

Understanding the Role of Free Radicals, Oxidative Stress, and Antioxidants: A Comprehensive Review

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Abstract: Oxidative stress, resulting from an imbalance between free radicals and antioxidants, profoundly influences physiological processes and disease pathogenesis. Free radicals, possessing unpaired electrons, exhibit transient stability but high reactivity, originating from endogenous metabolic processes and exogenous sources like environmental toxins. While essential at low levels, their accumulation leads to oxidative stress, contributing to cellular damage and disease progression. Antioxidants, including enzymatic (e.g., superoxide dismutase, catalase) and non-enzymatic (e.g., glutathione, vitamins C and E) varieties, play pivotal roles in neutralizing free radicals and mitigating oxidative damage. Natural antioxidants, particularly phenolic compounds abundant in plant-based foods, offer diverse health benefits, including anti-inflammatory, anticancer, and antimicrobial properties. Synthetic antioxidants like BHA and BHT are also utilized in food preservation. This review provides insights into the sources, types, and physiological impacts of free radicals, oxidative stress, and antioxidants. Understanding these mechanisms is essential for developing therapeutic interventions against oxidative stress-related disorders and promoting overall health.

Keywords: free radicals; oxidative stress; antioxidants; enzymatic antioxidants; non-enzymatic antioxidants; phenolic compounds; synthetic antioxidants.

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1. Introduction

In the intricate landscape of biological systems, a delicate equilibrium exists between oxidants and antioxidants, essential players in maintaining cellular homeostasis [1]. At the heart of this balance lie free radicals, molecular entities with unpaired electrons, possessing beneficial and detrimental roles within the body [2]. While pivotal in cellular signaling and immune response regulation, excessive production of free radicals can tip this equilibrium towards oxidative stress [3], a state implicated in numerous pathological conditions ranging from neurodegenerative diseases to cancer [4].

Antioxidants are central to combating oxidative stress, a diverse array of molecules that neutralize free radicals, safeguarding cellular integrity [5]. Enzymatic antioxidants, such as superoxide dismutase and catalase, alongside non-enzymatic counterparts like glutathione and vitamins C and E, form a robust defense network against oxidative damage [6]. Moreover, natural compounds abundant in fruits, vegetables, and herbs, notably phenolic compounds, offer multifaceted health benefits owing to their antioxidant properties [7].

This review aims to unravel the complexities surrounding free radicals, oxidative stress, and antioxidants. By exploring their sources, physiological roles, and implications in health and disease, we endeavor to provide a comprehensive understanding of these critical components in biological systems. Such insights are paramount for devising effective strategies to combat oxidative stress-related disorders and promote overall well-being in individuals of all ages.

2. Oxidative Stress

The imbalance between pro-oxidants and antioxidants is called oxidative stress [8]. This is caused by a lack of antioxidants or by the accumulation of free radicals, primarily the reactive oxygen species (ROS) and the reactive nitrogen species (RNS); after the stimulation of the endogenous and external environment, oxidative stress could lead to cell death and the dysfunction of physiology, which could ascribe to DNA damage, inflammation [9].

3. Free Radicals

Free radicals are atoms, molecules, or molecular fragments characterized by one or more unpaired electrons, conferring them with high reactivity and transient stability [10]. Typically uncharged, these highly reactive species have a short lifespan of less than 10^{-6} seconds within biological systems. Reactive oxygen species, including certain oxygen species [11], although initially non-reactive, can serve as precursors to free radical generation. Extensive research demonstrates that free radicals inflict oxidative damage upon various biomolecules within living organisms, including proteins, lipids, and nucleic acids [12]. This oxidative damage has been implicated in the pathogenesis of numerous diseases, such as respiratory disorders, cancer, cardiovascular diseases, atherosclerosis, and neuronal degeneration[3].

3.1. Types of free radicals.

They are generally classified (Table 1) into two major categories of radicals: reactive oxygen species (ROS) and reactive nitrogen species (RNS), which include the free radicals and the non-free radicals, where the first ones are more reactive and less stable than the second one because they contain at least one unpaired electron in the shells around the aromatic nucleus [3].

Table 1. Some examples of reactive oxygen and nitrogen species [13].

Reactive oxygen species (ROS)			
Radicals	Symbol	Non-radicals	Symbol
Superoxide	$O_2^{\bullet-}$	Hydrogen peroxide	H_2O_2
Hydroxyl radical	OH^{\bullet}	Hypochlorous acid	$HOCl$
Peroxyl radical	ROO^{\bullet}	Hypobromous acid	$HOBr$
Alkoxyl radical	RO^{\bullet}	Ozone	O_3
Hydroperoxyl radical	HO_2^{\bullet}	Singlet oxygen	$^1\Delta_g$
Lipid peroxyl radical	LOO^{\bullet}	Lipid peroxide	$LOOH$
Reactive nitrogen species (RNS)			
Radicals	Symbol	Non-radicals	Symbol
Nitric oxide	NO^{\bullet}	Nitrous acid	HNO_2
Nitrogen dioxide	NO_2^{\bullet}	Nitrosylation	NO^+
		Nitroxyl anion	NO^-
		Dinitrogen tetroxide	N_2O_4
		Dinitrogen trioxide	N_2O_3
		Peroxynitrite	$ONOO^-$

3.2. Sources of free radicals.

Free radicals are produced either from normal cell metabolism in situ, which means internal sources, or from external sources [14].

