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Potential applications of antioxidants - A Review

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Abstract

Antioxidants have attracted biomedical researchers due to the importance of this chemicals in preventing free radicals from causing biological cell damage which might cause cancer. Antioxidants biomedical compounds represent one of the most potential Martials that could be used to heal illness such as cancer. This short review will try to cover antioxidants enzymes types and its resource. Additionally, this review will explain briefly the uses of antioxidants in food preservative and industry which shows how important of these compounds in human been life.
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1. Introduction

Antioxidants are chemicals that interact with and neutralize free radicals, thus preventing them from causing damage. Antioxidants are also known as "free radical scavengers". [1]
Free radicals are highly reactive chemicals that have the potential to harm biological cells. They are created when an atom or a molecule (a chemical that has two or more atoms) either gains or loses an electron (a small negatively charged particle found in atoms). Free radicals are formed naturally in the body and play an important role in many normal cellular processes [2].
Production of ROS in mitochondria which is occurs by Electron transport chain produces superoxide anion in mitochondria by the reduction of molecular oxygen. ROS are generated by mitochondria, via the release of electrons from the electron transport chain and the reduction of oxygen molecules into superoxides (O_2-). Superoxides, through the reaction catalyzed by superoxide dismutase (SOD), are transformed into the much less reactive hydrogen peroxide moiety (H_2O_2). However, when hydrogen peroxide interacts with ions of transition metals such as iron and copper, the most reactive ROS, hydroxyl radicals (OH-) are formed (Fenton's reaction) [3].
Oxidative stress reflects an imbalance between the systemic manifestation of reactive oxygen species and a biological system's ability to readily detoxify the reactive intermediates or to repair the resulting damage. Oxidative stress is thought to contribute to the development of a wide range of diseases including Alzheimer's disease,[4] Parkinson's disease,[5] the pathologies caused by diabetes.[6]
Oxidative damage in DNA can cause cancer. Several antioxidant enzymes protect DNA from oxidative stress. It has been proposed that polymorphisms (alternative phenotypes, in the population of a species) in these enzymes are associated with DNA damage and subsequently the individual's risk of cancer susceptibility.[7]
Antioxidants are broadly divided into two; depends on its solubility [8]:

1. Hydrophilic antioxidants: Antioxidants react with oxidants in the cell cytoplasm and the blood plasma. For example: Ascorbic acid, Glutathione and Uric acid.
2. Hydrophobic antioxidants: Protect cell membranes from lipid peroxidation. For example: Carotenes, α-tocopherol and Ubiquinol. These compounds may be synthesized in the body or obtained from the diet.

1.1 Antioxidant enzyme

Antioxidant enzymes are the main line of defense against free radicals. Uncontrolled generation ROS are involved in a number of human disease states, including diabetes and cancer due to disturbance in cellular and molecular processes including cell growth, differentiation and proliferation. When cells are exposed to oxidative stress a defense system endorses the expression and regulation of number of antioxidant

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enzymes as a defense mechanism to protect them from the damage induced by free radicals.

1.2 Catalase

Catalase is a common enzyme found in nearly all living organisms exposed to oxygen (such as bacteria, plants, and animals) figure (1). It catalyzes the decomposition of hydrogen peroxide to water and oxygen.[9] It is a very important enzyme in protecting the cell from oxidative damage by reactive oxygen species (ROS).
Catalase is a tetramer of four polypeptide chains each over 50 amino acids long [10]. It contains four porphyrin heme (iron) groups that allow the enzyme to react with the hydrogen peroxide. the reaction is believed to occur in two stages

H_2O_2 + Fe(III)-E → H_2O + O=Fe(IV)-E(.+)
H_2O_2 + O=Fe(IV)-E(.+) → H_2O + Fe(III)-E + O_2[16]

Catalase is used in the food industry for removing hydrogen peroxide from milk prior to cheese production.[11] Another use is in food wrappers where it prevents food from oxidizing [12]. Catalase is also used in the textile industry, removing hydrogen peroxide from fabrics to make sure the material is peroxide-free [13].

