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OXIDATIVE STRESS AND ANTIOXIDANT DEFENCE SYSTEM: A REVIEW

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Abstract: Reactive oxygen species (ROS) are generated by living organisms as a result of normal cellular metabolism and environmental factors, such as air pollutants or cigarette smoke or radiations. ROS are highly reactive molecules and can damage cell structures such as carbohydrates, nucleic acids, lipids, and proteins and alter their functions. Oxidative stress is an imbalance between radical-generating and radical- scavenging activity, resulting in oxidative stress and tissue damage, (1). Oxidative stress occurs when there is imbalance in our cells due to either an increase in free radicals or decrease in antioxidants. Reactive oxygen metabolites generated during normal metabolism and metabolism stimulated by xenobiotics can enter into reactions that, when uncontrolled, can impair performance of dairy animals. Direct effects include peroxidative changes in membranes and other cellular components. Indirectly, competitive consumption of reducing equivalents can interfere with important metabolic functions and divert glucose from other pathways by inducing the monophosphate shunt. Normally, the body is protected by a wide range of antioxidant systems working in concert. Metal catalysts of oxidative reactions are removed in intracellular fluids by metal-binding macromolecules. Superoxide dismutases, glutathione peroxidase, and catalase within cells remove superoxide and peroxides before they react with metal catalysis to form more reactive species (2). Finally, peroxidative chain reactions initiated by reactive species that escaped enzymatic degradation are terminated by chain-breaking antioxidants, including water-soluble ascorbate, glutathione, and urate and lipid-soluble vitamin E, ubiquinone, and beta-carotene. To optimize performance, oxidative stress in high producing animals must be controlled by supplying all known antioxidant nutrients and by minimizing effects of substances that stimulate reactive oxygen metabolites (3)
Keywords: Antioxidant, Oxidant, Oxidative Stress, Reactive Oxygen Species.

Introduction

Oxidative stress is a disturbance in the balance between reactive species or free radicals and antioxidants. Under normal conditions, cells are able to balance the production of oxidants and antioxidants. Oxidative stress occurs when there is imbalance in our cells due to either an increase in free radicals or a decrease in antioxidants. Oxidative stress leads to the structural changes of the cell wall and hamper the process of maturation of cellular structures. It also lead to the change in the function and death eventually.

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Causes of Oxidative stress:

ENDOGENOUS SOURCE:

I. Body's normal use of oxygen such as respiration and some cell mediated immunefunctions

II. Immune cell activation

III. Inflammation

IV. Mental stress etc. EXOGENOUS SOURCE:

I. Environmental pollutants

II. Cigarette smoke

III. Radiations etc.

Free Radicals: When the cells use oxygen for cellular function, they naturally produce free radicals. Free radicals are the atoms having odd number of electrons. Free radicals thus produced cause severe oxidative stress and if not controlled may cause excessive cell damage and impair production and reproduction related activities. Free radicals are highly reactive and are capable of damaging almost all types of biomolecules like proteins, lipids, carbohydrates, nucleic acid etc. (4) Free radicals have been implicated in causation and progression of many diseases like cancer, cardiovascular disease, inflammatory diseases, respiratory diseases, diabetes, cataract, hypertension, anemia, vitiligo, Alzheimer's disease, Parkinson's disease etc.

Antioxidants:

Antioxidants are defined as substances that inhibit or delay the oxidation of biologically relevant molecules either by specifically quenching free radicals or by chelation of redox metals. Antioxidants may be considered as scavengers of free radicals.

Vitamin A, beta carotene, vitamin C, vitamin E and selenium are the naturally occurring antioxidants which are able to neutralize harmful free radicals produced through cellular activity and various stresses, (Chew, 1993).

Enzymatic Antioxidants:

I. Superoxide Dismutase (SOD):

Superoxide dismutase plays a serious role in oxidative stress by catalyzing the rapid dismutation of $O_2^{\bullet-}$ and thus reducing the danger of $^{\bullet}OH$ formation *via* metal-catalyzed reactions. Superoxide dismutases (SODs) are antioxidant enzymes that protect cells from toxic oxygen metabolites by converting superoxide into molecular oxygen and hydrogen

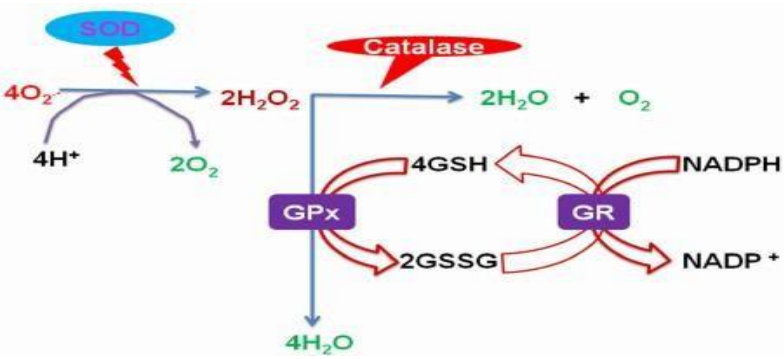
peroxide via cyclic reduction and oxidation of an active site metal. SOD out-competes damaging reactions of superoxide, thus protecting the cell from superoxide toxicity. (Quint *etal*., 2006)

II. Catalase:

Catalase is one of the crucial antioxidant enzymes that mitigates oxidative stress to a considerable extent by destroying cellular hydrogen peroxide to produce water and oxygen. Deficiency or malfunction of catalase is postulated to be related to the pathogenesis of many age-associated degenerative diseases like diabetes mellitus, hypertension, anemia, vitiligo, Alzheimer's disease, Parkinson's disease, bipolar disorder, cancer, and schizophrenia. Therefore, efforts are being undertaken in many laboratories to explore its use as a potential drug for the treatment of such diseases (7).

