Review article

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AN OVERVIEW OF ANTIOXIDANT ACT AS PRO-OXIDANT

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ABSTRACT

Antioxidants are the substance that decreases the damage occurs due to oxygen which is caused by free radicals. The well-known antioxidants, enzymes and other substances like vitamin C, vitamin E and beta carotene, which are capable of countering the destructive effects of oxidation. Inadequate levels of antioxidants enzymes will cause oxidative stress and damage to cells. Pro-oxidant are any endobiotic or xenobiotic that induces oxidative stress either by generation of reactive oxygen species or by inhibiting antioxidant systems. In fact pro-oxidant can form all reactive, free radical containing molecules in cells or tissues, although antioxidants functions against oxidative damage induced by free radicals, they might also exhibit pro-oxidant action and leading to oxidative damage. Antioxidant supplement helps in promoting the health, but later large case including of vitamin A, vitamin E and beta-carotene, singly or in altered combinations propose that supplementation has no effect on mortality, cancer risk or have increased cancer risk and does not reduce the risk of cardiovascular disease. Paradoxically, the agents which, are usually consider as antioxidants it will act as uncertain pro-oxidants and really increase oxidative stress. Antioxidants are the reducing agents that can also act as pro-oxidants; it depends upon the dose employed for a therapeutic purpose.

Keywords: Antioxidants, Vitamin C, Vitamin E, Beta carotene, Pro-oxidants

INTRODUCTION

Antioxidants are well known for the protection they afford our bodies from damaging free radicals. The free radicals are unstable molecules that oxidize other molecules, and are formed by our bodies as part of regular metabolism. The oxidized products are more unstable and react with other molecules to form a domino-like chain reaction, it forms to oxidative stress. Oxidative stress is the total mass employed in the organisms by the continuous production of free radicals. This stress might outcome from lifestyle choices, environmental factors and aging process too. By the time this free radical chain deceases out, it can be negatively control vital components of our cells. Free radicals are produced in the cells of the body by the metabolic method of converting food to energy. Finally this cells built-in antioxidant defense system that guards against reactive oxygen species and toxic free radicals [1]. Antioxidant defense system includes many of consistent substances that conserve a proper balance between the reduced/ oxidized antioxidants. The maintenance of the body's natural defense system can reduce the growth of disease [2]. Environmental factors, aging process and the body's normal metabolic functions can also generate pro-oxidants, which will act as toxins in the body. Pro-oxidants are free radicals that are the byproducts from body use of oxygen in the energy cycle. Pro-oxidants can cause same type of oxidative damage to the human body that can observe in peeled apple decay and turn brown color. Our body organs experience the similar type of decay and destruction over time from unhindered free radicals [2].

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ANTIOXIDANT

Antioxidants are the substance that decreases the damage occurs due to oxygen which is caused by free radicals. The well-known antioxidants are enzymes and other substances like vitamin C, vitamin E and beta carotene, which are capable of countering the destructive effects of oxidation. Antioxidants are commonly added to food products such as vegetable oils and prepared foods to prevent or delay their deterioration from their action. It also reduces the risks of cancer disease. Antioxidants will slow down the progression of macular degeneration. It is a molecule

that inhibits the oxidation of other molecules. Oxidation is a chemical process or reaction involving in the loss of electrons in the oxidation state. Oxidation reactions will produce free radicals ions. This free radicals will start form a chain reactions. These chain reactions when occur in the cell, it cause death or damage to the cells. Antioxidants can terminate or dismiss these chain reactions by removing the free radical intermediates, and inhibit the further oxidation reactions. By themselves it will oxidized, so antioxidants are often been used as a reducing agents, examples such as thiols, ascorbic acid (vitamin C), or polyphenols [3].

Plants and animals maintain multifaceted types of antioxidants, such as glutathione, vitamin A, vitamin C, and moreover enzymes such as superoxide dismutase, catalase and various peroxidases. Inadequate levels of antioxidants or inhibition of the antioxidant enzymes will cause oxidative stress and damage to cells. Oxidative stress will lead damage to cell structure and cell abnormalities by reactive oxygen species (ROS)and chronic inflammation. Oxidative stress plays a significant role in many diseases, including cancers, diabetes for human. Most of the antioxidants are widely used in the food supplements and have been investigated for the prevention of varies diseases such as coronary heart disease, cancer, diabetes and other disease [4].