3.2.1. Internal sources.

3.2.1.1. Mitochondria.

They are known as the "powerhouse of a cell" because they are responsible for 90% of the energy production in cells [15]. In addition, mitochondria are the main source of reactive oxygen species [16] because there are about 90% to 95% of cellular oxygen is used up in oxidative phosphorylation, and 3% from that pool can be converted to superoxide (Figure 1). Also, mitochondria produce H₂O₂ and OH• by Fenton reaction and dismutation of O₂ [17].

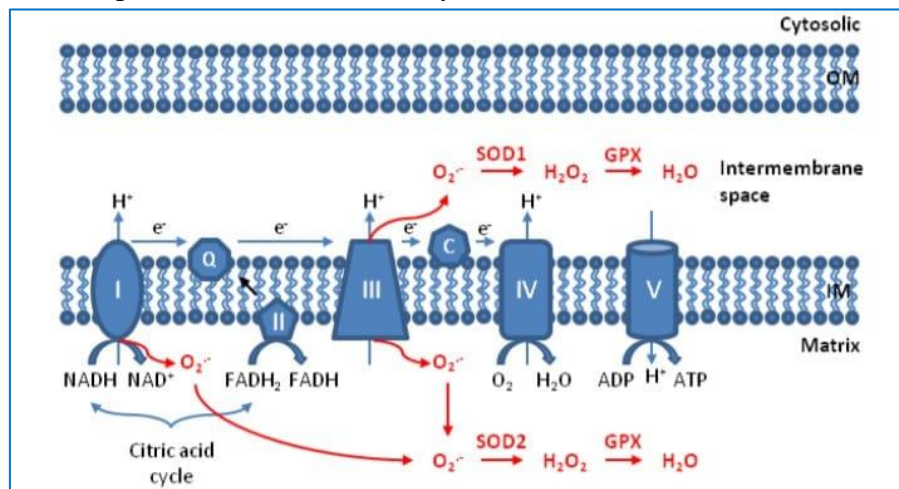


Figure 1. Production and disposal of mitochondria Reactive oxygen species (ROS) [18].

3.2.1.2. NADPH oxidase.

The NADPH oxidase (Figure 2) is the major enzymatic source of reactive oxygen species (ROS) generation in cells [19]. Using the NADPH as the electron donor, the NADPH oxidase catalyzes the production of superoxide by the reduction of oxygen by the following reaction (Equation 1):

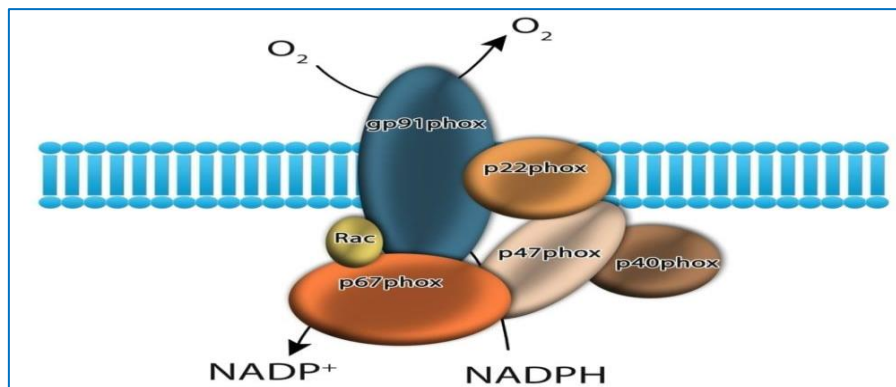


Figure 2. Schematic diagram of the structure of the active NADPH oxidase complex [17].

3.2.1.3. Lipoxygenases.

This enzyme is one of the reactive oxygen species (ROS) sources in blood vessel walls [20]. Also, it intervenes in the production of some kinds of reactive oxygen species (ROS) by stimulating the LBs [21], which suggests that LTB₄ treatment of fibroblasts and neutrophils results in reactive oxygen species (ROS) generation [17].

3.2.2. External sources.

According to [22], these are some of the external sources of free radicals: Environmental pollutants, Cigarette smoke, Radiation, Certain drugs, Industrial solvents, Alcohol, Ultraviolet light, Ozone, Pesticides, and anesthetic solvents.