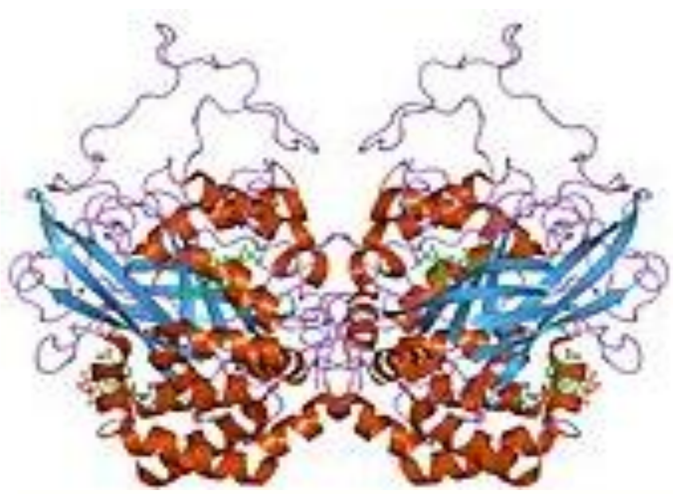

Figure 1: Catalase structure.

1.3 Glutathione

Glutathione (GSH) is an important antioxidant in plants, animals, fungi, and some bacteria and archaea, figure (2). Glutathione is capable of preventing damage to important cellular components caused by reactive oxygen species such as free radicals peroxides, lipid peroxides, and heavy metals [14].
The glutathione is considered the master antioxidant (about 5,000 times stronger than any other antioxidant) because it has the most "extra" electrons to share. For example:

- Vitamin E has 3 extra electrons to share.
- Vitamin C has 5 extra electrons to share.
- SOD has 10,000 extra electrons to share.
- Glutathione (GSH) has 1million extra electron to share.

It is a tripeptide with a gamma peptide linkage between the carboxyl group of the glutamate side chain and the amine group of cysteine, and the carboxyl group of cysteine is attached by normal peptide linkage to a glycine. glutathione can be reduced back by glutathione reductase, using NADPH as an electron donor.[15] The ratio of reduced glutathione to oxidized glutathione within cells is often used as a measure of cellular oxidative stress [16]

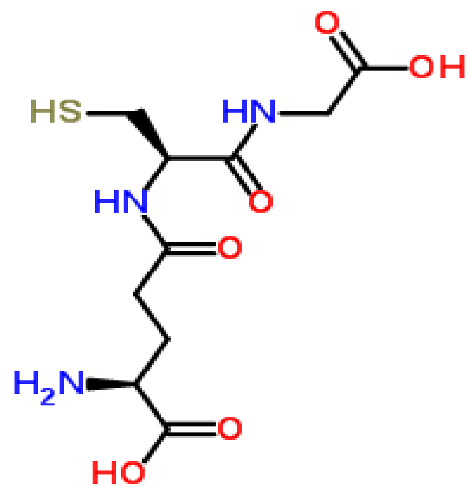

Figure 2: Glutathione structure.

Glutathione has multiple functions

- It maintains levels of reduced glutraedoxin and glutathione peroxidase [17].
- It is one of the major endogenous antioxidants produced by the cells, participating directly in the neutralization of free radicals and reactive oxygen compounds, as well as maintaining exogenous antioxidants such as vitamins C and E in their reduced (active) forms.[18]
- Regulation of the nitric oxide cycle is critical for life, but can be problematic if unregulated.[19]
- It has roles in progression of the cell cycle, including cell death [16].

