treatment of brittle fingernails and onychoschizia with biotin: scanning electron microscopy. *J Am Acad Dermatol*. 1990 Dec;23(6 Pt 1):1127-32. [PMID: 2273113]
14. Hochman LG, Scher RK, Meyerson MS. Brittle nails: response to daily biotin supplementation. *Cutis*. 1993 Apr;51(4):303-5. [PMID: 8477615]
15. Scheinfeld N, Dahdah MJ, Scher R. Vitamins and minerals: their role in nail health and disease. *J Drugs Dermatol*. 2007 Aug;6(8):782-7. Review. [PMID: 17763607]
16. Floersheim GL. Treatment of brittle fingernails with biotin [in German]. *Z Hautkr*. 1989 Jan 15;64(1):41-8. [PMID: 2648686]
17. Sedel F, Bernard D, Mock DM, et al. Targeting demyelination and virtual hypoxia with high-dose biotin as a treatment for progressive multiple sclerosis. *Neuropharmacology*. 2015 Sep 5. [Epub ahead of print] [PMID: 26327679]
18. Biotin: Monograph. *Alt Med Rev*. 2007;12(1):73-78. [on file]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

© XYMOGEN
DRS-304
Rev. 06/25/19



7 22537 51025 7

RelaxMax™

Neurotransmitter & Hormone Support*
Promotes Stress Resiliency*



Available in Unflavored & Cherry

Discussion

Inositol Present as the distinct isomer myo-inositol, inositol is a six-carbon cyclic polyalcohol that occurs naturally in all living cells. Fruits, beans, grains, and nuts contain some inositol; however, an 1800–2500–calorie daily diet has been shown to provide only 225–1500 mg of myo-inositol. Of the nearly 100% of ingested myo-inositol that is absorbed in the gastrointestinal tract, more than half becomes lipid bound. In contrast to low plasma concentration, the peripheral nerves have an extraordinarily high concentration of myo-inositol.^[1] Inositol is a precursor for the second-messenger phosphatidylinositol system, which affects mood status differently than precursors for neurotransmitters.^[2] Based upon validated scoring procedures, double-blind, controlled, random-order crossover clinical trials using up to 18 g of myo-inositol per day for a month have demonstrated effectiveness with minimal to no side effects.^{*[3,4]}

GABA (gamma-aminobutyric acid) GABA is an amino acid manufactured in brain cells from glutamate. This primary neurotransmitter, abundant in the cerebral cortex, increases the production of alpha waves (related to a relaxed, yet mentally focused state) while decreasing beta waves (associated with hyperactivity, nervousness, and fleeting thoughts). Sufficient GABA results in the smooth, calming, regular rhythmic flow of electrical impulses in the brain needed for emotional well-being.^[5] Supplementation in humans has shown support for the maintenance of healthy cortisol and secretory IgA levels while under stress.^{*[6]}

Taurine (2-aminoethanesulfonic acid) Taurine exists mainly in free form in the intracellular space of tissues. This conditionally essential amino acid maintains cell volume via osmoregulation, which is the process that corrects excessive or insufficient concentrations of electrolytes. Taurine also stabilizes cell membranes in the heart and brain—two electrically active tissues. Considered neuroprotective, taurine modulates the ability of mitochondria to buffer intracellular calcium during glutamate depolarization and excitotoxicity (the means by which neurons are overstimulated and damaged) and, thereby, may prevent cell death.^[7] In addition to its antioxidant and cytokine-

Clinical Applications

- » Supports Relaxed Mood*
- » Supports Inhibitory Neurotransmitter and Second Messenger Functions*
- » Supports Neurotransmitter Balance and Neuronal Stabilization*
- » Supports Healthy Blood Pressure Levels Already Within Normal Range*
- » Addresses Brain Osmotic Regulation, Glial Cell Function, and Effective Neuronal Transmission*

*RelaxMax™ is an innovative powdered drink mix. It contains a blend of ingredients that supports the body's natural synthesis of catecholamines, the inhibitory neurotransmitter GABA, hormonal balance, and healthy glucose metabolism. RelaxMax aims to promote a calm, relaxed, well-balanced emotional and physiological state.**

balancing functions, taurine is important to neurotransmission, neuroregulation, and cardiac function.^[8,9] Taurine supplementation also increases GABA.^{*[9]}

L-Theanine (N-ethyl-L-glutamine) L-Theanine, provided as Suntheanine®, is protected by more than 40 US and international patents for its various physiological efficacies and L-isomer-specific production processes. A naturally-occurring, biologically active, free-form amino acid, L-theanine gives green tea its characteristic taste. Although notable for its relaxation support, L-theanine may also support nerve health and cognition. Theanine lowers glutamate levels by preventing transport of glutamate's precursor, glutamine.^[10] It may also inhibit neurotransmission, cause inhibitory neurotransmission via glycine receptors, and thereby reduce neuronal overstimulation.^[11] L-theanine's ability to relax the mind without inducing drowsiness has been documented by an increase in alpha wave activity during EEG recording.^{*[12]}

Magnesium Sometimes referred to as the relaxation mineral and mainly found in the brain, bones, and muscles, magnesium assists in the transmission of nerve impulses and is essential to more than 300 enzymatic reactions in the body. Magnesium supplementation has been shown to support a healthy mood, including during the menstrual cycle when mood changes are common.^{*[13]}

More than one of the ingredients in RelaxMax may support a healthy body weight and healthy hormone, lipid, insulin, and glucose metabolism.^{*[14-16]}

RelaxMax™ Supplement Facts

Serving Size: 1 Scoop (about 3 g)
 Servings per Container: About 60

	Amount Per Serving	%Daily Value
Magnesium (as Albion® di-magnesium malate)	75 mg	18%
myo-Inositol	2 g	**
Taurine	500 mg	**
GABA (gamma-aminobutyric acid)	100 mg	**
L-Theanine (Suntheanine®)	50 mg	**

** Daily Value not established.

Other Ingredients: None.

DIRECTIONS: Dissolve one scoop of RelaxMax™ into 6 fl ounces of cool, pure water. Drink one to two times daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or preservatives.

Albion is a registered trademark of Albion Laboratories, Inc. Malate covered by U.S. Patent 6,706,904.



Suntheanine® is a registered trademark of Taiyo International, Inc. U.S. and International Patents Pending. U.S. Patent Nos. 6831103, 6589566, 6297280.

RelaxMax™ Cherry Supplement Facts

Serving Size: 1 Scoop (3.9 g)
 Servings Per Container: About 60

	Amount Per Serving	%Daily Value
Magnesium (as Albion® di-magnesium malate)	75 mg	18%
myo-Inositol	2 g	**
Taurine	500 mg	**
GABA (gamma-aminobutyric acid)	100 mg	**
L-Theanine (Suntheanine®)	50 mg	**

** Daily Value not established.

Other Ingredients: Natural cherry flavor (no MSG), malic acid, natural red beet powder, citric acid, and stevia.

DIRECTIONS: Dissolve one scoop of RelaxMax™ into 6 fl ounces of cool, pure water. Drink one to two times daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy protein, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

Albion is a registered trademark of Albion Laboratories, Inc. Malate covered by U.S. Patent 6,706,904.



Suntheanine® is a registered trademark of Taiyo International, Inc. U.S. and International Patents Pending. U.S. Patent Nos. 6831103, 6589566, 6297280.

References

- Clements, RS, Darnell B. Myo-inositol content of common foods: development of a high myo-inositol diet. *Am J Clin Nutr.* 1980 Sep;33(9):1954-67. <http://www.ajcn.org/content/33/9/1954>. Accessed October 24, 2011.
- Levine J, Barak Y, Gonzalves M. Double-blind, controlled trial of inositol treatment of depression. *Am J Psychiatry.* 1995 May;152(5):792-4. [PMID: 7726322]
- Palatnik A, Frolov K, Fux M, et al. Double-blind, controlled, crossover trial of inositol versus fluvoxamine for the treatment of panic disorder. *J Clin Psychopharmacol.* 2001 Jun;21(3):335-9. [PMID: 11386498]
- Fux M, Levine J, Aviv A, et al. Inositol treatment of obsessive-compulsive disorder. *Am J Psychiatry.* 1996 Sep;153(9):1219-21. [PMID: 8780431]
- Abdou AM, Higashiguchi S, Horie K, et al. Relaxation and immunity enhancement effects of gamma-aminobutyric acid (GABA) administration in humans. *Biofactors.* 2006;26(3):201-8. [PMID: 16971751]
- Locatelli V, Bresciani E, Tomiazio L, et al. Central nervous system-acting drugs influencing hypothalamic-pituitary-adrenal axis function. *Endocr Dev.* 2010;17:108-20. [Epub 2009 Nov 24] [PMID: 19955761]
- El Idrissi A. Taurine increases mitochondrial buffering of calcium: role in neuroprotection. *Amino Acids.* 2008 Feb;34(2):321-8. [Epub 2006 Sep 8] [PMID: 16955229]
- Fujita T, Ando K, Noda H, et al. Effects of increased adrenomedullary activity and taurine in young patient with borderline hypertension. *Circulation.* 1987 Mar;75(3):525-32. [PMID: 3815764]
- L'Amoreaux WJ, Marsillo A, El Idrissi A, et al. Pharmacological characterization of GABA receptors in taurine-fed mice. *J Biomed Sci.* 2010 Aug 24;17 Suppl 1:S14. [PMID: 20804588]
- Kakuda T, Hinoi E, Abe A, et al. Theanine, an ingredient of green tea, inhibits [3H] glutamine transport in neurons and astroglia in rat brain. *J Neurosci Res.* 2008 Jun;86(8):1846-56. [PMID: 18293419]
- Yamada T, Tershima T, Okubo T, et al. Effects of theanine, r-glutamylethylamide, on neurotransmitter release and its relationship with glutamic acid neurotransmission. *Nutr Neurosci.* 2005 Aug;(8)4:219-26. [PMID: 16493792]
- Nobre AC, Rao A, Owen GN. L-theanine, a natural constituent in tea, and its effect on mental state. *Asia Pac J Clin Nutr.* 2008;17 Suppl 1:167-8. [PMID: 18296328]
- Facchinetti F, Borella P, Sances G, et al. Oral magnesium successfully relieves premenstrual mood changes. *Obstet Gynecol.* 1991 Aug;78(2):177-81. [PMID: 2067759]
- D'Anna R, Di Benedetto V, Rizzo P, et al. Myo-inositol may prevent gestational diabetes in PCOS women. *Gynecol Endocrinol.* 2012 Jun;28(6):440-2. [PMID: 22122627]
- Unfer V, Carlomagno G, Dante G, et al. Effects of myo-inositol in women with PCOS: a systematic review of randomized controlled trials. *Gynecol Endocrinol.* 2012 Feb 1. [Epub ahead of print] [PMID: 22296306]
- Hedström, H. *GABA-Steroid Effects in Healthy Subjects and Women with Polycystic Ovary Syndrome* [dissertation]. Umeå, Sweden: Obstetrics and Gynecology Department of Clinical Sciences, Umeå University; 2011.

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

© XYMOGEN
 DRS-222
 Rev. 08/08/19



7 22537 51026 4

Resveratin™ Plus

Resveratrol/Pterostilbene Complex



Available in 60 capsules

Discussion

Resveratrol (RES) (3,5,4'-trihydroxystilbene) is a stilbenol derived from stilbene, a natural plant product. RES is found in varying amounts in grapes, various berries, plums, peanuts (and pines). Oral resveratrol is rapidly metabolized via sulfate conjugation by the intestine/liver.^[1] The methyl capping of all free hydroxyl groups (as in Pterostilbene) results in dramatically higher hepatic metabolic stability, intestinal absorption and membrane transport compared to unmethylated RES.^[2,3] Quercetin, pterostilbene and resveratrol are synergistic antioxidants, with quercetin seemingly aiding in the absorption of resveratrol.*^[4]

Stilbenols are polyphenolic compounds that have cell-protecting properties.^[5] For RES, this action has mostly been linked to growth and death regulatory pathways. Research published in 2008 also demonstrated RES's contribution to the maintenance of genome stability. Pterostilbene and quercetin, structurally-related and naturally-occurring, small polyphenols, show longer half-life in vivo than unmethylated resveratrol and have been shown to work synergistically to protect cellular health.*^[6]

As exciting as its role in chemoprotection, is resveratrol's ability to produce changes associated with longevity. These include increased insulin sensitivity, reduced IGF-1, increased AMP-activated protein kinase and peroxisome proliferator-activated receptor-gamma coactivator 1 alpha activity, increased mitochondrial number and improved motor function. RES opposed the effects of the high calorie diet in 144 of 153 significantly altered gene pathways.^[7] RES activates sirtuins including SIR2, a special longevity cellular^[8] and SIRT1 that helps protect nerve cells.*^[9]

In vitro, ex vivo and animal experiments have shown that the attributes of RES such as its powerful antioxidant activity, modulation of hepatic apolipoprotein and lipid synthesis, inhibition of platelet aggregation, and inhibition of human platelet and neutrophil production of pro-atherogenic eicosanoids favor protection against atherosclerosis.*^[10]

Clinical Applications

- » Methylation helps improve absorption and stability*
- » Powerful Antioxidant Support*
- » Supports Healthy Cellular Function*
- » Produces Changes Associated with Longer Lifespan (including activation of sirtuins)*
- » Supports Cardiovascular/Neurological Health*

*Resveratin™ Plus provides a complete bioflavonoid complex with resveratrol, quercetin, and pterostilbene. These three antioxidants work together synergistically. Pterostilbene, a new focus of scientific research, is methylated resveratrol, a bio-optimized form that complements resveratrol and quercetin. These compounds are being extensively studied in the areas of cardiovascular health and aging.**

Resveratrol's numerous anti-inflammatory properties may explain why it has so many far-reaching health benefits. It inhibits synthesis and release of pro-inflammatory mediators, modifies eicosanoid synthesis, and inhibits activated immune cells. By inhibiting either NF-(kappa)B or the activator protein-1 (AP-1), resveratrol also appears to inhibit inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2).^[11] Specific human dosing to support a healthy inflammatory response has not yet been established.*^[12]

EXCLUSIVE • PATENTED

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

Resveratin™ Plus Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Quercetin (as quercetin dihydrate)(from <i>Saphora japonica</i>)(bud)	250 mg	**
<i>trans</i> -Resveratrol (as <i>Polygonum cuspidatum</i> root extract)	75 mg	**
<i>trans</i> -Pterostilbene (pTeroPure®)	62.5 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), microcrystalline cellulose, stearic acid, magnesium stearate, silica, and medium-chain triglyceride oil.

DIRECTIONS: Take one capsule twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.



is a trademark of ChromaDex Inc.

**References**

1. Wenzel E, Somoza V. Metabolism and bioavailability of trans-resveratrol. *Mol Nutr Food Res*. 2005 May;49(5):472-81. [PMID:15779070]
2. Walle T, et al. High absorption but very low bioavailability of oral resveratrol in humans. *Drug Metab Dispos*. 2004 Dec;32(12):1377-82. [PMID:15333514]
3. Wen X, Walle T. Methylated flavonoids have greatly improved intestinal absorption and metabolic stability. *Drug Metab Dispos*. 2006 Oct;34(10):1786-92 [PMID: 16868069]
4. Morimitsu Y, Sugihara N, Furuno K. Inhibitory effect of flavonoids on sulfo- and glucurono-conjugation of acetaminophen in rat cultured hepatocytes and liver subcellular preparations. *Biol Pharm Bull*. 2004 May;27(5):714-7. [PMID: 15133252]
5. Fresco P, Borges F, Diniz C, Marques MP. New insights on the anticancer properties of dietary polyphenols. *Med Res Rev*. 2006 Nov;26(6):747-66 [PMID: 16710860]
6. Ferrer P, et al. Association between pterostilbene and quercetin inhibits metastatic activity of B16 melanoma. *Neoplasia*. 2005 Jan;7(1):37-47. [PMID:15736313]
7. Baur JA, et al. Resveratrol improves health and survival of mice on a high-calorie diet. *Nature*. 2006 Nov; 16;444(7117):337-42. [PMID: 17086191]
8. Stefani M, et al. The effect of resveratrol on a cell model of human aging. *Ann N Y Acad Sci*. 2007 Oct;1114:407-18. [PMID: 17804521]
9. Tang BL, Chua CESIRT1 and neuronal diseases. *Mol Aspects Med*. 2008 Jun;29(3):187-200 [PMID: 17397914]
10. Soleas GJ, Diamandis EP, Goldberg DM. Resveratrol: a molecule whose time has come? And gone? *Clin Biochem*. 1997 Mar;30(2):91-113 [PMID:9127691]
11. de la Lastra CA, Villegas I. Resveratrol as an anti-inflammatory and anti-aging agent: mechanisms and clinical implications. *Mol Nutr Food Res*. 2005 May;49(5):405-30 [PMID:15832402]
12. Hougee S, Faber J, Sanders A, de Jong RB, van den Berg WB, Garssen J, Hoijer MA, Smit HF. Selective COX-2 inhibition by a Pterocarpus marsupium extract characterized by pterostilbene, and its activity in healthy human volunteers. *Planta Med*. 2005 May;71(5):387-92. [PMID: 15931573]

Additional references available upon request

EXCLUSIVE • PATENTED

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

S-Acetyl Glutathione

Supports Natural Antioxidant Activity*



Available in 60 & 120 acid-resistant vegetarian capsules

Discussion

Reduced glutathione, commonly known as glutathione or GSH, is a tripeptide consisting of L-glutamine, L-cysteine, and glycine. It is ubiquitous in living systems. Glutathione biosynthesis can be affected by biochemical individuality and/or dietary factors. Chronic oxidative stress can also deplete cellular glutathione. Precursors to glutathione, such as whey protein, vitamin C, and glutamine, are often recommended to boost glutathione levels in the body; however, results are inconsistent. Biological individuality is such that not every body has equivalent ability to metabolize the precursor to raise glutathione.*

Why Not Give Pure Glutathione? Unfortunately, most oral forms of glutathione are foul smelling, but more importantly, the majority of an oral dose is oxidized before it can be absorbed and used by the cells. This formulation delivers a unique preparation of glutathione that overcomes these usual limitations. The stability of S-acetylglutathione through the intestinal wall and the plasma is well documented in the literature. Oral intake of S-acetylglutathione increases total glutathione and percent-reduced glutathione. Percent-reduced glutathione is a very significant biomarker of health status.*^[1-5]

Mechanism of Absorption S-acetylglutathione, a lipid-like compound, is taken up intact by chylomicrons in the gut. The acetyl bond is placed on its thiol group or sulfur group, which prevents oxidation and allows the molecule to pass diffusively into the cell after absorption in the gut. The bond is then cleaved by non-specific enzymes inside the cell. Acetylation prevents the breakdown of glutathione, and S-acetylglutathione does not require energy expenditure to be cleaved to reduced glutathione once it crosses the cell wall.*^[1-8]

Antioxidant Activity Glutathione functions extensively in tissues and organs throughout the body. It plays critical roles in protecting the body from oxidative stress, maintaining cellular functions, and supporting healthy immune function.^[1,4] Many factors can increase cellular exposure to oxidative insult, and therefore increase cellular consumption of nutrients—such as glutathione—that provide

Clinical Applications

- » Provides Intracellular Antioxidant Support*
- » Supports Healthy Cell Function and Healthy Aging*
- » Supports Detoxification*
- » Supports a Healthy Immune Response*
- » Supports Amino Acid Transport Across Cell Membranes*
- » Enhances Antioxidant Activity of Vitamins C and E*

*S-Acetyl Glutathione is an acetylated form of glutathione. This form is well-absorbed and more stable throughout the digestive tract than other forms on the market. Use of stomach acid-resistant capsules (DRcaps™) further protect stability. Laboratory data showed that S-acetyl glutathione increased intracellular glutathione and had a positive effect on many oxidative stress biomarkers.**

antioxidant activity. This may result in a fierce cycle of oxidative stress and challenges to detoxification. Complete biotransformation and protection from oxidative stress are important to maintaining cellular integrity and tissue health.*^[2,5]

Other Benefits of Maintaining Healthy Glutathione Levels Much information related to mitochondrial health has surfaced in the literature. Mitochondria, the energy-producing powerhouses of cells, are also the primary intracellular site of oxygen consumption and the major source of reactive oxygen species (ROS). S-acetylglutathione has been shown to cross the membrane of the mitochondria, increasing the organelle's activity and minimizing ROS.^[8,9] Reduction of ROS is associated with maintaining mitochondrial integrity and function, and improved mitochondrial health is believed to support overall health and energy.*

S-acetylglutathione has also been shown to decrease TNF-alpha, NF-kappa beta, and F-2 isoprostane.^[4,9-12] Additionally, there is mounting evidence that intracellular glutathione levels in antigen-presenting cells (e.g. macrophages) may influence the Th1/Th2 cytokine response pattern and promote a balanced immune reaction.*^[10]

EXCLUSIVE • PATENTED

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

S-Acetyl Glutathione Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
S-Acetyl Glutathione	200 mg	**
** Daily Value not established.		

Other Ingredients: HPMC (acid-resistant vegetarian capsule), microcrystalline cellulose, stearic acid, magnesium stearate, and silica.

DIRECTIONS: Take one to two capsules one to two times daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.

**References**

1. Locigno R, Pincemail J, Henno A, et al. S-Acetyl-glutathione selectively induces apoptosis in human lymphoma cells through a GSH-independent mechanism. *Int J Oncol.* 2002 Jan;20(1):69-75. [PMID: 11743644]
2. Lomaestro BM, Malone M. Glutathione in health and disease: pharmacotherapeutic issues. *Ann Pharmacother.* 1995 Dec;29(12):1263-73. [PMID: 8672832]
3. Cacciatori I, Cornacchia C, Pinnen F, et al. Prodrug approach for increasing cellular glutathione levels. *Molecules.* 2010 Mar 3;15(3):1242-64. [PMID: 20335977]
4. Vogel J, Cinatl J, Dauletbayev N, et al. Effects of S-acetylglutathione in cell and animal model of herpes simplex virus type 1 infection. *Med Microbiol Immunol.* 2005 Jan;194(1-2):55-59. [PMID: 14624358]
5. Ballatori N, Krance SM, Notenboom S, et al. Glutathione dysregulation and the etiology and progression of human diseases. *Biol Chem.* 2009 Mar;390(3):191-214. [PMID: 19166318]
6. Richman PG, Meister A. Regulation of gamma-glutamyl-cysteine synthetase by nonallosteric feedback inhibition by glutathione. *J Biol Chem.* 1975 Feb 25;250(4):1422-26. [PMID: 1112810]
7. Anderson ME, Powrie F, Puri RN, et al. Glutathione monoethyl ester: preparation, uptake by tissues, and conversion to glutathione. *Arch Biochem Biophys.* 1985 Jun;239(2):538-48. [PMID: 4004275]
8. Anderson ME, Nilsson M, Sims NR. Glutathione monoethyl ester prevents mitochondrial glutathione depletion during focal cerebral ischemia. *Neurochem Int.* 2004 Feb;44(3):153-59. [PMID: 14568558]
9. Kretzschmar M. Regulation of hepatic glutathione metabolism and its role in hepatotoxicity. *Exp Toxicol Pathol.* 1996 Jul;48(5):439-46. [PMID: 8765689]
10. Fraternali A, Paoletti MF, Casabianca A, et al. Antiviral and immunomodulatory properties of new pro-glutathione (GSH) molecules. *Curr Med Chem.* 2006;13(15):1749-55. [PMID: 16787218]
11. Kretzschmar M, Klinger W. The hepatic glutathione system—influences of xenobiotics. *Exp Pathol.* 1990;38(3):145-64. [PMID: 2192911]
12. Donnerstag B, Ohlenschlager G, Cinatl J, et al. Reduced glutathione and S-acetylglutathione as selective apoptosis-inducing agents in cancer therapy. *Cancer Lett.* 1996 Dec;110(1-2):63-70. [PMID: 9018082]

Additional references available upon request

EXCLUSIVE • PATENTED

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Saccharomycin[®] DF

DNA-Verified *Saccharomyces boulardii*



Available in 20 capsules, 60 capsules & 120 capsules

Discussion

Saccharomycin[®] DF is manufactured using a process that involves controlled temperature and low vacuum, eliminating the shock of freeze-drying. The drying procedure, which does not modify the water content of the preparation, slows down aging, cell deterioration, and contamination, leading to increased stability and greater resistance to gastric acid. This process does not require or contain dairy products or lactose.*

***Saccharomyces boulardii* (*S. boulardii*)** is a natural, non-pathogenic yeast that may help support and maintain the healthy ecology of the small and large intestines. In a 2010 systematic review and meta-analysis of 31 randomized placebo-controlled treatment arms in 27 trials comprising 5029 adults, "*S. boulardii* was found to be significantly efficacious and safe in 84% of those treatment arms."^[1] A study also suggested that *S. boulardii* can be used safely and effectively in children three months and older.^[2] A double-blind, randomized, placebo controlled study of children ages 3-59 months produced statistically significant positive results suggesting that *S. boulardii* may play an important role in supporting normal gastrointestinal function in young children.*^[3]

Extensively researched and published in European and American peer-reviewed journals, *Saccharomyces boulardii* appears to function through several mechanisms of action. With regard to maintaining normal GI function and transit time, research suggests that *S. boulardii* secretes a protease that may assist in directly degrading bacterial toxins and stimulating antibody production against those toxins.^[4-6] *S. boulardii* is also believed to support the natural inflammatory response, exert a trophic effect on intestinal mucosa, and positively support the immune system.^[3] These actions further support and help maintain the normal health and function of the intestinal brush border.*

This probiotic yeast appears to support normal gastrointestinal flora and integrity^[7,8]; promote production of intestinal enzymes and secretory IgA^[9]; and support cytokine balance through its effects on

Clinical Applications

- » Supports Gastrointestinal-based Immunity*
- » Supports Integrity and Function of Mucosal Cells*
- » Supports Healthy Gut Flora*

Saccharomycin[®] DF is a lactose-free, stomach acid-resistant, stable, European patent-pending formula containing DNA-verified *Saccharomyces boulardii*. This probiotic yeast supports other probiotic organisms in addition to intestinal barrier function and integrity. Research also suggests that *Saccharomyces boulardii* supports normal immune responses.*

IL-8, IL-6, IL-10, NF-kappaB, TNF-alpha, and PPAR-gamma.^[6,10,11] Research suggests a role for *S. boulardii* in the production of health-promoting short-chain fatty acids, including butyrate.*^[12] Research suggests that butyrate, in turn, plays an important role in maintaining the integrity, function, and normal flora of the intestines.^[13]

Following a multi-dose study in healthy volunteers, the concentration of *S. boulardii* in feces increased rapidly, reaching a steady state by day three in all subjects. Following completion of administration, the *S. boulardii* population declined consistently and was cleared from the bowel within five to seven days, indicating that the probiotic yeast did not permanently colonize the gastrointestinal tract.^[14] Saccharomycin DF provides 10 billion colony-forming units of *S. boulardii* in a two-capsule dose.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Saccharomycin® DF Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
<i>Saccharomyces boulardii</i> (10 billion CFU)	500 mg	**
** Daily Value not established.		

Other Ingredients: HPMC (capsule), microcrystalline cellulose, stearic acid, magnesium stearate, silica, and medium-chain triglyceride oil.
Europe Patent Pending #05425084.0
† Colony-Forming Units

DIRECTIONS: Take one to two capsules per day, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Not for use by infants under three months of age. Do not use if you have severe immune suppression or are taking antifungal medication. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically-modified organisms (GMOs), artificial colors, artificial sweeteners, or preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children. Does not require refrigeration.

**References**

1. McFarland LV. Systematic review and meta-analysis of *Saccharomyces boulardii* in adult patients. *World J Gastroenterol.* 2010 May 14;16(18):2202-22. [PMID: 20458757]
2. Vandenplas Y, Brunser O, Szajewska H. *Saccharomyces boulardii* in childhood. *Eur J Pediatr.* 2009 Mar;168(3):253-65. Review. [PMID: 19096876]
3. Riaz M, Alam S, Malik A, et al. Efficacy and Safety of *Saccharomyces boulardii* in Acute Childhood Diarrhea: A Double Blind Randomised Controlled Trial. *Indian J Pediatr.* 2011 Oct 14. [PMID: 21997865]
4. Can M, Beşirbellioğlu BA, Avci İY, et al. Prophylactic *Saccharomyces boulardii* in the prevention of antibiotic-associated diarrhea: a prospective study. *Med Sci Monit.* 2006 Apr;12(4):P119-22. [PMID: 16572062]
5. Castagliuolo I, Riegler MF, Valenick L, et al. *Saccharomyces boulardii* protease inhibits the effects of *Clostridium difficile* toxins A and B in human colonic mucosa. *Infect Immun.* 1999 Jan;67(1):302-7. [PMID: 9864230]
6. Im E, Pothoulakis C. [Recent advances in *Saccharomyces boulardii* research]. *Gastroenterol Clin Biol.* 2010 Sep;34 Suppl 1:S62-70. Review. French. [PMID: 20889007]
7. Krasowska A, Murzyn A, Dyjankiewicz A, et al. The antagonistic effect of *Saccharomyces boulardii* on *Candida albicans* filamentation, adhesion and biofilm formation. *FEMS Yeast Res.* 2009 Dec;9(8):1312-21. [PMID: 19732158]
8. *Saccharomyces boulardii*. Professional Monograph. Natural Standard Database <http://naturalstandard.com/databases/herbssupplements/sboulardii.asp>. Accessed February 14, 2012.
9. Buts JP, Bernasconi P, Vaerman JP, et al. Stimulation of secretory IgA and secretory component of immunoglobulins in small intestine of rats treated with *Saccharomyces boulardii*. *Dig Dis Sci.* 1990 Feb;35(2):251-6. [PMID: 2302983]
10. Dahan S, Dalmasso G, Imbert V, et al. *Saccharomyces boulardii* interferes with enterohemorrhagic *Escherichia coli*-induced signaling pathways in T84 cells. *Infect Immun.* 2003 Feb;71(2):766-73. [PMID: 12540556]
11. Pothoulakis C. Review article: anti-inflammatory mechanisms of action of *Saccharomyces boulardii*. *Aliment Pharmacol Ther.* 2009 Oct 15;30(8):826-33. Review. [PMID: 19706150]
12. Schneider SM, Girard-Pipau F, Filippi J, et al. Effects of *Saccharomyces boulardii* on fecal short-chain fatty acids and microflora in patients on long-term total enteral nutrition. *World J Gastroenterol.* 2005 Oct 21;11(39):6165-9. [PMID: 16273644]
13. Lewis K, Lutgendorff F, Phan V, et al. Enhanced translocation of bacteria across metabolically stressed epithelia is reduced by butyrate. *Inflamm Bowel Dis.* 2010 Jul;16(7):1138-48. [PMID: 20024905]
14. Blehaut H, Massot J, Elmer GW, et al. Disposition kinetics of *Saccharomyces boulardii* in man and rat. *Biopharm Drug Dispos.* 1989 Jul-Aug;10(4):353-64. [PMID: 2758101]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Saloxicin™

(*Salix alba/Boswellia serrata*)



Available in 120 capsules

Discussion

White Willow Bark (*Salix alba*) Willow bark has been used for thousands of years to help support eicosanoid and cytokine balance and to help relieve discomfort.^[1-3] Willow bark is currently approved by the German Commission E and the European Scientific Cooperative on Phytotherapy (ESCOP) for these purposes. Willow bark is also recognized in the United States for its role in supporting joint comfort.^[1] Willow bark contains glycosides, salicylates, flavonoids, tannins, aromatic compounds, and acids. A 2007 Cochrane review of the literature found moderate evidence that *Salix alba* positively affected eicosanoid metabolism and produced results that were comparable to those obtained by other commonly used compounds. Favorable results were obtained when the *Salix alba* in the studies was standardized to 120 mg or 240 mg salicin. Saloxicin™ provides a standardized 120 mg dose of salicin per serving.*^[4]

Various randomized placebo-controlled studies suggest that willow bark produces positive effects on joint discomfort. The usual dose of salicin is 240 mg per day,^[5] which is the intake recommendation for Saloxicin. Pharmacokinetic evaluations reveal that salicylic acid is the major metabolite of salicin, though other components of willow bark are believed to provide relief as well.^[6] The mechanism of action of white willow bark appears to involve an effect on both arachidonic acid-derived eicosanoids and cytokine compounds.*^[7]

5•Loxin®, a standardized *Boswellia serrata* extract enriched to 30% 3-O-acetyl-11-keto-β-boswellic acid (AKBA), is ten times more concentrated than ordinary *B serrata*. *Boswellia serrata* is an ayurvedic herb whose principle constituents—boswellic acid and alpha-boswellic acid—may help maintain healthy leukotriene metabolism by reducing the activity of the enzyme 5-lipoxygenase.^[8] 5-lipoxygenase (5-LOX) catalyzes the synthesis of unfavorable leukotrienes.*

A randomized, double-blind, placebo-controlled trial assessing the efficacy, safety, and tolerability of *Boswellia* extract produced statistically significant and clinically relevant decreases in knee

Clinical Applications

- » Affects the Production of Arachidonic Acid-Derived Eicosanoids*
- » Supports Cytokine Balance*
- » Supports Joint Comfort*
- » Contains 40 mg Proprietary Bioflavonoid Berry Blend*
- » Supports Antioxidant Mechanisms*

Saloxicin™ is formulated to support eicosanoid and cytokine balance and provide support for joint comfort. 5-LOXIN®, a patented *Boswellia* extract yielding concentrated 3-O-acetyl-11-keto-β-boswellic acid (AKBA), is found to inhibit the 5-lipoxygenase enzyme. Salicin from white willow bark is a natural inhibitor of both the COX-2 and 5-lipoxygenase enzymes. Bioflavonoid-rich BerryVin™ provides additional support for eicosanoid balance and antioxidant activity.*

discomfort, increases in knee flexion, and increases in walking distance.^[9] A randomized, double-blind, placebo-controlled study specifically designed with 5•Loxin resulted in statistically significant improvements in comfort and physical function and a significant reduction in matrix metalloproteinase (MMP) in synovial fluid.^[10] MMP represents a class of enzymes that selectively hydrolyze peptide bonds and degrade structural proteins; they play a crucial role in the degradation of joint tissues. 5•Loxin shows significant inhibition against several MMPs. It helps prevent the formation of human recombinant TNF-α inducible MMPs, which further facilitates the maintenance of healthy cartilage and cell-cycle regulation.*^[11,12]

BerryVin™ (40 mg) contains a blend of blueberries, strawberries, escobillo, and cranberries, along with grape and pomegranate extracts. This bioflavonoid-rich berry powder provides polyphenols, anthocyanins, ellagic acid, and an antioxidant capacity of 4000 TE/g to fight free radicals. It may also provide substantial antioxidant support for soft tissues. Bioflavonoids are thought to act synergistically to inhibit cyclooxygenases, lipoxygenases, and phospholipases, ultimately supporting healthy eicosanoid metabolism and favorable cytokine balance.*^[13,14]

Saloxicin™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Salicin (from white willow extract (<i>Salix alba</i>) (bark))	120 mg	**
<i>Boswellia serrata</i> extract (gum resin) (30% 3-O-Acetyl-11-keto- β -Boswellic acid [AKBA])(5-LOXIN®)	50 mg	**
High ORAC Berry Blend (strawberries, escobillo, blueberries, cranberries, grape extract, pomegranate extract)(whole fruit) (>4,000 TE/g)(>25% total polyphenols)(>10% anthocyanins) (>5,000 ppm ellagic acid)(BerryVin™)	40 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), tricalcium phosphate, microcrystalline cellulose, stearic acid, magnesium stearate, calcium silicate, and silica.
BerryVin™ is a trademark of Cyvex Nutrition, Inc.

