**ALA - Alpha Lipoic Acid**

Alpha-lipoic acid is also listed as: Dihydrolipoic acid; Lipoic acid; Lipolate; Thiotic acid.

Alpha-lipoic acid (ALA), a naturally occurring compound and a radical scavenger was shown to enhance glucose transport and utilization in different experimental and animal models. Clinical studies described an increase of insulin sensitivity after acute and short-term (10 d) parenteral administration of ALA. The effects of a 4-week oral treatment with alpha-lipoic acid were evaluated in a placebo-controlled, multi-center pilot study to determine see whether oral treatment also improves insulin sensitivity. Seventy-four patients with type-2 diabetes were randomized to either placebo (n = 19); or active treatment in various doses of 600 mg once daily (n = 19), twice daily (1200 mg; n = 18), or thrice daily (1800 mg; n = 18) alpha-lipoic acid. An isoglycemic glucose-clamp was done on days 0 (pre) and 29 (post). In this explorative study, analysis was done according to the number of subjects showing an improvement of insulin sensitivity after treatment. Furthermore, the effects of active vs. placebo treatment on insulin sensitivity were compared. All four groups were comparable and had a similar degree of hyperglycemia and insulin sensitivity at baseline. When compared to placebo, significantly more subjects had an increase in insulin-stimulated glucose disposal (MCR) after ALA treatment in each group. As there was no dose effect seen in the three different alpha-lipoic acid groups, all subjects receiving ALA were combined in the "active" group and then compared to placebo. This revealed significantly different changes in MCR after treatment (+27% vs. placebo; p < .01). This placebo-controlled explorative study confirms previous observations of an increase of insulin sensitivity in type-2 diabetes after acute and chronic intravenous administration of ALA. The results suggest that oral administration of alpha-lipoic acid can improve insulin sensitivity in patients with type-2 diabetes.
Alpha-lipoic acid is an antioxidant that is manufactured in the human body. Antioxidants are substances that work by attacking "free radicals," waste products created when the body turns food into energy. There are also many sources of free radicals in the environment such as ultraviolet rays, radiation, and toxic chemicals in cigarette smoke, car exhaust, and pesticides. Free radicals cause harmful chemical reactions that can damage cells in the body, making it harder for the body to fight off infections. As a result a person becomes more susceptible to long term diseases such as diabetes and liver damage.

Uses

General

Alpha lipoic acid is a vitamin-like substance that helps to make energy in your body. As an antioxidant, it is used to treat acquired immunodeficiency syndrome (AIDS). Alpha lipoic acid may also be used to treat diabetes and burning mouth syndrome. Alpha-lipoic acid works together with other antioxidants such as vitamins C and E. It is important for growth, helps to prevent cell damage, and helps the body rid itself of harmful substances.

Diabetes

Several studies suggest that treatment with ALA may help reduce pain, burning, itching, tingling, and numbness in people who have nerve damage (called peripheral neuropathy) caused by diabetes. Alpha-lipoic acid has been used for years for this purpose in Europe. Other studies have shown that alpha-lipoic acid speeds the removal of glucose (sugar) from the blood of people with diabetes and that this antioxidant may prevent kidney damage associated with diabetes in animals.

Liver Disease
Alpha-lipoic acid may prove useful in the treatment of chronic hepatitis because it relieves stress on the liver and helps rid the body of toxins. There have been several case reports of use of alpha-lipoic acid in combination with silymarin (milk thistle) and selenium (a substance with liver-protecting and antioxidant properties) to help treat hepatitis C (a serious type of hepatitis contracted from blood and bodily fluids that does not have an adequate cure or treatment).

It has also been used in conjunction with silymarin to treat *Amanita* poisoning. *Amanita* is a highly poisonous mushroom that causes liver damage.

**Brain Function and Stroke**

Because alpha-lipoic acid can pass easily into the brain, it has protective effects on brain and nerve tissue and shows promise as a treatment for stroke and other brain disorders involving free radical damage. Animals treated with alpha-lipoic acid, for example, suffered less brain damage and had a four times greater survival rate after a stroke than the animals who did not receive this supplement. While animal studies are encouraging, more research is needed to understand whether this benefit applies to people as well.

**Other**

Additional conditions for which alpha-lipoic acid may prove useful include heart failure, human immunodeficiency virus (HIV), cataracts, and glaucoma. More research is underway in these areas.

