R-Alpha Lipoic Acid →
The Practitioners ultimate tool

Alpha-Lipoic Acid (ALA), is a vitamin-like sulfur containing fatty acid. It's a naturally occurring derivative is octanoic acid with several biological functions in the body. It's known as the universal antioxidant and has been studied for its therapeutic and prophylactic potential since the 1950's. Best known for its ability to mitigate diabetic neuropathy and regulate glucose metabo-lism, ALA is being looked into as a potential tool in a wide range of patho-logical conditions.

In addition to being known as the 'Universal Antioxidant', ALA belongs to a class of compounds referred to as 'mitochondrial nutrients'. The effect ALA exerts on the mitochondria paired with its antioxidant properties are what afford it the systemic benefits it has in the body.

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Basic Biology

ALA is a thiol compound with many of its chemical properties stemming from the dithiol ring, whose sulfur components provide several benefits.

Two forms of ALA exist. S-Lipoic Acid and R-Lipoic acid. R-lipoic acid is the form that is found in nature. It is the biologically active version of ALA and is readily used by the body. On the contrary, S-Lipoic Acid is a man-made compound created to stabilize R-ALA, and reduce manufacturing costs.

Alpha-lipoic Acid is the oxidized form of lipoic acid and dihydrolipoic acid (DHLA)is the reduced form. When ALA is metabolized, it is quickly reduced to DHLA, which is suggested to have more potent antioxidant abilities than ALA. Together, they form a powerful redox couple that takes care of reactive oxygen species, chelates metals and facilitates the health of other antioxidants.

Used in the Krebs cycle, ALA is an essential coenzyme necessary for energy production, mainly in carbohydrate metabolism.

Overview of Biological Properties

- Neutralizes reaction oxygen species (ROS)
- Increases tissue concentrations of other antioxidants
- Chelates copper and iron
- Can stabilize metals with free radical properties such as manganese and zinc
- Crosses the blood-brain barrier
- Functions as a redox regulator of several proteins (myo-globin & prolactin)
- Contributes to gene transcription
- Promotes mitochondrial health as well as mitochondria biogenesis
- Indicated in energy metabolism (amino acid breakdown and carbohydrate metabolism)

Alpha Lipoic Acid as an Antioxidant

Many pathological processes involve a disrupted antioxidant to free radical ratio. When there are not enough antioxidants to neutralize free radicals, oxidative stress results. Oxidative stress damages healthy tissues and cells. Over time this damage can prompt, accelerate and contribute to both the onset and progression of chronic conditions.

Several factors contribute to the imbalance between free radicals and antioxidants. Environmental conditions such as pollution, dietary choices and lifestyle factors can all increase free radical load. The body is able to synthesize some antioxidants. However, the capacity is limited and declines with age. It is necessary to have a constant influx of antioxidants from exogenous sources such as food and supplements to restore the balance in the body.

