

The Ultimate Guide to Alpha Lipoic Acid

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 **ABUNDANCE & HEALTH**
HIGH PERFORMANCE NUTRIENTS



Alpha lipoic acid is an extremely important defence nutrient that can either be taken as a supplement, absorbed from the foods you eat or produced naturally by your body. It is an extraordinarily potent nutrient that really packs a powerful punch in a way that many other protective nutrients just can't compete with.

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Introduction

In the last decade there has been a surge of interest in the pharmacological properties of alpha lipoic acid and an increasing rise in the number of studies investigating this nutrient's, therapeutic potential for a range of health concerns. Let's find out why...

What is alpha lipoic acid?

Alpha lipoic acid is a sulphur containing fatty acid that is also referred to as lipoic acid and thioctic acid. It is derived from octanoic acid and is transported into the cells where it is rapidly reduced to dihydrolipoic acid (DHLA), the more bioactive form of alpha lipoic acid, which possesses the unique ability to neutralise free radicals.^{1,2,3}

What are free radicals?

Free radicals are unstable molecules produced naturally in the body during many of the natural metabolic and chemical processes, such as breathing, burning food for energy or fighting off infections.⁴ If free radicals overwhelm the body's ability to neutralise them, they may contribute to cellular oxidative stress, which has the potential to damage cells, proteins and DNA, a process that's associated with degenerative disease and ageing. Oxidative stress is believed to make a significant contribution to many inflammatory conditions, such as arthritis, respiratory diseases, heart disease, gastric ulcers, Type 2 diabetes, hypertension and many neurological disorders.⁵

Alpha lipoic acid is found in the mitochondria, the intracellular fluid and the phospholipid membranes of cells and this nutrient accumulates primarily in the heart, liver and skeletal muscle, but is found in other tissues as well.

Alpha lipoic acid exists in two forms, S-Lipoic acid or R-Lipoic acid, the latter being the naturally occurring and more biologically active form found in the body.⁶ Results from one comparative study, recorded plasma concentrations of R-Lipoic acid were as much as 40-50% higher than S-Lipoic acid in volunteers who received a 600mg oral dose of each.⁶



The many roles of alpha lipoic acid

Alpha lipoic acid functions as a cofactor in several important enzymatic complexes that are involved in the breakdown of amino acids and the generation of energy in the mitochondria.⁷

Converting glucose into energy

Mitochondria are tiny organelles within cells that take in nutrients and convert them into energy rich molecules for the cell to use. They are known as the powerhouses of cells and play a pivotal role not just in energy metabolism but also immune response and cell turnover.⁸

Supporting cellular defences

Around forty years ago, biologists discovered that as well as playing a key role in energy generation, alpha lipoic acid also has unique and powerful cell defence properties. These activities are shown to be more effective in supplemental form compared to food sources.

Effective as a supplement

Research shows that alpha lipoic acid contained in food, has very little impact on levels of free lipoic acid in human plasma or cells.⁹ Data suggests that alpha lipoic acid from food has a short half-life and uptake in the cells (about 30%), which is due to its reduced solubility, instability in the stomach and degradation by liver processes.¹⁰ However, the use of various innovative supplement formulations has greatly improved alpha lipoic acid's absorption and uptake into cells.

Unique set of attributes

A growing body of evidence suggests that orally supplied alpha lipoic acid isn't necessarily used as a metabolic cofactor, but instead generates a unique set of biochemical activities against a variety of biological mechanisms that culminate in disease.¹¹ These activities have been attributed to alpha lipoic acid's:

- **Contribution to cell defence functions**¹²
- **Ability to neutralise reactive oxygen species (ROS)**¹²
- **Significant effect on the tissue concentrations of many powerful antioxidants**¹³
- **Ability to form stable complexes with copper, manganese, zinc and other metals that act as free radicals**¹⁴
- **Ability to cross the blood-brain barrier**¹⁵

