

Alpha Lipoic Acid

Alpha Lipoic Acid (ALA) is not classified as a vitamin, yet is synthesized by the body and is conditionally essential. Alpha lipoic acid benefits include supporting glucose metabolism, and this is perhaps its best known feature.^{1,2,3} As a chiral molecule, it can be found in both isomeric forms (S and R) while the majority of non-specified supplemental forms are a racemic mixture of both.

Paying attention to the form is important. For example, if your target is healthy glucose metabolism, all oxidized forms (S, R, and racemic) will have an effect on glucose uptake; however, only the R form interacts with the insulin receptor itself.¹² It is also important to be watchful of dietary and nutrient interactions. Co-ingestion with medium chain triglycerides inhibits the already limited bioavailability which is approximately 30%.^{13,14} Conversely, acetyl-L-carnitine has been studied in combination with alpha lipoic acid and, when taken together, may support mitochondrial biogenesis and act upon the peroxisome proliferator-activated receptors (PPAR), gamma and alpha.*^{16,25}

ALA essentially has two purposes. Primarily, it acts as a co-enzyme in metabolic functions and secondarily to scavenge free radicals.* While it is a fatty acid by design, it is also water soluble suitable for both lipophilic and hydrophilic environments. It is also effective in both its oxidized and reduced forms.⁴ This unique motif equips ALA for the complex domain of the mitochondria and electron transport chain.*

In vivo, ALA's cofactor role is to assist in the production of energy originating biomolecules like acetyl-CoA and mitochondrial energy powerhouse enzymes like pyruvate dehydrogenase and alpha-ketoglutarate dehydrogenase.⁴ These enzymes seem to produce enough ALA endogenously and do not appear to respond to supplementation.⁴ Multiple basic science studies and clinical trials are aiming to fully understand the benefits of ALA.^{1,2,4,5,8,10,11,15,16,18,19,20,21,23}

Specifically, ALA has been studied in basic sciences with N-acetyl-cysteine (NAC).⁸ In mice, researchers observed the effects of doses of 20mg/kg on lipid peroxidation and dopamine levels.*^{9,10} ALA is also of interest in its role in heavy mineral metabolism.*^{11,15} In the diet, ALA can be found in muscle meats,⁴ spinach,^{5,6} kidney,^{5,6} liver,^{5,6} broccoli,^{5,6} and tomatoes.^{5,6} The amounts in foods are much less than in the dietary supplement form.

In addition, Alpha lipoic acid benefits include:

- ALA may act on AMP-activated protein kinase (AMPK).⁷
- Human clinical trials on ALA have emerged that are supportive for its use in heart, glucose metabolism, and nerve health.*^{18,19,23}

When considering ALA remember:

- Biotin and ALA have a similar structure, thus like with biotin, avoid avidin or the protein in raw egg whites as it can sequester the biomolecule.²²
- ALA acts on the Keap1-Nrf2 system. When this system is activated, genetic expression of NAD(P)H quinone oxidoreductase 1 (NQO1) and UDP-glucuronosyltransferase (UGT) are regulated by the Keap1 sensor.^{20,21}

- The ALADIN (I, II, and III), SYDNEY (I and II), and ORPIL clinical trials all used divided oral dosages up to 2400 mg per day with no apparent side effects; however selenium levels in the serum, heart, brain, and muscle tissues were all lowered along with manganese levels also decreasing in the heart.⁴
- Use caution with ALA when there is evidence or suspicion of 21-hydroxylase and/or 17 α -hydroxylase deficiencies. ALA is an inhibitor of NADPH-cytochrome-P450 reductase (POR) and can potentially have consequences for those with alterations in these genes.¹⁷
- Co-ingestion of monocarboxylic acids inhibits the absorption of ALA and that there is a very limited amount of ALA coming from food. Mitochondria efficiently recycle ALA under normal circumstances.

Many studies use 600 mg of oxidized alpha lipoic acid two to three times per day. Chronic high dosages of approximately 5-10 g per day have been shown to increase oxidative damage.^{4,24}

By Christy Williamson, MS

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