Alfa-Lipoic Acid - a useful antioxidant

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Abstract

Recent advances in free radical chemistry have shown considerable changes in therapeutic schedules in the treatment of cataract and diabetic cases. Alfa-Lipoic acid has been recommended for therapeutic use in recent years. It has shown its unique free radical scavenging potential as universal antioxidant. Due to its unique biochemical structure, it is capable to cross blood brain barrier and other biological membranes and neutrilize most of the toxic reactive oxygen species including hydroxyl radicals and free metal ions effectively. Detailed understanding about pharmacokinetics of Alfa-Lipoic acid may help to evaluate its therapeutic utility in a large array of disorders involving free radial injuries.

Keywords: Alfa-Lipoic acid; Free radical chemistry; Universal antioxidant; Reverse phase high performance liquid chromatography; Cataract; Oxidative neural disorders.

Introduction

In recent years Alfa-Lipoic acid has drawn considerable attention as a therapeutically important antioxidant. Alfa-Lipoic acid (Oxidized state) and Dihydrolipoic acid (Reduced state) form a dithiol redox body which plays the unique role of a universal antioxidant.

Lipoate requiring dehydrogenases systems eg, Pyruvate dehydrogenase complex, Alfa-ketoglutarate dhydrogenase complex etc, binds covalently with dihydrolipoate by the amide linkage of a lysine residue of the enzyme ie dihydrolipoate transacylase. FAD+ plays the role of proton acceptor molecule.

Mechanism of antioxidant functions

Alfa-Lipoic acid exhibits its antioxidant action in two phases. While converting itself into its reduced form, Alfa-Lipoic acid neutralizes one free radical (Phase-I) and subsequently in the process of regaining its original oxidized form, it neutralizes another free radical (Phase-II). Thus Alfa-Lipoic acid keeps on acting on free radicals with cyclical continuity and neutralizes most of the free radicals effectively.

It is one of the broad spectrum antioxidants capable of neutralizing a large array of reactive oxygen species eg, superoxide radicals, hydroxyl radicals, hypoclorous acid, peroxyl radicals, singlet oxygen and free metal ions.

Moreover, it enhances the actions of other antioxidants like vitamin C and Glutathione, which may in turn recycle vitamin E. Therefore, Alfa-Lipoic acid could prove itself as a potential therapeutic agent in various diseases with glutathione anomalies including HIV infection.

The unique chemical structure of lipoic acid is responsible for its solubility in water as well as in lipid (Hydrophobic bond) and therefore it can move across the blood brain barrier and other biological membranes.

Lipoic acid and its reduced product (Dihydrolipoic acid) exhibit hydrophobic binding to proteins such as albumin which can inhibit glycation reaction.

Furthermore, Lipoate can act as a redox regulator of proteins such as myoglobin, prolactin, thioredoxin and NF-kappa B

transcription factor.

Therefore, oxidative properties of Lipoic acid were reviewed in terms of:

1. reactions with reactive oxygen species (ROS);
2. interactions with other antioxidants;
3. beneficial effects in oxidative stress models or clinical conditions.

Method of estimation

Reverse phase high performace liquid chromatography with electrochemical detection having a lower limit of quantification of 1ng/ml.

Pharmacological actions

L-buthionine (S,R) – Sulfoximine (BSO) is a known inhibitor of glutathione synthesis. Administrating BSO to newly born animals leads to development of cataract. Most often BSO-treated animals are used as a potential model for therapeutic antioxidant trials in protecting them from developing cataract. It has been reported that optimal dose of Alfa-Lipoic acid can protect 60% of BSO-treated animals from cataract formation. Administration of Alfa-Lipoic acid leads to increase of plasma concentration of glutathione, ascorbate and Vitamin-E. Treatment with Alfa-Lipoic acid restores the glutathione peroxidase, catalase and ascorbate free radical reductase level in lens tissue but fails to influence glutathione reductase and superoxide dismutase levels.

Conclusion

Use of Alfa-Lipoic acid in the prevention of cataract has been recommended in the present day clinical practice. It seems to be an ideal substance in treating oxidative brain and other neural disorders involving free radical injuries. Since, most important thiol antioxidant gluthaione cannot be used as therapeutic agent, Alfa-Lipoic acid can play the role of a useful substitute for it. Use of Alfa-Lipoic acid as a therapeutic agent has also shown beneficial effects in the prevention of peripheral neuropathy and cardiac autonomic dysfunction in NIDDM, Artherosclerotic disorders, Alzheimer's & Parkinson's diseases.

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