

LE Magazine June 2008

REPORT

Reducing Aging Markers with Lipoic Acid

Why do some people age better than others?

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We know that part of the answer lies in genetics. However, premature aging also comes down to cellular damage, brought on by oxidative stress from free radicals that are constantly being formed through countless biochemical reactions in our bodies.

One of the secrets to slowing down aging is to aggressively combat this oxidative damage with long-acting antioxidants.

Lipoic acid is one of the most potent, versatile and longer-acting antioxidant vitamins known. Of all the major antioxidant vitamins only lipoic acid possesses the unique ability to work in both water-soluble and fat-soluble environments in the body. This ubiquitous property means that lipoic acid has access to all parts of our cells to neutralize damaging free radicals, which are implicated in many age-related diseases including heart disease and diabetes. Being able to navigate cellular membranes throughout the body also means that lipoic acid can also cross the blood-brain barrier to exert its protective effects against neurological and cognitive diseases, such as Alzheimer's disease.



As scientific research continues to advance, the discovery of newer, rapidly absorbed forms of lipoic acid will allow us to increase the broad-spectrum benefits of this universal antioxidant.

Every second, 24 hours a day, oxidative damage caused by free radicals occurs in our bodies through the energy-producing reactions that take place within mitochondria of our cells. The cumulative damage inflicted by free radicals can have numerous negative age-related effects. This free radical theory of aging is supported by many leading researchers, one key proponent being world-renowned biochemist, Bruce Ames, PhD, from the University of California, Berkeley. Dr. Ames and colleagues maintain that "oxidant by-products of normal metabolism cause extensive damage to DNA, protein, and lipid." They argue that "this damage (the same as that produced by radiation) is a major contributor to aging and to degenerative diseases of aging such as cancer, cardiovascular disease, immune-system decline, brain dysfunction, and cataracts."¹

Scientific research suggests that minimizing these deleterious free radical reactions by ensuring optimal antioxidant levels could therefore hold the key to effectively slowing aging and its unwanted consequences.

WHAT YOU NEED TO KNOW: REDUCING AGING MARKERS WITH LIPOIC ACID

- Cumulative damage inflicted by free radical reactions in the body's mitochondria can have numerous age-related effects by increasing oxidative stress and mitochondrial damage.
- Mitochondrial damage is a major contributor to aging and to degenerative diseases such as cancer, cardiovascular disease, diabetes, immune system decline, and brain dysfunction.
- One of the secrets to slowing down aging is to aggressively combat this oxidative damage with long-acting antioxidants.
- Lipoic acid is the most versatile and powerful antioxidant in the entire antioxidant defense network. Studies show that lipoic acid in combination with acetyl-L-carnitine can reverse mitochondrial decay and restore mitochondrial function to youthful levels.
- Some of the most impressive research on lipoic acid involves its role in fighting type 2 diabetes. Numerous studies have shown that lipoic acid improves glucose tolerance as well as the peripheral nerve complications associated with full-blown diabetes.

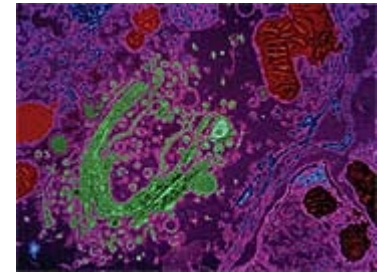
- Lipoic acid has a wide range of other health benefits, including preventing and treating atherosclerotic vascular diseases, helping to slow the progression of neurodegenerative diseases such as Alzheimer's disease, and having possible anticancer effects.
- As the amount of lipoic acid produced by the body decreases with aging, supplementation may be necessary to maintain adequate levels.
- A dramatic new study has unveiled an advanced new formulation of lipoic acid called sodium-R-lipoic acid, which is more potent and stable than pure R-lipoic acid. Sodium-R-lipoic acid is the next-generation lipoic acid, which reaches higher plasma levels of lipoic acid sooner than pure R-lipoic acid.

BOOSTING MITOCHONDRIAL HEALTH

Lipoic acid is considered to be a crucial anti-oxidant for a variety of mitochondrial reactions. Animal studies have shown that antioxidants such as lipoic acid can neutralize the excess production of free radicals within the mitochondria²⁻⁵ and reverse some of the mitochondrial decay caused by oxidative damage.^{3,5-8}

Mitochondrial disorders share several common consequences—reduced production of ATP (or energy), increased reliance on non-oxygen energy sources, and increased production of oxygen free radicals. The benefits of lipoic acid in mitochondrial disorders have been demonstrated in numerous studies.

