

Benfotiamine 150 + Alpha-Lipoic Acid 300

**Doctor's
BEST**

Science-Based Nutrition™



INGREDIENTS

Alpha-lipoic acid is a sulfur-containing fatty acid that performs vitamin-like roles in the body. Also known as thioctic acid or simply lipoic acid (LA), this compound functions as a coenzyme in the metabolism of carbohydrates, and was originally thought to belong to the B vitamin family.¹ LA is required for synthesis of acetyl CoA, a pivotal metabolite in the cellular process of transforming glucose (blood sugar) into energy. Since amounts of alpha-lipoic acid in supplements are up to 1000 times greater than the amounts of LA that could be obtained by diet, supplemental LA can introduce physiologic actions that food alone would not bestow.^{2,3} An intensively researched compound, alpha-lipoic acid taken orally is thought to go beyond its role as a metabolic cofactor and instead elicit a unique set of biochemical activities that can safely enhance many areas of health.⁴

Benfotiamine is a synthetic derivative of thiamin that has been shown in many studies to be far more bioavailable than actual thiamin.^{5,6} Benfotiamine taken orally is readily absorbed at higher doses, which is in sharp contrast to regular water-soluble forms of thiamin that exhibit a rapid decline in absorption when taken in doses above 5 mg.⁷ Human and rodent studies indicate that benfotiamine can greatly improve thiamin status, especially in comparison with regular forms of thiamin.⁸

BENEFITS

Recycles antioxidant nutrients such as Vitamin C and Vitamin E*

Comprehensive support against oxidative stress*

An ideal antioxidant would have the ability to quench a variety of free radical types, to neutralize free radicals in both watery and fatty environments, to bind (chelate) metal ions that can generate free radicals, and to recycle other antioxidants found in the body.⁹ Since alpha-lipoic acid meets all of these criteria, it was termed "the universal antioxidant."¹⁰ In the body, LA can be converted (reduced) to DHLA, or dihydrolipoic acid, a potent mitochondrial antioxidant. Unlike antioxidants such as glutathione, both the oxidized and reduced forms of LA are powerful antioxidants. DHLA is a crucial component of the "antioxidant network" that ties together interac-

tions between glutathione, ubiquinol (coenzyme Q10), vitamins C & E, and alpha-lipoic acid.¹¹ Together, these antioxidants work as a team. DHLA is responsible for regenerating vitamin C, which in turn recycles vitamin E; it also converts glutathione from its oxidized form back into its radical-scavenging reduced form, as well as being able to regenerate CoQ10.

The LA/DHLA pair is recognized as one of the most powerful biological antioxidant systems and is integral in a strategy to answer oxidative stress (the varying oxidative load that holds sway over diverse aspects of health and aging in general). Proving that benefits are tangible, a randomized, placebo-controlled, double-blinded trial of parallel design showed that 400 mg of LA taken orally for 4 weeks significantly decreased oxidative stress (as measured by the concentration of circulating reactive oxygen metabolites).¹² Prior to this was the ISLAND Study, in which 300 mg of LA taken orally for 4 weeks was shown to support endothelial function (in this case, vascular tone: specifically, relaxation of blood vessel walls) and markers of oxidative stress.¹³ Beyond bolstering glutathione and directly scavenging radicals, LA is also thought to enhance the defense system against oxidative stress via the activation of cell signaling pathways, enhancing the activation of anti-oxidative genes.¹⁴

Benfotiamine displays direct antioxidant action in vitro, and preliminary research with human subjects suggests that this activity can be advantageous in helping to safeguard the integrity of human DNA by increasing the antioxidant capacity of plasma.¹⁵ In the laboratory, when human, rat, and porcine kidney cells were exposed to toxins that assault the integrity of DNA, benfotiamine was able to reduce oxidative stress under these circumstances.¹⁶ Benfotiamine, like vitamins C and E, can deter the activation of NF-κB (a DNA-binding factor known to be activated by oxidative stress-generated reactive oxygen species) for more balanced immune responses, and recent in vitro results suggest that the beneficial antioxidant properties of benfo-

Supplement Facts

Serving Size 1 veggie capsule
Servings per container 60 servings

	Amount per serving	% Daily Value
Benfotiamine	150 mg	†
Alpha-Lipoic acid	300 mg	†
L-Leucine	10.5 mg	†

† Daily Value not established.

Other Ingredients: Modified cellulose (vegetarian capsule), silicon dioxide.

Suggested Adult Use: Take 1 capsule daily, with or without food, or as recommended by a nutritionally-informed physician.

Non-GMO / Gluten Free / Soy Free / Vegan
Store in a cool dry place.