Therapeutic potential

Research also suggests that alpha lipoic acid and DHLA may have an impact on genes and regulatory proteins which play key roles in metabolism and growth.^{16,17} These diverse actions suggest that alpha lipoic acid supports multiple mechanisms both physiologically and pharmacologically. Studies show that alpha lipoic acid is found to be lower in individuals in poor health, indicating the scope for further research on the potential therapeutic role this nutrient may play in some cases.¹⁸

1. How does alpha lipoic acid protect cells?

The human body uses oxygen as the primary oxidant in energy producing biological reactions, yet this aerobic mechanism is associated with the generation of highly reactive and potentially harmful (free radical) molecules. Oxidative damage occurs when there is an imbalance between free radical generation and the body's ability to neutralise these reactive products.¹⁹ Modern day lifestyles have increased our susceptibility to increasing levels of free radical damage due to poor diet, pollution, over exposure to sunlight, cigarette smoke and numerous other medicines, drugs and chemicals.

It is virtually impossible to escape from free radical damage, which is why it is so important to protect the body with a continuous supply of defence nutrients to help offset the potential cellular damage. This is not always straightforward because the body's ability to produce antioxidants to neutralise free radical damage is controlled by an individual's genetic makeup and is also affected by dietary choices and exposure to environmental pollutants.

Alpha lipoic acid's action as a defence nutrient is well-researched. It offers a uniquely efficient protective mechanism against the damaging effects of pro-oxidants. Alpha lipoic acid is unusual in that it functions in both fatty and watery sections of cells, whereas other nutrients with antioxidant properties are either water-soluble or fat-soluble substances^{20,21,22,23}. For example, vitamin C is a water-soluble compound that works to protect aqueous areas of the body, such as the inside of cells and blood from oxidative stress. Vitamin E is a fat-soluble compound utilised by the body to protect the mainly fatty composition of the cells such as the cell membranes.

This dual functionality gives alpha lipoic acid an unusually broad spectrum of action. Since alpha lipoic acid is easily absorbed through the gut and transported across cell membranes it offers protection against a wide variety of free radicals both inside and outside the cell including the DNA, allowing it to protect virtually all body tissues against free radicals.

2. Can alpha lipoic acid support antioxidant status?

When antioxidants neutralise a free radical, they become oxidised (inactivated), and are no longer able to neutralise additional free radicals. But evidence suggests alpha lipoic acid can regenerate vitamin C, vitamin E and glutathione, making them active once again. This antioxidant recharging ability of alpha lipoic acid helps extend the lifespan of these important and powerful defence nutrients.²⁵

3. Why is alpha lipoic acid important for energy production?

It's well established that alpha lipoic acid plays an essential role in the bio-energetic reactions of the mitochondria. Within these special cellular components, alpha lipoic acid acts as a cofactor for some of the key enzymes involved in generating energy from carbohydrates, proteins, fats and oxygen, holding a critical position in energy metabolism.²⁶

4. How is alpha lipoic acid involved in glucose uptake?

The binding of insulin to insulin receptors triggers a cascade of reactions that allows glucose to enter into cells, a process called glucose uptake.²⁷ Results from in-vitro research suggest that lipoic acid may enhance glucose uptake by helping to regulate the activity of a glucose transporter molecule, which stimulates insulin-signalling mechanisms.²⁸

5. Could alpha lipoic acid support heart health?

Oxidative stress is believed to be a major factor in a range of cardiovascular conditions, such as atherosclerosis, high blood pressure and heart failure. There are several defence nutrients involved in neutralising oxidative stress and alpha lipoic acid is one of them. The activity of protective defence nutrients such as alpha lipoic acid and vitamin C is believed to have a beneficial effect on oxidative stress measurements in relation to cardiovascular health.²⁹



How much alpha lipoic acid do you need?

Although there is no established recommended daily nutrient value for alpha lipoic acid, standard doses tend to range between 100-600mg a day.^{29,30} Levels used in scientific research range from 300mg to 1,200mg a day.³¹

What are the best food sources of alpha lipoic acid?