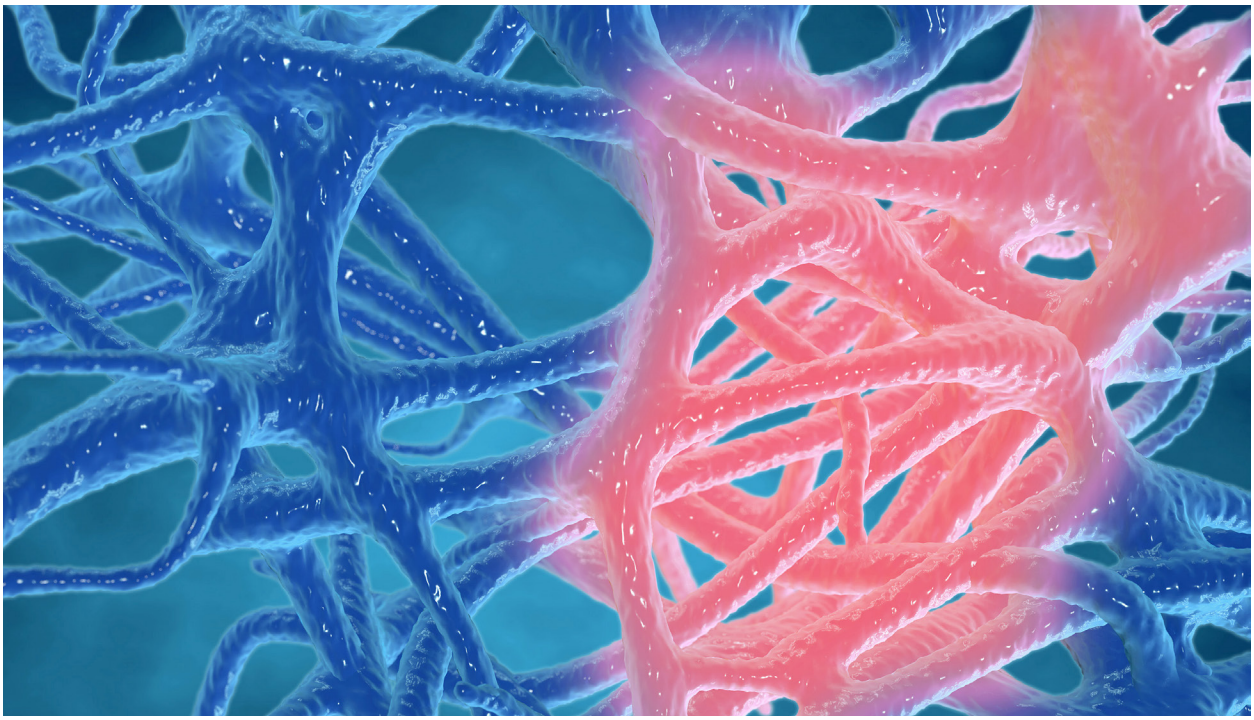
Alpha Lipoic Acid is a unique antioxidant in the sense that it is both water and fat soluble. This is in contrast to other antioxidants which are either fat soluble or water soluble but not both. This feature allows ALA to exert its effects intracellularly and extracellularly. It is able to easily penetrate tissues, independent of their composition and neutralize free radicals. For this reason, it has antioxidant properties in the brain, nervous system, throughout the cardiovascular system, in the liver and skeletal muscle among others.

ALA is found in the mitochondria, intracellular fluid and in the phospholipid cell membrane. This gives an indication of its wide range of therapeutic potential as an antioxidant.

ALA works as an antioxidant though:

- Neutralizing various reactive oxygen species
- Inhibiting reactive oxygen generators
- Repairing damage inflicted by oxidants
- Restoring other antioxidants, thus increasing systemic concentration
- Increases cellular resistance to hydrogen peroxide

ALA has a higher free radical scavenging capacity and is a more stable molecule in comparison to other antioxidants. Due to this, research has shown that ALA is able to regenerate other antioxidant agents, most notably- glutathione, vitamin C, vitamin E and CoQ10.



Alpha Lipoic Acid and Inflammation

Inflammation is a normal cellular process designed to heal the body from injury. However, chronic inflammation, like oxidative stress, is another key contributor to chronic illness.

ALA can inhibit the inflammatory cascade through and independent of its ROS scavenging abilities.

The oxidative stress that ensues from increased free radicals can prompt a chronic inflammatory response. Because ALA is efficient at quenching free radicals, it indirectly has a positive effect on inflammation.

ALA also exerts an effect on NF-Kb. Increased and long-term expression of NF-Kb is a characteristic of a number of pathological processes, due to its pro-inflammatory properties. ALA is able to inhibit NF-Kb and its downstream inflammatory markers such as TNA-a and IL-6. In addition to reducing proinflammatory mediators, it acts on inflammasomes, thereby increasing anti-inflammatory cytokines. Exerting a two-pronged effect on the inflammatory pathways.

Therapeutic Considerations for Alpha Lipoic Acid

Diabetes

Characterized by blood sugar dysregulation and insulin resistance, diabetes is a pathology that has myriad potential complications. ALA has been studied extensively for its role in mitigating insulin resistance and in glucose metabolism. A large body of research on ALA is centered around diabetic neuropathy. Since diabetes is a risk factor for cardiovascular events, the effects of ALA have been looked at in relation to risk factors for cardiovascular disease in both patients with diabetes and without. The research suggests ALA can decrease HbA1c and fasting blood glucose, reduce the risk for cardiovascular events, improve the lipid profile and clinically improve diabetic neuropathy.

