World Journal of
Biological and Pharmaceutical Research

Journal homepage: https://zealjournals.com/wjbpr/

ISSN: 2799-0338 (Online)

(RESEARCH ARTICLE)

Check for updates

Alpha-Lipoic Acid (ALA), fatty acid and promising chelating agent for neurological ailments

Abdulkareem AlMomen [1] and Eleonore Blaurock-Busch [2, *]

[1] *Medicine-Hematology, King Saud University and National Blood and Cancer Center, Riyadh, Kingdom of Saudi Arabia.*
[2] *Micro Trace Minerals Laboratory, Hersbruck, Germany.*

World Journal of Biological and Pharmaceutical Research, 2022, 03(01), 009–014

Publication history: Received on 23 May 2022; revised on 30 June 2022; accepted on 02 July 2022

Article DOI: https://doi.org/10.53346/wjbpr.2022.3.1.0038

Abstract

Alpha-lipoic acid, a sulphur-containing fatty acid, also known as thioctic acid, occurs as a coenzyme and component of the pyruvate dehydrogenase complex in the mitochondria of almost all living things with a cell nucleus. As a natural substance, it is considered a safe, well tolerated chelating agent. Unlike the hydrophilic chelating agents DMSA, DMPS or EDTA, which are prescription items, not easily available in some countries, the lipophilic α-lipoic acid (ALA) is a natural substance and as such not regulated as strictly. It has the ability to pass the blood brain barrier (BBB) and can thus penetrate all areas of the nervous system. Consequently, current research investigates whether and to what extent oral administration influences the development of metal-based multiple sclerosis (MS) and M. Alzheimer.

With our clinical research we could confirm ALAs metal-binding ability and the extend of urinary excretion for the metals Arsenic, Barium, Manganese, Mercury and Nickel following oral application. We established a treatment protocol, suitable for people of all ages and confirmed the safety of ALA, if given in moderate doses.

Keywords: Alpha-Lipoic Acid; Oral Chelation; Arsenic; Mercury; Multiple Sclerosis; Alzheimer

1. Introduction

Alpha-lipoic acid, a sulphur-containing fatty acid, also known as thioctic acid, occurs as a coenzyme and component of the pyruvate dehydrogenase complex in the mitochondria of almost all living things with a cell nucleus. It is a natural substance, and considered to be a safe, well tolerated, but weak chelating agent. Our research confirm this.

Furthermore, unlike the synthetic antidotes, which are listed by Poison Centers worldwide for the treatment of metal toxicities, ALA is easily available.

2. Function

As a coenzyme, α-lipoic acid (ALA) acts primarily in the case of oxidative decarboxylation in the hydrogen and acyl group transfer. It plays an important role in the pyruvate dehydrogenase complex of the mitochondria, the link between glycolysis and the citric acid cycle, and the α-ketoglutarate dehydrogenase complex in the citric acid cycle.

In the fight against free radicals, antioxidants lose their energy and the ability to protect the organism. Here, ALA shows a remarkable protective effect. With its reduced form of dihydrolipoic acid, ALA forms a biochemical redox system and

* Corresponding author: Eleonore Blaurock-Busch
Senior Researcher, Micro Trace Minerals Laboratory, Hersbruck Germany.

Copyright © 2022 Author(s) retain the copyright of this article. This article is published under the terms of the Creative Commons Attribution Liscense 4.0.

becomes a free radical scavenger and powerful antioxidant that can regenerate antioxidants such as vitamin C, vitamin E, coenzyme Q10 or glutathione that are, or have been used up in the body.

2.1. Use and medical research

ALA's use in cancer research seems promising since lipoic acid impairs the energy balance of cancer cells and thus stimulates the death of cancer cells.

The study of Korkina et al. 1993 brought astonishing discoveries. Children exposed to radioactive rays showed a reduction in free radicals after 28 days of ALA administration, reducing radiation damage. Furthermore, liver and kidney values improved, which was attributed to the improved excretion of radioactive metabolites. Similar study results have since been recorded internationally and can be found in the American National Library of Medicine.

