Extended Abstract

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Pharma Europe 2020: Free radical and their role in different clinical conditions - Nusrath Siddiqui- National Institute of Technology Rourkela

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Abstract

Free radicals and related species have attracted a great deal of attention in recent years. They are mainly derived from oxygen (reactive oxygen species/ROS) and nitrogen (reactive nitrogen species/RNS), and are generated in our body by various endogenous systems, exposure to different physicochemical conditions or patho physiological states. It has been estimated that the average person has around 10000–20000 free radicals attacking each body cell each day. Some free radicals are good in that they enable your body to fight inflammation, kill bacteria, and control the tone of smooth muscles, which regulate the working of internal organs and blood vessels. On the other hand increased or uncontrolled free radical activity might combine with other factors to cause some diseases such as neurodegenerative diseases, heart disease, cancers etc. Free radicals are very unstable and react quickly with other compounds, and try to capture the needed electron to gain stability. A chain reaction thus gets started. Once the process is started, it can cascade, and finally results in the disruption of a living cell. Generally, harmful effects of reactive oxygen species on the cell are most often like damage of DNA, oxidations of polydesaturated fatty acids in lipids, oxidations of amino acids in proteins, oxidatively inactivate specific enzymes by oxidation of co-factors. It play important role in phagocytosis, apoptosis, detoxification reactions as mediator and executioner of precancerous and infectious cells. It maintains cellular homeostasis in body by participating in various signaling pathways. The balance between the production of free radicals and the antioxidant defences in the body has important health implications.Under the normal conditions the antioxidant defense system within the body can easily handle free radicals that are produced. If there are too many free radicals produced and too few antioxidants, this may cause chronic damage.

Key words: Free radicals, ROS, chain reaction.

CHARACTERISTICS OF FREE RADICALS AND OXIDANTS

ROS and RNS are the terms collectively describing free radicals and other non-radical reactive derivatives also called oxidants. Radicals are less stable than non-radical species, although their reactivity is usually stronger.

A molecule with one or more unpaired electron in its outer shell is called a free radical (1-5). Free radicals are formed from molecules via the breakage of a bond such each fragment keeps one electron, by cleavage of a radical to offer another radical and, also via redox reactions (1, 2). Free radicals include hydroxyl (OH•), superoxide (O2•–), gas (NO•), dioxide (NO2•), peroxyl (ROO•) and lipid peroxyl (LOO•). Also, peroxide (H2O2), ozone (O3), singlet oxygen (1O2), acid (HOCl), acid (HNO2), peroxynitrite (ONOO–), dinitrogen trioxide (N2O3), lipid peroxide (LOOH), aren't free radicals and usually called oxidants, but can easily cause radical reactions in living organisms. Biological free radicals are thus highly unstable molecules that have electrons available to react with various organic substrates like lipids, proteins, DNA.

GENERATION OF FREE RADICALS AND OXIDANTS

Formation of ROS and RNS can occur in the cells by two ways: enzymatic and non-enzymatic reactions. Enzymatic reactions generating free radicals include those involved within the respiratory chain, the phagocytosis, the prostaglandin synthesis and the cytochrome P450 system (1-9). For example, the superoxide radical (O2•–) is generated via several cellular oxidase systems like NADPH oxidase, xanthine oxidase, peroxidases. Once formed, it participates in several reactions yielding various ROS and RNS like peroxide, hydroxyl (OH•), peroxynitrite (ONOO–), acid (HOCl), etc. H2O2 (a non-radical) is produced by the action of several oxidase enzymes, including aminoacid oxidase and xanthine oxidase. The last one catalyses the oxidation of hypoxanthine to xanthine, and of xanthine to uric acid. Hydroxyl radical (OH•), the foremost reactive radical in vivo, is made by the reaction of O2•– with H2O2 within the presence of Fe2+ or Cu+ (catalyst). This reaction is known as the Fenton reaction (3-8). Hypochlorous acid (HOCl) is produced by the neutrophil-derived enzyme, myeloperoxidase, which oxidizes chloride ions in the presence of H2O2. Nitric oxide radical (NO•) is formed in biological tissues from the oxidation of L-arginine to citrulline by nitric oxide synthase

Free radicals are often produced from non-enzymatic reactions of oxygen with organic compounds also as those initiated by

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ionizing radiations. The nonenzymatic process also can occur during organic process (i.e. aerobic respiration) in the mitochondria .

ROS and RNS are generated from either endogenous or exogenous sources. Endogenous free radicals are generated from immune cell activation, inflammation, mental stress, excessive exercise, ischemia, infection, cancer, aging. Exogenous ROS/RNS result from air and water pollution, cigarette smoke, alcohol, heavy or transition metals (Cd, Hg, Pb, Fe, As), certain drugs (cyclosporine, tacrolimus, gentamycin, bleomycin), industrial solvents, cooking (smoked meat, used oil, fat), radiation. .After penetration into the body by different routes, these exogenous compounds are decomposed or metabolized into free radicals.

BENEFICIAL ACTIVITIES OF FREE RADICALS AND OXIDANTS

At low or moderate concentrations, ROS and RNS are necessary for the maturation process of cellular structures and may act as weapons for the host defence system . Indeed, phagocytes (neutrophils, macrophages, monocytes) release free radicals to destroy invading pathogenic microbes as part of the body's defense mechanism against disease .The importance of ROS production by the system is clearly exemplified by patients with granulomatous disease. These patients have defective membrane-bound NADPH oxidase system which makes them unable to supply the superoxide radical ($O_2^{\bullet -}$), thereby leading to multiple and protracted infection (4, 5). Other beneficial effects of ROS and RNS involve their physiological roles in the function of a number of cellular signaling systems . Their production by nonphagocytic NADPH oxidase isoforms plays a key role in the regulation of intracellular signaling cascades in various types of nonphagocytic cells including fibroblasts, endothelial cells, vascular smooth muscle cells, cardiac myocytes, and thyroid tissue. For example, nitric oxide (NO) is an intercellular messenger for modulating blood flow, thrombosis, and neural activity .NO is also important for nonspecific host defense, and for killing intracellular pathogens and tumors. Another beneficial activity of free radicals is that the induction of a mitogenic response .In brief, ROS/RNS at low or moderate levels are vital to human Beings.

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