DIRECTIONS: Take two capsules twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep tightly closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

5-LOXIN® is a registered trademark of PL Thomas - Laila Nutra, LLC and is used under license. International Patents Pending.

**References**

1. Natural Standard Database. *Willow Bark* (*Salix* Spp.). Somerville, MA: Natural Standard; 2012. <http://naturalstandard.com/databases/herbssupplements/willowbark.asp#undefined>. Accessed August 2, 2012.
2. Singh AP. Salicin-A natural analgesic. *Ethnobotanical Leaflets*. 2003;1:1-4. <http://opensiuc.lib.siu.edu/eb/vol2003/iss1/8>. Accessed August 2, 2012.
3. Fiebich BL, Appel K. Anti-inflammatory effects of willow bark extract. *Clin Pharmacol Ther*. 2003 Jul;74(1):96; author reply 96-7. [PMID: 12844141]
4. Gagnier JJ, van Tulder MW, Berman B, et al. Herbal medicine for low back pain: a Cochrane review. *Spine*. 2007 Jan 1;32(1):82-92. [PMID: 17202897]
5. Maroon JC, Bost JW, Maroon A. Natural anti-inflammatory agents for pain relief. *Surg Neurol Int*. 2010 Dec 13;1:80. [PMID: 21206541]
6. Schmid B, Kötter I, Heide L. Pharmacokinetics of salicin after oral administration of a standardised willow bark extract. *Eur J Clin Pharmacol*. 2001 Aug;57(5):387-91. [PMID: 11599656]
7. Khayyal MT, El-Ghazaly MA, Abdallah DM, et al. Mechanisms involved in the anti-inflammatory effect of a standardized willow bark extract. *Arzneimittelforschung*. 2005;55(11):677-87. [PMID: 16366042]
8. Safayhi H, Boden SE, Schweizer S, et al. Concentration-dependent potentiating and inhibitory effects of *Boswellia* extract on 5-Lipoxygenase product formation in stimulated PMNL. *Planta Med*. 2000 Mar;66(2):110-3. [PMID: 10763581]
9. Kimmatkar N, Thawani V, Hingorani L, et al. Efficacy and tolerability of *Boswellia serrata* extract in treatment of osteoarthritis of knee—a randomized double blind placebo controlled trial. *Phytomedicine*. 2003 Jan;10(1):3-7. [PMID: 12622457]
10. Sengupta K, Alluri KV, Satish AR, et al. A double blind, randomized, placebo controlled study of the efficacy and safety of 5-Loxin for treatment of osteoarthritis of the knee. *Arthritis Res Ther*. 2008;10(4):R85. [PMID: 18667054]
11. Laila Impex Research Centre. 5-LOXIN® overview. PLT. <http://www.plthomas.com/540/97/5-loxin->. Accessed August 8, 2012.
12. Roy S, Khanna S, Krishnaraju AV, et al. Regulation of vascular responses to inflammation: inducible matrix metalloproteinase-3 expression in human microvascular endothelial cells is sensitive to antiinflammatory *Boswellia*. *Antioxid Redox Signal*. 2006 Mar-Apr;8(3-4):653-60. [PMID: 16677108]
13. Havsteen B. Flavonoids, a class of natural products of high pharmacological potency. *Biochem Pharmacol*. 1983 Apr 1;32(7):1141-8. [PMID: 6342623]
14. Kim HP, Son KH, Chang HW, et al. Anti-inflammatory plant flavonoids and cellular action mechanisms. *J Pharmacol Sci*. 2004 Nov;96(3):229-45. [PMID: 15539763]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

SAM-e & TMG/SAM-e

Methyl Donors



SAM-e & TMG is available in 30 Natural Lemon stick packs
SAM-e is available in 30 acid-resistant capsules

Discussion

S-adenosyl-L-methionine (S-AdoMet) is a naturally occurring substance formed in the body from the amino acid methionine and the “energy molecule” adenosine triphosphate (ATP). Formation of S-AdoMet is catalyzed by methionine adenosyltransferase and depends on cofactors including vitamin B6, vitamin B12, folate, and magnesium. S-AdoMet has been studied as a supportive nutrient in liver health, joint comfort, metabolic reactions, and healthy mood.^{*[1-4]}

Methylation S-AdoMet is the “universal” methyl donor for biochemical reactions throughout the body.^[5] This methyl transfer, or “transmethylation,” is critical to reactions involving proteins, phospholipids, DNA, RNA, creatine, hormones, development of cell membranes, degradation of histamine, and formation of norepinephrine and dopamine. ^[1,6] Eighty-five percent of transmethylation takes place in the liver, and healthy S-AdoMet levels appear to be essential to liver health and function.^{*[2,7]}

Antioxidant and Liver Support S-AdoMet is considered to be “critical” for synthesis of glutathione, a principal component of antioxidant and detoxification systems in the body.^[1] Following donation of a methyl group, S-AdoMet is converted to S-adenosyl-homocysteine (SAH). This biochemical reaction promotes the transsulfuration pathway in the liver that generates glutathione. Further metabolism of SAH involves trimethylglycine (TMG), also known as betaine anhydrous. TMG plays an important role in maintaining a healthy S-AdoMet:SAH ratio in the liver.*

During a national symposium, the roles of S-AdoMet and TMG in supporting liver health were reviewed with a focus on their participation in the vital processes of transmethylation and transsulfuration, their ultimate contribution to increased glutathione synthesis and its hepatoprotective effects, their promotion of a balanced S-AdoMet:SAH ratio, their activation of phosphatidylethanolamine methyltransferase, and the increase in phosphatidylcholine synthesis as a result of their administration.^[8] Ongoing animal studies suggest that S-AdoMet supports liver health^[9,10] and that exogenous S-AdoMet may positively affect cell-life regulation of hepatocytes.^[7] In certain human cohorts, researchers recommend further research into combining S-AdoMet with nutrients such as vitamin B6 to optimize outcomes.^{*[5]}

Healthy Mood Supplemental S-AdoMet appears to support a healthy mood, possibly due to its active role in methylation and its involvement in the formation of monoamine

Clinical Applications

- » Supports Biochemical Reactions Requiring Methyl Groups*
- » Supports Neurotransmitter Synthesis and Healthy Mood*
- » Facilitates Conversion of Homocysteine to Glutathione*
- » Supports Liver Health and Function*
- » Promotes Joint Comfort*

*SAM-e & TMG is a sweet, yet slightly tart lemon-flavored powder. SAM-e is encapsulated S-AdoMet. S-AdoMet (S-adenosyl-L-methionine) and TMG (trimethylglycine) are naturally occurring substances that act as methyl donors during vital biochemical processes in the body. Methylation is essential to normal cell health and function. It can decline with age or chronic alcohol consumption, and it can be limited in some individuals due to their genetic makeup. S-AdoMet donates methyl groups, which are needed for the synthesis of neurotransmitters, proteins, nucleic acids, and phospholipids. It supports glutathione production, liver health, joint comfort, and a healthy mood. TMG is another methyl donor. It is involved in the metabolism of homocysteine and the formation of S-AdoMet. TMG ultimately supports cardiovascular and neurological health, as well as normal cell-life regulation.**

neurotransmitters.^[3,11-13] Meta-analysis of earlier studies suggested that S-AdoMet showed greater support of a healthy mood when compared to placebo with an effect comparable to that of other treatments.^[14] A 30-day, double-blind, placebo-controlled, randomized study of 80 women suggested that there was a significant improvement in mood after the women received an oral dose of 1600 mg/d of S-AdoMet compared to placebo.^[15] Another study of 143 subjects who received an oral dose of 1600 mg/d of S-AdoMet suggested that S-AdoMet yielded positive results that were comparable to other treatments for supporting a healthy mood, but S-AdoMet was better tolerated.^[16] In a small (N=26), four-week, double-blind, randomized protocol comparing oral S-AdoMet with other treatments, 62% of the S-AdoMet group showed significant improvement in mood. The study revealed a significant correlation between plasma S-AdoMet levels and the degree of healthy mood support, regardless of treatment type.^{*[17]}

TMG Trimethylglycine is a naturally occurring compound (glycine attached to three methyl groups) that is found in food (estimated intake 0.5-2 g/d) and can be produced in the body from the precursor choline.^[18] TMG is thought to protect liver cells, support homocysteine metabolism and cardiovascular health, and may also support a healthy mood due to its role in S-AdoMet metabolism.^[3,9,18,19] When TMG donates a single methyl group, it is converted to dimethylglycine (DMG), which is capable of donating two methyl groups. TMG is thought to stimulate activity of the enzyme betaine-homocysteine methyltransferase (BHMT). BHMT, found in abundance in a healthy liver,^[20,21] is used by TMG to donate a methyl group to homocysteine. Once TMG adds a methyl group to homocysteine to produce methionine, the methionine can then be converted to S-AdoMet. A randomized, double-blind, crossover study of healthy volunteers suggested that TMG supplementation (at doses of 3 g and 6 g/d) has a dose-dependent effect on serum TMG levels and a significantly positive effect on maintaining healthy homocysteine levels.^[22] Together, S-AdoMet and TMG provide an abundant source of methyl groups and ultimately support a wide variety of biochemical reactions in the body.*

SAM-e XMOGEN’s SAM-e contains a minimum of 70% of the SS isomer of S-AdoMet, the form the body can use most readily. This relatively high concentration from Gnosis’ Adomix® not only makes SAM-e particularly bioavailable but also cost-effective. Each capsule is sealed in a nitrogen-purged blister pack to maximize protection from the environment.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

SAM-e & TMG Supplement Facts

Serving Size: 1 Stick Pack (about 2.6 g)

	Amount Per Serving	%Daily Value
Calories	5	
Total Carbohydrate	1 g	<1% [†]
Calcium (as calcium carbonate, calcium oxide, and calcium chloride anhydrous)	75 mg	6%
Betaine Anhydrous (trimethylglycine)	600 mg	**
S-adenosyl-L-methionine (as s-adenosyl-L-methionine 1,4-butanedisulfonate)	400 mg	**

[†]Percent Daily Values are based on a 2,000 calorie diet.
** Daily Value not established.

Other Ingredients: Xylitol, citric acid, malic acid, stearic acid, silica, natural lemon flavor, and turmeric extract (for color).

DIRECTIONS: Consume the contents of one stick pack daily away from meals, or as directed by your healthcare practitioner. Preferably pour a small amount of the contents of a stick pack directly into the mouth and allow contents to dissolve. Then repeat process until contents of the entire stick pack have dissolved in the mouth. Alternatively, contents may be added to 2-4 oz of water or preferred liquid; stir and drink within 15 minutes.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Use special caution in individuals with bipolar disorder. Do not use if stick pack is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

SAM-e Supplement Facts

Serving Size: 1 capsule

	Amount Per Serving	%Daily Value
S-adenosyl-L-methionine (as Adomix® S-adenosyl-L-methionine disulfate p-toluenesulfonate)	200 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), microcrystalline cellulose, ascorbyl palmitate, calcium oxide, silica, and calcium chloride anhydrous.

DIRECTIONS: Take one capsule daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Use special caution in individuals with bipolar disorder. Do not use if foil is punctured.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

Adomix Adomix® is a registered trademark of Gnosis S.p.A. Patent reference: PCT/IT2006/000610.

**References**

- Natural Standard Database. SAME. <http://naturalstandard.com/databases/herbssupplements/same.asp?#undefined>. Accessed October 21, 2012.
- Friedel HA, Goa KL, Benfield P. S-adenosyl-L-methionine. A review of its pharmacological properties and therapeutic potential in liver dysfunction and affective disorders in relation to its physiological role in cell metabolism. *Drugs*. 1989 Sep;38(3):389-416. [PMID: 2680435]
- Papakostas GI, Cassiello CF, Iovieno N. Folate and s-adenosylmethionine for major depressive disorder. *Can J Psychiatry*. 2012 Jul;57(7):406-13. [PMID: 22762295]
- Mayo Clinic. SAME. Updated September 1, 2012. http://www.mayoclinic.com/health/same/NS_patient-same/DSECTION=dosing. Accessed October 22, 2012.
- Halsted CH, Medici V. Vitamin-dependent methionine metabolism and alcoholic liver disease. *Adv Nutr*. 2011 Sep;2(5):421-7. [PMID: 22332083]
- Lu SC. S-Adenosylmethionine. *Int J Biochem Cell Biol*. 2000 Apr;32(4):391-5. [PMID: 10762064]
- Mato JM, Lu SC. Role of S-adenosyl-L-methionine in liver health and injury. *Hepatology*. 2007 May;45(5):1306-12. [PMID: 17464973]
- Purohit V, Abdelmalek MF, Barve S, et al. Role of S-adenosylmethionine, folate, and betaine in the treatment of alcoholic liver disease: summary of a symposium. *Am J Clin Nutr*. 2007 Jul;86(1):14-24. [PMID: 17616758]
- Kharbada KK. Alcoholic liver disease and methionine metabolism. *Semin Liver Dis*. 2009 May;29(2):155-65. [PMID: 19387915]
- Kharbada KK, Rogers DD 2nd, Mailliard ME, et al. A comparison of the effects of betaine and S-adenosylmethionine on ethanol-induced changes in methionine metabolism and steatosis in rat hepatocytes. *J Nutr*. 2005 Mar;135(3):519-24. [PMID: 15735087]
- Baldessarini RJ. Neuropharmacology of S-adenosyl-L-methionine. *Am J Med*. 1987 Nov 20;83(5A):95-103. [PMID: 3318448]
- Morgan AJ, Jorm AF. Self-help interventions for depressive disorders and depressive symptoms: a systematic review. *Ann Gen Psychiatry*. 2008 Aug 19;7:13. [PMID: 18710579]
- Miller AL. The methylation, neurotransmitter, and antioxidant connections between folate and depression. *Altern Med Rev*. 2008 Sep;13(3):216-26. [PMID: 18950248]
- Bressa GM. S-adenosyl-L-methionine (SAME) as antidepressant: meta-analysis of clinical studies. *Acta Neurol Scand Suppl*. 1994;154:7-14. [PMID: 7941964]
- Salmaggi P, Bressa GM, Nicchia G, et al. Double-blind, placebo-controlled study of S-adenosyl-L-methionine in depressed postmenopausal women. *Psychother Psychosom*. 1993;59(1):34-40. [PMID: 8441793]
- Delle Chiaie R, Pancheri P, Scapicchio P. Efficacy and tolerability of oral and intramuscular S-adenosyl-L-methionine 1,4-butanedisulfonate (SAME) in the treatment of major depression: comparison with imipramine in 2 multicenter studies. *Am J Clin Nutr*. 2002 Nov;76(5):1172S-6S. [PMID: 12418499]
- Bell KM, Potkin SG, Carreon D, et al. S-adenosylmethionine blood levels in major depression: changes with drug treatment. *Acta Neurol Scand Suppl*. 1994;154:15-8. [PMID: 7941961]
- Olthof MR, Verhoef P. Effects of betaine intake on plasma homocysteine concentrations and consequences for health. *Curr Drug Metab*. 2005 Feb;6(1):15-22. [PMID: 15720203]
- Yi EY, Kim YJ. Betaine inhibits in vitro and in vivo angiogenesis through suppression of the NF- κ B and Akt signaling pathways. *Int J Oncol*. 2012 Nov;41(5):1879-85. doi: 10.3892/ijo.2012.1616. [PMID: 22940742]
- Wang JA, Dudman NP, Lynch J, et al. Betaine:homocysteine methyltransferase—a new assay for the liver enzyme and its absence from human skin fibroblasts and peripheral blood lymphocytes. *Clin Chim Acta*. 1991 Dec 31;204(1-3):239-49. [PMID: 1819467]
- Pellanda H, Namour F, Fofou-Caillierez M, et al. A splicing variant leads to complete loss of function of betaine-homocysteine methyltransferase (BHMT) gene in hepatocellular carcinoma. *Int J Biochem Cell Biol*. 2012 Feb;44(2):385-92. [PMID: 22138536]
- Schwab U, Törrönen A, Meririnne E, et al. Orally administered betaine has an acute and dose-dependent effect on serum betaine and plasma homocysteine concentrations in healthy humans. *J Nutr*. 2006 Jan;136(1):34-8. Erratum in: *J Nutr*. 2007 Apr;137(4):1124. [PMID: 16365055]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

SedaLin™

Sleep Support*



Available in 60 capsules

Discussion

Human Studies A Home Use Test (HUT) performed in 2005 among a target group of 61 men and women using SedaLin™ for two weeks yielded very positive results.^[1] Seventy-four percent of respondents used the product according to the directions: Take seven or more capsules during the two-week test period. Of these respondents,

- » 83% said SedaLin helped them relax*
- » 91% said SedaLin helped reduce fatigue due to lack of sleep*
- » 91% said SedaLin helped ensure a good night's sleep*
- » 82% said SedaLin is an essential item to have on hand*

An open-label, single-center, observational survey that included 295 people (ages 18-87) with sleep difficulties was performed to obtain a subjective evaluation of the tolerability and effectiveness of SedaLin.^[2] Self-reported sleep difficulties included problems falling asleep, multiple wakings, and next-day tiredness due to a lack of sleep. Patients taking at least one 365 mg capsule of SedaLin one hour before going to bed every night for at least two weeks experienced the following:

- » 86% considered SedaLin relaxing*
- » 82.8% said SedaLin assisted in a restful sleep*
- » 82.8% said SedaLin was effective in reducing fatigue due to lack of sleep*
- » No significant adverse events

SedaLin (known as SEDITOL®) is a blend of a patented extract of *Magnolia officinalis* bark and a proprietary extract of *Ziziphus spinosa* seed. These herbs have been traditionally used in Asia for qi stagnation, for mild anxiety and nervousness, and to support normal, uninterrupted sleep.^{*,[3-5]}

Magnolia officinalis Magnolia bark is rich in a biphenol compound called honokiol and its isomer magnolol. In experimental animal studies, these compounds have been shown to enhance the activity of gamma-aminobutyric acid (GABA) A receptors and GABA binding,

Clinical Applications

- » Supports Calmness*
- » Supports Normal, Uninterrupted Sleep*

*SedaLin™ is an all-natural herbal blend of Magnolia officinalis and Ziziphus spinosa formulated to support restful sleep. To achieve maximum effectiveness, this non-addictive formula should be taken for a minimum of seven nights in a row and may be taken indefinitely.**

which may help the body cope with the neurologic effects emotions can have on behavior and well-being.^[4,6] Honokiol, administered by intraperitoneal injection in mice, was shown to promote NREM (non-rapid eye movement) sleep by modulating the benzodiazepine site of the GABA (A) receptor.^[5] And, in an experimental animal model of chronic mild stress, a mixture of honokiol and magnolol supported normal levels of 5-hydroxytryptamine (5-HT) and its metabolite 5-hydroxyindoleacetic acid (5-HIAA) in various brain regions. The combination also promoted healthy corticosterone levels and platelet adenyl cyclase (AC) activity. Researchers suggest that these findings provide a basis for further study into the influence of magnolol and honokiol on the serotonergic system, the HPA (hypothalamic-pituitary-adrenal) axis, and the AC-cAMP pathway in relation to mood and emotional behavior.^{*,[7]}

Ziziphus spinosa A primary use of *Z spinosa* seeds in Traditional Chinese Medicine is to support calmness and help individuals with occasional sleeplessness.^[8,9] In an experimental animal model, saponins and flavonoids extracted from the seeds showed a significant relaxing effect and helped prolong sleeping time.^[8] To investigate potential mechanisms, researchers tested the influence of spinosin—a flavonoid derived from ziziphus seeds—on pentobarbital-induced sleep in mice. They concluded that it potentiated sleep via a serotonergic mechanism.^{*,[10]}

Koetter et al^[3] studied the interactions of magnolia and ziziphus extracts with selected central nervous system receptors in a series of assays. Interactions with the adenosine A1 receptor, dopamine transporter and dopamine D5 receptor (antagonist activity), serotonin receptors (5-HT1B and 5-HT6 antagonist activity), and the GABA benzodiazepine receptor were demonstrated. It is suggested that these findings provide some insight into the combined activity of these extracts.*

SedaLin™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Seditol®† (a proprietary blend of a patented†† extract from <i>Magnolia officinalis</i> (bark) and an extract from <i>Ziziphus spinosa</i> (seed))	730 mg	**
** Daily Value not established.		

Other Ingredients: HPMC (capsule), magnesium stearate, stearic acid, microcrystalline cellulose, calcium silicate, and silica.

DIRECTIONS: Take one to two capsules before bedtime, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Do not take if pregnant or lactating. Do not take if currently taking any prescription medication or receiving medical treatment without consulting your physician. Keep out of the reach of children. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.



†Seditol® is a registered trademark of NPI, LLC.
††U.S. Patent No. US 6,814,987

**References**

1. Seditol sleep supplement. HUT: Final report. TRG Study #82-05013. Nanuet, NY: Target Research Group; April, 2005. Study on file.
2. LaValle J, Pelletier M, LaValle L, et al. A proprietary blend of Magnolia and Ziziphus extracts assists with sleep: an open-label assessment. Next Pharmaceuticals. http://www.nextpharmaceuticals.com/stage/pdfs/Seditol_Open2008.pdf. Accessed June 18, 2012.
3. Koetter U, Barrett M, Lacher S, et al. Interactions of Magnolia and Ziziphus extracts with selected central nervous system receptors. *J Ethnopharmacol*. 2009 Jul 30;124(3):421-25. [PMID: 19505549]
4. Alexeev M, Grosenbaugh DK, Mott DD, et al. The natural products magnolol and honokiol are positive allosteric modulators of both synaptic and extra-synaptic GABA(A) receptors. *Neuropharmacology*. 2012 Jun;62(8):2507-14. [PMID: 22445602]
5. Qu WM, Yue XF, Sun Y, et al. Honokiol promotes non-rapid eye movement sleep via the benzodiazepine site of the GABA(A) receptor in mice. *Br J Pharmacol*. 2012 Apr 27. doi: 10.1111/j.1476-5381.2012.02010.x. [Epub ahead of print] [PMID: 22537192]
6. Squires RF, Ai J, Witt MR, et al. Honokiol and magnolol increase the number of [3H] muscimol binding sites three-fold in rat forebrain membranes in vitro using a filtration assay, by allosterically increasing the affinities of low-affinity sites. *Neurochem Res*. 1999 Dec;24(12):1593-602. [PMID: 10591411]
7. Xu Q, Yi LT, Pan Y, et al. Antidepressant-like effects of the mixture of honokiol and magnolol from the barks of *Magnolia officinalis* in stressed rodents. *Prog Neuropsychopharmacol Biol Psychiatry*. 2008 Apr 1;32(3):715-25. [PMID: 18093712]
8. Jiang JG, Huang XJ, Chen J, et al. Comparison of the sedative and hypnotic effects of flavonoids, saponins, and polysaccharides extracted from Semen Ziziphus jujube. *Nat Prod Res*. 2007 Apr;21(4):310-20. [PMID: 17479419]
9. Peng WH, Hsieh MT, Lee YS, et al. Anxiolytic effect of seed of *Ziziphus jujuba* in mouse models of anxiety. *J Ethnopharmacol*. 2000 Oct;72(3):435-41. [PMID: 10996283]
10. Wang LE, Bai YJ, Shi XR, et al. Spinosin, a C-glycoside flavonoid from semen *Ziziphus spinosa*, potentiated pentobarbital-induced sleep via the serotonergic system. *Pharmacol Biochem Behav*. 2008 Sep;90(3):399-403. [PMID: 18466960]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

SYNOVX[®] AI

Joint Comfort Support*



Available in 60 vegetarian capsules

DISCUSSION

Type II Collagen

Type II collagen (CII) is the most abundant structural protein in cartilage. It provides tensile strength and toughness to the tissue. In some individuals, immune responses to endogenous CII may impact joint cartilage integrity and joint comfort. However, researchers have discovered that a repetitive low dose of chicken or bovine CII—when taken orally and in its native form—is able to support a naturally balanced and healthy joint environment in such individuals.^[1-3] This is accomplished through a natural mechanism called oral tolerization (or “oral tolerance”), which supports the body’s desensitization process to a specific antigen—in this case, CII.^[3] Oral tolerization using CII essentially works as follows:

- Orally administered native CII enters the Peyer’s patches (immune surveillance structures) in the gut-associated lymphoid tissue (GALT).*
- Dendritic cells in the GALT take up the CII and present it to T-cells to produce regulatory T-cells.*
- Regulatory T-cells change specific systemic immune responses via the production of certain regulatory cytokines (e.g., TGF-beta 1, IL-10 and IL-4).*
- Systemic immune tolerance to CII is induced by the body and endogenous CII is naturally protected.*

Human trials have been conducted to study the effects of oral CII in joint health.^[4-8] In a multicenter, double-blind, placebo-controlled trial, 205 individuals were enrolled at six different sites and randomized to receive a placebo or an oral dose (20, 100, 500, or 2,500 mcg) of CII for 24 weeks. Efficacy was assessed monthly, and responses were analyzed utilizing three sets of criteria. Positive effects were observed at the lowest dose of CII, and no side effects were detected.^[6] Trentham et al found beneficial effects on the size and comfort of joints in a randomized, double-blind, placebo-controlled trial involving 60 patients who were given 100-500 mcg/d of chicken CII for three months.^[2] Ausar et al found beneficial effects in 90% of the subjects who received 0.5 mg/day of CII for 12 weeks.^[5] Conversely, another 12-week study found no significant difference in benefit between three groups (placebo, 10 mg/d of CII, 1 mg/d of CII). There was, however, a higher prevalence of responders in the CII groups.^[7] Researchers have noted that differences in study results may be related to the dose, species, and formulation of the CII.^[8]

b-2Cool[®]

B-2Cool is a specially developed native CII that is extracted from chicken sternums. Its manufacturing process is strictly controlled to preserve the triple helix structure of the molecule and the specific epitopes of the native protein that are thought to account for maximum effectiveness.*

CLINICAL APPLICATIONS

- Supports Joint Comfort and Mobility*
- Has a Protective Effect on Endogenous Type II Collagen*
- Modulates Immune Cell and Cytokine Activity in Joints*
- Improves Knee Function*

*SynovX[®] AI provides a proprietary blend of ingredients that specifically targets tissues, immune cells, and cytokines in joints. Type II collagen is the main structural protein in cartilage, and research suggests that low-dose, native-form type II collagen—as found in b-2Cool[®]—positively influences the immune response in joints via a mechanism called oral tolerization (a desensitization process). Xanthohumol, from hops, and hesperidin complement the activities of b-2Cool to deliver specialized joint support. Let SynovX AI help you stay active and moving!**

Pre-Clinical Study

In an experimental study performed in rats, orally administered b-2Cool (1-10 mg/kg) had positive effects on cytokine (interleukin [IL]-1 beta) production as well as comfort, as measured by a paw pressure test at days seven and 14. The lower dose displayed effectiveness at day 14. Repeated administration of the b-2Cool supported healthy spontaneous motility and preserved endogenous collagen from damage. Efficacy was comparable to that induced by 250 mg/kg/d of glucosamine.*^[9]

Human Study

Bakilan et al demonstrated a superior effect, compared to baseline, of b-2Cool (40 mg/d) combined with a standard intervention (acetaminophen (AC)) versus the standard intervention alone. In this three-month clinical study (n = 39), statistically significant results in comfort and mobility were achieved in the group taking the combination. The researchers reported, “the results suggest that native type II collagen treatment combined with acetaminophen is superior to acetaminophen alone for symptomatic treatment of patients with knee osteoarthritis.”*^[10]

Hesperidin

Free radicals that are released by activated neutrophils and produced by other biochemical pathways can play a significant role in joint cartilage changes. As a citrus bioflavonoid, hesperidin (HES) has been studied for its positive effects on free radical production, COX-2 gene expression, and cytokine balance.^[11-13] HES is often combined with other natural and standard joint health agents.^[14,15] Animal models have demonstrated that administration of hesperidin leads to significant improvements in biochemical and histological features of experimentally challenged joint tissues.^[12,16] Hesperidin administration is associated with the suppression of T-lymphocyte proliferation and IL-2 production as well as downregulation of IL-1, IL-6, and tumor necrosis factor-alpha.*^[13]

Xanthohumol

Research suggests that hop extract, particularly xanthohumol (XN), helps support eicosanoid and cytokine balance and joint health.^[17-20] Specifically, XN has been found to be superior to other hops-derived compounds (including isoxanthohumol) for inhibiting hyaluronic acid export, supporting proteoglycan and collagen homeostasis, and supporting cytokine balance in bovine chondrocytes.^[18] XN appears to suppress production of nitric oxide, IL-1 beta, and TNF-alpha; induce nuclear translocation of Nrf2 (nuclear factor erythroid 2-related factor 2); and increase cellular glutathione.^[21] Furthermore, XN appears to confer additional support for cytokine balance by downregulating cellular toll-like receptor 4 (TLR4) protein content.*^[22]

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN[®] Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

SynovX® AI Supplement Facts

Serving Size: 2 Capsules



	Amount Per Serving	%Daily Value
SynovX AI Proprietary Blend Hesperidin (from <i>Citrus sinensis</i> (fruit), b-2Cool® native collagen type II, and xanthohumol (from <i>Humulus lupulus</i>)(hop cones)	469 mg	**
** Daily Value not established.		

Other Ingredients: Dicalcium phosphate, HPMC (capsule), microcrystalline cellulose, ascorbyl palmitate, silica, and medium-chain triglyceride oil.

DIRECTIONS: Take two capsules on an empty stomach, or use as directed by your healthcare practitioner. For best results, take the capsules at bedtime.

Consult a healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

is a registered trademark licensed by Bioiberica, S.A.

