Alpha Lipoic Acid

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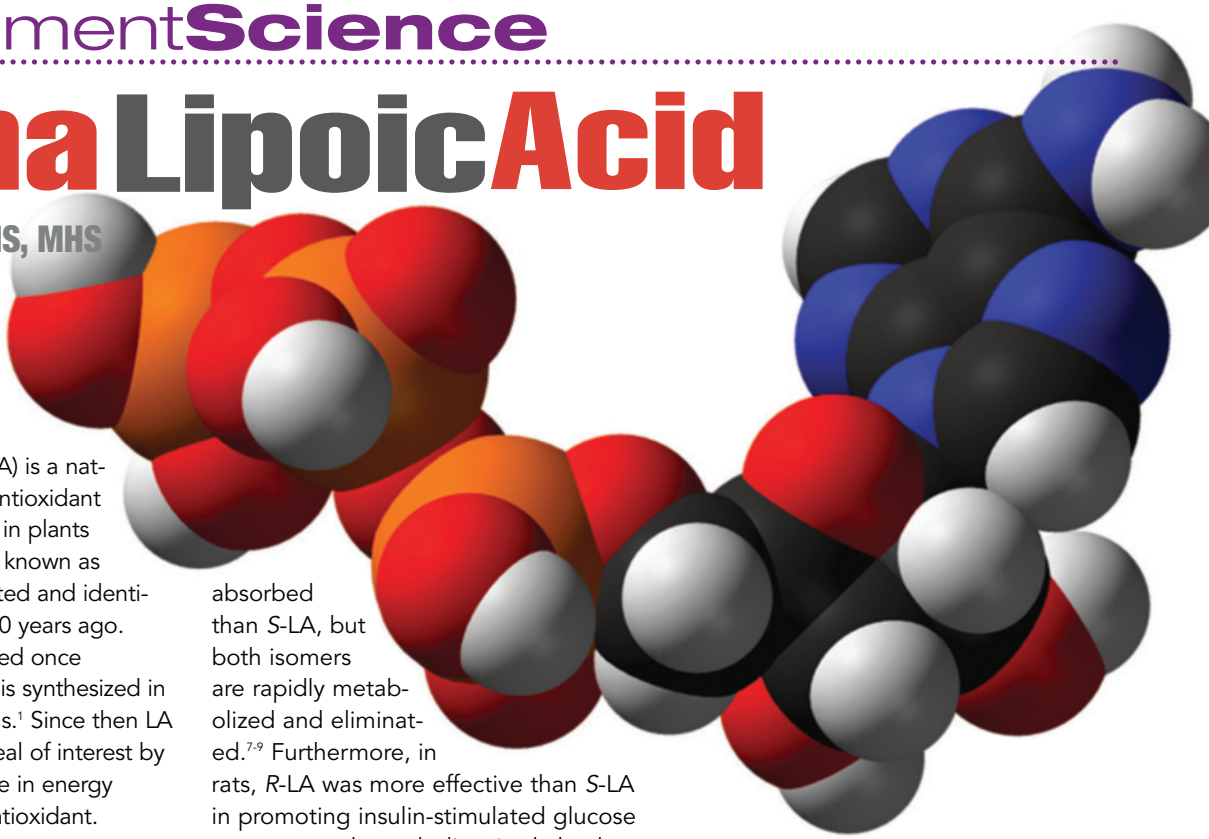

Alpha lipoic acid (LA) is a naturally occurring, antioxidant compound found in plants and animals. Also known as thiotic acid, LA was isolated and identified as a vitamin about 50 years ago. However, it was reclassified once researchers found that it is synthesized in small amounts by humans.[1] Since then LA has generated a great deal of interest by researchers due to its role in energy metabolism and as an antioxidant.

Introduction

Specifically, LA is involved in carbohydrate metabolism, and in the mitochondrial citric acid cycle, which produces adenosine triphosphate (ATP).[2] LA is both water and fat soluble, and can regenerate endogenous antioxidants. LA is about 30 percent absorbed from dietary or supplemental sources, and is reduced to dihydrolipoic acid (DHLA) in many tissues.[3-5] Exogenous LA, and the metabolite DHLA, have antioxidant activity and can scavenge free radicals both intra- and extra-cellularly.[6] Research has demonstrated that LA has other health benefits as well.

R-Lipoic Acid & Racemic Lipoic Acid

Before beginning the discussion, it is important to differentiate between the two types of LA. Basically there are two possible optical isomers that are mirror images of each other (*R*-LA and *S*-LA). Only the *R*-isomer is endogenously synthesized and bound to protein. Most supplements contain a 50/50 (racemic) mixture of *R*-LA and *S*-LA. Although direct comparisons of the bioavailability of oral racemic LA and *R*-LA supplements have not been published, after oral dosing with racemic LA, peak plasma concentrations of *R*-LA were found to be 40-50 percent higher than *S*-LA. This suggests that *R*-LA is better absorbed than *S*-LA, but both isomers are rapidly metabolized and eliminated.[7-9] Furthermore, in rats, *R*-LA was more effective than *S*-LA in promoting insulin-stimulated glucose transport and metabolism in skeletal muscle[10], and *R*-LA was more effective than racemic LA and *S*-LA in promoting healthy vision.[11]