III. Glutathione Peroxidase:

It detoxifies H2O2 to water, while reduced glutathione (G-SH) is converted to oxidized glutathione (GS-SG). The reduced glutathione can be regenerated by the enzyme glutathione reductase utilizing NADPH. The main biological role of catalase is to protect the organism from oxidative damage (8).



Non-enzymatic Antioxidants

I. Ascorbic Acid:

Ascorbate is taken into account a potent antioxidant thanks to its ability to donate electrons in an exceedingly wide selection of enzymatic and non-enzymatic reactions. It efficiently scavenges free radicals and inhibits lipid peroxidation. Ascorbic acid (vitamin C) is primary antioxidant present in biological systems to counter oxidative stress. Ascorbic acidis oxidized into monodehydroascorbate or ascorbate free radicals and then into dehydroascorbate (DHA) in the presence of free radicals or ROS.

II. Glutathione:

Body cells contain glutathione, which is a substance made from three amino acids: cysteine, glutamate, and glycine. Glutathione acts as an important antioxidant in the body. That means it

helps combat free radicals (6). These are molecules that can damage body's cells. Reduced glutathione (GSH) plays a key role in the biological antioxidant enzyme system. Thereduced glutathione (GSH) gets regenerated from the oxidized glutathione (GS-SG) through the participation of glutathione reductase and NADPH. Ability to synthesize glutathione seems to decrease as age advances, possibly because your body can't create as much. Lower glutathione levels appear to go hand-in-hand with poorer health. For instance, lower levels may play a role in many conditions (cancer, type II diabetes, hepatitis, HIV) that are more likely to develop in older people.

III. Carotenoids

Carotenoids, such as lycopene, β-carotene, xanthophyll, lutein, and zeaxanthin, are lipophilic antioxidants capable of detoxifying various ROS and most effectively capture the lipid peroxyl radical ($LOO^{\bullet}$), thus providing membrane protection. Carotenoids react with $LOO^{\bullet}$ and form lipid hydroperoxide (LOOH) and a carotenoid radical which will be regenerated by tocopherol, and both tocopherol and carotenoid radicals might be reduced by ascorbic acid subsequently (11). Among the different carotenoids β-carotene is the most important. It can act as an antioxidant under low partial pressure of oxygen. Lycopene, a fat soluble pigment is responsible for colour of certain fruits and vegetables. Lycopene possess antioxidant property. Lutein and zeaxanthin impart yellow or green colour to fruits and vegetables.

IV. Vitamin E and selenium:

Vitamin E (tocopherol) and tocotrienols are essential components of the cell membrane where they express both antioxidant and non-antioxidant functions. There are four tocopherol and tocotrienol isomers (α, β, γ, and δ). Tocopherols are a gaggle of lipophilic antioxidants and are synthesized by photosynthetic organisms and present in green, photosynthetically active parts of the plant only. The antioxidant activity of tocopherol is predicated on the electron donor properties of the chromanol ring. It is the most important lipid soluble intracellular antioxidant being capable of scavenging oxygen radicals and terminates free radical chain reaction while selenium is a cofactor of enzyme glutathione peroxidase that acts in aquous intracellular and extracellular compartments to catalyse destruction of peroxides (2). Supplementation of vitamin E and selenium increased the glutathione peroxidase activity along with decrease lipid peroxidation in many species. (10). Superoxide dismutase disproportionate superoxide (O_2^-) to hydrogen peroxide(H_2O_2), which is metabolized in the intracellular compartments by selenium dependent glutathione peroxidase.

$$O_2^- + O_2^- + 2H^+ \xrightarrow{\text{Superoxide dismutase}} H_2O_2 + O_2$$

$$2GSH + H_2O_2 \xrightarrow{\text{Glutathione peroxidase}} G\text{-}S\text{-}S\text{-}G + 2H_2O$$

α-Lipoic acid: It plays a key role in recycling other important antioxidants like ascorbic acid, tocopherol and glutathione. It is a vitamin like compound produced in the body.

V. Phenolic compounds:

Phenolic compounds are referred to as phytochemicals found in a large number of foods and beverages. The relative high diversity of these molecules produced by plants must be taken into account when methods of preparation are employed to obtain industrial or homemade products. Phenolic compounds comprise one (phenolic acids) or more (polyphenols) aromatic rings with attached hydroxyl groups in their structures. Their antioxidant capacities are related to these hydroxyl groups and phenolic rings (5).

Conclusion

Antioxidants plays an important role to prevent cancer and many other diseases. It also helps in slowing aging process and preventing heart diseases. Antioxidants may exhibit beneficial mutual influences like the synergism of synthetic phenolic antioxidants, or the regeneration of tocopherol from its oxidized form, tocopheroxyl radical, by reduced coenzyme Q or vitamin C.

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