Glucose Regulation

Hyperglycemia is a characteristic of metabolic disease and diabetes. Improving insulin sensitivity, and reducing blood sugar through non-insulin dependent mechanisms is important in the maintenance and prevention of diabetes. ALA has a positive effect on glucose regulation.

Mechanisms of Action

- Increase glucose uptake in insulin resistance and sensitive muscle tissue
- Encourages glucose transporters to migrate to the cell membrane, especially GLUT-4 in fat and skeletal muscle
- Increases insulin signaling pathway
- Activates AMPK resulting in lower plasma glucose and increased insulin sensitivity
- May inhibit insulin secretion from pancreatic beta cells

Note: The more metabolically compromised the individual, the lower the dose of ALA needed to see improvements. For full effects in mild to moderate metabolic pathology, a higher dose is needed.

Diabetic Neuropathy

Diabetic Neuropathy (DN) is a complication of diabetes that results from nerve damage. Excess oxidative stress is hypothesized to be a culprit in the onset and progression of diabetic neuropathy. ALA has a positive effect on nerve health and since the pathogenesis of DN is influenced by oxidative stress, ALA is a prime candidate for symptom management. Symptoms such as spontaneous burning, intense pain and numbness have been shown to subside with the introduction of ALA. A higher quality of life was also reported in a significant number of subjects. The proposed mechanism through which ALA works are:

- Improves nerve blood flow
- Improves nerve conduction
- Improved quality of life
- Median and peroneal sensory nerve velocity improved

Cardiovascular Health

The risk for cardiovascular disease (CVD) increases with diabetes, however independent of a di-abetes, CVD is still prevalent in the general population. ALA helps to reduce the risk for CVD by improving individual lipid profiles, promoting health cholesterol levels, supporting blood ves-sels and reducing inflammation.

- In diabetics ALA lowered CRP by up 30%, IL-6 by up to 29% and TNF-a by up to 22%
- Reduced amount of oxidized lipoproteins
- Improves endothelial dysfunction
- Relieves endoplasmic reticulum stress (a key marker in diabetes and CVD)
- Protects against the onset of atherosclerosis
- Increase the amount of LDL receptors in the liver
- Improves triglycerides

Weight Management

There's evidence that ALA can help support a healthy weight. The mechanisms that allow ALA to regulate weight are the same as it's metabolic benefits and include, increasing insulin sen-si-tivity, lowering triglycerides, promoting a healthy cholesterol profile and regulating glucose uptake.

The current understanding is that ALA in higher doses (approximately 800mg-1800mg) can produce moderate weight loss in clinically obese individuals. This might be due to the ability of ALA to activate hypothalamic AMPK. Research when paired ALA can have moderate effects in appetite suppression, and therefore, ALA can support individuals in their weight loss goals. While it can offer a weight loss effect on it's own, the research suggests pairing ALA with a targeted dietary strategy.

One study showed ALA can be used in conjunction with antipsychotics, to mitigate weight gain caused as a side effect of the medication (always check with your MD or ND before starting a supplement when on medication)

Cognitive Health

Science is now looking toward oxidative stress and inflammation as a contributing factor to the pathogenesis of neurological conditions. ALA is a neuroprotective agent and anti-inflammatory molecule that possesses the ability to reverse damage to the central nervous system to a signif-icant degree. Research has shown the efficacy of ALA in slowing down the progression of mild Alzheimer's, reducing the rate of cognitive decline and there is evidence for the use of ALA in multiple sclerosis. Further research is needed to understand the full range of effects of ALA on neural tissue and how these can be used in a clinical setting.

The proposed mechanisms of action in regard to ALA and cognition are:

- Reduces oxidative stress in neural tissue
- Crosses the Blood Brain Barrier
- Modulates insulin resistance in the brain
- Increases production of acetylcholine
- Readily enters both the central and peripheral nervous system
- Exerts a protective action on glioma cells
- Reduces migration of t-lymphocytes into the central nervous system (anti-inflammatory environment)
- Potential to chelate and a sequester excess iron
- In animal studies, ALA protected cortical neurons from cytotoxicity

Novel Conditions

New, exciting and promising research is continuously surfacing surrounding the therapeutic na-ture of ALA. Due to its antioxidant and anti-inflammatory properties along with its role in mito-chondrial and nerve health, it's hypothesized that ALA is a promising candidate for the manage-ment of several pathological conditions. The research that is currently emerging is fo-cusing on:

