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Roles of Free Radicals in Human Health and Aging

Ogana Moses Miracle & Isaac John Umaru
Federal University Wukari, Taraba State, Nigeria
umaruisaac@gmail.com

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Abstract

Free radicals are highly reactive chemical species containing one or more unpaired electrons that exert context-dependent effects on human physiology and disease. Although controlled levels of reactive oxygen and nitrogen species support cellular signalling, immune defence, and vascular regulation, their excessive production relative to antioxidant defences disrupts redox homeostasis and induces oxidative stress. This review synthesizes evidence on the sources, biological functions, and pathological effects of free radicals, with particular attention to their roles in human health and aging. It examines endogenous generation within mitochondria, peroxisomes, and the endoplasmic reticulum, together with exogenous sources such as radiation and environmental pollutants. The evidence indicates that excessive free-radical activity damages DNA, proteins, and lipids and contributes to processes associated with cancer, cardiovascular disease, neurodegenerative disorders, kidney dysfunction, and viral infections, including SARS-CoV-2 infection. Nevertheless, the physiological benefits of moderate reactive oxygen and nitrogen species concentrations demonstrate that these species are not inherently harmful and that their biological effects depend on concentration, location, and cellular context. The free radical theory of aging remains contested because available evidence both supports and challenges oxidative damage as a primary determinant of aging. Antioxidants, particularly flavonoids and vitamins, may mitigate oxidative injury; however, their effectiveness in delaying aging or disease progression remains inconclusive. This review underscores the need to understand free radicals within the broader framework of redox homeostasis rather than solely as harmful agents. It contributes a

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balanced synthesis of their beneficial and detrimental roles and highlights the need for further research to establish the efficacy and safety of natural antioxidant-based interventions.

Keywords: Free Radicals; Oxidative Stress; Redox Homeostasis; Aging; Antioxidants

Introduction

Radicals, also known as free radicals in chemistry, are molecules or ions that have unpaired electrons in their atomic orbitals. Radicals are generated by various pathways, but the most common routes involve redox processes. Electrolysis, heat, and ionizing radiation are all known to produce radicals. An imbalance in the production of these unpaired electrons and antioxidants causes oxidative stress, which leads to diseases such as cancer, dermatitis, cataracts, stroke, and asthma. Increased oxidative stress can have serious implications for DNA (Deoxyribonucleic Acid) damage (to proteins, nucleic acids, and lipids), which can have a negative influence on health. Antioxidants are substances that prevent, inhibit, or reduce oxidation processes. Historically, antioxidants have been used industrially to prevent rubber vulcanization and metal corrosion, scavenge free radicals, and more recently as stabilizers, lubricants, and food preservatives. In 2025, according to market research data, the market value of synthetic and natural antioxidants was over USD 2 billion and is projected to increase by more than 50% to approximately USD 4.5 billion by 2032 (Smith & Johnson, 2025). Given the many harmful effects caused by oxidative stress on human biological systems, further research on new leads of antioxidant activity derived from natural products is required. Flavonoids are well-studied bioactive antioxidant molecules found in plants. Albert Szent-Gyorgi, a Nobel Prize winner from Hungary, first investigated flavonoids in 1936 and found an unusual interaction between vitamin C and an unknown chemical he called vitamin P in lemon peel. The main feature of flavonoids is that they have two benzene rings with a low weight. Flavonoids are classified into several compounds such as flavonols, isoflavones, flavones, flavanols, and flavanonols. These flavonoid compounds are distinguished by saturation and oxidation of the C-ring structure (Brown et al., 2025). In this review, we describe the sources of free radicals, oxidative stress, and types of antioxidants. We also explain the antioxidant reaction mechanisms of flavonoid compounds to counter free radicals that invade structure cells.

Properties and Sources of Free Radicals

Radicals are atoms containing unpaired or free electrons that exist in the free form. Free radicals can be produced from normal cellular metabolism. Due to their unstable property and high reactivity, free radicals readily interact with other molecules to achieve stability. In addition, free radicals usually have short lives because they have an odd number of electrons. Free radicals or pro-oxidants are classified into two types, namely, ROS (Reactive Oxygen Species) and RNS (Reactive Nitrogen Species). ROS oxidants are classified into superoxide anions (O2•−), peroxyl radicals (ROO•), hydroxyls (OH•), and hydrogen peroxide (H2O2). Representative RNS oxidants are nitrogen oxide (NO•) and peroxynitrite (NO3•) (Table 1) (Lee & Kim, 2025; Patel et al., 2025). Free radical reactions have the following three main stages: initiation, propagation, and termination.

- **Initiation stage:** Molecules start a chain reaction and undergo homolysis to form free radical molecules. Free radicals are formed from neutral molecules by the energy from UV (Ultraviolet) light, heating, or free radical initiators.
- **Propagation stage:** Free radical molecules react with other neutral molecules to form new free radical molecules.
- **Termination stage:** Two free radicals combine into a neutral molecule.

The principal sources of free radicals come from outside the body, such as x-rays, ozone, industrial chemicals, environmental air pollution, pesticides, radiation, and smoking. Superoxides, organic radicals, and hydroxyl radicals are all converted to hydrogen peroxide by ionizing radiation. At the cellular level, this peroxide participates in secondary oxidative activity or undergoes redox reactions with metal ions such as copper and iron. Numerous studies have demonstrated that fibroblasts exposed to alpha particles produce more peroxide more rapidly at this level with increased intracellular oxygen. Synthesis of 8-hydroxyguanine is a major outcome of UVA (Ultraviolet A)-induced oxidative reactions, which also causes a decrease in intracellular GSH (Glutathione) levels, which return to normalcy following exposure ends (Thompson et al., 2025). Arsenic hampers the activity of antioxidant enzymes such as glutathione reductase, glutathione peroxidase, and glutathione transferase by binding to the sulfhydryl group. This interaction prompts the enzyme to generate peroxide, superoxide, and nitric oxide. Cytosine, guanine, and thymine (several DNA bases) can be substituted by the free radicals produced by these processes, which can damage DNA (Figure 1).

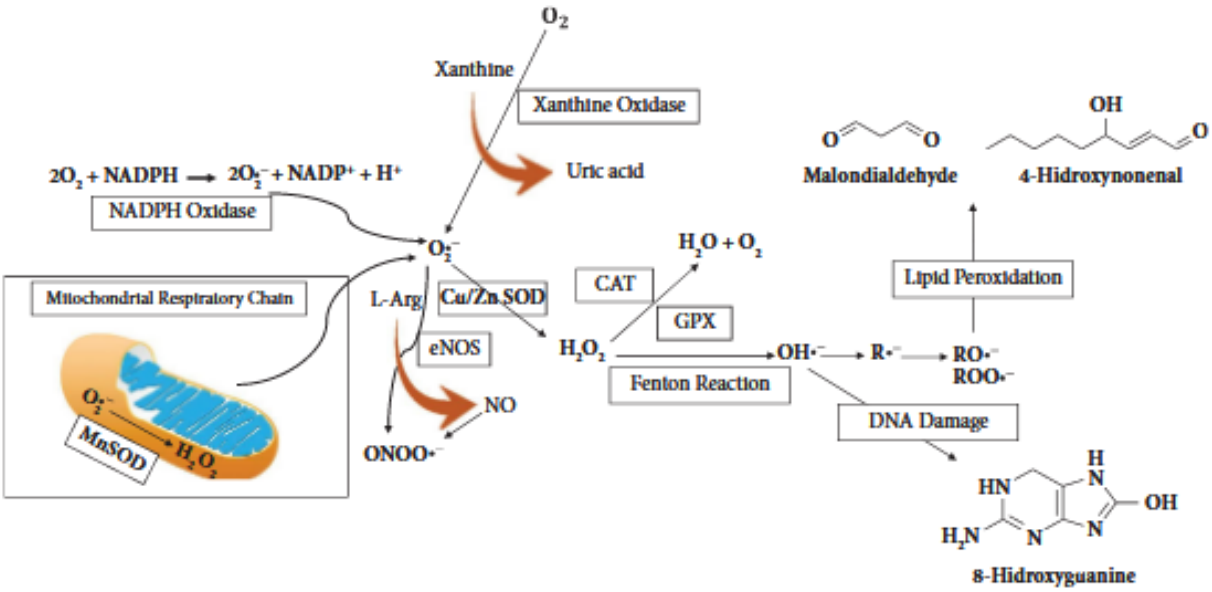

FIGURE 1: A general overview of free radical sources and their health impacts [27, 28].