Animal studies have shown that lipoic acid in combination with acetyl-L-carnitine restores mitochondrial function to youthful levels.^{3,9,10} These studies also show that the decline due to aging in physical activity, cognition, and heart and immune function can also be restored in good part with lipoic acid and acetyl-L-carnitine.^{3,9-11}



Investigators have also studied the efficacy of lipoic acid, creatine monohydrate, and coenzyme Q10, in patients with mitochondrial disorders. In a placebo-controlled study, this combination therapy favorably influenced surrogate markers of cellular energy dysfunction such as plasma lactate levels.¹²

A study published this year also found that treatment with lipoic acid and acetyl-L-carnitine significantly increases mitochondrial mass in fat cells (adipocytes) and promotes mitochondrial synthesis and adipocyte metabolism.¹³

Imagine keeping the powerhouses of your cells vibrant and strong throughout your life. This is what lipoic acid does for your mitochondria.

RECYCLING KEY ANTIOXIDANTS

Lipoic acid is one of the body's most important antioxidants particularly because it is the supplement that can also best regenerate glutathione. Glutathione, a compound produced from three amino acids cysteine, glutamic acid, and glycine, is a key endogenous antioxidant that cannot be efficiently administered orally since it is broken down in the digestive tract before it can reach cells. Glutathione can be found in the watery portion of the cell (known as the cytosol) as opposed to vitamin E, which is present in the fatty portion of each cell. The liver contains a tremendous amount of glutathione, which reflects its function in the body's detoxification processes.

Human aging is marked by a sharp decline in the synthesis and recycling of glutathione and other key antioxidants, such as vitamins C and E and coenzyme Q10, leaving the body vulnerable to increased oxidative damage. Lipoic acid can regenerate these anti-oxidants^{14,15} proving a useful weapon against numerous diseases that are associated with impaired energy utilization and increased oxidative stress, including type 2 diabetes, neurological diseases, and heart disease.

According to Lester Packer, PhD, one of the most noted researchers on antioxidants, "lipoic acid is the most versatile and powerful antioxidant in the entire antioxidant defense network."

IMPROVING INSULIN SENSITIVITY

Lipoic acid is a dietary supplement that is perhaps best known for being an insulin mimic because it increases glucose uptake in insulin-resistant cells.¹⁶⁻¹⁸ "Normal" levels of insulin are essential for glucose and amino acid metabolism. Insulin secreted by the

pancreas after a meal helps transport glucose and amino acids (the building blocks of protein) into the body's cells. Having "normal" levels of insulin, however, does not necessarily guarantee "optimal" benefits with regards to its effects. Dietary means of increasing insulin sensitivity therefore increase the efficiency by which the body transports glucose and amino acids into the muscle cells.

Some of the most impressive research on lipoic acid involves its role in fighting diabetes. Numerous studies have shown that treating insulin-resistant animals and patients with type 2 diabetes improves skeletal muscle glucose uptake and glucose tolerance.¹⁶⁻²⁰

To study the effects of lipoic acid on insulin sensitivity, European researchers treated 12 overweight adults, average age 53 years, suffering from type 2 diabetes with oral lipoic acid, 600 mg twice daily over a period of four weeks. Twelve subjects with normal glucose tolerance served as a control group in terms of insulin sensitivity. They found that lipoic acid treatment increased peripheral insulin sensitivity in patients with type 2 diabetes in this very short time period of just four weeks.²¹

Lipoic acid also shows dramatic benefits in overcoming peripheral nerve complications once diabetes has taken hold. Multiple pathogenic pathways are involved in these neuropathic effects and many treatments have been tried without success. In Germany, lipoic acid has been widely used for overcoming the painful symptoms of diabetic neuropathy.