3.3. Damages of free radicals.

In fact, free radicals with a small concentration have a very important physiological role, for example, expansion of blood vessels [3]. Still, the continual influx and generation of reactive oxygen species (ROS) either from internal or external sources would cause oxidative damage of cellular components and may impair many cellular functions [11]; this damage could be in:

3.3.1. Lipids.

As we know, cellular membranes are highly rich in unsaturated fatty acids, which is why they are vulnerable to oxidative damage. This damage has three stages and is known as lipid peroxidation[23].

3.3.2. Proteins.

Proteins are the most common targets for attack by Reactive oxygen species (ROS), predominantly by the OH[•], RO[•], and nitrogen-reactive radicals causing damage[24]. Hydrogen peroxide and superoxide radicals have weak effects on proteins except for proteins containing Sulfhydryl groups[25]. Following the oxidation, proteins are susceptible to many changes in their function, which include inactivation chemical fragmentation [11].

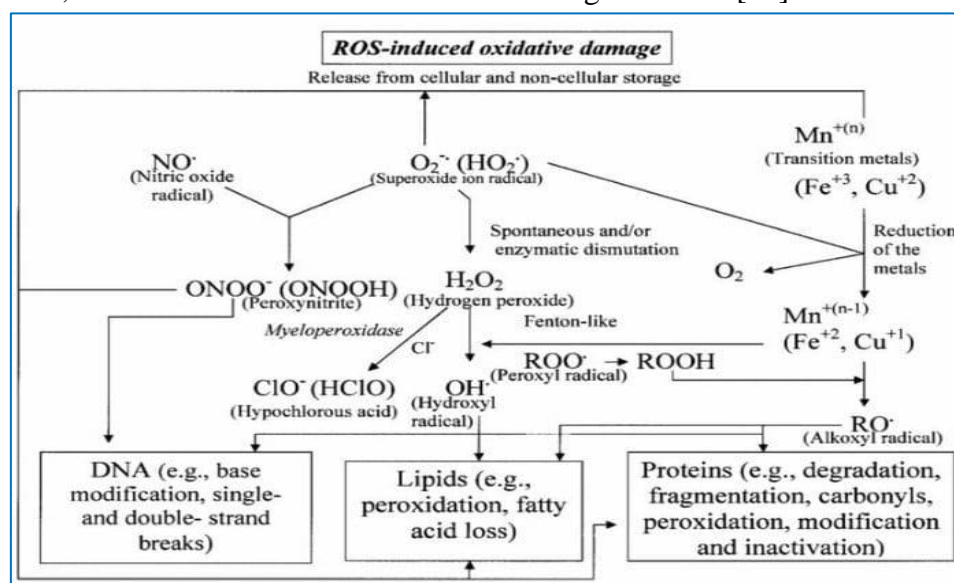


Figure 3. Reactive oxygen species (ROS)-induced oxidative damage [27].

3.3.3. DNA.

DNA is a very sensitive molecule for Reactive oxygen species (ROS) (Figure 3), which can cause several types of damage to it, such as modification of DNA bases, loss of purines (apurinic sites), DNA-protein cross-linkage, damage to the deoxyribose sugar and damage to DNA repair system [26].

4. Antioxidants

Antioxidants are defined as molecules that dispose of, scavenge, and inhibit the formation of Reactive oxygen species (ROS) or oppose their actions [28]. In other words, antioxidants are chemicals that bind with free radicals and nullify their effect by causing damage to biological molecules. They bind with them by giving up their electrons. This results in the termination of oxidative chain reactions, and the free radicals are no longer able to attack the cell. Antioxidants attain a state of free radicals after donating their electrons. It can accommodate the change in electrons without becoming reactive, which is why they are not harmful [29].

4.1. Classification of antioxidants.

Antioxidants can be divided into two dominant categories based on their sources:

4.1.1. Natural antioxidants.

According to [11], this category is the most important because they directly act on free radicals either by decomposing, scavenging, or converting free radicals to less reactive forms. This defense mechanism involves 2 groups.

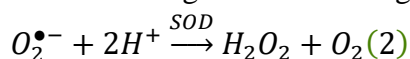
4.1.1.1. Enzymatic antioxidants.

The enzymatic antioxidants include superoxide dismutase (SOD), catalase, glutathione reductase (GRx) and glutathione peroxidase (GPx).

4.1.1.1.1. Superoxide dismutase (SOD).

Superoxidedismutases are metal-containing enzymes that catalyze the conversion of two superoxides into oxygen and hydrogen peroxide, which is less toxic than superoxide [30].

In other words, Superoxide dismutase (SOD) are proteins that stimulate the dismutation of superoxide to hydrogen peroxide according to the following reaction equation (2) [31]:



They exist in three forms in mammalian tissues and tissue distribution [32]: Copper zinc superoxidedismutase (CuZnSOD), Manganese superoxidedismutase (MnSOD), and extracellular superoxide dismutase (ECSOD).