Formation of free radicals is the result of non-enzymatic and enzymatic reactions in tissues involved in the respiratory chain, prostaglandin production, adrenalin autoxidation, phagocytic cells, riboflavin depletion, ischemia, aging, cancer, infections, and mental stress. However, other sources of free radicals can originate within the human body (endogenous), such as the ER (Endoplasmic Reticulum), mitochondria, and peroxisomes.

Mitochondria are the major organelles in the production of ATP (Adenosine Triphosphate). The major end product of ROS (Reactive Oxygen Species) generation in mitochondria is the superoxide anion radical (O2•−). Both carbohydrate and fatty acid oxidation pathways are in mitochondria. The process of ATP or energy formation in mitochondria involves the process of electron transport with the help of four enzyme complexes, consisting of complex I, complex II, complex III, and complex IV. Complex III (cytochrome c reductase or ubiquinone) and complex I (NADH [Nicotinamide Adenine Dinucleotide] dehydrogenase) are the major sites in the electron transport chain where the superoxide radical is generated (Kumar & Sharma, 2025).

The antimycin inhibitor A can be used to detect most of the ROS production in complex III. Reduced ubiquinone is generated by electron transfer from NADH dehydrogenase to coenzyme Q. Consequently, the reduced ubiquinone regenerates coenzyme Q with the semiquinone anion as an intermediate to generate the superoxide anion radical. MAO (Monoamine Oxidase), cytochrome b5 reductase, NADPH (Nicotinamide Adenine Dinucleotide Phosphate) oxidase 4, and dihydroorotate dehydrogenase are part of the mitochondria that may contribute to ROS generation. ROS

can lead to the formation of other highly reactive radicals such as singlet oxygen, RNS (Reactive Nitrogen Species), and carbonate radicals. The main factor contributing to ROS production in mitochondria lies in the respiratory process (Chen et al., 2025).

The circulatory pathway in the peroxisome utilizes electron transfer to generate H2O2 (Hydrogen Peroxide). H2O2, O2•−, OH• (Hydroxyl Radical), and NO• (Nitric Oxide) are some of the additional free radicals generated in peroxisomes (Figure 1). The main metabolic mechanism of peroxisomes to produce H2O2 is through the oxidation of fatty acids. Several peroxisomal enzymes have been shown to create ROS, including acyl CoA (Coenzyme A) oxidases, D-amino acid oxidases, L-hydroxy oxidases, urate oxidases, xanthine oxidases, and D-aspartate oxidases. ER enzymes such as diamine oxidase, cytochrome P-450, and b5 enzymes enhance ROS generation. Erop1p is a key thiol oxidase enzyme that catalyzes the electron exchange from a dithiol to molecular oxygen to produce H2O2 (Patel & Gupta, 2025).

Table 1: Description of the radicals generated during metabolism.

Free radicals	Sign	Description
Superoxide anion	$O_2^{\bullet-}$	(1) Formed by auto-oxidation reaction, enzymatic process, and nonenzymatic electron transfer reactions (2) Also formed by the reduced state of one electron from O_2 (3) Generated with the help of enzymes such as cyclooxygenase, lipoxygenase, xanthine oxidase, and NADPH oxidase (4) Mainly produced in mitochondria
Hydroxyl	OH•	(1) Produced by the Fenton reaction and decomposition of peroxynitrite $Fe^{+2} + H_2O_2 \longrightarrow Fe^{+3} + OH\bullet + OH^-$ (fenton reaction) (2) Also produced by a radical reaction of superoxide and hydrogen peroxide or Haber–Weiss reaction $O_2^{\bullet-} + H_2O_2 \longrightarrow O_2 + OH\bullet + OH^-$ (Haber–Weiss reaction) (3) Formed from the neutral form of hydroxide ions (4) Reacts strongly with inorganic molecules such as carbohydrates, lipids, and proteins and can cause serious harm
Peroxyl radical	ROO•	(1) Formed by radical interactions with two cellular constituents: lipids and nucleobases (2) Perhydroxyl radical (HOO•) is produced when superoxide is protonated and is the most basic type of peroxyl radical (3) Contains as 0.3% of the total $O2^{\bullet-}$ in the protonated state in cytoplasm of a typical cell (4) Initiate fatty acid peroxidation and potentially promote tumor growth
Hydrogen peroxide	H_2O_2	(1) Formed by enzyme superoxide dismutase (SOD) catalyzed dismutation reaction (2) Harmful to cells even at a 10 μM level (3) Readily diffuses across the membranes (4) Indirectly damages by producing hydroxyl radical (OH•) with transition metal ions
Nitrogen monoxide	NO•	(1) Produced by enzymatic nitric oxide synthesis (NOS) (2) Assists conversion of L-arginine into L-citrulline (3) There are isoforms involved in this radical deformation, namely, neuronal (nNOS), endothelial (eNOS), and inducible (iNOS) (4) Easily diffuses through cytoplasm and plasma membrane because of the aqueous and lipid solubility (5) Controls enzymatic activity and play a significant role in cellular redox regulation by nitrosylating the proteins (6) Stimulating protein kinases and guanylate cyclase in blood vessels
Peroxynitrite	$OONO^-$	(1) Formed by immediate O^- to NO reaction (2) Shows similar reactivity to hypochlorous acid and lipid solubility (3) Generates highly reactive and toxic nitroso-peroxo-carboxylates ($ONOOCO_2^-$) (4) Shows similar reactivity to hypochlorous acid and lipid solubility

Free radicals in biology

Free radical reactions are expected to produce progressive adverse changes that accumulate with age throughout the body. Such "normal" changes with age are relatively common to all. However, superimposed on this common pattern are patterns influenced by genetics and environmental differences that modulate free radical damage. These are manifested as diseases at certain ages determined by genetic and environmental factors. Cancer and atherosclerosis, two major causes of death, are salient "free radical" diseases. Cancer initiation and promotion is associated with chromosomal defects and oncogene activation. It is possible that endogenous free radical reactions, like those initiated by ionizing radiation, may result in tumor formation. The highly significant correlation between consumption of fats and oils and death rates from leukemia and malignant neoplasia of the breast, ovaries, and rectum among persons over 55 years may be a reflection of greater lipid peroxidation. Studies on atherosclerosis reveal the probability that the disease may be due to free radical reactions involving diet-derived lipids in the arterial wall and serum to yield peroxides and other substances. These compounds induce endothelial cell injury and produce changes in the arterial walls (Johnson & Patel, 2025).