- Migraines
- Autoimmune conditions, specifically MS and lupus
- Chronic Pain (carpal tunnel and lower back pain)
- Age related digestive disturbances
- Non-Alcoholic Fatty Liver Disease (NAFLD)

Supplementation and ALA

De novo synthesis of ALA occurs in small amounts in the body. The amount created internally isn't sufficient for the energy requirement of the cells, and therefore external sources such as food and supplements are recommended to fill the gap. Clinical conditions, such as diabetes can down-regulate the production of ALA in the body, and therefore baseline health should be taken into consideration when deciding if supplementation is updated and what dose!

Safety and Contraindications

Safety

Alpha Lipoic Acid has proven to have an excellent safety profile. A large meta analysis compiled data from several trials and observational studies that concluded supplementation with ALA wasn't associated with any adverse events.

It has been shown to be safe in several populations including but not limited to: smokers, those with cardiovascular disease, neurological disorders and diabetes. An observational study looked at the effects of ALA in pregnancy and determined that is safe. Although well tolerated in pregnancy, there is insufficient evidence for the use of ALA in a pediatric population.

In terms of prolonged supplementation, it's advisable to cycle supplements- however ALA has been declared safe for consistent use up to 4 years.

No adverse events have been described in the literature with doses up to 1,800mg. With this in mind, possible reactions can include nausea, vomiting, dizziness, cutaneous rash, hypotension and hypertension. These are not dose dependent and are rare.

Contraindications

Caution should be exerted with the use of some medications. Consult with your MD or ND when deciding to use ALA in combination with diabetic or thyroid medication or if undergoing chemotherapy.

Recommended Daily Intake (RDI)

Currently there are no government mediated guidelines for the RDI of ALA. A standard, preventative dose is up to 600mg a day; however, research shows that up to 1,800mg is safe and therapeutic. The ideal dose will vary from individual to individual.
Note: These amounts will be lower when using liposomal supplements due to their superior bioavailability.

Food Sources

ALA is found in various plant and animal foods, albeit with a few caveats.

Food Sources: Red meat, organ meats (kidney, heart and liver), spinach, broccoli, tomato, potatoes and peas.

Research shows that consuming foods that contain ALA has an insignificant impact on plasma and cellular levels. Current evidence suggests that ALA is broken down by stomach acid, and further degraded by the liver. This results in a short half-life and only a 30% uptake by cells. In addition to this, in dietary sources, ALA is bound to lysine- an amino acid. Human digestive enzymes are unable to break this bond, further reducing its bioavailability.

Different Types of Supplements

ALA supplements come in capsules, pills, liquids and liposomes. Intravenous ALA is also available through qualified health care professionals.

Unlike food sources, supplements contain free ALA, which has scientifically been shown to increase levels in the body. The amount of ALA found in supplements is estimated to be 1000 times greater than in food sources- making supplementation the most effective way to increase levels and reap the therapeutic and prophylactic benefits of ALA.