Furthermore, studies indicate that ALA was able to demonstrate a significant effect on normalizing blood sugar levels. Research has shown that this fatty acid activates the transport molecules Glut-1 and Glut-4, which are responsible for transporting glucose into the muscle cells, allowing glucose to be used as energy.

The improvement in insulin sensitivity has been demonstrated by the US biochemist Dr. Passwater as early as 1995 and has since been confirmed by researchers at an international level. Packer et al noticed that ALA, taken orally at doses of 600 mg/day, 1200 mg/day, or 1800 mg/day for 4 weeks resulted in a 25% improvement in insulin sensitivity.

According to the DAZ (German Pharmaceutical Journal), ALA also intervenes in the pathomechanisms of neurodegeneration and its disturbed neuronal energy metabolism. ALA shows a positive effect in dementia sufferers. In patients with mild to moderate Alzheimer's dementia, the additional administration of ALA to acetylcholinesterase inhibitors slowed down the progression of the disease. .

2.2. Trade names of available products as Mono-preparations

As a natural substance ALA is commercially available under various names as a dietary supplement. In the United States, this micronutrient is widely available as an over-the-counter nutritional supplement in the form of capsules, tablets, and aqueous liquids. The German Society for Nutrition (DGE) does not provide any guidelines for the use of this fatty acid. However, Germany allows ALA to be sold as a nutritional supplement, but also approved ALA as a drug for the treatment of diabetic neuropathy since 1966.

While the body can synthesize lipoic acid (LA), it can also be absorbed from the diet. Dietary supplementation in doses from 200–600 mg is likely to provide up to 1000 times the amount available from a regular diet. Gastrointestinal absorption is variable and decreases with the use of food. It is therefore recommended that dietary LA be taken 30–60 minutes before or at least 120 minutes after a meal. Maximum blood levels of LA are achieved 30–60 minutes after dietary supplementation, and it is thought to be largely metabolized in the liver.

2.3. Natural chelating substance with a special effect

Another function of ALA is its special ability to bind metals. Unlike the chemical chelating agents DMSA, DMPS, EDTA or DTPA, ALA can penetrate all areas of the central and peripheral nervous system. This effect is primarily due to its reduced form dihydrolipoic acid, a dithiol that has strong antioxidant properties and can form chelate bonds. ALA-chelate complexes are excreted almost exclusively via the bile ducts.

2.4. Current International Research

Since ALA can penetrate all areas of the nervous system, it is currently being investigated whether and to what extent oral administration influences the development of multiple sclerosis (MS). There is ample evidence that toxic metals such as mercury affect nerve function. Thus, a 'detoxification' of nerve cells should have a positive effect on their function. In the USA, a clinical study, now entering its second phase, is intended to show whether ALA treatment has a positive effect on the progression of the disease. The second part of this randomized 3-stage and placebo-controlled study is scheduled to be completed by the end of 2023. The VA Office of Research and Development funds the work. More information: https://clinicaltrials.gov/ct2/show/NCT03161028

2.5. Our Research

Hematologist and Metal Toxicologist Dr Abdulkareem AlMomen, Professor of Medicine at King Saud University and the National Blood and Cancer Center of Riyadh, Saudi Arabia has been collaborating with MTM Laboratories of Germany

for more than a decade. He has been researching and using the antioxidative and metal-binding effect of ALA for years. Prof. AlMomen has noted patient improvements but no side effects so far. He developed a treatment protocol for ALA that he has used on patients suffering from neurological ailments.

In addition to using ALA as a provocative agent, he does use it as a chelating agent for those who show elevated levels of potentially toxic elements after eliminating the source and as such he found dental amalgams to be such a source. He also states that constipation must be avoided. It should be treated prior to oral treatment.

2.6. Treatment Protocol

For chelating purposes and the treatment of a metal burden, 600 mg are given for 3 months, once daily for those who are under 40 kg and twice daily for those who are over 40 kg for 3 months.

For this study, samples had been submitted from patients who had been treated in the clinic of Prof AlMomen. According to his protocol oral ALA is given based on body weight.

- Up to 40 kg body weight: 600 mg
- 40-70 kg: 1200 mg for 40-70 kg
- >70 kg: 1800 mg
- Oral intake: before bedtime.
- Urine collection: in the morning, after rising.

