Multidisciplinary Reviews

REVIEW ARTICLE
Published Online: December 16, 2021
https://doi.org/10.29327/multi.2022002

The efficacy of Alpha Lipoic Acid in public health and veterinary medicine: a review paper

Zainab Abdul Hussein Saud[a*]

[a]Department of Public Health, College of Veterinary Medicine, University of Basrah, Basrah, Iraq.

*Corresponding author: zainab.saud@uobasrah.edu.iq

Abstract Alpha Lipoic Acid (ALA**)** is a fatty acid that mainly synthases mammals and plants. Alpha lipoic acid is found in trace amounts, soluble in water and fat. ALA plays an essential role in the body's synthases of glutathione, the body's most important endogenous antioxidant, supporting healthy vision, protecting cells from free radicals, and enhancing liver functions. Additionally, ALA helps dissolve toxic substances in the liver. In the present review, we described the history with the physical and biochemical properties of ALA besides highlighting its functions in living organisms. We also reviewed the benefits of using synthetic forms of ALA in domestic animals to prevent and treat medical disorders. In conclusion, in addition to its role in enhancing body functions, ALA also plays a major role as a valuable antioxidant that could give an advantage to its use as a promising treatment against the widespread infection in animals and humans.

Keywords: ALA, antioxidant, domestic animals, fatty acid, human

1. Introduction

Alpha lipoic acid was first named (potato growth factor) by Snell in 1937. Consisting of potato extract, ALA has been shown to assist *Lactobacillus* growth (Salinthone et al 2008). Dr. Lester was the first to isolate small amounts of ALA crystals from liver residue in 1951. These substances are called alpha lipoic acid since they can dissolve in lipid. In contrast, some scientists call it thioctic acid because it contains two sulfur (theion in Greek) and eight carbon (octo in Greek) atoms (Berkson 2010). Alpha lipoic acid was first described in Germany in 1957 as a treatment for acute toxicity caused by *Amanita phalloides* (mushrooms), a deadly poison widely distributed in Europe (Gomes and Negrato 2014).

As a co-factor for mitochondrial enzyme complexes that participate in energy production, plants and mammals synthesized ALA in trace quantities. ALA is similar in function to many of the B vitamins (Târtea et al. 2020). Some scientists classified alpha lipoic acid as a vitamin because the body produces it. ALA is found in small amounts in animals tissue with high metabolic activity, such as liver, kidney, and heart; it is also found in vegetables and fruit such as peas, tomatoes, rice bran, and spinach. ALA supplied by the diets is transported by the bloodstream into tissue and incorporated into cells, after which it is transported into mitochondria (Gorąca et al 2011; Saleh 2019; Salehi et al 2019).

2. Synonyms of Alpha Lipoic Acid

Due to the asymmetric carbon in alpha lipoic acid, there are two possible optical isomers: R-lipoic acid and S-lipoic acid; R-lipoic acid is the natural form, and S-lipoic acid is the synthetic form (Figure 1) (Carrier and Rideout 2013; Hofmann et al. 1995)**.** Alpha lipoic acid was named (R)-5-(1,2-dithiolan-3-yl) pentatonic acid.

Alpha lipoic acid has different names, including thioctic acid, 6,8-thioctic acid, 6,8-dithioctane acid, 1,2-dithiol-3-valeric acid, lipoate, and alpha-lipoic acid (Rentier et al 2015).

3. Alpha lipoic acid properties

The Alpha lipoic acid has antioxidants properties discovered in 1988; it has the same ability as vitamin C, vitamin E, and coenzyme Q 10 (Naji et al 2018; Shindyapina et al 2017). In addition to its ability to neutralize free radicals in intracellular and extracellular environments, ALA differs from antioxidants. It neutralizes free radicals within the aqueous and lipid regions of the cell (Naji 2017). The characteristics of ALA allow it to pass through cell membranes to neutralize free radicals. Vitamin C protects the watery portion of the cell from free radicals, while vitamin E can protect the fatty membrane, while AlA protects the watery and fatty portions (Naji and Zenad 2016; Park et al 2014).

