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Antioxidant Properties of Phenolic Compounds to Manage Oxidative Stress / A Review

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Abstract

Phenolic compounds are one of the most common and widespread groups of plant secondary metabolites. Phenolic compounds embrace a broad range of plant substances that possess in common an aromatic ring having one or more hydroxyl substituent. The beneficial effects of polyphenols are mainly attributed to their antioxidant properties, since they can act as chain breakers or radical scavengers depending on their chemical structures. Free radical are molecules which contain unpaired electron in the outer orbitals, and is highly reactive in the body by oxidizing (removing an electron from) other atoms, or sometimes reducing (donating their electron to) other atoms. Antioxidant refers to any molecule stable enough to donate an electron to a rampaging free radical and neutralize it, thus reducing its capacity to damage a target molecule. Due to the potential health concerns synthetic antioxidants, polyphenolic compounds which are found in different plants and their manufactured by-products, have been used as some alternative natural antioxidants to retard lipid oxidation in different food sources. Plant derived antioxidants are main components of phenolic compounds to trap the activities of free radicals. Medicinal plants, as source of remedies, are widely used as alternative therapeutic tools for the prevention or treatment of many diseases. The recent studies have investigated that the antioxidant effect of medicinal plants, alcoholic beverages, spices and essential oils products are mainly attributed to phenolic compounds such as flavonoids, phenolic acids, tannins etc.

Keywords: Phenolics, Antioxidant, Free Radical, Oxidative Stress

Introduction

Nature has been a source of medicinal agents from ancient time. Herbal medicine is still the most common source for primary health care constituting about 65-80% of the world's population, mainly in developing countries [1]. For centuries, humankind has been very dependent on plants as a source of carbohydrates, proteins, and fats for food and shelter. In addition to essential primary metabolites, higher plants synthesize a wide variety of the secondary metabolites [2]. Recently, there is growing interest in finding naturally occurring antioxidants for use in foods or medicinal materials to replace synthetic antioxidants, which are being restricted due to their carcinogenicity [3]. Antioxidants are secondary constituents or metabolites found naturally in plants. They are mainly phenolics serving in plant defense mechanisms to counteract reactive oxygen species (ROS) in order to avoid oxidative damage. Their antioxidant activity is related to their redox properties, ability to scavenge a variety of reactive species such as superoxide, hydroxyl and peroxyl radicals and hypochlorous acid, singlet oxygen quenching, metal ion chelation [4,5]. It was reported that the antioxidant activity of plant materials was well correlated with the content of their phenolic compounds [6].

Antioxidant is a molecule stable enough to donate an electron to a rampaging free radical and neutralize it, thus reducing its capacity to damage. These antioxidants delay or inhibit cellular damage mainly through their free radical scavenging property [7]. These low-molecular-weight antioxidants can safely interact with free radicals and terminate the chain reaction before vital molecules are damaged. Some of such antioxidants, including glutathione, ubiquinol, and uric acid, are produced during normal metabolism in the body [8]. Other lighter antioxidants are found in the diet. Although there is several enzymes system within the body that scavenges free radicals, the principle micronutrient (vitamins) antioxidants are vitamin E (α-tocopherol), vitamin C (ascorbic acid), and ß-carotene [9].

Polyphenolic compounds in the diet enhance the stability of low-density lipoprotein (LDL) to oxidation, and evidence exists that LDL oxidation plays a significant role in atherosclerosis and coronary heart disease [10]. The role of natural antioxidants in fruits and vegetables in the delay of the onset of atherogenesis and pathogenesis has received considerable attention [10]. In the last years, oxidative stress-related diseases/disorders have gained a special attention. Metabolic, neurodegenerative, cardiovascular, mitochondrial diseases and even cancer, are among the most frequent [11,12]. Some Classes of phenolic compounds in plants phenolics, benzoquinones (C_6), Hydroxybenzoic acids($C_6–C_1$), Acethophenones, phenylacetic acids ($C_6–C_2$), Hydroxycinnamic acids, phenylpropanoids (coumarins, isocoumarins, chromones, chromenes ($C_6–C_3$), Napthoquinones ($C_6–C_4$), Xanthones ($C_6–C_1–C_6$), Stilbenes, anthraquinones ($C_6–C_2–C_6$), Flavonoids, isoflavonoids ($C_6–C_3–C_6$), Lignans, neolignans ($(C_6–C_3)_2$, Biflavonoids ($C_6–C_3–C6_{)2}$, Lignins ($C_6–C_3$)n, Condensed tannins (proanthocyanidins or flavolans) ($C_6–C_3$ C_6) [13]. Numerous studies have been investigating the underlying triggering factors, in order to understand the mechanisms of action of free radicals, as well as to discover effective substances towards preventing and even reversing the occurrence of oxidative damages [14, 15]. Taking in to account these the main aims of this study is to analyze the antioxidants properties of phenolic compounds to manage oxidative stress and to understand the correlation between phenolics and antioxidants to combat different disease.

Natural Sources of Phenolic compounds

The Phenolic compounds are secondary metabolites of plants generally involved in the defense against ultraviolet radiation or aggression by pathogens [16], being the major antioxidants of our diet [17]. Their main dietary sources are fruits and plant-derived beverages such as fruit juices, tea, coffee, red wine, Vegetables, herbs, medicinal plants, beans, seaweeds and algae. Cereals, chocolate, and dry leguminous also contribute to the total Phenolic compound intake [18,19]. The total dietary intake is about 1g/day, being much higher than that of all other known dietary antioxidants, about 10 fold higher than that of vitamin C and 100 fold higher than those of vitamin E and carotenoids [17,20].