Although ALA is well tolerated, some patients cannot tolerate the usual dose (they get severe stomach pain). In such cases, Prof. AlMomen reduces the dose to 300 mg and sometimes to 100-150 mg/day.

Before the first treatment, a morning urine is taken. The patient can do this himself at home. If this is not possible, a spontaneous urine sample can be taken in the practice before ALA is given. This is called the Baseline Urine.

The morning urine of the day following the administration of lipoic acid is the Provocation Urine.

In both cases, 5-7ml are required for the laboratory test.

3. Material and Methods

Data from 537 urine provocation tests were statistically evaluated (see Table 2). Data obtained from ALA-provocation tests were compared to baseline urine test results. This comparison of ALA provocation urine test values and baseline urine test results allows an assessment of the ALA treatment.

We also compared ALA test values with urinary excretion values obtained after the administration of 500mg oral DMSA (Dimethyl succinic acid). DMSA is a chelating agent approved by the FDA (Food and Drug Association) for the oral treatment of lead intoxicated children. It is a prescription item. The DMSA test values used for this study were obtained predominantly from German clinics, using standard protocol.

A total of over 50 metals were analyzed via ICP-MS spectroscopy, utilizing cell technique. Table 1 lists elements and isotopes routinely tested. The elements Scandium, Yttrium and Holmium were used as Internal Standards.

4. Results and discussion

Urine samples were acidified with nitric acid before testing. All elements tested were statistically evaluated.

The oral administration of ALA noticeably increased the urinary excretion of Arsenic, Barium, Mercury and Nickel. Manganese binding and excretion via urine seemed insignificant. Lead was ‘chelated’ by DMSA, but not by ALA.

The following table contains and compares only test values of metals that indicate bonding with ALA. For the metals not mentioned, no ALA binding could be detected.

95%ile: The most common reference range is the interval of values containing 95% of a healthy population. It is commonly used for biochemical analytes such as metals in urine.

Table 1 Elements and Isotopes

Elements and Isotopes			
Element	**Isotop**	**Element**	**Isotop**
Lithium	7	Cesium	133
Beryllium	9	Barium	138
Boron	10	Lanthanum	139
Magnesium	24	Cerium	140
Aluminum	27	Praseodymium	141
Calcium	44	Neodymium	146
Titanium	49	Samarium	147
Vanadium	51	Europium	153
Chromium	52	Gadolinium	157
Manganese	55	Dysprosium	163
Iron	56	Erbium	166
Cobalt	59	Thulium	169
Nickel	60	Ytterbium	172
Copper	63	Lutetium	175
Zinc	66	Hafnium	178
Gallium	69	Tantalum	181
Germanium	74	Tungsten	182
Arsenic	75	Rhenium	185
Selenium	78	Iridium	193
Rubidium	85	Platinum	195
Strontium	88	Mercury	202
Zirconium	90	Thallium	205
Niobium	93	Lead	208
Molybdenum	98	Bismuth	209
Rhodium	103	Thorium	232
Palladium	105	Uranium	238
Silver	107	Cesium	133
Cadmium	111	Barium	138
Tin	118	Lanthanum	139
Antimony	123	Cerium	140
Iodine	127	Praseodymium	141
Tellurium	128	Neodymium	146

Table 2 Comparison of Urine Test Values (all in microgram/liter =mcg/l)

Element	DL	Baseline Norm (95%ile)	ALA N537 Mean	STD	95%ile	DMSA, 500mg Mean	N197 STD	95%ile
Arsenic	0.35	<15	26.7	108.4	74.7	11.9	28.5	90
Barium	0.1	<5.7	10.5	168.2	10.1	2.5	8	16.1
Mercury	0.4	<1	2.4	3	8	4.2	8.7	24.2
Manganese	0.75	<4.5	5	4	12.1	4.2	4.1	11.6
Nickel	0.5	<3	6.3	4.2	14.5	6.1	5.8	17.8
Lead	0.3	<5	1.7	4.7	5	8	10.5	27.8

DL= Detection Limit in mcg/l); STD= Standard Deviation; N=Number of Tests

4.1. Assessment

4.1.1. Arsenic and Barium

Both chelators, ALA and DMSA show a similar binding ability and increase in urinary excretion. However, the standard deviation of the ALA values for As and Ba is considerably higher than that obtained from DMSA provocation tests. This indicates a higher variation in ALA test results among samples. (Note: the standard deviation indicates how widely individual results are distributed within the dataset.) For ALA we see an unexpectedly high standard deviation of measured values. A substantial difference in patients' arsenic and barium exposure may be the cause. Further studies are needed to explain this.

