Antioxidants and their Impact on Human Health

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Abstract

The maintenance of cellular and physiological homeostasis relies on a delicate balance between oxidants and antioxidants. When reactive oxygen and nitrogen species (ROS and RNS) are produced in excess due to metabolic and environmental processes, they can induce oxidative stress, accelerate aging, and contribute to the development of chronic diseases, including respiratory, neurological, and cardiovascular disorders. Antioxidants counteract oxidative stress by neutralizing free radicals through mechanisms such as hydrogen atom transfer, electron donation, metal ion chelation, and enzymatic activation. These antioxidants are generally classified into two groups: enzymatic (e.g., glutathione peroxidase, catalase, and superoxide dismutase) and non- enzymatic (e.g., vitamins C and E, carotenoids, flavonoids, glutathione, and uric acid). While antioxidants generally protect against cellular damage, certain conditions, such as the presence of transition metals or high concentrations, can cause them to act as prooxidants. This phenomenon is currently being explored for its potential therapeutic applications in cancer treatment. Antioxidants, which are crucial for maintaining health and preventing disease, are derived from both endogenous synthesis and dietary sources, including fruits, vegetables, nuts, cereals, and beverages. Although the real-world effectiveness of antioxidants is influenced by factors like bioavailability, metabolism, and interactions, their activity is typically evaluated using in vitro tests (such as DPPH, ABTS, FRAP, and ORAC) and in vivo methods. In addition to their health benefits, antioxidants are widely used in industrial applications, cosmetics, and food preservation to prevent oxidation and prolong shelf life. Diets rich in antioxidants are linked to a reduced risk of disease, although the effects of high-dose supplements remain inconsistent. Therefore, the most effective way to promote long-term health and reduce issues related to oxidative stress is to obtain antioxidants through a well-balanced, nutrient-dense diet.

Introduction

The maintenance of physiological homeostasis relies on the balance between oxidants and antioxidants. This balance can be disrupted by reactive oxygen and nitrogen species (ROS and RNS), which are generated by both the body's normal metabolic processes and external factors.[1,2] These reactive species are produced endogenously by phagocytic cells during immune responses and within various cellular compartments, such as mitochondria and peroxisomes. Exogenous sources include cigarette smoke, xenobiotic compounds, UV radiation, and pollution. While these reactive species play crucial roles in cellular signaling and defense mechanisms, their excessive presence leads to oxidative stress, a condition associated with the development of numerous diseases.[3,4] The damaging effects of free radicals and other reactive species are counteracted by antioxidant molecules. These defense molecules, including substances like glutathione, uric acid, and ubiquinone, are both

synthesized by the body and obtained through the diet, with sources such as flavonoids and vitamins C, E, and A. Additionally, certain trace elements, such as zinc and selenium, are crucial for the function of antioxidant enzymes, even though they do not directly act as antioxidants themselves.[5,6] Beyond these well-known antioxidants, the total antioxidant capacity of blood is significantly influenced by circulating proteins, particularly albumin and alpha-1 antitrypsin. To preserve the delicate balance between oxidants and antioxidants, these proteins work in concert with other antioxidants to form a synergistic defense network that neutralizes ROS and RNS. This interconnected system of oxidative and antioxidative compounds plays a critical role in various physiological processes, with a particular focus on their relevance to chronic obstructive pulmonary disease (COPD).[7,8]

Classification of Antioxidants

Antioxidants inhibit the chemical process of oxidation, which can generate free radicals and trigger chain reactions that may damage cells. In essence, they protect cells from the harmful effects of these unstable molecules. Antioxidants neutralize free radicals by donating an electron, thereby stabilizing them and preventing further damage to other cellular components.[9,10]

Antioxidants can be classified in several ways based on their properties and functions.