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

tiamine could work against some forms of lipid peroxidation.⁵ An animal model suggests that during oxidative stress generated by excess glucose, benfotiamine has the capacity to reduce levels of superoxide and hydroxyl radicals in the heart.¹⁷

Supports healthy aging*

Disrupts formation of Advanced Glycation End Products (AGEs)*

Aging brings an accumulation of oxidized proteins that interfere with mitochondrial efficiency, and a reduction in mitochondrial mass that leads to imperfect energy homeostasis. Alpha-lipoic acid's status as a so-called "mitochondrial nutrient" helps to address these aging factors.^{18, 19}

Benfotiamine has several means of fighting the aging process. It can enhance transketolase activity by promoting tissue levels of thiamine diphosphate, leading to metabolic pathways favoring less production of Advanced Glycation End Products (AGEs). AGEs are formed by a complex series of reactions between reducing sugars and amino acids on proteins, lipids, and nucleic acids. Diet is a major external source of AGEs, with about 10% of AGEs from food remaining in the body after ingestion²⁰; bodily AGE levels are higher in smokers and individuals consuming AGE-rich diets.²¹ In food, AGEs are created by a non-enzymatic browning process called the Maillard reaction, which can contribute to desired colors, odors, and tastes (caramelized onions is one example of the reaction's results). However, this reaction is not restricted to food; in 1981, researchers discovered that the Maillard reaction also takes place within the body, and that it accelerates as we age (hence the term "AGE"). AGEs are especially a concern among proteins with a long half-life, such as serum albumin, lens crystalline, and collagen in the extracellular matrix. Internal AGEs may also be formed due to accumulation of super-reactive glucose metabolic intermediates within cells such as triosephosphates, affecting nearby proteins, lipids, and DNA.⁸

In a crossover study of 13 participants, a test meal with high AGE content was provided before and after 3 days of oral benfotiamine administration at a dose of 1,050 mg.²⁰ Measurements of endothelial function (behavior of cells lining the blood vessel walls) and oxidative stress were taken on both occasions. The high AGE meal significantly increased TBARS (an indicator of oxidative stress), yet this effect of the meal was reduced by supplemental benfotiamine when compared to the baseline meal as measured prior to supplementation. Although this was a high dose of benfotiamine, it nonetheless demonstrates a potential benefit of this form of thiamin at lower doses.

Helps maintain healthy glucose metabolism*

Alpha-lipoic acid is a key factor in the cellular process that metabolizes glucose for energy production. The impact of LA administration in promoting healthy blood sugar metabolism is evidenced in numerous animal and human studies.²²⁻²⁴ It serves as a component of several multi-enzyme complexes of oxidative metabolism, such as pyruvate dehydrogenase complex (PDC). Manipulation of PDC, a complex critical for glucose oxidation and homeostasis, is thought to be one reason that benefits have been shown from alpha-lipoic acid supplementation.²⁵ In skeletal muscle, LA is proposed to stimulate local glucose transporters.⁴ Alpha-lipoic acid is cited especially for its ability to reduce oxidative stress in the context of the important relationship between healthy blood sugar levels and vascular health.²⁶

Helps maintain nervous system health*

Alpha-lipoic acid has gained increasing attention for its support of both the central and peripheral regions of the nervous system. In a prominent long-term, placebo-controlled, multicenter trial of 460 subjects, 233 of the participants were randomly assigned to receive 600 mg of alpha-lipoic acid orally once daily. After 4 years, the group receiving LA had superior secondary nerve health outcome measures compared to the placebo group, especially in terms of small fiber and muscular function, and the LA was well tolerated by participants.^{27, 28}

The brain—as the most complex part of the central nervous system—is par-

ticularly vulnerable to oxidative stress due to its high rate of metabolism and its long-lived neurons. Higher brain levels of glutathione are associated with maintenance of a healthy brain,¹⁴ and LA excels at helping to maintain glutathione levels. One group of researchers found that alpha-lipoic acid decreased oxidative stress in the brain mitochondria of aged rats.²⁹ This kind of activity inside of neurons may help explain the observed effect of LA administration on cognitive upkeep in an animal model. Evidence of cognitive benefits has cropped up in multiple studies on normal old mice, including one where longer-term memory was enhanced by LA. The researchers suggested several mechanisms beyond decreased oxidative stress that could explain the cognitive support seen in these animal studies, including stimulated production of acetylcholine and enhancement of memory-related signaling pathways.¹⁹ Preliminary research with human subjects suggests that LA supports sustained cognitive function in older age.^{30, 31}

Benfotiamine also has a history of nerve-related research behind it, including a 3-week randomized, double-blinded, placebo-controlled pilot trial of 40 participants. In this short study, the group taking 400 mg benfotiamine daily had superior sensory function and other statistically significant outcome measures pertaining to nerve health.³² These findings are supported by results from other placebo-controlled trials in which benfotiamine was administered as tablets in doses ranging from 150 to 600 mg daily (higher doses showed the greatest benefit).^{33, 34} Thiamin is a cofactor for several enzymes in two metabolic pathways of brain glucose metabolism. As a special S-acyl thiamin derivative, benfotiamine has unique effects in supporting healthy brain glucose metabolism, and in mice, cognitive function (research in humans is needed to confirm this finding).³⁵

A LOGICAL MERGE

Benfotiamine and alpha-lipoic acid are two bioactive compounds that share common goals in particular areas of health, albeit via different mechanisms. Best Benfotiamine 150 + Alpha Lipoic Acid 300 is a sensible combination to oppose the oxidative stress that accelerates aging, to promote maintenance of healthy glucose metabolism, and to support a healthy nervous system.