REFERENCES

- Farboud A, Choy E. Serological investigation of IgG levels and subclasses in rheumatoid arthritis patients following ingestion of bovine type II collagen: results of a double blind, randomised controlled trial. *Clin Rheumatol*. 2011 Feb;30(2):193-99. [PMID: 20440528]
- Trentham DE, Dynesius-Trentham RA, Orav EJ, et al. Effects of oral administration of type II collagen on rheumatoid arthritis. *Science*. 1993 Sep 24;261(5129):1727-30. [PMID: 8378772]
- Park KS, Park MJ, Cho ML, et al. Type II collagen oral tolerance; mechanism and role in collagen-induced arthritis and rheumatoid arthritis. *Mod Rheumatol*. 2009;19(6):581-89. [PMID: 19697097]
- Barnett ML, Combitchi D, Trentham DE. A pilot trial of oral type II collagen in the treatment of juvenile rheumatoid arthritis. *Arthritis Rheum*. 1996 Apr;39(4):623-28. [PMID: 8630112]
- Ausar SF, Beltramo DM, Castagna LF, et al. Treatment of rheumatoid arthritis by oral administration of bovine tracheal type II collagen. *Rheumatol Int*. 2001 May;20(4):138-44. [PMID: 11411957]
- Barnett ML, Kremer JM, St Clair EW, et al. Treatment of rheumatoid arthritis with oral type II collagen. Results of a multicenter, double-blind, placebo-controlled trial. *Arthritis Rheum*. 1998 Feb;41(2):290-97. Erratum in: *Arthritis Rheum* 1998 May;41(5):938. [PMID: 9485087]
- Sieper J, Kary S, Sørensen H, et al. Oral type II collagen treatment in early rheumatoid arthritis. A double-blind, placebo-controlled, randomized trial. *Arthritis Rheum*. 1996 Jan;39(1):41-51. [PMID: 8546737]
- Choy EH, Scott DL, Kingsley GH, et al. Control of rheumatoid arthritis by oral tolerance. *Arthritis Rheum*. 2001 Sep;44(9):1993-97. [PMID: 11592359]
- Di Cesare Mannelli L, Micheli L, Zanardelli M, et al. Low dose native type II collagen prevents pain in a rat osteoarthritis model. *BMC Musculoskelet Disord*. 2013;14(1):228. doi:10.1186/1471-2474-14-228.
- Bakilan F, Armagan O, Ozgen M, et al. Effects of native type II collagen treatment on knee osteoarthritis: a randomized controlled trial. *Eurasion J Med*. 2016 Jun;48(2):95-101. [PMID: 27551171]
- Hirata A, Murakami Y, Shoji M, et al. Kinetics of radical-scavenging activity of hesperetin and hesperidin and their inhibitory activity on COX-2 expression. *Anticancer Res*. 2005 Sep-Oct;25(5):3367-74. [PMID: 16101151]
- Umar S, Kumar A, Sajad M, et al. Hesperidin inhibits collagen-induced arthritis possibly through suppression of free radical load and reduction in neutrophil activation and infiltration. *Rheumatol Int*. 2013 Mar;33(3):657-63. [PMID: 22527139]
- Li R, Li J, Cai L, et al. Suppression of adjuvant arthritis by hesperidin in rats and its mechanisms. *J Pharm Pharmacol*. 2008 Feb;60(2):221-28. [PMID: 18237470]
- Ahmed YM, Messiha BA, Abo-Saif AA. Protective effects of simvastatin and hesperidin against complete Freund's adjuvant-induced rheumatoid arthritis in rats. *Pharmacology*. 2015;96(5-6):217-25. [PMID: 26345515]
- Natural Medicines. Hesperidin. <https://naturalmedicines.therapeuticresearch.com/databases/health-wellness/professional.aspx?productid=1033>. Accessed October 18, 2016.
- Kawaguchi K, Maruyama H, Kometani T, et al. Suppression of collagen-induced arthritis by oral administration of the citrus flavonoid hesperidin. *Planta Med*. 2006 Apr;72(5):477-79. [PMID: 16557465]
- Hougee S, Faber J, Sanders A, et al. Selective inhibition of COX-2 by a standardized CO2 extract of *Humulus lupulus* in vitro and its activity in a mouse model of zymosan-induced arthritis. *Planta Med*. 2006 Feb;72(3):228-33. [PMID: 16534727]
- Stracke D, Schulz T, Prehm P. Inhibitors of hyaluronan export from hops prevent osteoarthritic reactions. *Mol Nutr Food Res*. 2011 Mar;55(3):485-94. [PMID: 20848398]
- Gao X, Deeb D, Liu Y, et al. Immunomodulatory activity of xanthohumol: inhibition of T cell proliferation, cell-mediated cytotoxicity and Th1 cytokine production through suppression of NF-kappaB. *Immunopharmacol Immunotoxicol*. 2009;31(3):477-84. [PMID: 19555200]
- Cho YC, Kim HJ, Kim YJ, et al. Differential anti-inflammatory pathway by xanthohumol in IFN-gamma and LPS-activated macrophages. *Int Immunopharmacol*. 2008 Apr;8(4):567-73. [PMID: 18328448]
- Lee IS, Lim J, Gal J, et al. Anti-inflammatory activity of xanthohumol involves heme oxygenase-1 induction via NRF2-ARE signaling in microglial BV2 cells. *Neurochem Int*. 2011 Feb;58(2):153-60. [PMID: 21093515]
- Peluso MR, Miranda CL, Hobbs DJ, et al. Xanthohumol and related prenylated flavonoids inhibit inflammatory cytokine production in LPS-activated THP-1 monocytes: structure-activity relationships and in silico binding to myeloid differentiation protein-2 (MD-2). *Planta Med*. 2010 Oct;76(14):1536-43. [PMID: 20309792]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

SYNOVX[®] CALM

Neuromuscular Relaxation Support*



Available in 60 vegetarian capsules

DISCUSSION

SynovX[®] Calm is part of the SynovX program of formulas, each targeted to address a specific concern related to joint health. For some individuals, even minor joint and muscular discomfort can make bedtime challenging. This specialized neuromuscular formulation features a select combination of botanical extracts traditionally used for calming, relaxation, and occasional sleeplessness complemented by bioavailable minerals that influence muscular contraction and relaxation. The combination of ingredients in SynovX Calm has yielded positive clinical results in similar products.*

Botanicals

Valerian Extract

Valerian (*Valeriana officinalis*) root has enjoyed broad historical applications, including for muscle pain and spasms, nervousness, stress, and occasional sleeplessness. Its effects can be attributed to its calming and soothing influence on the nervous system.^[1-3] Among the root's more than 150 possibly synergistic constituents, perhaps the most well understood are the valepotriates and valerenic acid. Valerenic acid binds to gamma-aminobutyric acid (GABA) receptors in the central nervous system, which produces a calming effect.^[3,4] GABA is the primary neurotransmitter involved in increasing the production of alpha waves (associated with a relaxed, yet mentally focused state) while decreasing beta waves (related to hyperactivity, nervousness, and fleeting thoughts). Valerian also shows effects on receptors for melatonin, the hormone that regulates the body's sleep-wake cycle.*^[5]

Passion Flower Extract

Passion flower (*Passiflora incarnata*) has a long history of traditional use for its calming and relaxing properties, and early evidence from both animal studies and human trials support these uses.^[7-11] The flavonoids in passion flower generate activity at the brain's receptors for GABA and benzodiazepines, which theoretically contribute to the calming and restful effects.*^[5]

Hops Extract

Hops are the female seed cones of the hop species *Humulus lupulus*, a medicinal plant used for a variety of purposes, including calming and relaxation. Although minimal evidence supports hops as a monotherapy, studies combining hops with valerian^[6,12] and hops with valerian plus passion flower have shown a modest improvement of sleep measures. In a 14-day randomized controlled trial (n = 91), a combination of hops extract (30 mg), valerian extract (300 mg), and passion flower extract (80 mg) taken at bedtime increased total duration of sleep, decreased nighttime awakenings, and reduced sleep latency.*^[13]

CLINICAL APPLICATIONS

- Traditionally-Used Botanicals That Address Relaxation and Occasional Sleeplessness*
- Muscular Calming Formula*
- Targeted Minerals That Promote Healthy Muscular Contraction/Relaxation*
- Contributes to Muscle Recovery Following Exercise*

*SynovX[®] Calm is designed to help relax tight/spastic muscles and ease occasional discomfort from overworked muscles. It features botanical extracts traditionally used to calm nerves and muscles and address occasional sleeplessness plus minerals to support healthy muscular contraction and relaxation.**

Sour Cherry Powder

Sour cherry (*Prunus cerasus*) is known to be rich in anthocyanins and polyphenolic compounds. Data also suggest that sour cherry naturally contains melatonin, which is critical in regulating the sleep-wake cycle.^[14] Several preliminary studies have also suggested sour cherry juice or freeze-dried concentrate may ease post-exercise muscle soreness.*^[15-17]

Minerals

Magnesium (TRAACS[®] magnesium bisglycinate chelate and magnesium taurate) Magnesium is provided as patented Albion[®] TRAACS[®] bisglycinate chelate comprised of magnesium bound to amino acids to create a chelate plus magnesium taurate. TRAACS chelates appear to be more readily absorbed through the intestinal mucosa than other mineral forms making an excellent delivery system for magnesium.*^[18]

As a cofactor for over 300 enzyme pathways, magnesium has a multitude of actions including a calming effect on the nervous system and the regulation of muscle contraction, which have both been demonstrated in animal and human studies.^[19,20] Magnesium affects permeability of excitable membranes and thereby acts as a "gatekeeper" to excitatory neurotransmitters.^[20] In addition to interacting with the GABA receptor, magnesium plays a role in the inhibition of the excitotoxin N-methyl-D-aspartate (NMDA) and thus promotes restfulness.*^[21,22]

Potassium (Albion[®] potassium glycinate complex)

Potassium is the most abundant intracellular electrolyte found in the body and is important for many functions, including muscle contraction and nerve impulse transmission.*

Calcium (Carbonate)

Calcium carbonate is an excipient used in SynovX Calm as a densifier. When present at greater than 2% of the Daily Value, calcium must be declared on a label. Although calcium carbonate is not intended to contribute to the formula's function, this excipient provides elemental calcium which plays a role in nerve transmission so that muscles and nerves function properly.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN[®] Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

SynovX® Calm Supplement Facts

Serving Size: 2 Capsules



	Amount Per Serving	%Daily Value
Calcium (as calcium carbonate)	85 mg	7%
Magnesium (as TRAACS® magnesium bisglycinate chelate and magnesium taurate)	75 mg	18%
Potassium (as Albion® potassium glycinate complex)	45 mg	1%
Valerian Extract (<i>Valeriana officinalis</i>)(root)(0.8% valerianic acids)	200 mg	**
Sour Cherry (<i>Prunus cerasus</i>)(cherry)	80 mg	**
Passion Flower Extract (<i>Passiflora incarnata</i>)(aerial part) (4% vitexin)	60 mg	**
Hops Extract (<i>Humulus lupulus</i>)(strobulus)(0.3% rutin)	30 mg	**

Other Ingredients: Capsule (hypromellose and water), ascorbyl palmitate, and silica.

DIRECTIONS: Take one or two capsules daily, or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. May cause drowsiness. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

Albion® and TRAACS® are registered trademarks of Albion Laboratories, Inc. U.S. Patent 7,838,042.

REFERENCES

- Bent S, Padula A, Moore D, et al. Valerian for sleep: a systematic review and meta-analysis. *Am J Med.* 2006 Dec;119(12):1005-12. [PMID: 17145239]
- Fernández-San-Martín MI, Masa-Font R, Palacios-Soler L, et al. Effectiveness of Valerian on insomnia: a meta-analysis of randomized placebo-controlled trials. *Sleep Med.* 2010 Jun;11(6):505-11. [PMID: 20347389]
- Hudson T. Valerian: A sleep aid and anxiolytic. Plant Intelligence Professional Resources. https://www.gaiaherbs.com/uploads/A_Research_Review_of_Valerian-1371566791.pdf. Accessed August 9, 2018.
- Benke D, Barberis A, Kopp S, et al. GABA A receptors as in vivo substrate for the anxiolytic action of valerianic acid, a major constituent of valerian root extracts. *Neuropharmacology.* 2009 Jan;56(1):174-81. [PMID: 18602406]
- Sarris J, Panossian A, Schweitzer I, et al. Herbal medicine for depression, anxiety and insomnia: a review of psychopharmacology and clinical evidence. *Eur Neuropsychopharmacol.* 2011 Dec;21(12):841-60. [PMID:21601431]
- Leathwood PD, Chauffard F, Heck E, et al. Aqueous extract of valerian root (*Valeriana officinalis* L.) improves sleep quality in man. *Pharmacol Biochem Behav.* 1982 Jul;17(1):65-71. [PMID: 7122669]
- Ingale AG, Hivrale AU. Pharmacological studies of *Passiflora* sp. and their bioactive compounds. *African Journal of Plant Science.* 2010 Oct 31;4(10):417-26. doi:10.1007/s00216-016-9376-4.
- Barbosa PR, Valvassori SS, Bordignon CL Jr, et al. The aqueous extracts of *Passiflora alata* and *Passiflora edulis* reduce anxiety-related behaviors without affecting memory process in rats. *J Med Food.* 2008 Jun;11(2):282-8. [PMID: 18598170]
- Miyasaka LS, Atallah AN, Soares BGO (2007). Cochrane Database of Systematic Reviews, 24: 1, CD004518.
- Reginatto FH, De-Paris F, Petry RD, et al. Evaluation of anxiolytic activity of spray dried powders of two South Brazilian *Passiflora* species. *Phytother Res.* 2006 May;20(5):348-51. [PMID: 16619361]
- Dhawan K, Kumar S, Sharma A. Antiasthmatic activity of the methanol extract of leaves of *Passiflora incarnata*. *Phytother Res.* 2003 Aug;17(7):821-2. [PMID:12916087]
- Morin CM, Koetter U, Bastien C, et al. Valerian-hops combination and diphenhydramine for treating insomnia: a randomized placebo-controlled clinical trial. *Sleep.* 2005 Nov;28(11):1465-71. [PMID: 16335333]
- Maroo N, Hazra A, Das T. Efficacy and safety of a polyherbal sedative-hypnotic formulation NSF-3 in primary insomnia in comparison to zolpidem: a randomized controlled trial. *Indian J Pharmacol.* 2013 Jan-Feb;45(1):34-9. [PMID: 23543804]
- Howatson G, Bell PG, Tallent J, et al. Effect of tart cherry juice (*Prunus cerasus*) on melatonin levels and enhanced sleep quality. *Eur J Nutr.* 2012 Dec;51(8):909-16. [PMID: 22038497]
- Kuehl KS, Perrier ET, Elliot DL, Chesnutt JC. Efficacy of tart cherry juice in reducing muscle pain during running: a randomized controlled trial. *J Int Soc Sports Nutr.* 2010 May 7;7:17. [PMID: 20459662]
- Levers K, Dalton R, Galvan E, et al. Effects of powdered Montmorency tart cherry supplementation on acute endurance exercise performance in aerobically trained individuals. *J Int Soc Sports Nutr.* 2016 May 26;13:22. [PMID: 27231439]
- Bell PG, Stevenson E, Davison GW, et al. The effects of Montmorency tart cherry concentrate supplementation on recovery following prolonged, intermittent exercise. *Nutrients.* 2016 Jul 22;8(7). [PMID: 27455316]
- Albion Minerals. <http://www.albionminerals.com/human-nutrition/products-trade/quality/traacs-ft-ir>. Accessed August 9, 2018.
- Laires MJ, Monteiro CP, Bicho M. Role of cellular magnesium in health and human disease. *Front Biosci.* 2004 Jan 1;9:262-76. [PMID: 14766364]
- Long S, Romani AM. Role of Cellular Magnesium in Human Diseases. *Austin J Nutr Food Sci.* 2014 Nov 18;2(10). [PMID: 25839058]
- Nielsen FH, Johnson LK, Zeng H. Magnesium supplementation improves indicators of low magnesium status and inflammatory stress in adults older than 51 years with poor quality sleep. *Magnes Res.* 2010 Dec;23(4):158-68. [PMID: 21199787]
- Papadopol V, Nechifor M. Magnesium in neuroses and neuroticism. In: Vink R, Nechifor M, editors. *Magnesium in the Central Nervous System* [Internet]. Adelaide (AU): University of Adelaide Press; 2011. Available from <http://www.ncbi.nlm.nih.gov/books/NBK507254/> [PMID: 29920008]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

SYNOVX[®] DJD

Nourishing and Supporting Joint Structures*



Available in 120 vegetable capsules

DISCUSSION

Years of joint tissue stress, underlying cytokine imbalance, and other factors can upset the equilibrium between anabolic and catabolic processes in the joints. The cooperative ingredients in SynovX DJD nourish joint tissues and help support balanced metabolic activity within them.*

Green-Lipped Mussel (GLM) (*Perna canaliculus*) XYMOGEN's GLMs are sourced from unpolluted waters off New Zealand and are guaranteed to be pure. They contain glycosaminoglycans (GAGs)—the principal components of cartilage and synovial fluid—as well as eicosatetraenoic acid, which promotes a healthy joint environment.^[1,2] GLMs have been shown to inhibit cyclooxygenase and lipoxygenase enzymes.^[2,3] Results of a systematic review of human randomized or placebo-controlled trials show that GLM supplementation (900-1200 mg/d) helps maintain healthy joint tissue and function.*^[1]

Hyal-Joint[®] Hyaluronic acid (HA) is responsible for the viscoelastic and lubricating properties of synovial fluid as well as for performing biophysical, biochemical, and cell-regulatory roles in joint synovial tissues. Given these critical tasks, HA has become a focus of proactive joint care. Hyal-Joint is a proprietary rooster comb extract rich in high-molecular-weight HA; it also contains collagen and other GAGs. Research suggests that Hyal-Joint supports the quality of synovial fluid by positively influencing synovial HA concentration and by reducing the expression of degradative factors in synovial fluid.^[4-8] Furthermore, scientific evidence shows that Hyal-Joint is two to four times more active than regular HA in nourishing and supporting the health of synovial fluid.^[7] This higher degree of activity comes from the unique composition of Hyal-Joint, which naturally contains key ingredients that benefit synovial fluid.*

CS BiO-ACTIVE[®] Chondroitin sulfate (CS) is a GAG required for the formation of proteoglycans found in joint cartilage. CS is thought to enhance joint health by supporting endogenous synthesis and preventing degradation of other joint GAGs. Oral administration of CS (800-1200 mg/d) has proven to positively influence joint space width, joint comfort, and fluid accumulation.^[9-12] The pharmaceutical grade, low-molecular-weight CS in CS BiO-ACTIVE has demonstrated higher bioavailability^[13] and greater biological activity^[14] than other CS

CLINICAL APPLICATIONS

- Helps Maintain Healthy Joints*
- Provides Joint Tissue Building Blocks*
- Supports a Healthy Joint Environment by Influencing the Activity of Cytokines, Catabolic Enzymes, and Oxidative Molecules*

*SynovX[®] DJD is designed to bolster what years of joint use can threaten in active individuals. This breakthrough formula contains critical joint building blocks and other nutrients that work cooperatively to nourish joint tissues and maintain a healthy joint environment. Let SynovX DJD help you stay active!**

sources. CS BiO-ACTIVE is the reference CS for the European Union Pharmacopoeia, and it was selected by the US National Institutes of Health for their glucosamine/chondroitin trial.^[15] In fact, most of the clinical research performed using CS has employed CS BiO-ACTIVE; and in all clinical trials and over 10 years of pharmacovigilance, CS BiO-ACTIVE has shown an excellent safety profile.*

Glucosamine Sulfate Glucosamine is an amino saccharide that research suggests stimulates chondrocytes, supports GAG synthesis, incorporates sulfur into cartilage, induces HA production, and modulates prostaglandin (e.g., PGE2) synthesis.^[16-18] Most of the scientific research done on glucosamine has been performed using glucosamine sulfate. Oral doses of 1,500 mg/d show clinical benefits in joint mobility and comfort.^[16,19] It is postulated that lower doses may nourish the joint tissues, especially in combination with chondroitin sulfate. Several studies confirm that the benefits of combining glucosamine sulfate and chondroitin sulfate outweigh taking them alone.*^[20-22]

Methylsulfonylmethane (MSM) As an organosulfur compound, MSM is thought to primarily benefit joint tissues by delivering sulfur. Sulfur helps maintain the strength and structure of connective tissue by forming cross-linkages through disulfide bonds—such as those found in GAGs.^[23] Research suggests that MSM may reduce joint tissue damage triggered by free radicals.^[24] One joint study shows that glucosamine and MSM achieve better results when combined than when administered individually.*^[25]

Vitamin C and Manganese Vitamin C is essential to the synthesis of collagen and to the maintenance of collagen integrity. Furthermore, an animal study suggests that serum ascorbate levels influence fluid accumulation in the joint.^[26] Manganese assists the growth and development of normal bone and the synthesis of cartilage. Pairing manganese with chondroitin and glucosamine in high doses has yielded positive effects on joints.^[27,28] and one combination study demonstrated a synergistic protective effect on joints.*^[21]

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN[®] Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

SynovX® DJD Supplement Facts

Serving Size: 2 Capsules		
	Amount Per Serving	%Daily Value
Vitamin C (ascorbic acid)	38 mg	42%
Manganese (as TRAACS® manganese bisglycinate chelate)	2.5 mg	109%
Methylsulfonylmethane (MSM)	500 mg	**
Green-Lipped Mussel (<i>Perna canaliculus</i>)	500 mg	**
Chondroitin Sulfate (as chondroitin sulfate sodium)(CS BIO-ACTIVE®)	300 mg	**
Glucosamine Sulfate Sodium Chloride	300 mg	**
Hyaluronic Acid (from Hyal-Joint®)	15 mg	**
** Daily Value not established.		



Other Ingredients: HPMC (capsule), ascorbyl palmitate, silica, and medium-chain triglyceride oil.
Contains: Crustacean Shellfish (shrimp and crab)

DIRECTIONS: Take two capsules daily, or as directed by your healthcare practitioner. Consult your practitioner prior to use. Individuals taking warfarin or other medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, dairy products, fish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or preservatives.

Hyal-Joint® Hyal-Joint® is a registered trademark licensed by Biolberica, S.A.

TRAACS® is a registered trademark of Albion Laboratories.

CS BIO-ACTIVE® CS B-BIOACTIVE is a registered trademark licensed by Biolberica, S.A.

REFERENCES

- Brien S, Prescott P, Coghlan B, et al. Systematic review of the nutritional supplement Perna Canaliculus (green-lipped mussel) in the treatment of osteoarthritis. *QJM*. 2008 Mar;101(3):167-79. [PMID: 18222988]
- McPhee S, Hodges LD, Wright PF, et al. Anti-cyclooxygenase effects of lipid extracts from the New Zealand green-lipped mussel, *Perna canaliculus*. *Comp Biochem Physiol B Biochem Mol Biol*. 2007 Mar;146(3):346-56. [PMID: 17197217]
- Treschow AP, Hodges LD, Wright PF, et al. Novel anti-inflammatory omega-3 PUFAs from the New Zealand green-lipped mussel, *Perna canaliculus*. *Comp Biochem Physiol B Biochem Mol Biol*. 2007 Aug;147(4):645-56. [PMID: 17543561]
- Castillo V, Bendele AM, Li K, et al. Effects of oral administration of Hyal-Joint® in 17 day rat developing type II collagen arthritis. *Osteoarthritis Cartilage*. 2010 Oct;18(Suppl 2):S244-45. doi:10.1016/S1063-4584(10)60572-9. Osteoarthritis Research Society International (OARSI) World Congress; September 23-26, 2010; Brussels, Belgium.
- Carmona JU, Argüelles D, Deulofeu R, et al. Effect of the administration of an oral hyaluronan formulation on clinical and biochemical parameters in young horses with osteochondrosis. *Vet Comp Orthop Traumatol*. 2009;22(6):455-59. [PMID: 19876524]
- Torrent A, Ruhl R, Theodosakis J, et al. Comparison of the efficacy of two products sold as orally-administered hyaluronan acid supplements, ib0004 and id386 on the endogenous in vitro synthesis of hyaluronan acid by human synoviocytes. *Osteoarthritis and Cartilage* 2009;17(1):S277-78.
- Torrent A, Ruhl R, Theodosakis J, et al. Comparative efficacy of IB0004, extracted hyaluronan acid (HA) and fermented HA on the synthesis of endogenous HA by human synoviocytes. *Osteoarthritis Cartilage*. 2009;17(Suppl 1):S278-79. [on file]
- Torrent A, Ruhl R, Martínez C, et al. Anti-inflammatory activity and absorption of a natural rooster comb extract (Hyal-Joint®). *Osteoarthritis and Cartilage*. 2010 Oct;18(Suppl 2):S246-47. doi:10.1016/S1063-4584(10)60577-8.
- Kahan A, Uebelhart D, De Vathaire F, et al. Long-term effects of chondroitins 4 and 6 sulfate on knee osteoarthritis: the study on osteoarthritis progression prevention, a two-year, randomized, double-blind, placebo-controlled trial. *Arthritis Rheum*. 2009 Feb;60(2):524-33. [PMID: 19180484]
- Möller I, Pérez M, Monfort J, et al. Effectiveness of chondroitin sulphate in patients with concomitant knee osteoarthritis and psoriasis: a randomized, double-blind, placebo-controlled study. *Osteoarthritis Cartilage*. 2010 Jun;18 Suppl 1:S32-40. [PMID: 20399899]
- Wildi LM, Raynauld JP, Martel-Pelletier J, et al. Chondroitin sulphate reduces both cartilage volume loss and bone marrow lesions in knee osteoarthritis patients starting as early as 6 months after initiation of therapy: a randomised, double-blind, placebo-controlled pilot study using MRI. *Ann Rheum Dis*. 2011 Jun;70(6):982-89. [PMID: 21367761]
- Hochberg MC, Clegg DO. Potential effects of chondroitin sulfate on joint swelling: a GAIT report. *Osteoarthritis Cartilage*. 2008;16 Suppl 3:S22-24. [PMID: 18768335]
- Adebowale A, Du J, Liang Z, et al. The bioavailability and pharmacokinetics of glucosamine hydrochloride and low molecular weight chondroitin sulfate after single and multiple doses to beagle dogs. *Biopharm Drug Dispos*. 2002 Sep;23(6):217-25. [PMID: 12214321]
- Tat SK, Pelletier JP, Mineau F, et al. Variable effects of 3 different chondroitin sulfate compounds on human osteoarthritic cartilage/chondrocytes: relevance of purity and production process. *J Rheumatol*. 2010 Mar;37(3):656-64. [PMID: 20110528]
- Barnhill JG, Fye CL, Williams W, et al. Chondroitin product selection for the glucosamine/chondroitin arthritis intervention trial. *J Am Pharm Assoc*. 2006 Jan-Feb;46(1):14-24. [PMID: 16529337]
- Dahmer S, Schiller RM. Glucosamine. *Am Fam Physician*. 2008 Aug 15;78(4):471-76. [PMID: 18756654]
- Igarashi M, Kaga I, Takamori Y, et al. Effects of glucosamine derivatives and uronic acids on the production of glycosaminoglycans by human synovial cells and chondrocytes. *Int J Mol Med*. 2011 Jun;27(6):821-27. [PMID: 21455564]
- Kapoor M, Mineau F, Fahmi H, et al. Glucosamine sulfate reduces prostaglandin E(2) production in osteoarthritic chondrocytes through inhibition of microsomal PGE synthase-1. *J Rheumatol*. 2012 Mar;39(3):635-44. [PMID: 22089456]
- Selvan T, Rajiah K, Nainar MS, et al. A clinical study on glucosamine sulfate versus combination of glucosamine sulfate and NSAIDs in mild to moderate knee osteoarthritis. *Scientific World Journal*. 2012;2012:902676. [PMID: 22577354]
- Tat SK, Pelletier JP, Vergés J, et al. Chondroitin and glucosamine sulfate in combination decrease the pro-resorptive properties of human osteoarthritis subchondral bone osteoblasts: a basic science study. *Arthritis Res Ther*. 2007;9(6):R117. [PMID: 17996099]
- Lippiello L, Woodward J, Karpman R, et al. In vivo chondroprotection and metabolic synergy of glucosamine and chondroitin sulfate. *Clin Orthop Relat Res*. 2000 Dec;(381):229-40. [PMID: 11127660]
- Clegg DO, Reda DJ, Harris CL, et al. Glucosamine, chondroitin sulfate, and the two in combination for painful knee osteoarthritis. *N Engl J Med*. 2006 Feb 23;354(8):795-808. [PMID: 16495392]
- Methylsulfonylmethane (MSM). Monograph. *Altern Med Rev*. 2003 Nov;8(4):438-41. [PMID: 14653770]
- Brien S, Prescott P, Lewith G. Meta-analysis of the related nutritional supplements dimethyl sulfoxide and methylsulfonylmethane in the treatment of osteoarthritis of the knee. *Evid Based Complement Alternat Med*. 2011;2011:528403. doi: 10.1093/ecam/nep045. [PMID: 19474240]
- Usha PR, Naidu MU. Randomised, double-blind, parallel, placebo-controlled study of oral glucosamine, methylsulfonylmethane and their combination in osteoarthritis. *Clin Drug Investig*. 2004;24(6):353-63. [PMID: 17516722]
- Simões SI, Eletério CV, Cruz ME, et al. Biochemical changes in arthritic rats: dehydroascorbic acid and ascorbic acid levels. *Eur J Pharm Sci*. 2003;18(2):185-89. [PMID: 12594012]
- Das A Jr, Hammad TA. Efficacy of a combination of FCHG49 glucosamine hydrochloride, TRH122 low molecular weight sodium chondroitin sulfate and manganese ascorbate in the management of knee osteoarthritis. *Osteoarthritis Cartilage*. 2000 Sep;8(5):343-50. [PMID: 10966840]
- Leffler CT, Philippi AF, Leffler SG, et al. Glucosamine, chondroitin, and manganese ascorbate for degenerative joint disease of the knee or low back: a randomized, double-blind, placebo-controlled pilot study. *Mil Med*. 1999 Feb;164(2):85-91. [PMID: 10050562]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

© XYMOGEN
DRS-167
Rev. 08/08/19



SYNOVX[®] METABOLIC

Joint Support for Overweight Patients*



Available in 30 capsules & 60 capsules

DISCUSSION

A paradigm shift is occurring in our understanding of how excess body fat affects joint health. At the heart of this new understanding, adipose tissue has emerged as a dynamic organ that releases several signaling molecules or mediators (e.g., adipokines).^[1,2] These adipose-generated mediators “communicate” with cells of joint tissues, sending messages that result in changes to cartilage and synovial fluid that ultimately affect joint health, function, and comfort.^[2] In a search to discover substances that can help change this cellular “communication” to a more healthy exchange, scientists tested a proprietary combination of hyaluronic acid and other glycosaminoglycans called Oralvisc[®], which is the main ingredient in SynovX Metabolic.*

In a double-blind, randomized, controlled study, an evaluation of the effects of Oralvisc (80 mg/day) on multiple mediators associated with joint tissue changes in overweight individuals was undertaken. The results were very promising:

Leptin is an adipokine (or adipocytokine), a cell-to-cell signaling protein that originates from adipose. It is one of the central mediators being investigated as a metabolic component that affects joint health.^[2] Leptin is not only thought to have synergistic actions with other damaging cytokines, including IL-1, TNF-alpha, and IFN-gamma,^[2] but it is also thought to affect joint tissues through activation of iNOS, stimulation of cartilage remodeling enzymes, induction of synovial membrane cytokines, and bone matrix regulation.^[3] Increased levels of leptin have been observed in the chondrocytes, synovial fluid, and osteophytes of human subjects; and increased levels of leptin are thought to play a role in cartilage homeostasis.^[2,4] It is postulated that supporting a reduction in levels of synovial and serum leptin will prove to be beneficial in cartilage homeostasis and turnover.*

Three months of supplementation with Oralvisc resulted in a significant ($P < 0.05$) decrease between initial and final—and between supplement and placebo—synovial and serum leptin levels, as measured by immunoassay.^[5] In addition, the supplemented group lost an average of 1.21 lb compared to an average 1.65 lb weight gain in the placebo group. The researchers concluded that reducing leptin levels could be beneficial to cartilage homeostasis and turnover, and that the weight loss could be due to the decrease in leptin levels associated with healthy joint function and changes in overall metabolism.*

CLINICAL APPLICATIONS

- Supports Joint Comfort and Function*
- Positively Affects the Synovial Cytokine and Chemokine Profile*
- Reduces Synovial Fluid Leptin and Serum Leptin*
- Reduces Levels of Key Signaling Molecules, Such as Bradykinin and Cytokines*

*SynovX[®] Metabolic is a cutting-edge option for those in need of joint support related to excess body fat. Exciting, new research shows that fat cells send messages (via leptin and other signaling molecules) to joint tissue cells. These messages can trigger a cascade of events that damage the health and integrity of joints. SynovX Metabolic works by changing the “communication” between these cells, resulting in a more naturally healthy joint environment that can help you stay comfortable and be active.**

The effect of Oralvisc on weight loss and leptin levels was also observed in diet-induced obese mice. Oralvisc (3 mg/mouse/day) resulted in faster loss of body fat compared to placebo. At sacrifice, supplemented mice had a 30% lower adiposity index and a 40% lower circulating leptin level than controls.^[6] Furthermore, preliminary research on mouse embryo fibroblasts suggested that Oralvisc can suppress adipogenic gene expression.*^[7]

Cytokines and Chemokines are cellular communication mediators; some of these activate chondrocytes and synovia to break down joint extracellular matrix and trigger a cascade of damaging events.^[8,9] As demonstrated in the clinical trial, Oralvisc supplementation resulted in a significant reduction in 12 serum and synovial cytokines and chemokines, including IL-1alpha, IL-1beta, and TNF-alpha, after the three-month period. In contrast, the placebo group did not display a reduction in these mediators; and, in some cases, the levels increased, suggesting progression of unhealthy catabolic signaling.*^[9]

Glycosaminoglycans (GAGs), such as hyaluronic acid (HA), have numerous functions within joints. For instance, HA has visco-elastic properties that reduce friction between cartilage surfaces, and it has metabolic properties that are critical for homeostasis of the synovial fluid.^[10,11] Damaging pathways triggered by signaling molecules result in changes to the synovial fluid environment and have been shown to result in an increase in HA turnover. When the researchers looked at the effect of Oralvisc on HA turnover in synovial fluid, they found that after 12 weeks of supplementation the mean rate of HA turnover declined by 45% ($P = 0.046$). In addition to the normalization in HA turnover, the researchers also noted that the dietary supplement supported joint comfort and function.*^[11]

Bradykinin, a peptide produced in the synovial membrane, is responsible for stimulating nociceptors and initiating the cytokine response to cellular insult. Researchers found that Oralvisc supplementation resulted in significantly lower ($P < 0.05$) serum bradykinin levels (14.44 ng/mL versus placebo 15.06 ng/mL).*

Continued on next page

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN[®] Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

SynovX® Metabolic Supplement Facts

Serving Size: 1 Capsule		
	Amount Per Serving	%Daily Value
Vitamin C (ascorbic acid)	15 mg	17%
ORALVISC® (proprietary, naturally occurring source of glycosaminoglycans (GAGs))	80 mg	**
** Daily Value not established.		

