IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Role of antioxidants in Oxidative stress-A Review

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Abstract

Antioxidants are compounds that prevent a molecule's oxidation when present at very low concentrations. It has the potential to nullify in living organisms the ill effects of oxidation caused by free radicals. The unpaired electrons of these free radicals are particularly reactive and neutralise human metabolism 's harmful reactions. The main enzymatic antioxidants of this protection mechanism are superoxide dismutase (SOD), glutathione peroxidase (GPX) and catalase, through which the free radicals produced during metabolic reactions are removed.

Key words: Antioxidants, SOD and GPX

Introduction

Antioxidants are a group of compounds in the body that kill single oxygen molecules, also referred to as free radicals, to protect against oxidative cell damage. They are important for good health and are naturally present in a wide range of foods and plants, including many fruits and vegetables. Vitamin C, Vitamin E, and beta-carotene are the most widely used antioxidants [1]. Free radicals are by-products of oxygen metabolism that can harm cells and are among the causes of many degenerative diseases, especially aging-related diseases. As a person ages, cell damage and extra antioxidant supplementation of the diet-rich foods can help slow the oxidative damage done to cells. Ironically, free radicals, which played a significant role in the creation of nucleic acids and other building blocks responsible for the origin and early development of protocells on Earth, have become a threat to the very nature of life during the course of evolution. Over the past two decades, awareness of the effects of free radical reactions on biological systems and safety by antioxidant defence mechanisms has increased rapidly [2].

Free Radicals

There has been a tumultuous history of the idea of free radicals in the biological system; in retrospect, that is not at all surprising because the study of radicals in organic chemistry has been clouded by controversy from the very beginning. Second, "radicals" were considered part of molecules (like the diethyl sulphide ethyl groups), and there was no difference between "free" and "bound" radicals [3]. Biomedical scientists have seen a great deal of interest in the role of free radical dependent oxygen in different diseases in recent years. In more than 100 disorders,

including arthritis and hemorrhagic shock to AIDS, "Reactive oxygen molecules" or "Free Radicals" have been implicated. This wide spectrum of diseases has increased the formation of free radicals in most, if not all, human diseases, contributing to cell and tissue injury [4-7].

Capable of independent life, free radicals contain one or more unpaired electrons, e.g. superoxide. From the exceptionally short half-lives of different species, the degree of free radical reactivity can be judged. This reactivity emerges from the unstable electronic structure of radicals; from other molecules from which they collide, they readily detach electrons and this molecule becomes a free radical capable of reacting in turn.

Superoxide RadicaI

Of all oxygen dependent molecules, superoxide is the best known free radical because it is the first intermediate in the sequential univalent oxygen reduction that leads to the formation of H_2O. Radical superoxide is unusual in that it can contribute to the formation of many other reactive species, including free radical hydroxyl [8-11]. Superoxide radical also interacts with H2O2 to generate the singlet oxygen molecule, another reactive oxygen species, although not a free radical. The enzyme SOD has three variants. The predominant copper-zinc containing enzymes are found in the cytoplasm while manganese SOD is located in the mitochondria.

Superoxide dismutase, catalase, and glutathione peroxidase are antioxidant enzymes that not only play an important but indispensable role in protecting biological systems from free radical attacks against antioxidants. It is normal to have SOD enzyme deficiency. Therefore, for cellular health, the enzyme is indispensable, protecting body cells from excessive oxygen radicals, free radicals and other harmful agents that promote ageing or cell death. With age, the levels of SODs decrease, while free radical formation increases. Proper daily SOD supplementation has been suggested to protect the immune system and substantially minimise one's disease chances and eventually slow down the ageing process.

Manganese superoxide dismutase

Mn-SOD is a homotetramer (96 kDa) containing one atom of manganese per subunit that cycles during the two-step superoxide dismutation from Mn (III) to Mn (II) and back to Mn (III). A major source of oxygen radicals is the respiratory chain in mitochondria. MnSOD is a key antioxidant enzyme with nuclear encoding that acts to eliminate these superoxide radicals

Copper, zinc superoxide dismutase

Other groups of copper, zinc superoxide dismutase Cu, Zn-SOD (SOD-1) are Throughout evolution, the enzyme preserved normally has two identical subunits of approximately 32 kDa, each containing a metal cluster, the active site consisting of a copper and a zinc atom bridged by a typical ligand: His 61

Hydroxyl Radicals

In biological environments, the hydroxyl radical is known to be potentially the most active oxidant. Because of its extremely brief hall life, however. Highly reactive hydroxyl radicals quickly react with a number of molecules, such as those in organic lipids, by removing or adding hydrogen to unsaturated bonds. Diffusion potential is limited to just around two molecular diameters before reacting. The biological importance of hydroxyl radical as oxidant was first observed during generation by x-ray irradiation [12-13].