Antioxidant Function

While LA and DHLA can both neutralize reactive oxygen species and reactive nitrogen species *in-vitro*[12], the real antioxidant value may be in the ability to "recycle" other antioxidants. Here's how it works: when an antioxidant scavenges a free radical, it loses or gains an electron, which causes the antioxidant to become a free radical. DHLA can correct the electron imbalance, so that the antioxidant is active again. In this way, DHLA can recycle vitamin E, vitamin C and glutathione.[13-16]

Certain metal ions such as iron and copper can induce oxidative damage via interactions with free radicals.[17] LA and DHLA have been shown to chelate (bind) with iron and copper, inhibiting oxidative damage *in-vitro*.[18] They have also been shown to inhibit excess iron and copper accumulation in animal research.[19,20]

In addition, LA has been found to increase glutathione levels *in-vitro* and in aged animals.[21,22] This is important given the role that glutathione plays as an intracellular antioxidant and in the detoxification and elimination of potential carcinogens and toxins.

Insulin Signaling & Diabetes

The binding of insulin to the insulin receptor in the body signals a process that ultimately increases the uptake of glucose into cells.[23,24] *In-vitro* research has shown that LA activates the insulin signaling cascade in cultured cells[25-27], resulting in increased glucose uptake.[28,29] Of course this raises the question as to whether supplementation with LA might improve glucose utilization in diabetics.

Small clinical studies (up to 20 type 2 diabetic patients) showed that an intravenous dose of 500-1,000 mg LA improved insulin sensitivity (insulin stimulated glucose disposal) by up to 50 percent compared to placebo.[30,31] In a four-week, placebo-controlled study, 72 type 2 diabetic patients received daily 600 mg, 1,200 mg or 1,800 mg of LA orally. The results were improved insulin sensitivity by 25 percent[32] with no significant differences among the three doses of LA. This suggests that 600 mg daily day may be the maximum effective Avenir 45 BookObliquedose.[33]

Diabetic Neuropathy

About 60-70 percent of all people with diabetes have some form of nerve damage, called diabetic neuropathy (or more accurately, neuropathies, since there is more than one kind). High blood sugar

levels over a long period of time damage nerves throughout the body, but those in the hands and feet are most often damaged. Symptoms of diabetic neuropathy can include pain and numbness, particularly in the hands and feet, or problems with digestion, the urinary tract, blood vessels and the heart. These symptoms can range between mild and extremely painful to the point of disability.[34]

Giving 600-1,200 mg oral or intravenous LA daily reduced symptoms of peripheral neuropathy in diabetics. LA improved symptoms such as burning, pain, numbness and prickling of the feet and legs. It also seems to improve objective measures such as ratings of nerve function decline and disability. Symptom improvement occurs within three to five weeks with oral and intravenous dosing.[35-43] Doses lower than 600 mg daily have not been shown to be effective.[44]

Memory Function

LA alone or in combination with other nutraceuticals has been found to improve measures of memory in animal models of age-associated memory decline.[45-48] An uncontrolled, open-label trial in nine patients with suboptimal memory function, who were also taking acetylcholinesterase inhibitors, reported that oral supplementation with 600 mg/day of LA appeared to stabilize memory function over a one-year period.[49]

Improved measures of memory in aged animals or in animal models of age-associated cognitive decline has been found when LA has been administered alone or in combination with other nutraceuticals.[50-56] In a one-year, uncontrolled, open-label trial of nine patients with probable Alzheimer's disease and related dementias who were also taking acetylcholinesterase inhibitors, daily oral supplementation with 600 mg of LA seemed to stabilize cognitive function.[57] Then the study was extended for four years to include 43 patients with probable Alzheimer's disease. The results were that patients with mild dementia or moderate-early dementia who took 600 mg LA daily along with acetylcholinesterase inhibitors experienced slower cognitive decline compared to the typical cognitive decline of Alzheimer's patients.[58] Unfortunately, this study did not use a control group so it is difficult to assess the value of the results.

Peripheral Artery Function

Preliminary clinical research suggests that taking LA 300 mg twice daily might reduce pain associated with exercise in people with suboptimal peripheral artery disease.[59] A randomized controlled trial assessed the effect of oral LA supplementation on flow-mediated vasodilation in 58 patients diagnosed with metabolic syndrome.[60] Oral supplementation with 300 mg/day of LA for four weeks improved flow-mediated vasodilation by 44 percent compared to placebo.

Vision

Animal research indicates R-lipoic acid can protect against the formation of cataracts.[61] Administration of racemic lipoic acid had no protective effect on lens antioxidants. R-lipoic acid also appeared to have greater bioavailability than racemic alpha-lipoic acid. In another study designed to mimic the radiation exposure experienced by astronauts, jet crews and military personnel who have suffered a radiation accident, R-lipoic acid was one of a number of nutrients that protected against radiation-associated protein leakage in the eye lens.[62]

Relationship to Biotin

Structurally, biotin is chemically similar to that of LA. Furthermore, high concentrations of LA can compete with biotin for transport across cell membranes.[63,64] In rats, high doses of injectable LA decreased the activity of two biotin-dependent enzymes by about 30-35 percent.[65] Nevertheless, it is unknown whether LA supplementation substantially increases the requirement for biotin in humans.[66] VR

For a full list of references, go to www.vitaminretailer.com.

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