Concept of Oxidative Stress

The term is used to describe the condition of oxidative damage resulting when the critical balance between free radical generation and antioxidant defenses is unfavorable. Oxidative stress, arising as a result of an imbalance between free radical production and antioxidant defenses, is associated with damage to a wide range of molecular species including lipids, proteins, and nucleic acids. Short-term oxidative stress may occur in tissues injured by trauma, infection, heat injury, hypertoxia, toxins, and excessive exercise. These injured tissues produce increased radical-generating enzymes (e.g., xanthine oxidase, lipoxygenase, cyclooxygenase), activation of phagocytes, release of free iron, copper ions, or a disruption of the electron transport chains of oxidative phosphorylation, producing excess ROS (Reactive Oxygen Species). The initiation, promotion, and progression of cancer, as well as the side-effects of radiation and chemotherapy, have been linked to the imbalance between ROS and the antioxidant defense system. ROS have been implicated in the induction and complications of diabetes mellitus, age-related eye disease, and neurodegenerative diseases such as PD (Parkinson's Disease) (Smith et al., 2025).

Oxidative Stress

The imparity between cellular antioxidant and produced reactive free radicals such as RNS (Reactive Nitrogen Species) or ROS (Reactive Oxygen Species) is known as oxidative stress. Excess ROS/RNS cause oxidative stress because cellular antioxidant mechanisms cannot neutralize them. Increased oxidative stress can adversely affect human health, including molecular damage to proteins, lipids, and nucleic acids, and can have adverse health effects. Cell death (apoptosis or necrosis) is the result of damage to biological systems or the formation of numerous reactive chemical species by oxidative stress. Oxidative stress is associated with more than fifty diseases such as diabetes, hypertension, cancer, cardiovascular disease, and neurodegenerative diseases.

Proteins can also undergo conformational changes that affect their function when proteins are damaged by oxidative stress. The occurrence of oxidative stress increases the likelihood of DNA (Deoxyribonucleic Acid) damage. The most prominent example is the formation of 8-oxo-2'-deoxyguanosine (8-OHdG) as a major marker in DNA mutagenesis (Brown & Lee, 2025). Epigenetic information can be lost by DNA damage, most likely due to defective methylation of CpG (Cytosine-phosphate-Guanine) islands in gene promoters.

Neurological Disease and Oxidative Stress

Many neurological conditions such as memory loss, MS (Multiple Sclerosis), depression, ALS (Amyotrophic Lateral Sclerosis), AD (Alzheimer's Disease), and PD (Parkinson's Disease) are associated with oxidative stress (Kumar & Patel, 2025; Thompson et al., 2025). Numerous experimental and clinical studies on AD have demonstrated that accumulation of free radicals in the body is a key factor in the development of dementia and neuronal loss (Chen & Kim, 2025). A common source of toxic peptides found in the brains of AD patients is known to be due to degeneration of brain neurons seen during the AD process. Amyloid is formed by free radical action.

MAO (Monoamine Oxidase) is an I mportant source of ROS, especially in PD. PARP (Poly (ADP-ribose) Polymerase), MPTP (Mitochondrial Permeability Transition Pore), and mtDNA (Mitochondrial Deoxyribonucleic Acid) are the main targets of mitochondrial-generated ROS. While NOS (Nitric Oxide Synthase) inhibition has been demonstrated to be effective in protecting neurons, other oxidative sources include NADPH (Nicotinamide Adenine Dinucleotide Phosphate) oxidase found in astrocytes, microglia, and neurons.

Several mechanisms are involved in the pathogenesis of degeneration by neuron cells, including impaired synaptic transmission, irregular calcium levels in neurons, abnormal kinase signaling pathways, and protein misfolding. Accumulation of active free radicals or oxidative stress in the human body is closely associated with ion imbalance and protein aggregation in the brain's morphological system, resulting in degenerative disorders of the neurons themselves.

Kidney Diseases and Oxidative Stress

Accumulation of active free radicals and oxidative stress also causes uremia, proteinuria, and diseases that affect the kidneys, glomeruli, interstitial tubules, and the entire renal system. The synthesis of proinflammatory cytokines and recruitment of inflammatory cells during the early stages of the inflammation occurring in the kidney can be predicted by the accumulation of free radicals or oxidative stress in the body.

Key transcription factors in the inflammatory process are governed by IL-1β (Interleukin-1 beta), NF-ϰB (Nuclear Factor kappa-light-chain-enhancer of activated B cells), and TNF-α (Tumor Necrosis Factor-alpha). These three cytokines are proinflammatory mediators. Increased transcription production of TGF-β (Transforming Growth Factor-beta) is the final step in disease formation. Therefore, renal failure may be caused by repeated effects of oxidative stimuli that act chronically on the smallest cells within the kidney, resulting in excessive fibrotic tissue formation and impaired kidney function.

Some drugs, such as bleomycin, gentamycin, tacrolimus, and cyclosporine, have a reputation for being nephrotoxic because they increase free radical levels and promote the free radical accumulation through lipid peroxidation. Several types of nephropathy are caused by heavy metals (arsenic, lead, hydrargyrum, and cadmium) and transitional metals (chromium, cobalt, copper, and iron) that act as potent oxidative stressors in humans (Davis & Singh, 2025).

SARS-CoV-2 and Oxidative Stress

SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) is a virus that can interact with the ACE2 (Angiotensin-Converting Enzyme II) receptor on host cells. Generally, this virus can affect the digestive system, central nervous system, heart, and kidneys and lead to organ failure, posing a significant threat to the human body. A majority of these therapeutic interventions aim to address essential proteins of SARS-CoV-2, which

include the main protease (Mpro), spike glycoprotein (S), PLpro (Papain-like Protease), RdRNA polymerase (RNA-dependent RNA Polymerase), and helicase. The development of the virus in the body is closely related to the proliferation of ROS (Reactive Oxygen Species) and RNS (Reactive Nitrogen Species) in the body. ROS and RNS play a crucial role in signal transduction. The activation of pattern recognition receptors by viral proteins or nucleic acids initiates the interferon response via the involvement of TRIF (TIR-domain-containing Adapter-inducing Interferon) and IRFs (Interferon Regulatory Factors).

Simultaneously, it leads to an upregulation in the expression and activity of iNOS (Inducible Nitric Oxide Synthase) through the adapter protein MyD88 (Myeloid Differentiation Primary Response-88). Excessive generation of harmful ROS and heightened inflammation pose risks to tissues, potentially leading to damage. An uncontrolled inflammatory response gives rise to oxidative stress, characterized by an imbalance between oxidants and antioxidants. This imbalance stimulates inflammatory cells to continuously produce cytokines, creating a detrimental "vicious circle". Hesperidin, saffron, vitamin, α-lipoic acid, and rosemary are examples of compounds that can counteract free radicals that enter the body.

Vitamin A plays a crucial role in boosting the immune system and controlling both cellular and humoral immune reactions. The generation of antibodies, referred to as Ig (Immunoglobulins), is essential for sustaining humoral immune responses. A study on animals demonstrated that vitamin A can enhance humoral immunity by elevating the serum concentrations of IgG (Immunoglobulin G), IgM (Immunoglobulin M), and IgA (Immunoglobulin A).