Other Ingredients: Microcrystalline cellulose, capsule (gelatin, carmine, and titanium dioxide), vegetable stearic acid, vegetable magnesium stearate, and silica.

DIRECTIONS: Take one capsule daily, or as directed by your healthcare practitioner. Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

ORALVISC® is a registered trademark licensed by Bioiberica, S.A.

Likewise, synovial fluid bradykinin decreased significantly ($P < 0.05$) in the supplemented group (-0.6 ng/mL versus placebo +0.29 ng/mL).^{*[12]}

The positive results observed for each metabolic parameter studied may have translated into the clinically significant improvements recorded in joint comfort and function as assessed by VAS (visual analog scale) and WOMAC (Western Ontario and McMaster Universities osteoarthritis index) scores.^{*[13]}

REFERENCES

1. Toussiot E, Streit G, Wendling D. The contribution of adipose tissue and adipokines to inflammation in joint diseases. *Curr Med Chem.* 2007;14(10):1095-100. [PMID: 17456023]
2. Issa RI, Griffin TM. Pathobiology of obesity and osteoarthritis: integrating biomechanics and inflammation. *Pathobiol Aging Age Relat Dis.* 2012 May 9;2(2012). [PMID: 22662293]
3. Iannone F, Lapadula G. Obesity and inflammation—targets for OA therapy. *Curr Drug Targets.* 2010 May;11(5):586-98. [PMID: 20199391]
4. Dumond H, Presle N, Terlain B, et al. Evidence for a key role of leptin in osteoarthritis. *Arthritis Rheum.* 2003 Nov;48(11):3118-29. [PMID: 14613274]
5. Wu W, Zvirbulis R, Zonca B, et al. An oral preparation containing hyaluronic acid (Oralvisc®) can significantly decrease the production of leptin levels in the serum and synovial fluid of osteoarthritic knee patients. Poster presented at: Orthopaedic Research Society (ORS) Annual Meeting. San Antonio, TX. January 26-29, 2013. [on file]
6. Reynés B, Petrov PD, Serrano A, et al. A glycosaminoglycan rich commercial preparation used in osteoarthritis management favors fat loss in diet-induced obese mice. *Ann Rheum Dis.* 2014;73:1060. doi:10.1136/annrheumdis-2014-eular.5581.
7. Petrov PD, Granados N, Chetrit C, et al. Synergistic effects of a mixture of glycosaminoglycans to inhibit adipogenesis and enhance chondrocyte features in multipotent cells. *Cell Physiol Biochem.* 2015;37(5):1792-806. [PMID: 26584280]
8. Kapoor M, Martel-Pelletier J, Lajeunesse D, et al. Role of proinflammatory cytokines in the pathophysiology of osteoarthritis. *Nat Rev Rheumatol.* 2011 Jan;7(1):33-42. [PMID: 21119608]
9. Wu W, Pasierb M, Zonca B, et al. An oral preparation containing hyaluronic acid (Oralvisc®) can act systemically to decrease serum and synovial fluid levels of inflammatory cytokines and chemokines in osteoarthritic knee patients. Poster presented at: Orthopaedic Research Society (ORS) Annual Meeting. San Antonio, TX. January 26-29, 2013. [on file]
10. Ghosh P, Guidolin D. Potential mechanism of action of intra-articular hyaluronan therapy in osteoarthritis: are the effects molecular weight dependent? *Semin Arthritis Rheum.* 2002 Aug;32(1):10-37. [PMID: 12219318]
11. Li KW, Wu W, Emson CL, et al. An oral preparation containing hyaluronic acid (Oralvisc®) can normalize the turnover of hyaluronic acid in synovial fluid of osteoarthritic knee patients. *Osteoarthritis Cartilage.* 2013 April;21(Suppl):S217. doi:10.1016/j.joca.2013.02.449.
12. Nelson F, Zvirbulis R, Zonca B, et al. An oral preparation containing hyaluronic acid (Oralvisc®) can reduce osteoarthritis knee pain and serum and synovial fluid bradykinin. *Osteoarthritis Cartilage.* 2013 April;21(Suppl):S150. doi:10.1016/j.joca.2013.02.320.
13. Nelson F, Zvirbulis R, Zonca B, et al. The effects of an oral preparation containing hyaluronic acid (Oralvisc®) on obese knee osteoarthritis patients determined by pain, function, bradykinin, leptin, inflammatory cytokines, and heavy water analyses. *Rheumatol Int.* 2015;35:43-52. doi:10.1007/s00296-014-3047-6.

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

© XYMOGEN
DRS-278
Rev. 08/08/19



SYNOVX® PERFORMANCE

Joint Mobility Support*



Available in 60 vegetarian capsules

DISCUSSION

SynovX® Performance provides primary support for joint lubrication and comfort in the face of aging, normal wear and tear, and robust physical activity. This unique formula addresses the health of the total joint, including articular cartilage (highly specialized connective tissue), the synovial membrane (a thin layer of tissue that contains synoviocytes), and the synovial fluid (the fluid that lubricates the joint). Providing early support for the joint's cartilage matrix can tip the balance in favor of anabolism (building up) versus catabolism (breaking down). A proprietary blend of ingredients makes SynovX Performance the early “go-to” formula for healthy joint maintenance.*

Hyal-Joint® This proprietary complex is rich in high-molecular-weight hyaluronic acid, along with polysaccharides and collagen. Hyaluronic acid (HA), the principal component of Hyal-Joint, is a lubricating substance produced naturally in the body.^[1] It is found in abundance in the synovial fluid and extracellular matrix of joints where it reduces friction between cartilage surfaces and helps maintain cytokine balance. Hyaluronic acid helps maintain the quality of the synovial fluid and the integrity of the synovial membrane, both key factors in the health of the joint itself. Oral HA is absorbed in the small intestine and has yielded positive results in human, animal, and cell studies.^[2,3] Cell studies suggest that high-molecular-weight HA has a positive effect on cytokine balance due to downregulation of IL-8, iNOS, aggrecanase-2, and TNF-alpha gene expression.^[4] In vitro efficacy studies found Hyal-Joint to be two to four times more effective than fermented HA in stimulating the synthesis of endogenous HA and improving the concentration and viscous properties of joint fluid.^[5-7]

Research on Hyal-Joint has yielded positive outcomes.^[8-14] A randomized, double-blind, placebo-controlled trial indicated that oral Hyal-Joint (80 mg/d) resulted in significant improvements in WOMAC (Western Ontario and McMaster Universities Osteoarthritis) scores compared to baseline, with a greater magnitude of improvement in physical function and total symptoms when compared to placebo. Hyal-Joint was found to improve several markers of quality of life in the study as well.^[2] Oral supplementation with Hyal-Joint resulted in a decrease in synovial effusion and occasional pain when compared to other treatment.^[8] Several other human studies showed varied positive effects of Hyal-Joint supplementation at 80 mg/d for three months.^[9-11] The observed benefits included improved joint mechanics, increased muscle strength and function, increased joint comfort and mobility, and reduced fluid accumulation. In one study, pre- and post-intervention peripheral blood samples taken in a

CLINICAL APPLICATIONS

- Supports Joint Mobility and Comfort*
- Supports Healthy Synovial Fluid*
- Supports Joint Integrity and Function*

*SynovX® Performance is a breakthrough formula designed for active adults who don't want to slow down or reduce their ability to perform athletic tasks—from walking to extreme sports. It promotes healthy joint fluid and synovial membranes, supports joint mobility, and helps support cytokine and eicosanoid balance. Keep the fluid in your joints healthy just as you would change the oil in your car to get more mileage. Let SynovX Performance help you stay active and perform well!**

subset of patients showed that supplementation improved gene expression related to GAG metabolism and extracellular matrix remodeling.*^[11]

Animal studies have yielded promising results suggesting that Hyal-Joint supports joint tissue at the cellular level^[12] and reduces synovial effusion.^[13] Hyal-Joint was found to lower levels of prostaglandin E2 (PGE2) in human fibroblasts cells which, in turn, supports eicosanoid balance in the body.*^[14]

Hesperidin A citrus bioflavonoid that has been studied for its effect on cytokine balance, hesperidin (HES) is often combined with other therapeutic agents.^[15] Research suggests that oral HES can support joint health; when administered, it significantly improved all clinical parameters measured,^[16] suppressed clinical scores, and improved histological features in the animal model.^[17] Hesperidin administration was associated with the suppression of T-lymphocyte proliferation and IL-2 production; downregulation of IL-1, IL-6, and TNF-alpha; and amelioration of pathological changes in a targeted rat population.*^[18]

Xanthohumol Hops are used traditionally to promote relaxation and healthy mood.^[19] However, current research suggests that hop extract, particularly xanthohumol (XN), helps support eicosanoid and cytokine balance and joint health.^[20-23] Specifically, XN was found to be superior to other hops-derived compounds (including isoxanthohumol) for inhibiting hyaluronic acid export, inhibiting proteoglycan and collagen loss, and supporting cytokine balance in bovine chondrocytes.^[21] XN appears to suppress production of nitric oxide, IL-1β, and TNF-α; induce nuclear translocation of Nrf2; and increase cellular glutathione.^[24] Furthermore, XN appears to confer additional support for cytokine balance by downregulating cellular toll-like receptor 4 (TLR4) protein content.^[25] SynovX Performance contains a concentrated extract of xanthohumol.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

SynovX® Performance Supplement Facts

Serving Size: 1 Capsule	Amount Per Serving	%Daily Value
SynovX Performance Proprietary Blend	490 mg	**
Hesperidin (from <i>Citrus sinensis</i>) (fruit), Hyal-Joint® (proprietary natural complex rich in high-molecular-weight hyaluronic acid, other polysaccharides, and collagen), and xanthohumol (from <i>Humulus lupulus</i>) (hop cones)		
** Daily Value not established.		

Other Ingredients: HPMC (capsule), dicalcium phosphate, ascorbyl palmitate, silica, and medium-chain-triglyceride oil.

DIRECTIONS: Take one capsule twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn, soy, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep tightly closed in a cool, dry place out of reach of children.

Hyal-Joint® Hyal-Joint® is a registered trademark licensed by Bioiberica, S.A.



REFERENCES

- Natural Medicines. Hyaluronic Acid. <https://naturalmedicines.therapeuticresearch.com/databases/health-wellness/professional.aspx?productid=1062>. Accessed January 11, 2016.
- Kalman DS, Heimer M, Valdeon A, et al. Effect of a natural extract of chicken combs with a high content of hyaluronic acid (Hyal-Joint) on pain relief and quality of life in subjects with knee osteoarthritis: a pilot randomized double-blind placebo-controlled trial. *Nutr J*. 2008 Jan 21;7:3. [PMID: 18208600]
- Bergin BJ, Pierce SW, Bramlage LR, et al. Oral hyaluronan gel reduces post operative tarsocrural effusion in the yearling Thoroughbred. *Equine Vet J*. 2006 Jul;38(4):375-8. [PMID: 16866209]
- Wang CT, Lin YT, Chiang BL, et al. High molecular weight hyaluronic acid down-regulates the gene expression of osteoarthritis-associated cytokines and enzymes in fibroblast-like synoviocytes from patients with early osteoarthritis. *Osteoarthritis Cartilage*. 2006 Dec;14(12):1237-47. [PMID: 16806998]
- Torrent A, Ruhí R, Theodosakis J, et al. Comparative efficacy of IB0004, extracted hyaluronic acid (HA) and fermented HA on the synthesis of endogenous HA by human synoviocytes. *Osteoarthritis Cartilage*. 2009;17(Suppl 1):S278-S279. [on file]
- Bioiberica. Hyal-Joint. http://www.hyal-joint.com/Information_on_the_ingredient.html. Accessed January 11, 2016.
- Torrent A, Ruhí R, Theodosakis J, et al. Comparison of the efficacy of two products sold as orally-administered hyaluronic acid supplements, IB0004 and ID386 on the endogenous in vitro synthesis of hyaluronic acid by human synoviocytes. *Osteoarthritis Cartilage*. 2009;17(Suppl 1):S277-S278.
- Möller I, Martínez-Puig D, Chetrit C. Oral Administration of a natural extract rich in hyaluronic acid for the treatment of knee OA with synovitis: a retrospective cohort study. *Clin Nutr Suppl*. 2009;4(2):171. <http://download.journals.elsevierhealth.com/pdfs/journals/1744-1161/PIIS1744116109703941.pdf>. Accessed January 11, 2016.
- Martínez-Puig D, Möller I, Fernández C, et al. Efficacy of oral administration of yoghurt supplemented with a preparation containing hyaluronic acid (Mobilee™) in adults with mild joint discomfort: a randomized, double-blind, placebo-controlled intervention study. *Mediterr J Nutr Metab*. 2013;6:63-68.
- Solà R, Valls RM, Martorell I, et al. A low-fat yoghurt supplemented with a rooster comb extract on muscle joint function in adults with mild knee pain: a randomized, double blind, parallel, placebo-controlled, clinical trial of efficacy. *Food Funct*. 2015 Nov 4;6(11):3531-39. [PMID: 26302034]
- Sánchez J, Bonet ML, Keijer J, et al. Blood cells transcriptomics as source of potential biomarkers of articular health improvement: effects of oral intake of a rooster combs extract rich in hyaluronic acid. *Genes Nutr*. 2014 Sep;9(5):417. [PMID: 25024048]
- Castillo V, Bendele AM, Li K, et al. Effects of oral administration of Hyal-Joint® in 17 day rat developing type II collagen arthritis. *Osteoarthritis and Cartilage*. 2010 Oct;18(Suppl 2):S244-S245. doi:10.1016/S1063-4584(10)60572-9.
- Carmona JU, Argüelles D, Deulofeu R, et al. Effect of the administration of an oral hyaluronan formulation on clinical and biochemical parameters in young horses with osteochondrosis. *Vet Comp Orthop Traumatol*. 2009;22(6):455-9. [PMID: 19876524]
- Torrent A, Ruhí R, Martínez C, et al. Anti-inflammatory activity and absorption of a natural rooster comb extract (Hyal-Joint®). *Osteoarthritis and Cartilage*. 2010 Oct;18(Suppl 2):S246-S247. doi:10.1016/S1063-4584(10)60577-8.
- Natural Medicines. Hesperidin. <https://naturalmedicines.therapeuticresearch.com/databases/health-wellness/professional.aspx?productid=1033>. Accessed January 13, 2016.
- Umar S, Kumar A, Sajad M, et al. Hesperidin inhibits collagen-induced arthritis possibly through suppression of free radical load and reduction in neutrophil activation and infiltration. *Rheumatol Int*. 2013 Mar;33(3):657-63. [PMID: 22527139]
- Kawaguchi K, Maruyama H, Kometani T, et al. Suppression of collagen-induced arthritis by oral administration of the citrus flavonoid hesperidin. *Planta Med*. 2006 Apr;72(5):477-9. [PMID: 16557465]
- Li R, Li J, Cai L, et al. Suppression of adjuvant arthritis by hesperidin in rats and its mechanisms. *J Pharm Pharmacol*. 2008 Feb;60(2):221-8. [PMID: 18237470]
- Natural Medicines. Hops. <https://naturalmedicines.therapeuticresearch.com/databases/food,-herbs-supplements/professional.aspx?productid=856>. Accessed January 13, 2016.
- Hougee S, Faber J, Sanders A, et al. Selective inhibition of COX-2 by a standardized CO2 extract of *Humulus lupulus* in vitro and its activity in a mouse model of zymosan-induced arthritis. *Planta Med*. 2006 Feb;72(3):228-33. [PMID: 16534727]
- Stracke D, Schulz T, Prehm P. Inhibitors of hyaluronan export from hops prevent osteoarthritic reactions. *Mol Nutr Food Res*. 2011 Mar;55(3):485-94. [PMID: 20848398]
- Gao X, Deeb D, Liu Y, et al. Immunomodulatory activity of xanthohumol: inhibition of T cell proliferation, cell-mediated cytotoxicity and Th1 cytokine production through suppression of NF-kappaB. *Immunopharmacol Immunotoxicol*. 2009;31(3):477-84. [PMID: 19555200]
- Cho YC, Kim HJ, Kim YJ, et al. Differential anti-inflammatory pathway by xanthohumol in IFN-gamma and LPS-activated macrophages. *Int Immunopharmacol*. 2008 Apr;8(4):567-73. [PMID: 18328448]
- Lee IS, Lim J, Gal J, et al. Anti-inflammatory activity of xanthohumol involves heme oxygenase-1 induction via NRF2-ARE signaling in microglial BV2 cells. *Neurochem Int*. 2011 Feb;58(2):153-60. [PMID: 21093515]
- Peluso MR, Miranda CL, Hobbs DJ, et al. Xanthohumol and related prenylated flavonoids inhibit inflammatory cytokine production in LPS-activated THP-1 monocytes: structure-activity relationships and in silico binding to myeloid differentiation protein-2 (MD-2). *Planta Med*. 2010 Oct;76(14):1536-43. [PMID: 20309792]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

SYNOVX[®] RECOVERY

Ultra-Pure Joint Support*



Available in 120 vegetable capsules

DISCUSSION

Nourishing and maintaining the connective tissue (cartilage) in our joints are essential to maintaining flexibility, exercising comfortably, and recovering effectively. Three high-quality ingredients are combined in SynovX Recovery to promote joint health and assist with recovery from temporary joint discomfort due to occasional overexertion or intensive activity.*

CS b-Bioactive[®] Chondroitin sulfate (CS) is the most abundant glycosaminoglycan (GAG) in the body. GAGs are the principal components of cartilage and synovial fluid. CS is thought to enhance joint health by supporting endogenous synthesis and preventing degradation of other joint GAGs. Oral administration of CS (800-1200 mg/d) has proven to positively influence brain response to patellar pressure, joint space width, joint comfort, and fluid accumulation.^[1-5] SynovX Recovery provides 1200 mg of CS in the recommended four-capsule-per-day dosage.*

The pharmaceutical grade, low-molecular-weight CS in CS b-Bioactive has demonstrated higher bioavailability^[6] and greater biological activity^[7] than other CS sources. CS b-Bioactive is the reference CS for the European Union Pharmacopoeia, and it was selected by the US National Institutes of Health for their glucosamine/chondroitin trial.^[8] In fact, most of the clinical research performed using CS has employed CS b-Bioactive; and in all clinical trials and over 10 years of pharmacovigilance, CS b-Bioactive has shown an excellent safety profile.*

In a landmark study, the comparable efficacy of 1200 mg/d of CS b-Bioactive versus standard intervention was tested. In this multicenter, randomized, double-blind, controlled and comparative study, 194 subjects were studied for a two-year period. According to quantitative magnetic resonance, subjects supplemented with CS b-Bioactive showed slower progression of cartilage volume loss in the first year when compared to subjects on standard intervention. Furthermore, both interventions were found to be equally effective on comfort, function, ease of movement, and fluid accumulation.^{*[9]}

CLINICAL APPLICATIONS

- Supports Joint Structure and Function*
- Supports Proteoglycan Synthesis for Healthy Connective Tissue*
- Helps Protect Cartilage Cells*
- Contributes to Muscle Recovery Following Exercise*

*SynovX[®] Recovery features methylsulfonylmethane (MSM) blended with naturally occurring, clinically researched glucosamine sulfate and chondroitin sulfate. Combined, these three ingredients provide targeted support for healthy joint structure and function.**

A comprehensive review published by Cochrane in 2015 included 43 randomized controlled trials including 4962 participants treated with chondroitin sulfate; 4148 participants given placebo or another control were included. The review revealed that chondroitin (alone or in combination with glucosamine) was better than placebo for supporting joint comfort in short-term studies.^{*[10]}

Glucosamine Sulfate Glucosamine is a naturally occurring amino saccharide (glucose with a nitrogen-containing amino group attached) that is a principle substrate for cartilage synthesis.^[11] Research suggests that glucosamine stimulates chondrocytes (cartilage cells), supports GAG synthesis, incorporates sulfur into cartilage tissue, induces hyaluronic acid (HA) production, and modulates prostaglandin (e.g., PGE2) synthesis.^[12-14] Prostaglandins (specialized hormone-like fatty acids produced in the body) regulate a wide variety of bodily functions, including cytokine production and balance. Glucosamine sulfate was found to inhibit the release of PGE2, the activity of NF-kappaB, and the synthesis of COX-2 enzymes in human chondrocytes.^{*[15]}

Most of the scientific research done on glucosamine has been performed using glucosamine sulfate. Oral doses of 1500 mg/d have shown clinical benefits in joint mobility and comfort.^[12,16] Four capsules per day of SynovX Recovery provide 1500 mg of glucosamine sulfate. It is postulated that even lower doses may nourish joint tissues, especially in combination with chondroitin sulfate.*

Several studies have confirmed that the benefits of combining glucosamine sulfate with chondroitin sulfate outweigh taking either alone.^[17-19] During a randomized, double-blind, placebo-controlled clinical trial that followed 605 participants for two years, all study groups who had received glucosamine sulfate (1500 mg/d), chondroitin sulfate (800 mg/d), or a combination of the two experienced an improvement in joint comfort. However, only the group that received a combination of glucosamine sulfate and chondroitin sulfate experienced a significant improvement in joint space.^{*[20]}

A phase IV, multicenter, randomized, double-blind, non-inferiority trial (n = 606) compared the effects of chondroitin sulfate plus glucosamine hydrochloride—1200 mg and 1500 mg, respectively—versus a standard intervention. At six months, both interventions produced equivalent effects on knee comfort (50% improvement),

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN[®] Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

ease of movement (~48% improvement), functional limitation (~45.95% improvement), and joint fluid accumulation (~50% improvement).^{*[21]}

Methylsulfonylmethane (MSM) As an organosulfur compound, MSM is thought to primarily benefit joint tissues by delivering sulfur. Sulfur helps maintain the strength and structure of connective tissue by forming cross-linkages through disulfide bonds—such as those found in GAGs.^[22] One joint study shows that glucosamine and MSM achieve better results when combined than when administered individually.^{*[23]} Research suggests that MSM may reduce joint tissue damage triggered by free radicals and support muscle recovery after exercise through its antioxidant capacity. Though relatively high doses of MSM were used in exercise studies, the one gram provided in two servings of SynovX Recovery can contribute to MSM dosing for exercise recovery.^{*[24-26]}

SynovX® Recovery Supplement Facts

Serving Size: 2 Capsules		
	Amount Per Serving	% Daily Value
Glucosamine Sulfate (as glucosamine sulfate sodium chloride)	750 mg	**
Chondroitin Sulfate (as chondroitin sulfate sodium)(CS Bio-ACTIVE®)	600 mg	**
Methylsulfonylmethane (MSM)	500 mg	**
** Daily Value not established.		

Other Ingredients: HPMC (capsule), ascorbyl palmitate, medium-chain triglyceride oil, and silica.
Contains: Crustacean shellfish (shrimp and crab).

DIRECTIONS: Take two capsules twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking warfarin or other medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, dairy products, fish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.

CS BIO-ACTIVE® CS B-BIOACTIVE is a registered trademark licensed by Bioterica, S.A.

REFERENCES

- Kahan A, Uebelhart D, De Vathaire F, et al. Long-term effects of chondroitins 4 and 6 sulfate on knee osteoarthritis: the study on osteoarthritis progression prevention, a two-year, randomized, double-blind, placebo-controlled trial. *Arthritis Rheum.* 2009 Feb;60(2):524-33. [PMID: 19180484]
- Möller I, Pérez M, Monfort J, et al. Effectiveness of chondroitin sulphate in patients with concomitant knee osteoarthritis and psoriasis: a randomized, double-blind, placebo-controlled study. *Osteoarthritis Cartilage.* 2010 Jun;18 Suppl 1:S32-40. [PMID: 20399899]
- Wildi LM, Raynaud JP, Martel-Pelletier J, et al. Chondroitin sulphate reduces both cartilage volume loss and bone marrow lesions in knee osteoarthritis patients starting as early as 6 months after initiation of therapy: a randomised, double-blind, placebo-controlled pilot study using MRI. *Ann Rheum Dis.* 2011 Jun;70(6):982-89. [PMID: 21367761]
- Hochberg MC, Clegg DO. Potential effects of chondroitin sulfate on joint swelling: a GAIT report. *Osteoarthritis Cartilage.* 2008;16 Suppl 3:S22-24. [PMID: 18768335]
- Monfort J, Pujot J, Contreras-Rodriguez O, et al. Effects of chondroitin sulfate on brain response to painful stimulation in knee osteoarthritis patients. *Ann Rheum Dis.* 2014;73:82. doi:10.1136/annrheumdis-2014-eular.4908.
- Adebowale A, Du J, Liang Z, et al. The bioavailability and pharmacokinetics of glucosamine hydrochloride and low molecular weight chondroitin sulfate after single and multiple doses to beagle dogs. *Biopharm Drug Dispos.* 2002 Sep;23(6):217-25. [PMID: 12214321]
- Tat SK, Pelletier JP, Mineau F, et al. Variable effects of 3 different chondroitin sulfate compounds on human osteoarthritic cartilage/chondrocytes: relevance of purity and production process. *J Rheumatol.* 2010 Mar;37(3):656-64. [PMID: 20110528]
- Barnhill JG, Fye CL, Williams W, et al. Chondroitin product selection for the glucosamine/chondroitin arthritis intervention trial. *J Am Pharm Assoc.* 2006 Jan-Feb;46(1):14-24. [PMID: 16529337]
- Pelletier JP, Raynaud JP, and Beaulieu A, et al. In a two-year double-blind randomized controlled multicenter study, chondroitin sulfate was significantly superior to celecoxib at reducing cartilage loss with similar efficacy at reducing disease symptoms in knee osteoarthritis patients [abstract]. *Arthritis Rheumatol.* 2015; 67 (suppl 10). <http://acrabstracts.org/abstract/in-a-two-year-double-blind-randomized-controlled-multicenter-study-chondroitin-sulfate-was-significantly-superior-to-celecoxib-at-reducing-cartilage-loss-with-similar-efficacy-at-reducing-disease-sym/>. Accessed January 8, 2016.
- Singh JA, Noorbaloochi S, MacDonald R, et al. Chondroitin for osteoarthritis. *Cochrane Database Syst Rev.* 2015 Jan 28;1:CD005614. [PMID: 25629804]
- Glucosamine. Natural Medicines. <https://naturalmedicines.therapeuticresearch.com/databases/food,-herbs-supplements/professional.aspx?productid=807>. Accessed January 13, 2016.
- Kelly GS. The role of glucosamine sulfate and chondroitin sulfates in the treatment of degenerative joint disease. *Altern Med Rev.* 1998 Feb;3(1):27-39. Review. [PMID: 9600024]
- Igarashi M, Kaga I, Takamori Y, et al. Effects of glucosamine derivatives and uronic acids on the production of glycosaminoglycans by human synovial cells and chondrocytes. *Int J Mol Med.* 2011 Jun;27(6):821-27. [PMID: 21455564]
- Kapoor M, Mineau F, Fahmi H, et al. Glucosamine sulfate reduces prostaglandin E(2) production in osteoarthritic chondrocytes through inhibition of microsomal PGE synthase-1. *J Rheumatol.* 2012 Mar;39(3):635-44. [PMID: 22089456]
- Largo R, Alvarez-Soria MA, Díez-Ortego I, et al. Glucosamine inhibits IL-1beta-induced NFkappaB activation in human osteoarthritic chondrocytes. *Osteoarthritis Cartilage.* 2003 Apr;11(4):290-98. [PMID: 12681956]
- Selvan T, Rajiah K, Nainar MS, et al. A clinical study on glucosamine sulfate versus combination of glucosamine sulfate and NSAIDs in mild to moderate knee osteoarthritis. *Scientific World Journal.* 2012;2012:902676. [PMID: 22577354]
- Tat SK, Pelletier JP, Vergés J, et al. Chondroitin and glucosamine sulfate in combination decrease the pro-resorptive properties of human osteoarthritis subchondral bone osteoblasts: a basic science study. *Arthritis Res Ther.* 2007;9(6):R117. [PMID: 17996099]
- Lippiello L, Woodward J, Karpman R, et al. In vivo chondroprotection and metabolic synergy of glucosamine and chondroitin sulfate. *Clin Orthop Relat Res.* 2000 Dec;(381):229-40. [PMID: 11127660]
- Clegg DO, Reda DJ, Harris CL, et al. Glucosamine, chondroitin sulfate, and the two in combination for painful knee osteoarthritis. *N Engl J Med.* 2006 Feb 23;354(8):795-808. [PMID: 16495392]
- Fransen M, Agalotiis M, Nairn L, et al. Glucosamine and chondroitin for knee osteoarthritis: a double-blind randomised placebo-controlled clinical trial evaluating single and combination regimens. *Ann Rheum Dis.* 2015 May;74(5):851-58. [PMID: 24395557]
- Hochberg MC, Martel-Pelletier J, Monfort J, et al. Combined chondroitin sulfate and glucosamine for painful knee osteoarthritis: a multicentre, randomised, double-blind, non-inferiority trial versus celecoxib. *Ann Rheum Dis.* 2016 Jan;75(1):37-44. [PMID: 25589511]
- Methylsulfonylmethane (MSM). Monograph. *Altern Med Rev.* 2003 Nov;8(4):438-41. [PMID: 14653770]
- Usha PR, Naidu MU. Randomised, double-blind, parallel, placebo-controlled study of oral glucosamine, methylsulfonylmethane and their combination in osteoarthritis. *Clin Drug Investig.* 2004;24(6):353-63. [PMID: 17516722]
- Brien S, Prescott P, Lewith G. Meta-analysis of the related nutritional supplements dimethyl sulfoxide and methylsulfonylmethane in the treatment of osteoarthritis of the knee. *Evid Based Complement Alternat Med.* 2011;2011:528403. [PMID: 19474240]
- Kalman DS, Feldman S, Scheinberg AR, et al. Influence of methylsulfonylmethane on markers of exercise recovery and performance in healthy men: a pilot study. *J Int Soc Sports Nutr.* 2012 Sep 27;9(1):46. [PMID: 23013531]
- Barmaki S, Bohlooli S, Khoshkharesh F, et al. Effect of methylsulfonylmethane supplementation on exercise - Induced muscle damage and total antioxidant capacity. *J Sports Med Phys Fitness.* 2012 Apr;52(2):170-74. [PMID: 22525653]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

SYNOVX® TENDON & LIGAMENT

Tendon and Ligament Support*



Available in 60 vegetable capsules

DISCUSSION

It is known that tendons and ligaments have a slower and more limited ability to self-repair than other tissues. However, healthy tendons and ligaments do indeed have an intrinsic capacity for repair, which is controlled by resident fibroblasts and their surrounding extracellular matrix (ECM).^[1] Fibroblasts (e.g., tenocytes) are responsible for producing the ECM and therefore the proteoglycans (protein/mucopolysaccharide complex) and collagen needed for tissue repair. The key is to stimulate this process. In vitro and in vivo research suggests SynovX Tendon & Ligament does just that. This proprietary blend of type I collagen and mucopolysaccharides combined with vitamin C supports the structural and functional needs of tendons and ligaments.*

Type I Collagen and Mucopolysaccharides Adult tendons are comprised mainly of type-I collagen molecules that are hierarchically organized into structural units. The molecular structure and organization of tendon and ligament collagen fibrils are key determinants in the ability of these tissues to endure mechanical force and fuel self-repair.^[1] While collagen provides much of tendon/ligament structure and strength, mucopolysaccharides are said to provide the “glue” that holds them together and allows them to stretch, flex, bend, and maintain their resilience. Mucopolysaccharides—also known as glycosaminoglycans or GAGs—are a critical component of ECM and are important in maintaining structural integrity, lubrication, and spacing of collagen fibers. Furthermore, mucopolysaccharides have been shown to increase collagen and non-collagenous protein synthesis in cultures of bovine tenocytes and ligament cells.*^[2]

Vitamin C This vitamin helps maintain tendon/ligament structure and biomechanical properties by stimulating collagen biosynthesis.*^[3-5]

In Vitro IL-1beta (interleukin-1beta) is a cytokine associated with adverse tendon/ligament changes. The effect of SynovX Tendon & Ligament in the presence of IL-1beta was studied in primary human tenocytes. Tenocyte cultures treated with 250, 500, and 1000 µg/ml of SynovX Tendon & Ligament showed no signs of cytotoxicity or other negative effects on the viability of cells. The major findings were that this formula counteracted the negative effects of IL-1beta by: (1) protecting tenocytes from degenerative morphological changes, cellular degeneration, and apoptosis, (2) reversing the downregulation of collagen type I and beta 1-integrin receptor expression, (3) increasing tenomodulin production, and (4) causing a significant dose- and time-dependent increase in proliferation and viability of tenocytes. These

CLINICAL APPLICATIONS

- Promotes the Body's Processes of Tendon/Ligament Self-Repair*
- Supports Tendon/Ligament Function*
- Protects and Promotes Collagen Biosynthesis*
- Supports Tendon/Ligament Comfort*

*SynovX® Tendon & Ligament is an advanced formula designed to bolster tendon/ligament comfort and recovery. Whether repetitive use or something more acute is your challenge, preliminary research suggests that SynovX Tendon & Ligament can support the stability, health, and proliferation of tendon and ligament cells and thereby promote the body's ability for self-repair. Let SynovX Tendon & Ligament help you stay active.**

results demonstrated that SynovX Tendon & Ligament supports tenocyte viability and proliferation and type I collagen synthesis.^[1] Furthermore, the treated cells appeared healthy; displayed an abundant and well-organized ECM; and exhibited high levels of euchromatin, indicating that the cells were very active and had a high rate of protein (i.e., collagen) biosynthesis.

