The Role of Antioxidants in Human Health: Biochemical Insights

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ABSTRACT

Sies introduced the "oxidative stress," in 1980 by highlighting the imbalance between prooxidants and antioxidants that contribute to chronic diseases. However, oxygen is essential for life involved in numerous biological processes and can cause cellular damage through oxidative events. Mitochondria generates free radicals like reactive oxygen species (ROS) and reactive nitrogen species (RNS) in their energy cycle which play dual roles in cellular functions. Antioxidants are present in both endogenous and exogenous forms and are vital in maintaining health by counteracting free radical damage. Carotenoids are a group of dietary antioxidants that are crucial for human health. Free radicals are produced through normal oxygen utilization and various environmental factors that may be beneficial and harmful. Therapeutically antioxidants reduce oxidative stress by neutralizing free radicals like enzymatic (e.g., superoxide dismutase) and non-enzymatic antioxidants (e.g., vitamins) play critical roles. Dietary antioxidants obtained from plant compounds and metal ion complexes bolster antioxidant defence and are essential for maintaining cellular homeostasis and reducing oxidative challenges.

1. Introduction:

Oxygen contains oxidative properties that make it essential for life and significantly influence the various biological processes. However, oxygen through oxidative events can cause cellular damage. However, in mitochondria cells produce energy and free radicals as by-products during ATP (adenosine triphosphate) production, including reactive oxygen species (ROS) and reactive nitrogen species (RNS). These both toxic and beneficial roles in the body and maintaining a balance between these effects is crucial. These reactive species support cellular redox signaling and immune function at low or moderate levels and at high levels, they produce oxidative stress that damages cell functions and structures. The toxic effects of oxygen were not fully understood before Gershman's free radical theory. Gershman and Gilbert suggested the harmful effects of ionizing radiation during World War II and a study on free radical biochemistry emerged. Gershman observed that oxygen toxicity is due to partially reduced forms of oxygen, and in the same year, Commoner, Townsend, and Pake identified free radicals in biological materials through electron paramagnetic resonance (EPR). Later, the aging process was linked with free radicals by Denham Harman (1956). These innovative studies show extensive research into free radicals in biological systems [2].

Now, oxidative stress from free radicals is recognized as a key mechanism in many disorders including cardiovascular, neurological, and others. Approximately 5% of inhaled oxygen is transformed into harmful reactive oxygen species (ROS) like superoxide, hydroxyl radicals, and hydrogen peroxide. However, the increase in the risk of oxidative stress-related diseases is the result of modern lifestyle factors, including unhealthy habits, chemical exposure, pollution, smoking, drugs, illness, and stress. These diseases' occurrence can be reduced by lowering free radical generation and improving antioxidant status. Recently, many antioxidants have been utilized therapeutically to treat diseases associated with oxidative stress. Few studies display, that the disease risk increased due to low absorption of antioxidants and low blood levels. For instance, the risk of cancer may be doubled through insufficient intake of fruits and vegetables. However, health can be protected from oxidative stress through a diet rich in antioxidants and natural antioxidant supplements are increasingly recognized as essential [1].

Table 1. Types of Antioxidants

Endogenous Antioxidants	Exogenous Antioxidants
Enzymatic	**Nutritional**
Catalase	Carotenoids
Superoxide dismutase	Vitamin C
Glutathione	Vitamin E
Glutamyl trans peptidase	Phytochemicals
Non-Enzymatic	**Supplementations**
Uric acid	β-carotene
Ubiquinone	Coenzyme Q10
Tocopherol	Lipoic acid
Retinol	Glutathione
Glutathione	Phytoestrogens
Melatonin	Polyphenol
Nuclear factor erythroid 2-related factor 2 (NRF2)	
Mineral elements	
Selenium	
Zinc	
Manganese	
Copper	

2. Revisiting Carotenoids as dietary Antioxidants for Health and Disease Prevention

"Carotenoids" are yellow, red, and orange pigments with long-chain hydrocarbons and conjugated double bonds. Nature carotenoids are over 1100 and mostly as C-40 tetraterpenoid metabolites in plants, though C-45 and bacteria contain C-50 carotenoids. However, these are classified into hydrocarbon carotenoids (carotenes and lycopene) and oxygenated carotenoids (xanthophylls) that depend upon their oxygen content. Furthermore, animals cannot prepare carotenoids that make them exogenous nutrients. Moreover, birds and fish collect carotenoids through oxidative modification after ingestion. On the other side, mammals like humans exhibit different patterns of absorption and accumulation. Humans are unique indiscriminate accumulators that absorb over 40 dietary carotenoids. Subsequently, α-carotene, β-carotene, lycopene, β-cryptoxanthin, lutein, and zeaxanthin are six major carotenoids, that accumulate in human plasma and tissues. In addition, carrots, tomatoes, leafy greens, and tropical fruits are included in the major dietary sources [8].

