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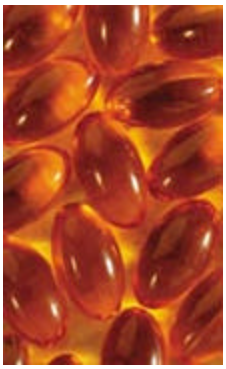
Alpha-Lipoic Acid: A Versatile Antioxidant

By Yousry Naguib, PhD



Alpha-lipoic acid (also known as thioctic acid) is produced in the body, and found in food sources such as liver, brewer's yeast, and potatoes. Red meat is among the rich sources of alpha-lipoic acid (ALA). ALA was first isolated in 1957, and is chemically known as 1,2-dithiolane-3-pentanoic acid.

ALA plays key roles in health, as an antioxidant, and as a cofactor for a number of vital enzymes responsible for metabolism of glucose, fatty acids and other sources for cellular energy.

ALA is used to restore liver health, treat diabetes-related neuropathy, and help regulate blood sugar, prevent diabetic retinopathy, and provide protection against oxidative processes involved in the degenerative diseases.

Recycling Antioxidants

As an antioxidant ALA is unique in that it is both water- and fat-soluble; thus it can offer protection against free radicals throughout the body. ALA can regenerate other antioxidants such as vitamin C, vitamin E, and glutathione, thus prolonging their existence in the body.

Vitamin C, vitamin E, and glutathione work together to protect tissues, cells, and DNA from free radical damage. Vitamin E is a potent fat-soluble antioxidant that works primarily to scavenge lipid peroxyl radicals, which are formed in fatty tissues and membranes. Vitamin C is a water-soluble antioxidant that has the ability to regenerate vitamin E from its free radical form. And the oxidized free radical form of ascorbic acid can be regenerated by ALA.1

Glutathione is an amino acid that acts as an essential antioxidant inside of biological cells, and its oxidized free radical form can be recycled by other antioxidants including ALA and the antioxidant coenzyme called NADPH (nicotinamide adenine dinucleotide phosphate, reduced form).

Glutathione provides protection against cataract formation, liver damage, and cancer.

All these antioxidants are interlinked and ALA plays a major role in recycling many of these key antioxidants in the body.

ALA is readily absorbed when taken orally, and once inside cells is reduced to dihydrolipoic acid, which can then be released by the cell. Urinary excretion of ALA is maximal three to six hours after oral administration of ALA.2

Diabetes and ALA

Diabetes is one of the major degenerative diseases in the United States. It is a major risk factor for the development of cardiovascular disease, and can lead to complications such as kidney disease, nerve damage and blindness.

In diabetes mellitus the body's cells experience a relative starvation (leading to increased food intake) for glucose because of the lack of insulin action.

There are two major types of diabetes mellitus, Type I and Type II. Type I is known as insulin-dependent diabetes mellitus, and requires insulin injection. Type I is characterized by almost a complete lack of pancreatic cell function such that no, or very little insulin is released. Type II, known as non-insulin dependent diabetes mellitus, is characterized by decreased release of insulin from the pancreas.

ALA has been used in Europe to treat and prevent complications associated with diabetes, including neuropathy, and cataracts. ALA is also found to reverse neuropathy, aid glucose utilization, and help diabetics reduce their reliance on insulin.

Studies in Europe show that taking 600 mg twice a day improved the symptoms of diabetic neuropathy, which is marked by numbness and tingling in the hands and feet3.

The ability of ALA to restore diabetic nerve function after only four months of high-dose oral treatment was demonstrated in a 1997 German study4. Seventy-three diabetic patients with damaged autonomic nervous systems were randomly assigned to receive either 800 mg per day of ALA or a placebo.

After four months, the ALA group had a statistically significant improvement in the sympathetic system and no change for the parasympathetic, whereas the placebo-group showed continuing deterioration of both sympathetic and

parasympathetic systems. Symptoms due to autonomic nerve disorder increased in the placebo group, but decreased with ALA.

In a multicenter, double-blind, placebo-controlled study, 328 patients with Type II diabetes and symptomatic peripheral neuropathy were randomly assigned to treatment with intravenous infusion of ALA or placebo for three weeks.

Symptoms (pain, burning, parestheia, and numbness) in the feet decreased significantly in the ALA-group taking 600 mg daily, as compared to the placebo. No significant adverse events were observed. The study concluded that intravenous treatment with ALA (600 mg daily) for three weeks is safe and effective in reducing symptoms of diabetic peripheral neuropathy in Type II diabetes5.