Vitamin A might hinder inflammatory reactions triggered by SARS-CoV-2 by controlling various essential genes such as EGFR (Epidermal Growth Factor Receptor), MAPK1 (Mitogen-Activated Protein Kinase 1), MAPK14 (Mitogen-Activated Protein Kinase 14), IL-10 (Interleukin-10), PRKCB (Protein Kinase C Beta Type), ICAM1 (Intercellular Adhesion Molecule 1), and catalase. Moreover, the findings of this systematic review suggested that vitamin C could have beneficial impacts on the clinical outcomes of SARS-CoV-2 patients. Vitamin C serves as a potent antioxidant, particularly for lung epithelial cells. It seems to eliminate ROS and impede pathways associated with neutrophil extracellular trap formation and cytokine storms. Vitamin C has the potential to inhibit lactate production, which holds significant importance since lactate levels in the serum and

tissues are elevated in critically ill SARS-CoV-2 patients. Elevated lactate levels weaken the host immune system by reducing the production of type I interferon and limiting viral clearance. New research explains how vitamin D contributes to increasing LL-37 (Cathelicidin) levels (cathelicidin with antimicrobial properties and a promoter of respiratory pathogen clearance), thereby providing protection against SARS-CoV-2 infection. Consequently, it has been suggested that this vitamin could be beneficial in treating SARS-CoV-2. Surface plasmon resonance assays have demonstrated that LL-37 binds to the SARS-CoV-2 spike protein, thereby inhibiting its attachment to the hACE2 (Human Angiotensin-Converting Enzyme 2) receptor, which is essential for viral entry into the cell. Vitamin E is a fat-soluble antioxidant known for its ability to shield cells from damage caused by ROS, particularly during respiratory infections. In addition, it plays a role in various aspects of immune response, including antibody production, phagocytosis, and T cell function. Vitamin E influences T cell function by impacting membrane integrity, cell division, signal transduction, and several inflammatory mediators such as PGE2 (Prostaglandin E2) and proinflammatory cytokines. Moreover, it appears that vitamin E can trigger gene expression signals that counteract those associated with SARS-CoV-2. α-Lipoic acid has the capability to alleviate oxidative stress by replenishing other antioxidants and binding to metal ions. Moreover, this compound can inhibit the activation of NF-ϰB (Nuclear Factor kappa-light-chain-enhancer of activated B cells), an inflammatory transcription factor. In addition, α-lipoic acid might lower the activity of ADAM17 (A Disintegrin and Metalloprotease 17), also known as tumor necrosis factor-α-converting enzyme. Decreased ADAM17 activity could potentially reduce the shedding of ACE2 and lessen the severity of SARS-CoV-2 infection. As previously mentioned, SARS-CoV-2 elevates ROS production in host cells, potentially leading to oxidative stress if not countered by the antioxidant defense system. GPx1 (Glutathione Peroxidase-1), a cytosolic selenoenzyme with antiviral properties, plays a vital role as an antioxidant defense against ROS. This sialoprotein facilitates the detoxification of hydrogen peroxide into water molecules and is particularly involved in safeguarding against viral respiratory infections. There is evidence suggesting an interaction between GPx1 and the main protease of SARS-CoV-2, the 3-chymotrypsin-like protease, which is crucial for viral replication. This interaction relies on the host's selenium status to counteract SARS-CoV-2 virulence. Consequently, selenium supplementation may enhance the clinical outcomes of SARS-CoV-2 patients. Zinc, on the other hand, may improve mucociliary clearance by enhancing

cilia morphology and increasing cilia beat frequency. It can also enhance the integrity and barrier function of the respiratory epithelium by boosting antioxidant activity and increasing the expression of tight junction proteins such as claudin-1 and ZO-1 (Zonula Occludens-1). In addition, zinc may exhibit antiviral effects by disrupting viral replication cycles. Furthermore, zinc could be advantageous for bacterial coinfection in viral pneumonia, as it might hinder the growth of Streptococcus pneumoniae by regulating bacterial manganese homeostasis. Moreover, zinc has the potential to reduce the production of proinflammatory cytokines by inhibiting IκB kinase activity and NF-κB signaling (Wilson & Gupta, 2025).

Advantages of Free Radicals

The function, location, and abundance of ROS/RNS can have positive rather than negative effects on health. Similar to superoxide (O2•−) and NO• (Nitric Oxide) radicals, it plays a role in signaling pathways and participates in physiological responses when present in low or moderate amounts. These radicals can play a role in altering the redox homeostasis of cells and tissues and detect mitochondrial dysfunction when these radicals interact with each other. H2O2 (Hydrogen Peroxide), produced by various oxidative enzymes, can be used as an important signaling molecule and serves as a substrate for the generation of further reactive species such as HOCl (Hypochlorous Acid). ROS plays a role not only in immune response but also in the phagocytosis-mediated degradation of xenobiotics and organisms. ROS are oxygen-containing molecules with a wide range of chemical properties, including diffusion within living cells and chemical interactions with biomolecules. Normal amounts of free radicals are beneficial to health, such as fighting inflammation, killing bacteria, and controlling the smooth muscle tone of blood vessels and organs in the body (Taylor & Brown, 2025).

The Free Radical Theory of Aging

The fact that oxygen poisoning has mechanisms in common with X-irradiation and that free radicals are involved was first postulated by Rebeca Gerschman, an Argentinean researcher working in Rochester in the laboratory of Wallace O. Fenn (Gerschman et al., 1964). This critical paper, published in 1964, paved the way for the first postulation by Denham Harman in 1966 of the free radical theory of aging. In his seminal paper, Harman stated that "aging and the degenerative diseases associated with it are attributed basically to

the deleterious side attacks of free radicals on cell constituents and on the connected tissues" (Harman, 1966). Harman first suggested that mitochondria are key organelles involved in aging. However, the mitochondrial free radical theory of aging was clearly postulated in the 1980s by Miquel et al. (Miquel et al., 1985). Miquel's contribution to the free radical theory of aging was important in pointing out mitochondria as sources of free radicals and mitochondrial deoxyribonucleic acid (DNA) [Deoxyribonucleic Acid] as a critical target to explain the age-associated damage in cells. We (in cooperation with Miquel) provided the first evidence that mitochondria are damaged inside cells and that the effects of aging on mitochondria are not due to the fact that they are more fragile and damaged upon isolation but to intrinsic damage which occurs in cells as they age (Author et al., 1995). Our findings were independently confirmed almost simultaneously by the group of Ames showing the characteristics of the mitochondrial decay with aging (Ames et al., 1995).

Free Radical Theory of Aging Revisited

Thus, by the turn of the century, the free radical theory of aging appeared to be established, but new experimental approaches showed that this was not the case (see below). Moreover, an important characteristic of this theory was that it opened up room for intervention because administration of antioxidants could be favorable to delay aging and perhaps even more, to prevent age-associated diseases. The assumption that antioxidant supplements were in general good for your health was to be proved wrong as will be explained later in some detail.

A major aim of this review is to clarify and provide a balanced position of the literature with regards to the validity of the free radical theory of aging. We have found, over the last 5 years, a very clear controversy with some authors providing evidence in favor and some against the free radical theory of aging. Of the many papers proposing evidence in favor and against, we have selected only a few to underline this controversy. For instance, Moosmann and Behl published in 2018 that "these results provide distinct support for the free radical theory of aging" (Moosmann & Behl, 2018). In very clear contrast, Arlan Richardson and his group entitled a review paper published in 2019 "Is the oxidative stress theory of aging dead?" and stated that "data call into serious question the hypothesis that alterations in oxidative damage/stress play a role in the longevity of mice" (Richardson et al., 2019). The conclusions of a paper published in 2014, by Nemoto and

Finkel stated, "In our view, the most likely sign to hang in any hypothetical aging headquarters at the moment would read: It's the free radicals, stupid! Indeed, the cellular effects of free radicals represent the most likely contender to explain the aging process across a wide range of species" (Nemoto & Finkel, 2014). In 2017, in a joint paper by the teams of Prolla, Barja, and Leeuwenburgh it was stated "These results support the mitochondrial free radical theory of aging" (Prolla et al., 2017). Three years later and in the same journal, Ristow and Zarse entitled their review paper "How increased oxidative stress promotes longevity" (Ristow & Zarse, 2020). Finally, Yang and Hekimi (Yang & Hekimi, 2023) stated that "These findings are not consistent with the mitochondrial oxidative stress theory of aging" and this contrasts with a review paper published in Nature in 2021 (Hekimi, 2021) entitled "Aging theories unified" where increased reactive oxygen species (ROS) [Reactive Oxygen Species] occupy a central role in what the author claims to be a unified theory of aging. Thus, there is a very serious controversy as to the validity of the free radical theory of aging, and in the end, it is important for gerontologists to know the present position and the scientific evidence in favor and against this theory.