**Dietary Sources**

Good food sources of alpha-lipoic acid include spinach, broccoli, beef, yeast (particularly Brewer's yeast), and certain organ meats (such as the kidney and heart).

**Available Forms**

Alpha-lipoic acid supplements are available in capsule form.
How to Take It

Pediatric

There are no known scientific reports on the pediatric use of alpha-lipoic acid. Therefore, it is not currently recommended for children.

Adult

Alpha-lipoic acid can be purchased in dosages ranging 30 mg to 100 mg tablets. Currently there are no established recommended doses for supplementation. For general antioxidant support, the recommended dose of ALA is 20 mg to 50 mg per day.

Manufacturers of alpha-lipoic acid suggest one or two 50-mg capsules daily as a dietary supplement.

Studies that have been successful in improving nerve function in diabetics have used 600 mg of alpha-lipoic acid per day in divided doses.

Do not take alpha lipoic acid without talking to your doctor first if you are taking:

- Medicines used to lower blood sugar (examples: metformin Glucophage, Glynase, pioglit)
- Take alpha lipoic acid on an empty stomach

Precautions

Because of the potential for side effects and interactions with medications, dietary supplements should be taken only under the supervision of a knowledgeable healthcare provider. This is especially true for those who are pregnant or breastfeeding.

Skin rash has been reported rarely from alpha-lipoic acid.
Finally, because alpha-lipoic acid has been associated with improved blood sugar control, people with diabetes should follow their blood sugar levels carefully when taking this supplement in order to avoid hypoglycemia (low blood sugar). Your doctor may decide that a reduction in dosage of insulin or oral blood sugar-lowering drugs is needed if you are taking this supplement.

Possible Interactions

If you are currently being treated with any of the following medications, you should not use alpha-lipoic acid without first talking to your healthcare provider.

Amikacin and Gentamicin

In an animal study, alpha-lipoic acid supplements reduced side effects, particularly toxicity to the ear, associated with these antibiotics. Additional studies are needed to confirm these effects in people.

Cisplatin and Cyclophosphamide

The use of alpha-lipoic acid supplements in animals protected against toxic side effects associated with these medications.

Thyroid-regulating Medications, Levothyroxine

Rats given alpha-lipoic acid supplements had altered thyroid hormone function, but improved cholesterol levels. Blood hormone levels and thyroid function tests should be monitored closely in people taking thyroid hormones who are also taking alpha-lipoic acid.

Dosage:
The amount depends on the strength of the medicine and the reason you are taking alpha lipoic acid.
Side Effects:
Stop taking your medicine right away and talk to your doctor if you have any of the following side effects.

- Allergic reaction: Itching or hives, swelling in your face or hands, swelling or tingling in your mouth or throat, chest tightness, trouble breathing, or rash.

Other Side Effects:
This medicine may also cause other side effects. Tell your doctor if you have side effects that you think are caused by this medicine.

- A feeling of "pins and needles" in your body
- Headache
- Hives, skin rash
- Muscle cramps

Linus Pauling Institute on ALA

Introduction

Alpha-lipoic acid (LA), also known as thioctic acid, is a naturally occurring compound that is synthesized in small amounts by plants and animals, including humans. Endogenously synthesized LA is covalently bound to specific proteins, which function as cofactors for several important mitochondrial enzyme complexes. In addition to the physiological functions of protein-bound LA, there is increasing scientific and medical interest in potential therapeutic uses of pharmacological doses of free LA. LA contains two thiol (sulfur) groups, which may be oxidized or reduced. The reduced form is known as dihydrolipoic acid (DHLA), while the oxidized form is known as LA. LA also contains an asymmetric carbon, meaning 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. Free LA supplements may contain either R-LA or a 50/50 (racemic) mixture of R-LA and S-LA.

**Metabolism and Bioavailability**

**Endogenous Biosynthesis**

LA is synthesized de novo from an 8-carbon fatty acid (octanoic acid) in mitochondria, where protein-bound LA functions as an enzyme cofactor. Recent evidence suggests that LA can be synthesized “on site” from octanoic acid that is already covalently bound to LA-dependent enzymes. The final step in LA synthesis is the insertion of two sulfur atoms into octanoic acid. This reaction is catalyzed by lipoil synthase, an enzyme that contains iron-sulfur clusters, which are thought to act as sulfur donors to LA. The gene for lipoil synthase has recently been cloned, and research is underway to learn more about its regulation.

