Antioxidants and Their Impact on Human Health

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Abstract:

In recent years, significant attention has been directed toward the field of free radical chemistry. Our bodies naturally produce free radicals, reactive oxygen species (ROS), and reactive nitrogen species (RNS) that are naturally generated within the human body as by-products of various metabolic processes and endogenous production due to exposure to various external environmental factors. Maintaining a balance between these reactive species and antioxidants is crucial for normal physiological functions. Oxidative stress is a key contributor to cellular and molecular damage, affecting vital biomolecules such as lipids, proteins, and nucleic acids. This cumulative damage is implicated in the pathophysiology of numerous chronic and degenerative diseases, including cardiovascular disorders, neurodegenerative conditions (e.g., Alzheimer's and Parkinson's diseases), diabetes mellitus, inflammatory diseases, and various types of cancer. Antioxidants can be derived from both natural and synthetic sources and function by scavenging free radicals, chelating metal ions, or up-regulating endogenous antioxidant defences. Natural antioxidants, commonly found in fruits, vegetables, herbs, and spices, include polyphenols, carotenoids, and essential vitamins. On the other hand, synthetic antioxidants such as butylated hydroxytoluene (BHT) and butylated hydroxyanisole (BHA) are widely used in the food and pharmaceutical industries to prevent oxidation and prolong shelf life.

This review aims to provide a comprehensive overview of the various types of antioxidants, their mechanisms of action, and their sources. Furthermore, it highlights the critical role of antioxidants—both natural and synthetic—in the prevention of oxidative stress-related diseases and their potential applications in health promotion and disease management.

Keywords: Free radicals, antioxidants, oxidation, oxidative stress

Introduction:

The "oxygen paradox" highlights that while oxygen is essential for life, it also generates harmful free radicals, leading to oxidative stress. [1] These reactive by-products can damage vital biomolecules. To counter this, the body relies on water- and fat-soluble antioxidants. A proper balance between oxidative stress and antioxidant defences is crucial for maintaining health.[2]

Generation of free radicals and their sources

Free radicals are naturally produced during normal respiration and various cellular activities. Among them, oxygen-centred free radicals—such as superoxide, hydroxyl radicals, peroxyl radicals, alkoxy radicals and nitrogen oxide are particularly significant in triggering oxidative stress.[3] These reactive species originate from two main sources: internal (endogenous) and external (exogenous). A summary of the primary endogenous and exogenous sources of free radicals is provided in Table 1.

Table no.1: Endogenous and exogenous sources of free radicals [4]

Endogenous Sources of Free Radicals		External Sources of Oxidative Stress	
Mitochondrial respiration	Essential process of life that generates superoxide anion radical	Air pollution	Exposure to particulate matters in polluted air can produce significant oxidative stress, increasing the risk for asthma, cardiovascular diseases, chronic pulmonary obstructive diseases (COPD), and lung cancer.
Autoxidation	Autooxidation of many biological molecules (hemoglobin, myoglobin, catecholamines, etc.) in the human body can produce free radicals. Superoxide is the primary free radical formed	Inorganic particles in air	Ingestion of mineral particles from dust in individuals working in industry may cause oxidative stress, particularly if air contains fine mineral dust (quartz, silica, and asbestos)
Enzymatic reaction	Many enzymatic reactions involving xanthine oxidase, lipoxygenase, aldehyde oxidase, etc. can generate free radicals	Tobacco smoking	Oxidants present in tobacco smoke can damage lungs causing COPD and even raising risk of lung cancer
Respiratory burst	This is a processs in which phagocytes consume a large amount of oxygen during phagocytosis	Some medications	Medications such as bleomycin, adriamycin, and sulfasalazine may produce oxidative stress
Metal ions	Metal ions such as copper ion and ferrous ion, which are essential for the body, can react with hydrogen peroxide to produce free radicals	Industrial solvents	Some industrial solvents, such as chloroform and carbon tetrachloride, if inhaled may cause oxidative damage
Strenuous exercise infection	May produce free radicals because the immune system may try to neutralize invading microorganisms with a burst of free radicals	Exposure to radiation	Exposure to excessive ultraviolet light, prolonged exposure to the sun (sunbathing), and treatment with radiation as part of cancer therapy increase oxidative stress
Ischemia/ reperfusion	May activate xanthine oxidase, producing free radicals		

Effect of oxidative stress on body

Oxidative stress plays a critical role in the onset and progression of many health conditions, including atherosclerosis, cancer, aging, and various inflammatory diseases like arthritis, lupus, and respiratory distress syndrome.[5] It is also linked to ischemic events (e.g., heart attacks, strokes), genetic disorders (e.g., hemochromatosis), immune dysfunctions (e.g., AIDS), and neurological disorders such as Alzheimer's, Parkinson's, and muscular dystrophy. [6,7] Additionally, it contributes to complications in organ transplantation, gastric ulcers, hypertension, and preeclampsia.

