



Role of Free Radicals in Environmental Pollution

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Abstract: Free radicals and oxidants play a twofold part as both toxic and useful compounds, as they can be either detrimental or helpful to the body. They are unbalanced, extremely reactive particles which are generated both inside and outside the body. They are designated as electron hungry molecules produced when oxygen is metabolized by the body. They travel via cells disturbing their organisation and instigating cellular damage. The changes induced by free radicals are understood to be a major cause of aging, disease development and death.

Keywords: Free radical, Environmentally Persistent Free Radicals (EPFRs), reactive oxygen species (ROS), Oxidative stress, Particulate Matter (PM).

I. Introduction

Various evidences have been seen indicating a range of toxicants, both natural and man-made, that pose significant risk to human health. Health risk ranges from a simple allergy to the development of cancers. The cost involved in the prevention and treatment of these diseases is huge and is increasing at a faster rate. People living in poor or underdeveloped countries are at much higher risk of developing these conditions than those living in developed countries due to the lack of medical treatment or the lack of understanding of health risks. On the other hand, there is a major threat from synthetic toxicants in developed countries as large number of chemicals is synthesized, more food additives/ preservative are utilized, and more petroleum based pollution is present in air [1]. An atom or group of atoms having an unpaired electron is termed as a free radical, which is very unstable. In order to stabilize itself, it takes electrons from other atoms with which they make contact with making the donor atom unstable and promoting a chain reaction. This procedure happens rapidly with a huge number of particles being influenced in a matter of nanoseconds. They are both naturally occurring and manmade. Body's immune system uses natural free radicals to eradicate viruses and bacteria; however foreign free radicals originating from toxins, tobacco smoke, or pollutants, are capable of causing cell damage and induce an inflammatory reaction causing a large range of biological damage. These free radicals have a very short life span [2].

Environmentally Persistent Free Radicals (EPFRs) are free radicals having a much longer life span thus are more persistent in the ambient environment and are also biologically active by the formation of cell damaging reactive oxygen species (ROS) [2]. EPFRs are produced in thermal processes and combustion including hazardous waste incineration and diesel combustion. These processes generate minute particles called Particulate Matter (PM). PM is categorized as ultrafine (0.1 μm and smaller), fine (0.1-2.5 μm) and coarse (2.5-10 μm). Ultrafine particles have the potential to enter in to the deepest section of the lungs (the alveolar region) and 90% of them are formed from combustion. These particles offer ideal breeding ground for EPFR formation. Initially free radicals form a loose bond with the surface of the particle. Then the loosely bonded free radical chemically binds with the metals present in the particle so as to stabilize its unpaired electron, forming the EPFR. This procedure increases the half-life of the EPFR up to few days instead of the fractions of a second of a normal free radical by reducing the metal [2].

A condition where steady-state ROS concentration chronically increases, altering cellular metabolism, its regulation and damaging cellular components is termed as oxidative stress. Release of antioxidants, expression of genes coding for antioxidant enzymes and increase in the concentration of ROS scavengers is due to activation of oxidative manifestation [3]. These reactive oxygen species (ROS) stimulate oxidative stress where the immune response of the body is accelerated [2]. Oxidative stress is an inevitable characteristic of aerobic life. It is the consequence of an imbalance between the formation of reactive oxygen species (ROS) and antioxidant reaction in living beings [4]. Reactive oxygen species are stimulated by substances like pesticides, metal ions and petroleum pollutants. Free radicals are also formed during usual cellular metabolism. The main endogenous source of ROS is mitochondrial respiration [3]. Free radicals are constantly produced throughout normal cellular metabolism and do not generally pose significant threat to human health as they are eliminated by extensive defensive mechanism like reduced glutathione, SOD and ascorbate. Due to improper removal of free radical, damage to critical lipids, proteins and DNA is induced. Such type of damage is generally not accurately repaired, so it could cause tissue/organ toxicity, and may also induce tumor formation [1]. Increase in formation of ROS can alter gene expression, cause oxidation of proteins and lipids and change cell redox status [3]. Heart and lung dysfunction as well as DNA damage is caused

when this mechanism is started by free radicals. Health risks may vary from a simple allergy to the development of various types of cancers [2].

II. Detailed pathway for the formation of free radicals

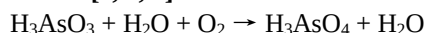
The common toxicants are halogenated compounds (carbon tetrachloride and chloroform), metals (arsenic, lead, and copper), air pollutants (sulphur dioxide, sulphur trioxide and ozone) and to various drugs (hydralazine and arsenic trioxide). These toxicants work on the theme of their biotransformation in vivo and the production of free radicals (oxidative stress) [1].