In nature, Phenolic compound are usually found conjugated to sugars and organic acids [18,20]. They can be classified according to two major types, flavonoids and non-flavonoids and in different classes, which depend on the number of phenol rings and on the structural elements linking these rings [21,22]. Nevertheless, there is still some controversy in associated to the classes of Phenolic compounds to be considered [23]. Nonflavonoids and phenolic acids are abundant in foods. Flavonoids, the target class of polyphenols, may be divided into different subclasses according to the degree of oxidation of the heterocyclic ring anthocyanins, flavonols, flavans, flavanol, flavones, and isoflavones [24]. Most of them are known to possess antioxidative activities. Different antioxidative compounds identified in various natural plant sources are summarized in Figure 1 below.

The mode of their antioxidative action may vary, depending on the structural and compositional characteristics of the individual phenolic compound. Phenolic compounds with varying antioxidative activities from diverse natural sources have been reported.

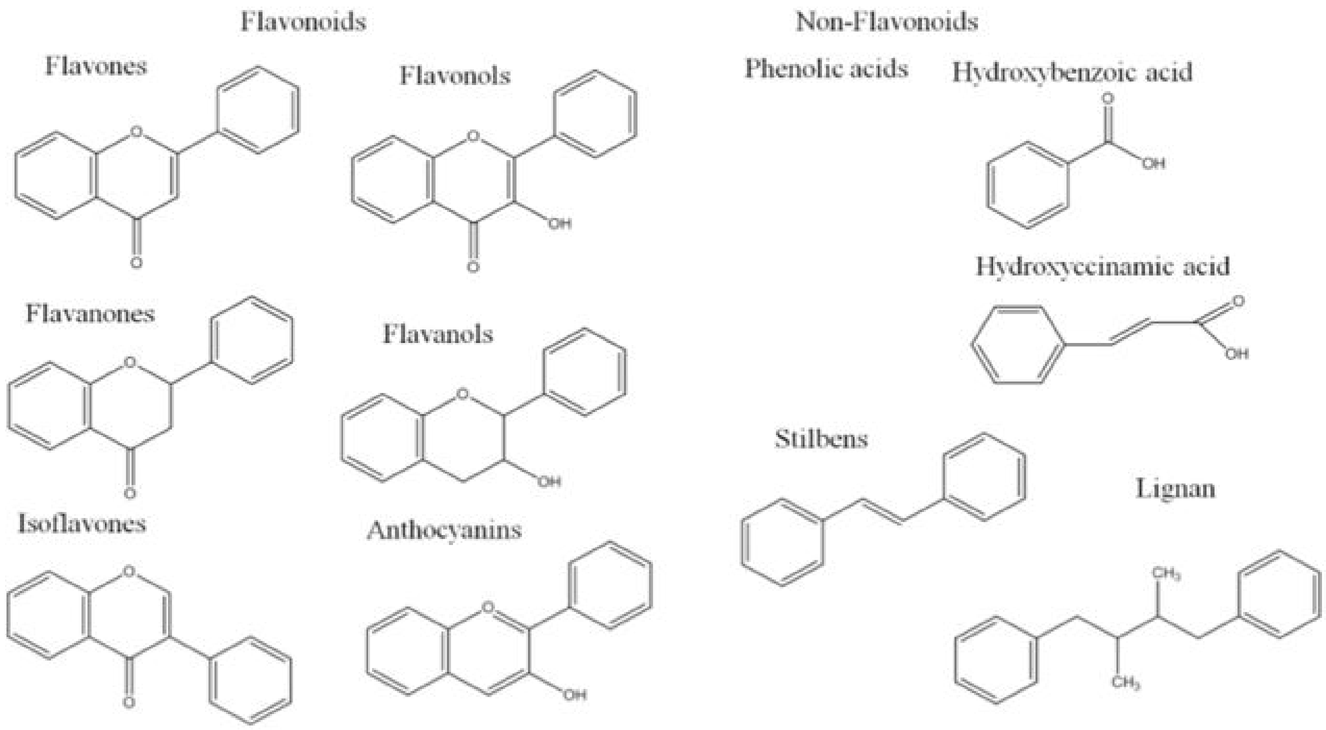

Figure 1: Chemical structure of subclasses of the flavonoids and non-flavonoids

Phenols as natural source of plant foods

Phenolic compounds as food components represent, with more than 6000 identified substances, the largest group of secondary metabolites in plant foods. They are characterized by a large range of structures and functions, but generally possessing an aromatic ring bearing one or more hydroxy substituents [25]. They are usually found in plants bound to sugars as glycosides [26]. Plant phenols are present in many foodstuffs as color imparting ingredients (e.g. anthocyanins in red wines, red cabbage, eggplant, strawberry, blueberry, raspberry, plum, cherry etc [25-27].

Plants have always been used by humans to relieve and cure many diseases [28]. Today, in many parts of the world traditional medicine replaces conventional medicine [29]. With multiple biological activities, many medicinal plants have antioxidant activity that is attracting more and more the attention of several research teams for its role in the fight against several diseases such as cancer, the atherosclerosis, cerebral cardiovascular events, diabetes, hypertension, and Alzheimer's disease [30,31].