A number of clinical studies have demonstrated its therapeutic effectiveness in diabetic neuropathy and many researchers believe this may be due to its strong antioxidant power in improving the pathophysiology of damaged nerves. One placebo-controlled study involving 328 diabetic patients with peripheral nerve problems revealed that 600 mg daily intravenous treatment with lipoic acid is safe and effective for overcoming characteristic symptoms such as pain, burning, and itching in the feet after just three weeks of treatment.²²

SUPPLEMENTING WITH LIPOIC ACID

As the amount of lipoic acid produced by the body decreases with aging, supplementation may be necessary to maintain adequate levels. Scientific studies showing the health benefits of alpha-lipoic acid have used doses ranging from 300 to 1,800 mg/day. For optimal benefits, some nutritionists recommend that it is taken with biotin and vitamin B complex. Remember that R-lipoic acid is twice as potent as alpha-lipoic acid. That's because alpha lipoic acid consists of only 50% active R-lipoic and 50% inactive S-lipoic acid.

While there are several forms of lipoic acid on the market, many of them have been shown to be relatively unstable in the body. This property undermines their bioavailability, which leads to poor absorption.⁴⁴

In a dramatic new study, researchers have overcome these polymerization problems by developing an advanced new formulation of lipoic acid, which is being referred to as the next-generation lipoic acid. This new discovery converts the biologically active "R" form of lipoic acid to sodium-R-lipoic acid (NaRLA) to create a more stable, potent product.

A preliminary study has indicated that NaRLA is superior to other forms of lipoic acid by achieving dramatically higher plasma levels of lipoic acid sooner than pure R-lipoic acid.⁴⁴ The authors of this study refer to this unique formulation as the most bioavailable form of lipoic acid. This enhanced potency, says one of the study's co-authors, reflects a maximum plasma concentration that is 10-30 times higher than pure R-lipoic acid.⁴⁵

Unlike other forms of lipoic acid, NaRLA is completely water-soluble, which offers an innovative solution in that it does not have to be restricted to capsules and tablets, but can also be taken as a powdered drink mix.

These impressive findings offer an effective and well-tolerated application for the vast array of health benefits conferred by lipoic acid.

Another placebo-controlled three-week study with 600 mg oral lipoic acid given three times a day in 24 patients with diabetes found that neuropathic symptoms decreased by 47% in the supplemented group compared with only 24% in the control group.²³

Yet another short-term study found that just five weeks of oral supplementation with 600-1,800 mg/day of lipoic acid also improves painful symptoms of diabetic neuropathy.²⁴

In addition, lipoic acid has been shown to be beneficial in renal complications associated with diabetes. This was seen in a study in which supplementing with 600 mg/day of lipoic acid for 18 months slowed the progression of kidney damage in 84 patients with diabetic nephropathy.²⁵

ANTI-OBESITY, ANTIHYPERTRIGLYCERIDEMIC, AND ANTI-INFLAMMATORY EFFECTS

Add to these impressive benefits a long list of other health applications for lipoic acid. In another particular study,²⁶ scientists investigated whether lipoic acid inhibits atherosclerosis in animal (mice) models of human atherosclerosis. They discovered that supplementation with lipoic acid significantly reduced atherosclerotic lesion formation in the large blood vessels of these mice. This was associated with approximately 40% less body weight gain and lower triglycerides levels. According to these scientists, “dietary lipoic acid supplementation inhibits atherosclerotic lesion formation in two mouse models of human atherosclerosis, an inhibition that appears to be due to the ‘anti-obesity,’ antihypertriglyceridemic, and anti-inflammatory effects of lipoic acid. Lipoic acid may be a useful adjunct in the prevention and treatment of atherosclerotic vascular diseases.”²⁶ Lipoic acid supplementation also prevents the development of high blood pressure and high blood glucose, presumably through its antioxidative properties.²⁷

LIPOIC ACID HELPS WITH BRAIN FUNCTION

Alzheimer’s is a neurodegenerative disease that currently has no known cure. It is thought that oxidative stress might play a key role in neuro-degenerative and cognitive disorders due to the higher vulnerability of neuronal tissues to free-radical damage. A recent study revealed that anti-oxidants such as lipoic acid may have clinical value in slowing down the progression of Alzheimer’s disease. In this open-label study, nine patients with Alzheimer’s disease received 600 mg of lipoic acid daily in addition to standard acetylcholinesterase drugs for 12 months. Encouraged by findings that treatment led to a “stabilization of cognitive functions in the study group,” the investigators extended their analysis to 43 patients over an observation period of up to 4 years. During this longer time period, they found that the disease progressed very slowly in patients with mild dementia. They also noted that the rate of disease progression was dramatically lower than data from other long-term studies, leading to the conclusion that “alpha-lipoic acid might be a successful ‘neuroprotective’ therapy option for Alzheimer’s disease.”²⁸

