Following are some studies about ALA in various aspects.
There may be others, I really would not know.

best wishes,
Moria

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Toxicol Appl Pharmacol 1992 May;114(1):88-96
Effect of lipoic acid on biliary excretion of glutathione and metals.

Gregus Z, Stein AF, Varga F, Klaassen CD
Department of Pharmacology, University Medical School of Pecs, Hungary.

Several metals are excreted in bile as glutathione complexes, and their biliary excretion is facilitated by increased hepatobiliary transport of glutathione. The present study analyzed the effect of lipoic acid (LA; thioctic acid; 37.5-300 mumol/kg, iv), an endogenous disulfide which can be reduced in vivo to a dithiol, on the hepatobiliary disposition of
glutathione-related thiols and the biliary excretion of metals (10 mumol/kg, iv) in rats. Administration of LA enhanced the biliary excretion of reduced glutathione in a dose-dependent fashion. Despite increasing glutathione output, LA (150 mumol/kg, iv) did not increase, but rather decreased, the biliary excretion of methylmercury, cadmium, zinc, and copper, which are transported into bile in a glutathione-dependent manner, as indicated by a marked reduction in their biliary excretion after diethyl maleate- induced glutathione depletion. In contrast, biliary excretion of inorganic mercury,
which is minimally affected by glutathione depletion, was dramatically enhanced (12- to 37-fold) by LA administration. Following injection of LA, the concentrations of endogenous disulfides in arterial blood plasma (e.g., cystine, glutathione disulfide, cysteine-glutathione, protein- cysteine, and protein-glutathione mixed disulfides) were considerably diminished,
while the levels of endogenous thiols (e.g., glutathione and cysteine) were increased.
This finding indicates that LA, probably after enzymatic conversion to dihydrolipoic acid, can reduce endogenous disulfides to thiols. It appears that LA induces the transport of glutathione into bile by the temporary formation of dihydrolipoic acid-glutathione mixed disulfide, which after being translocated into bile is cleaved to LA and reduced glutathione.
Because the glutathione molecule thus transported into bile cannot complex metals at the thiol group, this might be the mechanism for the observed failure of the LA-induced increase in biliary excretion of glutathione to enhance the hepatobiliary transport of metals that are transported into bile as glutathione complexes (i.e., methylmercury, cadmium, zinc, and copper).
The observations also raise the possibility that endogenous dihydrolipoic acid, by forming a stable complex with mercuric ion, may play the role of a carrier molecule in the hepatobiliary transport of inorganic mercury.

Comment by Andy Cutler:

This is an excellent and useful paper. I suggest people get the actual paper and read it rather than relying on the abstract if they are going to draw conclusions about what they will or won't do.

This paper actually did have a large influence on determining the LA chelation protcol as follows: I don't suggest LA until some months after organic mercury exposure ceases so that it all converts to inorganic form, I suggest using half maximum zinc dosage once chelation starts, and I suggest not chelating more than half the time and taking frequent breaks from it to avoid perturbing copper and zinc balance.

Unusually for a biomedical paper these guys presented their data in enough detail that I was able to extract a rate law for LA and mercury - and found it was the same as the info I got on rates from the Russian paper on LA for mercury poisoning.

This is a rat paper, not one with human subjects, but most of the fundamentals of biochemistry remain the same among all mammals. The things you have to watch out for are papers where vitamin C is relevant (since rats make their own and we need to eat it) and papers where the blood/brain barrier is relevant (since ours works much differently and much better than the one rats have).

Andy Cutler

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TITLE: Protective role of DL-alpha-lipoic acid against mercury-induced neural lipid peroxidation.

AUTHORS: Anuradha B; Varalakshmi P
AUTHOR AFFILIATION: Department of Medical Biochemistry, Dr AL
Mudaliar
Post Graduate Institute of Basic Medical Sciences, Madras University,
Taramani, Madras, 600 113, India.
SOURCE: Pharmacol Res 1999 Jan;39(1):67-80
CITATION IDS: PMID: 10051379 UI: 99162510
ABSTRACT: Experimental neurotoxicity in rat models was induced by an intramuscular injection of mercuric chloride. dl-alpha-lipoic acid was administered as an antidote in three protocols of experimental design. Two protocols of short-term exposure of mercury was designed, one
with prophylactic therapy and the other with curative therapy of lipoic acid.
The third protocol was with prophylactic therapy of lipoic acid on
long-term exposure of mercury. Enhanced lipid peroxidation, depleted non-enzymic and perturbed enzymic antioxidant status were observed in cerebral cortex, cerebellum and sciatic nerves of the toxic groups. The ameliorating effect of lipoic acid and its therapeutic efficacy during various modes of therapy, on the antioxidant status was established in the nervous
tissues.