ALA can also neutralize a diverse range of free radicals, including singlet oxygen, peroxyl, superoxide, and hydroxyl radicals, peroxynitrite and hypochlorite, and other antioxidants that neutralize a single type of free radical. Therefore ALA is called a "universal antioxidant" (Naji and Zenad 2016).

In mitochondria, ALA plays an integral role in energy production, acting as a co-factor of multi-enzymatic complexes for protein metabolism and carbohydrate regulation after energy production (Shay et al 2009). When antioxidants scavenge a free radical, they oxidize and lose the ability to fight future free radicals until reduced.

ALA is important in regenerating or recycling other antioxidants such as vitamin C and coenzyme Q10, which turn vitamin E into antioxidant chains by oxidizing it and recycling it (Naji and Zenad 2015; Shay et al 2009). Dihydrolipoic acid can reduce oxidized antioxidants, restoring them to their initial capacity (Jones et al 2002; Saleh et al 2019).

ALA increases glutathione levels, which plays a vital role as an intracellular antioxidant, protecting the body from free radicals and removing and detoxifying potential toxins and carcinogens (Alabada and Saleh 2020; Attia et al 2020). Lastly, the ALA bind or chalet with heavy metals to form complex with Mg, Fe, Cu, Zn, Ni, and Cd and protect the cell from damage (Naji et al 2018).

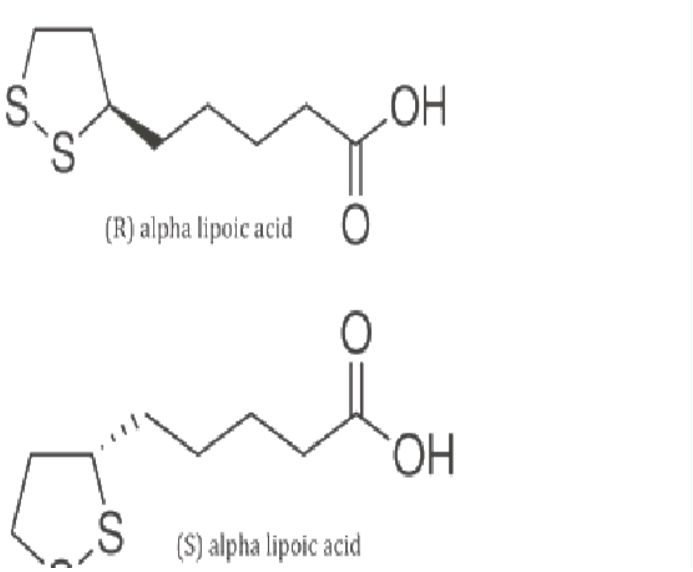

Figure 1 Structure of R and S alpha lipoic acid enantiomeric forms. *Source:* Carrier and Rideout (2013)

4. Alpha lipoic acid in veterinary medicine

Several studies have used ALA as an antioxidant in animals; the dose of ALA used in acute cadmium toxicity studies was 50 mg/kg IM twice with 12-hour intervals. The dose for chronic cadmium toxicity studies was 10 mg/kg orally every 48 h for 90 days, respectively. However, the findings of the mentioned studies suggest that ALA has played a significant role as an antioxidant to protect tissues and organs against cadmium toxicity (Naji and Zenad 2015).

Several scientists have documented that ALA therapy is beneficial for animals. Researches have shown that alpha-lipoic acid improves glucose metabolism and insulin resistance in rats; studies have also shown that alpha-lipoic acid is protective on the retinas of experimental mice models with diabetes (Budin et al. 2009).

A study applied on cattle used ALA to enhance the bovine secondary preantral follicles development and growth (Zoheir et al 2017); the study proved that adding ALA to culture medium improved the development rate of secondary preantral follicles. As a result of media enrichment with 250 and 500 uM of ALA, the number and development of active follicles increased due to the upregulation of growth regulation genes and downregulation of apoptosis-induced genes. Moreover, ALA is used as a supplement to enhance cattle embryo development which varies depending on the ALA concentration (Fabra et al. 2020).

In the horse, Alpha Lipoic acid has improved insulin activity and glucose utilization in both humans and animals. Recently, researchers examined glucose and insulin dynamics and leptin serum concentrations in pony mares supplemented with lipoic acid (Anthony et al 2021; Berg et al 2012).