Chemical Composition and Properties of phenolic compounds

Phenolic compounds are one of the most common and widespread groups of plant secondary metabolites. The term "phenolic compounds" embrace a broad range of plant substances that possess in common an aromatic ring having one or more hydroxyl substituent. They most frequently occur combined with sugar, as glycosides, and thus make them tend to be water-soluble. There are several classifications of phenolics, but the most spread one is based on the number of phenolic cycles in the molecule [32]. Several subclasses of phenols can be distinguished according to the number of phenol rings and to the structural elements that join these rings. According to this principle, the following compounds are belonging to phenolics: simple phenols and benzoquinones (e.g., catechol), phenolic and hydroxycinnamic acids (e.g., caffeic, ferulic acid), phenylpropenes (e.g., eugenol), coumarins, naphthoquinones, stilbenoids (resveratrol), anthraquinones, flavonoids (e.g., quercetin, genistein), flavanones, isoflavonoids, anthocyanins, lignans, lignins, and polyphenols (e.g., tannins) [33].

The beneficial effects of polyphenols are mainly attributed to their antioxidant properties, since they can act as chain breakers or radical scavengers depending on their chemical structures [34]. Polyphenols might also trigger changes in the signaling pathways and subsequent gene expression [35]. It is possible that the distinct chemical and receptor-mediated activities of polyphenols might result in similar outcomes via different pathways [36]. Under some circumstances, polyphenols can exhibit pro-oxidative effects.

Depending on their particular structures, polyphenols exhibit a wide range of properties. They include yellow, orange, red, and blue pigments, as well as various compounds involved in food flavour. The major flavours associated with polyphenols are bitterness and astringency. Other major polyphenol characteristics include their radical-scavenging capacity, which is involved in antioxidant properties, and their ability to interact with proteins. The latter is responsible for astringency perception (resulting from interactions of tannins with salivary proteins), for formation of haze and precipitates in beverages, and for inhibition of enzymes and reduced digestibility of dietary proteins [37]. Polyphenols are believed to be potent scavengers of peroxyl radicals, mainly because of the presence of high mobility of hydrogen in their molecular structures [38].

Catechin, epicatechin and gallates of epicatechin are major catechins with dietary importance for human health. In recent years, catechins have been used as natural antioxidant in oils and fats against lipid oxidation, supplement for animal feeds both to improve animal health and to protect animal products, as antimicrobial agent in foodstuffs and as health functional ingredient in various foods and dietary supplements [37]. It has been also demonstrated that the increased consumption of mint, tea or tea enriched with mint may contribute to the improvement in quality of healthy life by increasing the antioxidant defence and delaying the onset of various degenerative diseases caused by oxidative stress [39].

Function of Phenolic Compounds

Numerous phenolic compounds are responsible for color, taste, and texture of plants and therefore play an important role for plants and for human diet. The most relevant phenolics for the human nutrition are flavonoids, isoflavonoids, anthocyanins, phenolic acids, and polyphenols [40]. Flavanols as quercetin, rutin, hesperidin, naringin, and tangeritin are found in high concentrations in onions, apples, red wine, broccoli, tea, and Ginkgo biloba [41]. The most common in the American diet are quercetin (70%), kaempferol (16%), and myricetin (6%) [42]. Flavonoids have been reported to possess a wide range of activities in the prevention of common diseases, including cancer, neurodegenerative diseases, and gastrointestinal disorders [43]. Quercetin has demonstrated significant anti inflammatory activity because of direct inhibition of several initial processes of inflammation. It inhibits the manufacture and the release of histamine and other allergic and inflammatory mediators and might be of therapeutic benefit by treatment of cardiovascular diseases [44]. Numerous studies have shown the accumulation of flavonoids in in vitro cultures, e.g. in callus culture of Crataegus sinaica [45] as well as in suspension cultures of Glycyrrhiza echinata [46]. Lipid oxidation is an extremely multifaceted process which involves various reactions that produce several physical and chemical alterations [47]. Rapid donation of a hydrogen atom to lipid radicals by these phenolic antioxidants could be one of the ways to impede lipid oxidation. The effectiveness of phenolic compounds in decelerating lipid oxidation is associated with their free radical-scavenging activity showing figure 2 below. Figure 2: Scheme showing oxidation of a polyunsaturated fatty acid (PUFA) and the role of phenolic (PP) compounds in the prevention of lipid oxidation [46].