1.4 Superoxide dismutase

Superoxide dismutase has been found in almost all organisms living in the presence of oxygen, including some anaerobic bacteria, supporting the notion that superoxide is a key and general component of oxidative stress. Superoxide dismutase (SOD) is an enzyme that facilitates the breakdown of the toxic superoxide radical into either ordinary molecular oxygen (O2) or hydrogen peroxide (H_2O_2).
The general form, applicable to all the different metal-coordinated forms of SOD, can be written as follows:

- M(n+1)+-SOD + O_2^- → Mn+-SOD + O_2
- Mn+-SOD + O_2^- + 2H+ → M(n+1)+-SOD + H_2O_2

Where M = Cu (n=1); Mn (n=2); Fe (n=2); Ni (n=2).
There are three major families of superoxide dismutase, depending on the protein fold and the metal cofactor.

1.4.1 Copper and zinc-SOD

Most commonly used by eukaryotes, including humans. The cytosols of virtually all eukaryotic cells contain an SOD enzyme with copper and zinc (Cu-Zn-SOD), figure (3). The bovine Cu-Zn enzyme is a homodimer of molecular weight 32,500. It was the first SOD whose atomic-detail crystal structure was solved, in 1975.[8] It is an 8-stranded beta-barrel, with the active site held between the barrel and two surface loops. The two subunits are tightly joined back-to-back, mostly by hydrophobic and some electrostatic interactions. The ligands of the copper and zinc are six histidine and one aspartate side-chains; one histidine is bound between the two metals [20].

Figure 3: Cu-Zn –SOD structure

1.4.2 Iron or manganese

Used by prokaryotes and protists, and in mitochondria and chloroplasts, Iron– Many bacteria contain a form of the enzyme with iron (Fe-SOD); some bacteria contain Fe-SOD, others Mn-SOD, and some (such as E. coli) contain both, figure (4). Fe-SOD can also be found in the chloroplasts of plants. The 3D structures of the homologous Mn and Fe-SOD have the same arrangement of alpha-helices, and their active sites contain the same type and arrangement of amino acid side-chains. They are usually dimers, but occasionally tetramers.

1.4.3 Manganese

Nearly all mitochondria, and many bacteria, contain a form with manganese (Mn-SOD): For example, the Mn-SOD found in human mitochondria. The ligands of the manganese ions are 3 histidine side-chains, an aspartate side-chain and a water molecule or hydroxy ligand, depending on the Mn oxidation state (respectively II and III [21].

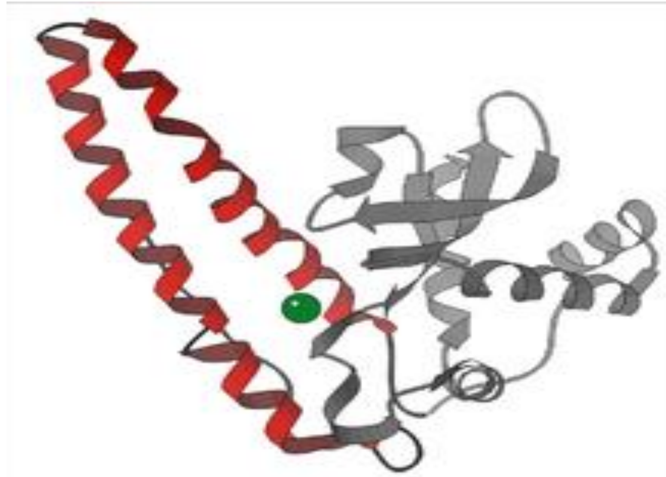

Figure 4: Fe-Mn-SOD structure.

1.4.4 Nickel

SOD was first isolated in 1996 from *Streptomyces* bacteria and is primarily found in prokaryotic organisms.[2] It has since been observed in cyanobacteria and a number of other aquatic microbes, figure (5).This has a hexameric structure built from right-handed 4-helix bundles, and each containing N-terminal hooks that chelate a Ni ion.it provides most of the interactions critical for metal binding and catalysis and is, therefore, a likely diagnostic of NiSOD [22].