^[1] In another in vitro test, human tenocytes incubated with SynovX Tendon & Ligament for 10 days showed a strong stimulatory effect on cell proliferation that exceeded the proliferation seen in cells incubated with (IGF-1) insulin-like growth factor 1 (positive control).^[6] In addition, cells remained viable and showed large amounts of endoplasmic reticulum, which is needed for synthesis of ECM.*

In Vivo A prospective observational study performed by Nadal et al demonstrated the effects of SynovX Tendon & Ligament on the health of epicondyles, plantar fascia, Achilles tendons, or supraspinatus tendons. Patients were selected on the basis of clinical assessment and ultrasound results. For three months, all of the patients received 20 to 30 physical therapy sessions and the study group received two caps/d of SynovX Tendon & Ligament.^[7] Comfort, quality of life (SF-36), and physiotherapist assessments were performed before intervention began and also at 30-, 60-, and 90-day intervals during intervention. In every assessment, patients given SynovX Tendon & Ligament showed numerical or statistically significant improvements after two to three months of supplementation compared to controls.^[7] Researchers concluded that supplementing with SynovX Tendon & Ligament improved comfort level and biomechanical properties without adverse effects.*

Several other human studies using SynovX Tendon & Ligament have demonstrated its positive effects on tendon comfort and structure.^[8-10] For instance, in a randomized placebo-controlled study (n = 60) designed to test the effects of SynovX Tendon & Ligament versus placebo on Achilles, supraspinatus, lateral epicondyle, and plantar fascia comfort and tendon structure, Binh et al found that subjects taking SynovX Tendon & Ligament (two caps/day) had significantly greater comfort at 90 days. At the end of the study, ultrasound assessment showed no signs of structural issues in the supplemented group.^[8] In a prospective, randomized, controlled trial,

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

59 subjects were assigned to one of three groups: eccentric training, eccentric training plus SynovX Tendon & Ligament, or passive stretching plus SynovX Tendon & Ligament. Compared to physical therapy alone, the researchers found that supplementation with SynovX Tendon & Ligament provided additional benefits associated with comfort at rest and exercise recovery as well as changes in tendon thickness and vascularization in certain subjects.*^[9]

SynovX™ Tendon & Ligament Supplement Facts

Serving Size: 2 Capsules		
	Amount Per Serving	%Daily Value
Vitamin C (ascorbic acid)	60 mg	67%
TENDOACTIVE® Proprietary Blend Mucopolysaccharides and Type I Collagen	520 mg	**
** Daily Value not established.		

Other Ingredients: HPMC (capsule), microcrystalline cellulose, ascorbyl palmitate, silica, and medium-chain triglyceride oil.

DIRECTIONS: Take two capsules daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

TENDOACTIVE® is a registered trademark licensed by Bioiberica, S.A.



REFERENCES

- Shakibaei M, Buhrmann C, Mobasheri A. Anti-inflammatory and anti-catabolic effects of TENDOACTIVE® on human tenocytes in vitro. *Histol Histopathol*. 2011 Sep;26(9):1173-85. [PMID: 21751149]
- Lippiello L. Collagen synthesis in tenocytes, ligament cells and chondrocytes exposed to a combination of glucosamine HCl and chondroitin sulfate. *Evid Based Complement Alternat Med*. 2007 Jun;4(2):219-24. [PMID: 17549239]
- Grosso G, Bei R, Mistretta A, et al. Effects of vitamin C on health: a review of evidence. *Front Biosci*. 2013 Jun 1;18:1017-29. [PMID: 23747864]
- Omeroğlu S, Peker T, Türközkan N, et al. High-dose vitamin C supplementation accelerates the Achilles tendon healing in healthy rats. *ArchOrthop Trauma Surg*. 2009 Feb;129(2):281-86. [PMID: 18309503]
- Zanoni JN, Lucas NM, Trevizan AR, et al. Histological evaluation of the periodontal ligament from aged Wistar rats supplemented with ascorbic acid. *An Acad Bras Cienc*. 2013 Mar;85(1):327-35. [PMID: 23460436]
- Shakibaei M, Csaki C, Mobasheri A. In vitro study of tendinopathy in humans: report on adhesion and proliferation assay, electron microscopy, immunofluorescence, and western blot analysis with Bioiberica compounds. Barcelona, Spain: Bioiberica, S.A.; 2006. [on file]
- Nadal F, Bové T, Sanchís D, et al. Effectiveness of treatment of tendinitis and plantar fasciitis by Tendoactive™. [OARS abstract 473]. *Osteoarthritis Cartilage*. 2009 Sept; 17(suppl 1):S253.
- Hai Binh B, Ramirez P, Martinez-Puig D. A randomized, placebo-controlled study to evaluate efficacy and safety of a dietary supplement containing mucopolysaccharides, collagen type I and vitamin C for management of different tendinopathies. *Ann Rheum Dis*. 2014;73:299. doi:10.1136/annrheumdis-2014-eular.5477.
- Balius R, Alvarez G, Barb F, et al. Management of Achilles tendinopathy in reactive versus degenerative stage: a prospective, randomized, controlled trial evaluating the efficacy of a dietary supplement associated to eccentric training or passive stretching. *Ann Rheum Dis*. 2014;73:299-300. doi:10.1136/annrheumdis-2014-eular.5533.
- Arquer A, Garcia M, Laucirica JA, et al. The efficacy and safety of oral mucopolysaccharide, type I collagen and vitamin C treatment in tendinopathy patients. *Apunts Med Esport*. 2014;49(182):31-36. http://apps.elsevier.es/watermark/ct_servlet?_f=10&pident_articulo=90346457&pident_usuario=0&pcontactid=&pident_revista=276&ty=146&accion=L&origen=bronco%20&web=www.apunts.org&lan=en&fichero=276v49n182a90346457p df001.pdf. Accessed January 7, 2016.

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

© XYMOGEN
DRS-277
Rev. 08/08/19



T-150

Support for the Thyroid*



Available in 60 Capsules & 120 Capsules

Discussion

Thyroid Hormone Production The thyroid is a small gland with a sizeable role in the body. Its primary function is the concentration of iodine and the production of crucial thyroid hormones thyroxine (T4) and triiodothyronine (T3). T4 is converted to T3 by the body. Between them, T3 is the more potent, biologically active hormone. It regulates the metabolic rate within cells and affects fundamental functions throughout the body. Thyroid hormone production depends on the presence of iodine and the amino acid L-tyrosine in adequate amounts. T4 contains tyrosine and four iodine molecules, while T3 contains tyrosine and three iodine molecules. Production of thyroid hormones can be disrupted by several factors in the environment, including heavy metals (lead, cadmium, mercury, fluoride), pesticides, dysbiosis, hormonal fluctuations, antibiotic residues, chemicals, other xenobiotics, or lack of nutrients required for thyroid hormone synthesis.*^[1]

The Thyroid Gland's Manifold Effects The thyroid gland does not work alone; it interacts intimately with the liver, the kidneys, and the hypothalamus, pituitary, and adrenal glands. Communicating via the intricate matrices of the hypothalamic-pituitary-adrenal (HPA) axis and the hypothalamic-pituitary-thyroid (HPT) axis, these key players coordinate the body's response to stress and its quest for homeostasis.*^[1,2]

Thyroid hormone activates over 100 enzymes in the body, exerting a significant effect on growth and metabolic rate. The metabolic rate reflects the body's transformation of nutrients into energy. Thyroid hormone, and its influence on metabolic rate, plays a fundamental role in appetite, weight maintenance, energy levels and mood, gastrointestinal regularity, tolerance to temperature changes, and healthy hair and nails.*^[3,4]

Glandular Support Glandular extracts have a century-old history of supporting healthy thyroid levels. A linear relationship between thyroid extract and serum levels of thyroxine and triiodothyronine in children has been observed.*^[3,5]

Clinical Applications

- » Provides Essential Nutrient, Herbal, and Glandular Support for Production of Thyroid Hormones*

*T-150 is a comprehensive BSE-free, bovine, multi-glandular, mineral and herbal formula to support healthy thyroid function.**

Micronutrient, Amino Acid, and Herbal Support Production of thyroid hormone is fundamentally dependent on the presence of L-tyrosine and iodine, while conversion of T4 to T3 is facilitated by selenium. Bladderwrack (*Fucus vesiculosus*), dulse, kelp, and Irish moss are natural sources of iodine for support of endogenous thyroid hormone production.*^[6]

The combination of foundational elements with supportive nutrients in XyMOGEN's T-150 represents a comprehensive approach to thyroid support.*

T-150 Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Iodine (from organic Icelandic kelp)(<i>Laminaria digitata</i>)(stem and leaf)	40 mcg	27%
Selenium (as L-selenomethionine)	50 mcg	91%
Dulse (<i>Rhodymenia palmata</i>)(whole plant)	400 mg	**
Thyroid Gland (from New Zealand bovine)	150 mg	**
Adrenal Gland (from Argentina bovine)	50 mg	**
Irish Moss (<i>Chondrus crispus</i>)(whole plant)	40 mg	**
L-Tyrosine	30 mg	**
Anterior Pituitary Gland (from Argentina bovine)	15 mg	**
Bladderwrack (<i>Fucus vesiculosus</i>)(whole plant)	15 mg	**
Spleen (from Argentina bovine)	5 mg	**
Thymus Gland (from Argentina bovine)	5 mg	**
** Daily Value not established.		

Other Ingredients: HPMC (capsule), vegetable stearic acid, silica, vegetable magnesium stearate, microcrystalline cellulose, and medium-chain triglyceride oil. May contain traces of fish and crustacean shellfish.

DIRECTIONS: Take one capsule daily with water (away from food), or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, dairy products, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

STORAGE: Keep closed in a cool, dry place out of reach of children.

**References**

1. Baker SM, Bennett P, Bland JS, et al. *Textbook of Functional Medicine*. Gig Harbor, WA: The Institute for Functional Medicine; 2010.
2. Tsigos C, Chrousos GP. Hypothalamic-pituitary-adrenal axis, neuroendocrine factors and stress. *J Psychosom Res*. 2002 Oct;53(4):865-71. [PMID: 12377295]
3. Gaby AR. Sub-laboratory hypothyroidism and the empirical use of Armour thyroid. *Altern Med Rev*. 2004 Jun;9(2):157-79. [PMID: 15253676]
4. Bodó E, Kromminga A, Bíró T, et al. Human female hair follicles are a direct, nonclassical target for thyroid-stimulating hormone. *J Invest Dermatol*. 2009 May;129(5):1126-39. [Epub 2008 Dec 4] [PMID: 19052559]
5. Weill J, Debruxelles P, Fulla Y, et al. [Management of primary hypothyroidism in childhood treated with thyroid extract (author's transl)] [Article in French]. *Arch Fr Pediatr*. 1980 Jan;37(1):29-34. [PMID: 7469681]
6. Krinsky DI, LaValle JB, Hawkins EB, et al. *Natural Therapeutics Pocket Guide*. 2nd ed. Hudson, OH: Lexi-Comp, Inc.; 2003.

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

TestoPlex™ Plus

Supports Vitality, Virility, and Vigor*



Available in 60 capsules and 120 capsules

Discussion

Five percent of males aged 40-50 years and as many as 70% of males over 70 years are confronted with "hypogonadism." Low testosterone levels have been associated with a decline in libido, erectile dysfunction, lack of energy, less physical strength and endurance, loss of height, decreased enjoyment in life, low mood, feeling grumpy, falling asleep after dinner, and decreased work performance.^[1,2] Some studies suggest that low testosterone may also contribute to cognitive decline.^{*[3,4]}

Although sometimes thought of as a male hormone, a review study of the clinical significance of testosterone has shown its positive association with sexual function and a healthy libido in women.^{*[5]}

Most circulating testosterone is bound to sex hormone-binding globulin (SHBG). Only the lesser amount of testosterone not bound to SHBG is considered bioavailable.^[6] TestoPlex Plus features a blend of ingredients designed to support healthy androgen biosynthesis, which includes modulating the influence of SHBG.*

Shilajit is a naturally occurring, mineral-rich phytocomplex with many bioactive components, including fulvic acids. It comprises rock humus, rock minerals, and organic substances that have been compressed by layers of rock mixed with marine organisms and microbial metabolites.^[7] Shilajit has a rich history of use in Indian ayurvedic and siddha medicine as a health and wellness optimizer. It is known as a *rasayana* because of its rejuvenating qualities, which include heightening physical performance and relieving fatigue.^{*[8]}

According to an article in the *American Journal of Clinical Nutrition*, weightlifters use shilajit to promote better strength, recovery, and muscular hypertrophy and also to combat physical stress, but human data on these uses are lacking.^{*[9]}

Animal and human studies have documented the safety of shilajit. The oral median lethal dose (LD50) is > 200 grams, and chronic use at doses of 0.2–1.0 g/kg body weight appear to be safe.^{*[7]}

Upwards of 50 studies on shilajit suggest that it has a positive effect on testosterone levels and adaptogenic, antioxidant, cytokine-balancing, immunomodulatory, and antidiabetic activities.^[10] Fulvic acid, the main bioactive component in shilajit, blocks tau proteins self-aggregation suggesting it may have a role in supporting cognition.^{*[11]}

PrimaVie® shilajit at a dose of 250 mg/capsule consumed twice daily after major meals for 90 days was evaluated in 75 healthy male volunteers aged 45–55 for its testosterone secretion efficacy and its stimulation effects. This double-blind placebo-controlled study revealed that PrimaVie shilajit, when compared to placebo, significantly ($P < 0.05$) increased total testosterone, free testosterone, and dehydroepiandrosterone (DHEA). The levels of testosterone synthesis-supportive gonadotropic hormones were well-maintained.^{*[7]}

Another study further demonstrated the safety and also the spermatogenic nature of shilajit. Infertile males ($n = 35$) took 100 mg of PrimaVie shilajit twice daily after major meals for 90 days. At completion, 28 of the subjects had significant ($P < 0.001$)

Clinical Applications

- » Supports Healthy Testosterone Levels*
- » Supports Healthy Libido and Performance*
- » Supports Overall Vitality*
- » Optimizes Physical Strength and Endurance*
- » Supports Cognition*

*TestoPlex™ Plus features two safe, clinically-tested, standardized, and patented ingredients designed to support vitality and general physical and mental well-being in men and women. Numerous studies have demonstrated that PrimaVie® shilajit and LJ100® Eurycoma longifolia support healthy androgen biosynthesis, which includes modulating the influence of sex hormone-binding globulin.**

improvement compared to baseline values of factors related to fertility. Furthermore, at the study's completion, the semen's content of malondialdehyde (MDA), a marker for oxidative stress, was reduced. High-performance liquid chromatography (HPLC) revealed that the semen had constituents of PrimaVie shilajit. Compared to baseline, serum levels of testosterone rose 23.5% ($P < 0.001$) and follicle-stimulating hormone (FSH) rose 9.4% ($P < 0.05$). Liver and kidney profiles were unchanged.^{*[12]}

In addition, the safe use of PrimaVie shilajit in either gender was demonstrated in an experimental study on skeletal muscle adaptation in human subjects ($n = 16$), ages 21–70 years. Participants were given 250 mg of PrimaVie with no adverse effects during the 12-week study period.^{*[13]}

Eurycoma longifolia root (Malaysian ginseng) is considered a tonic and an adaptogen for supporting healthy libido, energy, sports performance, and weight management by promoting healthy testosterone levels and freeing testosterone from SHBG. Eurypeptides activate the CYP-17 enzyme, which plays a key role in production of DHEA, progesterone, testosterone, and pheromone via the metabolism of pregnenolone. A systemic review and meta-analysis of randomized controlled studies ($n = 139$) concluded that the herbal extract "may have clinical effect on erectile function. However, more efficacy trials are warranted to further support current evidence."^{*[14]}

LJ100® *Eurycoma longifolia* is a root extract whose safety and efficacy is backed by animal and at least 12 human clinical studies. Compound isolation, a patented water-extraction process, and technologically advanced manufacturing methods ensure the purity of this ingredient and allow for the capture of the potent, biologically active eurypeptides.*

A randomized, placebo-controlled, two-month study ($n = 20$) focused on the outcomes of LJ100 on various parameters in male volunteers aged 38–58 who had varied health conditions and consumed either a placebo or 200, 400, or 600 mg of LJ100. The herb-consuming volunteers showed improvement in sexual desire and performance. Also, testosterone and DHEA levels were high-normal when compared to baseline; HDL cholesterol improved; those who had type-2 diabetes showed improvement in blood glucose levels; and insulin-like growth factors (IGF-1) were high-normal (lower levels of IGF-1 are correlated with higher body fat). Compared to those on placebo, the majority of the volunteers on LJ100 had high-normal levels of thyroxine suggesting higher metabolism. Blood and lipid panels and liver and renal function profiles, electrolytes, and various tumor markers including prostate-specific antigen (PSA) were within normal range.^{*[15]}

The benefits of LJ100 are not limited to males or particular age groups. Two studies, one in middle-aged and one in senior males and females, demonstrated the herb's promotion of healthy fitness, vitality, and vigor concomitant with an increase in free testosterone and a decline in SHBG.^{*[16,17]}

In summary, it appears that the combination of these two herbs supports healthy testosterone levels in men and women which, in turn, supports vitality, virility, and vigor.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

TestoPlex™ Plus Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
PrimaVie® Shilajit (10.3% Dibenzo- pyrones (DBPs) & Dibenzo- pyrone Chromoproteins (DCPs))(50% fulvic acids with DBP Core Nucleus)	500 mg	**
LJ100® <i>Eurycoma longifolia</i> Extract (22% bioactive eurypeptides, 40% glyco saponins)(root)	200 mg	**

** Daily Value not established.

Other Ingredients: Capsule (hypromellose and water), microcrystalline cellulose, dicalcium phosphate, ascorbyl palmitate, and silica.**DIRECTIONS:** Take two capsules in the morning, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tampo seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.**DOES NOT CONTAIN:** Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

PrimaVie® is protected under US patents 6,969,612 and 6,440,712 and is a trademark of Natreon, Inc.

LJ100® is the registered trademark of HP Ingredients. Worldwide patent WO/02/17946 Bioactive Fraction of *Eurycoma Longifolia*. US patent 7,132,117 Bioactive Fraction of *Eurycoma Longifolia*.**References**

- Korenman SG, Morley JE, Mooradian AD, et al. Secondary hypogonadism in older men: its relation to impotence. *J Clin Endocrinol Metab.* 1990 Oct;71(4):963-969. [PMID: 2205629]
- Vermeulen A, Kaufman JM. Diagnosis of Hypogonadism in the aging male. *Aging Male.* 2002 Sept;5(3):170-6. [PMID: 12471777]
- Beauchet O. Testosterone and cognitive function: current clinical evidence of a relationship. *Eur J Endocrinol.* 2006 Dec;155(6):773-81. [PMID: 17132744]
- Wahjoepramono EJ, Asih PR, Aniwiyanti V, et al. The effects of testosterone supplementation on cognitive functioning in older men. *CNS Neurol Disord Drug Targets.* 2016;15(3):337-43. [PMID: 26553159]
- Davis SR, Wahlin-Jacobsen S. Testosterone in women—the clinical significance. *Lancet Diabetes Endocrinol.* 2015 Dec;3(12):980-92. [PMID: 26358173]
- Mayo Clinic. Test ID: TTFB. Testosterone, Total, Bioavailable, and Free, Serum. <http://www.mayomedicallaboratories.com/test-catalog/Clinical+and+Interpretive/83686>. Accessed April 20, 2017.
- Pandit S, Biswas S, Jana S, et al. Clinical evaluation of purified Shilajit on testosterone levels in healthy volunteers. *Andrologia.* 2015 Jun;48(5):570-5. [PMID: 26395129]
- Surapaneni DK, Adapa SR, Preeti K, et al. Shilajit attenuates behavioral symptoms of chronic fatigue syndrome by modulating the hypothalamic-pituitary-adrenal axis and mitochondrial bioenergetics in rats. *J Ethnopharmacol.* 2012 Aug 30;143(1):91-9. [PMID: 22771318]
- Bucci LR. Selected herbals and human exercise performance. *Am J Clin Nutr.* 2000 Aug;72(2 Suppl):624S-36S. [PMID: 10919969]
- Stohs SJ. Safety and efficacy of shilajit (mumie, moomiyo). *Phytother Res.* 2014 Apr;28(4):475-9. [PMID: 23733436]
- Carrasco-Gallardo C, Guzmán L, Maccioni RB. Shilajit: a natural phytocomplex with potential procognitive activity. *Int J Alzheimers Dis.* 2012;2012:674142. [PMID: 22482077]
- Biswas TK, Pandit S, Mondal S, et al. Clinical evaluation of spermatogenic activity of processed shilajit in oligospermia. *Andrologia.* 2010 Feb;42(1):48-56. [PMID: 20078516]
- Das A, Datta S, Rhea B, et al. The human skeletal muscle transcriptome in response to oral shilajit supplementation. *J Med Food.* 2016 Jul;19(7):701-9. [PMID: 27414521]
- Kotirum S, Ismail SB, Chaiyakunapruk N. Efficacy of tongkat ali (*Eurycoma longifolia*) on erectile function improvement: systematic review and meta-analysis of randomized controlled trials. *Complement Ther Med.* 2015 Oct;23(5):693-8. [PMID: 26365449]
- Tambi MI, Kadir AB. LJ100, a potent adaptogen, maintains healthy aging in men. *Int J Androl.* 2005;28(suppl 1): 25-44.
- Sarina MY. Effects of strength training and LJ100 supplementation on strength and muscle size in middle-aged women. Presented at: 4th Asia-Pacific Conference on Exercise and Sport Science & 8th International Sports Science Conference; July 15-17, 2009; Malaysia.
- Henkel RR, Wang R, Bassett SH, et al. Tongkat ali as a potential herbal supplement for physically active male and female seniors—a pilot study. *Phytother Res.* 2014 Apr;28(4):544-550. [PMID: 23754792]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

UritraX™

Concentrated Urinary Tract Support*



Available in about 50 servings powder

Discussion

Amino acid and sugar complexes called lectins may be produced by certain organisms allowing them to adhere to the inside walls of the bladder and urinary tract, where they may continue to thrive.^[1]

D-mannose is a simple sugar produced in the body and occurring naturally in certain fruits, especially cranberries and pineapples. The adult dose of UritraX™ is more concentrated in D-mannose than these fruits or juices, and studies suggest that D-mannose is ten times more effective than cranberries.^[2]

Nearly all ingested mannose gets excreted through the kidneys and into the urine.^[3,4] Research suggests that lectins, present in the urinary tract and bladder, adhere to the D-mannose more readily than they do to the walls of the urinary tract. This action helps support the body's ability to flush out these unwanted particles through the urine.^[5] D-mannose users report that they can feel the effect in 24-48 hours.^[6]

UritraX™ is not capable of killing either “friendly” or harmful bacteria. It simply supports the naturally protective “flushing out” mechanism of the urine.^[6]

Clinical Applications

- » Helps Maintain a Healthy Environment for the Urinary Tract's Mucosal Surface*

*UritraX™ features D-mannose, a simple sugar that occurs naturally in cranberries and pineapple. Research suggests that D-mannose interferes with lectin adhesion to the bladder wall, thereby supporting a healthy urinary tract.**

UritraX™ Supplement Facts

Serving Size: 1 Scoop (about 936 mg)

	Amount Per Serving	%Daily Value
D-Mannose	900 mg	**
** Daily Value not established.		

Other Ingredients: None.**DIRECTIONS:** Mix one scoop in 2-4 oz of water one to three times daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.**DOES NOT CONTAIN:** Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.**References**

1. Michaels EK, Chmiel JS, Plotkin BJ, Schaeffer AJ, "Effect of D-mannose and D-glucose on Escherichia coli bacteria in rats". *Urol Res* 1983;11(2):97-102
2. Zafriri D, Ofek I, Adar R, Pocino M, Sharon N. Inhibitory activity of cranberry juice on adherence of type 1 and type P fimbriated Escherichia coli to eukaryotic cells. *Antimicro Agents Chemother* 1989; 33:92-98
3. Toyota S, et al. [article in Japanese], [Anti-bacterial defense mechanism of the urinary bladder. Role of d-mannose in urine], *Nippon Hinyokika Gakkai Zasshi*. 1989 Dec;80(12):1816-23
4. Ganda OP, et al. Metabolic effects of glucose, mannose, galactose, and fructose in man. *J Clin Endocrinol Metab*. 1970 Oct;49(4):616-22
5. Sharon N, Ofek I, "Safe as mother's milk:carbohydrates as future anti-adhesion drugs for bacterial diseases". *Glycoconj J* 2000 Jul-Sep, 17 (7-9):659-64. Review
6. Wright, Jonathan, D-Mannose and Infection, "Nutrition & Healing", June 1999, Vol 6, Issue 6
7. Amacker-Francoys I, et al. The metabolisable hexoses D-glucose and D-mannose enhance the expression of IRS-2 but not of IRS-1 in pancreatic beta-cells. *Exp Clin Endocrinol Diabetes*. 2005 Sep;113(8):423-9 [PMID: 16151975]
8. Sharon N, Ofek I, "Safe as mother's milk:carbohydrates as future anti-adhesion drugs for bacterial diseases". *Glycoconj J* 2000 Jul-Sep, 17 (7-9):659-64. [PMID: 11421356]
9. D-Mannose. www.naturaldatabase.com {accessed 3.26.07}

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*The statements in this document have not been evaluated by the Food and Drug Administration. Products listed are not intended to diagnose, treat, cure, or prevent any disease.

VegaPro™

Proprietary Vegan Protein Complex



Available in 14 servings

Discussion

Adequate, good-quality protein helps the body sustain proper functioning. For instance, the amino acid supply (from dietary protein) is used to build functional proteins needed for healthy immune function and to produce the enzymes and hormones needed for metabolism, digestion, and other important processes like detoxification and bone remodeling.^[1-4] XYMOGEN developed VegaPro to offer practitioners and patients a “clean,” unadulterated vegetable protein that enables a high level of protocol personalization.*

“Clean” Protein VegaPro is an excellent choice of supplementary protein for vegans and those who are sensitive to sugar (including lactose), sweeteners, or flavorings.^[5-7] It is also free of gluten. VegaPro provides protein from pea and rice sources, avoiding major food allergens including milk, egg, soy, and wheat. The pea protein in VegaPro is non-GMO and is naturally obtained by simple water extraction, keeping all the nutritional qualities intact.*

Flexible Formulation Aside from providing clean, easily digestible vegetable protein, the advantage of VegaPro is its flexibility. While other protein supplements provide high levels of various micronutrients, making it difficult to add protein to a patient’s nutritional protocol, VegaPro is not enriched with extra micronutrients. Therefore, practitioners can design personalized protocols for their patients by directing them to add selected supplements to a VegaPro shake or take encapsulated or tableted micronutrient supplements along with VegaPro. Additionally, VegaPro can easily be added to any functional food formula—if added protein is desired—without the concern of getting too much of any micronutrient. Because this formula is free of sugars and flavorings, it can be added to any approved beverage; or it can be mixed with pure water for a mild, earthy, pea soup taste.*

Excellent Quality Proteins for dietetic foods must provide good basic nutritional quality, which, in this case, means a high protein level, a well-balanced amino acid profile, and good digestibility. At 98% digestibility, pea protein is considered highly digestible and matches

Clinical Applications

- » Provides Sugar-Free, Unadulterated Vegetable Protein for Broad Applications*
- » Excellent for Those Sensitive to Sugar, Sweeteners, or Flavorings*
- » Excellent for Those Sensitive to Gluten or Milk, Egg, or Soy Proteins*
- » Can Be Used As Part of an Elimination Diet Protocol*
- » Can Provide Additional Protein to Any Functional Food or Dietary Supplement Protocol*
- » May Support Feelings of Hunger Satisfaction*

VegaPro™ is a sugar-free source of unadulterated vegetable protein sourced from non-GMO peas and rice, providing 17 grams of high-quality protein in every scoop. This flexible formula can be mixed with pure water or any beverage approved by your practitioner. Because it does not provide additional micronutrients, it can easily be added to any functional food formula, when additional protein is desired; or micronutrients can be mixed with VegaPro in accordance with recommendations by your practitioner. VegaPro is an excellent choice of supplementary protein for those who are sensitive to gluten; sugars, including lactose; sweeteners; or flavorings. Furthermore, the use of pea and rice proteins in VegaPro avoids major food allergens including milk, egg, soy, and wheat.

that of beef, milk, and soy protein digestibility. The protein content of the pea protein features a well-balanced amino acid profile (listed on reverse side), including a high content of lysine, arginine, and branched-chain amino acids (leucine, isoleucine, and valine). Amino acid scoring provides a way to predict how efficiently protein will meet a person’s amino acid needs. Because pea protein alone is incomplete, combining it with rice protein makes VegaPro a complete protein with an amino acid score of 100%.*

Satisfaction: An Added Benefit of Increasing Protein Intake Signals that originate from the gut, in response to mechanical (gastric distention) and chemical changes that occur after the ingestion of food, let us know when we’ve had enough to eat. Among the macronutrients, proteins have been identified as having the greatest impact in this regard. Actually, the effect of high-protein foods is not only observed immediately after their consumption by a stronger feeling of satisfaction but also at a later meal by supporting a lower food intake.*^[8]

Added Amino Acids L-Glutamine is an energy substrate for most cells—especially intestinal epithelial cells and immune cells. It is also an essential component for numerous metabolic functions.^[9,10] Glycine, an inhibitory (calming) neurotransmitter, is an important constituent of collagen and a building block for other substances such as coenzyme A, nucleic acids, creatine phosphate, purines, bile, and other amino acids. Taurine is a derivative of sulfur-containing cysteine with many healthful clinical applications, including the support of stable cell membranes, cardiovascular health, glucose tolerance, detoxification, and bile salt synthesis.*^[11]

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

VegaPro™ Supplement Facts

Serving Size: 1 Scoop (about 21 g)
 Servings Per Container: About 14

	Amount Per Serving	% Daily Value
Calories	80	
Total Fat	1 g	1% [‡]
Total Carbohydrate	1 g	<1% [‡]
Dietary Fiber	1 g	4%
Protein	17 g	
Iron (naturally occurring)	3 mg	17%
Sodium (naturally occurring)	300 mg	13%

[‡] Percent Daily Values are based on a 2,000 calorie diet.
Other Ingredients: VegaPro™ (XYMOGEN's proprietary blend of pea protein isolate, taurine, rice protein concentrate, glycine, and L-glutamine).