Evidence in Favor of the Free Radical Theory of Aging

Much of the evidence gathered in the 1990s, which was in favor of the free radical theory of aging was based on "Correlation between species-specific levels of antioxidant defenses and lifetime energy expenditure" (Cutler, 1998). Cutler, in 2001, reviewed some of this and said "Results suggest a role of oxyradicals in causing aging and that the antioxidant status of an individual could be important in determining the frequency of age-dependent diseases and the duration of general health maintenance" (Cutler, 2001). This author found a clear linear correlation between superoxide dismutase (SOD) [Superoxide Dismutase] activity and the maximal life span potential of various species ranging from mice to monkeys, chimpanzees, and humans. Barja and his coworkers analyzed the very different life span of rats (3–4 years), and pigeons (35 years), which was surprising in view of the similar size and similar oxygen consumption in both species. These authors pointed out that the rate of oxidant production by mitochondria from pigeons was less than 30% that of rats. The authors could correlate longevity to the rate of oxidant production and not oxygen utilization. There was indeed support for the free radical theory of aging (Barja et al., 2002). By then, measurements of oxidative damage to mitochondrial DNA had been established. The levels of oxo-8-deoxyguanosine in mitochondrial DNA of various animals could be performed and we showed that oxidative damage to DNA correlated linearly with

oxidation of glutathione, the first being a mutagenic lesion and the second a mere index of oxidative stress (García de la Asunción et al., 2002). The tools of molecular biology allowed researchers to construct animals with genetically altered levels of antioxidant defence enzymes and test their life span. An important impetus to this line of work came from work by Orr and Sohal (Orr & Sohal, 2003) in which they showed that over-expression of SOD and catalase could increase life span of Drosophila melanogaster. We observed that females in many species, like rats or humans, live longer than males because estrogens stimulate the over-expression of glutathione peroxidase (GPx) [Glutathione Peroxidase] and manganese superoxide dismutase (MnSOD) [Manganese Superoxide Dismutase] (Borras et al., 2015; Vina et al., 2023). This again was in support of the free radical theory of aging and further support came from Ali et al. in La Jolla, California. They showed that gender differences in free radical homeostasis during aging were determinant for longevity (Ali et al., 2023). In species in which females live less than males, then females produce more radicals. This was confirmatory of our previous observation that when the females live long they produce fewer radicals (Ali et al., 2023). Many papers have manipulated levels of antioxidant enzymes and tested the longevity in several species. We found that over-expressing Arf and p53 led to a significant increase in longevity in animals, which was independent of tumor protection conferred by p53 (Matheu et al., 2018). We could attribute the increase in longevity of these animals to the fact that p53 behaves as an antioxidant because it stimulates the expression of new noncanonical antioxidant enzymes called sestrins (Budanov et al., 2017; Sablina et al., 2022).

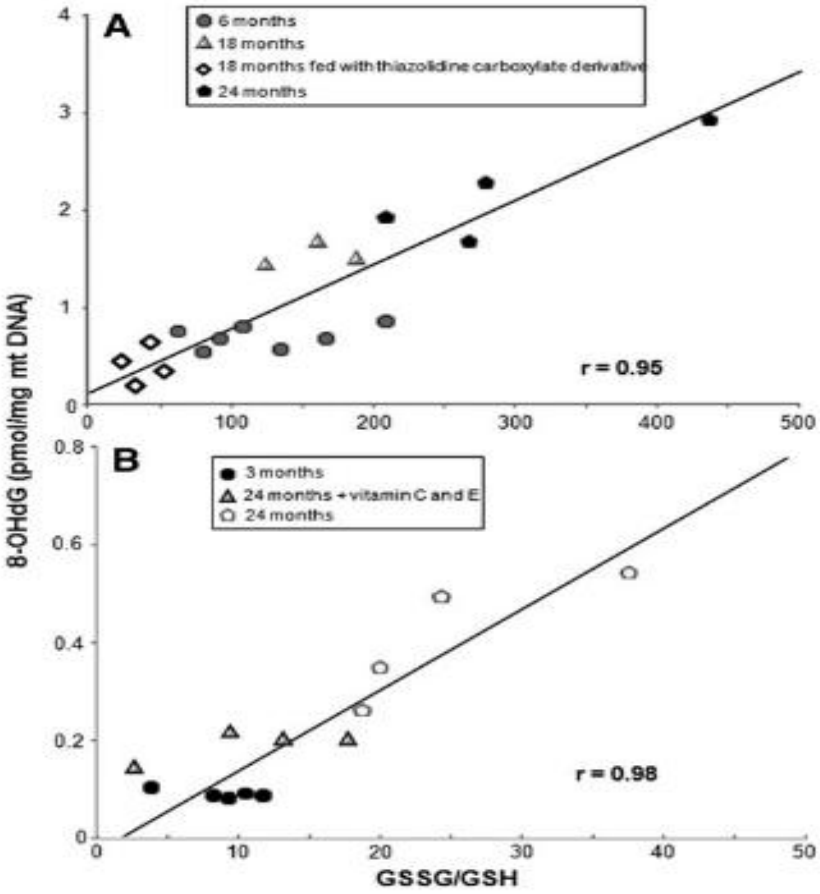

FIG. 2 Relationship between mitochondrial GSSG/GSH

[Oxidized Glutathione/Reduced Glutathione] and levels of 8-OHdG [Oxo-8-deoxyguanosine] in mitochondrial DNA from livers of mice (A) and rats (B). Lines of regression and correlation coefficients (r) are shown. Redrawn from García de la Asunción et al. (2002).

Evidence Against the Free Radical Theory of Aging

In pure logical terms, a single result that does not fit with a theory is sufficient to disprove its general validity (Popper, 2018). This, of course, does not indicate that all experiments that support the theory are invalid, or even that the theory is not a "useful" one in that it has fostered research and it has offered a general framework for many experiments, some of which have been discussed above. When studying the evidence that does not support the free radical theory of aging, it is important to highlight the biology of naked mole rats. These animals live much longer than ordinary rats. The maximal life span of these animals may go as far as 25 years compared with 3–4 years in ordinary rats. According to the free radical theory of aging, oxidative damage should be much less in the

naked mole rats than in ordinary rats. This is not the case and, in fact, the naked mole rats show higher oxidative damage than the control, ordinary rats (Andziak et al., 2021). However, one must keep in mind that the naked mole is adapted to limited oxygen tension in the tunnels where it lives and has a low metabolic rate. Moreover, work by Perez et al. has shown that these animals exhibit increased efficiency of cysteine reduction mechanisms leading to improved sensitivity to protein repair and degradation (Perez et al., 2019). Thus, even if increased longevity coincides with a more oxidized state, the naked mole rat does not constitute an irrefutable proof of failure of the free radical theory of aging. On the other hand, there are mutants of Caenorhabditis elegans, for instance, the NUO-6 that show higher oxidative stress than the controls and that live longer than the controls (Yang & Hekimi, 2023). However, when NUO-6 mutants are treated with a powerful antioxidant, such as N-acetyl cysteine, then they are under less oxidative stress, but they also live less.