Antioxidants also have been used in the industry use, such as preservatives in food and cosmetics, and to prevent the degradation of rubber and gasoline [5]. Moreover antioxidants such as vitamin C, vitamin E, β-carotene, α-lipoic acids and honey have been shown to ameliorate hyperglycemia through increased beta cell mass and insulin secretion [6-9]. In patients with type 1 diabetes mellitus, the supplementation of vitamin E and/or vitamin C combination ameliorated oxidative stress and improved endothelium-dependent vasorelaxation [10, 11]. It was found that supplementation with combined chromium (Cr) and vitamins C and E ameliorated oxidative stress, reduced fasting blood glucose, glycated hemoglobin (HbA1c) and insulin resistance in type 2 diabetes mellitus [12]. Similarly, a study reported that vitamin E supplementation significantly reduced malondialdehyde (MDA) levels and increased the concentrations of GSH in type 1 diabetic patients[13]. In type 1 diabetes mellitus patients, vitamins C and E supplementation ameliorated oxidative stress markers, improved vascular dysfunction, creatinine clearance and retinal blood flow [14].

The α-lipoic acid (LA) supplementation markedly protected the beta cells, reduced cholesterol levels, and attenuated albuminuria and glomerular mesangial expansion in diabetic mice. The supplementation with alpha lipoic acid significantly improved DN and oxidative stress in the diabetic mice [15]. Green tea, which is well-researched for its antioxidant and anti-inflammatory properties, has been shown to be renoprotective. Catechin (CTN), a component of green tea, is responsible for the renoprotection. Antioxidants could play a role in the management of diabetes mellitus and its renal complications. However, considering that diabetes mellitus is a disorder with multiple etiology, antioxidant supplementation alone is likely to be less effective. The usage of antioxidants in pharmacology is intensively to be studied, particularly for treating for neurodegenerative disorders and stroke.

PRO-OXIDANT

Pro-oxidant can be define as to any endobiotic or xenobiotic that induces oxidative stress either by generation of ROS or by inhibiting antioxidant systems. In fact pro-oxidant can form all reactive, free radical containing molecules in cells or tissues. Although antioxidants functions against oxidative damage induced by free radicals, they might also exhibit pro-oxidant action, leading to oxidative damage [16, 17]. Antioxidants are the reducing agents that can also act as pro-oxidants. For example, vitamin C is a powerful antioxidant, which reduces oxidizing substances such as hydrogen peroxide [18].Moreover, it reduces the metal ions that generate free radicals ions through the Fenton reaction [19, 20].

$2\ Fe3+ + Ascorbate \rightarrow 2\ Fe2+ + Dehydroascorbate$

$2\ Fe2+ + 2\ H2O2 \rightarrow 2\ Fe3+ + 2\ OH\cdot + 2\ OH-$

The comparative significance of the antioxidant and pro-oxidant activities of antioxidants is aquit interesting area of current research. Vitamin C, which employs its effects as a vitamin by oxidizing polypeptides, appears to have a commonly antioxidant action in the human body[19, 21]. Moreover the data are less available for dietary antioxidants, such as vitamin E, [22] or polyphenols [23]. Likewise, the pathogenesis of diseases relating to hyperuricemia likely involves uric acid direct and indirect pro-oxidant properties. Paradoxically, the agents which, are usually consider as antioxidants it will act as uncertain pro-oxidants and really increase oxidative stress. In addition ascorbate, therapeutically important conditional pro-oxidants include uric acid and

sulfhydryl amino acids such as homocysteine. Characteristically, this involves some transition-series metal such as iron or copper as catalyst. The potential role of the pro-oxidant role of uric acid in example atherosclerosis and ischemic stroke, and another example is the postulated role of homocysteine in atherosclerosis.

ANTIOXIDANT ACT AS A PRO-OXIDANT

Ascorbic acid is a strong antioxidant, and it has been shown to reduce the oxidative indices against ischemia/reperfusion injury. Paradoxically, ascorbic acid has also been shown to have pro-oxidant property [24]. The pro-oxidant action of ascorbic acid was revealed in a study by Seo and Lee (2002) who demonstrated that ascorbic acid acts as an antioxidant in low dose while surprisingly it exhibits pro-oxidant action in high dose [24].Likewise, Park and Lee (2008) reported that ascorbic acid might act not only as an antioxidant but also as a pro-oxidant during cold ischemia/reperfusion in the liver [25]. In detail, cold ischemia/reperfusion was noted to decrease the reduced to oxidized glutathione ratio, whereas it increased the level of lipid peroxidation and mitochondrial swelling [25]. These changes were noted to be prevented by exposing the liver to 0.5 mM ascorbic acid but were however augmented at 2 mM ascorbic acid [25], confirming that ascorbic acid might be an antioxidant or pro-oxidant depending upon the dose employed for a therapeutic purpose.

