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# Primary and Secondary Antioxidants

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***Abstract:*** **The process of removing hydrogen or electrons from a substance is called oxidation. Different kinds of free radicals are generated as a result of oxidation reactions which trigger various chain reactions and have a tendency to cause damage to the system. These chain reactions are stopped by antioxidants which quench the free radical intermediates thereby retarding the oxidation reactions. The antioxidants are agents which aid in the *reduction.***

***Keywords:*** **Primary enzyme antioxidants, Secondary Antioxidants , Catalase , Glutathione.**

## 1. INTRODUCTION

The redox reaction is shown in figure 1.

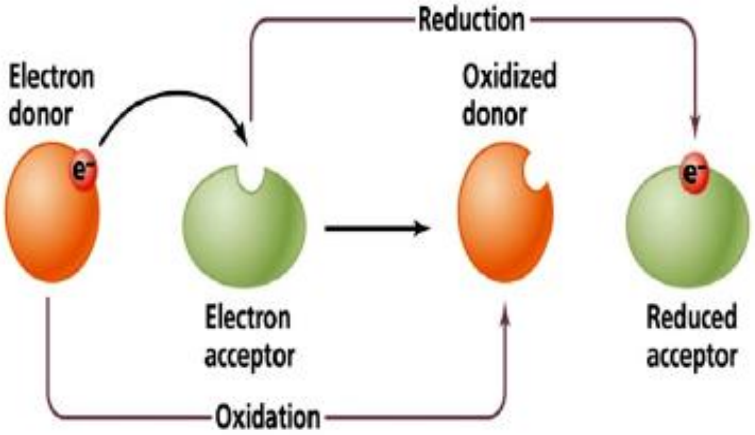


**Figure 1: Schematic representation of redox reaction**

## 2. CLASSIFICATION OF ANTIOXIDANTS

The antioxidants are broadly categorised into two types, based on their mode of action as enzymatic and non-enzymatic antioxidants. The enzymatic antioxidants are further classified as primary enzymatic defences or chain breaking antioxidants while the second type is called the secondary enzymatic defences or preventive antioxidants. The free radicals are degraded completely by the enzymatic antioxidants to hydrogen peroxide and finally to water, which act in the presence of various cofactors like iron, zinc, copper and manganese. The primary defence comprises of three significant enzymes namely catalase, glutathione peroxidase and superoxide dismutase. The peroxides are reduced to selenoles by donation of two electrons by glutathione peroxidase and the use of peroxides for the Fenton reaction is also prevented. The function of catalase is to transform hydrogen peroxide to molecular oxygen and water. Superoxide dismutase transforms superoxide anions into hydrogen peroxides.

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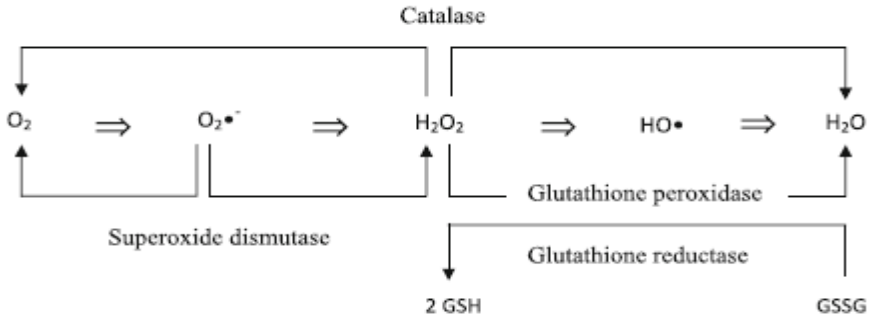


**Figure 2: The mechanism of enzymatic antioxidants**

The two secondary enzymatic antioxidants are glucose-6-phosphate dehydrogenase and glutathione reductase. The nicotinamide adenine dinucleotide phosphate (NADP) is a coenzyme used in the anabolic reactions which is regenerated by glucose-6-phosphate thereby generating a reducing atmosphere. The glutathione which acts as the antioxidant is reduced by the secondary enzyme defence- glutathione reductase.

The size of the antioxidants is another basis for their classification and is categorised as large molecule antioxidants and small molecule antioxidants. The primary enzymes belong to the class of large molecule antioxidants. The reactive oxygen species are eliminated by a process called radical scavenging by small molecule antioxidants like glutathione, vitamin C, carotenoids and vitamin E.

