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What are the molecular mechanisms of oxidant and antioxidant compounds?

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Core tip

The antioxidant compounds react in one-electron reactions with reactive oxygen species (ROX) and reactive nitrogen species (RNS) and prevent oxidative damage.

Introduction

In the biology system, reactive oxygen species (ROS) and reactive nitrogen species (RNS) are produced during cellular metabolism which have important roles in apoptosis, cell signaling, gene expression and ion transportation (1,2). On the other hand, excessive amounts of ROS and RNS can attack many molecules such as protein, unsaturated fatty acids, RNA and DNA that named oxidative stress. During times of environmental stress and cell dysfunction, ROS and RNS levels can increase and cause significant cellular damage. Oxidative stress increase risk for many diseases such as inflammatory disease, cardiovascular disease, cancer, diabetes, Alzheimer disease, cataracts, autism and aging (2,3).

The generation of ROS initiates with uptake of oxygen, activation of NADPH oxidase, and the production of the superoxide anion radical ($O_2^{\cdot-}$). The reactive species can also be generated by the myeloperoxidase (MPO) that is present in the neutrophil cytoplasmic granules. RNS like nitric oxide ($NO^{\cdot}$) is produced by the enzyme nitric oxide synthase. The inducible nitric oxide synthase (iNOS) is capable of constantly producing large amount of $NO^{\cdot}$, which acts as an $O_2^{\cdot}$ quencher. Then, $NO^{\cdot}$ reacts to $O_2^{\cdot}$ and produces peroxynitrite ($ONOO^-$) which is a very strong oxidant; hence, each can modulate the effects of other (4). Superoxide ($O_2^{\cdot-}$), a main cellular free radical, involves in a large number of deleterious changes that often associated with an increase in peroxidative processes. Although $O2^{\cdot-}$ itself is not so reactive to biomolecules, it can help in generation of more powerful $HO^{\cdot}$ and $ONOO^-$ radicals. Therefore, neither $NO^{\cdot}$ nor $O_2^{\cdot-}$ is a strong oxidant radicals, peroxynitrite is a potent and versatile oxidant that can attack a wide range of biological targets (4).

$NO^{\cdot} + O_2^{\cdot-} \rightarrow ONOO^-$

Peroxynitrite can react with the aromatic amino acid residues in the enzyme and biological compounds resulting in the nitration of the aromatic amino acids and enzyme inactivation.

However, cells are normally able to defend themselves against ROS or RNS damage by antioxidant compounds. Antioxidants can be categorized based on their activity including enzymatic and non-enzymatic antioxidants. The antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GSHPx) in presence of their cofactors such as copper, zinc, manganese, andiron convert oxidative products to hydrogenperoxide (H_2O_2) and then to water (5,6). Non-enzymatic antioxidants such as vitamin C, vitamin E, plant polyphenol, carotenoids and glutathione work by interrupting free radical chain reactions. The antioxidant enzymes can diminish the levels of lipid hydroperoxide and H_2O_2; thus they are essential in the prevention of lipid peroxidation and maintaining the structure and function of cell membranes. SOD enzymes located in the cytosol and mitochondria, change $O_2^{\cdot-}$ into oxygen and H_2O_2 in presence of the metal ion cofactors such as copper, zinc, or manganese. The enzyme CAT present in the peroxisome, changes H_2O_2 to oxygen and water. The enzyme GSHPx located both in the cytoplasm and extracellularly in almost every human tissue converts the H_2O_2 in to the water. The biochemical function of GSHPx is to reduce lipid hydroperoxides to their corresponding alcohols and to reduce free

hydrogen peroxide to water.

The non-enzymatic antioxidants are categorized, the natural antioxidants and the synthetic antioxidants. Vitamin E (a-tocopherol), an efficient lipid soluble antioxidant, acts as a 'chain breaker' during lipid peroxidation in cell membranes and low-density lipoprotein (LDL) (7). Its activity is to interrupt lipid peroxyl radicals (LOO^{o}) and to terminate the lipid peroxidation chain reactions.

LOO^{o} + a -tocopherol–OH → LOOH + a-tocopherol–O^{o}

Then tocopheroxyl radical, fairly stable in normal circumstances, acts to initiate lipid peroxidation itself, which is an essential criterion of a good antioxidant. Vitamin C (ascorbic acid), a water-soluble free radical scavenger, regenerates vitamin E in cell membranes in combination with glutathione or compounds capable of donating reducing equivalents. Then, vitamin C alters to the ascorbate radical by providing an electron to the lipid radical in order to terminate the lipid peroxidation chain reaction. Finally, the pairs of ascorbate radicals react quickly to produce one molecule of ascorbate and one molecule of dehydroascorbate that the dehydroascorbate does not have any antioxidant capacity. Therefore, the dehydroascorbate is converted back into the ascorbate by the addition of two electrons with the help oxidoreductase (4). So, it is important to know molecular pathway function of antioxidant/oxidant compounds.

Conclusion

ROS and RNS, the radical derivatives of oxygen or nitrogen are the most important free radical in biological systems that induce oxidative stress. On the other hand, antioxidants may directly react with the reactive radicals then destroy them by accepting or donating electron(s) to eliminate the unpaired condition of the radical.

Thus, understanding the reaction molecular mechanism of oxidants/antioxidants is crucial to find an appropriate treatment modality.

Authors' contribution

EA and HN wrote the manuscript equally.

Conflicts of interest

The authors declared no competing interests.

Ethical considerations

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