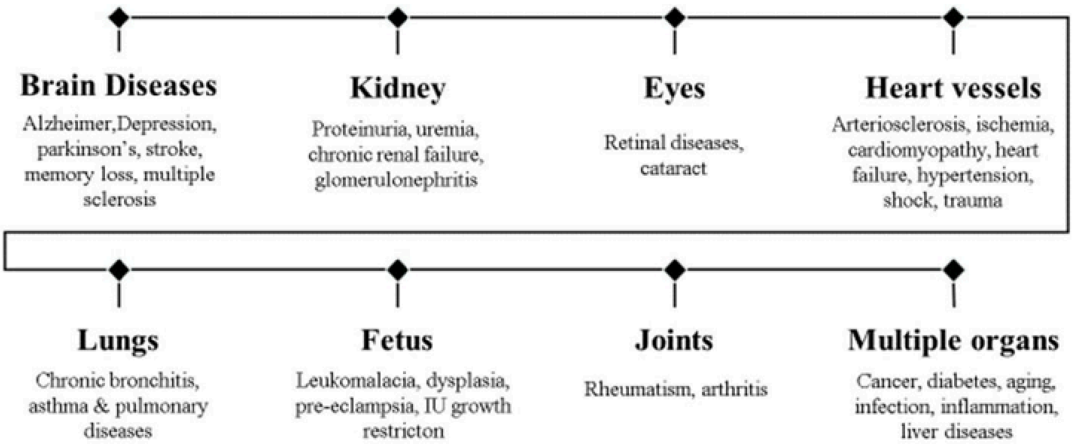

Figure 1: Various diseases associated with oxidative stress conditions

Cardiovascular diseases

Heart disease is the leading cause of death, with oxidative processes playing a key role in its development. Oxidation of polyunsaturated fats in LDL contributes to atherosclerosis, as free radicals from vascular cells trigger lipid peroxidation.[8] This leads to vascular damage, foam cell formation, and plaque buildup. Oxidized LDL is both atherogenic and toxic to endothelial cells.

Carcinogenesis

Reactive oxygen and nitrogen species (ROS/RNS) promote cancer by damaging DNA, causing mutations, and activating carcinogens. Antioxidants like beta-carotene, vitamin C, and vitamin E help counteract these effects. Beta-carotene protects through antioxidant, immune-boosting, and photoprotective actions. [9]

Free radical and aging

Aging is driven by free radical-induced cellular damage, leading to functional decline and age-related diseases. Reducing oxidative stress or free radical production may slow aging.

[10] Since oxidative stress increases with age, a diet rich in antioxidants can help protect cells, enhance quality of life, and possibly extend lifespan.

Oxidative damage to protein and lipids [11]

Proteins can be oxidatively modified through amino acid alteration, peptide bond cleavage, or cross-linking via lipid peroxidation products, with methionine, cysteine, arginine, and histidine being especially vulnerable. Such damage increases protein susceptibility to degradation and can impair the function of enzymes, receptors, and transport systems. Oxidized proteins may also form reactive groups that further damage cell membranes and disrupt cellular function.

Lipids oxidative stress and biomolecular oxidation contribute to aging, atherosclerosis, inflammation, cancer, and drug toxicity. A key mechanism is lipid peroxidation, driven by free radicals, especially in polyunsaturated fatty acids of cell membranes. Initiated by hydroxyl radicals, it leads to a chain reaction forming lipid hydroperoxides and reactive by-products like alkanes, malondialdehyde, and isoprostanes. These by-products serve as biomarkers and are associated with various diseases, including neurodegeneration, ischemia-reperfusion injury, and diabetes.

Oxidative damage to DNA

DNA and RNA are highly susceptible to oxidative damage, especially during aging and cancer. Oxidative stress from UV radiation or free radicals increases modified nucleotides like glycol, dTG, and 8-hydroxy-2'-deoxyguanosine (8-OHdG).[12] Mitochondrial DNA is particularly vulnerable, linking its damage to several diseases. 8-OHdG is a key biomarker for assessing oxidative stress.

