

## Aspects Relating of the Oxidative Stress to Living Organisms

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Free radicals (pro-oxidants) are compounds belonging to the radical groups; they are active biochemically and biologically, and they destroy cell membranes, nuclei, and cytoplasm, producing and maintaining an intense oxidative stress. This is a consequence of the presence of one or several free electrons on the last layer of an atom in the molecule. Free radicals are oxygenated electron-deficit anions that do not make up salts, acids, or bases, but keep this reactive (free) form [1].

Oxygen electronic structure explains why the element, though a free diradical (two unpaired electrons) have low reactivity. Oxygen is essential for aerobic bodies' life, but, in concentrations that are too high, it can turn toxic. Molecular oxygen in fundamental state is inert, and its partial reduction results in active oxygen species—the most dangerous free radicals [2]. This group of compounds is called Reactive Oxygen Species (ROS). ROS is a term including not only oxygen radicals (O and H), but also oxygen non-radical derivatives, including hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>), hypochlorous acid (HOCl), and ozone (O<sub>3</sub>) [3]. Even if ROS are not true free radicals, these species are molecule reactive [4].

Under physiological conditions, ROS are produced in small amounts in the cells [5].

The interaction between these species and lipid membranes, nucleic acids, proteins and enzymes or other small molecules, leads inevitably to cell lesions (Figure 1).

These cell lesions are one of the factors leading to ageing and degenerative diseases at cell level, there are several types of reactive species.

The variety of free radicals in nature resulted from different processes (ultraviolet radiations, gamma radiations, action of specific particles, etc.) makes their classification difficult [6,7].

From the point of view of the nature of the element containing free electrons, free radicals can be: superoxide, peroxide, hydroxide, nitric oxide, nitrite, nitrate, alkoxyl (Table 1).

Cell production of ROS roots in enzymatic and non-enzymatic sources.

Electron transfer from proteins or enzymatic systems can lead to ROS as a result of electron transfer reactions. This "unintentional" generation of ROS in mitochondria represents 1–2% of the total O<sub>2</sub> consumed in reducing conditions. Body oxygen content represents 65% and inhaled air oxygen content is 21%. Cells generate aerobic energy, reducing O<sub>2</sub> to water.

Oxygen can be used in catabolic and anabolic processes, allowing larger amounts of energy than possible in its absence [8].

Oxygen has a particular electronic structure in its fundamental state, with two non-participating electrons on the last layer, each of which is localised on an orbital n\* (Figure 2).

These two electrons have the same quantum number of spin; thus, if O<sub>2</sub> tries to oxidate a compound by accepting two electrons, they need to have a parallel spin number to occupy the free spaces in the orbitals n\*

(in an orbital, two electrons have anti-parallel spins +1/2 and -1/2) [9].

This particularity asks for a restriction of oxidations, determining higher or lower reactivity, depending on the nature of the electron donor (Table 2).

All oxidations in nature are based on these two pathways, even if the forms may seem varied.

Peroxides and superoxides are anions that have oxidative action (peroxides, alkoxyls, nitrosamines, acrolein) derive from H<sub>2</sub>O<sub>2</sub> and from other sources/processes, like the anions resulted from the degradation (rancidisation, proteolytic degradation, etc.) of lipid-rich foods (lipid peroxides, lipid alkoxyls) or from food processing (frying, refreezing, etc.).

Hypochlorous acid behaves like free radicals (but they do not belong to this class).

Other sources of free radicals are nitrosamines and unsaturated aldehydes (acrolein), very active and destructive because of their action on cell membranes [10].

Evolutionally, nature has selected and included in the composition of the organisms, reactions generating free radicals with multiple roles: functional, intracellular communication, or destructive, cytotoxic. If, at molecular level, the main target of the free radicals is the free or protein groups SH, at cellular level, the major goal is cell membranes.