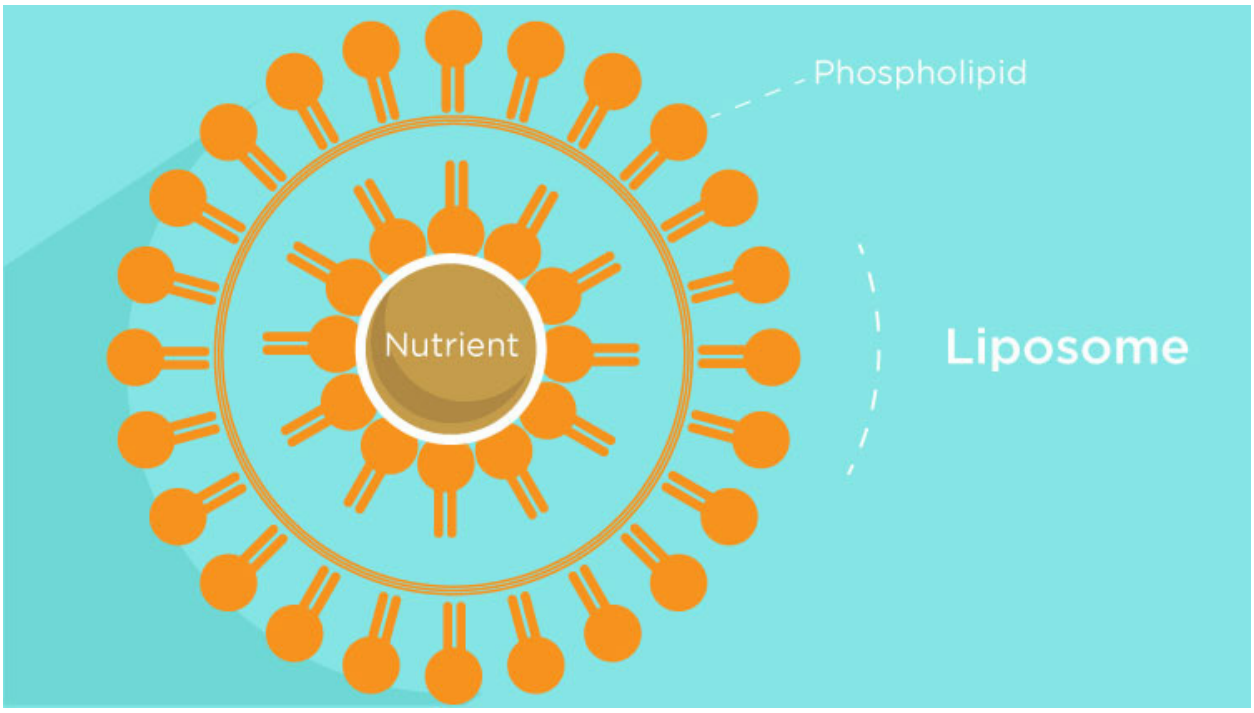
As mentioned previously, two forms of ALA exist; S-ALA and R-ALA. R-ALA is found in nature and it is the form that the body produces internally, whereas S-ALA is a synthesized version. R-ALA exerts a greater biopotency in metabolic pathways in comparison to S-ALA, along with a higher availability. Research found that plasma concentrations of ALA increased up to 50%more with R-ALA vs S-ALA at the same dose.

Many supplements use both forms in their formulations. This is because S-ALA is more cost effective than R-ALA and can be used to stabilize R-ALA – which is the less stable of the two and can be damaged easily. A quality and more efficacious supplement contains only the biologically active form: R-ALA.

NOTE: Most supplements will provide this info on the label, but always check the ingredients on the back to be sure.

Who Benefits from ALA Supplementation?

- Those with high stress lifestyles
- Those who have metabolic dysfunction (pre-diabetes, diabetes)
- Older adults
- Those at high risk for chronic illness
- Those experiencing age-related health issues