Antioxidants

Antioxidants are stable molecules that neutralize free radicals by donating electrons, thereby preventing cellular damage as shown in figure 2. Some, like glutathione, ubiquinol, and uric acid, are naturally produced in the body, while others—such as vitamins E, C, and beta- carotene—must be obtained through the diet. These antioxidants halt harmful chain reactions and play a key role in protecting cells from oxidative stress. Antioxidants function through various roles such as radical scavenging, hydrogen/electron donation, peroxide decomposition, singlet oxygen quenching, and metal chelation. [13,14,15] They exist as enzymatic and non- enzymatic forms in both intra- and extracellular environments to neutralize ROS. Their action involves two main mechanisms: chain-breaking by electron donation and removal of ROS initiators. Antioxidants may also act via metal ion chelation, co-antioxidant activity, or gene expression regulation.

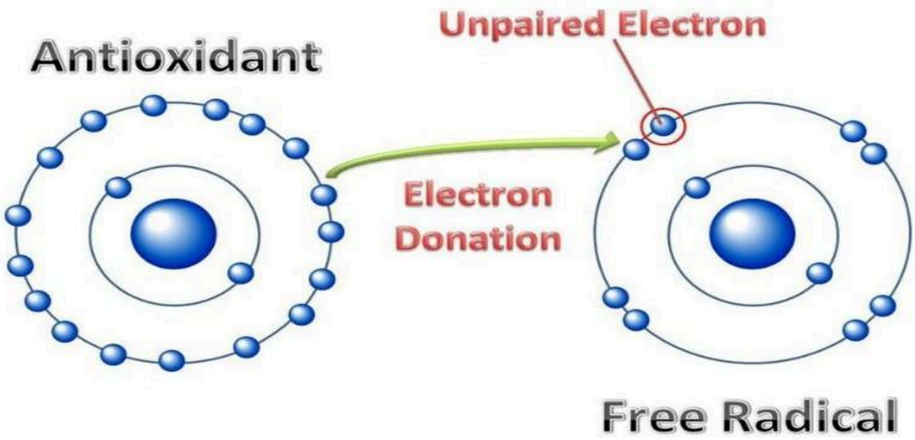

Figure 2: Mechanism of action of an antioxidant action

Antioxidants defend the body through four levels: prevention, radical scavenging, repair/de novo synthesis, and adaptation. [16]

1. **Preventive antioxidants** reduce hydroperoxides and hydrogen peroxide to non-radical forms, preventing free radical formation. Key enzymes include glutathione peroxidase, catalase, and PHGPX, which also targets membrane-bound phospholipids.

2. **Radical-scavenging antioxidants** neutralize existing free radicals to halt chain reactions. Hydrophilic scavengers include vitamin C, uric acid, and albumin, while lipophilic ones include vitamin E and ubiquinol, with vitamin E being especially potent.

3. **Repair/de novo antioxidants** involve enzymes like proteases and DNA repair systems that remove or fix oxidized molecules, preventing damage buildup.

4. **Adaptation** refers to the body's ability to upregulate antioxidant production in response to oxidative stress signals.

Enzymatic antioxidants

Cells combat oxidative stress through a network of antioxidant enzymes. Superoxide dismutases (SODs) convert harmful superoxide radicals into hydrogen peroxide, which is then broken down into water and oxygen by catalase and peroxidases. SODs are present in nearly all aerobic cells and come in three types based on metal cofactors: Cu/Zn, Fe, and Mn. In humans, SOD1 (cytoplasm), SOD2 (mitochondria), and SOD3 (extracellular) protect different cellular compartments. Catalase, found in nearly all oxygen-exposed organisms, especially in the liver, rapidly breaks down hydrogen peroxide to prevent cellular damage. [16,17,18]

Non-enzymatic antioxidants Vitamin C and Vitamin E

Ascorbic acid (vitamin C) is a monosaccharide antioxidant essential in humans, who must obtain it from the diet. Unlike humans, most animals synthesize it naturally. [19] Within cells, it is kept in its reduced form by glutathione through enzymes like protein disulfide isomerase and glutaredoxins. As a reducing agent, it neutralizes ROS, including hydrogen peroxide. Additionally, it serves as a substrate for ascorbate peroxidase, especially important in plant stress resistance.

Vitamin E consists of eight tocopherols and tocotrienols, with α-tocopherol being the most studied due to its high bioavailability. It acts as a key lipid-soluble antioxidant, protecting cell membranes from oxidation by reacting with lipid radicals in the lipid peroxidation chain. This process prevents the continuation of the reaction. The oxidized α-tocopheroxyl radicals can be recycled back to their active form by other antioxidants like ascorbate, retinol, or ubiquinol. [20].

