Antioxidant Therapy by Lipoic Acid in Various Illnesses: Reactive Oxygen Species and Oxidative Stress

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Abstract

Lipoic acid (LA) is an effective antioxidant that possesses therapeutic properties in the treatment of various illnesses, including multiple sclerosis (MS), Alzheimer's disease (AD), Parkinson's disease (PD), diabetes, cognitive decline, depression, memory loss, and hemorrhage. Additionally, mechanistic aspects of lipoic acid are addressed.

Keywords: Lipoic acid; Antioxidant; Illness; Reactive oxygen species; Oxidative stress

Abbreviations: LA: Lipoic Acid; OS: Oxidative Stress; OS: Reactive Oxygen Species; AO: Antioxidant; ROS: Reactive Oxygen Species; AD: Alzheimer's Disease; PD: Parkinson's Disease; MS: Multiple Sclerosis; MDA: Malondialdehyde; TBARS: Thiobarbituric Acid Reactive Substances; GSH: Glutathione

Introduction

The unifying theme of reactive oxygen species (ROS) - oxidative stress (OS) - antioxidant (AO) has been used successfully to rationalize a wide range of physiological activities. There is a plethora of experimental evidence supporting the ROS-OS-AO theoretical framework [1-3]. This evidence includes the generation of the common ROS, lipid peroxidation, degradation products of oxidation, depletion of AOs, effect of exogenous AOs, and DNA oxidation and cleavage products, as well as electrochemical data. This comprehensive unifying mechanism is consistent with the frequent observation that many substances display a variety of activities (e.g. multiple drug properties), as well as toxic effects. It is important to recognize that mode of action in the biodomain is often involved with many physiological actions and is multifaceted. In addition to the ROS-OS-AO approach, other aspects may pertain, such as, enzyme inhibition, allosteric effects, receptor binding, electrochemistry, cell signaling, metabolism and physical factors.

Lipoic acid (LA) (Figure 1) is a potent AO, which has been reported to alleviate a wide variety of illnesses involving ROS-OS. The present article addresses the following ones: multiple sclerosis (MS), Alzheimer’s disease, diabetes, cognitive decline, depression, memory loss, and hemorrhage. The dithiol metabolite (dihydro LA) (Figure 2) from reduction is even more potent as an AO [4,5]. Two possible mechanisms (Scheme 1) of thiol AO activity are presented which has received recent attention. A number of AOs can also act as pro-oxidant under the appropriate conditions. Application to thiols is presented in (Scheme 2).
Discussion

Since ROS and OS are known to play a role in MS, LA was investigated as an AO. LA was shown to exert protective effects including decrease in OS and prevention of apoptosis [6]. There is also reduction of redox signaling. LA is reduced to a dithiol which is a more powerful AO. OS plays a major role in MS and inflammation. A study of the A0lipoic acid demonstrated improvement among MS patients [7]. LA lessoned hypertension, while decreasing levels of superoxide and malondialdehyde (MDA) [8]. AO capacity was enhanced. AOs characterized by enhanced OS and decreased AOs [9]. Focus was on recovery from ROS by use of AOs, such as LA, n-acetylcysteine and vitamin E. A multi-targeted approach is recommended. Therapeutic use of LA in diabetes was studied [10]. OS is a factor in many diseases. Therefore, beneficial effects are noted from use of AOs, such as LA. Various factors are involved in depression, including oxidative and nitrosative stress, as well as damage to lipid membranes and decrease in AO levels [11]. Promising compounds for reversal of the adverse affects include LA. OS is importantly involved in brain diseases, such as Alzheimer’s disease (AD) and Parkinson’s disease (PD). LA is known to bestow neuroprotection via the AO property [12]. A study found that LA was able to improve memory. Reversal of OS was observed, together with a favorable effect on lifespan [13]. Elevated MDA levels after hemorrhage were reduced by LA treatment [14]. The acid lessons cerebral vasospasms by its strong AO property. AD arises from ROS and RNS resulting in OS [15]. AOs such as LA, offer treatments for neurodegenerative diseases. LA and the dithiol derivative are strong AOs which are promising for neuroprotection via the AO property [16]. The role of OS is addressed.

Hemorrhage is associated with ROS, DNA fragmentation, malondialdehyde (MDA) formation plus decrease in glutathione (GSH). LA treatments reversed the adverse factors [17]. The disulfide enhances AO activity and inhibited free radical generation. OS occurs during seizures such as epilepsy [18]. Brain damage is induced by oxidative processes. A strong protective effect was achieved by use of LA. Aging dogs develop cognitive decline and oxidative damage [19]. These animals trialed with an AO diet, including LA, showed cognitive improvement. The aged brain shows increases in ROS. The AO diet improves cognition by maintaining mitochondrial homeostasis. Lipopolsaccharides (LPS) generate ROS that play a role in brain injury [20]. LPS induced OS and shocked with increase in thiobarbituric acid-reactive substances (TBARS) and H2O2. Addition of LA after LPS increased thiol content and decreased TBARS and H2O2. LA protects the brain against OS [21]. LA exerts many biofunctions, in part by destroying ROS. The review discusses treatment of various diseases involving OS. LA may be effective in treatment of MS, AD and diabetes. 

References