1. **Based on Solubility**

i. **Water-soluble (hydrophilic) antioxidants**: These antioxidants operate primarily in the aqueous environments of the body, such as blood plasma and the cytosol of cells. Examples include glutathione, uric acid, and vitamin C (ascorbic acid).

ii. **Lipid-soluble (hydrophobic) antioxidants:** These function mainly in lipid-rich areas, such as cellular membranes, where they help protect lipids from peroxidation. Notable examples include carotenoids like beta-carotene and vitamin E (tocopherols and tocotrienols).[11,12]

2. **Based on Nature:**

i. **Natural Antioxidants:** These are derived from plant or animal sources and are primarily obtained through the diet. Common examples include minerals such as zinc and selenium, vitamins like C, E, and A, and various phytochemicals such as flavonoids, carotenoids, and polyphenols.

ii. **Synthetic Antioxidants:** These are man-made compounds with antioxidant properties, commonly used in industrial applications and as food preservatives. Examples include butylated hydroxytoluene (BHT) and butylated hydroxyanisole (BHA).[13–15]

3. **Based on Their Mode of Action:**

i. **Primary Antioxidants (Chain-Breaking Antioxidants):** These antioxidants directly neutralize free radicals by converting them into less reactive and more stable molecules, effectively interrupting the chain reaction of oxidation. Examples include phenolic compounds and vitamin E.

ii. **Secondary Antioxidants (Preventive Antioxidants):** These act by inhibiting the formation of free radicals or by decomposing peroxides and hydroperoxides before they can propagate oxidative damage. Examples include metal chelators like EDTA and antioxidant enzymes such as glutathione peroxidase, catalase, and superoxide dismutase.[16–

4. **Based on Their Source**

    i. **Endogenous Antioxidants:** These are produced naturally within the body. They include enzymatic antioxidants such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), as well as non-enzymatic antioxidants like glutathione, lipoic acid, and uric acid.

    ii. **Exogenous (Dietary) Antioxidants:** These are obtained from external sources, primarily through the diet. Examples include carotenoids, flavonoids, and vitamins C, E, and A, along with other phytochemicals found in fruits, vegetables, and various plant-based foods.[4,19,20]

5. **Based on their Chemical Nature**

    i. **Enzymatic:** These are enzymes that facilitate the breakdown of oxidizing agents and help neutralize reactive species. Key examples include glutathione peroxidase, catalase, and superoxide dismutase.

    ii. **Non-Enzymatic:** This group comprises a wide variety of compounds that scavenge free radicals or inhibit oxidative reactions through non-enzymatic mechanisms. It includes minerals (such as zinc and selenium), vitamins (such as C, E, and A), and phytochemicals (like flavonoids, carotenoids, and polyphenols).[21–23]

Antioxidants and Their Dietary Sources

Antioxidants are compounds that protect cells from the harmful effects of free radicals, unstable molecules that can damage proteins, lipids, and DNA. This cellular damage has been linked to aging and the progression of various diseases. Antioxidants are either produced naturally by the body or obtained through the diet.

Antioxidants in Food

A significant portion of the antioxidants we consume comes from our diet, particularly from a variety of plant-based foods. A diverse and nutrient-rich diet is the most effective way to ensure adequate antioxidant intake.

Key Dietary Sources of Antioxidants

1. **Fruits**: Berries (such as blueberries, strawberries, and raspberries), citrus fruits (including oranges, lemons, and grapefruits), apples, grapes, cherries, and many other fruits are rich in various antioxidants.[24,25]

2. **Vegetables**: Cruciferous vegetables (like broccoli and Brussels sprouts), leafy greens (such as spinach and kale), as well as colorful vegetables like peppers, carrots, and tomatoes, are excellent sources of dietary antioxidants.

3. **Nuts and Seeds:** Almonds, walnuts, flaxseeds, and chia seeds are rich in antioxidants such as vitamin E and selenium.

4. **Legumes:** Beans and lentils are excellent sources of polyphenols, which possess strong antioxidant properties.

5. **Whole Grains:** Whole grains contain antioxidants like tocotrienols and phytic acid.

6. **Herbs and Spices:** Many herbs and spices, including cloves, cinnamon, ginger, and turmeric, are potent sources of antioxidants.

7. **Coffee and Tea:** Both beverages are rich in polyphenolic compounds, contributing significantly to antioxidant intake.

8. **Dark Chocolate:** A good source of flavanols, a type of polyphenol known for its antioxidant effects.

Polyphenols:

Polyphenols are a diverse group of plant-derived compounds known for their strong antioxidant properties. They are broadly categorized into several subclasses:

Flavonoids: Found abundantly in dark chocolate, tea, coffee, fruits, and vegetables.[26–35] Subtypes include:

i. **Anthocyanins:** Responsible for the vibrant colors of cherries, red cabbage, and berries.

ii. **Flavanols:** Present in apples, cocoa, and tea, catechins in green tea are a prominent example.

iii. **Flavones:** Found in foods like celery and parsley.

iv. **Flavanones:** Common in citrus fruits.

v. **Isoflavones:** Primarily found in soybeans.