Glutathione

Glutathione is a cysteine-containing peptide synthesized in cells and found in most aerobic organisms. It acts as a key antioxidant through its thiol group, which serves as a reducing agent and can cycle between oxidized and reduced forms. Maintained by glutathione reductase, it protects cells by reducing oxidants and supporting redox balance. [21]

Melatonin

Melatonin (N-acetyl-5-methoxytryptamine) is a hormone found in animals and some other organisms, including algae. It is a potent antioxidant capable of crossing cell membranes and the blood–brain barrier.[22] Unlike other antioxidants, melatonin does not undergo redox cycling; once oxidized, it forms stable end-products and cannot be regenerated, making it a terminal or "suicidal" antioxidant.

Natural antioxidants

Synthetic antioxidants like BHT and BHA are commonly used in foods, cosmetics, and medicines to prevent oxidation, especially in oil- and fat-containing products. However, due to their volatility, instability at high temperatures, potential carcinogenicity, and growing consumer preference for safer alternatives, there's a shift toward natural antioxidants. Natural antioxidants from dietary and medicinal plants are gaining popularity due to their safety, low cost, and health benefits. A wide variety of vegetables (e.g., potatoes, spinach, tomatoes), fruits (e.g., berries, cherries, citrus), and beverages like green and black tea (rich in phenolics) [23] have shown strong antioxidant activity as show in figure 3. Indian medicinal plants such as neem, turmeric, holy basil, ginger, and green tea are also rich in antioxidant compounds, making them valuable alternatives to synthetic antioxidants in food, cosmetic, and therapeutic industries.

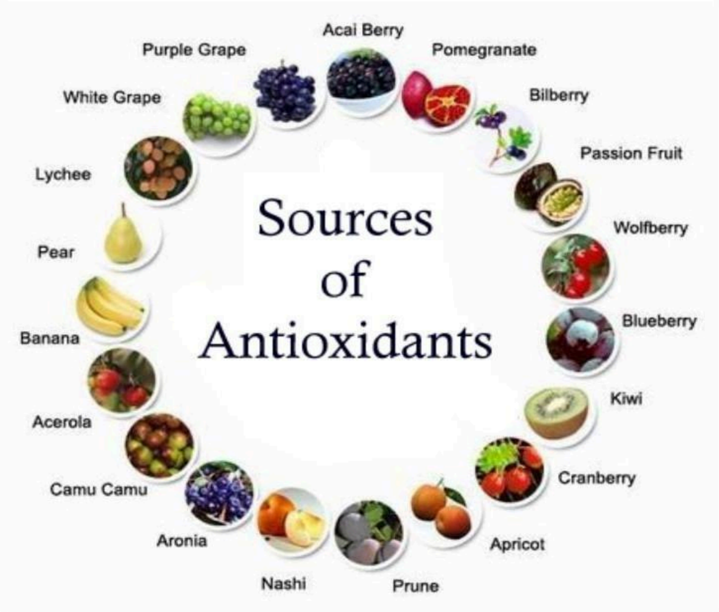

Figure 3: Source of natural antioxidants

Indian functional foods having antioxidant activity

In recent years, preventive medicine has highlighted the vital role of nutrition in reducing the risk of chronic diseases, leading to increased interest in functional foods and nutraceuticals. Functional foods are those that offer health benefits beyond basic nutrition, helping to enhance physiological functions or reduce disease risk. Examples include broccoli (rich in sulforaphane), carrots (β-carotene), and tomatoes (lycopene), as well as Indian green vegetables and spices like mustard and turmeric.[24,25] Nutraceuticals include dietary supplements, herbal products, fortified foods, and beverages. Flavonoids, commonly found in plants, are key nutraceutical compounds known for their antioxidant, anti-inflammatory, antiallergic, antiviral, and anticancer properties.

Conclusion

Free radicals contribute to chronic diseases like heart issues, inflammation, cataracts, and cancer. Antioxidants neutralize this damage, prompting interest in natural sources due to concerns over synthetic ones. Plant-based foods, Indian spices, and medicinal plants are rich in antioxidants, offering a safe, affordable way to boost health, especially in areas with limited medical access.

References:

1. Mohammed, A.A., & Ibrahim, AA. (2004). Pathological roles of reactive oxygen species and their defence mechanism. Saudi Pharm J, 12:1-18.

2. Bagchi K., & Puri S. (1998). Free radicals and antioxidants in health and disease. East Mediterranean Health Jr, 4:350-60.

3. Lien Ai Pham-Huy., & Hua He, Chuong Pham-Huy. (2008). Free Radicals, Antioxidants in Disease and Health. Int J Biomed Sci.Jun; 4 (2):89–96.