Comment of Andy Cutler:
Above paper showing efficacy of LA for brain mercury problems

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TITLE: Effect of mercury on rabbit myelin CNP-ase in vitro.

AUTHORS: Domanska-Janik K; Bourre JM
SOURCE: Neurotoxicology 1987 Spring;8(1):23-32
CITATION IDS: PMID: 3031563 UI: 87173849
ABSTRACT: 2',3'-cyclic nucleotide 3'-phosphodiesterase (CNPase) catalyzes hydrolysis of 2',3'-cyclic nucleotides to form the corresponding 2'-monophosphates. Rabbit myelin fraction with CNPase specific activity between 30-40 mumoles/min/mg protein was incubated in the presence of various inorganic and organic heavy metal compounds: HgCl2; (CH3Hg)OH; Pb(NO3)2; Pb(C2H302)2.3H20; (C2H5)2Pb; (C2H5)3SnCl. The enzyme has been shown to be almost exclusively sensitive to mercurials in microM concentration range.
This would arise from the high solubility of mercurials in organic solvents, which allows them to penetrate into hydrophobic regions of the enzyme to react with active sulfhydryl groups. CNP-ase inhibition by methylmercury was biphasic: A reversible, non-competitive inhibition with an apparent Ki = 1 microM occurred after a 5 min preincubation time of the enzyme with the inhibitor. In the case of longer preincubation time, as well as in the presence of HgCl2, the graph of enzyme activity versus protein concentration intercepted the abscissa to the right of the origin, indicating that mercurials are irreversible inhibitors of the enzyme. After 45 min of preincubation of the inhibitors with the enzyme 1 nmol of HgCl2
completely blocks CNP-ase activity equivalent to 15.6 micrograms of myelin protein, whereas 1 nmole of Met-Hg blocks activity in 9.9 micrograms proteins.
This apparently irreversible inhibition of CNP-ase activity by HgCl2 could be fully restored by the use of an excess of hydrophobic low molecular weight thiols, lipoic acid being the most efficient. Dithiothreitol, a hydrophilic complexing agent, was potent to reverse the inhibition caused by Met-Hg only during the short time experiments. Both low molecular weight thiols, and also EDTA in the case of inorganic mercury could prevent the inhibition of CNP-ase by mercurials, if preincubated for 15 min with the inhibitors, prior to the addition of the enzyme. The irreversible type of inhibition of CNP- ase by Met-Hg was only partially reversed in the presence of low molecular weight thiols. This suggests that the formation of a metal-mercaptide complex is not the only mechanism of inhibition by methylmercury. The possibility of lipid peroxidation triggered by methylmercury with subsequent inhibition of the enzyme activity was not supported by the experimental results. In fact, myelin associated CNP-ase activity appears to be very resistant to the structural membrane alterations caused by lipid peroxidation.

Comment of Andy Cutler:
above paper showing that LA actually can remove the emplaced mercury and fix the problem.

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TITLE: [Protective effect of lipoic acid amide in experimental mercurialism]
VERNACULAR TITLE: Zashchitnyi effekt amida lipoevoi kisloty pri eksperimental'nom merkurializme.
AUTHORS: Leskova GE
SOURCE: Gig Tr Prof Zabol 1979 Jun;(6):27-30

Comment by Andy Cutler:
The above paper actually DOES have an english abstract at the end of it even though medline didn't pick it up. I plowed through it because it had really good kinetic data on LA/mercury. They showed 50% reduction in brain and other organ mercury over controls with use of LA, and also measured increase in fecal and independently urinary excretion of mercury (where the fecal rate law in my book came from for LA), and also sliced and diced rats to figure out exactly how much mercury was left in a variety of organs in controls and treated animals.

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TITLE: [Protective action of lipoic amide in poisoning by organic mercury compounds (experimental data)]
VERNACULAR TITLE: O zashchitnom deistvii amida lipoevoi kisloty pri intoksikatsii rtutnoorganicheskimi soedineniiami (eksperimental'nye dannye)
AUTHORS: Trakhtenberg IM; Leskova GE; Verich GE
SOURCE: Gig Tr Prof Zabol 1974 Sep;(9):25-8

Comment by Andy Cutler:
above paper showing that LA is effective when the mercury is still present in the organic form.