R-lipoic acid occurs naturally in a wide variety of plant and animal foods. However, it is bound to lysine, an amino acid found within protein molecules, so it's not present as free alpha lipoic acid.³² The body cannot benefit from it in the same way as it does with the alpha lipoic acid that your body produces. This is thought to be because human digestive enzymes are unable to break the bond between alpha lipoic acid and lysine.³²

FOODS TYPICALLY HIGH IN ALPHA LIPOIC ACID INCLUDE:

KIDNEY	TOMATOES
HEART	PEAS
LIVER	BRUSSELS SPROUTS
SPINACH	BREWER'S YEAST
BROCCOLI	

Although alpha lipoic acid is found naturally in food, it is not likely that enough alpha lipoic acid is consumed in the typical Western diet. Whereas high oral doses of supplemental free alpha lipoic acid lead to significant increases within the body.³³ Studies have identified that approximately 30-40% of an oral dose of standard alpha lipoic acid is absorbed.³⁴

Are there risk factors for an alpha lipoic acid deficiency?

Animal studies have shown that a deficiency of alpha lipoic acid may result in a failure to thrive, brain atrophy, reduced muscle mass and increased lactic acid accumulation. No such states have been demonstrated in humans, except in rare cases of inherited mutations in the biological pathways that synthesise lipoic acid.³²

Six quick facts about alpha lipoic acid

1. Alpha lipoic acid was first isolated from insoluble liver extracts in 1951.
2. It was first used around 1959 for the treatment of acute poisoning by *Amanita phalloides*, otherwise known as 'death cap' (from mushrooms).³⁵
3. In much of the world alpha lipoic acid is regulated as a medicine. In fact, intravenous alpha lipoic acid is classed as a medicine in all countries.³⁶
4. Germany has approved the use of intravenous alpha lipoic acid for diabetic neuropathy since 1959 and is available by prescription.³²
5. Although alpha lipoic acid is synthesised in small amounts in the human body it is not sufficient for the energy needs of the cell, so it must be obtained via food or supplementation.¹⁷
6. Considering its role in many biochemical processes, lipoic acid was once included as part of the B vitamin family. Nowadays, the overall consensus by scientific experts is that lipoic acid is not a vitamin.³⁷

Are there different types of alpha lipoic acid supplements?

When looking for a supplement make sure you don't get confused between alpha lipoic acid and the omega 3 alpha linolenic acid because they can both be abbreviated to ALA.³⁸

Alpha lipoic acid supplements are available as liposomes, tablets, capsules and liquids. Your health care provider may also be able to provide it intravenously.³⁸ Unlike alpha lipoic acid found in foods, supplements contain free alpha lipoic acid. Supplemental alpha lipoic acid is available in three different forms:

- **R-Alpha-Lipoic Acid (R-ALA)**
- **S-Alpha-Lipoic Acid (S-ALA)**
- **Mixed R-ALA & S-ALA**

Not all forms of ALA are created equal. According to research R-ALA is more readily digested and absorbed into the cells than S-ALA.³² R-ALA is the form that is present in nature, whereas S-ALA is synthetic. It may be obtained through many chemical procedures of thioctic acid and stops the important activities of R-ALA, such as the interactions with enzymes, proteins and genes.¹⁷

Many supplement companies produce alpha lipoic acid synthetically in the S form. This is because in standard products it is cheaper to produce and is more stable. Some companies use a mix of the two.

Superior absorption with liposomal R-ALA

Supplements containing R-ALA in liposomal delivery form are considered superior to standard oral supplements because of their many advantages. Liposomes protect the alpha lipoic acid from oxidation and degradation in the acidic environment of the stomach and increase the absorption and uptake in cells compared to other conventional pharmaceutical delivery forms such as tablets and capsules.

It is worth noting that the amounts of alpha lipoic acid available in supplement form (200-600mg) may be as much as 1000 times greater than is possible to obtain from the diet.