4. Sefren Geiner Tumilaar., Ari Hardianto., Hirofumi Dohi., & Dikdik Kurnia. (2024). A Comprehensive Review of Free Radicals, Oxidative Stress, and Antioxidants: Overview, Clinical Applications, Global Perspectives, Future Directions, and Mechanisms of Antioxidant Activity of Flavonoid Compounds. J Chemistry, 31 May. Vol. 2024, 11-20

5. Sies H. (1985) Oxidative stress: Introductory remarks. In: Sies H, editor. Oxidative Stress. San Diego: Academic Press, 1-7.

6. Docampo R. Antioxidant mechanisms. In: Marr J, Müller M, editors. (1995). Biochemistry and Molecular Biology of Parasites. London: Academic Press, 147-60.

7. Rice-Evans CA., & Gopinathan V. (1995). Oxygen toxicity, free radicals and antioxidants in human disease: Biochemical implications in atherosclerosis and the problems of premature neonates. Essays Biochem, 29, 39-63.

8. Esterbauer H., Pubi H., & Dieber-Rothender M. (1991). Effect of antioxidants on oxidative modification of LDL. Ann Med,23, 573-81.

9. S. Wu., H. Lu., & Y. Bai. (2019). Nrf2 in cancers: a double-edgedsword. Cancer Medicine, 8(5), 2252–2267.

10. Sastre J., Pellardo FV., & Vina J. (1996). Glutathione, oxidative stress and aging. Age ,19,129-39.

11. A. Phaniendra, D. B., Jestadi., & L. Periyasamy. (2015). Free radicals: properties, sources, targets, and their implication in various diseases. Indian Journal of Clinical Biochemistry, 30(1), 11–26.

12. M. Rinnerthaler,, J. Bischof., M. Streubel., A. Trost., & K. Richter. (2015). Oxidative stress in aging human skin. Biomolecules, vol. 5, no. 2, pp. 545–589.

13. I. Gulcin. (2020).Antioxidants and antioxidant methods: an updated overview. Archives of Toxicology, 94(3), 651–715.

14. E. Da Pozzo., M. De Leo., & I. Faraone et al. (2018). Antioxidant and antisenescence efects of bergamot juice. Oxidative Medicine and Cellular Longevity, 1–14.

15. A. Elsayed Azab., A Adwas., A. S. Ibrahim Elsayed., A. A Adwas., S. Ibrahim Elsayed., & F. A. Quwaydir. (2019). Oxidative stress and antioxidant mechanisms in human body. Journal of Applied Biotechnology & Bioengineering, 6(1), 43–47.

16. C. D. Fernando., & P. Soysa. (2015). Optimized enzymatic colorimetric assay for determination of hydrogen peroxide (H_2O_2) scavenging activity of plant extracts. Methods X, 2, 283–291.

17. S. Bardaweel., M. Gul, M. Alzweiri., A. Ishaqat., H. Alsalamat., & R. Bashatwah. (2018). Reactive oxygen species: the dual role in physiological and pathological conditions of the human body. Te Eurasian Journal of Medicine, 50 (3), 193–201.

18. C. Winterbourn. (2020). "Biological chemistry of superoxide radicals. ChemTexts, 6, 7–13.

19. J. Kocot., D. Luchowska-Kocot., M. Kiełczykowska., I. Musik., & J. Kurzepa. (2017). Does vitamin C infuence neurodegenerative diseases and psychiatric disorders? .Nutrients, 9(7) , 659–729.

20. M. Yaman., J. Çatak., & H. Ugur. (2021). The bioaccessibility of water-soluble vitamins: a review. Trends in Food Science & Technology, 109, 552–563.

21. C. Gaucher., A. Boudier., J. Bonetti., I. Clarot., P. Leroy., & M. Parent. (2018). Glutathione: antioxidant properties dedicated to nanotechnologies. Antioxidants, 7(5), 62–21.

22. D. Kopustinskiene and J. Bernatoniene (2021). Molecular mechanisms of melatonin- mediated cell protection and signaling in health and disease. Pharmaceutics, 13(2), 129–219.

23. B. Salehi., P. L. Jornet., & E. P.-F. Lopez et al. (2019). Plant-derived ´ bioactives in oral mucosal lesions: a key emphasis to curcumin, lycopene, chamomile, aloe vera, green tea and cofee properties. Biomolecules, 9, 1–23.

24. Roberfroid MB. (1999). What is beneficial for health? The concept of functional food. Food Chem Toxicol, 37, 1034-41.

25. Krishnaswamy K. (1996). Indian functional food: Role in prevention of cancer. Nutr Rev, 54, 127-31.