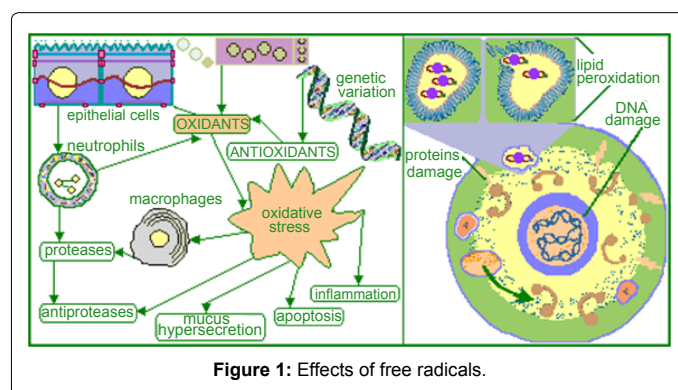


Figure 1: Effects of free radicals.

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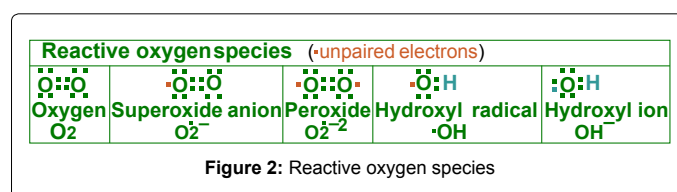
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| Species/Common Name  | Systematic Name/Alternative and Comments                                      |
|--|---|
| CO/carbon monoxide   | carbon monoxide/Oxidomethanediyl ( $\text{CH}_3^\bullet$ )                    |
| CO <sub>2</sub> /carbon dioxide  | carbon dioxide/dioxidomethane   |
| CO <sub>2</sub> <sup>-</sup> /carbon dioxide radical anion             | dioxidocarbonate ( $\bullet$ 1-)/oxidooxomethyl radical                       |
| CO <sub>3</sub> <sup>-</sup> /carbonate radical                        | trioxidocarbonate ( $\bullet$ 1-)   |
| H <sup>•</sup> /hydrogen atom  | monohydrogen ( $\bullet$ )  |
| H <sub>2</sub> O/water   | dihydrogen monoxide/oxidane   |
| H <sub>2</sub> O <sub>2</sub> /hydrogen peroxide                       | dihydrodioxide/dioxidane  |
| H <sub>3</sub> C <sup>•</sup>  | methyl radical  |
| HNO <sub>2</sub>   | nitrous acid  |
| HNO <sub>3</sub>   | nitric acid   |
| HO <sup>•</sup> /hydroxyl radical                                      | hydridooxygen/oxidanyl  |
| HO <sub>2</sub> <sup>-</sup> /hydridodioxide (1-)                      | dioxidanide, hydrogendioxide (1-)/hydrogenperoxide (1-)                       |
| HO <sub>2</sub> <sup>•</sup> /hydroperoxyl, but is obsolete            | Hydridodioxide ( $\bullet$ ) dioxidanyl/hydrodioxyl, perhydroxyl              |
| HO <sub>3</sub> <sup>•</sup> /hydrogen trioxide radical                | hydridotrioxide ( $\bullet$ )/trioxidanyl                                     |
| HOCO <sup>•</sup>  | hydroxidooxidocarbon ( $\bullet$ )  |
| HOCO <sub>2</sub>  | hydroxidodioxidocarbon ( $\bullet$ )  |
| HOCl/hypochlorous acid   | hydrogenoxidochlorate   |
| HOBr/hypobromous acid  | hydrogenoxidobromate  |
| HOI/hypoiodous acid  | hydrogenoxidiodate  |
| HOSCN/hypothiocyanous acid   | hydrogenoxidothiocyanate  |
| HON <sub>2</sub> <sup>•</sup>  | hydroxidonitrogen(2 $\bullet$ ) (triplet)/hydrogen oxidonitrate(2 $\bullet$ ) |
| HOOCO/ (hydridodioxido)  | oxidocarbon( $\bullet$ )  |
| HOONO/peroxynitrous acid   | hydrogenoxidoperoxidonitrate/nitrosodioxidane                                 |
| (NO) <sub>2</sub> <sup>•</sup>   | bis (oxidonitrate) ( $n - n$ ) ( $\bullet$ 1-)                                |
| N <sub>2</sub> O/nitrous oxide   | dinitrogen monoxide   |
| N <sub>2</sub> O <sup>•</sup>  | oxidodinitrate ( $\bullet$ 1-)  |
| N <sub>2</sub> O <sub>3</sub>  | dinitrogen trioxide   |
| N <sub>3</sub> <sup>•</sup> /azidyl radical                            | trinitrogen ( $2n - n$ )( $\bullet$ )   |
| NO <sup>•</sup> /nitric oxide, but is obsolete                         | oxidonitrogen ( $\bullet$ )/oxoazanyl, nitrogen monoxide                      |
| NO-(2 $\bullet$ )/nitroxyl   | oxidonitrate (2 $\bullet$ 1-) (triplet)                                       |
| NO <sub>2</sub> <sup>-</sup> /nitrite                                  | dioxidonitrate (1-)   |
| NO <sub>2</sub> <sup>•</sup> /nitrogen dioxide                         | dioxidonitrogen   |
| NO <sub>2</sub> <sup>2-•</sup>   | dioxidonitrate( $\bullet$ 2-)   |
| NO <sub>3</sub> <sup>•</sup> /nitrate                                  | trioxidonitrate (-)   |
| NO <sub>3</sub> <sup>-</sup> /nitrogen trioxide                        | trioxidonitrogen ( $\bullet$ )/nitrosoxidanyl                                 |
| NO <sub>3</sub> <sup>2-•</sup>   | trioxidonitrate ( $\bullet$ 2-)   |
| O <sup>•</sup> /radical anion of HO <sup>•</sup>                       | oxide ( $\bullet$ 1-)/oxidanidyl  |
| O <sub>2</sub> <sup>•</sup> /superoxide                                | dioxide ( $\bullet$ 1-)/dioxidanidyl  |
| O <sub>2</sub> <sup>•+</sup> /   | dioxygen ( $\bullet$ 1+)  |
| O <sub>2</sub> <sup>2•</sup> /oxygen, usually O written O <sub>2</sub> | dioxygen (triplet)/dioxidanediyl  |
| O <sub>3</sub> /ozone  | trioxygen   |
| O <sub>3</sub> <sup>•</sup> /ozonide                                   | trioxide ( $\bullet$ 1-)/trioxidanidyl  |
| OCl <sup>•</sup> /hypochlorite   | oxidochlorate (1-)  |
| OB <sup>•</sup> /hypobromite   | oxidobromate (1-)   |
| OI <sup>•</sup> /hypoiodite  | oxidiodate (1-)   |
| OSCN <sup>•</sup> /hypothiocyanate                                     | oxidothiocyanate (1-)   |
| OCOO <sup>•</sup>  | (dioxido) oxidocarbonate ( $\bullet$ 1-)                                      |
| ONOO <sup>•</sup> /peroxynitrite                                       | oxidoperoxidonitrate (1-)/nitrosodioxidanide                                  |
| ONOOH/peroxynitrous acid   | hydrogen-oxidoperoxinitrate/nitrosodioxidane                                  |
| ONOO <sup>•</sup>  | (dioxido)oxidonitrogen ( $\bullet$ )/nitrosodioxidanyl                        |

