GENERATION & MODE OF ACTION OF FREE RADICALS & OXIDATIVE STRESS WITH SPECIAL EMPHASIS ON HEALTH & DISEASE PREVENTION

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ABSTRACT

The normal functioning of cells is dependent on a proper balance of pro oxidants and antioxidants. The former promote the release of oxidants to provide energy needed for cell functioning. In this process, different biochemical reactions take place which continuously produce free radicals. Living cells continually generate free radicals or reactive oxygen species (ROS) through the respiratory chain during energetic metabolism. Human body has various intrinsic mechanisms to counteract oxidative stress by producing antioxidants, or through externally derived foods and/or supplements. However whenever there is excess of free radicals their accumulation in the body generates a phenomenon called oxidative stress. As we age, this oxidative and/or nitrosative damages elicit a number of late-onset diseases after ROS/RNS accumulate to certain levels. Cumulative tissue injury thus caused by free radical is now known to underlie the pathogenesis of clinical conditions such as cancer, arthritis, arteriosclerosis, and neurodegenerative diseases. Oxidative stress is marked with expression of specific biomarkers whose specificity towards the various disease condition needs validation. During this process of release of energy to perform normal activities of life, electrons are transferred between the molecules resulting in many Reactive Oxygen Species and the non-oxygen free radicals in the body. However, excessive oxidative stress or inadequacy in a normal cell's antioxidant defence system (or both) can cause the cell to experience oxidative stress. Tumour cells usually have an imbalanced redox status resulting in the damage to DNA, proteins and lipids. Higher levels of DNA damage and deficient DNA repair may predispose individuals to cancer. In this review, summarize the source, balance, maintenance, generation, mode of action and physiological functions of ROS, oxidative stress and its toxic mechanisms underlying a number of diseases and also the biomarkers implicated in selected human diseases and prevented by using antioxidants, functional foods, nutraceuticals and phytochemicals.

Keywords: Antioxidants, Oxidative stress, Free radicals, Nutraceuticals, phytochemicals, Oxidants, Oxidation, Reduction

INTRODUCTION

Free radicals have been implicated in over a hundred disease conditions in humans, including arthritis, hemorrhagic shock, atherosclerosis, advancing age, ischemia and reperfusion injury of many organs, Alzheimer and Parkinson's disease, gastrointestinal dysfunctions, tumour promotion and carcinogenesis, and AIDS (Debasis Bagchi et al., 2000). Oxidative stress can be caused in result of free radicals formation. Aging and different chronic diseases including diabetes, cancer and cardiovascular diseases could be caused by oxidative stress. Antioxidants are important factor to maintain optimal cellular and human body health (Sunil Kumar, 2014). Functional food components are potentially beneficial components found naturally in foods or added to them as functional ingredients (Raquel G et al.). Phytochemicals, as plant components with discrete bio-activities towards animal biochemistry and metabolism are being widely examined for their ability to provide health benefits (Cora J et al., 2000). Within the last decade, we have observed distinct changes in the understanding of the role of foods in human health promotion. The first frontier of scientific investigations has moved from the primary role of food as the source of energy and body-forming substances to the more subtle action of biologically active food components on human health. In the industrialized world, there has been an explosion of consumer interest in the active role of foods in the well-being and life prolongation as well as in the prevention of initiation, promotion and development of cancer, cardiovascular diseases and osteoporosis. At the moment, the most important and the most frequently used functional food compounds are probiotics, prebiotics, plant antioxidants, vitamins and calcium. It has been given high priority in the production of probiotics and prebiotics, and the extraction of bioactive components from plant materials by enzyme and fermentation technology to reduce loss of these compounds as well as by genetic engineering to intensify their biosynthesis (Włodzimierz Grajek et al., 2005).

Free radicals

A free radical can be defined as any molecular species capable of independent existence that contains an unpaired electron in an atomic orbital (V.Lobo. et al., 2010). Free radicals are well documented for playing a dual role in our body as both deleterious and beneficial species. It is highly unstable because of its atomic or molecular structure.

Generation and sources of free radicals

Free radicals can be formed from both endogenous and exogenous substances. They are continuously forming in cell and environment. Different sources of free

radicals are as follows:

☐ UV radiations, X-rays, gamma rays and microwave radiation.

☐ Oxygen free radicals in the atmosphere considered as pollutants.

☐ In mitochondria-catalyzed electron transport reactions, oxygen free radical produced as by product.

☐ Interaction with chemicals, automobile exhausts fumes, smoking of cigarettes & cigars.