**Dietary and Supplemental Alpha-Lipoic Acid**

Exogenous LA from the diet can be activated with ATP or GTP by lipoate activating enzyme, and transferred to LA-dependent enzymes by lipoil transferase. Consumption of LA from foods has not yet been found to result in detectable increases of free LA in human plasma or cells. In contrast, high oral doses of free LA (50 mg or more) result in significant but transient increases in free LA in plasma and cells. Pharmacokinetic studies in humans have found that about 30-40% of an oral dose of racemic LA is absorbed. Oral LA supplements are better absorbed on an empty stomach than with food. Taking racemic LA with food decreased peak plasma LA concentrations by about 30% and total plasma LA concentrations by about 20% compared to fasting. After oral dosing with racemic LA, peak plasma concentrations of R-LA were found to be 40-50% higher than S-LA, suggesting R-LA is better absorbed than S-LA. Both isomers are rapidly metabolized and excreted. Plasma LA concentrations generally peak in one hour or less and decline rapidly.
In cells, LA is quickly reduced to DHLA, and studies in vitro indicate that DHLA is rapidly exported from cells.

**Biological Activities**

**Protein-Bound Alpha-Lipoic Acid**

-LA is an essential cofactor for several mitochondrial enzyme complexes that catalyze critical reactions related to energy production and the catabolism (breakdown) of alpha-keto acids and amino acids (17). In each case, R-LA is covalently bound to a specific lysine residue in one of the proteins in the enzyme complex. The pyruvate dehydrogenase complex catalyzes the conversion of pyruvate to acetyl-coenzyme A (CoA), an important substrate for energy production via the citric acid cycle. The alpha-ketoglutarate dehydrogenase complex catalyzes the conversion of alpha-ketoglutarate to succinyl CoA, another important citric acid cycle intermediate. The activity of the branched-chain ketoacid dehydrogenase complex results in the catabolism of the branched-chain amino acids, leucine, isoleucine and valine. The glycine cleavage system is a multi-enzyme complex that catalyzes the oxidation of glycine to form 5,10 methylene tetrahydrofolate, an important cofactor in nucleic acid synthesis.

**Free Alpha-Lipoic Acid**

When considering the biological activities of supplemental free LA, it is important to keep in mind the limited and transient nature of the increases in plasma and tissue LA.

**Antioxidant Activities**

**Scavenging Reactive Oxygen and Nitrogen Species:**

Reactive oxygen species (ROS) and reactive nitrogen species (RNS) are highly reactive compounds with the potential to damage DNA,
proteins and lipids (fats) in cell membranes. Both LA and DHLA can directly scavenge (neutralize) physiologically relevant ROS and RNS in the test tube. However, it is not clear whether LA acts directly to scavenge ROS and RNS in vivo. The highest tissue concentrations of free LA likely to be achieved through oral supplementation are at least 10 times lower than those of other intracellular antioxidants, such as vitamin C and glutathione. Moreover, free LA is rapidly eliminated from cells, so any increases in direct radical scavenging activity are unlikely to be sustained.

Regeneration of Other Antioxidants:

When an antioxidant scavenges a free radical, it becomes oxidized itself and is not able to scavenge additional ROS or RNS until it has been reduced. DHLA is a potent reducing agent with the capacity to reduce the oxidized forms of several important antioxidants, including vitamin C and glutathione. DHLA may also reduce the oxidized form of alpha-tocopherol (the alpha-tocopheroxyl radical) directly or indirectly, by reducing the oxidized form of vitamin C (dehydroascorbate), which is able to reduce the alpha-tocopheroxyl radical. Coenzyme Q\textsubscript{10} is an important component of the mitochondrial electron transport chain that also has antioxidant activity. DHLA can also reduce oxidized forms of coenzyme Q\textsubscript{10}, which may also reduce the alpha-tocopheroxyl radical. Although DHLA has been found to regenerate oxidized antioxidants in the test tube, it is not known whether DHLA effectively regenerates other antioxidants under physiological conditions.

Metal Chelation:

Redox-active metal ions, such as free iron and copper, can induce oxidative damage by catalyzing reactions that generate highly reactive free radicals. Compounds that chelate (bind) free metal ions in a way that prevents them from generating free radicals offer promise in the treatment of neurodegenerative and other chronic diseases, in which metal-induced oxidative damage may play a role. Both LA and
DHLA have been found to inhibit copper- and iron-mediated oxidative damage in the test tube, and to inhibit excess iron and copper accumulation in animal models.