DIRECTIONS: Blend, shake, or briskly stir one level scoop (21 g) into 8-12 oz room temperature or chilled, pure water; or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

Typical Amino Acid Profile Per Serving:

Alanine	890 mg	Methionine	230 mg
Arginine	1,790 mg	Phenylalanine	1,140 mg
Aspartic Acid	2,370 mg	Proline	930 mg
Cysteine	210 mg	Serine	1,090 mg
Glutamic Acid	3,480 mg	Taurine	500 mg
Glycine	910 mg	Threonine	800 mg
Histidine	520 mg	Tryptophan	210 mg
Isoleucine	930 mg	Tyrosine	790 mg
Leucine	1,730 mg	Valine	1,040 mg
Lysine	1,470 mg		



References

1. Kerstetter JE, O'Brien KO, Insogna KL. Low protein intake: the impact on calcium and bone homeostasis in humans. *J Nutr.* 2003 Mar;133(3):855S-61S. [PMID: 12612169]
2. Protein intake and metabolism in frail elderly - Geriatric Nutrition. BNET – The CBS Interactive Business Network Web site. http://findarticles.com/p/articles/mi_m0887/is_10_22/ai_110727292/. Published October, 2003 (in *Nutrition Research Newsletter*). Accessed July 22, 2011.
3. Chernoff R. Protein and older adults. *J Am Coll Nutr.* 2004 Dec;23(6 Suppl):627S-30S. [PMID: 15640517]
4. Evans WJ. Protein nutrition, exercise and aging. *J Am Coll Nutr.* 2004 Dec;23(6 Suppl):601S-09S. [PMID: 15640513]
5. Rigamonti E, Parolini C, Marchesi M, et al. Hypolipidemic effect of dietary pea proteins: Impact on genes regulating hepatic lipid metabolism. *Mol Nutr Food Res.* 2010 May;54 Suppl 1:S24-30. [PMID: 20077421]
6. Jürgens H, Haass W, Castañeda TR, et al. Consuming fructose-sweetened beverages increases body adiposity in mice. *Obes Res.* 2005 Jul;13(7):1146-56. [PMID: 16076983]
7. Stanhope KL, Schwarz JM, Keim NL, et al. Consuming fructose-sweetened, not glucose-sweetened, beverages increases visceral adiposity and lipids and decreases insulin sensitivity in overweight/obese humans. *J Clin Invest.* 2009 May;119(5):1322-34. doi:10.1172/JCI37385. [PMID: 19381015]
8. Johnstone AM, Stubbs RJ, Harbron CG. Effect of overfeeding macronutrients on day-to-day food intake in man. *Eur J Clin Nutr.* 1996 Jul;50(7):418-30. [PMID: 8862477]
9. Oliveira GP, Dias CM, Pelosi P, et al. Understanding the mechanisms of glutamine action in critically ill patients. *An Acad Bras Cienc.* 2010 Jun;82(2):417-30. [PMID: 20563423]
10. Walsh NP, Blannin AK, Robson PJ, et al. Glutamine, exercise and immune function. Links and possible mechanisms. *Sports Med.* 1998 Sep;26(3):177-91. [PMID: 9802174]
11. Yatabe Y, Miyakawa S, Ohmori H, et al. Effects of taurine administration on exercise. *Adv Exp Med Biol.* 2009;643:245-52. [PMID: 19239155]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Vinpocetine

Brain Support Formula*



Available in 60 Capsules

Discussion

Vinpocetine is derived from vincamine, an alkaloid extracted from the periwinkle plant (*Vinca minor*). It has been used extensively in Eastern Europe, and more recently in the United States, to support cerebrovascular health and healthy cognitive and mental function during aging. Vinpocetine's roles in supporting brain function are multi-modal and include its influence on cerebral circulation, its support of antioxidant activity in the brain, and its role in supporting neuronal health.^[1-3] Together, these varied actions support overall brain tissue health and function.*

Brain Function The safety and effectiveness of vinpocetine have been tested and validated by in vitro, animal, and human studies. Many human studies demonstrate support of healthy cognitive and mental function—primarily related to improved capillary blood flow and cellular metabolism. Supplementation has also been associated with improved quality of life and support of cerebrovascular function and healthy blood flow.^[4-7] It is important to note that absorption of vinpocetine is thought to be significantly higher when given with food. One study found the relative bioavailability under non-fasting conditions was approximately 60% to 100% higher than under fasting conditions.*^[8]

Cerebral Blood Flow Neurons are completely reliant on a continuous supply of oxygen and glucose, which is delivered to them by the blood. Vinpocetine may affect phosphodiesterases (PDEs), enzymes that typically act on smooth muscle tissues, such as those in arterial walls, and prevent them from relaxing. Supporting normal action of PDEs promotes healthy vascular smooth muscle function and cerebral blood flow.^[2,9] Other research suggests that vinpocetine may improve oxygen-release from hemoglobin, help maintain normal blood viscosity, and increase and maintain red blood cell flexibility—making red blood cells better able to squeeze through tiny capillaries.*^[3,10]

Antioxidant Effects Neurological tissue is particularly susceptible to oxidative stress due to its high demand for oxygen, high levels of polyunsaturated fatty acids in neural membrane phospholipids, and

Clinical Applications

- » Supports Healthy Brain Function*
- » Supports Brain Antioxidant Activity*
- » Supports Blood Flow to the Brain*
- » Supports Oxygenation of Brain Tissue*

*Vinpocetine is a powerful antioxidant that protects the brain and enhances its function by increasing blood flow and oxygenation.**

low antioxidant defenses. Furthermore, reactive oxygen species (ROS) can produce complex structural and functional changes within the vessel walls of the cerebral vasculature; such changes carry broad implications for cerebral perfusion (flow to brain) and blood-brain barrier (BBB) permeability.^[11,12] Scavenging these radicals, therefore, should be considered an important part of supporting cerebrovascular health. Because vinpocetine readily crosses the BBB and is taken up by brain tissue, its support of antioxidant activity in the brain has been investigated. In various experimental models, vinpocetine has been shown to directly support the neutralization of ROS.*^[12-14]

Vinpocetine influences neuronal sodium, calcium, and to a lesser degree, potassium ion channels. Vinpocetine's inhibition of voltage-sensitive sodium (Na⁺) channels and reduction of intracellular calcium (Ca²⁺) levels is thought to moderate the excitotoxicity of neurotransmitters. This activity may be an important aspect of vinpocetine's effect on nerve cell integrity.^[1,15] In other research, the cytokine-modulating mechanisms of vinpocetine suggest another avenue by which it may protect brain tissue and neurons—namely inhibition of TNF- α -induced NF- κ B activation and the subsequent generation of certain signaling molecules.*^[16,17]

Vinpocetine Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Vinpocetine	10 mg	**
** Daily Value not established.		

Other Ingredients: Microcrystalline cellulose, HPMC (capsule), stearic acid, magnesium stearate, and silica.

DIRECTIONS: Take one to two capsules daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

CAUTIONS: Do not use if you are pregnant, or lactating, or allergic to any ingredient. Do not use if you have low blood pressure, are taking blood-thinning agents, or are within two weeks before or after undergoing surgery.

STORAGE: Keep closed in a cool, dry place out of reach of children.

**References**

1. Hadjiev D. Asymptomatic ischemic cerebrovascular disorders and neuroprotection with vinpocetine. *Ideggyogy Sz.* 2003 May;56(5-6):166-72. [PMID: 12861957]
2. Muravyov AV, Yakusevich VV, Chuchkanov FA, et al. Hemorheological efficiency of drugs, targeting on intracellular phosphodiesterase activity: in vitro study. *Clin Hemorheol Microcirc.* 2007;36(4):327-34. [PMID: 17502703]
3. Vinpocetine. Monograph. *Altern Med Rev.* 2002 Jun;7(3):240-43. [PMID: 12126465]
4. Valikovics A. Investigation of the effect of vinpocetine on cerebral blood flow and cognitive functions [in Hungarian]. *Ideggyogy Sz.* 2007 Jul;60(7-8):301-10. [PMID: 17713111]
5. Chukanova EI. Efficacy of cavinton in the treatment of patients with chronic blood flow insufficiency. Russian multicenter clinical-epidemiological program "CALIPSO" [in Russian]. *Zh Nevrol Psikhiatr Im S S Korsakova.* 2010;110(12):49-52. [PMID: 21311488]
6. Chukanova EI. Cavinton in the complex treatment of patients with chronic cerebrovascular insufficiency [in Russian]. *Zh Nevrol Psikhiatr Im S S Korsakova.* 2009;109(9):35-39. [PMID: 19770831]
7. Bagoly E, Fehér G, Szapáry L. The role of vinpocetine in the treatment of cerebrovascular diseases based in human studies [in Hungarian]. *Orv Hetil.* 2007 Jul;148(29):1353-58. [PMID: 17631470]
8. Lohmann A, Dingler E, Sommer W, et al. Bioavailability of vinpocetine and interference of the time of application with food intake. *Arzneimittelforschung.* 1992;42:914-17. [PMID: 1418055]
9. Truss MC, Stief CG, Uckert S, et al. Initial clinical experience with the selective phosphodiesterase-I isoenzyme inhibitor vinpocetine in the treatment of urge incontinence and low compliance bladder. *World J Urol.* 2000;18:439-43. [PMID: 11204266]
10. Tohgi H, Sasaki K, Chiba K, et al. Effect of vinpocetine on oxygen release of hemoglobin and erythrocyte organic polyphosphate concentrations in patients with vascular dementia of the Binswanger type. *Arzneimittelforschung.* 1990 Jun;40(6):640-43. [PMID: 2396997]
11. Chrissobolis S, Faraci FM. The role of oxidative stress and NADPH oxidase in cerebrovascular disease. *Trends Mol Med.* 2008 Nov;14(11):495-502. [PMID: 18929509]
12. Horvath B, Marton Z, Halmosi R, et al. In vitro antioxidant properties of pentoxifylline, piracetam, and vinpocetine. *Clin Neuropharmacol.* 2002 Jan-Feb;25(1):37-42. [PMID: 11852295]
13. Deshmukh R, Sharma V, Mehan S, et al. Amelioration of intracerebroventricular streptozotocin induced cognitive dysfunction and oxidative stress by vinpocetine—a PDE1 inhibitor. *Eur J Pharmacol.* 2009 Oct;620(1-3):49-56. [PMID: 19699735]
14. Solanki P, Prasad D, Muthuraju S, et al. Preventive effect of piracetam and vinpocetine on hypoxia-reoxygenation induced injury in primary hippocampal culture. *Food Chem Toxicol.* 2011 Apr;49(4):917-22. [PMID: 21193009]
15. Sitges M, Nekrassov V. Vinpocetine selectively inhibits neurotransmitter release triggered by sodium channel activation. *Neurochem Res.* 1999 Dec;24(12):1585-91. [PMID: 10591410]
16. Jeon KI, Xu X, Aizawa T, et al. Vinpocetine inhibits NF-kappaB-dependent inflammation via an IKK-dependent but PDE-independent mechanism. *Proc Natl Acad Sci U S A.* 2010 May;107(21):9795-800. [PMID: 20448200]
17. Medina AE. Vinpocetine as a potent antiinflammatory agent. *Proc Natl Acad Sci U S A.* 2010 Jun;107(22):9921-22. [PMID: 20495091]

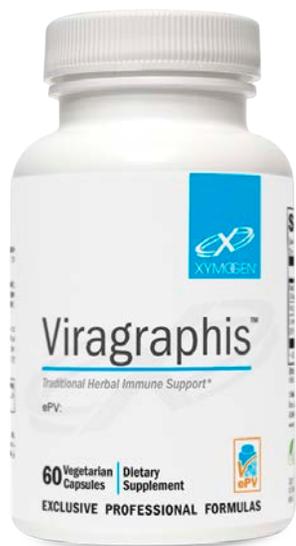
Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Viragraphis™

Traditional Herbal Immune Support*



Available in 60 capsules

Discussion

Herbs have been used to support health and well-being throughout history and across cultures and are the cornerstone of many ancient medical systems, including Ayurveda and Traditional Chinese Medicine (TCM). Viragraphis™ comprises three herbs that have been used traditionally and specifically to support the body's immune system.*

Andrographis Extract (*Andrographis paniculata*) Andrographis has been used widely in traditional medical systems as a bitter herb that works quickly to support upper respiratory health and immune response.^[1] TCM categorizes andrographis as “bitter” and “cold.” The herb has been used to support temperature regulation, respiratory health, immune function, and cytokine and eicosanoid balance.^[1-4] A randomized, double-blind, placebo-controlled study investigated the use of 1200 mg/day (standardized to 4% andrographolides) in 158 adult patients. Results revealed that individuals receiving the herb had a significant improvement in several of the parameters measured when compared to placebo. A “high degree of effectiveness” was observed by day two of treatment.*^[5]

Research on andrographolide, a major constituent of andrographis, suggests that this bioactive component supports immune activity in human cells by increasing proliferation of lymphocytes, production of interleukin-2, tumor necrosis factor-alpha, and cluster of differentiation (CD) marker expression.^[6,7] A phase I dose-escalating trial of andrographolide was conducted in a select group of individuals. A significant rise in mean CD4(+) lymphocytes was observed in individuals receiving 10 mg/kg andrographolide ($p = 0.002$).^[8] It was noted in the study that prolonged use of concentrated andrographolide may lead to dose-related (5-10 mg/kg) adverse effects for some individuals,^[1] a point that should be considered when calculating individual dosing. Acute toxicology studies in rodents noted no observed adverse effects at doses up to 5 g/kg of andrographolide. Researchers did note significant increases in white blood cell and lymphocyte counts as well as a reduction in urea, suggesting that andrographolide had immune-stimulant and renal protective effects.^[9] Andrographolide is standardized to 50% in Viragraphis.*

Clinical Applications

- » Supports Healthy Immune and Respiratory Function*
- » Supports Healthy Cytokine and Eicosanoid Balance*
- » Designed as a Fast-Acting, Short-Term Formula*

*Viragraphis™ features three herbs that have been used traditionally for immune support and stimulation. Contemporary research on these herbs—andrographis, licorice root, and indigowoad—confirms the wisdom of their historical use. XYMOGEN's Viragraphis formula may be especially helpful in supporting cytokine balance and respiratory function.**

Licorice Root Extract (*Glycyrrhiza glabra*) Medicinal use of licorice dates back to ancient Greece, China, India, and Egypt. Contemporary research suggests that its active component glycyrrhizin supports the human immune system in the presence of pathogens.^[10,11] A 2004 study found that glycyrrhizin more effectively supported immune function than other compounds studied (ribavirin, 6-azauridine, pyrazofurin, and mycophenolic acid).^[12] Research suggests that mechanisms of action for glycyrrhizin include induction of T-cell interferon-gamma and interference with the pathogen's membrane.*^[11]

Licorice also appears to play a role in maintaining a healthy mucous membrane (including that of the respiratory tract), stimulating mucus production, and supporting eicosanoid balance in the body.^[13] Long-term intake of high doses of glycyrrhizin may deplete potassium and exacerbate hypertension.^[13,14] Although general dosing for standardized glycyrrhizin ranges from 40 to 360 mg per day,^[10,13] and Viragraphis provides approximately 40 mg of standardized glycyrrhizin per two-capsule dose, short-term supplementation with Viragraphis is recommended.*

Indigowoad 10:1 Root Extract (*Isatis indigotica*) Indigowoad is commonly used in TCM to support the immune system and upper respiratory tract. A closer look at the mechanism of action for indigowoad root extract in animals revealed that the extract significantly increased spleen weight as well as the number of circulating white blood cells, lymphocytes in particular. The same study found that the indigowoad extract stimulated macrophage phagocytic activity and reduced the suppressive effect that hydrocortisone has on the immune system.^[15] A human neutrophil cell study indicated that the isaindigotone derivative of *I. indigotica* was able to scavenge superoxide free radicals and inhibit 5-lipoxygenase and leukotriene B(4) metabolism, ultimately supporting a healthy eicosanoid balance.*^[16]

Viragraphis™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Andrographis Extract (<i>Andrographis paniculata</i>)(stem) (50% andrographolide)	375 mg	**
Indigowoad 10:1 Extract (<i>Isatis indigotica</i>)(root)	300 mg	**
Licorice Extract (<i>Glycyrrhiza glabra</i>)(root)(25% glycyrrhizin)	158.4 mg	**
** Daily Value not established.		

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, silica, and medium-chain triglyceride oil.

DIRECTIONS: Take two capsules daily, or as directed by your healthcare practitioner. Recommended for short-term use.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Consult your healthcare practitioner if you have uncontrolled hypertension. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

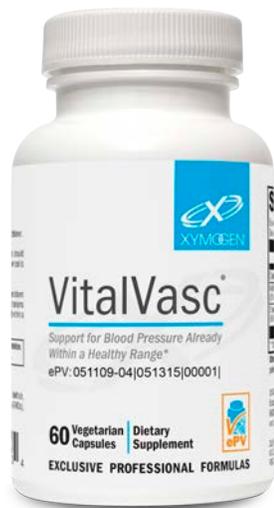
**References**

1. Natural Standard Database. Andrographis. <http://www.naturalstandard.com/databases/herbssupplements/all/andrographis.asp>. Accessed January 30, 2013.
2. Akbar S. Andrographis paniculata: a review of pharmacological activities and clinical effects. *Altern Med Rev*. 2011 Mar;16(1):66-77. [PMID: 21438648]
3. Abu-Ghefreh AA, Canatan H, Ezeamuzie CI. In vitro and in vivo anti-inflammatory effects of andrographolide. *Int Immunopharmacol*. 2009 Mar;9(3):313-8. [PMID: 19110075]
4. Sheeja K, Shihab PK, Kuttan G. Antioxidant and anti-inflammatory activities of the plant *Andrographis paniculata* Nees. *Immunopharmacol Immunotoxicol*. 2006;28(1):129-40. [PMID: 16684672]
5. Cáceres DD, Hancke JL, Burgos RA, et al. Use of visual analogue scale measurements (VAS) to assess the effectiveness of standardized *Andrographis paniculata* extract SHA-10 in reducing the symptoms of common cold. A randomized double-blind placebo controlled study. *Phytomedicine*. 1999 Oct;6:217-23. [PMID: 10589439]
6. Kumar RA, Sridevi K, Kumar NV, et al. Anticancer and immunostimulatory compounds from *Andrographis paniculata*. *J Ethnopharmacol*. 2004 Jun;92(2-3):291-5. [PMID: 15138014]
7. Rajagopal S, Kumar RA, Deevi DS, et al. Andrographolide, a potential cancer therapeutic agent isolated from *Andrographis paniculata*. *J Exp Ther Oncol*. 2003 May-Jun;3(3):147-58. [PMID: 14641821]
8. Calabrese C, Berman SH, Babish JG, et al. A phase I trial of andrographolide in HIV positive patients and normal volunteers. *Phytother Res*. 2000 Aug;14(5):333-8. [PMID: 10925397]
9. Bothiraja C, Pawar AP, Shende VS, et al. Acute and subacute toxicity study of andrographolide bioactive in rodents: Evidence for the medicinal use as an alternative medicine. *Comparative Clinical Pathology*. June 2012. doi:10.1007/s00580-012-1539-x.
10. Natural Standard Database. Licorice. <http://www.naturalstandard.com/databases/herbssupplements/licorice.asp?#undefined>. Accessed February 4, 2013.
11. Fiore C, Eisen M, Krausse R, et al. Antiviral effects of *Glycyrrhiza* species. *Phytother Res*. 2008 Feb;22(2):141-8. [PMID: 17886224]
12. Cinatl J, Morgenstern B, Bauer G, et al. Glycyrrhizin, an active component of liquorice roots, and replication of SARS-associated coronavirus. *Lancet*. 2003 Jun 14;361(9374):2045-6. [PMID: 12814717]
13. Krinsky DL, LaValle JB, Hawkins EB, et al. *Natural Therapeutics Pocket Guide*. 2nd ed. Hudson, OH: Lexi-Comp; 2003.
14. Isbrucker RA, Burdock GA. Risk and safety assessment on the consumption of Licorice root (*Glycyrrhiza* sp.), its extract and powder as a food ingredient, with emphasis on the pharmacology and toxicology of glycyrrhizin. *Regul Toxicol Pharmacol*. 2006 Dec;46(3):167-92. Review. [PMID: 16884839]
15. Xu YM, Lu PC. Experimental studies on immunostimulatory effects of the *Isatis indigotica* polysaccharide [in Chinese]. *Zhong Xi Yi Jie He Za Zhi*. 1991 Jun;11(6):357-9, 325-6. [PMID: 1889106]
16. Molina P, Tárraga A, Gonzalez-Tejero A, et al. Inhibition of leukocyte functions by the alkaloid isaindigotone from *Isatis indigotica* and some new synthetic derivatives. *J Nat Prod*. 2001 Oct;64(10):1297-300. [PMID: 11678654]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.



Available in 60 vegetarian capsules

Discussion

Adequate functioning of the endothelium is critical to allow blood vessels to fully dilate in response to changes in blood flow and to deter constriction of vessels. Diminished nitric oxide (NO) availability and an imbalance of endothelium-derived relaxing and contracting factors contribute to endothelial dysfunction, which is linked to the development of numerous vascular conditions.^[1] Each of the food-derived extracts in VitalVasc have exhibited improvements in clinical markers of vascular health.*

Cordiant™

It has been suggested that hesperidin alters endothelial cells to permit natural dilation and control of blood flow and pressure. In isolated and cultured endothelial cells, hesperidin stimulates the production of endothelial NO synthase, the NO-producing enzyme that triggers arterial dilation which, in turn, increases healthy blood flow.^[2,3] A randomized, placebo-controlled, double-blind, crossover trial examined whether oral hesperidin administration (500 mg/day for three weeks) improved endothelial function in 24 individuals with metabolic syndrome. The results revealed a significant increase in flow-mediated dilation (FMD) in the metabolic syndrome patients compared to the patients on placebo.*^[4]

Another name for hesperidin is hesperetin 7-rutinoside. As discussed above, the rutinoside hesperidin is widely studied and has been linked to several major health-promoting effects. However, the low solubility and complex metabolism of rutinosides in the gastrointestinal system have limited their absorption. Each capsule of VitalVasc contains 250 mg of Cordiant, a unique pharmaceutical grade rutinoside orange peel extract that contains a high concentration of rutinoside-2S. The high ratio of the more active “S” form in Cordiant makes it unique. Compared to other rutinoside preparations, which contain nearly equal amounts of the “S” to “R” forms, Cordiant has shown greatly improved bioavailability.*^[5,6]

Cordiant has been studied for its effect in activating endothelial production of NO. In a randomized placebo-controlled trial, subjects received a three-week intervention of 500 mg/day of Cordiant resulting in an 18% higher FMD score, a direct marker of endothelial function, compared to those receiving placebo. Additionally, concentrations of high-sensitivity C-reactive protein (hs-CRP) and serum amyloid A (SAA) were reduced as was circulating E-selectin, indicating reduced obstruction of the endothelium.*^[4]

An additional randomized, double-blind, placebo-controlled study evaluated the effect of 450 mg of daily Cordiant on endothelial function in 68 overweight subjects for a six-week period. Although no significant changes in fasting or postprandial FMD were observed in a group of patients with a

Clinical Applications

- » Supports Cardiovascular Health*
- » Provides Antioxidant Support*
- » Promotes the Maintenance of Healthy Blood Pressure Levels That Are Already Within the Healthy Range*

*VitalVasc® combines three safe, standardized, food-derived extracts that have been shown to support antioxidant activity or nitric oxide synthesis or both. These mechanisms contribute to arterial health and the maintenance of blood pressure that is already within a healthy range.**

baseline FMD of less than 3%, those with a baseline greater than or equal to 3% showed significant improvement in endothelial function. Circulating adhesion molecules sVCAM-1 and sICAM-1 were reduced along with systolic and diastolic blood pressure in both groups regardless of baseline FMD. The findings suggested that Cordiant has a promising role in the preservation of endothelial function and healthy blood flow in overweight individuals.*^[7]

Grape Seed Extract

Grape seed extract is a rich source of oligomeric proanthocyanidins (OPCs), which donate electrons or protons to reactive oxygen species (ROS) and act as scavengers.^[8] Oxidative stress can increase vascular endothelial permeability, formation of oxidized LDL, and activation of phagocytic cells. Grape seed extract has been investigated for its ability to interfere with oxidative stress, benefiting cholesterol and blood pressure.*^[9,10]

When utilized as a dietary supplement, grape seed extract has been suggested for lowering blood pressure in individuals with mildly elevated levels. In a double-blind placebo-controlled study, supplementing with 300 mg per day of grape seed extract for eight weeks (n=66) resulted in a statistically significant decrease in both systolic (average reduction of 8 mmHg) and diastolic blood pressure (average reduction of 5mmHg) in adults with prehypertension (mildly elevated blood pressure). Levels in the placebo group were not reduced.*^[11]

In another double-blind placebo-controlled study, 27 subjects with metabolic syndrome were given 150 or 300 mg per day of grape seed extract for four weeks. Both systolic and diastolic blood pressures were lowered after treatment with grape seed extract as compared with placebo. A decrease in oxidation of LDL particles also occurred in the treatment group.*^[12]

Each capsule of VitalVasc contains 75 mg of Enovita®, a grape seed extract standardized to 95% proanthocyanidins. Enovita has shown efficacy in maintaining healthy blood pressure when associated with diet and lifestyle modification. A four-month duration study evaluated two dosages (150 mg/day and 300 mg/day) of Enovita in 119 subjects with borderline hypertension (defined as pre-hypertension) (120-139 mmHg/80-89 mmHg) and stage 1 hypertension (140-159 mmHg/90-99 mmHg).^[13] The participants utilized nondrug dietary (reduction in salt, alcohol, and caffeinated drinks) and lifestyle (regular exercise, sleep time improvement, relaxation, and smoking reduction) interventions. Blood pressure and heart rate were the primary endpoints, with blood pressure normalization being significantly higher in the Enovita supplementation groups compared to control starting from the fourth week of supplementation.*^[14]

VitalVasc® Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Cordiat™ Rutinoid (from <i>Citrus sinensis</i>) (fruit)	250 mg	**
Arthricor® Olive Extract Blend (<i>Olea europaea</i>) (fruit) (9% hydroxytyrosol, 4% oleuropein, 1% tyrosol)	125 mg	**
Novovita® Grape Extract (<i>Vitis vinifera</i>) (seed) (95% proanthocyanidins)	75 mg	**

** Daily Value not established.

Other Ingredients: HPMC, dicalcium phosphate, maltodextrin, ascorbyl palmitate, and silica.

DIRECTIONS: Take one capsule twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

Arthricor is a trademark of Eight-IP.

Novovita® is a registered trademark of Indena S.p.A.

Cordiat is a trademark of BioActor B.V.

Olive Extract

The evidence linking the Mediterranean diet to cardiovascular health has grown substantially in recent years^[15-17] with specific research suggesting that olive oil and its phenolic constituents are primary beneficial contributors.^[18-22] Phenolic compounds have been shown to have a protective effect against LDL oxidation,^[20,23,24] and additional studies have demonstrated the ability of olive *leaf* extracts to significantly reduce blood pressure measurements.^[25] Olive polyphenolic compounds have also been linked to an increase in the production of NO.^{*[26,27]}

Each capsule of VitalVasc provides 125 mg of Arthricor® olive extract blend with three polyphenols—hydroxytyrosol, oleuropein, and tyrosol at levels supportive of vascular health.*

References

- Hadi HA, Carr CS, Al Suwaidi J. Endothelial dysfunction: cardiovascular risk factors, therapy, and outcome. *Vasc Health Risk Manag.* 2005 Sep; 1(3):183-198. [PMID: 17319104]
- Chiou CS, Lin JW, Kao PF, et al. Effects of hesperidin on cyclic strain-induced endothelin-1 release in human umbilical vein endothelial cells. *Clin Exp Pharmacol Physiol.* 2008 Aug;35(8):938-43. [PMID: 18430059]
- Liu L, Xu DM, Cheng YY. Distinct effects of naringenin and hesperetin on nitric oxide production from endothelial cells. *J Agric Food Chem.* 2008 Feb 13;56(3):824-9. [PMID: 18197618]
- Rizza S, Muniyappa R, Iantorno M, et al. Citrus polyphenol hesperidin stimulates production of nitric oxide in endothelial cells while improving endothelial function and reducing inflammatory markers in patients with metabolic syndrome. *J Clin Endocrinol Metab.* 2011 May;96(5):E782-92. [PMID: 21346065]
- Hua S, Song C, Geczy CL, et al. A role for acute-phase serum amyloid A and high-density lipoprotein in oxidative stress, endothelial dysfunction and atherosclerosis. *Redox Rep.* 2009;14 (5): 187-96. [PMID: 19843373]
- BioActor. Cordiat™ Formulation Has a >100% Improved Bioavailability Compared to Standard Rutinoid. Bioavailability Study Report. Maastricht, Netherlands: Bioactor B.V.; 2013. [available on request]
- Salden BN, Bouke N, Troost FJ, et al. Randomized clinical trial on the efficacy of hesperidin 2S on validated cardiovascular biomarkers in healthy overweight individuals. *Am J Clin Nutr.* 2016 Dec;104(6):1523-1533. [PMID: 27797708]
- Cook NC, Samman S. Flavonoids – chemistry, metabolism, cardioprotective effects, and dietary sources. *J Nutr Biochem.* 1996;7:66-76. doi: [http://dx.doi.org/10.1016/S0955-2863\(95\)00168-9](http://dx.doi.org/10.1016/S0955-2863(95)00168-9).
- Lum, H., Roebuck, KA. Oxidant stress and endothelial cell dysfunction. *Am J Physiol Cell Physiol.* 2001 Apr;280(4):C719-C741. [PMID: 11245588]
- Shi J, Yu J, Pohorty JE, et al. Polyphenolics in grape seeds—biochemistry and functionality. *J Med Food.* 2003 Winter;6(4):291-9. [PMID: 14977436]
- Robinson M, Lu B, Edirisinghe I, et al. Effect of grape seed extract on blood pressure in subjects with pre-hypertension. *J Pharm Nutr Sci.* 2012;2(2):155-159. <http://www.lifescienceglobal.com/pms/index.php/jpans/article/view/916/411>. Published May 11, 2012. Accessed May 7, 2017.
- Sivaprakasapillai B, Edirisinghe I, Randolph J, et al. Effect of grape seed extract on blood pressure in subjects with the metabolic syndrome. *Metabolism.* 2009 Dec;58(12):1743-1746. [PMID: 19608210]
- Pimenta E, Oparil S. Management of hypertension in the elderly. *Nat. Rev Cardiol.* 2012 Mar 13;9(5):286-96. [PMID: 22411292]
- Belcaro G, Ledda A, Hu S, et al. Grape seed procyanidins in pre-and mild hypertension: a registry study. *Evid Based Complement Alternat Med.* 2013;2013:313142. [PMID: 24171039]
- Estruch R, Ros E, Salas-Salvadó J, et al. Primary prevention of cardiovascular disease with a Mediterranean diet. *N Engl J Med.* 2013 Apr 4;368(14):1279-90. [PMID: 23432189]
- Mayor S. Mediterranean diet reduces cardiovascular events in people with heart disease, study shows. *BMJ.* 2016 Apr 24;353:i2348. [PMID: 27114468]
- Chiva-Blanch G, Badimon L, Estruch R. Latest evidence of the effects of the Mediterranean diet in prevention of cardiovascular disease. *Curr Atheroscler Rep.* 2014 Oct;16(10):446. [PMID: 25115436]
- Fitó M, Cladellas M, de la Torre R, et al. Anti-inflammatory effect of virgin olive oil in stable coronary disease patients: a randomized, crossover, controlled trial. *Eur J Clin Nutr.* 2008 Apr;62(4):570-74. [PMID: 17375118]
- Ruano J, López-Miranda J, de la Torre R, et al. Intake of phenol-rich virgin olive oil improves the postprandial prothrombotic profile in hypercholesterolemic patients. *Am J Clin Nutr.* 2007 Aug;86(2):341-46. [PMID: 17684203]
- Gimeno E, de la Torre-Carbot K, Lamuela-Raventós RM, et al. Changes in the phenolic content of low density lipoprotein after olive oil consumption in men. A randomized crossover controlled trial. *Br J Nutr.* 2007 Dec;98(6):1243-50. [PMID: 17617938]
- Bogani P, Galli C, Villa M, et al. Postprandial anti-inflammatory and antioxidant effects of extra virgin olive oil. *Atherosclerosis.* 2007 Jan;190(1):181-86. [PMID: 16488419]
- Guasch-Ferré M, Hu FB, Martínez-González MA, et al. Olive oil intake and risk of cardiovascular disease and mortality in the PREDIMED Study. *BMC Med.* 2014 May 13;12:78. [PMID: 24886626]
- Castañer O, Covas MI, Khymenets O, et al. Protection of LDL from oxidation by olive oil polyphenols is associated with a downregulation of CD40-ligand expression and its downstream products in vivo in humans. *Am J Clin Nutr.* 2012 May;95(5):1238-44. [PMID: 22440854]
- Raederstorff D. Antioxidant activity of olive polyphenols in humans: a review. *Int J Vitam Nutr Res.* 2009 May;79(3):152-65. [PMID: 20209466]
- Cherif S, Rahal N, Haouala M, et al. A clinical trial of a titrated Olea extract in the treatment of essential arterial hypertension. *J Pharm Belg.* 1996 Mar-Apr;51(2):69-71. [PMID: 8786521]
- Visioli F, Bellosta S, Galli C. Oleuropein, the bitter principle of olives, enhances nitric oxide production by mouse macrophages. *Life Sci.* 1998;62(6):541-6. [PMID: 9464466]
- Rocha BS, Gago B, Barbosa RM, et al. Dietary polyphenols generate nitric oxide from nitrite in the stomach and induce smooth muscle relaxation. *Toxicology.* 2009 Nov 9;265(1-2):41-8. [PMID: 19778575]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Xcellent C™

Advanced Vitamin C Formula



Available in 120 capsules

Discussion

Vitamin C (ascorbic acid) is a water-soluble vitamin that is essential to humans and must be obtained exogenously. While most mammals are able to synthesize vitamin C, humans are unable to. This is because humans lack one of the enzymes required to synthesize vitamin C from glucose. Stress, smoking, pollution, radiation and heavy metal exposure, immune challenge, and temperature change all increase the human requirement for vitamin C. Well-known functions of this versatile vitamin include antioxidant protection from free radicals and oxidative processes; synthesis of collagen, carnitine, and neurotransmitters; and immune stimulation and support.^[1-3] Vitamin C functions as a cofactor for several metabolic enzymes and is involved in protein metabolism. It also plays a lesser-known role in the deactivation of histamine.^{*[4,5]}

Collagen is a fundamental component of bone, tendons, ligaments, and blood vessels. Vitamin C's role in collagen formation makes it vital to maintaining skin, capillary, gum, joint, and skeletal health.^[1,3,6] Vitamin C's role in promoting and maintaining collagen, and consequently skin integrity, was recognized as early as the 1930s in published surgical journals.^{*[7]}

Synthesis of carnitine depends on vitamin C, highlighting vitamin C's role in energy production. Carnitine is the "car" that shuttles fatty acids into the mitochondria where they can be converted to the energy-yielding molecule adenosine triphosphate (ATP). Synthesis of certain hormones and neurotransmitters depends on vitamin C as well. It is required for the conversion of dopamine to norepinephrine—a neurotransmitter that is of great importance in maintaining healthy mood and brain function.^{*[3]}

Protecting tissues and organs from oxidative damage is believed to be pivotal in maintaining health in the body.^[8,9] Ascorbate, the reduced form of vitamin C (the form found in Xcellent C™), is a generous donor of electrons, allowing it to counteract oxidative free radicals. This property makes ascorbate an ideal antioxidant that can protect cells and tissues as well as regenerate other antioxidants. In turn, various

Clinical Applications

- » High-Potency Vitamin C Formula Provides 750 mg Vitamin C per Capsule
- » Formulated with BioPerine® to Enhance Nutrient Bioavailability*
- » Supports Immune and Antioxidant Systems*
- » Supports Production of Collagen, Carnitine, and Neurotransmitters*
- » Buffered with Minerals to Help Prevent Potential Stomach Upset*

*Xcellent C™ is a high-potency vitamin C formula with the addition of 7.5 mg of BioPerine® per capsule. BioPerine, a proprietary black pepper extract, is present to promote absorption and bioavailability of vitamin C. Vitamin C provides valuable antioxidant protection and is necessary for the production of collagen, an integral component of blood vessels, tendons, ligaments, and bone. This essential water-soluble vitamin is required for the synthesis of neurotransmitters and carnitine as well. Xcellent C contains buffering minerals to help prevent potential stomach upset.**

nutrients and compounds, such as glutathione and alpha-lipoic acid, are able to regenerate vitamin C and extend its antioxidant protection. Recognizing the importance of vitamin C as a protective antioxidant, the Institute of Medicine, an independent and non-profit organization that provides advice on health and science to decision makers and the public, recommended increasing vitamin C requirements for smokers due to their exposure to toxins and oxidative elements in cigarette smoke.^[1] Additionally, vitamin C is able to limit the formation of carcinogens, such as nitrosamines.^{*[1]}

Vitamin C supplementation has been studied for more than six decades with respect to moderating the severity or duration of acute immune challenges.^[1,3,10] Benefits are most notable in cases of extreme physical stress.^[2] Within three meta-analyses, in a subgroup of six studies, vitamin C reduced signs of acute immune challenge by an average of 50% in marathon runners, skiers, and soldiers that had been physically stressed or exposed to cold temperatures.^{*[11]}

Adequate intake and retention is necessary to maintain vitamin C status in the body. Total stores can range from 300 mg (considered too low to maintain health) to 2000 mg. The highest concentrations can be found in leukocytes, eyes, adrenal and pituitary glands, and the brain.^[1] Relatively low levels are maintained in plasma, so plasma vitamin C measurement may not be useful in the assessment of vitamin C status. According to pharmacokinetic studies, an oral dose of 1.25 g vitamin C per day will produce mean peak plasma concentrations of 135 micromol/L (approximately twice the level reached by consuming 200-300 mg/d of ascorbic acid from foods rich in vitamin C).^[1] The Linus Pauling Institute at Oregon State University recommends a base dose of 250 mg vitamin C twice a day.^[3] For optimal health, Dr. Pauling recommends 2.3 g or more per 2500 kJ.^[12] Individual tolerance should be determined, as some ascorbic acid is metabolized to oxalic acid and excreted in the urine. Bowel tolerance to higher doses of vitamin C may vary from individual to individual as well.*

Xcellent C™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Vitamin C (as calcium ascorbate, magnesium ascorbate, and potassium ascorbate)	1500 mg	1667%
Calcium (as calcium ascorbate)	130 mg	10%
Black Pepper Extract (<i>Piper nigrum</i>)(fruit)(95% piperine) (BioPerine®)	15 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), stearic acid, medium-chain triglyceride oil, magnesium stearate, and silica.
BioPerine is a registered trademark of Sabinsa Corp. BioPerine is protected by US patents 5,536,506; 5,744,161; 5,972,382; and 6,054,585.