☐ Burning of organic matter during cooking, forest fires, volcanic activities.

☐ Industrial effluents, excess chemicals, alcoholic intake, certain drugs, asbestos, certain pesticides and herbicides, some metal ions and fungal toxins& xenobiotics (Saikat Sen et al., 2010).

☐ Exercise.

Table 1: Free radicals in biology

Free radicals	Description
$O_2^{\cdot-}$, superoxide anion	One-electron reduction state of O_2, formed in many autoxidation reactions and by the electron transport chain. Rather unreactive but can release Fe^{2+} from iron–sulfur proteins and ferritin. Undergoes dismutation to form H_2O_2 spontaneously or by enzymatic catalysis and is a precursor for metal-catalyzed OH formation
H_2O_2, hydrogen peroxide	Two-electron reduction state, formed by dismutation of $O_2^{\cdot-}$ or by direct reduction of O_2. Lipid soluble and thus able to diffuse across membranes
OH, hydroxyl radical	Three-electron reduction state, formed by Fenton reaction and decomposition of peroxynitrite. Extremely reactive, will attack most cellular components
ROOH, organic hydroperoxide	Formed by radical reactions with cellular components such as lipids and nucleobases
RO, alkoxy and ROO, peroxy radicals	Oxygen centered organic radicals. Lipid forms participate in lipid peroxidation reactions. Produced in the presence of oxygen by radical addition to double bonds or hydrogen abstraction
HOCl, hypochlorous acid	Formed from H_2O_2 by myeloperoxidase. Lipid soluble and highly reactive. Will readily oxidize protein constituents, including thiol groups, amino groups, and methionine
$ONOO^-$, peroxynitrite	Formed in a rapid reaction between $O_2^{\cdot-}$ and NO. Lipid soluble and similar in reactivity to hypochlorous acid. Protonation forms peroxynitrous acid, which can undergo homolytic cleavage to form hydroxyl radical and nitrogen dioxide

☐ Ischemia/reperfusion injury.

☐ Environmental pollutants.

☐ Radiation.

☐ Ozone (V.Lobo. et al., 2010).

Mode of action of free radicals

Free radicals generally involved in chain reactions, a series of reactions leads to regenerates a radical that can begin a new cycle of reactions. Free radical actions take three distinct identifiable steps:

☐ **Initiation step:** formation of radicals.

☐ **Propagation step:** in this step

required free radical is regenerated repeatedly as a result of chain reaction, which would take the reaction to completion.

☐ **Termination step:** destruction of radicals (Saikat Sen et al., 2010).

The majority of free radicals that damage biological systems are oxygen-free radicals, and these are more generally known as "reactive oxygen species" (ROS). These are the main by-products formed in the cells of aerobic organisms, and can initiate autocatalytic reactions so that molecules to which they react are themselves converted into free radicals to propagate the chain of damage. ROS can be (i) generated during UV light irradiation and by X-rays and gamma rays (ii) produced during metal catalyzed reactions (iii) are present in the atmosphere as pollutants (iv) are produced by neutrophils and macrophages during inflammation, and (iv) are by-products of mitochondrial catalyzed electron transport reactions, and various other mechanisms (Khalid Rahaman, 2007).

Oxidative stress

Oxidative stress, defined as a disturbance in the balance between the production of reactive oxygen species (free radicals) and antioxidant defences, is discussed in relation to its possible role in the production of tissue damage (D.John Betteridge,2000).

Generation & mode of action of oxidative stress

The oxidative damage to DNA overtime could cause changes to both the structure and functions of chromosomes, which can lead to cancer and chronic diseases. Oxidative stress is cellular proteins. This plays a role in the causation of cataracts. Free radicals can interfere with protein function leading to irregular, abnormal metabolism and rapid aging. The increase in free radicals may be secondary to the disease process (Chinwe Elochukwu, 2015).

Free radicals and oxidative stress with special emphasis on health and diseases

Oxygen derived free radical reactions have been implicated in the pathogenesis of many human diseases including:

☐ Neurodegenerative disorder like alzheimer's disease, parkinson's disease, multiple sclerosis, amyotrophic lateral sclerosis, memory loss and depression.

☐ Cardiovascular disease like atherosclerosis, ischemic heart disease, cardiac hypertrophy, hypertension, shock and trauma.

☐ Pulmonary disorders like inflammatory lung diseases such as asthma and chronic obstructive pulmonary disease.