Dietary carotenoid's primary function in humans is provitamin A activity. α-Carotene, β-carotene, and β-cryptoxanthin convert to retinal in the small intestine and the other carotenoids remain unchanged when absorbed. Likewise, carotenoids offer many health benefits including immune support, gap junction formation, and adipocyte function, and their blood levels reflect fruit and vegetable intake. The carotenoids gained attention for their antioxidant properties with vitamins C and A. Later, this concept was refined to include the disruption of redox signaling. However, it was identified that the redox signaling was affected by new metabolites and a new interest in carotenoids' antioxidant role in human health [3].

3. The Biochemical Dynamics of Free Radicals and Antioxidants

The normal utilization of oxygen by the body results in the continuous production of free radicals. Oxygen is an essential element for life and is employed by cells to generate energy and lead to the generation of free radicals by the mitochondria. They produce by-products that are reactive oxygen species (ROS) and reactive nitrogen species (RNS) that stem from cellular redox processes. A particular affinity is offered to free radicals for lipids, proteins, carbohydrates, and nucleic acids. The triphenyl methyl radical was discovered by Gomberg in 1900 and was the first organic free radical identified. Furthermore, ROS/RNS are pollutants of the atmosphere and can be generated through various mechanisms such as UV light irradiation, metal-catalyzed reactions, inflammatory cell activation, mitochondrial-catalyzed electron transport reactions, and enzymatic processes. The effects of ROS depend on their concentration and environment and can be beneficial and harmful in biological systems. Despite this, ROS plays physiological roles in cellular responses to stress and defense against infectious agents, the high concentrations can cause damage to cell structures that can lead to oxidative stress [5].

4. The Therapeutic Potential of Antioxidants:

Increased production of free radicals or a reduction in the concentration of antioxidants can produce oxidative stress, resulting in an imbalance of pro-oxidants and antioxidants. H Pro-oxidants or free radicals, contain one or

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more unpaired electrons and are characterized as highly reactive and unstable although highly reacting with other molecules. Generally, many metabolic pathways in the human body generate reactive oxygen species (ROS) or free radicals that particularly target carbohydrates, fats, proteins, and nucleic acids. Moreover, the endogenous sources of ROS are mitochondria, xanthine oxidase, peroxisomes, inflammation, phagocytosis, arachidonic acid pathways, exercise, and ischemia/reperfusion injury as well as free metal ions, respiratory burst, cigarette smoke, industrial solvents. On the other side, exogenous conditions including environmental pollutants and UV irradiation. Additionally, incomplete reduction of unreactive dioxygen can lead to Reactive Oxygen Species (ROS) synthesis. Therefore, ROS has superoxide anion (O2−), hydrogen peroxide (H2O2), hydroxyl radical (OH), singlet oxygen, nitric oxide (NO), and some others that cause cellular damage, dissemination, and DNA harm. The primary ROS is a superoxide ion that can interact with other molecules to make secondary ROS through enzyme and metal-catalyzed pathways [4].

At higher concentrations, the ROS produces dual behavior and can damage biological systems while proper amounts have positive effects like protecting against infection. The peptide chains are broken through ROS by oxidizing various amino acids and influence lipid peroxidation by disrupting biological membranes. The oxidation of sulfhydryl groups leads to conformational changes, degradation, and unfolding, and lipid peroxidation generates unsaturated aldehydes, isoprostanes, and reactive substances of thiobarbituric acid, capable of inducing oxidative stress and impairing cellular proteins in the case of protein. Many diseases of oxidative stress are treated through several approved antioxidant drugs [7].

5. Plant Compounds and Metal Ion Complexes: Antioxidant Defense

On Earth, living organisms evolved in an oxygen-rich environment and led to permanent exposure to reactive oxygen species (ROS) as by-products of oxygen metabolism. However, to secure proper development and homeostasis, it is essential to reduce the level of ROS through efficient mechanisms. Preventing free radical formation, neutralizing ROS, and repairing damaged molecules are three levels that operate the antioxidant protection system. Hydrophilic and lipophilic antioxidant compounds are sourced from vegetables, fruits, and dietary supplements. Although the hydrophilic antioxidants are easily absorbed, the lipophilic ones require fats for absorption and remain in the body longer. Antioxidants are also classified as enzymatic or non-enzymatic. Superoxide dismutase, catalase, and glutathione peroxidase are enzymes that play critical roles in ROS removal while vitamins, and polyphenols, scavenge free radicals directly or indirectly are non-enzymes. The various antioxidants are crucial in overall health and ensure cellular and tissue redox balance [6].

6. Conclusion:

In conclusion, oxidative stress is characterized by an imbalance between prooxidants and antioxidants that plays a significant role in various chronic diseases. The Gershman and subsequent research pioneers discovered the free radicals and their toxic effects, marking a turning point in understanding the mechanisms. Modern lifestyle factors contribute to increased oxidative stress-related disorders and highlight the importance of securing a balance between free radicals and antioxidants. Carotenoids exhibit significant health benefits among other antioxidants and contribute to maintaining redox balance. The biochemical dynamics of free radicals and antioxidants can be understood by shedding light on their roles in cellular processes and disease pathogenesis. Overall, a diet contains antioxidants, and supplementation with natural antioxidant strategies helps to prevent oxidative stress-related diseases and promote overall well-being.

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