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Gen Pharmacol 1997 Sep;29(3):315-31 Related Articles, Books, LinkOut

The pharmacology of the antioxidant lipoic acid.

Biewenga GP, Haenen GR, Bast A
Leiden/Amsterdam Center for Drug Research, Vrije Universiteit,
Department of Pharmacochemistry, The Netherlands.

1. Lipoic acid is an example of an existing drug whose therapeutic effect has been related to its antioxidant activity.

2. Antioxidant activity is a relative concept: it depends on the kind of oxidative stress and the kind of oxidizable substrate (e.g., DNA, lipid, protein).

3. In vitro, the final antioxidant activity of lipoic acid is determined by its concentration and by its antioxidant properties. Four antioxidant properties of lipoic acid have been studied: its metal chelating capacity, its ability to scavenge reactive oxygen species (ROS), its ability to regenerate endogenous antioxidants and its ability to repair oxidative damage.

4. Dihydrolipoic acid (DHLA), formed by reduction of lipoic acid, has more antioxidant properties than does lipoic acid. Both DHLA and lipoic acid have metal-chelating capacity and scavenge ROS, whereas only DHLA is able

to regenerate endogenous antioxidants and to repair oxidative damage.

5. As a metal chelator, lipoic acid was shown to provide antioxidant activity by chelating Fe2+ and Cu2+; DHLA can do so by chelating Cd2+.

6. As scavengers of ROS, lipoic acid and DHLA display antioxidant activity in most experiments, whereas, in particular cases, pro-oxidant activity has been observed. However, lipoic acid can act as an antioxidant against the pro-oxidant activity produced by DHLA.

7. DHLA has the capacity to regenerate the endogenous antioxidants vitamin E, vitamin C and glutathione.

8. DHLA can provide peptide methionine sulfoxide reductase with reducing equivalents. This enhances the repair of oxidatively damaged proteins such as alpha-1 antiprotease.

9. Through the lipoamide dehydrogenase-dependent reduction of lipoic acid, the cell can draw on its NADH pool for antioxidant activity additionally to its NADPH pool, which is usually consumed during oxidative stress.

10. Within drug-related antioxidant pharmacology, lipoic acid is a model compound that enhances understanding of the mode of action of antioxidants in drug therapy.

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Archives of Biochemistry and Biophysics vol 86 pp 90-4 (1960) By R R Grunert

The Effect of DL-alpha-lipoic acid on heavy-metal intoxication in mice and dogs

[andArchives of Biochemistry and Biophysics vol 86 pp 90-4 (1960) By R R Grunert

The Effect of DL-alpha-lipoic acid on heavy-metal intoxication in mice and dogs

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Free Radic Biol Med 1999 Jun;26(11-12):1418-26 Related Articles, Books, LinkOut

Neuroprotective effects of alpha-lipoic acid and its positively charged amide analogue.

Tirosh O, Sen CK, Roy S, Kobayashi MS, Packer L

Department of Molecular and Cell Biology, University of California, Berkeley 94720-3200, USA.

Elevated levels of extracellular glutamate have been linked to reactive oxygen species mediated neuronal damage and brain disorders. Lipoic acid is a potent antioxidant that has previously been shown to exhibit neuroprotection in clinical studies. A new positively charged water soluble lipoic acid amide analog, 2-(N,N-dimethylamine) ethylamido lipoate HCl (LA-plus), with a better cellular reduction and retention of the reduced form was developed.
This novel antioxidant was tested for protection against glutamate induced cytotoxicity in a HT4 neuronal cell line. Glutamate treatment for 12 h resulted in significant release of LDH from cells to the medium suggesting cytotoxicity. Measurement of intracellular peroxides showed marked (up to 200%) increase after 6 h of glutamate treatment. Compared to lipoic acid, LA-plus was more effective in (1) protecting cells against glutamate induced cytotoxicity, (2) preventing glutamate induced loss of intracellular GSH, and (3) disallowing increase of intracellular peroxide level following the glutamate challenge. The protective effect of LA-plus was found to be independent of its stereochemistry. The protective function of this antioxidant was synergistically enhanced by selenium. These results demonstrate that LA-plus is a potent protector of neuronal cells
against glutamate-induced cytotoxicity and associated oxidative stress.

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Gig Tr Prof Zabol 1979 Jun;(6):27-30 Related Articles, Books, LinkOut

[Protective effect of lipoic acid amide in experimental mercurialism].

[Article in Russian]
Leskova GE

Comment from Andy Cutler:
This one refers to LA's neuroprotective effect (which has been around for a while so it is hard to find papers since everyone knows it by now)

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