

LIPOSOMAL



ERGO-THIONE+

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Ergo-Thione+ is a masterful liposomal formulation of the endogenous and exogenous water-soluble antioxidants ergothioneine, glutathione, vitamin C, and selenium from methylselenocysteine. Each compound works independently and in concert with one another via a network of antioxidant, detoxification, and repair enzymes of the glutathione, thioredoxin, and ascorbate systems.

Ergothioneine, a naturally occurring sulfur-containing amino acid, serves as the hub, connecting the other antioxidants in the formula, and has an extremely unique ability to function "on-demand", concentrating in damaged tissues. It is able to quench oxidative stress when physiologic needs arise without shutting down necessary pro-oxidant signaling.



Supplement Facts

Serving Size: 5 mL (1 tsp.) Servings Per Container: 20	Amount Per Serving	% Daily Value
Vitamin C (as Sodium Ascorbate)	600 mg	667%
Selenium (as Methylselenocysteine)	150 mcg	273%
Sodium	65 mg	3%
L-Ergothioneine	20 mg	**
Opitac™ Glutathione	200 mg	**
Phosphatidylcholine (from purified sunflower seed lecithin)	260 mg	**

**Daily Value not established

Other Ingredients: Glycerin, water, ethanol, tocopherol, natural flavorings, natural citrus oils

EDUCATION

The human body has multiple sophisticated antioxidant, detoxification, and repair systems woven together in a network supersystem. Numerous antioxidant defenses including vitamin C, selenium, glutathione, ergothioneine, vitamin E, and CoQ10 come together synergistically to manage oxidative stress and are critical components in the finely tuned balance of a healthy antioxidant system.¹

ERGOTHIONEINE

Ergothioneine is a naturally occurring, sulfur-containing, thiohistidine betaine amino acid that is readily absorbed and stored in most, if not all, tissues of the body. It is one of the few molecules which can cross the blood-brain barrier.² Ergothioneine plays a prominent role in the antioxidant network; in particular, evidence shows that it increases glutathione levels and in turn, glutathione reverses the oxidation of ergothioneine.^{3,4,5} This is of particular significance, given that glutathione turns over very rapidly; with some stressors its levels fall up to 90% in minutes. Multiple mechanisms do exist to regenerate glutathione, but with major tissue insults, these are heavily taxed and ergothioneine may afford a more stable mode of cellular protection. Remarkably, it is not metabolized to any notable extent, and the half-life of dietary ergothioneine is approximately one month.⁶

Antioxidant and Cytoprotective Effects

Ergothioneine has potent antioxidant activity against hydroxyl, peroxy and peroxynitrite radicals, as well as activated oxygen species.^{7,8} It also helps maintain glutathione levels in the liver and kidneys.⁹ A very unique attribute of this antioxidant is that it does not impede normal oxidative cell signaling. For example, administration of ergothioneine to young healthy individuals

indicated that ergothioneine is not a primary defense against oxidative stress, but instead acts as a secondary antioxidant buffer whenever the redox homeostasis is disturbed and/or when primary antioxidants are depleted through chronic exposure to oxidative stress.¹⁰ This is consistent with earlier animal studies demonstrating that ergothioneine does not interfere with the important roles of ROS/RNS in healthy tissues, but does answer the call when oxidative damage becomes excessive due to tissue injury, toxin exposure or disease.² This may be a deliberate, adaptive cytoprotective mechanism to minimize oxidative damage which could contribute to further injury.^{2,11}

The antioxidant properties and cytoprotective benefits of ergothioneine prove to be vast. It supports the cardiovascular system by protecting the endothelium via scavenging of reactive oxygen/nitrogen species and increasing glutathione and nitric oxide, among other mechanisms.¹² It also protects the endothelium from insults such as high glucose or oxidized-LDL exposure.^{13,14,15}

Hyperglycemia has a pro-oxidant effect on the vascular endothelium and ergothioneine exerts a beneficial effect through the upregulation of SIRT expression and downregulation of NF- κ B signaling.¹⁶ Ergothioneine may also protect the liver and kidneys from the negative impact of elevated blood glucose.¹⁷

Research also shows that ergothioneine supplementation decreases TNF- α , IL-1 β , and IL-6, among others, to support a healthy inflammatory response.^{12,18}

Activates Major Longevity Pathways

In addition to its antioxidant effects, ergothioneine is reported to have anti-senescence, anti-inflammatory, and anti-neurodegenerative properties via impacts on major longevity signaling pathways.¹⁹ Unfortunately, not only do blood levels of ergothioneine decline with age,^{20,21,22} but they are also significantly decreased in individuals with a variety of age-related disorders, suggesting that lower blood levels of ergothioneine could be a risk factor for age-related disorders making supplementation beneficial.²³ Interestingly, ergothioneine has been proposed as a “longevity vitamin” due to its presence in almost all human cell and tissue types.²⁴ To this end, there is increasing evidence suggesting that ergothioneine is positively correlated with healthy aging and longevity.²⁵

