

THE REVIEW OF

NATURAL PRODUCTS

TOPIC:

ALPHA LIPOIC ACID

DATE OF ISSUE:

OCT 1998

REPLACES
MONOGRAPH DATED:

N/A

SCIENTIFIC NAME(S): 1,2-dithiolane-3-pentanoic acid; 1,2-dithiolane-3-valeric acid; 6,8-thioctic acid; alpha-lipoic acid; 5-(1,2-dithiolan-3-yl) valeric acid.

COMMON NAME(S): Alpha-lipoic acid, lipoic acid, thioctic acid, acetate replacing factor, biletan, lipoicin, thioctacid, thioctan.

PRODUCT(S): eg, Alpha Lipoic Acid Extract (Pharmacist's Ultimate Health, et al).

SOURCE: Lipoic acid is a fat-soluble, sulfur-containing, vitamin-like antioxidant. It is not a true vitamin because it can be synthesized in the body and is not necessary in the diet of animals. Lipoic acid functions in the same manner as many B-complex vitamins. Good sources of lipoic acid are yeast and liver.^{1,2} Other sources include spinach, broccoli, potatoes, kidney, heart, and skeletal muscle.³

HISTORY: In the 1930s, it was found that a certain "potato growth factor" was necessary for growth of certain bacteria.³ In 1951, a fat-soluble coenzyme factor was discovered from work done on lactic acid bacteria. Reed et al, isolated this naturally occurring d-form and found it to be an important growth factor for many bacteria and protozoa. This compound was isolated and identified as "alpha lipoic acid."⁴

CHEMISTRY: Alpha lipoic acid is a molecule with 2 sulfur high-energy bonds. It functions as a coenzyme with pyrophosphatase in carbohydrate metabolism to convert pyruvic acid to acetyl-coenzyme A (Kreb's cycle) to produce energy.¹

PHARMACOLOGY: Pharmacokinetics and bioavailability of different enantiomers of alpha lipoic acid (ALA) have been performed in 12 subjects.⁵ Pharmacology of ALA has been studied in the areas of **oxidation, diabetes, AIDS, cancer, and liver ailments.**

Oxidation: ALA's antioxidant properties have been demonstrated. It has the ability to chelate metals and to scavenge free radicals.⁶ ALA is easily absorbed and transported across cell membranes; thus, free radical protection occurs both inside and outside of cells. It is also water- and fat-soluble, which makes it effective against a broader range of free radicals than vitamin C (water-

soluble) and vitamin E (fat-soluble) alone.² ALA administration also increases intracellular levels of glutathione, an important antioxidant.⁷ ALA regenerates or recycles antioxidant vitamins C and E³ but in one report, had no effect on vitamin E tissue concentration in animals, contradicting this effect.⁶

The body routinely converts ALA to dihydrolipoic acid, an even more powerful antioxidant. Both forms "quench" the dangerous peroxy radicals, which are responsible in part for heart, lung, and neurological disease and inflammation as well.⁹ In oxidative stress models such as ischemia, reperfusion injury, and radiation injury, ALA has been shown to be beneficial.^{10,11}

Diabetes: ALA has been shown to be beneficial in type 1 and type 2 diabetes. ALA has prevented various pathologies associated with this disease, such as reperfusion injury, macular degeneration, cataracts, and neuropathy.^{2,3,10,12} ALA reduced diabetic neuropathy in rats, which was improved in a dose-dependent manner. In part, the mechanism was suggested to be caused by reduction of the effects of oxidative stress.¹² ALA is approved in Germany to treat diabetic neuropathy. High doses (600 mg/day) improve this condition.²

ALA also improves the diabetic condition by improving blood sugar metabolism. It facilitates better conversion of sugar into energy.² In 13 non-insulin-dependent diabetes mellitus patients, ALA increased insulin-stimulated glucose disposal. Metabolic clearance rate for glucose rose by 50% compared with the control group.¹³

ALA improves blood flow to peripheral nerves and stimulates regeneration of nerve fibers.² A German study evaluating 800 mg/day ALA in diabetics with damaged autonomic nervous systems was compared against placebo. After 4 months, sympathetic systems showed improvement and autonomic nerve disorder decreased in the ALA group.¹⁴

Antioxidants in general may lead to regression of diabetic

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complications. When ALA was compared with antioxidant vitamin E, results failed to justify the higher cost of ALA over less-expensive and equally effective nutritional antioxidants.²

