ALA SAP

Science-based α-lipoic acid for optimal antioxidant protection

α-Lipoic acid (ALA) is a fat-soluble antioxidant. One of the leading causes of cellular breakdown is free-radical damage. ALA is one of the few substances that can cross the blood-brain barrier. ALA supplementation causes increased levels of glutathione, which helps the body dispose of toxins and glucose (sugar) from the blood, which is very helpful for those with diabetes and the prevention of eye disease.

ACTIVE INGREDIENTS

Each vegetable capsule contains:

α-Lipoic acid	275 mg
Biotin	50 mcg

Also contain: Vegetable magnesium stearate, microcrystalline cellulose, and silicon dioxide in a vegetable capsule made of vegetable carbohydrate gum and purified water.

Contains no: Gluten, soy, wheat, corn, eggs, dairy, yeast, citrus, preservatives, artificial flavour or colour, starch, or sugar.

This product is non-GMO and vegan friendly.

ALA SAP (antioxidant) contains 60 capsules per bottle.

DIRECTIONS FOR USE

Adults: Take 1 capsule twice daily or as directed by your healthcare practitioner.

2 capsules provide 550 mg of α-lipoic acid.

INDICATIONS

Supplementing with **ALA SAP** provides a daily dose of 550 mg of the antioxidant lipoic acid to optimize antioxidant levels throughout the day. Scientific research has shown that ALA offers protection against free radicals both inside and outside the cell wall, while other antioxidants may provide only extracellular protection. ALA is able to regenerate other antioxidants like vitamin E, vitamin C, and glutathione. In addition to antioxidant properties, ALA helps the body use glucose, hence its potential for helping people with diabetes. An antioxidant is any chemical, natural or synthetic, that neutralizes toxins or free radicals, thus protecting our cells from damage.

INCREASED BIOAVAILABILITY

- NFH brand **ALA SAP** consists of two forms, the *R*(+) and *S*(–) optical isomers, in equal amounts. A racemic mixture is one that has equal amounts of left- and right-handed enantiomers of a chiral molecule. Racemic ALA attempts to mimic the body's natural form of α-lipoic acid.
- α-Lipoic acid full-release promotes glutathione and antioxidant status. **ALA SAP** is pharmaceutical-grade α-lipoic acid with biotin.
- Since one study has shown that ALA may reduce the activity of biotin when taken at very high doses, we have added 33% of the daily requirement of biotin to compensate.

PURITY, CLEANLINESS, AND STABILITY

All ingredients listed for all **ALA SAP** lot numbers have been tested by a third-party laboratory for identity, potency, and purity.

Scientific Advisory Panel (SAP): adding nutraceutical research to achieve optimum health

NFH®

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WHAT IS α-LIPOIC ACID?

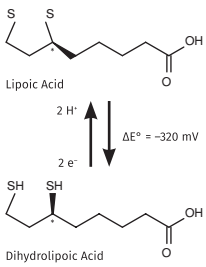
α-Lipoic acid (ALA), also known as thioctic acid, is considered a powerful metabolic antioxidant. In the body, ALA is reduced to a dithiol form, dihydrolipoic acid (DHLA), by NADH or NADPH.[1]

ALA was first discovered in 1951 as a vital cofactor in the pyruvate dehydrogenase complex of the citric acid cycle, essential in the production of cellular energy and the breakdown of α-keto acids and amino acids.[2] Initially, ALA was considered a vitamin; however, *R*-ALA is naturally synthesized de novo by plants and animals, is both water- and fat-soluble, and is widely found in cellular membranes and cytosol.[1, 2]

Whereas endogenously synthesized ALA functions in a protein-bound form, scientific and medical interest surrounds the therapeutic use of supplemental free ALA for its ability to quench free radicals, interaction with other antioxidants, and function in chronic disease prevention.

STRUCTURE AND FUNCTION OF ALA

α-Lipoic acid, chemically named 1,2-dithiolane-3-pentanoic acid, and its reduced form DHLA consist of an 8-carbon fatty acid chain (octanoic acid) containing two sulfur atoms, with a chiral center at the C3 carbon atom.[1] ALA and DHLA naturally occur in the *R* configuration.[3]



The high chemical reactivity of ALA and DHLA is primarily centered in their dithiolane rings and the position of the two sulfur atoms in the rings creates an exceptionally high electron density with a reduction potential of –0.32 V. As compared to the reduced glutathione/oxidized glutathione (GSH/GSSG) couple at –0.24 V, DHLA holds a higher cellular reducing potential, offering more protection from oxidative damage than GSH, a recognized cellular protector.[4]

Whereas most antioxidants are active only in lipid or aqueous phase, ALA is amphipathic and active in both lipid and aqueous phases.[3]

NATURAL *R*-FORM VERSUS SYNTHETIC *S*-FORM OF LIPOIC ACID

ALA exists as two different enantiomers: the biologically active *R*-isomer and the *S*-isomer.[2, 4] Whereas the *S*-isomer is part of supplemented synthetic racemic mixtures, trace amounts of *S*-ALA are found in biological tissues. Maximal absorption and plasma concentration levels are ~50% higher for the *R*-isomer versus the *S*-isomer.[1] The *R*-form of ALA is the only enantiomer naturally synthesized and used in biological systems.[1]

BIOAVAILABILITY

Dietary ALA is concentrated in animal tissues with high metabolic activity such as the kidney, heart and liver.[2, 4] Non-animal sources include spinach, broccoli, tomato, garden pea, Brussels sprouts and rice bran.