A number of other studies also support the clinical value of lipoic acid as a neuroprotective treatment for Alzheimer’s,²⁹⁻³¹ especially during the early stages of the disease.²⁹ Researchers have identified a number of mechanisms through which lipoic acid may help prevent cognitive decline. They believe lipoic acid may help increase the production of acetylcholine, an essential chemical messenger in the brain that is deficient in Alzheimer’s disease sufferers.²⁹ A recent study also suggests that lipoic acid combats oxidative vulnerability induced by exposing rats to amyloid-beta fibrils—neurotoxic protein fragments that are implicated in Alzheimer’s disease.³²



Parkinson’s disease is a degenerative disorder in which individuals suffer from various motor impairments that may also be helped by lipoic acid supplementation. Part of the brain called the substantia nigra is negatively affected in this disease. Scientists believe that oxidative stress might play a role in the degeneration of nerve cells in this area. Accordingly, an important biochemical feature of Parkinson’s is a significant early depletion of glutathione, a potent antioxidant mentioned earlier, which may ultimately result in free radical-induced damage, mitochondrial dysfunction, and neuronal cell death. Test tube, or in vitro, data suggest that pre-treatment of PC12 cells (a model of primary neuronal cells used by scientists) with lipoic acid may lessen the depletion of glutathione and preserve the activity of mitochondria.³³ Other work indeed shows that lipoic acid pre-treatment helps protect against radiation-induced DNA damage, indicating that “alpha-lipoic acid is a potent neuroprotective antioxidant.”³⁴

LIPOIC ACID MAY DECREASE BODY FAT

Although not typically thought of as a ‘weight-loss’ agent, lipoic acid does exert effects that might be worthwhile for those looking to trim their waists. Studies have shown that lipoic acid supplementation can decrease fat accumulation in mice.^{42,43} Lipoic acid also reduces body weight and prevents the development of diabetes in diabetes-prone obese rats by reducing triglyceride accumulation in non-adipose tissues thus improving insulin sensitivity.⁴³ So should you take lipoic acid if you want to lose weight? From a general health standpoint, it is wise to take lipoic acid anyhow. And if your waistline shrinks, then even better!

ANTICANCER EFFECT

Lipoic acid has also been investigated as an anticancer therapy,³⁵ because of its ability to preferentially induce apoptosis³⁶ and inhibit cancer cell proliferation.³⁷ In one amazing case study, the authors describe the long-term survival of a patient with pancreatic cancer without any toxic adverse effects. Pancreatic cancer is one of the most virulent forms of cancer that has a very poor prognosis. In this case study, the subject was treated with intravenous lipoic acid and low-dose naltrexone combined with a healthy lifestyle program. The patient was informed in October 2002 that there was little hope for his survival. By January 2006, however, he was back at work, symptom-free, and without appreciable progression of his malignancy. Furthermore, several other patients are on this treatment protocol and appear to be doing well. The authors believe that this



treatment protocol should be studied and considered, given its lack of toxicity and limited but impressive results.³⁸

Researchers have also studied the effects of lipoic acid on abnormal ovarian cell development. They found that lipoic acid selectively inhibits the growth of tumorigenic ovarian cells by increasing levels of a marker that halts abnormal cell division and reducing levels of proinflammatory cytokines in the body.³⁹

REJUVENATION EFFECTS

In addition to its disease-protective benefits, lipoic acid can also help fight the 'cosmetic' ravages of aging. For instance, one study investigated whether a cream containing 5% lipoic acid could improve the appearance of skin damaged by photoaging. The investigators took 33 women, average age 54 years, and treated half their faces twice daily with the lipoic acid cream and the other half using a control cream without lipoic acid. They discovered that after 12 weeks of treatment, lipoic acid improved clinical characteristics related to photoaging of facial skin, according to the women's self-evaluation as well as clinical and photographic evaluations.⁴⁰

Scientists are still unraveling the clues behind the impact of aging on cellular and tissue responses, which may result from unchecked inflammation, an altered balance of protein synthesis and degradation, and subsequent downstream effects on the rate and quality of wound healing.⁴¹

CONCLUSION

Lipoic acid has demonstrated multiple beneficial biological effects that make it a must-have in every aging human's supplement "toolbox."

If you have any questions on the scientific content of this article, please call a Life Extension Health Advisor at 1-800-226-2370.

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