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FREE RADICAL PRODUCTION IN BIOLOGICAL SYSTEM - A MINI REVIEW

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ABSTRACT

Free radicals are chemical species that have an ability to exist independently with unpaired electrons. They can be both beneficial and detrimental depending on its concentration in the cell. It is beneficial in host defense mechanisms against pathogens when its levels are low in the cell. However, and overload leads to oxidative stress than can presdispose many diseased conditions like inflammation, atherosclerosis, cancer, neurodegenerative disorders, etc. These free radicals in the body exist as reactive oxygen species (ROS) or reactive nitrogen species (RNS), and their effects are understood by their chemical properties.

KEYWORDS: free radicals, prooxidants, hydrogen peroxide, hydroxyl radicals, superoxide ion radicals

INTRODUCTION

Free radicals can be both beneficial and toxic depending on the balance between pro-oxidant and antioxidant homeostasis. They are produced either from normal cell metabolism in situ or from external sources (pollution, cigarette smoke, radiation, medication) [1-2]. As a prooxidant, it helps in apoptosis, immunity, protein phosphorylation, activation of several transcriptional factors, differentiation in the cell and host defense mechanism against pathogens provided they are at low levels. An overload and accumulation of free radicals in the body, however, can generate a phenomenon called oxidative stress as they cannot gradually be neutralized [3-4]. This phenomenon has been correlated to being the origins of diseased conditions like inflammation, atherosclerosis, hypertension, cancer, ischaemic disease, Alzheimer's disease, Parkinsonism, etc [5-7]. The mini review focuses on the types of free radicals generated and their chemical properties, thus exploring its impact on maintaining healthy cells in the body.

FREE RADICALS

A free radical is any chemical species with a capacity to exist independently while containing an unpaired electron in its atomic orbital. The presence of an unpaired electron leads to many radicals being unstable and highly reactive by either donating an electron to or accepting an electron from other molecules. Therefore, they can behave as oxidants or reductants [8]. Oxygen-containing free radicals such as superoxide anion radical, hydroxyl radical, hydrogen peroxide, oxygen singlet, peroxynitrite radical, nitric oxide radical, and hypochlorite are highly reactive in the nucleus and cell membranes targeting DNA, proteins, carbohydrates, and lipids resulting in many disease states due to the damage caused [9].

PRODUCTION OF SOME ROS AND RNS IN OUR BODY

Free radicals such as reactive nitrogen species (RNS) and reactive oxygen species (ROS) are naturally produced from metabolic processes in the human body such as enzymatic reactions

involved in the respiratory chain, phagocytosis, prostaglandin synthesis, and cytochrome P-450 system. or from exposure to external sources like X-rays, UV-rays, ozone, air pollutants, and industrial chemicals [10-12].

Hydrogen Peroxide (H_2O_2): Hydrogen peroxide is produced in a dismutation reaction catalyzed by superoxide dismutase (SOD) in the body (Eq. 1). Though it is not a free radical, it can cause damage to the cell at concentrations as low as 10 µM by easily penetrating the biological membranes, while at higher levels, it can lead to inactivation of cellular energy producing enzymes such as glyceraldehhyde-3-phosphate dehydrogenase. H_2O_2 has no direct effect on DNA. However, by Fenton reaction wherein in the presence of transition metal ions, hydroxyl radical (OH−) are produced, it can damage the DNA [13].

$$O_2 + O_2^{\bullet-} + 2H_2O \xrightarrow{SOD} H_2O_2 + O_2 \quad \text{- (1)}$$

Hydroxyl Radical (OH·): Hydroxyl radical is the neutral form of hydroxide ion formed in a Fenton reaction (Eq. 2) wherein H_2O_2 reacts with transition metal ions (Fe^{+2} or Cu^{+}), often complexed to different proteins [14]. When the body is under stress conditions, an excess of superoxide radical ($O_2^{\bullet-}$) is produced which causes the release of free iron from ferritin (a storage protein). These in turn participate in Fenton reaction to form $OH^{\bullet}$. $OH^{\bullet}$ is also formed by the Haber–Weiss reaction between $O_2^{\bullet-}$ and H_2O_2 (Eq. 3) [15].

This highly reactive free radical can strongly react with both organic and inorganic molecules. It also reacts with DNA, proteins, carbohydrates and lipids causing damage to the cells more severe than those cause by other ROS [16-17].

$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + OH^{\bullet} + OH^{-}$ (Fenton Reaction) -(2)

$O_2^{-} + H_2O_2 \rightarrow O_2 + OH^{\bullet} + OH^{-}$ (Haber-Weiss reaction)- (3)

Superoxide Ion Radical ($O_2^{\bullet}$): Superoxide anion radical is formed mostly in the mitochondria by enzymatic process by enzymes such as xanthine oxidase, lipooxygenase, cyclooxygenase and NADPH dependent oxidase, autooxidation reaction and by a nonenzymatic electron transfer to molecular oxygen [18-21]. Under physiological pH it can exist as $O_2^{\bullet-}$ while at low pH, as hydroperoxyl radical ($HOO^{\bullet}$) [22]. $HOO^{\bullet}$ can easily enter the phospholipid bilayer than the charged form ($O_2^{\bullet-}$) [23].

Peroxyl Radical ($ROO^{\bullet}$): Peroxyl Radical ($ROO^{\bullet}$) is formed by reactions of molecular oxygen with carbon-centered radicals in living systems [24]. The simplest form of peroxyl radical is perhydroxyl radical (HOO•). Peroxyl radicals initiates fatty acid peroxidation and can also promote tumor development [25].

Nitric Oxide or Nitrogen Monoxide ($NO^{\bullet}$): The molecule is generated in tissues by the isoforms of nitric oxide synthases (NOS) namely neuronal NOS (nNOS), endothelial NOS (eNOS) and inducible NOS (iNOS). These enzymes convert L-arginine to L-citrulline [26]. In this reaction one of the terminal guanido nitrogen atoms oxidizes to produce $NO^{\bullet}$.

Due to its solubility in aqueous and lipids it readily diffuses through plasma membrane and cytoplasm [27]. The $NO^{\bullet}$ is beneficial as it is an important intracellular second messenger involved in many biological activities such as blood pressure regulation, smooth muscle relaxation, neurotransmission, immune regulation and defensive mechanisms [28].

CONCLUSION: Imbalance between pro-oxidant and antioxidant homeostasis are considered to predispose a majority of disease conditions like inflammation, cancer, atherosclerosis, ischaemic disease, Alzheimer's disease, Parkinsons, etc. Antioxidant principles from natural resources have shown promise in correcting the imbalance. Therefore, by understanding the nature of free radicals, molecular mechanisms of their effect can help direct target-oriented antioxidant research and isolation from natural resources.

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