**Induction of Glutathione Synthesis:**

Glutathione is an important intracellular antioxidant that also plays a role in the detoxification and elimination of potential carcinogens and toxins. Studies in animals have found that glutathione synthesis and tissue glutathione levels are significantly lower in aged animals than in younger animals, leading to decreased ability of aged animals to respond to oxidative stress or toxin exposure. LA has been found to increase glutathione synthesis in cultured cells and in the tissues of aged animals fed LA. Recent research suggests that LA may increase glutathione synthesis in aged animals by increasing the expression of gamma-glutamylcysteine ligase (GCL), the rate-limiting enzyme in glutathione synthesis and by increasing cellular uptake of cysteine, an amino acid required for glutathione synthesis.

**Modulating Signal Transduction**

**Insulin Signaling:**

The binding of insulin to the insulin receptor (IR) triggers the autophosphorylation of several tyrosine residues on the IR. Activation of the IR in this manner stimulates a cascade of protein phosphorylations, resulting in the translocation of glucose transporters (GLUT4) to the cell membrane and increased cellular glucose uptake. LA has been found to increase GLUT4 translocation to cell membranes and to increase glucose uptake in cultured adipose (fat) and muscle cells. Although LA does not appear to bind to the IR like insulin, it can activate the insulin signaling cascade in cultured cells, possibly by acting as a mild oxidizing agent.

**PKB/Akt-dependent Signaling:**
In addition to insulin signaling, phosphorylation and dephosphorylation of other cell signaling molecules affect a variety of cellular processes, including metabolism, stress responses, proliferation and survival. One such molecule is protein kinase B also known as Akt (PKB/Akt). The addition of LA to cultured cells has been found to activate PKB/Akt-dependent signaling resulting in increased survival of neurons. LA administration improved nitric oxide-dependent vasodilation in aged rats by increasing PKB/Akt-dependent phosphorylation of endothelial nitric oxide synthase (eNOS), which increases eNOS catalyzed production of nitric oxide.

Redox-Sensitive Transcription Factors:

Transcription factors are proteins that bind to specific sequences of DNA and promote or repress the transcription of selected genes. Some transcription factors are sequestered outside the nucleus until some sort of signal induces their translocation to the nucleus. Oxidative stress or changes in the balance between oxidation and reduction (redox status) in a cell can trigger the translocation of redox-sensitive transcription factors to the nucleus. One such family of redox-sensitive transcription factors, known as nuclear factor-kappa B (NF-KB), regulates a number of genes related to inflammation and cell cycle control, which are involved in the pathology of diabetes, atherosclerosis and cancer. Physiologically relevant concentrations of LA added to cultured cells have been found to inhibit NF-KB nuclear translocation. Another redox-sensitive transcription factor known as Nrf2 enhances the transcription of genes that contain specific DNA sequences known as antioxidant response elements (AREs). LA has been found to enhance the nuclear translocation of Nrf2 and the transcription of genes containing AREs in vivo, including genes for GCL, the rate-limiting enzyme in glutathione synthesis.
LA deficiency has not been described, suggesting that humans are able to synthesize enough to meet their needs for enzyme cofactors.

**Disease Treatment**

**Diabetes Mellitus**

Chronically elevated blood glucose levels are the hallmark of diabetes mellitus (DM). In type 1 DM, insulin production is insufficient due to autoimmune destruction of the insulin-producing beta-cells of the pancreas. Type 1 DM is also known as insulin-dependent DM, because exogenous insulin is required to maintain normal blood glucose levels. In contrast, impaired cellular glucose uptake in response to insulin (insulin resistance) plays a key role in the development of type 2 DM. Although individuals with type 2 DM may eventually require insulin, type 2 DM is also known as noninsulin-dependent DM because interventions that enhance insulin sensitivity may be used to maintain normal blood glucose levels.