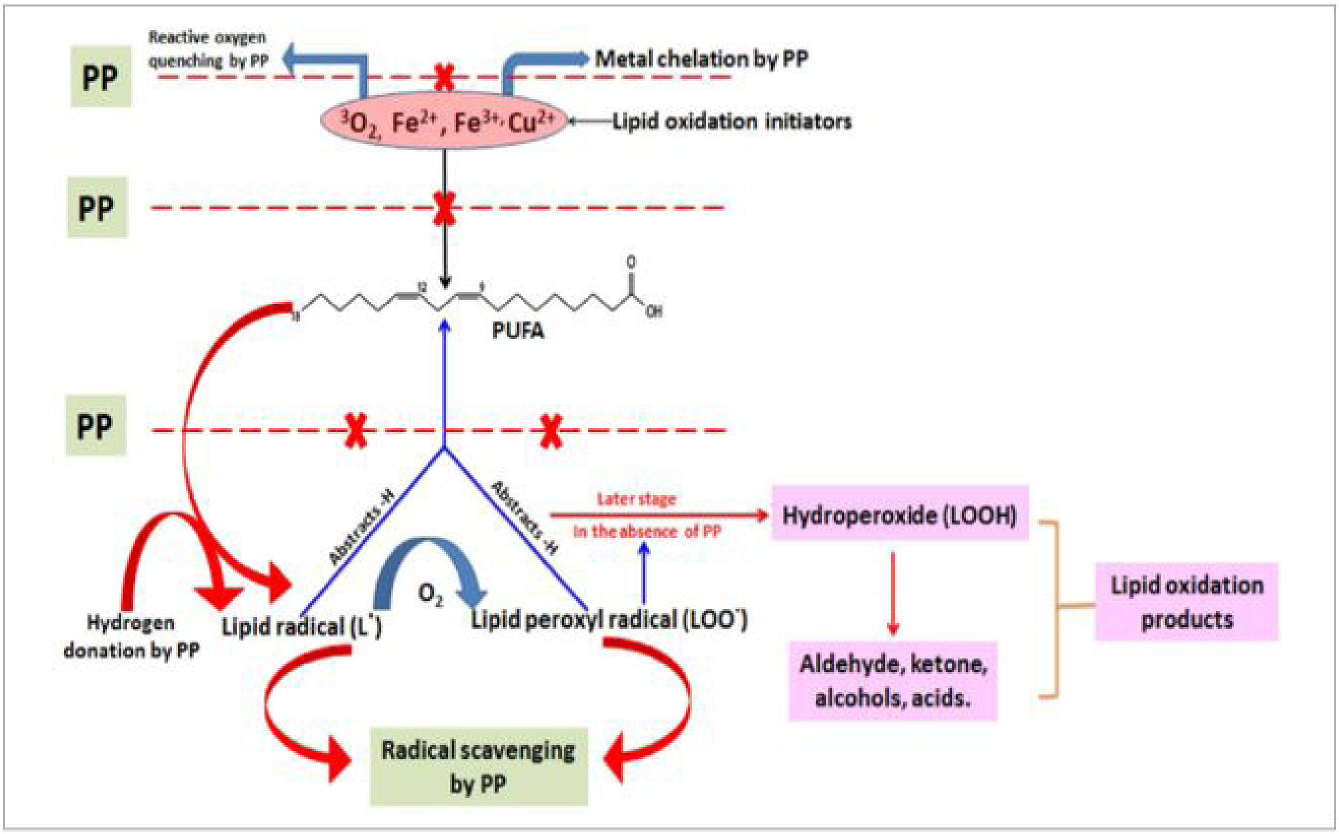

Figure 2: Scheme showing oxidation of a polyunsaturated fatty acid (PUFA) and the role of phenolic (PP) compounds in the prevention of lipid oxidation [45]

Free radicals

The term 'free radicals' is defined as the reactive molecular species that contain unpaired electrons in their outermost orbital [48,49]. Free radicals can be formed from molecules by the homolytic fission of a chemical bond and via redox reactions, which is a far more common process in biological systems [48]. In popular scientific/biomedical literature, 'free radical' is used in a broad sense and also includes related reactive species such as 'excited states' that lead to free radical generation or those species that result from free radical reactions.

Usually, free radicals are very short-lived and derived from two elements: oxygen and nitrogen, thus creating highly reactive molecules like reactive oxygen species (ROS) and reactive nitrogen species (RNS). ROS include superoxide anion radicals ($O_2^{-\bullet}$), reactive hydroxyl radicals ($OH^\bullet$), hydroperoxyl radical ($HO_2^\bullet$) and other species like hydrogen peroxide (H_2O_2), hypochlorous acid (HOCl) and singlet oxygen ($^1O_2$) [50]. The nitrogen-derived free radicals are nitric oxide ($NO^\bullet$), nitrogen dioxide (NO_2), peroxy-nitrite anion ($ONOO^-$) [51]. Free radical are molecules which contain unpaired electron in the outer orbitals, and is highly reactive in the body by oxidizing (removing an electron from) other atoms, or sometimes reducing (donating their electron to) other atoms. The major source of reactive oxygen species are mitochondria, produced by electron transport chain in aerobic respiration as byproducts. Although most electrons reach the third pump of the electron transport system, about 1% to 3% reacts with oxygen prematurely to form the superoxide radical [52]. A molecule is only a free radical if it possesses one or more unpaired electrons. The following figure shows the free radical molecule in a certain particle.