☐ Diseases associated with premature infants, including bronchopulmonary, dysplasia, periventricular leukomalacia, intraventricular hemorrhage, retinopathy of prematurity and necrotizing enterocolitis.

☐ Autoimmune disease like rheumatoid arthritis.

☐ Renal disorders like glomerulonephritis and tubulointerstitial nephritis, chronic renal failure, proteinuria, uraemia.

☐ Gastrointestinal diseases like peptic ulcer, inflammatory bowel disease and colitis.

☐ Tumours and cancer like lung cancer, leukaemia, breast, ovary, rectum cancers etc.

☐ Eye diseases like cataract and age related of retina.

☐ Ageing process.

☐ Diabetes.

☐ Skin lesions.

☐ Immuno depression.

☐ Liver disease, pancreatitis.

☐ AIDS.

☐ Infertility (Saikat Sen et al., 2010).

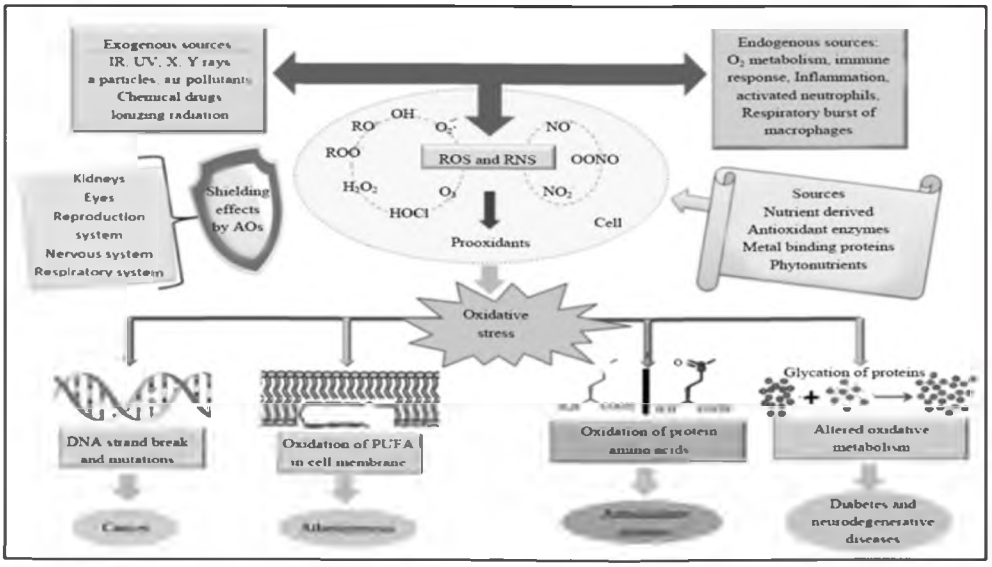


Fig.3: Synopsis of free radical formation, oxidative stress and pathogenesis of chronic diseases

Disease prevention by using antioxidants, functional foods, phytochemicals and related with other compounds

Several epidemiological studies have shown that a proper diet, in which plant foods provide the major portion of caloric intake, may reduce the development of certain diseases like cancer and atherosclerosis. Although fats and proteins in plants, as opposed to those of animal origin, are responsible to some extent for these protective effects, the contribution of other plant food components may also be relevant (Francesco Visioli et al.,2000). The phytochemicals present in functional foods that are responsible for preventing disease and promoting health have been studied extensively to establish their efficacy and to understand the underlying mechanism of their action (Bs Narasinga Rao, 2003). Antioxidants are substances that may protect cells from the damage caused by unstable molecules known as free radicals (A. A. Hamid et al., 2015).

CONCLUSION

New eating habits, actual trends in production and consumption have a health, environmental and social impact. Continuous usage of the same vegetable oil which is not even properly stored and re-using the already fried oil (rancid) lead to generation of free radicals through lipid peroxidation. The important roles of reactive oxygen species in diseases related to aging and the necessity and benefits of antioxidative nutraceuticals in the prevention of diseases and promotion of healthy aging have been extensively reported in recent years. The phytochemicals present in functional foods that are responsible for preventing disease and promoting health have been studied extensively to establish their efficacy and to understand the underlying mechanism of their action. In recent years, there has been a great deal of attention toward the field of free radical chemistry. Free radicals reactive oxygen species and reactive nitrogen species are generated by our body by various endogenous systems, exposure to different physiochemical conditions or pathological states. A balance between free radicals and antioxidants is necessary for proper physiological function. If free radicals overwhelm the body's ability to regulate them, a condition known as oxidative stress ensues.

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