**Glucose Utilization**

There is limited evidence that high doses of LA can improve glucose utilization in individuals with type 2 DM. A small clinical trial in 13 patients with type 2 DM found that a single intravenous infusion of 1000 mg of racemic LA improved insulin-stimulated glucose disposal (insulin sensitivity) by 50% compared to a placebo infusion. In an uncontrolled pilot study of 20 patients with type 2 DM, intravenous infusion of 500 mg/day of racemic LA for 10 days also improved insulin sensitivity measured 24 hours after the last infusion. A placebo-controlled study of 72 patients with type 2 DM found that oral administration of racemic LA at doses of 600 mg/day, 1200 mg/day or 1800 mg/day improved insulin sensitivity by 25% after 4 weeks of treatment. There were no significant differences among the three doses of LA, suggesting that 600 mg/day may be the maximum effective dose. Data from animal studies suggests that the R-isomer of LA may be more effective in improving insulin sensitivity than the
S-isomer, but this possibility has not been tested in any published human trials.

The effect of LA supplementation on long-term blood glucose (glycemic) control has not been well-studied. In an uncontrolled pilot study of a controlled-release form of oral racemic LA, 15 patients with type 2 DM took 900 mg/day for 6 weeks and 1200 mg/day for another 6 weeks in addition to their current medications. At the end of 12 weeks, plasma fructosamine concentrations decreased by about 10%, but glycosylated hemoglobin (HbA1c) levels did not change. Plasma fructosamine levels reflect blood glucose control over the past 2-3 weeks, while HbA1c values reflect blood glucose control over the past 2-4 months. At present, it is not clear whether oral or intravenous LA therapy improves long-term glycemic control in individuals with type 2 DM.

**Diabetic Neuropathy**

Intravenous and oral LA are approved for the treatment of diabetic neuropathy in Germany. More than 20% of diabetic patients develop peripheral neuropathy, a type of nerve damage that may result in pain, loss of sensation and weakness, particularly in the lower extremities. In addition to the pain and disability caused by diabetic neuropathy, it is a leading cause of lower limb amputation in diabetic patients. The results of several large randomized controlled trials indicate that maintaining blood glucose at near normal levels is the most important step in decreasing the risk of diabetic neuropathy. However, such intensive blood glucose control may not be achievable in all diabetic patients. A meta-analysis that combined the results of four randomized controlled trials, including 1258 diabetic patients, found that treatment with 600 mg/day of intravenous racemic LA for 3 weeks significantly reduced the symptoms of diabetic neuropathy to a clinically meaningful degree.

The efficacy of oral LA in the treatment of diabetic neuropathy is less clear. A short-term study of 24 patients with type 2 DM found that
the symptoms of peripheral neuropathy were improved in those who took 1800 mg/day of oral racemic LA for 3 weeks compared to those who took a placebo. A much larger clinical trial randomly assigned more than 500 patients with type 2 DM and symptomatic peripheral neuropathy to one of the following treatments: 1) 600 mg/day of intravenous racemic LA for 3 weeks followed by 1800 mg/day of oral racemic LA for 6 months, 2) 600 mg/day of intravenous racemic LA for 3 weeks followed by oral placebo for 6 months, or 3) intravenous placebo for 3 weeks followed by oral placebo for 6 months. Although symptom scores did not differ significantly from baseline in any of the groups, assessments of sensory and motor deficits by physicians improved significantly after 3 weeks of intravenous LA therapy. Motor and sensory deficits were also somewhat improved at the end of 6 months of oral LA therapy, but the trend did not reach statistical significance. In the longest controlled trial of oral LA therapy, 299 patients with diabetic peripheral neuropathy were randomly assigned to treatment with 1200 mg/day of racemic LA, 600 mg/day of racemic LA or a placebo. However, after 2 years of treatment, only 65 of the original participants were included in the final analysis. In that subgroup, those who took either 1200 mg/day or 600 mg/day of LA showed significant improvement in electrophysiological tests of nerve conduction compared to those who took the placebo.

Another neuropathic complication of diabetes is cardiovascular autonomic neuropathy, which occurs in as many as 25% of diabetic patients. Cardiovascular autonomic neuropathy is characterized by reduced heart rate variability, and is associated with increased risk of mortality in diabetic patients. In a randomized controlled trial of 72 patients with type 2 DM and reduced heart rate variability, oral supplementation with 800 mg/day of racemic LA for 4 months resulted in significant improvement in 2 out of 4 measures of heart rate variability compared to placebo.

Overall, the available research suggests that treatment with 600 mg/day of intravenous LA for 3 weeks significantly reduces the
symptoms of diabetic peripheral neuropathy. Although the benefit of long-term oral LA supplementation is less clear, there is some evidence to suggest that oral LA may be beneficial in the treatment of diabetic peripheral neuropathy (600-1800 mg/day) and cardiovascular autonomic neuropathy (800 mg/day).