What exactly are liposomes?

A liposome is a tiny spherical fluid filled sac surrounded by a phospholipid bilayer, which closely resembles the structure of human cell membranes. The ability of liposomes to encapsulate water-soluble or fat-soluble substances allows these vesicles to become highly effective nutrient delivery systems. Liposomes are often composed of naturally derived phospholipids, such as phosphatidylcholine.

The phospholipid protective shield encapsulating the nutrients forms a barrier, which is normally resistant to the action of enzymes, pH, and free radicals within the body. This protects the contents from degradation until the nutrients are released at the target cell, organ, or tissue. Because of the high biocompatibility, biodegradability, low toxicity, and capability to encapsulate fat and water-soluble compounds, liposomes are found to be the most successful nutrient carrier system known to date.³⁹

Why are phospholipids so important?

Historically phospholipids were only thought to be useful as structural components of cell membranes to aid flexibility and fluidity or forms of energy storage in cells. However, data uncovered over the last 30 years shows they also have an important role in cell physiology.^{40,39} They have been identified as playing an important role in regulating and organising a whole range of cellular functions including:

- **Cell signalling**
- **Cell structure**
- **Processes related to growth and immune surveillance**
- **Pathways for substances to cross membranes**
- **Apoptosis (programmed cell death)**

Phospholipids also work as emulsifiers to enhance fatty acid absorption and act as lubricating surfaces for structures like joints that require smooth motion.⁴⁰

The best-known phospholipid is phosphatidylcholine (also known as lecithin), which is an important component of the omega 3 fatty acids EPA and DHA found in cell membranes, which are known to contribute to the normal function of the heart.

Why choose a liposomal form of alpha lipoic acid?

Liposomal supplements offer more superior absorbency due to their unique delivery system. This is possible because the R-ALA is encapsulated in a protective phospholipid bilayer. This microscopic bubble protects the R-ALA from the powerful activity of the digestive juices, alkaline solutions, and free radicals of the body and transports it unharmed to the target tissues where it is instantly taken into the cell. What's more, because liposomes are delivered rapidly to the bloodstream and cells, they are far less energy dependent.

Liposomal encapsulation is a technology that prevents gastrointestinal degradation and assures high absorption into the blood. What's more it is also thought to target the intracellular space and reach into cellular compartments such as the mitochondria or nuclei.⁴¹ In addition to this superior delivery of nutrients, liposomes also effectively protect their contents from oxidation until they have reached their destination.

Liposomal Altrient R-ALA is manufactured by LivOn labs in the US using unique patented Liposomal Encapsulation Technology (LET).



The top 5 advantages of Altrient ALA

1. Altrient R-ALA contains liposomal R-ALA which is the most biologically active and rapidly absorbed form of alpha lipoic acid.
2. S-Lipoic Acid in conventional products is chemically synthesised and cannot provide the same benefits.
3. Altrient R-ALA preserves the stability of alpha lipoic acid in the gastric environment.
4. One sachet of Altrient R-ALA provides 1000mg of phospholipids, which includes 500mg of phosphatidylcholine.
5. Altrient R-ALA provides alpha lipoic acid in convenient portable sachets that are gluten free and vegan friendly.



How safe is alpha lipoic acid?

In general, high-dose alpha lipoic acid administration in adults has been found to have few serious side effects, however it has not been studied in children, so it is not recommended for paediatric use.⁴² There is insufficient evidence to support its use during pregnancy except under medical supervision. There have been no reported side effects in oral administration of up to 1,800mg daily. Doses of 500-1,000mg have been well-tolerated in placebo-controlled studies.

Adverse interactions

Care should be taken when combining alpha lipoic acid with certain medications.⁴² Professional advice should be sought from your healthcare provider, particularly relating to diabetes, chemotherapy and thyroid medication. Alpha lipoic acid may also lower the level of vitamin B1 in the body.