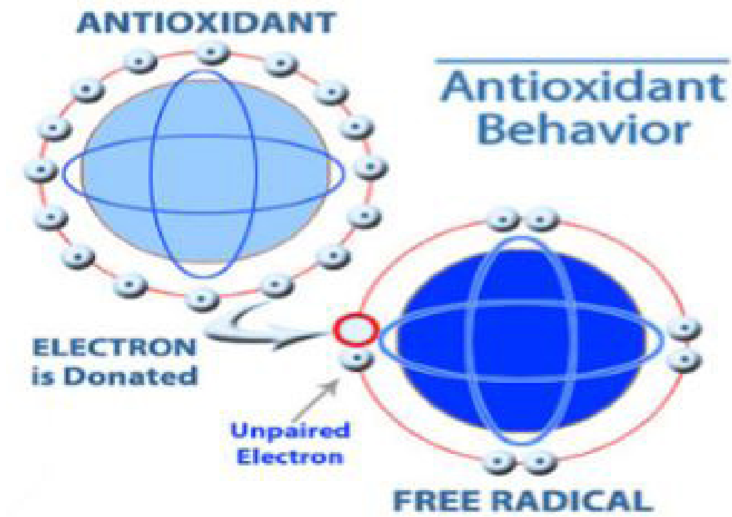

Figure 3: Free Radical Molecule

Oxidative stress and antioxidant protection mechanisms

In general, free radicals as necessary intermediates are produced in a variety of normal biochemical reactions and a homeostatic balance exists between free radical generation and quenching under normal physiological conditions [53]. Oxidative stress occurs when this balance is disrupted by excessive production of reactive oxygen species. Oxidative stress is defined as an imbalance between the production of free radicals and reactive metabolites, so-called oxidants or ROS, and their elimination by protective mechanisms referred to as antioxidants. This imbalance leads to damage of important biomolecules and cells, with potential impact on the whole organism [54]. The harmful effects of ROS are balanced by the action of antioxidants, example like enzymes present in the body [55]. Despite the presence of the cell's antioxidant defense system to counteract oxidative damage from ROS, oxidative damage accumulates during the life cycle and has been implicated in diseases, aging and age-dependent diseases such as cardiovascular disease, cancer, neurodegenerative disorders, and other chronic conditions [56].

Oxidative stress is linked to altered redox regulation of cellular signaling pathways and the formation of many types of cancer cells and oncogenic stimulation [57]. It appears that the DNA damage and activation of ROS to AP-1 and NF-kB pathways of signal transduction leads to the transcription of genes involved in cell growth regulation and initiation of cancerous conditions. Lipid peroxidation products are formed with the abstraction of a hydrogen atom from an unsaturated fatty acid [55]. The lipid peroxidation process influences membrane fluidity as well as the integrity of biomolecules associated with the membrane (membrane bound proteins or cholesterol). These highly oxidizable lipids may then, in turn, attack nearby proteins causing the formation of an excess of protein carbonyls [58]. A major development over the past two decades has been the realization that free radical mediated peroxidation of membrane lipids and oxidative damage of DNA are associated with a variety of chronic health problems [59] such as cancer, atherosclerosis, [60] neurodegenerative diseases [61]. Therefore, inhibition of oxidative damage by supplementation of antioxidants becomes an attractive therapeutic strategy to reduce the risk of these diseases [55].

Antioxidants are central to the redox balance in the human body. The term 'antioxidant' refers to any molecule stable enough to donate an electron to a rampaging free radical and neutralize it, thus reducing its capacity to damage a target molecule [48, 49]. Antioxidants may exert their effects by different mechanisms, such as suppressing the production of active species by reducing hydroperoxides and H_2O_2 and also by sequestering metal ions, termination of chain reaction by scavenging active free radicals, repairing and/or clearing damage of cell. Similarly, some antioxidants also induce the biosynthesis of other antioxidants or defence enzymes [62]. Humans have several mechanisms to counteract oxidative stress, either by producing antioxidants from endogenous antioxidant systems or externally supplied through exogenous antioxidants.

The endogenous antioxidant systems, including enzymatic and non-enzymatic antioxidants, play a crucial role in maintaining optimal cellular functions. The major antioxidant enzymes directly involved in the neutralization of ROS and

RNS are superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione reductase (GRx) [63]. SOD, the first line of defense against free radicals, catalyzes the dismutation of $O_2^{-\bullet}$ to O_2 and to the less-reactive species H_2O_2 by reduction. In humans there are three forms of SOD: cytosolic Cu, Zn-SOD, mitochondrial MnSOD, and extracellular SOD (EC-SOD) [64]. The H_2O_2 is transformed into water and oxygen by CAT or GPx. The selenoprotein GPx enzyme removes H_2O_2 by using it to oxidize reduced glutathione (GSH) into oxidized glutathione (GSSG). Glutathione reductase, a flavoprotein enzyme, regenerates GSH from GSSG, with NADPH as a source of reducing power (Figure 4)