4.1.1.1.2. Catalase (CAT).

Catalase catalyzes the decomposition of hydrogen peroxide to molecular oxygen and water, thereby completing the detoxifying reaction started by superoxide dismutase(SOD)[33].

Catalase was the first antioxidant enzyme to be characterized. It is located mostly within the peroxisomes of cells, which contain most enzymes capable of generating hydrogen

peroxide. It consists of four protein subunits, each containing a heme group and molecule of NADPH [34].

It may be found in bone marrow, heart, kidney, liver, blood, and mucous membranes, as in mitochondria and endoplasmic reticulum [35].

4.1.1.1.3. Glutathione reductases (GRx).

Glutathione reductases (GRx) is a flavine nucleotide-dependent enzyme [34], and it has a similar tissue distribution to glutathione peroxide [11]. It has been found in the prostate gland, seminal vesicles, and Sertoli cells[13].

The Role of glutathione reductases (GRx) is to generate glutathione (GSH) from GSSG using NADPH in order to increase the ratio of reduced to oxidized glutathione[36].

4.1.1.1.4. Glutathione peroxidases (GPx).

They are a family of selenium-containing enzymes that catalyze the reduction of H₂O₂ and organic peroxides, including phospholipid peroxides [37].

It is found in the liver and kidneys and is found in almost all tissues. Its subcellular location is usually the cytosol and mitochondria. It catalyzes the oxidation of reduced glutathione (GSH), decomposing hydrogen peroxide or other species, such as hydrogen peroxide and lipid hydroperoxide, and acts as a substrate for these enzymes [34].

4.1.1.1.5. Other enzymatic antioxidants.

Superoxide dismutase (SOD), catalase, glutathione reductase (GRx), and glutathione peroxidase (GPx) were the most known enzymatic antioxidants. Still, there are other enzymes may also participate in the enzymatic control of oxygen radicals and their products, such as Glutathione S-transferase (GST), Ceruloplasmin, Transferring, and Hemeoxygenase (HO)[13].

4.1.1.2. Non-enzymatic antioxidants.

They are also known as synthetic antioxidants or dietary supplements[13]. They are usually low-molecular-weight antioxidant (LMWA) compounds capable of preventing oxidative damage either by directly interacting with Reactive oxygen species (ROS) or indirectly by chelating metals [11].

4.1.1.2.1. Glutathione (GSH).

An endogenous tripeptide protects cells against free radicals by donating either a hydrogen atom or an electron [38]. It is the most abundant thiol protein in mammalian cells, and this molecule has three precursors: cysteine, glutamine acid, and glycine [39]. Glutathione exists as GSH in its reduced form, and 2 of the GSH molecules can be joined via oxidation at their Sulfhydrylgroups of the cysteine residue into a disulfide bridge to form GSSG which is the oxidized form [11].

4.1.1.2.2. Ascorbic acid (Vitamin C).

This vitamin (Figure 4) is considered one of the organism's most powerful antioxidant agents due to its capacity to donate two electrons from its double link at positions two and three in such a way that it interacts with FR, blocking their harmful effects[40]. It is a water-soluble

vitamin, one of the important molecules the human body needs [41]. It is widely distributed in various tissues [42]. This molecule scavenges the superoxide radical anion, hydrogen peroxide, hydroxyl radical, singlet oxygen, and reactive nitrogen oxide. Vitamin C has been found in citrus fruits, peppers, strawberries, tomatoes, broccoli, Brussels sprouts, and other leafy vegetables [13].

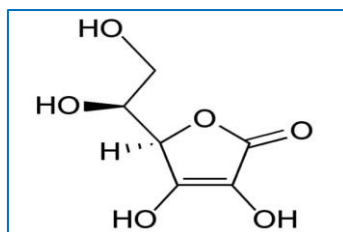


Figure 4. Chemical structure of ascorbic acid or vitamin C [43].

4.1.1.2.3. α -tocopherol (Vitamin E).

It is a fat-soluble vitamin with high antioxidant properties [42]. Vitamin E involves 2 subgroups: tocopherols and tocotrienols [13, 43]. These subgroups can further be divided into four lipophilic molecules, meaning there are eight isoforms of Vitamin E [34, 42]. The major difference between tocopherols and tocotrienols is the side chain. The first one has a saturated phytol tail, while the second one possesses an unsaturated side chain [42].

Vitamin E (Figure 5) functions as an efficient "chain breaker" during lipid peroxidation in cell membranes and various lipid particles, including low-density lipoprotein (LDL). Its Role is to scavenge lipid peroxy radicals and to terminate the lipid peroxidation chain reactions [11]. This vitamin has been found in high concentrations in palm oil, rice bran, and oily plants [43].