DIRECTIONS: Take two capsules twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

**References**

1. NIH Office of Dietary Supplements. Dietary Supplement Fact Sheet: Vitamin C. <http://ods.od.nih.gov/factsheets/VitaminC-HealthProfessional/>. Accessed September 3, 2012.
2. Schlueter AK, Johnston CS. Vitamin C: overview and update. *Journal of Evidence-Based Complementary & Alternative Medicine (JEBCAM)*. 2011; 16(1):49-57. <http://chp.sagepub.com/content/16/1/49.full.pdf+html>. Accessed August 23, 2012.
3. Linus Pauling Institute. Vitamin C. Updated November 2009. <http://lpi.oregonstate.edu/infocenter/vitamins/vitaminC/>. Accessed August 15, 2012.
4. Johnston CS. The antihistamine action of ascorbic acid. *Subcell Biochem*. 1996;25:189-213. [PMID: 8821975]
5. Strohle A, Wolters M, Hahn A. Micronutrients at the interface between inflammation and infection—ascorbic acid and calciferol: part 1, general overview with a focus on ascorbic acid. *Inflamm Allergy Drug Targets*. 2011 Feb;10(1):54-63. [PMID: 21184650]
6. MacKay D, Miller AL. Nutritional support for wound healing. *Altern Med Rev*. 2003 Nov;8(4):359-77. [PMID: 14653765]
7. Lanman TH, Ingalls TH. Vitamin C deficiency and wound healing: An experimental and clinical study. *Ann Surg*. 1937 Apr;105(4):616-25. [PMID: 17856964]
8. Jacob RA, Sotoudeh G. Vitamin C function and status in chronic disease. *Nutr Clin Care*. 2002 Mar-Apr;5(2):66-74. [PMID: 12134712]
9. Li Y, Schellhorn HE. New developments and novel therapeutic perspectives for vitamin C. *J Nutr*. 2007 Oct;137(10):2171-84. [PMID: 17884994]
10. Wintergerst ES, Maggini S, Hornig DH. Immune-enhancing role of vitamin C and zinc and effect on clinical conditions. *Ann Nutr Metab*. 2006;50(2):85-94. [PMID: 16373990]
11. Douglas RM, Hemilä H, Chalker E, et al. Vitamin C for preventing and treating the common cold. *Cochrane Database Syst Rev*. 2007 Jul 18;(3):CD000980. [PMID: 17636648]
12. Pauling L. Evolution and the need for ascorbic acid. *Proc Natl Acad Sci USA*. 1970 Dec;67(4):1643-8. [PMID: 5275366]
13. BioPerine®. About BioPerine®. <http://www.bioperine.com/about-bioperine.html>. Accessed September 4, 2012.

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

© XYMOGEN
DRS-184
Rev. 08/08/19



Xcellent E™

Bio-Enhanced Tocopherol/Tocotrienol Complex*



Available in 60 softgels

Discussion

Vitamin E, in its natural form, comprises eight different compounds: alpha-, beta-, gamma-, and delta-tocopherols and alpha-, beta-, gamma-, and delta-tocotrienols. Both tocopherols and tocotrienols are important to human health. Known as the “master antioxidant,” vitamin E has the ability to attenuate oxidative stress, and its antioxidant-related effects on various organs and systems have been the focus of vast research. More recently, non-antioxidant mechanisms have been proposed, such as those that affect cell-signal transduction and gene expression.^[1] Though the vast majority of research has been on alpha-tocopherol, recent mechanistic studies indicate that other isomers of vitamin E, such as gamma- and delta-tocopherols and tocotrienols, have superior antioxidant and cell-signaling properties that offer greater health benefits.*^[2,3]

Tocotrienols

Studies have demonstrated that tocotrienols have superior antioxidant activity compared to tocopherols. Tocotrienols also exhibit biological activities related to neuroprotection, radioprotection, cell-life regulation, cytokine modulation, and lipid metabolism that are not shared by tocopherols.^[3-5] Many of these benefits are thought to be mediated via their carboxychromanol metabolites.^[2,6] Among other actions, tocotrienols have been shown to inhibit HMG-CoA reductase (3-hydroxy-3-methylglutaryl-coenzyme A reductase), attenuate transcription factor NF-κB activation, and inhibit COX-2.^[7,8] Given these mechanisms, in addition to their antioxidant mechanisms, tocotrienols have a very broad range of applications. Due to the poor absorption and low bio-availability of tocotrienols, scientists developed EVNol SupraBio™.*

EVNol SupraBio: Bio-enhanced tocotrienol/tocopherol complex

EVNol SupraBio is a natural, full-spectrum tocopherol and tocotrienol complex extracted and concentrated from the red palm fruits (*Elaeis guineensis*) of sustainable plantations in Peninsular Malaysia. This vitamin E complex also contains minute amounts of other phytonutrients such as plant squalene, phytosterols, coenzyme Q10, and mixed carotenoids that are naturally extracted together with

Clinical Applications

- » Offers Antioxidant Protection for Cell Membranes and Lipids*
- » Supports Healthy Cytokine and Eicosanoid Balance*
- » Supports Neuroprotection and Cognitive Health*
- » Supports Cardiovascular, Nervous, and Reproductive Systems*
- » Supports Liver Health*
- » Provides Mixed Tocopherols and Tocotrienols for Comprehensive Vitamin E Nutrition*

*Xcellent E™ features EVNol SupraBio™ full-spectrum palm tocopherol/tocotrienol complex. EVNol SupraBio's patented bio-enhancing technology has been shown to increase tocotrienol absorption rates in humans by an average of 250%. Tocotrienols confer unique health benefits not provided by tocopherols. This means Xcellent E not only enables superior absorption but also more comprehensive vitamin E benefits than tocopherol-only formulas.**

tocotrienols. This patented formula contains a precise mixture of oil and approved food emulsifiers at optimum ratio and processing that self-emulsifies in the gastrointestinal tract to facilitate and provide a rapid and consistent absorption of tocotrienols into the plasma, independent of dietary fat or food intake.*

EVNol SupraBio Human Absorption Studies

Kholsa et al were the first to establish that oral supplementation of EVNol SupraBio resulted in a peak plasma level 12- to 13-fold the level established for neuroprotection.^[9] Later, in a two-period, two-sequence, crossover study performed in healthy human volunteers, researchers demonstrated that the SupraBio system increased the rate and extent of absorption of individual tocotrienols by an average of 250% compared to a regular tocotrienol oil extract.^[10] Moreover, EVNol SupraBio is the only tocotrienol/tocopherol complex in the market that has been the subject of an actual human tissue distribution study. In that study, Patel et al demonstrated that orally supplemented tocotrienols from EVNol SupraBio are absorbed into plasma and delivered and accumulated in vital organs, including the brain.*^[11]

EVNol SupraBio Human Clinical Studies

EVNol SupraBio is a heavily researched tocopherol/tocotrienol product that has been scientifically substantiated with human clinical studies on brain health, liver support, beauty, and cardiovascular health.^[11-18] For example, in a randomized, placebo-controlled, two-year neuroprotection study (n = 121), supplementation with 200 mg/d EVNol SupraBio attenuated the progression of injury to brain white matter.^[12] Three other studies demonstrated the positive effects of EVNol SupraBio on parameters of liver health^[11,13,14], and studies related to cardiovascular health suggested that 50-200 mg/d EVNol SupraBio supports healthy lipid (cholesterol, low-density lipoprotein, triglyceride) metabolism and showed a trend toward improved arterial compliance (the ability to expand and contract).^[15,16] Supplementation has also been shown to support the desired immune response to vaccine.^[17] And in a randomized, double-blind, placebo-controlled trial (n = 38), volunteers

Continued on next page

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Xcellent E™ Supplement Facts

Serving Size: 1 Softgel

	Amount Per Serving	%Daily Value
Vitamin E (as d-alpha tocopherol)	33.5 mg	223%
EVNol SupraBio™ Bio-Enhanced Natural Full Spectrum Tocotrienol/Tocopherol Complex	164.5 mg	**
Total Mixed Tocotrienols	25 mg	**
d-Gamma Tocotrienol	11.5 mg	**
d-Alpha Tocotrienol	7.4 mg	**
d-Delta Tocotrienol	4.1 mg	**
d-Beta Tocotrienol	822.5 mcg	**
Total Mixed Tocopherols	125 mg	**
Typical Composition:		
d-Gamma Tocopherol	75 mg	**
d-Delta Tocopherol	30 mg	**
d-Alpha Tocopherol	17.5 mg	**
d-Beta Tocopherol	2.5 mg	**

** Daily Value not established.

Other Ingredients: Sunflower oil, softgel (bovine gelatin, vegetable glycerin, and purified water), and polyglycerol esters of fatty acids.**DIRECTIONS:** Take one softgel twice daily, or use as directed by your healthcare practitioner.

Consult a healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.**DOES NOT CONTAIN:** Wheat, gluten, corn, yeast, soy protein, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

EVNol SupraBio is a trademark of ExcelVite Inc. and protected by US patent 6,596,306.

with hair loss who were given 100 mg of EVNol SupraBio daily experienced a 34.5% increase in number of hairs at the end of eight months, compared to a 0.1% increase in the placebo group.^[18] The higher activity of tocotrienols in certain organs may, in part, be explained by the fact that the unsaturated side-chain of tocotrienols allow more efficient penetration into tissues, such as brain and liver tissues, that have saturated fatty layers.*^[3,13]

It is clear from the emerging data that tocopherols and tocotrienols have complementary, unique, and important functions.^[3] Providing a formula that supplies the full spectrum of natural vitamin E isomers is an important option for practitioners and their patients.*

References

1. Azzi A, Meydani SN, Meydani M, et al. The rise, the fall and the renaissance of vitamin E. *Arch Biochem Biophys.* 2016 Apr 1;595:100-08. [PMID: 27095224]
2. Jiang Q, Yin X, Lill MA, et al. Long-chain carboxychromanols, metabolites of vitamin E, are potent inhibitors of cyclooxygenases. *Proc Natl Acad Sci U S A.* 2008 Dec 23;105(51):20464-69. [PMID: 19074288]
3. Ahsan H, Ahad A, Iqbal J, et al. Pharmacological potential of tocotrienols: a review. *Nutr Metab (Lond).* 2014 Nov 12;11(1):52. [PMID: 25435896]
4. Osakada F, Hashino A, Kume T, et al. Alpha-tocotrienol provides the most potent neuroprotection among vitamin E analogs on cultured striatal neurons. *Neuropharmacol.* 2004 Nov;47(6):904-15. [PMID: 15527824]
5. Fu JY, Che HL, Tan DM, et al. Bioavailability of tocotrienols: evidence in human studies. *Nutr Metab (Lond).* 2014 Jan 13;11(1):5. [PMID: 24410975]
6. Jiang Q. Natural forms of vitamin E: metabolism, antioxidant, and anti-inflammatory activities and their role in disease prevention and therapy. *Free Radic Biol Med.* 2014 Jul;72:76-90. [PMID: 24704972]
7. Singh VK, Hauer-Jensen M. γ-tocotrienol as a promising countermeasure for acute radiation syndrome: current status. *Int J Mol Sci.* 2016 May 3;17(5):pii:E663. [PMID: 27153057]
8. Peh HY, Tan WS, Liao W, et al. Vitamin E therapy beyond cancer: tocopherol versus tocotrienol. *Pharmacol Ther.* 2016 Jun;162:152-69. [PMID: 26706242]
9. Khosla P, Patel V, Whinter JM, et al. Postprandial levels of the natural vitamin E tocotrienol in human circulation. *Antioxid Redox Signal.* 2006 May-Jun;8(5-6):1059-68. [PMID: 16771695]
10. *Tocotrienols – A Potent and Unique Form of Natural Vitamin E from Red Palm Oil/Palm Fruits.* 6th ed. Edison, NJ: ExcelVite Inc.;2016.
11. Patel V, Rink C, Gordillo GM, et al. Oral tocotrienols are transported to human tissues and delay the progression of the model for end-stage liver disease score in patients. *J Nutr.* 2012 Mar;142(3):513-19. [PMID: 22298568]
12. Gopalan Y, Shuaib IL, Magosso E, et al. Clinical investigation of the protective effects of palm vitamin E tocotrienols on brain white matter. *Stroke.* 2014 May;45(5):1422-8. [PMID: 24699052]
13. Magosso E, Ansari MA, Gopalan Y, et al. Tocotrienols for normalisation of hepatic echogenic response in nonalcoholic fatty liver: a randomised placebo-controlled clinical trial. *Nutr J.* 2013 Dec 27;12(1):166. [PMID: 24373555]
14. Thendiono J, Arguillas M. The effect of vitamin E (mixed tocotrienol) on the liver stiffness measurement measured by transient elastography (fibroskan) among NAFLD patients. Presented at: 23rd Conference Meeting of the Asian Pacific Association for the Study of Liver; June 6-10, 2013; Singapore. <http://www.excelvite.com/wp-content/uploads/2015/04/EFFECT1.pdf>. Accessed June 6, 2016.
15. Ajuluchukwu JN, Okubadejo NU, Mabayoje M, et al. Comparative study of the effect of tocotrienols and -tocopherol on fasting serum lipid profiles in patients with mild hypercholesterolaemia: a preliminary report. *Niger Postgrad Med J.* 2007 Mar;14(1):30-33. [PMID: 17356586]
16. Rasool AH, Rahman AR, Yuen KH, et al. Arterial compliance and vitamin E blood levels with a self emulsifying preparation of tocotrienol rich vitamin E. *Arch Pharm Res.* 2008 Sep;31(9):1212-17. [PMID: 18806966]
17. Mahalingam D, Radhakrishnan AK, Amom Z, et al. Effects of supplementation with tocotrienol-rich fraction on immune response to tetanus toxoid immunization in normal healthy volunteers. *Eur J Clin Nutr.* 2011 Jan;65(1):63-69. [PMID: 20859299]
18. Beoy LA, Woei WJ, Hay YK. Effects of tocotrienol supplementation on hair growth in human volunteers. *Trop Life Sci Res.* 2010 Dec;21(2):91-99. [PMID: 24575202]

Additional references available upon request

Note on Vitamin E Activity and International Units (IUs)

Only alpha-tocopherol contributes to IU of vitamin E activity: 1 mg d-alpha tocopherol equals 1.49 IU vitamin E activity. Other naturally occurring forms of vitamin E (beta-, gamma-, delta-tocopherol) and tocotrienols do not contribute toward meeting the vitamin E requirement. Hence, the IU is calculated based on alpha-tocopherol alone in all formulations. Other isomers of vitamin E are expressed as "mg." Each gram of EVNol SupraBio 20% contains approximately 152 mg d-mixed tocotrienols and 35-60 mg d-alpha-tocopherol. Hence, the minimum vitamin E activity in 1 gram of EVNol SupraBio 20% = 35 mg d-alpha-tocopherol x 1.49 = 52.15 IU.

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

© XYMOGEN
DRS-312
Rev. 08/08/19



XenoProtX™

Comprehensive Support for Detoxification*



Available in 120 capsules

Discussion

Xenobiotics (chemicals foreign to a living organism) have the potential to disrupt metabolism and negatively affect cellular health.^[1-3] Classes of xenobiotics include pesticides, petroleum-based plastic compounds, industrial chemicals, and xenoestrogens. XenoProtX™ comprises an array of compounds to support detoxification and elimination of these potentially toxic molecules. Man-made xenoestrogens (including BPA, DDT, and DES), act as endocrine disruptors and can alter hormonal function in sensitive tissues including breast, uterus, cervix, and prostate.^[4,5] Xenoestrogens at very low levels are believed to disrupt neurotransmitter balance, glucose homeostasis, normal reproduction, and healthy metabolism.^[6] Detoxification of xenobiotics is a complex process that requires micronutrients, phytonutrients, energy, and adequate antioxidant support for safe and effective completion.^[6]

Antioxidant and Detoxification Support Several nutrients support antioxidant activity, both phases of detoxification, and the health and function of the liver (the major site of detoxification). **Milk thistle extract** contains silymarin, a compound found to limit the entry of hepatotoxins, donate sulfhydryl groups for detoxification, and increase hepatic glutathione by over 35%.^[7] Its action in the liver reduces fat peroxidation and fibrous tissue formation, supports a normal immune and inflammatory response, promotes protein synthesis and tissue regeneration, and supports glucuronidation and glutathione levels.^[8] **Alpha-lipoic acid** is both water- and fat-soluble. It supports glutathione metabolism, helps regenerate antioxidant vitamins C and E, and helps maintain the ratio of reduced-to-oxidized CoQ10 in mitochondria.^[7] The redox couple of lipoic acid and dihydrolipoic acid stabilizes NF-kappaB transcription and may help support healthy immune functions in the body.^[9,10] **Methylselenocysteine (MSC)** is considered a well-tolerated form of the trace element selenium and may support normal cell-life regulation.^[11] Selenium provides antioxidant support via glutathione peroxidase and manganese superoxide dismutase (MnSOD) activity.^[12] **N-acetyl-cysteine (NAC)** may significantly increase glutathione in the body, which, in turn, is incorporated into crucial antioxidant and detoxification enzymes. Glutathione supports antioxidant activity, phase II detoxification,

Clinical Applications

- » Provides Micronutrients, Phytonutrients, and Cofactors that Support Detoxification of Xenobiotics and Xenoestrogens*
- » Supports Healthy Estrogen Metabolism*
- » Supports Antioxidant Mechanism and Glutathione Production*

*XenoProtX™ is a comprehensive formula designed to support phase I and phase II liver detoxification of environmental pollutants, endocrine disruptors, estrogen metabolites, xenoestrogens, and other toxins. XenoProtX also supports antioxidant activity throughout the detoxification process. Micronutrients, phytonutrients, and activated cofactors provide additional support for energy production, cellular protection, and liver function during crucial metabolic biotransformation processes.**

and the normal breakdown of metabolites, toxins, and other compounds. NAC supports phase II sulfation reactions as well.^[7] **Calcium D-glucarate** has been added to support glucuronidation. **5-methyltetrahydrofolate (5-MTHF)** is present as Quatrefolic® (a stable, bioavailable form of folate) to support methylation, energy generation, and phase I and phase II activity.*

Phytonutrients A variety of phytonutrients support antioxidant activity in the body. **Green tea catechins** have been found to assist in free-radical scavenging, support detoxification through modification of phase I and phase II enzymes, and support normal cell-life regulation via multiple signaling pathways.^[13,14] Bioflavonoids, including **resveratrol, quercetin**, and the highly absorbable FlavitPURE™ form of **dihydroquercetin (DHQ)**, support phase I detoxification as well as intermediary antioxidant protection.^[11] **Pterostilbene**, a highly absorbable, methylated form of resveratrol, is thought to work together with quercetin in supporting normal cell-life regulation.^[15] **Turmeric extract** provides curcumin, a phytonutrient valued for its promotion of antioxidant activity, support of metabolic detoxification, and modulation of cytokine production.^[16,17] BioPerine®, a patented form of piperine from **black pepper**, has been added to enhance the absorption of nutrients, particularly curcumin.*^[18]

Xenoestrogen Metabolism XenoProtX provides **diindolymethane (DIM)** and **glucoraphanin** as SGS™. DIM promotes healthy estrogen metabolism and creates a better balance of estrogen metabolites (2-OH, 4-OH, 16-alpha-OH) through phase I cytochrome P450 enzyme induction and promotion of 2-hydroxylation.^[19,20] The action of DIM is complemented by glucoraphanin, which supports long-term antioxidant activity and phase II detoxification of less-desirable estrogen metabolites and xenoestrogens.^[21,22] Glucoraphanin and its metabolite sulforaphane are found to be effective, long-acting, indirect antioxidants and significant inducers of phase II detoxification enzymes.^[23,24] These actions may help support healthy estrogen balance and may be crucial for the health of estrogen-sensitive tissue.*

EXCLUSIVE • PATENTED

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XYMOGEN® Exclusive Professional Formulas
800-647-6100 | www.xymogen.com

XenoProtX™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Folate (as Quatrefolic® (6S)-5-methyltetrahydrofolic acid, glucosamine salt)	200 mcg	50%
Calcium (naturally occurring)	75 mg	8%
Selenium (as methylselenocysteine)	15 mcg	21%
Calcium-D-Glucurate	250 mg	**
Green Tea Aqueous Extract (<i>Camellia sinensis</i>)(leaf)(80% polyphenols, 60% catechins, 30% EGCG, 6% caffeine)	250 mg	**
Alpha-Lipoic Acid	100 mg	**
N-Acetyl-L-Cysteine	100 mg	**
Milk Thistle Extract (<i>Silybum marianum</i>)(seed)(80% silymarin)	100 mg	**
DIM (diindolylmethane)	75 mg	**
Quercetin (as quercetin dihydrate)(from <i>Sophora japonica</i>)(bud)	50 mg	**
Turmeric Extract (<i>Curcuma longa</i>)(rhizome)(95% curcuminoids)	50 mg	**
<i>trans</i> -Resveratrol (as <i>Polygonum cuspidatum</i> root extract)	18.5 mg	**
<i>trans</i> -Pterostilbene (pTeroPure®)	15.5 mg	**
Glucoraphanin (from broccoli extract)(<i>Brassica oleracea italica</i>)(seed)(truebroc™)	15 mg	**
Dihydroquercetin (from Larch Tree Extract)(<i>Larix dahurica</i> , <i>Larix gmelinii</i> , <i>Larix sibirica ledeb.</i> , <i>Larix cajanderi</i> , <i>Larix czekanowskii</i> , <i>Larix russica</i> , <i>Larix sukaczewij</i>)(saw logs)(DHQvital™)	5 mg	**
Black Pepper Extract (<i>Piper nigrum</i>)(fruit)(BioPerine®)	5 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), tricalcium phosphate, stearic acid, magnesium stearate, and silica.

DIRECTIONS: Take two capsules daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

pTeroPure is a trademark of ChromaDex, Inc.
BioPerine is a registered trademark of Sabinsa Corp. BioPerine is protected by US patents 5,536,506; 5,744,161; 5,972,382; and 6,054,585.



DHQvital DHQvital is a trademark of Berg Imports, LLC

Quatrefolic Quatrefolic® is a registered trademark of Gnosis S.p.A. Produced under US patent 7,947,862.

Produced under US patent 5,725,895; 5,968,505; 5,968,567; 6,177,122; and 6,242,018 licensed from Brassica Protection Products LLC; truebroc is a trademark of Brassica Protection Products LLC.

References

- Gaby AR. *Nutritional Medicine*. Concord, NH: Fritz Perlberg Publishing; 2011.
- Colborn T, vom Saal FS, Soto AM. Developmental effects of endocrine-disrupting chemicals in wildlife and humans. *Environ Health Perspect*. 1993 Oct;101(5):378-84. Review. [PMID: 8080506]
- Alexander BJ, Ames BN, Baker SM, et al. *Textbook of Functional Medicine*. Gig Harbor, WA: The Institute for Functional Medicine; 2010.
- Singleton DW, Khan SA. Xenoestrogen exposure and mechanisms of endocrine disruption. *Front Biosci*. 2003 Jan 1;8:s110-8. Review. [PMID: 12456297]
- Nadal A, Ropero AB, Laribi O, et al. Nongenomic actions of estrogens and xenoestrogens by binding at a plasma membrane receptor unrelated to estrogen receptor alpha and estrogen receptor beta. *Proc Natl Acad Sci U S A*. 2000 Oct 10;97(21):11603-8. [PMID: 11027358]
- Liska DJ. The detoxification enzyme systems. *Altern Med Rev*. 1998 Jun;3(3):187-98. Review. [PMID: 9630736]
- Krinsky DL, LaValle JB, Hawkins EB, et al. *Natural Therapeutics Pocket Guide*. 2nd ed. Hudson, OH: Lexi-Comp; 2003.
- Pradhan SC, Girish C. Hepatoprotective herbal drug, silymarin from experimental pharmacology to clinical medicine. *Indian J Med Res*. 2006 Nov;124(5):491-504. [PMID: 17213517]
- Suzuki YJ, Aggarwal BB, Packer L. Alpha-lipoic acid is a potent inhibitor of NFkappa B activation in human T cells. *Biochem Biophys Res Commun*. 1992 Dec 30;189(3):1709-15. [PMID: 1482376]
- Baur A, Harrer T, Peukert M, et al. Alpha-lipoic acid is an effective inhibitor of human immuno-deficiency virus (HIV-1) replication. *Klin Wochenschr*. 1991 Oct 2;69(15):722-4. [PMID: 1724477]
- Bhattacharya A. Methylselenocysteine: a promising antiangiogenic agent for overcoming drug delivery barriers in solid malignancies for therapeutic synergy with anticancer drugs. *Expert Opin Drug Deliv*. 2011 Jun;8(6):749-63. [PMID: 21473705]
- Shilo S, Pardo M, Aharoni-Simon M, et al. Selenium supplementation increases liver MnSOD expression: molecular mechanism for hepato-protection. *J Inorg Biochem*. 2008 Jan;102(1):110-8. [PMID: 17804075]
- Brown MD. Green tea (*Camellia sinensis*) extract and its possible role in the prevention of cancer. *Altern Med Rev*. 1999 Oct;4(5):360-70. Review. [PMID: 10559550]
- Shankar S, Ganapathy S, Srivastava RK. Green tea polyphenols: biology and therapeutic implications in cancer. *Front Biosci*. 2007 Sep 1;12:4881-99. Review. [PMID: 17569617]
- Ferrer P, Asensi M, Segarra R, et al. Association between pterostilbene and quercetin inhibits metastatic activity of B16 melanoma. *Neoplasia*. 2005 Jan;7(1):37-47. [PMID: 15736313]
- Jurenka JS. Anti-inflammatory properties of curcumin, a major constituent of *Curcuma longa*: a review of preclinical and clinical research. *Altern Med Rev*. 2009 Jun;14(2):141-53. [PMID: 19594223]
- Choi H, Chun YS, Shin YJ, et al. Curcumin attenuates cytochrome P450 induction in response to 2,3,7,8-tetrachlorodibenzo-p-dioxin by ROS-dependently degrading AhR and ARNT. *Cancer Sci*. 2008 Dec;99(12):2518-24. [PMID: 19018768]
- Shoba G, et al. Influence of piperine on the pharmacokinetics of curcumin in animals and human volunteers. *Planta Med*. 1998 May; 64 (4):353-6. [PMID: 9619120]
- Dalessandri KM, Firestone GL, Fitch MD, et al. Pilot study: effect of 3,3'-diindolylmethane supplements on urinary hormone metabolites in postmenopausal women with a history of early-stage breast cancer. *Nutr Cancer*. 2004;50(2):161-7. [PMID: 15623462]
- Kim EJ, Shin M, Park H, et al. Oral administration of 3,3'-diindolylmethane inhibits lung metastasis of 4T1 murine mammary carcinoma cells in BALB/c mice. *J Nutr*. 2009 Dec;139(12):2373-9. [PMID: 19864400]
- Bolton JL, Thatcher GR. Potential mechanisms of estrogen quinine carcinogenesis. *Chem Res Toxicol*. 2008 Jan;21(1):93-101. Review. [PMID: 18052105]
- Keum YS. Regulation of the Keap1/Nrf2 system by chemopreventive sulforaphane: implications of posttranslational modifications. *Ann N Y Acad Sci*. 2011 Jul;1229:184-9. Review. [PMID: 21793854]
- Boddupalli S, Mein JR, Lakkanna S, et al. Induction of phase 2 antioxidant enzymes by broccoli sulforaphane: perspectives in maintaining the antioxidant activity of vitamins A, C, and E. *Front Genet*. 2012;3:7. Epub 2012 Jan 24. [PMID: 22303412]
- Sulforaphane glucosinolate. Monograph. *Altern Med Rev*. 2010 Dec;15(4):352-60. Review. [PMID: 21194251] p. 352.

EXCLUSIVE • PATENTED

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XymoBolX™

Anabolic Amino Acid Complex*



Available in Natural Lemon & Natural Fruit Punch

Discussion

The amino acid (AA) formula that comprises XymoBolX was meticulously developed and studied by internationally recognized researchers in the fields of muscle metabolism and aging and longevity. Seventeen years of research have resulted in this particular blend of the nine essential amino acids (EAAs)—including the branched-chain amino acids leucine, isoleucine, and valine—plus arginine, proportioned in the most optimal ratios for muscle anabolism.^[1-22] XymoBolX is designed for both young and elderly individuals who are seeking to stimulate muscle protein synthesis, hasten muscle recovery, and promote muscle strength and function.*

Quality Not Quantity

Amino acids are potent stimulators of muscle protein synthesis in both the young and the elderly. Of the AAs, data indicate that EAAs are primarily responsible for this biological process.^[9] Moreover, studies demonstrate that there is no additional benefit to muscle protein synthesis from adding non-essential AAs to an EAA supplement.^[21] For instance, the addition of 22 g of non-essential AAs to 18 g of EAAs produced no additional benefit to net muscle balance when compared to the provision of 18 g of EAAs alone.^[21] Likewise, a 15 g EAA supplement—with the nine EAAs in similar ratios to XymoBolX—had twice the impact on muscle protein synthesis than that of an equal amount (15 g) of a high-quality protein.*^[14]

Why Include Arginine?