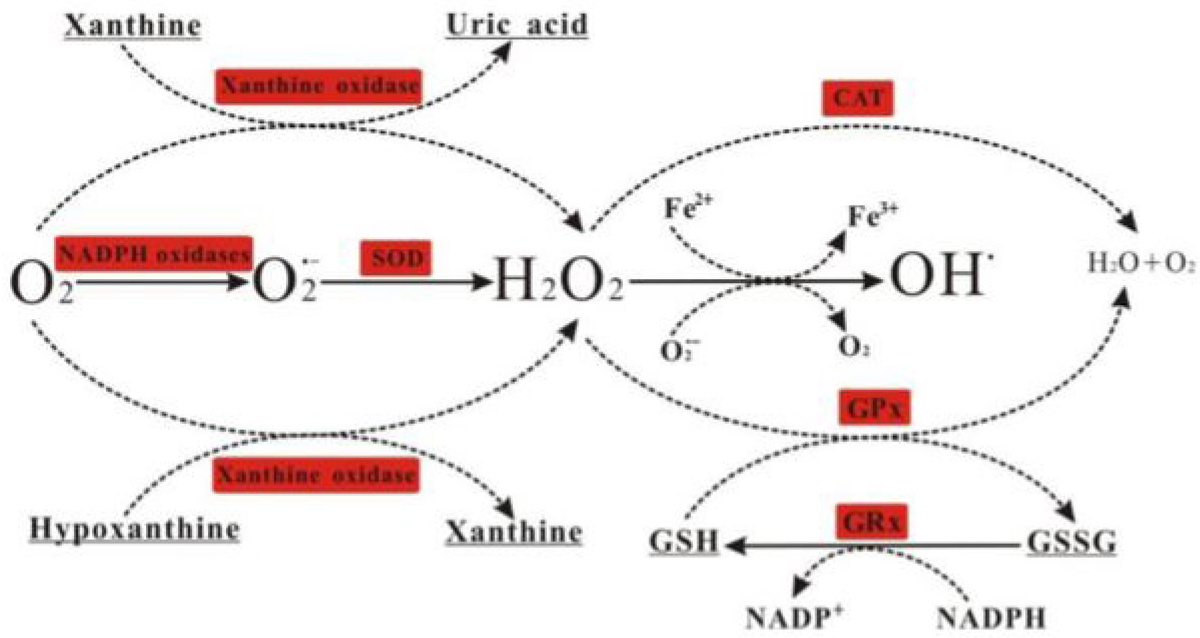

Figure 4: A schematic diagram showing the production of free radicals via different routes and the interaction between intracellular antioxidants [63]

Antioxidants and its heath implications

Antioxidants are any substances that directly scavenge ROS or indirectly act to up-regulate antioxidant defenses or inhibit ROS production [65]. During human evolution, endogenous defenses have gradually improved to maintain a balance between free radicals and oxidative stress. The antioxidant activity can be effective through various ways: as inhibitors of free radical oxidation reactions (preventive oxidants) by inhibiting formation of free lipid radicals; by interrupting the propagation of the autoxidation chain reaction (chain breaking antioxidants); as singlet oxygen quenchers; through synergism with other antioxidants; as reducing agents which convert hydroperoxides into stable compounds; as metal chelators that convert metal pro-oxidants (iron and copper derivatives) into stable products; and finally as inhibitors of pro-oxidative enzymes (lipooxigenases) [66-68]. The human antioxidant system is divided into two major groups, enzymatic antioxidants and non-enzymatic oxidants (Figure 5).

There has been growing indication over the past decades, that particular human diseases and oxidative stress may be prohibited by counting plant foods in the diets, that contain enormous quantities of antioxidants, for example, vitamins C, E or natural antioxidants such as tannins, phenolics, coumarins, flavonoids and terpenoids. Dietary antioxidants perform as scavengers of free radicals, a metal ligand, radical chain reaction inhibitors, antioxidant enzyme cofactors, and oxidative enzyme inhibitors [69]. The increment in the interest of broadening the antioxidants that could be utilized as food constituents to avoid food oxidation. Additionally, phenolic extracts obtained from plant substances, for instance, green tea, aromatic herbs and grape seeds are recognized to possess antimicrobial properties to encounter foodborne pathogens [70].

Antioxidants are divided into two classes: preventive antioxidants and chain breaking antioxidants. Preventive antioxidants inhibit oxidation by reducing the rate of chain initiation. In most cases hydroperoxide product, ROOH of the oxidation is the cause for the initiation process. Preventive antioxidants convert the hydroperoxides to molecular products that are not potential sources of free radical [71]. Most biological preventive antioxidants are also peroxide decomposers. Most biological preventive antioxidants are also peroxide decomposers. Carotenoids, flavonoids, cinnamic acids, benzoic acids, folic acid, ascorbic acid, tocopherols and tocotrienols are some of the antioxidants produced by the plant for their sustenance. Some of the widely known antioxidants are beta-carotene, ascorbic acid and alpha tocopherol [72].

Antioxidants have important preventive roles not only on undesirable changes in the flavor and nutritional quality of food, but also on tissue damage in various human diseases. They are effective in prevention of degenerative illnesses, such as different types of cancers, cardiovascular and neurological diseases, cataracts and oxidative stress dysfunctions [73,74]. Chronic diseases such as arteriosclerosis and cancer, which are the leading causes of death in the Western world, are likely to be mediated by free radical and lipid per oxidation mechanisms [75]. Antioxidants have been investigated and reported to play a specific role in the treatment of these diseases/disorders [76]. In the last decades, several epidemiological studies have shown that dietary intake of foods rich in natural antioxidants was correlated with reduced risk of coronary heart disease [77]. Dietary and natural antioxidants present in foods and other biological materials have attracted considerable interest because of their presumed safety and potential nutritional and therapeutic or health effects [78, 79].

People who have taken the antioxidant rich foods could be healthier in their entire life. They help us the shelf life process for living and non-living organism as well. Health-associated diseases, for example, coronary disease, diabetes, muscular degeneration and cancer are all impacted by damage due to cellular oxidative reactions. There has been growing attention in the response mechanism of antioxidants and whether they precisely interrupt or eradicate free radicals from human cells.