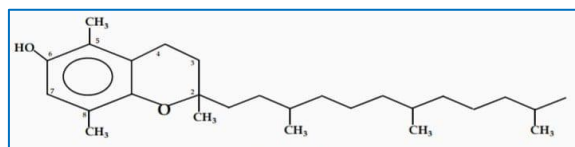


Figure 5. Chemical structure of vitamin E (α -tocopherol) [40].

4.1.1.2.4. Retinol (Vitamin A).

Vitamin A (Figure 6), also called trans-retinol, is an isoprenoid alcohol that performs several important functions in the organism [40]. It is produced as a result of the breakdown of β -carotene and is a carotenoid produced in the liver [34]. As such, it is considered a vital antioxidant that prevents human low-density lipoprotein (LDL) against copper-stimulated oxidation, eliminates FR, and protects the DNA in its mutagenic action [11, 40].

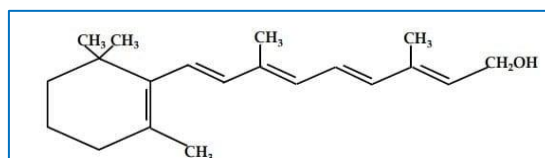


Figure 6. Chemical structure of Vitamin A (Retinol) [40].

4.1.1.2.5. Other non-enzymatic antioxidants.

There are other substances that may contribute to the maintenance of oxidative homeostasis, such as bioflavonoids, flavonoids, carotenoids, lycopene, hydroxycinnamates, carnitine, taurine, selenium, albumin, uric acid, lipoic acid [11, 13].

The most common and widely used antioxidants are phenolic compounds (Table 2), which are highly numerous in number and chemically diverse [18]. They can be classified in many ways based on their chemical structure, composition, solubility in various solvents, or the pathway by which they are synthesized [44].

Table 2. Major groups of phenolic compounds [45].

Class	Sub-class	Molecular species
Phenolic acids	Hydrobenzoic acids	gallicacid,ellagicacid, vanillicacid
	Hydroxycinnamic acids	ferulicacid,o-andp-coumaricacid,caffeic acid,sinapicacid
Flavonoids	Flavonols	quercetin,kaempferol
	Flavones	apigenin,luteolin
	Isoflavones	genistein,daidzein, glycitein
	Flavanones	naringenin,hesperitin
	Anthocyanidins and anthocyanins	cyanidin, delphinidin, malvidin, pelargonidin, peonidin, petunidin
	Flavan-3-ols	catechins,epicatechin, epigallocatechingallate
	Flavanolols	silymarin, silibinin
Non-flavonoid polyphenols	Dihydrochalcones	phloridzin,aspalathin
	Tannins	condensedcatechins
	Curcuminoids	curcumin
	Stilbenes	cinnamicacid, resveratrol
	Lignans	secoisolarici-resinol, sesamin

4.2. Phenolic compounds.

Phenolic compounds are the most widely distributed secondary metabolites, ubiquitously present in the plant kingdom, and their chemical structure is based on at least one aromatic ring bonded to one or more hydroxyl groups. They are mainly synthesized from the amino acid phenylalanine [46], which is converted to cinnamic acid; despite the structural diversity, the groups of compounds are often referred to as "Polyphenols".

These molecules represent a variety of functions in plant growth and development; they regulate seed germination and defense responses during excessive sun exposure, injuries, infection, and heavy metal stress [47].

They are derived from pentose phosphate, shikimate[48], and phenylpropanoid pathways in plants[49]. These molecules are usually divided into simple phenols and more complex derivatives. Each one of these groups includes others.

4.2.1. Sources.

Phenolic compounds are widespread in plant foods, especially in fruits, vegetables, grains, seeds, cereals, legumes, and beverages such as coffee and fruit juice [50].

4.2.2. Classification.

As we said before, phenolics possess an aromatic ring bearing one or more hydroxyl groups, and these rings are synthesized in the shikimate acid pathway from amino acid phenylalanine. That is why phenolic compounds can be classified in a number of ways, and they are classified into many groups based on the number of carbons in the molecule.

4.2.3. Role and importance of phenolic compounds.

Many studies have reported the advantages of phenolics, such as their anti-aging, anti-inflammatory, and antioxidant properties [45]. In addition to the above, there are relevant antioxidant enzymes to counter oxidants. Polyphenols, especially flavonoids, phenolic acids, and tannins have the important property of inhibiting α -glucosidase and α -amylase, which are key enzymes responsible for the digestion of dietary carbohydrates to glucose. The high antioxidant capacity makes polyphenols an important key factor that is involved in the chemical defense of plants and predators and plant-plant interferences [51]. Another valuable property of phenolic compounds is their ability to chelate heavy metal ions, such as iron and copper ions, due to suitable functional groups hydroxyl and carboxyl [47].