A. Haloalkanes

Reaction of chlorine with alkanes produces haloalkanes, which have been utilized in industry as cleaners, solvents, antiseptics and anesthetics. Some of them are also present in drinking water and in chlorinated swimming pools as contaminants. Generally, haloalkanes are very hepatotoxic and known human carcinogens. Carbon tetrachloride is predominantly metabolized via cytochrome P-450 (CYP2E1), but other isozymes of cytochrome P450 like CYPB1, CY2B2 and CYP3A are also capable of metabolizing carbon tetrachloride [5]. Bio-transformation of carbon tetrachloride by cytochrome P-450 results in the development of a carbon-centred free radical (trichloromethyl radical); due to its high reactivity, covalently binds to various cellular macromolecules as well as DNA and cytochrome P-450 (suicidal inactivation). Construction of DNA adducts along with carbon tetrachloride metabolites is thought to cause cancer [6]. Carbon tetrachloride radical in presence of oxygen reacts with lipids to form lipid peroxy radicals, which results in lipid peroxidation and lipid degradation (liver steatosis). Carbon tetrachloride's hepatotoxicity is both dose- and time dependent [1].

B. Inorganic arsenic

Inorganic arsenic is a pollutant in soil, water and air. In humans, it gets readily absorbed and has shown to stimulate formation of tumors in the liver, prostate, bladder and skin. It undergoes a sequence of methylation steps using S-adenosyl-L-methionine as the active methyl donor and the methylated form of arsenic is believed to be the ultimate carcinogen in vivo. A variety of mechanisms for arsenic toxicity have been projected, like inhibition of critical enzyme functions varying cellular signaling, affecting the glutathione redox system and formation of free radicals [6]. It has also been seen to produce free radicals which increase the production of 8-oxo-deoxyguanosine, a biomarker of oxidative DNA damage. Recent studies have shown that the development of oxidized DNA requires biomethylation of inorganic arsenic and is linked to an accelerated alteration to a cancer phenotype. It appears that the formation of free radicals and free radical-induced DNA oxidation plays a major role in the formation of tumors in vivo [1, 7, 8].



C. Smog

Smog is formed by the reaction of sunlight with nitrogen compounds, ozone, hydrocarbons, and various gases mainly released in automobile exhaust. It is a major health problem in the developed countries. Individuals with pre-existing heart or lung diseases are predominantly at risk from breathing this smog. Sulphur dioxide, nitric oxides and ozone are well recognized oxidants present in smog and cause cellular and organ damage by production of free radical species. Sulphur dioxide reacts with water to generate sulphite ($\cdot\text{SO}_3^-$) and sulphate ($\cdot\text{SO}_4^-$) anion radicals. Sulphite induces allergenic reactions, damaging sensitive proteins and cause broncho-constriction. Nitric oxide readily reacts with molecular oxygen to produce highly reactive peroxynitrite, which oxidizes proteins, DNA and lipids. Ozone is major pollutant of photochemical smog which is toxic in nature. Ozone causes alveolar epithelial damage, lung inflammation and cellular DNA damage due to its strong oxidizing capability. These damages are triggered by free radicals produced by the breakdown of secondary ozonides which is a reaction product of ozone with unsaturated lipids.

D. Hydrazines

Hydrazines are found in edible mushrooms and are used in medicine. They are in general toxic and are treated as environmental pollutants, which cause carcinogenicity, liver toxicity and mutagenicity. The least toxic hydrazines are hydralazine that causes lung tumors, DNA damage and critical forms of systemic lupus erythematosus. It has been proved by various studies that hydrazine derivatives produce free radicals on oxidation by cytochrome P-450, metal ions and peroxidases, causing DNA oxidation and damage [1].

III. Conclusion

Human Beings can generally handle free radicals but when antioxidants are inaccessible or if the free radical creation becomes extreme, harm may befall [8]. It is significant to note that free radicals accrue with age. The consequence of oxidative stress in the etiology of numerous chronic and deteriorating diseases advocates that

antioxidant therapy characterises a promising way for treatment [9]. In the future, a therapeutic tactic to increase the antioxidant capability of cells may be used to reinforce the long term effective treatment. Nevertheless, various queries about antioxidant supplements in disease prevention remain unresolved. More research is desirable before this supplementation could be formally suggested as a therapy.

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