**Table 1:** Formulae and IUPAC Recommended Names of Simple Compounds Containing C, H, and O in Free Radical Biology



| No. | Species/Abbreviation                       | Name  |
|-----|--|---|
|     | Asc; AscH <sup>-</sup> ; Asc <sup>•-</sup> | ascorbate, general; ascorbate monoanion; ascorbate radical                  |
|     | CAT  | catalase  |
|     | HRP  | peroxidase  |
|     | GPx  | glutathione peroxidase  |
|     | GR   | glutathione disulfide reductase; often referred to as glutathione reductase |
|     | Grx  | glutaredoxin  |
|     | GSH  | glutathione, not reduced glutathione (a misnomer)                           |
|     | GST  | glutathione S transferase   |
|     | LDL  | low density lipoprotein   |
|     | OH <sup>-</sup>                            | hydroxide anion, not to be confused with HO <sup>•</sup>                    |
|     | PUFA                                       | polyunsaturated fatty acid  |
|     | RO <sup>•</sup>                            | alkoxyl radical; not alkoxy   |
|     | ROO <sup>•</sup>                           | alkyl dioxygen ( $\bullet$ ), alkylidoxyl, alkylperoxyl radical; not peroxy |
|     | SOD  | superoxide dismutase  |

\*These are commonly used abbreviations. Others appear in the literature.

**Table 2:** Common Abbreviations.

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