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References

1. Alpha-Lipoic Acid. Monograph. <http://archive.foundationalmedicinereview.com/publications/11/3/232.pdf>. [Accessed 5.5.20.]
2. Hagen T.M. et al. Alpha-lipoic acid as a dietary supplement: Molecular mechanisms and therapeutic potential. *Biochimica et Biophysica Acta* 1790 2009; 1149-1160.
3. Linus Pauling. Alpha-lipoic acid. <http://lpi.oregonstate.edu/mic/dietary-factors/lipoic-acid>. [Accessed 6.5.20]
4. Live Science. What are free radicals? <https://www.livescience.com/54901-free-radicals.html>. [Accessed 11.5.20.]
5. Bilaska A, Wlodeck L. Review. Lipoic acid – the drug of the future? *Pharmacological Reports*. 2005; 57, 570-577.
6. Arcaro M. et al. Effects of 1-month α -lipoic acid supplementation on humans oxidative status: a pilot study. *Progress in Nutrition* 2017; Vol. 19, N. 1: 14-25.
7. Alpha-Lipoic Acid. Monograph. <http://archive.foundationalmedicinereview.com/publications/11/3/232.pdf>. [Accessed 5.5.20.]
8. Xia, M., Zhang, Y., Jin, K. et al. Communication between mitochondria and other organelles: a brand-new perspective on mitochondria in cancer. *Cell Biosci*. 2019; 9, 27.
9. Goraca A and Skibaska B. The Protective Effect of Lipoic Acid on Selected Cardiovascular Diseases Caused by Age-Related Oxidative Stress. *Oxidative Medicine and Cellular Longevity* 2015; 313021:1-11.
10. Salehi B, Berkay Yilmaz Y, Antika G, et al. Insights on the Use of α -Lipoic Acid for Therapeutic Purposes. *Biomolecules*. 2019;9(8):356.
11. Hagen T.M. et al. Alpha-lipoic acid as a dietary supplement: Molecular mechanisms and therapeutic potential. *Biochimica et Biophysica Acta* 1790 2009; 1149-1160.
12. Salehi B, Berkay Yilmaz Y, Antika G, et al. Insights on the Use of α -Lipoic Acid for Therapeutic Purposes. *Biomolecules*. 2019;9(8):356.
13. Linus Pauling. Alpha-lipoic acid. <http://lpi.oregonstate.edu/mic/dietary-factors/lipoic-acid>. [Accessed 6.5.20]
14. Sigel H, Priejs B, McCormick DB, Shih JC. Stability and structure of binary and ternary complexes of alpha-lipoate and lipoate derivatives with Mn²⁺, Cu²⁺, and Zn²⁺ in solution. *Arch Biochem Biophys* 1978;187:208-214.
15. Hagen T.M. et al. Alpha-lipoic acid as a dietary supplement: Molecular mechanisms and therapeutic potential. *Biochimica et Biophysica Acta* 1790 2009; 1149-1160.
16. Linus Pauling. Alpha-lipoic acid. <http://lpi.oregonstate.edu/mic/dietary-factors/lipoic-acid>. [Accessed 6.5.20]
17. Salehi B, Berkay Yilmaz Y, Antika G, et al. Insights on the Use of α -Lipoic Acid for Therapeutic Purposes. *Biomolecules*. 2019;9(8):356.
18. Live Science. What are free radicals? <https://www.livescience.com/54901-free-radicals.html>. [Accessed 11.5.20.]
19. Lobo V, Patil B, Phatak A, Chandra N. Free radicals, antioxidants and functional foods: Impact on human health. *Pharmacogn Rev*. 2010;4(8):118-126.
20. Alpha-Lipoic Acid. Monograph. <http://archive.foundationalmedicinereview.com/publications/11/3/232.pdf>. [Accessed 5.5.20.]
21. Dotson JD. What are the Primary Functions of Phospholipids. <https://sciencing.com/primary-functions-phospholipids-7349125.html>. [Accessed 14.5.20]