It is important to note that flavonoids such as myricetin, baicalein, and quercetin as well as ascorbic acid were noted to cleave plasmid pBR322 DNA and calf thymus DNA potently. However, addition of catalase was noted to protect the DNA from the strand breaks caused by flavonoids [26]. The authors of this study concluded that the mutagenic and carcinogenic action of flavonoids might be because of pro-oxidant effects of the compounds [26].

Yoshino et al. (2002) reported that gallic acid and its alkylesters (polyphenolic compounds with anti-oxidative activity) also acted as a pro-oxidant, causing a copper-dependent DNA damage. Treatment of DNA from plasmid pBR322 and calf thymus with gallic acid plus copper ion was shown to cause a strand scission and the formation of 8-hydroxy-2'-deoxyguanosine in DNA. However, addition of catalase was shown to protect the DNA from the gallic acid/copper-dependent strand breaks and the formation of 8-hydroxy-2'-deoxyguanosine [27]. This study concluded that the cytotoxic effect of gallate compounds might be due to their pro-oxidant action dependent on the reducing activity [27]. The anticancer and apoptosis inducing properties of green tea are mediated by its polyphenolic constituents particularly catechins [28]. Green tea polyphenol (-)-epigallocatechin-3-gallate (EGCG) is considered as an effective chemopreventive and apoptosis-inducing agents. Plant polyphenols are naturally occurring antioxidants; however it is important to note that they might also have pro-oxidant properties [28]. The copper oxidized catechins were suggested to be more efficient pro-oxidants as compared to their un-oxidized forms [28].

Yoshino et al. (2004) reported that curcumin, a well-known antioxidant in a principal ingredient of turmeric, acted as a pro-oxidant causing a copper-dependent DNA damage and apoptosis. Treatment of DNA from plasmid pBR322 and calf thymus with curcumin plus copper ion was shown to cause the strand scission and the formation of 8-hydroxy-2'-deoxyguanosine in DNA. However, addition of catalase was shown to protect DNA from the curcumin-dependent injuries [29].This study suggested that the pro-oxidant action of curcumin might be related to the conjugated beta-diketone structure of this compound [29].

NEGATIVE HEALTH EFFECTS OF ANTIOXIDANTS

Some antioxidant supplements may promote disease and increase mortality in humans under certain conditions [30, 31].Hypothetically, free radicals induce an endogenous response that protects against exogenous radicals (and possibly other toxic compounds) [32].Free radicals may increase life span [30]. This increase may be prevented by antioxidants, providing direct evidence that toxic radicals may mitohormetically exerts life extending and health promoting effects [30,31].Early studies suggested that antioxidant supplements might help promote the health, but later large trials including of vitamin A, vitamin E and beta-carotene, singly or in altered combinations propose that supplementation has no effect on mortality [31, 33, 34]. Taking of antioxidants as a randomized trials including beta carotene, vitamin E, vitamin C and selenium have shown no effect on cancer risk or have increased cancer risk [35-41]. Supplementation with selenium or vitamin E does not reduce the risk of cardiovascular disease [42,43].

CONCLUSION

In the recent years, antioxidants and pro-oxidants have been extensively studied and it seems that most of the

antioxidants are perform as pro-oxidants; it all be determined by their concentration and the nature of neighboring molecules. The controversy around the antioxidants is because the capacity to display antioxidant and pro-oxidant behavior depends on various factors.The main conclusion is that antioxidants do have an impact on our health, but the big question is the method of administration (food vs. supplements) and quantity that might be debatable. The fact that potent antioxidants in vitro may not have any effect in vivo should not discourage further research but rather stimulate it. It is true that antioxidants are beneficial and display a useful role in human homeostasis, but so are prooxidants; the academic community should search deeper into the kinetics and in vivo mechanisms of antioxidants to uncover the optimal concentrations or desired functions in order to push forward against many disease.

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