What are Liposomes

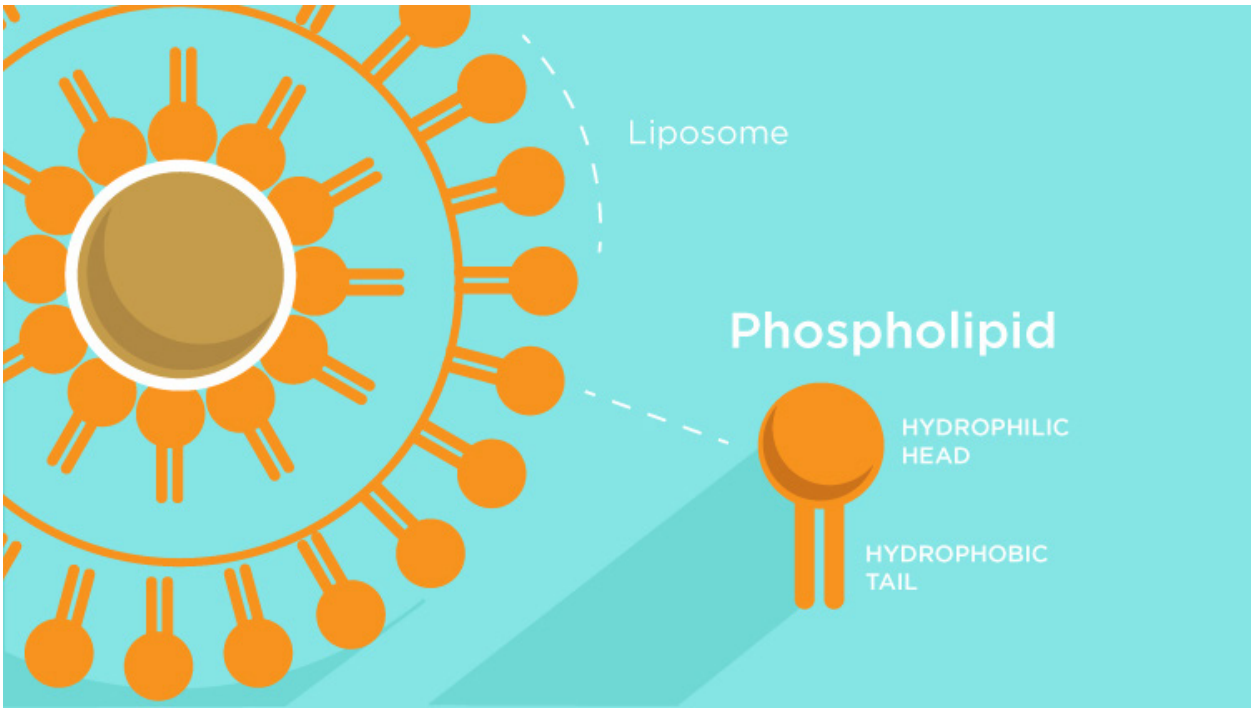
Liposomes are microscopic nano particles made of essential phospholipids. The phospholipids form a bubble, and encapsulate the nutrient of choice - in this case R-Alpha-Lipoic Acid.

The structure of a liposome allows superior absorption because none of the proteins involved in nutrient specific transportation are needed. Instead, liposomal vitamins get absorbed intact, as a fat through the small intestine where it then enters the bloodstream. Once in the bloodstream the liposomes attach to cells and the nutrient is released through the cell membrane.

LivLong Lypo-Spheric® Vitamin C is manufactured in the USA by LivOn Labs and uses a patented process called Liposomal Encapsulation Technology (LET)- each sachet contains 100mg of bioavailable Vitamin C and 1000mg of essential phospholipids. Each scahet is the equivialnt to taking 3000-4000mg of a conventional vitamin C supplement.

The Lypo-Spheric® Advantage

Not all liposomal vitamins are created equal. Encapsulation via phospholipids has been shown to have superior absorption compared to emulsion formulas. For this reason, Lypo-Spheric® uses Liposomal Encapsulation Technology to encapsulate Vitamin C in essential phospholipids, such as phosphatidylcholine. This process is what is responsible for the high, clinically proven absorption rate of Lypo-Spheric® products.



Benefits of Phospholipids

Phospholipids regulate several biological functions, such as cellular signalling and genetic expression. The fatty acids that make up phospholipids inhibit inflammatory pathways and phospholipids as a whole provide cellular protection from pathogens and harmful chemicals.

Phosphatidylcholine is the most abundant phospholipid in the body, and is considered essential as the body cannot synthesize it on its own. The cellular membrane is made up of 90% phosphatidylcholine but as the cellular membranes become compromised with age, the concentration of phosphatidylcholine decreases substantially.

The health of the cell membrane is critical to overall health. Due to it's fatty acid composition, the cell membrane is susceptible to free radical damage, which has ripple effects throughout the body. It is essential to provide the body with the building blocks to maintain and repair the delicate membrane.

Each packet of Lypo-Spheric® Vitamin C contains 1000mg of essential phospholipids that not only provide the best oral delivery of ALA, but also provide the material to keep cell membranes healthy from a structural and functional standpoint.

Why Use Phospholipids to Make Liposomes?

Lypo-Spheric® products use phospholipids because they are both hydrophilic and hydrophobic, which allows them to create an ideal liposome which is able to encapsulate nutrients for superior bioavailability.

4 Advantages to Lypo-Spheric R-Alpha Lipoic Acid

1. Contains only the bioactive form, R-ALA
2. Thanks to LET, the ALA is protected from the stomach acid/gastric juices and is delivered to cells intact
3. Lower dose is needed due to superior absorption
4. Contains essential phospholipids

The LivLong Team

** This guide is intended for informational purposes only, and is not to be used as medical advice.

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