



## Basic Concept of Free Radicals in Pharmacology

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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.  $\text{CCl}_2\text{O}_2$  and  $\text{CCl}_3$ . 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 by product 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

- **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].

- **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 peroxy intermediates are formed. [6].
- **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].
- **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

- **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].
- **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].

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