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Review Article
ABHI Publications since 2013
International Journal of Pharmacy and Engineering (IJPE)
ISSN 2320-849X

BASIC CONCEPT OF FREE RADICALS IN PHARMACY

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Abstract

Free radicals are chemical entities that can be thought of as fragments of molecules because they have an unpaired electron and are frequently very reactive. They are continuously created in cells, either accidentally as by-products of metabolism or purposefully, for example, during phagocytosis.The oxygen atom and its radical derivatives (superoxide and hydroxyl radicals), hydrogen peroxide, and transition metals are the most significant reactants in free radical biochemistry in aerobic cells. To stop the generation of free radicals or reduce their destructive effects, cells have evolved a wide range of antioxidant defenses. These include proteins that bind transition metals, enzymes that break down peroxides, and a variety of substances that scavenge free radicals. Biomolecules can be oxidized by reactive free radicals produced inside cells, which can cause cell death and tissue damage. Due to these species' short lifespans, it is very challenging to prove that they are involved in the pathogenesis of a disease.

Keyword-Reactive oxygen species,NADPH, Free radicals,Endothelium-derived relaxing factor

Received: December 25th 2023, Accepted: December 30th 2023,

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Introduction

Before the evolution of humans or their ancestors, the human body has been attacked by a harmful class of chemical agents. Although they are also known as "reactive oxygen species" and go by the abbreviation "ROS," they are known as "free radicals." Free radicals are produced by oxygen and compounds with a lot of oxygen[1].

Atoms or molecules that have unpaired electrons are known as free radicals. In atoms or molecules, electrons are found in pairs in certain orbitals. Free radicals can have one of three charges: positive, negative, or zero [2].

Free radicals are frequently produced by NADPH cytochrome P-450 reductase or other flavin-containing reductases, while cytochrome P-450 itself may also be involved, as is the case when carbon tetrachloride is reduced to produce radicals. CCl_2O_2 and CCl_3. A persistent amount of free radicals in the cell, as well as the depletion of reduced cofactor and hypoxia, are all possible outcomes of the recycling cycle in which many radicals can participate [3].

TYPES OF FREE RADICALS- [4]

Reactive oxygen species (ROS), which include the superoxide ion, hydrogen peroxide, hydroxyl radical, and singlet oxygen, are the most common types of free radicals that originate from oxygen atoms.

Superoxide ion (or reactive oxygen species)-It is a kind of oxygen that has one additional electron. This free radical has the potential to harm DNA, mitochondria, and other large molecules.

Hydrogen peroxide-It contributes to the creation of several reactive oxygen species. Peroxidases use hydrogen peroxide, a byproduct of oxygen metabolism, to do their job of neutralizing it.

Singlet oxygen-Our immune system creates singlet oxygen throughout the body. Cholesterol is oxidized by singlet oxygen.

Hydroxyl radical-In the electron transport chain, it is produced by the reduction of an oxygen molecule. It is the hydroxide ion's neutral form. Because of their great reactivity, hydroxyl radicals play a significant role in radical molecular biochemistry.

SOURCES OF REACTIVE FREE RADICALS-

1) Mitochondrial Cytochrome Oxidases-The mitochondrial cytochrome oxidase system adds four electrons to the free radicals, which are produced as typical by-products of cell metabolism under normal conditions in biological systems, to regulate their reduction and produce water [5].

2) Drug metabolism-ROS are produced by the cytochrome P450 and B5 systems, which are primarily engaged in drug metabolism, as well as the microsomal and nuclear membrane electron transport systems. In both the presence and absence of mixed-function oxidase substrates, NADPH oxidation produces ROS (O_2 and H_2O_2) as well. In the mechanism of cytochrome P450-driven processes, oxy and then peroxyintermediates are formed. [6].

3) Transition Metals-Conditions (such as hemolysis, for example) that cause the formation of transition metal ions (such as those of iron and copper) may noticeably increase the toxicity of ROS. H_2O_2 may be changed into OH by iron and copper ions. In the presence of unbound transition metal ions, the well-known antioxidant ascorbic acid [7].

