Summary

Alpha lipoic acid, the antioxidant nutritional supplement, is notable both for chelating inorganic mercury and for crossing cell membranes including the blood-brain barrier. Alpha lipoic acid should not be taken by individuals with mercury amalgam dental fillings since it can mobilize mercury from the fillings, equilibrating it throughout the body and across the blood-brain barrier. In addition, alpha lipoic acid may have neurotoxic effects in individuals who have a toxic metal burden, particularly if the dosing protocol neglects pharmacokinetics. Assessment of an individual’s toxic metal burden is difficult since there are no reliable diagnostic tests. Thus, alpha lipoic acid should be used with extreme caution.

Alpha lipoic acid

Alpha lipoic acid is widely recommended as an over-the-counter antioxidant and anti-aging nutritional supplement. (Discuss these properties. Packer. Ames.)

However, two of its little-known properties suggest its use may have neurotoxic effects in some individuals. First, both alpha lipoic acid (ALA), a disulfide, and its metabolite, dihydrolipoic acid (DHLA), a dithiol, chelate metals, notably inorganic mercury.

Second, as lipophiles, ALA and DHLA cross cell membranes including the blood-brain barrier. As lipophilic chelators, they facilitate equilibrium across cell membranes including the blood-brain barrier, thus can be expected to redistribute toxic metals into the brain.

Principles of chelation

A chelator is a molecule that can bind to a metal atom via two or more functional groups (in this case thiols or thiolates), as a caliper, such that the resulting molecule takes the form or a ring having some degree of stability. The word chelate is derived from the Greek word for claw.

A chelator has varying affinities for different metals. No chelator binds just a single target metal, but some chelators have a high degree of selectivity depending on environmental conditions. Chelators may either potentiate or attenuate the toxicity of a particular metal. For example, DMPS (2,3-dimercapto-1-propanesulfonic acid) and DMSA (dimercaptosuccinic acid) attenuate the toxicity of inorganic mercury but potentiate the toxicity of certain forms of organic mercury. (Cutler thinks this is not true.)

In biological systems, chelation is a dynamic and probabilistic process; its effectiveness is a function of the chemical and biological properties of the metal and the chelator, and of the conditions within the biological system. Furthermore, the response to a chelating agent is subject to considerable individual variation.

Effective as these agents are in binding metals in the test tube, their task within the body is indeed formidable since they must compete successfully with the myriad of ligands within the body which themselves bind metals very tightly. Thus reversal of heavy metal poisoning is always a difficult and often an impossible task for the clinician.

When chelators are used to treat toxic metal poisoning, some degree of redistribution, in which the metals bind and damage new targets, is inevitable.

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Certain chelators can increase urinary excretion of toxic metals but fail to relieve symptoms and may even exacerbate neurological sequelae.\textsuperscript{15} Catsch

In other words, some chelators may actually increase mercury levels within the brain while reducing the total body burden. Such redistribution may not be apparent when simple endpoints like urinary excretion are the main observation.

\textit{Enhanced excretion induced by a drug is meaningless from the therapeutic point of view if it is not paralleled by a decrease of the metal concentration in the critical organ(s). A drug might even cause a shift of the metal to the critical organ, thus aggravating its toxicity.}\textsuperscript{16} Catsch

Anecdotally, ill people have had severe adverse reactions to ALA, even at low doses.\textsuperscript{17}

Since chelation is complicated and may exacerbate toxicity, pharmacokinetics -- the step-by-step analysis of the absorption, metabolism, and excretion of a drug within a biological system -- is a key consideration.\textsuperscript{18} Andersen, 19 Cutler, 20 Catsch

**Cutler protocol**

Independent chemist, Andrew Cutler has authored a self-help manual advocating a pharmacokinetics-based low, frequent dose oral chelation protocol using 25 mg alpha lipoic acid every three hours -- with some adjustments for metabolic individuality -- with treatment rounds lasting several days, and with breaks lasting at least as long as the treatment round, and with recovery alleged to progress over the course of one to three or more years.

**Simplistic studies**

Despite the importance of pharmacokinetics as described in the literature and as inherent in the principles of toxicology, the mercury literature is rife with studies that overlook this concept, often describing administration of a chelator to animals or humans without regard to pharmacokinetics, and subsequent measurement of urinary metal excretion as the simple endpoint. Though these studies don't necessarily claim therapeutic benefits from this increased excretion, they may falsely imply such. (Give examples).

**No reliable diagnostic tests**

Since ALA can redistribute toxic metals into the brain, assessment of an individual's toxic metal burden would be worthwhile. Unfortunately, there are no reliable diagnostic tests. Elevated blood and urine mercury levels reveal only recent, not chronic, exposures. A porphyrins panel can reveal moderate to severe metal toxicity, but since porphyrins are easily destroyed by heat, light, or motion, the rate of false negatives is high.

A trace mineral analysis of hair can be informative, but there are no standard guidelines for interpretation, thus counterintuitive results are easily misinterpreted. Specifically, since mercury impairs mineral transport, hair mercury may appear low when the body burden is high. But mercury poisoning can be inferred from a hair test if the results for most “essential minerals” appear abnormally high and/or low instead of average, suggesting impaired mineral transport -- one of the toxic mechanisms of mercury.

**Conclusion**

Use of alpha lipoic acid as a nutritional supplement without consideration of its metal chelating properties, its lipophilic nature, and its pharmacokinetics, may yield neurotoxic redistribution of toxic metals. The lag time between the administration of the agent and the perception of toxicity may be great enough that this connection is overlooked by patient and clinician.

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\textsuperscript{17} Personal knowledge of author, who facilitates the Bay Area Chronic Mercury Poisoning Support Group.


\textsuperscript{19} Cutler AH. Amalgam Illness: Diagnosis and Treatment. noamalgam.com: 1979.