AIDS: Patients with HIV have a compromised antioxidant defense system, which may benefit from ALA's role as an effective antioxidant.² A small pilot study was conducted administering 150 mg ALA 3 times daily to HIV patients. It increased glutathione in all 10 patients and increased vitamin C in most patients as well. In addition, it improved the T-helper lymphocyte to T-helper suppressor cell ratio in 6 of 10 patients.²

ALA significantly inhibits replication of HIV by reducing the activity of reverse transcriptase, the enzyme which makes virus from DNA of lymphocytes.² In another report, ALA was found to also inhibit activation of "nuclear factor kappa-B," a substance involved in AIDS progression.¹⁵

Cancer: There is limited information available concerning ALA's role in cancer. Its mechanism of action and anticarcinogenic and cytoprotective effects have been addressed.¹⁶ ALA administration, in conjunction with cyclophosphamide, lowered the toxic effects of this anticancer drug when tested in animals.¹⁷

Liver ailments: ALA has been used as an antidote to *Amanita* mushroom poisoning.⁴ A review on mushroom intoxications employing ALA and other antidotes is available.¹⁸

Various: Various reports on ALA pharmacology include the following: Suppression of T-4 metabolism, exerting a lipid-lowering effect in rats,¹⁹ treatment in Wilson's disease,⁴ and cardiovascular disease.³

TOXICOLOGY: No adverse effects from ALA supplementation have been reported in either animal or human studies, even with large doses or extended use.² Its use in diabetes may warrant a reduction in dose of insulin or other oral diabetic medications. Close monitoring of blood sugar levels must be performed. In addition, ALA use may spare vitamins C and E, as well as other antioxidants.²

SUMMARY: ALA is a vitamin-like, "universal antioxidant." It functions to produce energy and has been studied in a number of areas. Its ability to scavenge free radicals has been clearly demonstrated. Its use in diabetes, AIDS, cancer, and liver ailments offer promising results such as reduction of pathologies associated with these diseases. No adverse events from ALA supplementation have been reported.

PATIENT INFORMATION – Alpha Lipoic Acid

Uses: Alpha lipoic acid has been used as an antioxidant for the treatment of diabetes and HIV. It also has been used for cancer, liver ailments, and various other conditions.

Side effects: No adverse effects have been reported.

¹ Ensminger A, et al. *Foods and Nutrition Encyclopedia*, 2nd edition. Boca Raton, FL: CRC Press Inc. 1994:1318-19.

² Murray M. *Encyclopedia of Nutritional Supplements*. Rockin, CA: Prime Publishing. 1996:345-48.

³ Ley B. *The Potato Antioxidant, Alpha Lipoic Acid*. BI Publications. 1996.

⁴ Budavari S, et al, eds. *The Merck Index*, 11th ed. Rahway: Merck and Co. 1989.

⁵ Hermann R, et al. *European J Pharm Sci* 1996;4(3):167-74.

⁶ Nichols T. *All Med Rev* 1997;2(3):177-83.

⁷ Busse E, et al. *Arzneimittel-Forschung* 1992;42(6):829-31.

⁸ Podda M, et al. *Biochem Biophys Res Commun* 1994;204:96-104.

⁹ Whitteman M, et al. *Feds Letters* 1996;379:74-76.

¹⁰ Schonheit K, et al. *Biochimica et Biophysica Acta* 1995;1271:335-42.

¹¹ Cao X, et al. *Free Radical Research* 1995;23:385-70.

¹² Nagamatsu M, et al. *Diabetes Care* 1995;18:1160-67.

¹³ Jacob S, et al. *Arzneimittel-Forschung* 1995;45(8):872-74.

¹⁴ Ziegler D, et al. *Diabetes Care* 1997;20:868-73.

¹⁵ Suzuk Y, et al. *Biochemical and Biophysical Research Communications* 1992;189:1709-15.

¹⁶ Dovichova I. *Ceska A Slovenska Farmacie* 1996;45(5):237-41.

¹⁷ Berger M, et al. *Arzneimittel-Forschung* 1993;33(9):1286-88.

¹⁸ Lampe K. *Global Toxicology* 1974;7(1):115-21.

¹⁹ Segermann J, et al. *Arzneimittel-Forschung* 1991;41(12):1294-98.