4) Nitric Oxide synthase-Endothelium-derived relaxing factor (EDRF), which is created by vascular endothelial cells, is thought to be comparable to NO. Nitric oxide is recognized to be involved in several important physiological processes, including the regulation of systemic blood pressure, digestion, platelet aggregation, and other processes. It is synthesized in a wide range of tissues. The primary enzyme for the production of NO is tissue-specific **[**8].

BIOCHEMICAL TARGETS OF FREE RADICALS IN THE BODY

A) Proteins-Free radicals may cause proteins to oxidatively degrade. Free radicals generated by the mitochondrial electron transport chain can promote protein breakdown. To encourage the production of new proteins, oxidative proteins destroyed damaged proteins [5].

B) DNA- The poly (ADP-ribose) synthetase enzyme is activated as a result of free radical damage to DNA. To assist in DNA repair, this breaks NAD+ [9].

ROLE OF FREE RADICALS IN HEALTH AND DISEASE

- Oxidative damage to DNA, proteins and other macromolecules has been linked to the development of a wide range of disorders, including heart disease and cancer. Both heart disease and many cancers may be prevented or slowed down by antioxidants, according to research [10].
- Heart and blood vessels (arteries, capillaries, and veins) are involved in a class of disorders known as cardiovascular illnesses. Heart conditions, vascular conditions, and kidney, peripheral arterial disease, and the brain. Most Relative to other diseases, CVDs account for of all deaths[11].
- Nox1 protein overexpression is a key early development in the prostate cancer's emergence. Having prostatic tumors Significantly increased ROS and Nox1 levels[12].
- Cigarette smoke particulates contain a complex mixture of numerous carcinogens and stable ROS with very long half-lives. These ROs can damage the tissues,

resulting in the progressive transformation of cells into the malignant form, which leads to an increased frequency of mutations caused by oxidative damage to DNA and eventually leads to lung cancer[13].

- People who have high blood pressure have a higher risk of stroke, heart disease, kidney failure, and early death. Free In part, oxidative stress brought on by radicals causes hypertension and endothelial dysfunction[14].
- According to epidemiological findings, those with diets high in fruits and vegetables have lower cancer rates. This has given rise to the hypothesis that these diets include components, potentially antioxidants, that guard against the onset of cancer. In-depth scientific research is currently being done on this subject. As of now, no large, well-designed studies have demonstrated that increasing the antioxidant content of one's diet lowers the risk of acquiring cancer. Additionally, antioxidants are known to slow down aging and prevent certain illnesses. strokes and heart conditions. Consequently, from the standpoint of public health, it is too early to make recommendations in relation to the prevention of disease and antioxidant supplements[15].

The Advantages of Radicals

- They regulate the blood flow through our arteries to prevent infection, maintain mental acuity, and sustain our focus.
- Some free radicals act as signaling molecules, activating and deactivating genes, similar to how antioxidants .
- Immune cells produce some free radicals, such as NO and superoxide, in extremely high concentrations to harm germs and viruses.
- Some free radicals kill cancer cells, and some cancer medications work by boosting the body's level of free radicals.[16]

Conclusion

Free radicals are a very reactive species of molecules.Atherosclerosis and coronary artery disease are both caused by protein and lipid radical damage in plasma lipoproteins; proteins can also cause autoimmune disorders.Ionizing radiation exposure, nonenzymatic processes involving transition metal ions, and the respiratory burst of activated macrophages all result in the production of oxygen radicals.Enzymes that eliminate superoxide ions and hydrogen peroxide, enzymatic reduction of lipid peroxides connected to glutathione oxidation, and nonenzymatic interaction of lipid peroxides with vitamin E all provide protection against radical damage.Radicals play a crucial role in the cell signaling that causes DNA damaged

cells to apoptose. High antioxidant doses may quench the risk of radical signaling is rising as a result of cancer occurrence.

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