- **The Radical Signaling Disruption Theory of Aging**

In the introduction to this review, we have reproduced the formulation of the free radical theory of aging by Denham Harman in the 1960s (Harman, 1966). Harman proposed that aging and age-associated diseases could be attributed to the deleterious effects of free radicals. Present-day evidence does not support this statement. An interesting modification of the free radical theory of aging has been put forward by Sohal and Orr (Sohal & Orr, 2021). They propose "The redox stress theory of aging." If free radicals cause a stress that cells can cope with, then damage will not occur because antioxidant defenses will overwhelm such stress. Only if the stress is of such magnitude that it deranges cellular signaling mechanisms, age-associated damage will take place. Keeping this in mind, we would like to propose "The cell signaling disruption theory of aging." This theory postulates that ROS cause aging inasmuch as they alter—sometimes irreversibly—the signaling network of the cell. If the cell can cope with the stress caused by relatively mild action of ROS, then adaptation takes place and damage does not occur. If, however, the cell is overwhelmed by the action of radicals, subcellular damage and aging will take place. Indeed, radicals serve as signals and interaction between them is tightly balanced. For instance, nitric oxide (NO) [Nitric Oxide], a radical, is a powerful vasodilator (Ignarro, 2006). But it reacts swiftly with superoxide (another radical) yielding peroxynitrite (Pryor & Squadrito, 2005). The latter does not have vasodilating properties and thus, interaction with superoxide prevents the vasodilating effects of NO. Steady state levels of superoxide are elevated in aging as shown by our group (Author et al., 1995), as well as by

that of Ames and coworkers (Ames et al., 1995). This results in more NO being removed and is important to explain the low vascular reactivity of the old. Free radicals are involved in the age-associated damage to macromolecules and this may cause a derangement in ROS-mediated cell signaling causing stress and diseases. This is exemplified, for instance, by the altered reactivity of NF-ϰB [Nuclear Factor kappa-light-chain-enhancer of activated B cells] or activator protein 1 in aging (Troen, 2020) by the lack of reactivity of p38 and PGC-1α [Peroxisome Proliferator-Activated Receptor Gamma Coactivator 1-alpha] (Derbre et al., 2020). A "modified" free radical theory of aging, which is in keeping with the majority of experiments reported in this review, is that aging is caused by a disruption of the whole signaling network involving ROS. This "modified" theory does not imply that radicals always cause damage (as in the original theory) or that the more oxidative stress the less longevity. There may be interventions, completely independent of ROS (like up-regulation of telomerase) that promote longevity without affecting ROS or oxidative stress.

Finally, our view is that, in general terms, we cannot support the idea of proposing antioxidant supplementation for the general population. There are many cases (like for instance exercise training) in which antioxidant supplementation is bad for you. And in general terms, it is much better to increase endogenous defences by nutritional or physiological manipulation than administering antioxidant compounds, such as vitamin C or E.

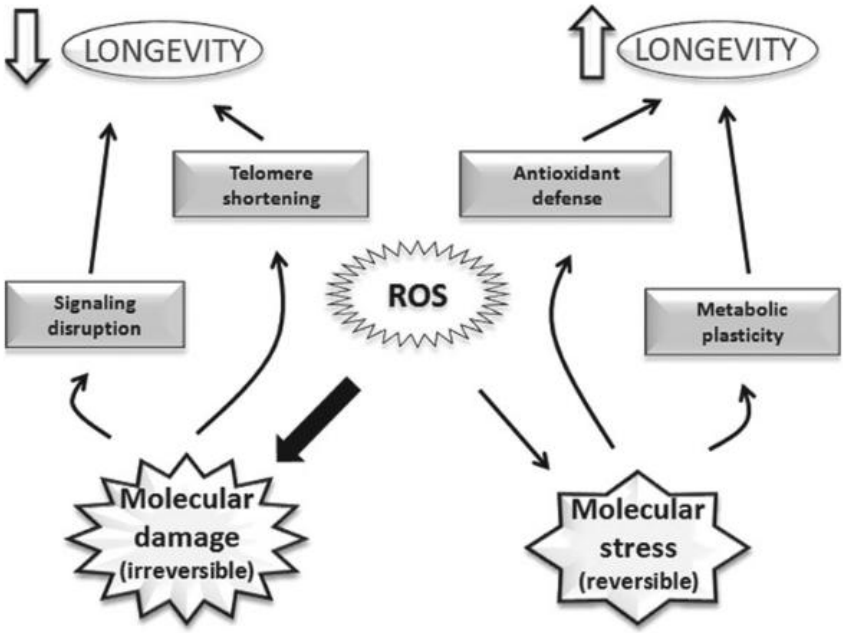

FIG. 3. The double edge sword of free radicals.

They have hermetic effects. When radicals cause severe effects on biomolecules it causes damage (i.e., irreversible alterations), whereas when the aggression is mild, a stress is caused and this may have signalling effects, as well as the already-mentioned hormetic effects.

Antioxidant Defenses

Antioxidants are substances capable of donating an electron to unquenched free radicals to neutralize them and reduce their potential for harm (Smith & Johnson, 2025). Cellular damage is mostly delayed or prevented by these antioxidants' ability to scavenge free radicals. Due to their low molecular weight, these antioxidants can easily interact with some free radicals to stop a series of reactions. Antioxidants can be divided into several major categories, including water-soluble and liposoluble, biological, and synthetic. Water-soluble antioxidants are found in vegetables and fruits and are best absorbed by the body. On the other hand, the body quickly removes them through urine. Both vitamin C and polyphenols are examples of water-soluble antioxidants. Antioxidants that are absorbed in the presence of lipids are known as liposoluble or fat-soluble antioxidants. Therefore, without lipids, the body is unable to absorb and utilize these antioxidants. However, note that they are difficult to remove from cells and tissues and can build up over time, preventing you from getting adequate amounts. A prime example of a fat-soluble antioxidant is vitamin E. There are two categories of antioxidants, namely, biological antioxidants and synthetic antioxidants. Enzymatic and nonenzymatic biological antioxidants are further classified into two categories. Antioxidants-involved enzymes can break down ROS (Reactive Oxygen Species), thus protecting the body from free radical damage. SOD (Superoxide Dismutase), catalase, and GPx (Glutathione Peroxidase) are the main classes of enzymatic antioxidants. On the other hand, GR (Glutathione Reductase) and TRxR (Thioredoxin Reductase) are the secondary enzymes of antioxidants.

Primary Enzymatic Antioxidants

In human biological systems, SOD (Superoxide Dismutase) contains external body fluids and aerobic cells (Kumar & Patel, 2025; Thompson et al., 2025). This enzyme accelerates the radical conversion of superoxide anions into H2O2 (Hydrogen Peroxide) and oxygen (Chen & Lee, 2025; Gupta & Sharma, 2025). There are three main types of SOD (all bound to metal cofactors).