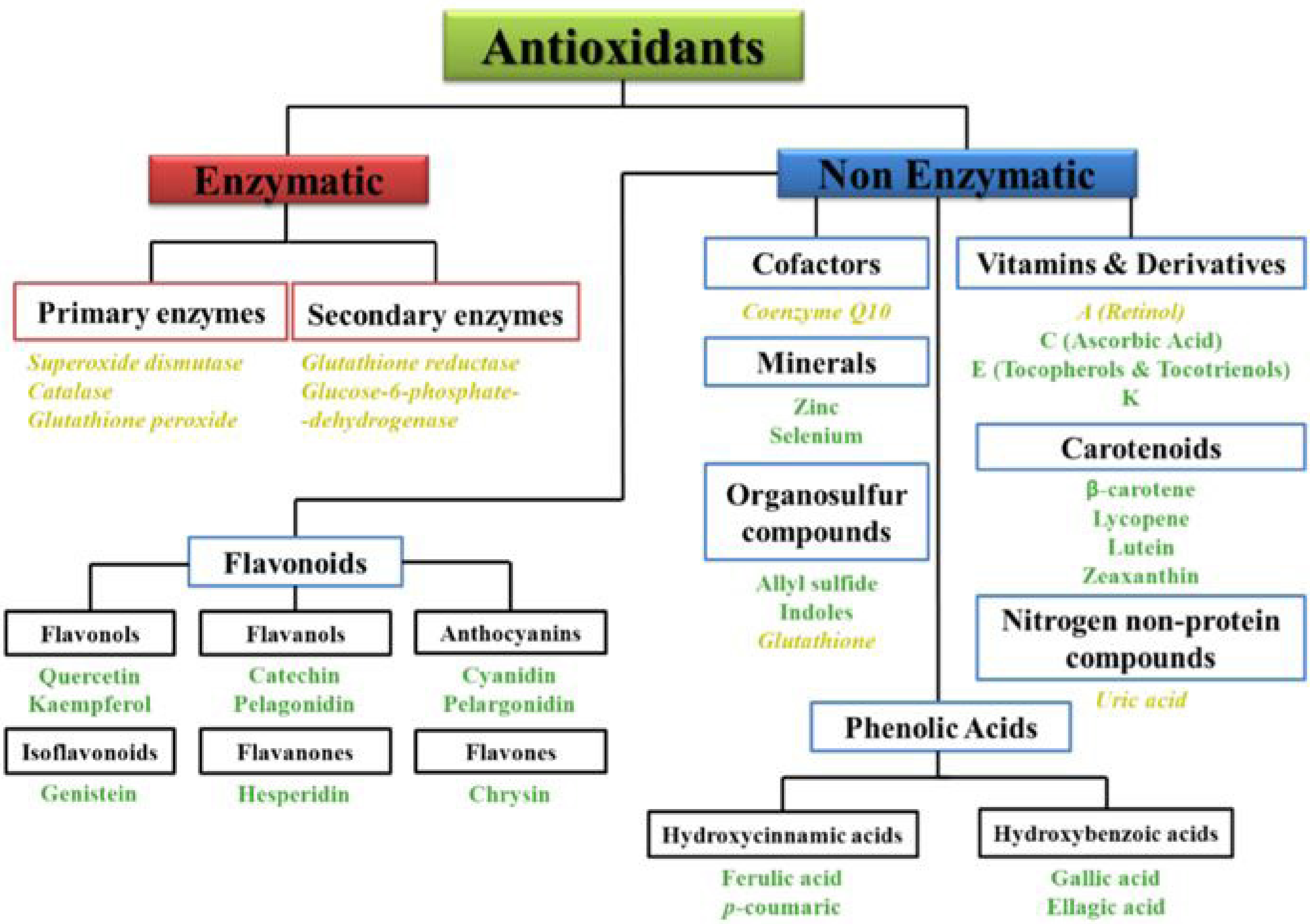

Figure 5: Natural antioxidants separated in classes. Green words represent exogenous antioxidants, while yellow ones represent endogenous antioxidants [80]

Antioxidant mechanisms

The role of antioxidants is to lower or terminate chain reactions by removing free radicals or inhibiting other oxidation reactions by being oxidized themselves. So, antioxidants are often reducing agents such as polyphenols or thiols [81]. Although oxidation reactions are vital for cells, they have damaging effects; hence, plants and animals contain various antioxidants, such as vitamins C and E and glutathione, as well as different enzymatic systems which catalyze the antioxidants reactions as catalase, superoxide dismutase (SOD) and peroxidases. The defects in or inhibition of these antioxidant enzymes will lead to oxidative stress and may damage and lyse the cells [82]. The mechanisms which followed by antioxidant defense are: 1) Blocking of free radicals production of 2) oxidants Scavenging 3) The converting toxic free radicals into less toxic substances 4) Blocking the production of secondary toxic metabolites and mediators of inflammation 5) Blocking of the chain propagation of the secondary oxidants 6) Repairing the injured molecules 7) Initiation and enhancing the endogenous antioxidant defense system. All of these defense mechanisms act hand by hand for protection of the body from oxidative stress. The antioxidant systems in the human body consist of powerful non-enzymatic and enzymatic antioxidants [83].

The possible mechanisms of action of antioxidants were first explored when it was recognized that substance with anti-oxidative activity is likely to be the one that itself readily oxidized. In the literature, much more effort has been spent on developing nonenzymatic antioxidant assays covering a wide range of HAT- and ET-based assays and methods for measuring ROS/RNS scavenging activity. Recently, synthetic and natural phenolic antioxidants have been summarized, together with their mode of action, health effects, degradation products, and toxicology [84].

Hydrogen Atom Transfer Based Methods (HAT): hydrogen atom transfer based method measure the capability of an antioxidant to quench free radicals (generally peroxyl radicals) by Hydrogen atom donation. Peroxyl radicals are generally chosen as the reactive species in these assays because of their higher biological relevance and longer half-life (compared to hydroxyl and superoxide radicals). The HAT mechanism of antioxidant action, in which the hydrogen atom ($H^{\bullet}$) of a phenol (ArOH) is transferred to an $ROO^{\bullet}$ radical, can be summarized by the reaction.