For both elements, DMSA excretion values are comparatively more stable than those obtained from ALA

4.1.2. Mercury

Both, ALA and DMSA show good bonding. While DMSA shows a stronger effect on mercury binding and urinary excretion, it is hydrophilic and therefore cannot pass the blood brain barrier (BBB).

Mercury tends to accumulate in nerve tissue, and according to studies by Calgary University and other researchers, mercury is highly toxic to neurons. ALA, however, is lipophilic and thus able to cross the BBB. Therefore, ALA seems of greater importance in the detoxification of brain tissue. ALA offers a promising treatment of metal-related neurological diseases.

4.1.3. Manganese

Both agents show similar, yet insignificant bonding.

4.1.4. Nickel

ALA and DMSA are similarly effective.

4.1.5. Lead

ALA showed no binding. As expected, DMSA bound lead as it has been approved by the FDA (Food and Drug Administration) for lead detoxification in children

5. Conclusion

Our data confirmed that ALA is a promising natural and 'soft' chelating agent. ALA seems particularly useful for detoxifying the elements Arsenic, Barium, Nickel and Mercury. Since ALA is a lipophilic substance, its use in eliminating mercury from nervous tissue is most promising and warrants further studies, especially for the treatment of neurological diseases such as Alzheimer, Autism or Multiple Sclerosis.

The data provided here demonstrated ALAs chelating ability for the elements Arsenic, Barium, Nickel and Mercury. However, in his daily practice, Prof. AlMomen who oversaw all clinical processes noted that the metal-binding efficacy of oral ALS is reduced in patients with constipation.

He points out another benefit of ALA Chelation: ALA does not affect essential minerals such as calcium and magnesium. Therefore, additional mineral supplementation is not required. However, he does provide specific supplements for deficient essential elements such as chromium, selenium, and zinc, if needed.

It must be emphasized that ALA is metabolized in the liver and ALA-chelate complexes are excreted almost exclusively via the bile ducts. Hence, urine metal excretion values may not show the extent to which ALA binds and eliminates toxins.

We recognize the need for further studies and recommend, in addition to urine testing to add faecal material for the evaluation of metal excretion after ALA treatment. Comparing the metal concentration from urine and faecal specimen should allow us to evaluate how metal binding and excretion via bile ducts correlate or contrast with urinary measurements. Such studies may provide much needed information about ALA's role in the treatment of chronic metal burden

Compliance with ethical standards

Acknowledgments

The authors appreciate the assistance of Holger Bürner, IT Director at Micro Trace Minerals Laboratories.

Disclosure of conflict of interest

Both authors declare that there is no conflict of interest.

References

[1] Biewenga GP. Et al. The Pharmacology of the Antioxidant Lipoic Acid. In: Gen Pharmacol. 1997; 29(3): 315–331.

[2] Biewenga GP. Et al. The role of lipoic acid in the treatment of diabetic polyneuropathy. In: Drug Metab Rev. 1997; 29(4): 1025–1054.

[3] Berkson B, Whitaker J. The Alpha Lipoic Acid Breakthrough: The Superb Antioxidant That May Slow Aging, Repair Liver Damage, and Reduce the Risk of Cancer, Heart Disease, and Diabetes. Publ. Harmony/Rodale. 1998.

[4] Roney J, The role of thiols, dithiols, nutritional factors and interacting ligands in the toxicology of mercury. In: Toxicology. 234, Nr. 3, 2007, S. 145-156.

[5] Packer L, Tritschler HJ, Wessel K: Neuroprotection by the metabolic antioxidant alpha-lipoic acid. In: Free radical biology & medicine. 22, Nr. 1-2, 1997; S. 359-378.