ALA has been documented to be ten times more toxic in cats than in humans, dogs, or rats. Typical signs of ALA toxicity in cats include reduced food intake, hypersensitivity, vomiting, hypersalivation, ataxia, and elevated hepatic enzymes. These signs might be observed followed inoculation of 60 mg/kg of ALA. In contrast, a lower dose of ALA (30 mg/kg) in cats caused mild hepatocellular changes (Loftin and Herold 2009).

In dogs, LD50 of ALA has been reported as 400–500 mg/kg, and the clinical signs include hypoglycemia, ataxia, vomiting, tremors, lethargy, seizures, weakness, and hypersalivation. However, changes in renal or hepatic functions tests have been reported (Anthony et al 2021).

5. Final considerations

ALA plays an essential role as a supplement widely used to enhance body functions. As an antioxidant, ALA has more additional properties than Vitamin C, Vitamin E, and Vitamin B. In addition, ALA is used to treat various diseases affecting humans and animals since it has a detoxification effect. Enhancement of liver function by ALA can be achieved by synthesizing certain antioxidants such as glutathione, which increase growth.

Conflict of Interest

I declare that there are no conflicts of interest.

Funding

The current review did not receive any financial support

References

Alabada, HKM, Saleh WMM (2020) Vitamin D Effectiveness and Pathology in Humans and Domestic Animals. Multidisciplinary Reviews 3:e2020010.

Anthony, RM, Jennifer MM, Kathy LG (2021) Alpha-Lipoic Acid as a Nutritive Supplement for Humans and Animals: An Overview of Its Use in Dog Food. Animals 11:1454.

Anthony, R M, Jennifer M.M, Dennis EJ, John JB, Kathy LG (2021) Alpha-Lipoic Acid Is an Effective Nutritive Antioxidant for Healthy Adult Dogs. Animals 11:274.

Attia, EAH, Zaki RM, Elkordy AA (2020) An Overview of the Antioxidant Effects of Ascorbic Acid and Alpha Lipoic Acid (in Liposomal Forms) as Adjuvant in Cancer Treatment. Antioxidants 9:359.

Berg , MDL, Rottinghaus GE, Chen Y, Berg EP, Ganjam VK, Keisler DH (2012) The Effects of Lipoic Acid Supplementation on Blood Glucose and Insulin Concentrations in Pony Mares. The Professional Animal Scientist 28:632–38.

Berkson, BB (2010) 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. Harmony.

Budin, SB, Othman F, Louis SR, Abu AB, Radzi M, Osman K, Das K, Mohamed J (2009) Effect of Alpha Lipoic Acid on Oxidative Stress and Vascular Wall of Diabetic Rats." Rom J Morphol Embryol 50:23–30.

Carrier, BC, Rideout CT (2013) Anti-Obesity and Lipid-Lowering Properties of Alpha-Lipoic Acid. J. Hum. Nutr. Food Sci 1:1002.

Fabra, MC., Izquierdo L, Anchordoquy JM, Anchordoquy JP, Carranza-Martín AC, Nikoloff N, Furnus CC (2020) Effect of Alpha-Lipoic Acid during Preimplantation Development of Cattle Embryos When There Were Different in Vitro Culture Conditions. Animal Reproduction Science 221:106550.

Gomes, MB, Negrato CA (2014) Alpha-Lipoic Acid as a Pleiotropic Compound with Potential Therapeutic Use in Diabetes and Other Chronic Diseases. Diabetology & Metabolic Syndrome 6:1–18.

Gorąca, AG, Huk-Kolega H, Piechota A, Kleniewska P, Ciejka E, Skibska B (2011) Lipoic Acid-Biological Activity and Therapeutic Potential. Pharmacological Reports 63:849–58.

Hofmann, MH, Mainka P, Tritschler H, Fuchs J, Zimmer G (1995) Decrease of Red Cell Membrane Fluidity And-SH Groups Due to Hyperglycemic Conditions Is Counteracted by α-Lipoic Acid1. Archives of Biochemistry and Biophysics 324:85–92.