Also, phenolics are responsible for the color (such as yellow, red, blue pigments, and orange), taste, and flavor (such as eugenol and vanillin) of foods and protect the plant against insects, fungi, bacteria, and viruses [46].

4.2.4. Phenolic groups.

4.2.4.1. Phenolic acids.

Phenolic acids are simple molecules represented as the basic unit of phenolic compounds, and they consist of 2 subgroups: hydroxybenzoic and hydroxycinnamic acids [45]. Phenolic acids have interesting biological properties, and according to many studies, they have diverse functions, including photosynthesis, enzyme activity, protein synthesis, and structural compounds. A large number of phenolic acids are present in vegetable foods, such as nuts and fruits [46].

4.2.4.2. Flavonoids.

The term "flavonoid" is generally used to describe a broad collection of natural products with low molecular weight, and it is from the Latin word "Flavus," which means yellow [52]. Flavonoids were originally described as Vitamin "P" [53].

Flavonoids are one of the largest groups of plant secondary metabolites. The general structure of a molecule (Figure 7) is based on a 15-carbon skeleton (connected by a three-carbon bridge (C6-C3-C6) [54], which consists of two aromatic rings, A and B, linked via a heterocyclic benzopyran ring, where the 2-phenylchroman considered as the basic unit for it [55].

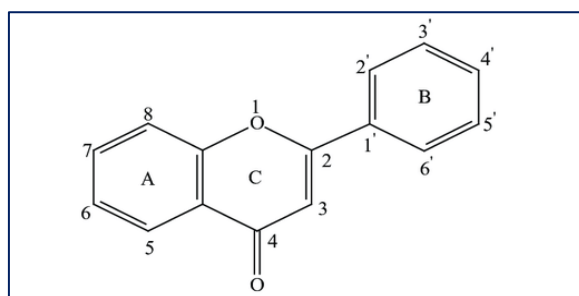


Figure 7. The basic unit of flavonoids.

Flavonoids are one of the most widespread groups of plant substances, and they occur in the root, leaf, flowers, bark, fruits, vegetables, seeds, and pollen. They also exist in cacao, coffee, and tea [45]. These compounds could be found as glycosides dissolved in water. About

2% of the total carbon photosynthesized is converted to Flavonoids, which contribute to the myriad of bright colors in plant tissues [56].

Flavonoids (Figure 8) have been classified into a variety of classes: chalcones, flavones, flavonols, flavandiols, flavonols, isoflavonoids, proanthocyanidins, and their derivatives anthocyanidins. The various classes of flavonoids differ in the level of oxidation and pattern of substitution of ring C. In contrast, individual compounds within a class differ in the pattern of substitution of the A and B rings [57].

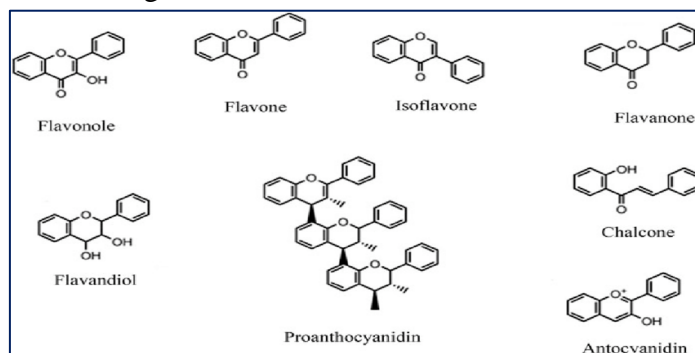


Figure 8. The different structures of flavonoid classes [58].

4.2.4.2.1. Biological activity of flavonoids.

Flavonoids possess many biochemical properties, but the best-described property of almost every group of flavonoids is their capacity to act as antioxidants. The antioxidant activity of flavonoids depends upon the arrangement of functional groups in the nuclear structure [59]. The configuration, substitution, and total number of hydroxyl groups substantially influence several mechanisms of antioxidant activity, such as radical scavenging and metal ion chelation ability [60]. This activity is due to a combination of the flavonoids iron chelating and free radical scavenger properties, as well as the inhibition of oxidase enzymes such as lipoxygenase, NADPH oxidase, and xanthine oxidase [61].

Fruits and vegetables have an enormous amount of flavonoids, which have been used as cancer chemopreventive agents [62]. Flavonolquercetin is contained in dietary fruits and vegetables, especially onions and apples. Quercetinflavonol is inversely associated with the incidence of cancer of the prostate, lung, stomach, and breast [63]. Many biological properties of flavonoids are sometimes proven to be cancer chemopreventive. For example, the natural resources of Anthocyanidins have the potential to fight against colorectal cancer[64], the sources of flavones (leek, kale, parsley, broccoli, pepper) used to treat breast, thyroid, stomach, lung, oral, and colon cancer[65].