Phenolic Acids: These occur in whole grains, fruits, and vegetables. Notable examples include ferulic acid and caffeic acid.[36–39]

Lignans: Found in whole grains, flaxseeds, and sesame seeds.

Stilbenes: The most well-known example is resveratrol, found in red wine and grapes.

Carotenoids:

Carotenoids are antioxidant-rich pigments found in a wide range of fruits and vegetables. They play important roles in health, including supporting vision and reducing oxidative damage. [40,41]

i. **Lycopene:** Found in tomatoes, watermelon, and pink grapefruit; known for its potent antioxidant activity.

ii. **Lutein and Zeaxanthin:** Present in leafy green vegetables and eggs, these carotenoids are especially important for maintaining eye health.

The Role of Antioxidants in Health and Disease

By neutralizing harmful free radicals and reducing oxidative stress, an underlying factor in the development and progression of various diseases and the aging process, antioxidants play a vital role in maintaining overall health.

Age and Antioxidants

Oxidative stress, caused by an imbalance between free radical production and the body's ability to counteract or detoxify their harmful effects, is considered a key contributor to aging. Over time, the accumulation of oxidative damage to lipids, proteins, and DNA can lead to cellular dysfunction and senescence, ultimately contributing to the decline in physiological and functional capacity associated with aging.[42–45]

Combating the Effects of Aging

Both endogenous and dietary antioxidants play a crucial role in protecting the body from oxidative damage by neutralizing free radicals before they can harm cellular structures. Their benefits in the aging process may include:

Protecting Cellular Integrity: By mitigating oxidative stress, antioxidants help preserve the function of cells and tissues.

Supporting Healthy Aging: They may contribute to slowing down certain age-related declines in physiological function.

Reducing the Risk of Age-Related Diseases: Chronic oxidative stress has been linked to a range of age-associated illnesses, and antioxidants may help lower this risk.

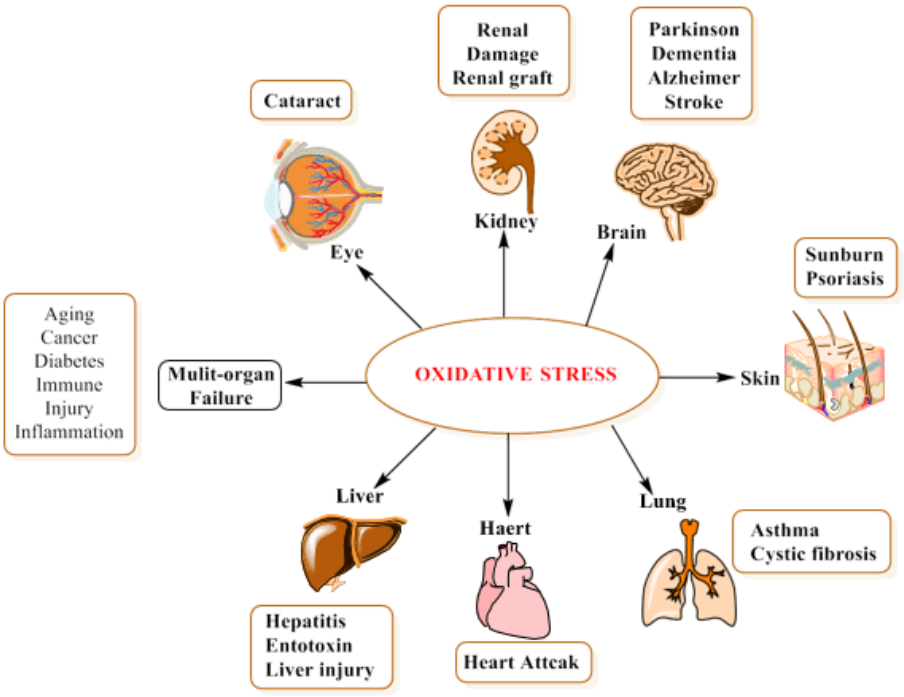

Figure 1. Oxidative stress causes different diseases

Chronic Diseases and the Role of Antioxidants

There is growing recognition that oxidative stress is a key contributor to the development and progression of many chronic illnesses. Due to their ability to neutralize free radicals, antioxidants may offer protective benefits or help manage these conditions.