In healthy young adults, sufficient arginine can be synthesized to meet normal demands. However, during rapid growth or in response to stress, there are heightened needs for arginine that may not be fully met. Furthermore, there is evidence that arginine has a unique stimulatory effect on muscle protein synthesis. While all mechanisms have not been fully elucidated and are likely multifactorial, it is known that arginine converts to nitric oxide, which relaxes blood vessels and improves blood flow to muscles. Last, arginine availability influences its own catabolism and that of other amino acids by controlling ureagenesis. A critical finding that solidified the need to add arginine to the EAA formulation was that without it, plasma arginine decreases; therefore, the rate of protein synthesis is potentially reduced.*^[17]

Essential Amino Acids and Exercise

The effectiveness of EAA intake is amplified by ingestion before exercise

Clinical Applications

- » Supports Muscle Protein Synthesis in the Young and the Elderly*
- » Supports Muscle Recovery After Exercise*
- » Supports Muscle Strength and Function*

*XymoBolX™ represents a breakthrough in the use of amino acids for muscle protein synthesis. Over 20 human trials have been conducted to arrive at this specific, patent-pending combination of amino acids in the most effective, anabolic ratios. Whether you want to support muscle strength and function or prevent muscle loss associated with inactivity or aging, XymoBolX provides the right amino acids in the right ratios to help you meet your goals and stay healthy.**

because of the increased delivery of amino acids to the muscles.^[6,21] In fact, results from acute studies have shown that exercise and EAA intake have additive effects on muscle protein synthesis.^[17] Furthermore, branched-chain AAs (BCAAs), have been demonstrated to hasten post-exercise muscle recovery. Data show that BCAA (e.g., leucine) supplementation before and after exercise helps decrease exercise-induced muscle damage, promotes muscle protein synthesis, and modulates exercise-related cytokine production.^[23,24] For example, leucine-enriched EAA supplementation (total EAA was 10 g of which 1.85 g were leucine) prolonged the anabolic response and the sensitivity of skeletal muscle to AAs.^[25] Børsheim et al propose that over time, exercise will increase the beneficial effects of EAA supplementation on lean body mass and strength and improve functional parameters of muscles.*^[17]

Muscle Loss with Aging

Beginning in the fourth decade of life, there is a natural and gradual decline in muscle mass (catabolism), strength, and function as a result of the innate metabolic changes and the more sedentary lifestyle that accompany aging. Studies using EAA supplementation at doses of 6.7 to 45 g/d in advanced age, bed rest, and recovery from surgery have demonstrated important benefits. These benefits include stimulation of muscle protein synthesis, enhancements in muscle strength, and improvements in functional parameters of the studied muscle(s).*^[11,14,15,17,20,22]

In the Elderly

Protein supplements are often used to help ward off muscle-related losses in the elderly. According to Ferrando et al, "Increasing protein intake to 1.4 g/kg/d in the elderly with EAA supplementation indicates the potential for preserving muscle function."^[20] Because non-essential AAs are not as effective as EAAs for muscle anabolism, supplements containing significant calories in the form of non-essential AAs may be inadequate to maximize anabolic efficiency in the elderly.^[9] Furthermore, the elderly tend to use protein supplements as calorie substitutes and reduce their food intake.^[9,20] In these cases, it becomes critical that the AA supplement be low-calorie, so as not to influence satiety, and highly efficient to confer maximum benefits to skeletal muscle.^[20] A high proportion of leucine is another factor that is required for optimal stimulation of muscle protein synthesis in the elderly.^[15] Additionally, there is evidence that the presence of carbohydrates in a nutritional supplement for the elderly is not beneficial and may actually impair muscle anabolism.^[9,17] XymoBolX is a highly efficient blend of EAAs plus arginine that provides zero carbohydrates.*

XymoBoiX™ Natural Lemon Flavor Supplement Facts

Serving Size: 1 Scoop (about 6.8 g)
Servings Per Container: About 30

	Amount Per Serving	%Daily Value
Calories	5	
Sodium	60 mg	3%
L-Leucine	1,639 g	**
L-Lysine HCL	707.85 mg	**
L-Valine	450 mg	**
L-Isoleucine	436.5 mg	**
L-Arginine	405 mg	**
L-Threonine	382.5 mg	**
L-Phenylalanine	274.5 mg	**
L-Methionine	135 mg	**
L-Histidine	67.5 mg	**
L-Tryptophan	2.7 mg	**

** Daily Value not established.

Other Ingredients: Citric acid, malic acid, natural flavors (no MSG), sea salt, stevia, and riboflavin (for color).

DIRECTIONS: Dissolve one scoop (6.8 g) into 8-12 oz of room-temperature water and consume once per day between meals, or use as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

References

1. Biolo G, Fleming RY, Maggi SP, et al. Transmembrane transport and intracellular kinetics of amino acids in human skeletal muscle. *Am J Physiol.* 1995 Jan;268(1 Pt 1):E75-84. [PMID: 7840186]
2. Volpi E, Ferrando AA, Yeckel CW, et al. Exogenous amino acids stimulate net muscle protein synthesis in the elderly. *J Clin Invest.* 1998 May 1;101(9):2000-07. [PMID: 9576765]
3. Tipton KD, Gurkin BE, Matin S, et al. Nonessential amino acids are not necessary to stimulate net muscle protein synthesis in healthy volunteers. *J Nutr Biochem.* 1999 Feb;10(2):89-95. [PMID: 15539275]
4. Volpi E, Mittendorfer B, Wolf SE, et al. Oral amino acids stimulate muscle protein anabolism in the elderly despite higher first-pass splanchnic extraction. *Am J Physiol.* 1999 Sep;277(3 Pt 1):E513-20. [PMID: 10484364]
5. Volpi E, Sheffield-Moore M, Rasmussen BB, et al. Basal muscle amino acid kinetics and protein synthesis in healthy young and older men. *JAMA.* 2001 Sep 12;286(10):1206-12. [PMID: 11559266]
6. Tipton KD, Rasmussen BB, Miller SL, et al. Timing of amino acid-carbohydrate ingestion alters anabolic response of muscle to resistance exercise. *Am J Physiol Endocrinol Metab.* 2001 Aug;281(2):E197-206. [PMID: 11440894]
7. Børsheim E, Tipton KD, Wolf SE, et al. Essential amino acids and muscle protein recovery from resistance exercise. *Am J Physiol Endocrinol Metab.* 2002 Oct;283(4):E648-57. [PMID: 12217881]
8. Tipton KD, Børsheim E, Wolf SE, et al. Acute response of net muscle protein balance reflects 24-h balance after exercise and amino acid ingestion. *Am J Physiol Endocrinol Metab.* 2003 Jan;284(1):E76-89. [PMID: 12388164]
9. Volpi E, Kobayashi H, Sheffield-Moore M, et al. Essential amino acids are primarily responsible for the amino acid stimulation of muscle protein anabolism in healthy elderly adults. *Am J Clin Nutr.* 2003 Aug;78(2):250-58. [PMID: 12885705]
10. Paddon-Jones D, Sheffield-Moore M, Katsanos CS, et al. Differential stimulation of muscle protein synthesis in elderly humans following isocaloric ingestion of amino acids or whey protein. *Exp Gerontol.* 2006 Feb;41(2):215-59. [PMID: 16310330]
11. Paddon-Jones D, Sheffield-Moore M, Zhang XJ, et al. Amino acid ingestion improves muscle protein synthesis in the young and elderly. *Am J Physiol Endocrinol Metab.* 2004 Mar;286(3):E321-28. [PMID: 14583440]
12. Børsheim E, Aarsland A, Wolfe RR. Effect of an amino acid, protein, and carbohydrate mixture on net muscle protein balance after resistance exercise. *Int J Sport Nutr Exerc Metab.* 2004 Jun;14(3):255-71. [PMID: 15256687]
13. Katsanos CS, Kobayashi H, Sheffield-Moore M, et al. Aging is associated with diminished accretion of muscle proteins after the ingestion of a small bolus of essential amino acids. *Am J Clin Nutr.* 2005 Nov;82(5):1065-73. [PMID: 16280440]
14. Paddon-Jones D, Sheffield-Moore M, Urban RJ, et al. Essential amino acid and carbohydrate supplementation ameliorates muscle protein loss in humans during 28 days bedrest. *J Clin Endocrinol Metab.* 2004 Sep;89(9):4351-58. [PMID: 15356032]
15. Katsanos CS, Kobayashi H, Sheffield-Moore M, et al. A high proportion of leucine is required for optimal stimulation of the rate of muscle protein synthesis by essential amino acids in the elderly. *Am J Physiol Endocrinol Metab.* 2006 Aug;291(2):E381-87. [PMID: 16507602]
16. Fitts RH, Romatowski JG, Peters JR, et al. The deleterious effects of bed rest on human skeletal muscle fibers are exacerbated by hypercortisolemia and ameliorated by dietary supplementation. *Am J Physiol Cell Physiol.* 2007 Jul;293(1):C313-20. [PMID: 17409123]
17. Børsheim E, Bui QU, Tissier S, et al. Effect of amino acid supplementation on muscle mass, strength and physical function in elderly. *Clin Nutr.* 2008 Apr;27(2):189-95. [PMID: 18294740]
18. Børsheim E, Bui QU, Tissier S, et al. Amino acid supplementation decreases plasma and liver triacylglycerols in elderly. *Nutrition.* 2009 Mar;25(3):281-88. [PMID: 19041223]
19. Katsanos CS, Aarsland A, Cree MG, et al. Muscle protein synthesis and balance responsiveness to essential amino acids ingestion in the presence of elevated plasma free fatty acid concentrations. *J Clin Endocrinol Metab.* 2009 Aug;94(8):2984-90. [PMID: 19454587]
20. Ferrando AA, Paddon-Jones D, Hays NP, et al. EAA supplementation to increase nitrogen intake improves muscle function during bed rest in the elderly. *Clin Nutr.* 2010 Feb;29(1):18-23. [PMID: 19419806]
21. Wolfe RR. Skeletal muscle protein metabolism and resistance exercise. *J Nutr.* 2006 Feb;136(2):525S-28S. [PMID: 16424140]
22. Ferrando A, Bamman M, Schutzler H, et al. Increased nitrogen intake following hip arthroplasty expedites muscle strength recovery. *J Aging Res Clin Practice* 2013;2(4):369-75. [on file]
23. Negro M, Giardina S, Marzani B, et al. Branched-chain amino acid supplementation does not enhance athletic performance but affects muscle recovery and the immune system. *J Sports Med Phys Fitness.* 2008 Sep;48(3):347-51. [PMID: 18974721]
24. Matsumoto K, Koba T, Hamada K, et al. Branched-chain amino acid supplementation attenuates muscle soreness, muscle damage and inflammation during an intensive training program. *J Sports Med Phys Fitness.* 2009 Dec;49(4):424-31. [PMID: 20087302]
25. Dickinson JM, Gundermann DM, Walker DK, et al. Leucine-enriched amino acid ingestion after resistance exercise prolongs myofibrillar protein synthesis and amino acid transporter expression in older men. *J Nutr.* 2014 Nov;144(11):1694-702. [PMID: 25332468]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

XymoDine™

Supra-Dose Iodine



Available in 90 capsules

Discussion

Iodine is an essential trace element, recognized for its traditional role in thyroid hormone synthesis. Iodine is directly incorporated into thyroxine (T4) and the biologically active form of the thyroid hormone triiodothyronine (T3). Thyroid hormones regulate metabolism and energy production throughout the body and, in turn, affect core body temperature, growth, reproduction, protein synthesis (including the formation of hair and skin), and neuromuscular function.*^[1,2]

In addition to its well-known role in thyroid health, iodine has antioxidant activity, and it plays a critical role in intellectual development, endocrine function, and breast and reproductive system health.^[2-8] Approximately 15-20 mg of iodine is concentrated in the thyroid and thyroid hormones, while 70% of the body's iodine is distributed in other tissues, including the mammary glands, ovaries, eyes, gastric mucosa, cervix, and salivary glands.*^[3,8,9]

Sources of Iodine

Iodine must be obtained from the diet or in supplement form. Iodine intake through seaweed consumption, such as in Japanese populations, is naturally higher than in other populations. Current estimates put Japanese daily intake of iodine from seaweed at 1-3 mg/d^[10]; but previous estimates have been much higher, such as 5.3-13.8 mg/d, and even as high as 50-80 mg/d.^[2,3] In other regions, the iodine content of food is dependent upon the presence and availability of iodine in the soil in which food is grown. In many countries, table salt and cattle feed have been fortified with iodine to help consumers meet minimum intake requirements. For instance, universal salt iodization was instituted to reduce the prevalence of goiter.^[11] It is interesting to note that over the last 25 years, the consumption of (iodized) table salt by US citizens has decreased by 65% as a result of people trying to reduce their sodium intake for health reasons.*^[2]

Iodine Sufficiency

Iodine sufficiency is a controversial topic. The US RDI for iodine is 150 mcg/d for adults, which governing bodies consider to be adequate. The tolerable upper limit is set at 1 mg/d. Among functional medicine practitioners, there is no consensus on the actual human requirement

Clinical Applications

- » Supports a Healthy Synthesis of Thyroid Hormones*
- » Helps Maintain Healthy Breast Tissue*

*XymoDine™ is a superior iodine formulation created to enhance thyroid support and offer long-term, consistent results. XymoDine contains the ideal balance of potassium iodide and molecular iodine (I₂).**

for iodine sufficiency. Some believe that individual iodine requirements hinge upon the exposure to or consumption of goitrogens—substances in food or the environment that interfere with iodine utilization or thyroid hormone production. Examples of goitrogens include toxic halides (fluoride and bromide), organochlorides, perchlorates, cabbage, Brussels sprouts, soybean isoflavones, and several other foods.*^[1]

According to some iodine experts, the requirement of the whole human body for iodine is about 14 mg/d or more (6 mg/d needed for the thyroid gland, the rest for extra-thyroidal tissues).^[12] Although there is not a consensus, many experts agree that the focus of sufficiency cannot reside solely with the thyroid, but rather it must address *whole body* sufficiency.*^[2]

Doses ranging from 3 mg/d up to 50 mg/d have been used successfully in clinical practice.^[2,11,13] It is postulated that intakes that reflect those of seaweed-consuming Japanese would come closer to meeting whole body sufficiency. Furthermore, it is a little-known fact that under certain circumstances, high doses of potassium iodide (up to 130 mg) can be used to saturate the thyroid and protect it in the event of a nuclear accident.*^[14]

Breast Health

Next to the thyroid gland, the breasts and ovaries concentrate the most iodine.^[3,9] The relationship between breast health and iodine levels has been reported on for decades, and it has been proposed that inadequate iodine prohibits normal breast architecture to develop.^[11] Moderately high doses of supplemental iodine have been used to promote breast comfort after animal and human studies suggested that such a protocol would have positive effects. A randomized, double-blind, placebo-controlled, multicenter clinical trial (N = 111) investigated the effect of supraphysiologic doses of iodine on breast health in women with normal thyroid function. The 3 and 6 mg/d doses resulted in significant improvement in breast comfort.^[5] According to Ghent et al, certain breast tissue “reacts differently to sodium iodide, protein-bound iodide and molecular iodine. Molecular iodine is nonthyrotropic and was the most beneficial.”^[4] It is important to note that individuals with a history of autoimmune thyroid pathologies were excluded from the study.*

Continued on next page

XymoDine™ Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	%Daily Value
Iodine (7500 mcg as potassium iodide and 5000 mcg as molecular iodine)	12,500 mcg	8333%

Other Ingredients: Microcrystalline cellulose, HPMC (capsule), silica, magnesium stearate, and sodium copper chlorophyllin.

DIRECTIONS: Take one capsule daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, corn, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

**Iodine Supplementation**

Supplemental iodine has been found to be safe and well-tolerated in the inorganic, non-radioactive iodine/iodide form.^[12] XymoDine reflects the forms and ratios of iodine found in Lugol's solution—a liquid combination of molecular iodine and potassium iodide that has been safely and effectively employed since 1829.^[3,15,16] XymoDine provides 12.5 mg of iodine per capsule, with a breakdown of 5 mg of molecular iodine and 7.5 mg of potassium iodide. The provision of 12.5 mg of iodine per capsule allows healthcare practitioners to easily titrate iodine dosage as required. Due to the “high-potency” dose of iodine in XymoDine, individuals should consult their healthcare practitioner prior to use regarding any medical conditions, including thyroid conditions, and any possible interactions with medications. High doses should be monitored by a knowledgeable healthcare professional.*

Testing is an important aspect of supra-dose iodine supplementation and should guide the use of iodine in mg doses. Experts use spot/urine testing and load testing with subsequent (24/h) urine analysis to help determine iodine need and sufficiency.*

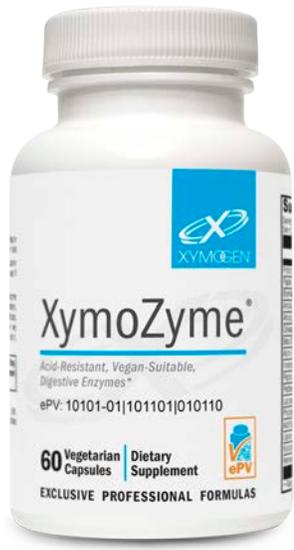
References

1. Linus Pauling Institute: Micronutrient Information Center. Iodine. <http://lpi.oregonstate.edu/infocenter/minerals/iodine/#safety>. Accessed March 19, 2015.
2. Miller D. Extrathyroidal benefits of iodine. *Journal of American Physicians and Surgeons*. 2006;11(4):106-10. <http://www.jpands.org/vol11no4/millerd.pdf>. Accessed March 17, 2015.
3. Patrick L. Iodine: deficiency and therapeutic considerations. *Altern Med Rev*. 2008 Jun;13(2):116-27. [PMID: 18590348]
4. Ghent WR, Eskin BA, Low DA, et al. Iodine replacement in fibrocystic disease of the breast. *Can J Surg*. 1993 Oct;36(5):453-60. [PMID: 8221402]
5. Kessler JH. The effect of supraphysiologic levels of iodine on patients with cyclic mastalgia. *Breast J*. 2004 Jul-Aug;10(4):328-36. [PMID: 15239792]
6. Stadel BV. Dietary iodine and risk of breast, endometrial, and ovarian cancer. *Lancet*. 1976 Apr 24;1(7965):890-91. [PMID: 58152]
7. Cann SA, van Netten JP, van Netten C. Hypothesis: iodine, selenium and the development of breast cancer. *Cancer Causes Control*. 2000 Feb;11(2):121-27. [PMID: 10710195]
8. Natural Medicines: Iodine. <https://naturalmedicines.therapeuticresearch.com/databases/food,-herbs-supplements/professional.aspx?productid=35>. Accessed March 20, 2015.
9. Iodine and the body. Iodine Research Web site. <http://iodineresearch.com/ovaries.html>. Accessed March 30, 2015.
10. Zava TT, Zava DT. Assessment of Japanese iodine intake based on seaweed consumption in Japan: A literature-based analysis. *Thyroid Res*. 2011 Oct 5;4:14. [PMID: 21975053]
11. Brownstein D. Clinical experience with inorganic non-radioactive iodine/iodide. http://www.optimox.com/pics/Iodine/IOD-09/IOD_09.htm. Accessed March 17, 2015.
12. Abraham GE. Orthoiodosupplementation: iodine sufficiency of the whole human body. http://www.optimox.com/pics/Iodine/IOD-02/IOD_02.htm. Accessed March 17, 2015.
13. Flechas JD. Orthoiodosupplementation in a primary care practice. http://www.optimox.com/pics/Iodine/IOD-10/IOD_10.htm. Accessed March 18, 2015.
14. Frequently asked questions on potassium iodide (KI). US Food and Drug Administration Web site. <http://www.fda.gov/drugs/EmergencyPreparedness/bioterrorismdrugpreparedness/ucm072265.htm>. Updated October 27, 2014. Accessed January 22, 2013.
15. Abraham GE. The safe and effective implementation of orthoiodosupplementation in medical practice. *The Original Internist*. 2004; 11:17-36. [On file]
16. Abraham GE, Flechas JD, Hakala JC. Optimum levels of iodine for greatest mental and physical health. *The Original Internist*. 2002;9:5-20. [On file]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.



Available in 60 capsules and 120 capsules

Discussion

Digestion Food must be broken down into its component parts in order to be absorbed into the bloodstream. Though salivary secretions, chewing, gastric acid, and pepsin begin the process of digestion, the majority of digestion takes place farther down the gastrointestinal tract in the small intestine. Once food leaves the stomach and enters the small intestine, digestive enzymes begin the monumental task of turning it into the building blocks and fuel that the body needs for structural support and metabolic processes. Digestive enzymes are produced primarily in the pancreas and brush border of the small intestine, and the health and function of these organs is vital to effective digestion and absorption. Proteolytic enzymes, amylases, and lipases are responsible for the digestion of proteins, carbohydrates, and fats. The complete digestion of these macronutrients produces small peptides, amino acids, monosaccharides and disaccharides, and free fatty acids that can easily pass through the intestinal microvilli and enter the bloodstream. Healthy digestion assures that incompletely digested molecules and proteins don't enter the bloodstream where they may be recognized as "foreign" by a vigilant immune system.*^[1,2]

Pancreatic and Intestinal Enzymes Pancreatic production of proteases, amylases, and lipases is complemented by intestinal production of lactase, maltase, sucrase, enterokinase, and various peptidases, highlighting the importance of the pancreas and the intestines in the digestive process. The enzyme lactase is required to break down lactose into glucose and galactose before the intact lactose can draw excess water into the bowel, and before colonic bacteria can break it down into volatile gases and acids. Though lactose (a disaccharide found only in mammals' milk) is readily digested by most infants, normal production decreases as a child is weaned onto whole foods and may eventually cease in adulthood. Exogenous administration of lactase can support lactose digestion effectively and allow for continued consumption of milk-based products.^[3,4] Maintaining a healthy gastrointestinal flora helps support brush border function and digestive capacity as well.*^[5]

Clinical Applications

- » Supports Healthy Digestion of Macronutrients and Enhances Nutrient Absorption*
- » Supports Breakdown of Polysaccharides in Beans and Cruciferous Vegetables*
- » Helps Support Pancreatic and Brush Border Enzyme Function*
- » Supports Breakdown of Lactose*

*XymoZyme® is a cost-effective, non-prescription, broad-spectrum, digestive enzyme formula suitable for vegans and designed to support the digestion of fat, protein, carbohydrate, fiber, and lactose. This comprehensive formula contains lipase, proteases, alpha-galactosidase, hemicellulase, papain, lactase, and other key digestive enzymes. XymoZyme works in a wide pH range—unlike porcine pancreatin, which works in a narrow pH range.**

Digestion of Plant-Based Compounds XymoZyme contains several principle digestive enzymes as well as a complement of enzymes designed to break down plant compounds and fibers that humans would otherwise be unable to digest. Raffinose and melibiose, carbohydrates commonly found in legumes, can be broken down by the intestinal enzyme alpha-galactosidase. In the absence of this enzyme, these carbohydrates pass into the large intestine, where microbes can ferment them and produce volatile gases. Exogenous administration of alpha-galactosidase, present in XymoZyme, supports the digestion of these plant-based compounds and has been used safely and effectively.^[6,7] Beta-glucanase, hemicellulase, pectinase, xylanase, and dipeptidyl peptidase (DPPIV) are also present and improve the digestibility of plant-based foods by breaking down plant cell walls, fibers, and proteins. Phytase is present to facilitate the breakdown of indigestible phytates from grains and seeds, and release phosphorus, calcium, inositol, and other nutrients for absorption. Bromelain and papain offer additional support for protein digestion. The enzyme invertase catalyzes sugar to glucose and fructose.*

XymoZyme incorporates amylase, lipase, proteases, hemicellulase, bromelain, papain, lactase, DPPIV, and other key digestive enzymes to provide a comprehensive formulation that functions in a wide pH range to support and facilitate healthy digestion. It has been formulated to allow flexible dosing that can be adjusted for individual needs.*

XymoZyme® Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Protease (pH 3.0-9.0)	120,000 HUT	**
Papain (from papaya)	50,000 TU	**
Bromelain (from pineapple)	120 GDU	**
Amylase	4,000 SKB	**
Amyloglucosidase (glucoamylase)	30 AG	**
Cellulase	4,000 CU	**
Beta-Glucanase	50 BGU	**
Alpha-Galactosidase	400 GAL	**
Invertase	2,000 Sumner	**
Peptidase (29 DPPIV)	2,400 HUT	**
Pectinase	70 Endo PG	**
Lactase	700 ALU	**
Phytase	20 U	**
Acid Stable Protease (pH 2.0-3.5)	400 HUT	**
Lipase	1,200 FIP	**
Xylanase	300 XU	**
Hemicellulase	200 HCU	**
** Daily Value (DV) not established.		

Other Ingredients: HPMC (capsule), microcrystalline cellulose, stearic acid, magnesium stearate, and silica.

DIRECTIONS: Take one to two capsules daily, or use as directed by your healthcare practitioner. If necessary, capsules may be opened and contents sprinkled over food.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, or artificial sweeteners.

Maltodextrin (derived from corn) is used to standardize enzyme activity.

**References**

1. Bland J, Liska D, Jones DS, et al. *Clinical Nutrition A Functional Approach*. 2nd ed. Gig Harbor, WA: The Institute for Functional Medicine. 2004.
2. Whitcomb DC, Lowe ME. Human pancreatic digestive enzymes. *Dig Dis Sci*. 2007 Jan;52(1):1-17. Review. [PMID: 17205399]
3. Sanders SW, Tolman KG, Reitberg DP. Effect of a single dose of lactase on symptoms and expired hydrogen after lactose challenge in lactose-intolerant subjects. *Clin Pharm*. 1992 Jun;11(6):533-8. [PMID: 1534729]
4. Heyman MB; Committee on Nutrition. Lactose intolerance in infants, children, and adolescents. *Pediatrics*. 2006 Sep;118(3):1279-86. Review. [PMID: 16951027]
5. Zaouche A, Loukil C, De Lagausie P, et al. Effects of oral *Saccharomyces boulardii* on bacterial overgrowth, translocation, and intestinal adaptation after small-bowel resection in rats. *Scand J Gastroenterol*. 2000 Feb;35(2):160-5. [PMID: 10720113]
6. Di Stefano M, Miceli E, Gotti S, et al. The effect of oral alpha-galactosidase on intestinal gas production and gas-related symptoms. *Dig Dis Sci*. 2007 Jan;52(1):78-83. [PMID: 17151807]
7. Ganiats TG, Norcross WA, Halverson AL, et al. Does Beano prevent gas? A double-blind crossover study of oral alpha-galactosidase to treat dietary oligosaccharide intolerance. *J Fam Pract*. 1994 Nov;39(5):441-5. [PMID: 7964541]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Zinc Glycinate

Proprietary Zinc Formula

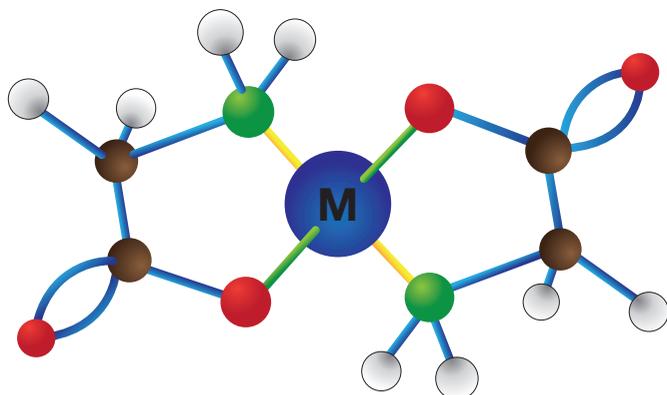


Available in 120 capsules

Discussion

Zinc is an essential trace mineral and serves important roles in the body. More than 300 enzymes depend on zinc for their normal activities in cellular metabolism. As a cofactor, zinc participates in carbohydrate and protein metabolism as well as copper-zinc superoxide dismutase (CuZnSOD) antioxidant activity. Zinc's role in supporting immune function includes regulating T lymphocytes, natural killer cells, CD4 cells, and interleukin II.^[1] A review of the research suggests that "zinc supplementation can significantly reduce the morbidity and mortality of apparently well-nourished children and shorten the time to recovery from acute [health problems]."^{*[2]}

Zinc's pivotal role in protein metabolism translates into a pivotal role in wound healing, DNA synthesis, normal inflammatory response, and normal growth and development during childhood, adolescence, and pregnancy.^[3] Zinc helps maintain the structural integrity of cell membranes; it assists them in their normal function and protects them from oxidative damage.^[4] Research in human subjects of various ages suggests that zinc supplementation decreases oxidative stress markers, supports a normal response to inflammation, and appears to



Zinc Bisglycinate Courtesy of Albion Laboratories, Inc.

Clinical Applications

- » Supports Enzymatic Reactions and Protein Metabolism*
- » Promotes Immune and Reproductive Health*
- » Supports Antioxidant Activity*
- » Plays a Role in Sensory Perception*

***Zinc Glycinate** is a fully reacted, proprietary TRAACS® amino acid chelate formulated for enhanced absorption. As an essential mineral, zinc serves catalytic, structural, and regulatory functions in the body. Zinc ultimately supports immune and neurological function, growth, taste acuity, nutrient metabolism, and reproductive health.**

be a factor in balancing TH1 and TH2 immune cell activity.^[5,6] Skin and mucous membranes also depend on zinc for their maintenance and integrity.^{*[3,7]}

Zinc and vitamin A have a fundamental relationship as zinc is required for synthesis of retinol-binding protein—the protein that transports vitamin A in the blood. Zinc is also essential to the production of an enzyme that converts vitamin A to one of its active forms, and this helps support vitamin A's vital role in night vision.^[4] Zinc supports healthy vision in general, especially as we age.^[8] Zinc's role in sensory perception extends not only to vision but also to normal taste and smell acuity.^{*[1,4,5,9]}

Zinc is highly concentrated in the liver, pancreas, kidneys, bone, muscles, eyes, prostate gland, sperm, skin, hair, and nails.^[1] The mineral is required for sperm maturation and fetal development. The endocrine system relies on adequate zinc status to assist in the regulation of insulin activity and the conversion of thyroxine (T4) to the active thyroid hormone triiodothyronine (T3).^[1] Zinc's regulatory role extends to gene expression, cell signaling, and nerve impulse transmission, as well as normal apoptosis.^{*[4]}

The body has no specialized system for storing zinc, so daily intake and absorption is essential.^[3] Phytates—elements found in plant-based, high-fiber foods—can bind minerals (including zinc) and inhibit their absorption. Therefore, the bioavailability of dietary zinc may be compromised.^[8] Other minerals, including iron, calcium, and copper, can interfere with zinc absorption, further affecting zinc nutrition.^[4] Gastrointestinal and urinary zinc losses should be considered as well. Assessment of overall zinc status must take into account not only intake but also absorption and retention. Zinc Glycinate—an Albion® TRAACS amino acid chelate—is a high-potency source of zinc formulated for enhanced absorption. In this form, zinc is coupled with two glycine molecules to facilitate its absorption across the intestinal wall and reduce interference from phytates and competing minerals.^{*[10]}

Zinc Glycinate Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%Daily Value
Zinc (as TRAACS® zinc bisglycinate chelate)	20 mg	182%

Other Ingredients: Microcrystalline cellulose, HPMC (capsule), stearic acid, magnesium stearate, and silica.

DIRECTIONS: Take one capsule daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

DOES NOT CONTAIN: Wheat, gluten, corn, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.



TRAACS® and the Albion Gold Medallion design are registered trademarks of Albion Laboratories, Inc.

**References**

1. Pelton R, LaValle JB, Hawkins EB, et al. *Drug-Induced Nutrient Depletion Handbook*. 2nd ed. Hudson, OH: LexiComp, Inc. 2001.
2. Cuevas LE, Koyanagi A. Zinc and infection: a review. *Ann Trop Paediatr*. 2005 Sep;25(3):149-60. [PMID: 16156979]
3. Dietary Supplement Fact Sheet: Zinc. Office of Dietary Supplements, National Institutes of Health. <http://ods.od.nih.gov/factsheets/ZincHealthProfessional/>. Updated September 20, 2011. Accessed July 24, 2012.
4. Linus Pauling Institute. Zinc. <http://lpi.oregonstate.edu/infocenter/minerals/zinc/>. Updated March 14, 2011. Accessed July 24, 2012.
5. Prasad AS. Zinc in human health: effect of zinc on immune cells. *Mol Med*. 2008 May-Jun;14(5-6):353-7. Review. [PMID: 18385818]
6. Beck FW, Prasad AS, Kaplan J, et al. Changes in cytokine production and T cell subpopulations in experimentally induced zinc-deficient humans. *Am J Physiol*. 1997 Jun;272(6 Pt 1):E1002-7. [PMID: 9227444]
7. Schwartz JR, Marsh RG, Draelos ZD. Zinc and skin health: overview of physiology and pharmacology. *Dermatol Surg*. 2005 Jul;31(7 Pt 2):837-47; discussion 847. Review. [PMID: 16029676]
8. Prasad AS. Discovery of human zinc deficiency: 50 years later. *J Trace Elem Med Biol*. 2012 Jun;26(2-3):66-9. [PMID: 22664333]
9. Stewart-Knox BJ, Simpson EE, Parr H, et al. Zinc status and taste acuity in older Europeans: the ZENITH study. *Eur J Clin Nutr*. 2005 Nov;59 Suppl 2:S31-6. [PMID: 16254578]
10. Zinc: A Mineral of Complex Biological Activity. Albion Human Nutrition Research Notes. 2004 Mar;13(1):1-3. <http://www.albionhumannutrition.com/search?searchword=zinc+2004+March&ordering=newest&searchphrase=all&limit=50>. Accessed July 24, 2012.

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.