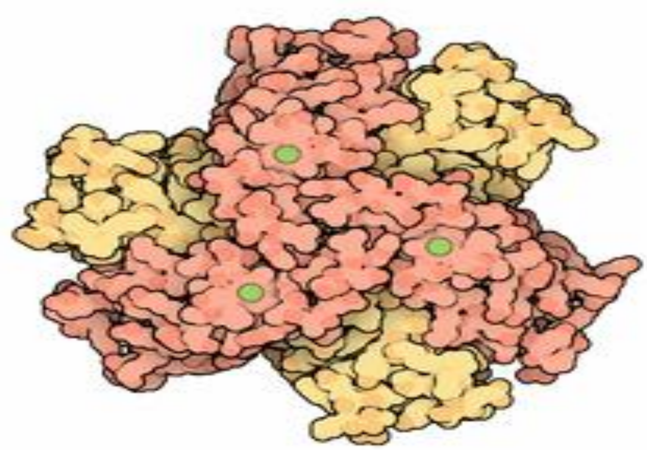

Figure 5: Ni-SOD structure

Antioxidant in food body produces some antioxidants, get them in certain foods and vitamins [23]. Common antioxidants include

- Vitamin A: is in milk, butter, eggs, and liver.
- Vitamin C: is in most fruits and vegetables. Eat fruits such as berries, oranges, kiwis, cantaloupes, and papayas. Eat vegetables such as broccoli, bell peppers, tomatoes, cauliflower, Brussels sprouts, and kale.
- Vitamin E: is in some nuts and seeds. For example, almonds, sunflower seeds, hazelnuts, and peanuts. You can find it in green leafy vegetables such as spinach and kale. You also can find it in soybean, sunflower, corn, and canola oils.
- Beta-carotene: is in brightly colored fruits and vegetables. Eat fruits such as peaches, apricots, papayas, mangoes, and cantaloupes. Eat vegetables such as carrots, peas, broccoli, squash, and sweet potatoes. It also is in some leafy green vegetables such as beet greens, spinach, and kale.
- Lycopene: is in pink and red fruits and vegetables. This includes pink grapefruits, watermelon, apricots, and tomatoes.
- Lutein: is in green leafy vegetables such as spinach, collards, and kale. You also can find it in broccoli, corn, peas, papayas, and oranges.
- Selenium: is in pasta, bread, and grains, including corn, wheat, and rice.

Uses of antioxidant

- Food preservatives: Antioxidants are used as food additives to help guard against food deterioration. Exposure to oxygen and sunlight are the two main factors in the oxidation of food, so food is preserved by keeping in the dark and sealing it in containers or even coating it in wax, as with cucumbers. These preservatives include natural antioxidants such as ascorbic acid (E300) and tocopherols (E306), as well as synthetic antioxidants such as propyl gallate (E310), tertiary butylhydroquinone , butylated hydroxyanisole E320) and butylated hydroxytoluene (E321).[24]

Industrial uses

Several industrial products contain antioxidants. Some of these include:

- Antioxidants are added to fuels and lubricants to prevent oxidation, and in gasolines to prevent the polymerization - this polymerization of gasoline leads to residues that can damage the engines.
- Antioxidants are added to polymers such as rubbers, plastics and adhesives to prevent their oxidative damage and loss of strength and flexibility. Polymers with double bonds are especially vulnerable and benefit with this addition.

  The breakdown leads to ozonolysis or cracking. Ozone cracking is especially damaging to elastomers such as natural rubber, polybutadiene and other double-bonded rubbers [25].

2. Conclusion

In conclusion antioxidants play a very important role in human life. The study of these compounds might open a wide range of scoops that can be used to open many avenues in drugs and food industry. This short review might be used by the researchers in this field to have an initiative idea of antioxidants enzymes types and resources. Which might lead to new discovery of how it can be used to benefit the human been.

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