Being a low molecular weight antioxidant, dietary or oral ALA is readily absorbed and has the ability to cross the blood-brain barrier, entering the brain and cerebrospinal fluid.[1, 2, 4] Although ALA is synthesized de novo in the mitochondria via lipoic acid synthase, potentially therapeutic levels are only reached with supplementation of free ALA.

Pharmacokinetic studies have shown that about 20–40% of oral racemic ALA is absorbed.[1] Furthermore, with plasma levels peaking 2 h after supplementation, ALA is rapidly metabolized and excreted, returning to presupplementation levels in 4 h. Supplementing oral ALA with food decreases maximal and total plasma ALA; however, *S*-ALA uptake appears to be more adversely affected than the *R*-isomer.

Therapeutic doses in humans range from 200 to 1800 mg/d ALA,[4] and it has been observed that an oral dose of 600 mg/d provides the optimum risk-to-benefit ratio.[6]

SAFETY

ALA supplementation has been found to be safe and associated with very few serious side effects.[6] The no-observed-adverse-effect level (NOAEL) for ALA is considered to be 60 mg/kg_{bw}/d. Safety analysis showed a dose-dependent increase in nausea, vomiting, and vertigo with oral supplementation over 600 mg/d.[5] Theoretically, since ALA improves insulin-mediated glucose uptake, coadministration of oral ALA with insulin or oral antidiabetic agents could potentially increase the risk of hypoglycaemia in diabetic patients; however, clinical trials did not observe any significant drug interactions.[7] Due to similarity in structure, high concentrations of oral ALA can compete with biotin for transport across cell membranes.[8]

ANTIOXIDANT ACTIVITY

ALA and DHLA are powerful antioxidants; however, the antioxidant activity of DHLA is superior to ALA.[3] Their functions include:[1, 2, 9]

1. **Direct free-radical scavenging properties**, quenching hydroxyl radicals, hypochlorous acid, peroxynitrate, and singlet oxygen. DHLA also scavenges superoxide and peroxyl radicals.
2. **Regeneration of endogenous antioxidants**, such as vitamin C, coenzyme Q_{10}, and glutathione, which in turn can recycle vitamin E. Unlike ascorbic acid, DHLA can be recycled from ALA and therefore is not destroyed by quenching free radicals. Furthermore, ALA administration has been shown to increase GSH synthesis.
3. **Chelation of metals**, such as iron, copper, mercury and cadmium, which can stimulate free-radical damage by generating highly toxic hydroxyl radicals. ALA and DHLA can chelate these redox-active transition metals followed by increased excretion, explaining ALA and DHLA's role in heavy metal detoxification.
4. **Reparation of oxidized proteins**, such as methionine, which is important for proteins with low turnover rate.

Finally, there are in vitro cases of DHLA's prooxidant activity; however ALA can act as an antioxidant against DHLA's potential prooxidant activity,[9] and the prooxidant effect of ALA and DHLA has not been observed in vivo and warrants further investigation.[1]

MODULATING SIGNAL TRANSDUCTION

ALA and DHLA stimulate certain signal transduction pathways, leading to therapeutic benefits.[1] In the insulin signaling pathway, ALA induces GLUT transporters to the cell membrane, resulting in increased intracellular glucose uptake, and ALA also acts as a mild oxidizing agent.

ALA can activate Akt-dependent pathways, affecting protein kinase B activity responsible for cell survival, increased glycogen metabolism, and suppression of apoptosis. Furthermore, ALA and DHLA inhibit nuclear factor-κB activity,[1, 2] a redox-sensitive transcription factor that regulates a number of genes associated with inflammatory process, diabetes, heart disease, cancer and AIDS.

ALA AND NUTRITIONAL SCIENCE

Diabetes Mellitus and Polyneuropathies

ALA and DHLA are understood to be effective in the prevention and/or treatment of diabetic complications associated with insulin resistance via ALA's ability to increase glucose uptake and actions as an antioxidant. Experimental and clinical studies report supplemental ALA significantly reduces symptoms of diabetic pathologies, including cataract formation, vascular damage, and polyneuropathy.[2]

Recent clinical trials of patients receiving a daily oral dose of 600 mg ALA for 3 weeks observed a significant reduction in pain, paresthesia, and numbness associated with chronic distal symmetric polyneuropathy.[10]

Other Diseases

As a potent antioxidant, ALA and DHLA may reduce the risk of cardiovascular disease via beneficial actions on LDL oxidation, blood lipid profiles, plaque formation, and hypertension.[4]

In vascular disease, a clinical trial in 58 patients with metabolic syndrome supplemented oral ALA 300 mg/d for 4 weeks and observed a 44% improvement in flow-mediated vasodilation, a measure of endothelial health.[6]

Finally, ALA supplementation may benefit diseases and conditions with oxidative stress as a part of their etiologies, such as Parkinson's disease, Alzheimer's disease, amyotrophic lateral sclerosis, and aging; however, future clinical trials are needed to establish dosage, safety and efficacy.[1]

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