Nickel superoxide dismutase

Ni-SOD was isolated from Streptomyces sp. cytosolic fraction. It is made up of four identical 13.4 kDa subunits, stable at pH 4.0-8.0 and up to 70 degrees Celsius. It is inhibited by cyanide and H2O2, but azide inhibits it very little. The composition of amino acids ranges from iron, manganese and zinc-copper SODs. The apoenzyme, which lacked nickel, had no ability to mediate the conversion of hydrogen peroxide to superoxide anion, strongly suggesting that Ni plays important activity.

Catalase

Catalase (EC 1.11.1.6) is a tetrameric haeminenzyme consisting of 4 identical subunits of 60 kDa arranged tetrahedrally. Consequently, it comprises 4 classes of ferriprotoporphyrin per molecule and has a molecular mass of approximately 240 kDa. One of the most effective enzymes known is catalase. It is so effective that at any concentration, it can not be saturated by H_2O_2. To form water and molecular oxygen, CAT reacts with H_2O_2 [14]. CAT is a natural antioxidant enzyme present in almost all oxygen-using living tissues. The enzyme uses either iron or manganese as a cofactor and catalyses water and molecular oxygen to degrade or decrease hydrogen peroxide (H2O2), thereby completing the SOD-imitated detoxification method. It is abundant in cells, where it constantly scouts for molecules of hydrogen peroxide. CAT is highly effective; it can break down millions of molecules of hydrogen peroxide in one second. The enzyme is predominantly found in peroxisomes, but is absent from mammalian cell mitochondria. Mitochondria found in the heart of the rat are the only exception. This means that another enzyme known as glutathione peroxidase in mammalian cell mitochondria performs the breakdown of hydrogen peroxide into water and oxygen [17].

In an aerobic organism, H_2O_2 is enzymically catabolized by catalase and other peroxidases. H_2O_2, detoxified by CAT and GPX, is used in animals. Catalase protects cells from the peroxide of hydrogen formed within them. Although CAT is not essential under normal conditions for some types of cells, it plays an important role in the acquisition of oxidative stress tolerance in the adaptive response of cells.

CAT also reacts successfully with hydrogen donors with peroxidase activity, such as methanol, ethanol, formic acid, or phenols. CAT operations take place in two stages. A hydrogen peroxide molecule oxidises the heme into an oxyferryl species. If one oxidation equivalent is eliminated from iron and one from the porphyrin ring, a porphyrin cation radical is produced. A second molecule of hydrogen peroxide serves as a reduction agent to regenerate the enzyme in the resting state, creating an oxygen and water.

However, hydrogen peroxide helps to influence certain physiological processes at low levels, such as signalling in cell proliferation, cell death, metabolism of carbohydrates, mitochondrial function, and platelet activation and maintenance of normal thiol redox balance.

Glutathione peroxidase

As the most relevant example of glutathione peroxidase (EC1.11.1.19), selenium-containing peroxidases catalyse the reduction of a number of GSH-using hydroperoxides (ROOH and H2O2) protect mammalian cells against oxidative damage. In mammals, there are at least five GPX isoenzymes found. While their expression is universal, each isoform 's levels differ depending on the type of tissue.

Fatty acid hydroperoxides and H2O2 are reduced by cytosolic and mitochondrial glutathione peroxidase (cGPX or GPX1) at the expense of glutathione. In most tissues, GPX1 and the phospholipid hydroperoxide glutathione peroxidase GPX4 (or PHGPX) are present. In both the cytosol and the membrane fraction, GPX4 is found. The

phospholipid hydroperoxides, fatty acid hydroperoxides, and cholesterol hydroperoxides formed by peroxidized membranes and oxidised lipoproteins can be reduced directly by PHGPX [15-16].

Conclusion

Superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX) activities constitute a first-line antioxidant defence system which plays a key and fundamental role in biological systems' overall defence mechanisms and strategies.

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