Jones, WJ, Li X, Qu ZC, Perriott L, Whitesell RR, May JM (2002) Uptake, Recycling, and Antioxidant Actions of α-Lipoic Acid in Endothelial Cells. Free Radical Biology and Medicine 33:83–93.

Loftin, EG., Herold LV (2009) Therapy and Outcome of Suspected Alpha Lipoic Acid Toxicity in Two Dogs. Journal of Veterinary Emergency and Critical Care 19:501–6.

Naji,HA (2017) The Effect of Zinc and Copper Deficiency on Hematological Parameters, Oxidative Stress and Antioxidants Levels in the Sheep. Basrah Journal of Veterinary Research 16:344–55.

Naji, HA, Ahmed JA, Alsaad KM (2018) chronic copper poisoning of sheep at Basrah governorate, Iraq. Basrah Journal of Veterinary Research 17:3.

Naji, HA, Zenad MM (2016) Hematological and Histopathological Changes Induced by Cadmium Chloride Toxicity in Sheep, with Using Alpha Lipoic Acid as Antioxidant. Basrah Journal of Veterinary Research 15:83–96.

Naji, HA, Zenad MM (2015) Oxidative Stress in Sheep Induced by Cadmium Chloride Toxicity, with Therapeutic Effects of Alpha Lipoic Acid. J. Anim. Feed Res 5:142–47.

Park, SP, Karunakaran U, Jeoung NH, Jeon JH, Lee IK (2014) Physiological Effect and Therapeutic Application of Alpha Lipoic Acid. Current Medicinal Chemistry 21:3636–45.

Rentier, CR, Pacini G, Nuti F, Rovero P, Papini AM (2015) Lipoylated Peptides and Proteins. Pp. 235–52 in Peptidomimetics II. Springer.

Saleh, WMM (2019) Clinical and Hematological Profiles Due to Cases of Minerals Deficiency in Local Ewes at Basra, Iraq. Adv. Anim. Vet. Sci. 7:315–20.

Saleh, WMM, Naji HA, Lafta MH, Al-Husseiny SH, Ali F (2019) Clinical and Bacteriological Diagnosis of Foot-Rot in Beef Bulls in Basra. Biomedical Journal 1:5.

Salehi, BS, Yılmaz YB, Antika G, Tumer TB, Mahomoodally MF, Lobine D, Akram M, Riaz M, Capanoglu E, Sharopov F (2019) Insights on the Use of α-Lipoic Acid for Therapeutic Purposes. Biomolecules 9:356.

Salinthone, SS, Yadav V, Bourdette DN, Carr DW (2008) Lipoic Acid: A Novel Therapeutic Approach for Multiple Sclerosis and Other Chronic Inflammatory Diseases of the CNS. Endocrine, Metabolic & Immune Disorders-Drug Targets (Formerly Current Drug Targets-Immune, Endocrine & Metabolic Disorders) 8:132–42.

Shay, KP, Moreau RF, Smith EJ, Smith AR, Hagen TM (2009) Alpha-Lipoic Acid as a Dietary Supplement: Molecular Mechanisms and Therapeutic Potential. Biochimica et Biophysica Acta (BBA)-General Subjects 1790:1149–60.

Shindyapina, AV, Komarova TV, Sheshukova EV, Ershova NM, Tashlitsky VN, Kurkin AV, Yusupov LR, Mkrtchyan GV, Shagidulin MY, Dorokhov YL. (2017) The Antioxidant Cofactor Alpha-Lipoic Acid May Control Endogenous Formaldehyde Metabolism in Mammals. Frontiers in Neuroscience 11:651.

Târtea, GCl, Florescu DR, Mihailovici AR, Donoiu L, Istrătoaie O (2020) Alpha-Lipoic Acid and Vitamin B Complex Slow down the Changes in Mice Diabetic Cardiomyopathy. Romanian Journal of Morphology and Embryology 61:521.

Zoheir KMA, Harisa GL, Allam AA, Yang L, Li X, Liang A, Abd-Rabou AA, Harrath AH (2017) Effect of Alpha Lipoic Acid on in Vitro Development of Bovine Secondary Preantral Follicles. Theriogenology 88:124–30.