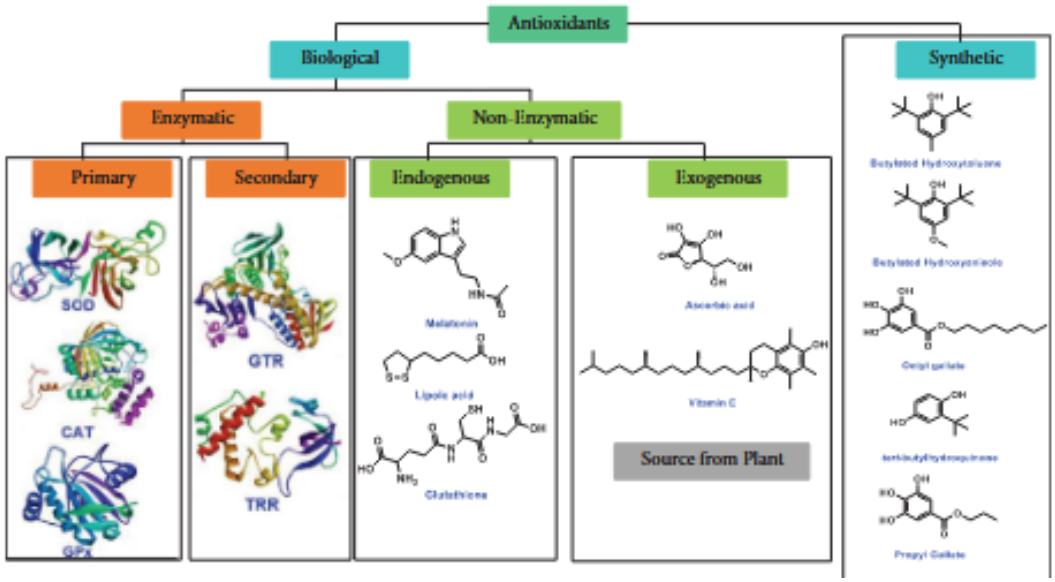

Fig. 4 schematic approaches for the classification of antioxidant

Glutathione has thiol groups' antioxidant characteristics because it can be oxidized and reduced reversibly and has a thiol group in its system. Glutathione is a cellular antioxidant because of its importance in maintaining the cell's redox state and its high concentration. Glutathione is a peptide that is produced in cells from amino acids. Glutathione can directly react with oxidants in cells and diminish other metabolites (Davis & Singh, 2025). Coenzyme Q10 (2, 3-dimethoxy-5-methyl-6-poly-isoprene Para benzoquinone), often called ubiquinone, is generated via isoprenoid oligomerization and the mevalonate pathway that begins with IPP (Isopentenyl Pyrophosphate) and DMAPP (Dimethylallyl Pyrophosphate) (Wilson & Brown, 2025). Ubiquinone is an antioxidant molecule that is fat-soluble and protects the body from lipid peroxidation and oxidative damage. It can scavenge certain ROS and regenerate other oxidized antioxidants (Taylor & Kim, 2025).

Exogenous Nonenzymatic Antioxidants

Extracorporeal or exogenous antioxidants must be taken regularly because their synthetic pathways are usually in plant cells or microorganisms. Vitamins, flavonoids, and carotenoids are examples of extracorporeal molecules that exhibit antioxidant activity. DHA (Dehydroascorbic Acid) can be produced by two-electron oxidation of vitamin C or AA (Ascorbic Acid). AA is found in tomatoes, pineapples, watermelons, and all citrus fruits (Figure 3). The main function of AA is to scavenge ROS in the form of O2 (Superoxide), H2O2 (Hydrogen Peroxide), organic peroxides, HClO (Hypochlorous Acid), or OH• (Hydroxyl Radical) (Patel & Gupta, 2025). On the other hand, other vitamins such as vitamin E can be defined as highly bioavailable water-soluble vitamins with antioxidant

properties (Brown & Lee, 2025). α-Tocopherol protects membranes from oxidation by interacting with radicals in the peroxidation reaction chain. This can prevent continued propagation and remove free radical intermediates (Smith & Taylor, 2025). Flavonoids can be classified as compounds with high oxidant activity because they are highly effective in reducing ROS such as superoxide anions and peroxyl radicals through the mechanism of HAT (Hydrogen Atom Transfer) (Kumar & Chen, 2025; Thompson & Patel, 2025). Flavonoids also can chelate some metal ions and block the formation of free radicals such as quercetin, an example of a flavonoid that can be an iron chelator and iron stabilizer (Johnson & Gupta, 2025). Catechol derivatives can also block the Fenton reaction in the formation of other free radicals (Brown et al., 2025; Davis & Kim, 2025). Carotenoids have the biological activity of scavenging ROS. β-Carotene, one of the most abundant carotenoids found in carrots, pumpkins, and mangoes, has been proposed as a cancer chemopreventive agent (Wilson & Sharma, 2025; Taylor & Singh, 2025).

Synthetic Antioxidants

Synthetic antioxidants interact with free radical species through metal ion binding, oxygen deactivation, radical to non-radical species conversion, and UV (Ultraviolet) radiation saturation (Smith & Brown, 2025). Examples of synthetic antioxidants include PG (Propyl Gallate), OG (Octyl Gallate), TBHQ (Tert-Butylhydroquinone), BHT (Butylhydroxytoluene), and BHA (Butylhydroxyanisole) (Figure 3) (Johnson & Patel, 2025; Kumar & Lee, 2025). BHT is less effective than BHA due to the two sterically hindered tert-butyl groups. BHA is very effective in controlling the oxidation of short-chain lipids. BHA and BHT are less effective in inhibiting ROS activity when compared to TBHQ (Chen & Gupta, 2025; Thompson & Singh, 2025). This is due to the two para-hydroxyl groups responsible for the antioxidation activity of TBHQ (Davis & Taylor, 2025). PG is known as a safe antioxidant because it can preserve oils and foods from spoilage caused by peroxide formation (Kumar & Lee, 2025). In addition, PG stabilizes foods and cosmetics. OG can be defined as a food preservative composed of gallic acid and 1-octanol ester. BHT and BHA are very commonly used antioxidants in the diet industry (Patel & Sharma, 2025).

Single Electron Transfer via Proton Transfer (SET-PT)

SET-PT (Single Electron Transfer via Proton Transfer) is one of the mechanisms of action of antioxidants in counteracting free radicals. The mechanism of SET (Single

Electron Transfer) is the provision of one electron to the free radical compound so that the free radical becomes its less reactive anion form. After that, the anion of the free radical will react with hydrogen ions to form a stable compound (Kumar & Brown, 2025). In this mechanism, the antioxidant donates one electron to the free radical so that the antioxidant becomes radicalized; therefore, the ability to donate electrons is crucial to the antioxidant activity. Here is the general process of SET:

$$A - OH + B\bullet \longrightarrow A - OH\bullet^{+} + B^{-}$$ (Gupta & Lee, 2025).

Anions are an energetically stable species with an odd number of electrons resulting from electron transfer mechanisms. Radical cations ($A - OH\bullet^{+}$) are relatively stable and difficult to react with other chemical species (Thompson & Sharma, 2025). Aromatic ring structures produced by the reaction with radicals in $A - OH\bullet^{+}$ can be dispersed throughout the molecule (Davis & Chen, 2025). As shown in Figure 6, antioxidant species can cause to stabilize radicals. The most important limitation in determining radical irrigation in the single electron transfer process comes from the IP (Ionization Potential). Lower IP value makes it easier to withdraw electrons and react with radicals, resulting in increased antioxidant activity (Wilson & Patel, 2025).

Transition Metal Chelation (TMC)

TMC (Transition Metal Chelation) is an antioxidant mechanism to chelate metals that form multiple coordination bonds between organic molecules. It involves the formation or presence of two or more separate coordinate bonds between a polydentate (multiple bonded) ligand and a single central metal atom. This process often occurs in the human body (Taylor & Kumar, 2025).