Also, the sources of isoflavonoids, such as soy flour and soy milk, fight against prostate, breast, and kidney cancer[66]. The mechanism of action of flavonoids in the molecular study is downregulation of mutant p53 protein, cell cycle arrest, tyrosine kinase inhibition, inhibition of heat-shock proteins, estrogen receptor bonding capacity, and inhibition of expression of Ras proteins [67].

Inflammation is the complex biological of vascular tissues to harmful stimuli, such as pathogens, damaged cells, and chemical irritation[68]. It is initiated by migrating immune cells from blood vessels and releasing mediators at the site of damage[69]. Many types of cells involved with the immune system have been shown to alter their behavior in the presence of flavonoids [70]. A number of flavonoids, such as hesperidin, apigenin, luteolin, and quercetin, are reported to possess anti-inflammatory and analgesic effects[71]. Flavonoids may

specifically affect the function of enzyme systems critically involved in generating inflammatory processes, especially tyrosine and serine-threonine protein kinases [72].

In the last decade, many studies have been developed to figure out the antiviral activity of flavonoids. Actually, most of these studies were concentrated on showing the effect of flavonoids against human immunodeficiency virus (HIV). Most of the work related to antiviral compounds revolves around inhibiting various enzymes associated with the virus's life cycle. The studies show the ability of flavonoids to inhibit the multiplication of HIV by inhibiting Human immunodeficiency virus 1 (HIV-1) reverse transcriptase [73]. In addition, the flavonoids chrysin, acacetin, and apigenin prevent HIV- activation via a novel mechanism that probably involves the inhibition of viral transcription [74].

A lot of studies have realized the antibacterial activity of flavonoids, especially the ones with hydrophilic substituents such as prenyl groups. This activity depends on structure, substituting the aromatic rings [75]. Several flavonoids have been shown to possess potent antibacterial activity, such as flavones, flavanones, flavanols, chalcones, isoflavonoids, bioflavonoids, and galangin. The antibacterial mechanisms of flavonoids are summed as follows: inhibition of nucleic acid synthesis, inhibition of cytoplasmic membrane function, inhibition of energy metabolism, inhibition of the attachment and biofilm formation, inhibition of the porin of the cell membrane, alteration of the membrane permeability and attenuation of the pathogenicity [76].

4.2.4.2.2. Importance of flavonoids in plants.

According to a lot of studies, flavonoids carry out functional roles of amazing significance in plant-environment interaction. One of these roles is protecting plants from germs and parasites and their ability to protect cell tissues from UV damage [77]. In addition, flavonoids have been used as a way of classification based on the colors they give for fruits and flowers [78], and they could regulate auxin movement and catabolism because of their ability to create auxin gradients translate into phenotypes with different morphoanatomical features, do they have a role as a growth regulator [79].

4.2.4.3. Complex phenols (Tannins).

The name "tannin" is derived from the French "Tanin" (tanning substance), and it is used for a range of natural polyphenols [80]. According to Bate-Smith and Swain, tannins are water-soluble phenolic compounds with a molar mass between 500 and 3000 [81]. They may be subdivided (Figure 9) into hydrolyzable tannins are derivatives of Gallic acid (3, 4, 5-trihydroxy benzoic acid) [82], and condensed tannins are usually referred to as Proanthocyanidins [83].

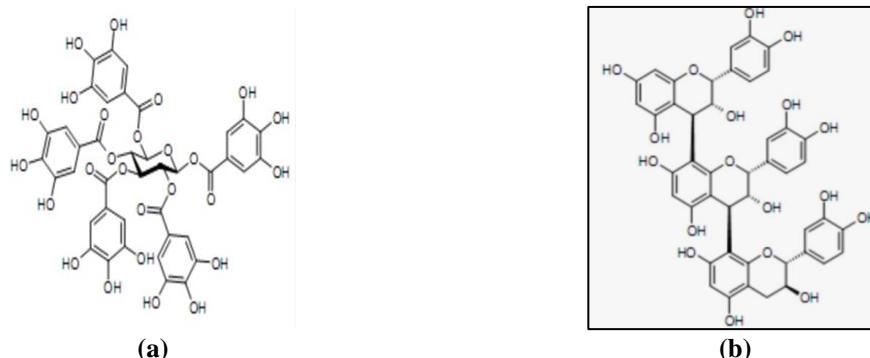


Figure 9. The basic structure of tannin is (a) Hydrolyzable tannins; (b) condensed tannins [83].

4.2.4.3.1. Sources of tannins.

The main sources of tannins are grape, muscadine grape, peach, blackberry, apple juice, raspberries, pomegranate, walnuts, olive, plum, haricot bean, chick-pea, lentils, tea, cocoa, coffee, chocolate and immature fruits [45].

4.2.4.3.2. Properties of tannins.

They are widely distributed in plants and occur in especially high amounts in the bark of certain trees and ingalls [84].