**Vascular Disease**

The inner lining of blood vessels, known as the endothelium, plays an important role in preventing vascular disease. Endothelial function is often impaired in diabetic patients, who are at high risk for vascular disease. Intra-arterial infusion of racemic LA improved endothelium-dependent vasodilation in 39 diabetic patients, but not in 11 healthy controls. Endothelial function can be assessed noninvasively by using ultrasound to measure flow-mediated vasodilation, which is endothelium-dependent. A randomized controlled trial assessed the effect of oral LA supplementation on flow-mediated vasodilation in 58 patients diagnosed with the metabolic syndrome, a condition of abnormal glucose and lipid (fat) metabolism. Oral supplementation with 300 mg/day of LA for 4 weeks improved flow-mediated vasodilation by 44% compared to placebo. Diabetic patients are also at high risk of microvascular disease, which may contribute to diabetic neuropathy. In an uncontrolled study, oral supplementation with 1200 mg/day of racemic LA for 6 weeks improved a measure of capillary perfusion in the fingers of 8 diabetic patients with peripheral neuropathy. While these results are encouraging, long-term randomized controlled trials are needed to determine whether LA supplementation can reduce the risk of vascular complications in individuals with diabetes.

**Multiple Sclerosis**

Feeding high doses of LA to mice with experimental autoimmune encephalomyelitis (EAE), a model of multiple sclerosis (MS), has been found to slow disease progression. In these animals, LA feeding appeared to inhibit the migration of inflammatory T cells into the
brain and spinal cord, possibly by inhibiting the activity of an enzyme known as matrix metalloproteinase (MMP)-9. A small pilot study designed to evaluate the safety of LA in 30 people with relapsing or progressive MS found that treatment with 1200-2400 mg/day of oral LA for 2 weeks was generally well-tolerated, and that higher peak serum levels of LA were associated with greater decreases in serum MMP-9 levels. However, this pilot study was not designed to assess the clinical benefit of LA. Larger, long-term clinical trials are needed to assess the safety and efficacy of LA in the treatment of MS.

**Cognitive Decline and Dementia**

LA alone or in combination with other antioxidants or L-carnitine has been found to improve measures of memory in animal models of age-associated cognitive decline, including rats, mice and dogs. However, it is not clear whether oral LA supplementation can slow cognitive decline related to aging or other pathology in humans. An uncontrolled, open-label trial in 9 patients with Alzheimer’s disease and related dementias, who were also taking acetylcholinesterase inhibitors, reported that oral supplementation with 600 mg/day of racemic LA appeared to stabilize cognitive function over a one-year period. However, the significance of these findings is difficult to assess without a control group for comparison. A randomized controlled trial found that oral supplementation with 1200 mg/day of racemic LA for 10 weeks was of no benefit in treating HIV-associated cognitive impairment. Although studies in animals suggest that LA may be helpful in slowing age-related cognitive decline, randomized controlled trials are needed to determine whether LA supplementation is effective in preventing or slowing cognitive decline associated with age or neurodegenerative disease.

**Sources**

**Endogenous Biosynthesis**

R-LA is synthesized endogenously by humans and bound to proteins
**Food Sources**

R-LA occurs naturally in foods covalently bound to lysine in proteins (lipoyllysine). Although LA is found in a wide variety of foods from plant and animal sources, quantitative information on the LA or lipoyllysine content of food is limited and published databases are lacking. Animal tissues that are rich in lipoyllysine (~1-3 mcg/g dry wt) include kidney, heart and liver, while edible plants that are rich in lipoyllysine include spinach and broccoli. Somewhat lower amounts of lipoyllysine (~0.5 mcg/g dry wt) have been measured in tomatoes, peas and Brussels sprouts.

**Supplements**

Unlike LA in foods, LA in supplements is free, meaning it is not bound to protein. Moreover, the amounts of LA available in dietary supplements (200-600 mg) are likely as much as 1000 times greater than the amounts that could be obtained in the diet. In Germany, LA is approved for the treatment of diabetic neuropathies and is available by prescription. LA is available as a dietary supplement without a prescription in the US. Most LA supplements contain a racemic (50/50) mixture of R-LA and S-LA (d,l-LA). Supplements that claim to contain only R-LA are usually more expensive, and information regarding their purity is not currently available. Since taking LA with a meal decreases its bioavailability, it is generally recommended that LA be taken on an empty stomach (one hour before or two hours after eating).