In a two-year follow-up study involving 65 patients with Type I and Type II diabetes, Ziegler and coworkers in Germany found that a combination of intravenous and oral administration ALA at levels of 600 or 1,200 mg daily for two years resulted in an improvement of the sensory nerve and tibial nerve conduction velocities6.

In another recent study, Ziegler and coworkers examined the effects of ALA on diabetic neuropathy in a seven-month, multicenter, randomized, controlled trial involving 509 patients who were assigned to receive either 600 mg ALA or placebo once daily intravenously for three weeks, followed by three times a day orally for six months. The symptoms of neuropathy were significantly improved in the ALA group as compared to the placebo. There were no significant side effects in both groups7.

Ziegler and coworkers also reviewed 15 clinical trials that assessed the therapeutic efficacy and safety of ALA in diabetic polyneuropathy8. They found that: (a) short-term treatment for three weeks using 600 mg ALA intravenously per day appears to reduce the symptoms of diabetic neuropathy, (b) oral treatment for four to seven months tends to reduce neuropathic deficits and improves cardiac autonomic neuropathy, and (c) ALA possesses a highly favorable safety profile.

To shed some light on the mechanism by which ALA exerts its beneficial effects on diabetic neuropathy, German researchers examined the effects of ALA on microcirculation in patients with diabetes mellitus and peripheral neuropathy. Patients were divided into two groups - the first group received 1,200 mg ALA orally per day for more than six weeks; the second

group received a one-time intravenous injection of 600 mg ALA or placebo. Both groups showed a significant improvement in microcirculation, suggesting that ALA might exert its beneficial effects at least partially by improving microcirculation9.

An earlier German study on patients with Type II diabetes, comparable in age, body-mass index, and degree of insulin resistance at baseline, showed that administration of ALA (1,000 mg given intravenously) significantly increased insulin-stimulated whole body glucose disposal by about 50 percent, whereas the control-group did not show any significant change10.

A study at Mayo Foundation in Rochester, MN, demonstrated that ALA improves neuropathy and reduces oxidative stress in diabetic peripheral nerves. After one-month of supplementation with ALA, patients showed improved blood flow of diabetic neuropathy and glutathione levels in the diabetic nerves in a dose-dependent manner11.

Heart Diseases

Oxidation of low-density lipoprotein (LDL) by free radicals has been implicated in the formation of arterial cholesterol deposits associated with atherosclerosis. Vitamin E plays a critical role in protecting LDL against free radical oxidations. A study published in 1992 showed that dihydrolipoic acid recycles vitamin E by synergistically interacting with ascorbate12. ALA has also been shown to reduce ischemia/reperfusion injury to the heart and brain13.

Other Health Benefits

The potential therapeutic use of ALA in preventing cataracts has been demonstrated in an animal study. Rats given ALA had 60 percent protection from cataract formation, leading the researchers to conclude that ALA protects glutathione in the lens.

ALA was also found to protect ascorbate and vitamin E, and to restore the activities of the enzymes glutathione peroxidase and catalase in the lenses of the treated animals. The study concluded that ALA could be of potential therapeutic value in preventing cataracts and their complications14.

A 1995 study suggested that ALA taken in the amount of 150 mg daily for one month improves visual function in people with glaucoma15.

ALA has also been suggested to benefit HIV-positive people. When 12 people with AIDS were given ALA, their glutathione

levels increased by 100 percent, vitamin C levels by 90 percent, T4 cells by 66 percent, and oxidative stress declined in 70 percent16. Researchers at the University of California, Berkeley, also found that ALA protects Nuclear Factor kappa-B (a protein complex involved in cancer and the progression of AIDS) from activating the transcription factor that causes HIV to replicate17.

Recommended Dose

Typically, doses of 20 to 50 mg of ALA per day are recommended for healthy individuals for antioxidant protection. Diabetics are recommended to take 200 mg ALA three times daily. A dose of 800 mg ALA per day has been proven helpful in treating diabetic neuropathy, and only150 mg ALA per day has been found useful for glaucoma18.

Side Effects

Side effects of ALA are rare but can include skin rash and the potential of hypoglycemia in diabetics.

Summary

Alpha-lipoic acid is a versatile antioxidant. It quenches a variety of free radicals and helps to recycle other antioxidants such as vitamins C and E, and glutathione. Alpha-lipoic acid has been shown to reduce symptoms of neuropathy, prevent diabetic retinopathy, and lower blood glucose levels in diabetics. ALA may also be useful in the treatment of ischemia/reperfusion injury and cellular oxidative stress. ***VR***
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Vitamin Retailer Magazine, Inc.,
A-2 Brier Hill Court, East Brunswick, NJ 08816
Phone: (732) 432-9600 **Fax:** (732) 432-9288 info@vitaminretailer.com