**Primary enzyme antioxidants**

**a. Catalase**

A group of enzymes containing peroxidases and catalases are termed as hydroperoxidases, which are responsible for modulating the levels of peroxides in the tissues. Additionally, the peroxidic bond is broken by the enzyme oxidoreductase in a heterolytic manner. The oxidation of hydrogen peroxide is catalysed by enzyme catalase through disproportion reaction to generate oxygen. The enzyme has three significant domains according to its structural conformation. It has a reduced NADPH moiety which is attached to the NADPH binding domain and a heme molecule at the active site. The third domain is the complex secondary structure which is formed during tetramerization by the coiling of the long peptide loops. The enzyme catalase present in the mammals is a homotetramer where the single monomers of protein have no activity of degrading the peroxide. The catalytic activity of the enzyme is to convert hydrogen peroxide to water and oxygen. This enzyme belongs to Fe-protoporphyrin IX which has a protein comprising of peroxidases, cytochromes and globins. One molecule of hydrogen peroxide is converted to water by the catalase heme $Fe^{3+}$ thus forming a $Fe^{4+}O$ (oxy ferryl species) along with a porphyrin cation radical. The second hydrogen peroxide molecule is oxidised to oxygen and another molecule of water by the reaction intermediate.

Its peroxidatic activity is to oxidise alcohols having low molecular weight in the presence of minimum concentration of hydrogen peroxide. This activity takes place when the amount of hydrogen peroxide for completing the catalytic cycle is not sufficient. The intermediate formed during the catalytic cycle oxidises the alcohol to aldehyde and water. The crystal structure of heme indicated that the active centre of the catalase is buried within the protein. The most convenient path lies perpendicular to the plain of the heme for the hydrogen peroxide molecule to reach the active site.

**b. Glutathione peroxidase**

Glutathione belongs to the class of tripeptide which is found in microorganisms and plants as well as animal tissues. The reduction of organic hydroperoxide and hydrogen peroxide by glutathione is catalysed by glutathione peroxidase. The enzyme glutathione peroxidase prevents oxidative damage in the body. There are two types of glutathione peroxidase in human tissues. One type of the enzyme contains selenium in its active site while the other is cationic isoenzymes of glutathione S-transferases.

The glutathione S-transferase belong to the family of multifunctional detoxification enzymes. The conjugation of the glutathione with a wide range of carcinogens and electrophilic toxins are catalysed by this enzyme. A huge number of isoenzymes are responsible for the activity of this enzyme.

**c. Superoxide dismutase**

There are three kinds of superoxide dismutase with three different kinds of protein folds. They combine with three different kinds of metals to form Cu,Zn SOD, MNSOD/FeSOD and NiSOD. The disproportionation reaction takes place

in the case of all three SOD, where reduction and oxidation of the metal ion take place alternately. The rate of SOD catalysis is similar to the limits of diffusion. The arrangement within the protein chain of all the three SOD is varied. The redox potential of the metal ion is changed conveniently for proper disproportionation of the superoxide. These three SOD are a source for proton and the enzymatic activity is controlled by inhibition of the product.

**Secondary enzyme antioxidants**

**a. Glutathione reductase**

Glutathione reductase enzyme falls into the class of secondary enzymatic antioxidants. The reduction of oxidised glutathione is catalysed by this enzyme in presence of NADPH to form reduced glutathione. It maintains a high ratio between the reduced glutathione and oxidised glutathione and intracellular oxidised glutathione pool. This enzyme is present at high level in patients suffering from cancer.

**b. Glucose-6-phosphate dehydrogenase**

The initial step of the pentose phosphate route is catalysed by glucose-6-phosphate dehydrogenase. The reaction proceeds to generate NADPH and defends the red blood cells from oxidative damage. This is the only route for the generation of NADPH in the red blood cells. NADPH is responsible for maintaining the redox potential in the cells and is also a cofactor for enzyme glutathione reductase. The elasticity and normal structure of the red blood cells is maintained by oxidised glutathione. Additionally, the iron is maintained in the ferrous state which is necessary for carrying oxygen. The hydrogen peroxide present in the red blood cells are removed by glutathione peroxidase with the help of reduced glutathione. The reaction oxidises the reduced glutathione which is again regenerated by glutathione reductase with the help of NADPH. In this process, NADPH gets oxidised which is again reduced by glucose-6-phosphate dehydrogenase.

## 3. CONCLUSION

Antioxidants are substances that scavenge the free radicals produced in the body during various oxidation reactions. They protect the body from the reactive free radicals which are capable of causing damage to the body. The primary enzymatic antioxidants comprise of glutathione peroxidase, catalase and superoxide dismutase. These enzymes have the primary structure of proteins where they are long chain polymers of different amino acids. The amino acids are connected to each other by peptide bonds to form the polymer. The secondary antioxidant enzyme comprises of glutathione reductase and glucose-6-phosphate dehydrogenase. these compounds behave as antioxidants with the aid of NADPH. The structure of these enzymes is mainly formed by secondary bonds like intramolecular hydrogen bonding, disulphide linkages and van der Waals bond. The straight chain formed due to the primary structure gets coiled due to the presence of these bonding interactions within the chain. The active site of the enzyme remains buried within the coil.

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