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

SCIENTIFIC REFERENCES

1. Reed L, De Busk B, et al. Crystalline alpha-lipoic acid; a catalytic agent associated with pyruvate dehydrogenase. *Science*. 1951; 114: 93-4.
2. Singh U and Jialal I. *Nutr Rev*. 2008; 66: 646-57.
3. Wollin SD and Jones PJ. *J Nutr*. 2003; 133: 3327-30.
4. Shay KP, Moreau RF, et al. Alpha-lipoic acid as a dietary supplement: molecular mechanisms and therapeutic potential. *Biochim Biophys Acta*. 2009; 1790: 1149-60.
5. Shoeb M and Ramana KV. *Free Radic Biol Med*. 2012; 52: 182-90.
6. Anon. Benfotiamine. Monograph. *Altern Med Rev*. 2006; 11: 238-42.
7. European Commission. Opinion of the Scientific Committee on Food on the tolerable upper intake level of Vitamin B1. European Commission Health & Consumer Protection Directorate-General Scientific Committee on Food. 2001. 1-8.
8. Balakumar P, Rohilla A, et al. *Pharmacol Res*. 2010; 61: 482-8.
9. Packer L, Witt EH, et al. alpha-Lipoic acid as a biological antioxidant. *Free Radic Biol Med*. 1995; 19: 227-50.
10. Kagan VE, Shvedova A, et al. Dihydrolipoic acid--a universal antioxidant both in the membrane and in the aqueous phase. Reduction of peroxy, ascorbyl and chromanoxyl radicals. *Biochem Pharmacol*. 1992; 44: 1637-49.
11. Packer L, Kraemer K, et al. *Nutrition*. 2001; 17: 888-95.
12. Gianturco V, Bellomo A, et al. *Arch Gerontol Geriatr*. 2009; 49 Suppl 1: 129-33.
13. Sola S, Mir MQ, et al. *Circulation*. 2005; 111: 343-8.
14. Yamada T, Hashida K, et al. alpha-Lipoic acid (LA) enantiomers protect SH-SY5Y cells against glutathione depletion. *Neurochem Int*. 2011; 59: 1003-9.
15. Schupp N, Dette EM, et al. *Naunyn Schmiedebergs Arch Pharmacol*. 2008; 378: 283-91.
16. Schmid U, Stopper H, et al. Benfotiamine exhibits direct antioxidative capacity and prevents induction of DNA damage in vitro. *Diabetes Metab Res Rev*. 2008; 24: 371-7.
17. Katare RG, Caporali A, et al. *Circ Heart Fail*. 2010; 3: 294-305.
18. Goraca A, Huk-Kolega H, et al. Lipoic acid - biological activity and therapeutic potential. *Pharmacol Rep*. 2011; 63: 849-58.
19. 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; 33: 194-203.
20. Stirban A, Negrean M, et al. *Diabetes Care*. 2006; 29: 2064-71.
21. Goh SY and Cooper ME. *J Clin Endocrinol Metab*. 2008; 93: 1143-52.
22. Golbidi S, Badran M, et al. *Front Pharmacol*. 2011; 2: 69.
23. Jacob S, Ruus P, et al. *Free Radic Biol Med*. 1999; 27: 309-14.
24. Kamenova P. *Hormones (Athens)*. 2006; 5: 251-8.
25. Korotchkina LG, Sidhu S, et al. R-lipoic acid inhibits mammalian pyruvate dehydrogenase kinase. *Free Radic Res*. 2004; 38: 1083-92.
26. Muellenbach EA, Diehl CJ, et al. *Metabolism*. 2008; 57: 1465-72.
27. Ziegler D, Low PA, et al. *Diabetes Care*. 2011; 34: 2054-60.
28. Papanas N and Maltezos E. *Angiology*. 2012; 63: 81-3.
29. Palaniappan AR and Dai A. Mitochondrial ageing and the beneficial role of alpha-lipoic acid. *Neurochem Res*. 2007; 32: 1552-8.
30. Hager K, Marahrens A, et al. *Arch Gerontol Geriatr*. 2001; 32: 275-282.
31. Holmquist L, Stuchbury G, et al. *Pharmacol Ther*. 2007; 113: 154-64.
32. Haupt E, Ledermann H, et al. *Int J Clin Pharmacol Ther*. 2005; 43: 71-7.
33. Winkler G, Pal B, et al. *Arzneimittelforschung*. 1999; 49: 220-4.
34. Stracke H, Gaus W, et al. *Exp Clin Endocrinol Diabetes*. 2008; 116: 600-5.
35. Pan X, Gong N, et al. *Brain*. 2010; 133: 1342-51.



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