Cardiovascular Diseases

One major area of interest is the role of antioxidants in protecting against cardiovascular diseases, particularly atherosclerosis—the buildup of plaque in the arterial walls, which can lead to heart attacks and strokes. Oxidative stress plays a central role in both the initiation and progression of

atherosclerosis by: Promoting the oxidation of low-density lipoprotein (LDL) cholesterol, which contributes to plaque

formation. Triggering inflammation and endothelial dysfunction within blood vessels. Enhancing the recruitment of immune cells, further accelerating arterial damage.[46–48]

LDL Oxidation: Free radicals can oxidize low-density lipoprotein (LDL) cholesterol, making it more likely to be taken up by macrophages in the arterial walls. This leads to the formation of foam cells—a hallmark of early atherosclerosis. Antioxidants such as vitamin E, carotenoids, and polyphenols can help prevent LDL oxidation, thereby slowing plaque development.

Endothelial Dysfunction: The endothelium, which lines the interior of blood vessels, can be damaged by oxidative stress, impairing its ability to regulate blood flow and prevent plaque accumulation. Antioxidants help protect endothelial function by reducing oxidative damage.

Inflammation: Oxidative stress promotes inflammation within the arteries, contributing to the formation and destabilization of atherosclerotic plaques. Some antioxidants also possess anti- inflammatory properties, which may further support vascular health.

Antioxidants and Their Role in Cancer Prevention

Antioxidants may help prevent or slow the progression of cancer, a disease marked by uncontrolled cell growth often triggered by genetic mutations, by counteracting oxidative stress. Oxidative stress is believed to contribute to cancer development through several key mechanisms:

Cell Proliferation and Survival: - Oxidative stress can activate signaling pathways that promote uncontrolled cell division and inhibit apoptosis (programmed cell death), both of which are critical in tumor formation. Certain antioxidants may help interfere with these pro-cancer pathways.[49,50]

DNA Damage: - Free radicals can directly damage DNA, leading to mutations that initiate or accelerate cancer development. By neutralizing these free radicals, antioxidants help protect DNA and maintain genetic stability.[51–53]

Chronic Inflammation: - Persistent inflammation, often driven by oxidative stress, creates a microenvironment that supports tumor growth and metastasis. Antioxidants with anti- inflammatory properties may help disrupt this process and reduce cancer risk.

Neurodegenerative Diseases and the Role of Antioxidants

Antioxidants may play a protective role in neurodegenerative diseases such as Parkinson's disease (PD) and Alzheimer's disease (AD), where the progressive loss of structure and function in neurons leads to cognitive and motor decline. Oxidative stress is believed to be a major contributor to the onset and progression of these conditions through several mechanisms[54–57]:

Brain Vulnerability: Due to its high oxygen consumption and abundance of easily oxidizable lipids, the brain is particularly susceptible to oxidative damage.

Protein Misfolding and Aggregation: Oxidative stress can promote the misfolding and accumulation of abnormal proteins, key features in neurodegenerative diseases. For instance, alpha-synuclein aggregation is associated with PD, while amyloid-beta plaques are characteristic of AD.

Neuronal Dysfunction and Cell Death: Persistent oxidative damage impairs neuronal function and can ultimately lead to

neuronal death, contributing to the progressive nature of these disorders. By counteracting oxidative stress, antioxidants may help slow disease progression and preserve cognitive and motor function.

Conclusion

Antioxidants play an indispensable role in preserving human health by combating oxidative stress, a key factor in aging and the onset of numerous chronic diseases. Through their ability to neutralize free radicals, antioxidants help maintain cellular integrity, support healthy aging, and potentially reduce the risk of conditions such as cardiovascular diseases, cancer, and neurodegenerative disorders.

They are classified based on various criteria, including solubility, source, chemical nature, and mode of action, and are sourced both endogenously and from a diverse range of dietary components, particularly plant-based foods. While the therapeutic potential of antioxidants is well- documented, their effectiveness is influenced by factors such as bioavailability, metabolism, and interactions with other nutrients.

Ultimately, a balanced, nutrient-rich diet rich in natural antioxidants remains the most reliable and beneficial approach for supporting long-term health and mitigating the damaging effects of oxidative stress. Though not a cure-all, antioxidants are an essential piece of the complex puzzle of disease prevention and healthy living.

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