22. Hagen T.M. et al. Alpha-lipoic acid as a dietary supplement: Molecular mechanisms and therapeutic potential. *Biochimica et Biophysica Acta* 1790 2009; 1149-1160.
23. Lipoic Acid. <https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/lipoic-acid>. [Accessed 6.5.20]
24. Scholich H, Murphy ME, Sies H. Antioxidant activity of dihydrolipoate against microsomal lipid peroxidation and its dependence on alpha-tocopherol. *Biochem Biophys Acta* 1989;1001:256-261.
25. Serhiyenko A et al. Alpha-lipoic acid and diabetic cardiac autonomic neuropathy. *MOJ Public Health*. 2019;8(1): 8-10.
26. Lipoic Acid. <https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/lipoic-acid>. [Accessed 6.5.20]
27. Linus Pauling. Alpha-lipoic acid. <http://lpi.oregonstate.edu/mic/dietary-factors/lipoic-acid>. [Accessed 6.5.20]
28. Kip A et al. The Antihyperglycemic Drug α -Lipoic Acid Stimulates Glucose Uptake via Both GLUT4 Translocation and GLUT4 Activation. *Diabetes* 2001; 50(6): 1464-1471.
29. Examine.com. Alpha-Lipoic Acid. <https://examine.com/supplements/alpha-lipoic-acid/>. [Accessed 12.5.2.]
30. Janson M. Orthomolecular medicine the therapeutic use of dietary supplements for anti-aging. *Clinical Interventions in Aging* 2006;1(3) 261-265.
31. RxList. Alpha-lipoic acid. https://www.rxlist.com/alpha-lipoic_acid/supplements.htm. [Accessed 7.5.20]
32. Linus Pauling. Alpha-lipoic acid. <http://lpi.oregonstate.edu/mic/dietary-factors/lipoic-acid>. [Accessed 6.5.20]
33. Janson M. Orthomolecular medicine the therapeutic use of dietary supplements for anti-aging. *Clinical Interventions in Aging* 2006;1(3) 261-265.
34. Bigioni M, Carbonelli MG, Fusco MA et al. Alpha-lipoic acid supplementation: a tool for obesity therapy? *Curr Pharm Des*. 2010;16(7):840-6.
35. Salehi B, Berkay Yilmaz Y, Antika G, et al. Insights on the Use of α -Lipoic Acid for Therapeutic Purposes. *Biomolecules*. 2019;9(8):356.
36. Kaczor T ND, FBNO. Highlighting Alpha Lipoic Acid in Diabetes. A review of the literature on ALA. *Natural Medicine Journal* 2020; 12, 5.
37. Bilaska A, Wlodeck L. Review. Lipoic acid – the drug of the future? *Pharmacological Reports*. 2005; 57, 570-577.
38. University of Maryland. Alpha Lipoic Acid. <https://umm.edu/health/medical/altmed/supplement/alphalipoic-acid>. [Accessed 14.5.20]
39. Fraziano M et al. The Multitrole of Liposomes in Therapy and Prevention of Infectious Diseases. *Front Immunol* 2018.
40. Dotson JD. What are the Primary Functions of Phospholipids. <https://sciencing.com/primary-functions-phospholipids-7349125.html>. [Accessed 14.5.20]
41. Levy T (2008). GSH Master Defender Against Disease, Toxins and Aging. LivOnBooks: USA.
42. Albens BC. What is Nuclear Factor Kappa B (NF-kB) Doing in and to the Mitochondrion? *Cell Dev Biol*. 2019, 7, 154: 1-7.
43. Jialil I, Singh U. Alpha-lipoic acid supplementation and diabetes. *Nutr Rev*. 2010; 70 (8):42.
44. Pizzino G, Irrera N, Cucinotta M, et al. Oxidative Stress: Harms and Benefits for Human Health. *Oxid Med Cell Longev*. 2017;:8416763.



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