Tannins can be complex with proteins, starch, vitamins, and minerals at moderate pH and dissociate at lower pH. This ability to make complexes has caused the leather tanning' properties [85].

Because of their high chemical reactivity, tannins have played an important role in thermosetting systems for several decades, such as tannin-based adhesives and tannin-based foam material [86].

They cause a bitter taste in immature fruits.

Figure 10 represents the diagrammatic representation of the sites of enzymatic and non-enzymatic antioxidants in the cell.

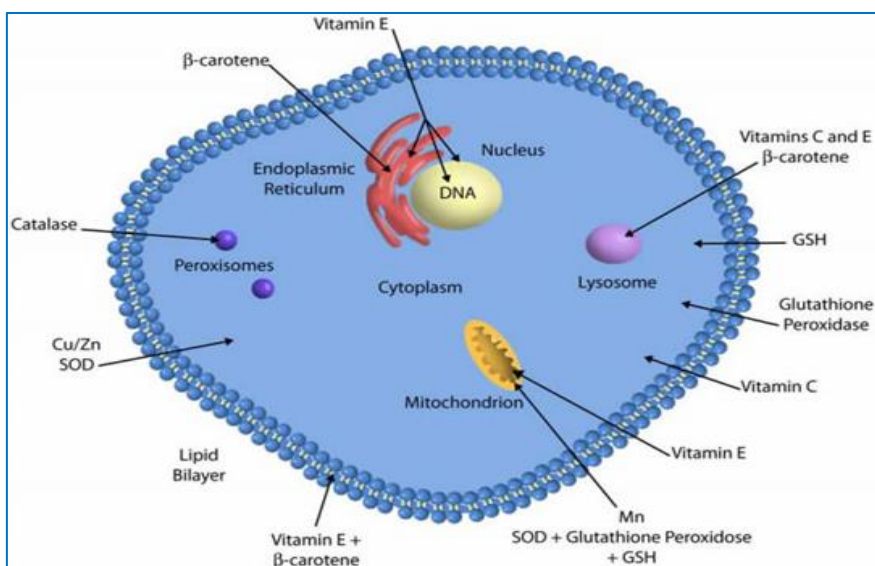


Figure 10.Diagrammatic representation of the site of enzymatic and non-enzymatic antioxidants [34].

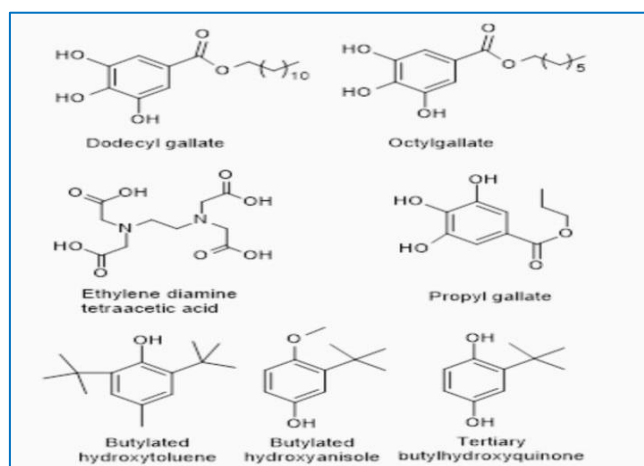


Figure 11. Structures of some synthetic antioxidants [87].

4.3. Synthetic antioxidants.

They are chemically synthesizing compounds (Figure 11) since they do not occur naturally [61]. Butylhydroxyanisol (BHA), butylhydroxytoluene (BHT), propyl gallate (PG), and Tertiary butyl hydroquinone (TBHQ) are types of synthetic antioxidants that are used as additives in foods to prevent the oxidation of lipid [6].

5. Conclusions

Oxidative stress represents a critical factor in the pathophysiology of numerous diseases, resulting from the delicate balance between reactive oxygen species (ROS) and the body's antioxidant defenses. While free radicals are essential at physiological levels for signaling and immune responses, their excessive accumulation leads to cellular and molecular damage. Antioxidants, both enzymatic and non-enzymatic, play a fundamental role in neutralizing these reactive species and maintaining cellular homeostasis. The exploration of natural antioxidants, particularly phenolic compounds from plant-based sources, has revealed their multifaceted benefits, ranging from mitigating oxidative damage to exhibiting anti-inflammatory, anticancer, and antimicrobial properties. Additionally, synthetic antioxidants continue to play a pivotal role in food preservation and industrial applications, albeit with ongoing evaluation of their safety profiles. Understanding the interplay between oxidative stress and antioxidant mechanisms provides valuable insights into potential therapeutic and preventative strategies for managing oxidative stress-related disorders. Future research should focus on advancing our knowledge of antioxidant bioavailability, synergistic effects, and the development of targeted interventions to harness their full potential in promoting health and combating diseases.

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Conflicts of Interest

The authors declare no conflict of interest.

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