Neuroprotection

Ergothioneine is found in high levels in the brain, suggesting a neuroregulatory function. Research has found that concentrations of this amino acid are lower in patients with cognitive impairment, neurologic degeneration, and frailty than in healthy subjects. The neuroprotective effect of ergothioneine may stem from promotion of neurogenesis, induction of neurotrophic factors, promotion of neuronal maturation, antioxidant and anti-inflammatory effects, and protection against various neurotoxins.^{26,27} A recent RCT in humans showed that 5 mg/day of ergothioneine enhanced memory and cognitive function.²⁸

Mitochondrial Function

SIRT3 is an enzyme which is involved in almost all aspects of mitochondrial metabolism and homeostasis, protecting mitochondria from a variety of damage and functioning in metabolism regulation, modulating inflammation, inhibition of oxidative stress, and regulation of apoptosis and autophagy.²⁹ Ergothioneine has been shown to activate the SIRT3 pathway.³⁰

Recently, ergothioneine was shown to improve aerobic exercise performance (duration and speed) in mice. This outcome was not only due to antioxidant effects, but also to improvement in mitochondrial respiration and increased generation of ATP. Remarkably, ergothioneine generated these effects without impairing mitochondrial recovery. It simultaneously reduced metabolic stress, inflammation, and oxidative stress in muscle tissue, and improved post-exercise muscle recovery.³¹

Improves Sleep Architecture

A final – but vital – application in which ergothioneine demonstrates positive effects is sleep. A double-blind, randomized controlled clinical trial in people with reported high anxiety and sleep complaints demonstrated that 20 mg/day of ergothioneine significantly improved subjective and objective sleep difficulties.³² Specifically, it improved sleep architecture and reduced the frequency of waking after sleep onset. A daily dose of ergothioneine improved sleeping difficulty regardless of timing of ingestion, which offers a unique advantage over other compounds typically used to improve sleep.

GLUTATHIONE

Glutathione is well known as our master antioxidant and is present in every single cell of the body. Glutathione offers comprehensive, broad-spectrum antioxidant protection, binding to a wide array of damaging molecules.³³

Glutathione is a key mitochondrial antioxidant, providing essential protection to the energy powerhouses of our cells.³⁴ It

is critical to our immune system function, helps dampen inflammation, is a key player in autoimmunity, and may confer protection from multiple disease states.^{34,35,36,37,38}

Studies reveal that daily liposomal administration of glutathione is effective at elevating stores of glutathione and impacting immune function, including elevating natural killer (NK) cell cytotoxicity by up to 400% and elevating lymphocyte proliferation by up to 60%.³⁹

Like ergothioneine, glutathione may also provide protection for the heart and brain. Glutathione is the most abundant antioxidant in the heart and lowered levels play an important role in the development of common cardiovascular conditions.⁴⁰ Neurodegenerative conditions are linked to increased mitochondrial oxidative stress and lowered levels of mitochondrial glutathione.⁴¹ The increased oxidative stress noted in mild cognitive impairment and neurodegenerative conditions has been attributed to lowered levels of glutathione in the brain.^{41,42}

VITAMIN C

Vitamin C is a powerful water-soluble nutrient with pleiotropic functions; it fortifies the body against oxidative stress, boosts endogenous levels of glutathione,⁴³ regulates immunity, modulates inflammation, and serves as a cofactor in the biosynthesis of connective tissue, among many other roles.

Emerging research indicates a link between vitamin C status and cognitive function, with a significant association between plasma vitamin C concentration and performance on tasks involving attention, focus, and working memory.⁴⁴ The brain is also highly vulnerable to damage from free radicals and the antioxidant activities of vitamin C play a critical role in protecting delicate brain tissue from such damage, thereby inhibiting harmful brain oxidative stress.⁴⁵

Vitamin C at doses greater than 500 mg per day has been found to support blood vessel integrity and combat vascular free radical damage, improving endothelial function.^{46,47}

Vitamin C also harmonizes with ergothioneine in providing additional protection from oxidative stress induced by hyperglycemia.⁴⁸

SELENIUM (AS METHYLSELENOCYSTEINE)

Selenium is a trace mineral with diverse functions throughout the body. Methylselenocysteine, a form prevalent in many foods including Allium, Brassica, and Astragalus species, is a less bio-accumulating form of selenium. It is an essential cofactor for antioxidant enzymes which protect cells from oxidative damage⁴⁹ and are essential for cell growth and survival.⁵⁰ Within the overlapping antioxidant systems, selenium is required as a cofactor and is interconnected with vitamin C and ergothioneine.⁵¹

This micronutrient also plays a role in brain health and cognitive function. Decreased antioxidant system function is related to cognitive decline, and deficiency of selenium may contribute to cognitive decline among aging people.⁵²

Selenium supplementation improved markers of oxidative stress and cognitive test improvement in individuals with mild cognitive impairment; similarly, improvement in selenium levels and mini-mental score was also observed in patients with neurodegenerative conditions.⁵³

Selenium dovetails with ergothioneine and glutathione in providing mitochondrial protection: optimal plasma selenium levels may be important to minimize chronic exercise-induced oxidative effects and mitochondrial changes.⁵⁴

Quicksilver Delivery Systems® improve upon liposomal and emulsification technology with smaller, more stable particles made from the highest-grade ingredients available. In addition to exceptional absorption rates, these tiny liposomal and nanoemulsified particles increase diffusion across mucus membranes, enhance lymphatic circulation of nutrients and support cellular delivery.