**Racemic vs. R-LA Supplements**

R-LA is the isomer that is synthesized by plants and animals and functions as a cofactor for mitochondrial enzymes in its protein bound form. 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% higher than S-LA, suggesting R-LA is better
absorbed than $S$-LA, but both isomers are rapidly metabolized and eliminated. In rats, $R$-LA was more effective than $S$-LA in enhancing insulin-stimulated glucose transport and metabolism in skeletal muscle, and $R$-LA was more effective than racemic LA and $S$-LA in preventing cataracts. However, virtually all of the published studies of LA supplementation in humans have used racemic LA. At present, it is not clear whether $R$-LA supplements are more effective than racemic LA supplements in humans.

**Safety**

**Adverse Effects**

In general, LA supplementation has been found to have few serious side effects. Intravenous administration of racemic LA at doses of 600 mg/day for 3 weeks and oral racemic LA at doses as high as 1800 mg/day for 6 months and 1200 mg/day for 2 years did not result in serious adverse effects when used to treat diabetic peripheral neuropathy. Two minor anaphylactoid reactions and one severe anaphylactic reaction, including laryngospasm, were reported after intravenous LA administration. The most frequently reported side effects to oral LA supplementation are allergic reactions affecting the skin, including rashes, hives and itching. Gastrointestinal symptoms, including abdominal pain, nausea, vomiting and diarrhea have also been reported. Malodorous urine has also been noted by people taking 1200 mg/day of LA orally.

**Pregnancy and Lactation**

The safety of LA supplements in pregnant and lactating women has not been established.

**Drug Interactions**

Because there is some evidence that LA supplementation improves insulin-mediated glucose utilization, it is possible that LA supplementation could increase the risk of hypoglycemia in diabetic
patients using insulin or oral antidiabetic agents. Consequently, blood glucose levels should be monitored closely when LA supplementation is added to diabetes treatment regimens. Co-administration of a single oral dose of racemic LA (600 mg) and the oral antidiabetic agents, glyburide or acarbose, did not result in any significant drug interactions in one study of 24 healthy volunteers.

**Nutrient Interactions**

**Biotin**

The chemical structure of biotin is similar to that of LA, and there is some evidence that high concentrations of LA can compete with biotin for transport across cell membranes. The administration of high doses of LA by injection to rats decreased the activity of two biotin-dependent enzymes by about 30-35%, but it is not known whether LA supplementation substantially increases the requirement for biotin in humans.

Alpha Lipoic Acid (ALA) is the only antioxidant that is both fat and water soluble. This is important because Alpha Lipoic Acid can access all parts of the cell, giving it tremendous ability to trap free radicals wherever they may be. One of the leading causes of the symptoms we know as aging is free radical damage. ALA is one of the very few substances that can actually cross the blood/brain barrier to enter the brain and go directly where it is needed most. ALA supplementation causes increased levels of glutathione, which helps the body dispose of toxins. This is important as glutathione protects the brain from free radical damage, and low levels of glutathione in the brain are associated with brain disorders such as stroke, dementia, Parkinson’s and Alzheimer’s disease. Test results have caused excitement regarding Alzheimer's & Alpha Lipoic Acid. Results of a small test showed ALA treatment led
to a stabilization of cognitive functions in the Alzheimer's study group. Researchers at UC Berkeley have found that cells bathed in ALA inhibit the growth of a protein linked with the growth of cancerous tumors. They believe that this has significant implications in cancer prevention.

Nearly everyone knows someone who has suffered from a stroke. They hit quickly and usually without warning, often leaving the victim crippled in the wake. Research is showing a strong connection between stroke recovery and Alpha Lipoic Acid.

For those concerned with cataracts and glaucoma, experiments with Alpha Lipoic Acid are delivering some exciting results!

ALA is also crucial for energy production. It helps break down sugar for the production of ATP, the fuel used by cells to keep the body running.

ALA is known as a network antioxidant. Normally once an antioxidant has eliminated a free radical, it is lost forever. Lipoic acid is the only antioxidant with the unique ability to regenerate/recycle itself, and other antioxidants such as vitamins C & E, so that they can continue destroying free radicals.