Flavonoids utilize the TMC mechanism to exert their antioxidant activity (Smith & Gupta, 2025). Such processes are catalyzed by switchover metals such as Fe (Iron), Co (Cobalt), Mn (Manganese), and Cu (Copper). Chelation, on the other hand, is susceptible to specific conditions, such as metal ions not attaching to proteins or other chelator molecules. As shown in Figure 7, the formation of OH• (Hydroxyl Radical) in the Fenton reaction can be reduced by adding metals or metal chelators. This can suppress the reduction of Fe3+ (Ferric Iron) (Brown & Singh, 2025). Flavonoids contain chelating properties that bind to metal ions within structural cells and prevent oxidation. Some flavonoids have the opportunity to bind heavy or transitional metal ions such as iron and

copper that are important in free radical generation and oxidation processes (Chen & Thompson, 2025).

Flavonoids have the adequate ability to combat incoming free radicals. Nevertheless, the nature of the flavonoid structure can be an important consideration in the reducing power and chelating potential of metals. For example, the metal chelating and free radical scavenging properties of catechol depend on the influence of two hydroxyl groups, two conjugated bonds on the active carboxylic group, and the B ring (Smith & Kumar, 2025).

Actual Limitations of Flavonoids

The current limitations on the utilization of flavonoids in medical, pharmaceutical, food, and cosmetic sectors are primarily influenced by the following two key factors:

Chemical and biophysical attributes, encompassing issues like poor solubility, chemical stability, bioavailability, and metabolic stability (including hepatic, intestinal, and intestinal microflora metabolism).

Challenges associated with plant production, including the low yield of these secondary metabolites relative to biomass and complexities involved in enhancing biosynthesis, as well as intricate methods for isolation, extraction, and purification (Johnson & Patel, 2025).

A primary issue concerning flavonoids is their limited bioavailability. Following oral intake, only a small fraction of flavonoids is absorbed in the upper gastrointestinal tract, including the oral cavity, while a considerable portion reaches the small intestine and can interact with the intestinal microbiota in the colon. Some flavonoids may undergo metabolism by liver enzymes, such as CYP (Cytochrome P450), leading to the formation of active metabolites (Brown & Taylor, 2025; Gupta & Lee, 2025). The absorption of flavonoids in the human body varies depending on the molecular structure conformation and pH levels. Once absorbed by the intestinal epithelium, flavonoids undergo transformation into conjugated metabolites, such as glucuronides, sulfates, and methylated metabolites. These transformations occur initially in the intestine and subsequently in the liver (Thompson & Sharma, 2025). The aglycones of flavonoids, characterized by their small molecular size and high hydrophobicity, enter the liver through the hepatic portal vein, where two primary metabolic reactions occur, i.e., oxidation reactions facilitated by CYP enzymes (phase I) and conjugation reactions (phase II). Flavonoid glycosides, on the

other hand, have higher hydrophilicity and molecular weight and can only be absorbed after undergoing hydrolysis into aglycones or phenolic acids by the intestinal microbiota. The rapid metabolic elimination of flavonoids underscores the importance of developing innovative approaches to enhance their delivery (Davis & Chen, 2025; Wilson & Patel, 2025).

Future Directions of Flavonoid Compounds

Flavonoids, vital secondary metabolites synthesized by plants and microorganisms, boast a multitude of biological activities. The recognition of these properties has sparked a growing interest in leveraging flavonoids across various industries including medical, pharmaceutical, and cosmetic, food, and nutraceutical sectors. Current research and development endeavors surrounding flavonoids primarily focus on their identification, extraction techniques, exploration of novel functionalities, and applications for promoting health. Techniques such as molecular docking, advanced extraction methodologies, and integration into diverse delivery systems are being employed to enhance flavonoid yield, solubility, and stability. These innovations pave the way for the advancement of new industrial manufacturing technologies aimed at harnessing the potential benefits of flavonoids (Taylor & Patel, 2025). One prospective solution to tackle the limitations associated with flavonoids involves the extensive adoption and advancement of nanotechnology. Nanotechnology presents promising prospects across various scientific domains including medicinal chemistry, healthcare, and pharmaceutical science. The unique characteristics of nanoparticles, such as their minute size and large surface area, render them particularly suitable for applications in the medical and pharmaceutical sectors. Their capability to enhance the efficacy of plant-derived products, augment the production of secondary plant metabolites compared to biomass, mitigate adverse effects, and boost bioavailability makes them an ideal avenue for addressing flavonoid challenges (Kumar & Lee, 2025). Nanovesicle systems such as liposomes and ethosomes, along with cyclodextrins and dendrimers, micro- and nanoparticles, nanostructured lipid carriers, SLN (Solid Lipid Nanoparticles), and nano micelles represent prevalent examples of biocompatible and biodegradable nanoparticles (Thompson & Singh, 2025). Another research investigation delves into the distinctive attributes of nano micelles, which facilitate efficient delivery and enhanced bioavailability of diverse nutrients, including flavonoids. Nano micelles offer numerous advantages stemming from their size and structural makeup. They bolster drug stability, shield them from elimination by the MPS (Mononuclear

Phagocyte System), and result in extended blood circulation (Brown & Sharma, 2025). There is undeniable evidence supporting the use of nanotechnology for precisely targeting the delivery of flavonoids to enhance their bioavailability. Nonetheless, thus far, these delivery systems for flavonoids have mainly been replicated in laboratory settings (in vitro), with limited application in human models. In the foreseeable future, conducting clinical trials holds the potential to significantly enhance both the efficacy and safety profiles of utilizing flavonoids as novel therapeutic approaches for human diseases (Chen & Gupta, 2025).

Conclusion

Free radicals can be produced by normal metabolism in the body and affect human biological systems. When the balance of pro-oxidant and antioxidants is disturbed, oxidative stress accumulates and causes severe damage to structural cells and tissues such as lipids, protein, and nucleic acids. This causes tissue damage in a variety of illness situations, including diabetes, neurological diseases, cancer, and others, hastening disease development. Flavonoids hold promise as natural compounds with potential health benefits, but their clinical applications require rigorous investigation to overcome existing limitations. Global perspectives from various continents provide valuable insights into dietary patterns and their associations with health outcomes. Future research should focus on addressing challenges in study design, enhancing bioavailability, and elucidating mechanisms of action to unlock the full potential of favonoids in promoting human health. In this review, we focused on favonoids as potent antioxidant because favonoids as secondary metabolites sourced from plants can prevent the development of free radicals. The presence of hydroxyl groups on the favonoids structure becomes a determining factor in the scavenging of free radicals. In fact, the position of the hydroxyl group on the B ring can be a metal chelation agent that makes the favonoids molecular structure a good antioxidant.

Recommendation

- It is important to remember that the body requires both free radicals and antioxidants. Having too many or too few of either may lead to health problems.

Lifestyle and dietary measures that may help reduce oxidative stress in the body include:

i. Eating a balanced diet rich in fruits and vegetables
ii. Limiting intake of processed foods, particularly those high in sugars and fats
iii. Exercising regularly
iv. Quitting smoking
v. Reducing stress
vi. Avoiding or reducing exposure to pollution and harsh chemicals
vii. Maintaining a healthy body weight

• Oxidative stress is a state that occurs when there is an excess of free radicals in the body's cells. The body produces free radicals during normal metabolic processes.

• Oxidative stress can damage cells, proteins, and DNA, contributing to aging. It may also play a role in the development of a range of health conditions, including diabetes, cancer, and neurodegenerative diseases such as Alzheimer's.

• The body naturally produces antioxidants to counteract these free radicals. A person's diet is also an important source of antioxidants.

• Making certain lifestyle and dietary changes may help reduce oxidative stress. These may include maintaining a healthy body weight, regularly exercising, and eating a healthy diet rich in fruits and vegetables.

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