Where the aryloxy radical (ArO•) formed from the reaction of antioxidant phenol with peroxyl radical is usually stabilized by resonance. The AH and ArOH species denote the protected biomolecules and antioxidants, respectively. Effective phenolic antioxidants need to react more quickly than biomolecules with free radicals to protect the latter from oxidation [85].

$$ROO^{\bullet} + AH/ArOH \rightarrow ROOH + A^{\bullet}/ArO^{\bullet}$$

Electron Transfer Based Methods (ET): The electron transfer mechanism of antioxidant action with a biologically relevant radical is based on the reactions.

$$ROO^{\bullet} + AH/ArOH \rightarrow ROO^{-} + AH^{\bullet+}/ArOH^{\bullet+}$$

$$AH^{\bullet+}/ArOH^{\bullet+} + H_2O \leftrightarrow A^{\bullet}/ArO^{\bullet} + H_3O^{+}$$

$$ROO^{-} + H_3O^{+} \leftrightarrow ROOH + H_2O$$

Application of Antioxidants

Recently, antioxidants have attracted considerable attention in relation to radicals and oxidative stress, cancer prophylaxis and therapy, and longevity [86]. Phenols and polyphenols are the target analytes in many such cases; they may be detected by enzymes like tyrosinase or other phenol oxidases, or even by plant tissues containing these enzymes [87,88]. The total antioxidant potential is a relevant tool for investigating the relationship between dietary antioxidants and pathologies induced by the oxidative stress.

The consumption of fruits and vegetables, as well as of grains and nuts, has been associated with reduced risk of chronic diseases [89,90]. Among food components fighting against chronic diseases, great attention has been paid to phytochemicals, plant-derived molecules endowed with steady antioxidant power. The cummulative and synergistic activities of the bioactive molecules present in plant food are responsible for their enhanced antioxidant properties. Hence, an appropriate investigation of the role of dietary antioxidants in disease prevention should be based on a complete database of antioxidant-rich food stuffs [89]. The importance of TAC as a novel instrument to estimate the relationship between diet and oxidative stress-induced disease is presented in recent studies. Table 1 below shows the application of antioxidants in different matrices.

Table 1: Widely used antioxidants and their applications [91,71]

Antioxidant	Plant sources	Applications
Beta-Carotene $C_{40}H_5$	Elaeis oleifera, Elaeis Guineensis Momordica Cochinchinnensis Spreng Eurycoma Longifolia Zanthoxylum Myriacanthum	Reported to be anodyne, antidotal, aphrodisiac, diuretic, and vulnerary. Oil palm is a folk remedy for headaches, rheumatism and is used as a liniment for indolent tumors. Used as a coloring and flavoring agent in steamed glutinous rice, male aphrodisiac, stomach ache and antitumor agent.
Alpha-Tocopherol $C_{29}H_{50}O_2$	Citrus Hystrix Calamus Scipronum Averrhoa Belimbi	Fruit used as preservative, flavoring in both savory and sweet food. Leaves used as hair shampoo and as medicine. The buds of these canes are eaten as food and have medical and antiseptic properties. They are commonly used for treatment of fever and aches. The syrup of the fruit is useful in relieving thirst, febrile excitement, and also in some slight cases of hemorrhage from the bowels, stomach and internal hemorrhoids
Ascorbic Acid $C_6H_8O_6$	Apium Graveolens Sauropus Androgynous	Arthritis, Back Pain (lower), Nervousness, Rheumatism. Insect and disease resistance.
PalmiticAcid $CH_3(CH_2)_{14}COOH$	Elaeis Oleifera, Elaeis Guineensis	Anodyne, antidotal, aphrodisiac, diuretic and vulnerary. Oil palm is source of palmitic acid and is a folk remedy for cancer, headaches, and rheumatism.
Beta Sitosterol $C_{29}H_{50}O$	Morinda Citrifolia Alpinia Officinarum Sida Acuta	Diabetes, high blood pressure, arthritis, skin afflictions, and conditions of aging Flatulence, dyspepsia, vomiting and sickness at stomach, and recommended as a remedy for stomach cancer. Entire plant for stomach ache
Selenium	Astragalus Valeriana Officinalis Achillea Millefolium	Prevents severe side effects of chemotherapy in patients with cancer. Inhibits the growth of murine renal cell carcinoma. Activation of immune system. Sedative activity. General tonic for the cardio-vascular system, lowers blood pressure, and slows heartbeat.
Anthraquinone $C_{14}H_8O_2$	Cassia Acutifolia	Antihelminthic, antibacterial, laxative, diuretic, for treatment of snakebites and uterine disorders.
Tannicacid $C_{76}H_{52}O_{46}$	Costus Spinosa	Tanning of leather.
Quercetin $C_{15}H_{10}O_7$	Blumea Balsamifera	Treatment for the swelling of pancreas.

Conclusion

Phenolic compounds are commonly found in both edible and non-edible plants, and they have been reported to have multiple biological effects, including antioxidant activity. The principal sources of polyphenols are fruits and beverages such as tea, red wine, and coffee, but vegetables, leguminous plants, and cereals are also good sources. The beneficial effects of polyphenols have been ascribed to their strong antioxidant activity that is, their ability to scavenge oxygen radicals and other reactive species. Antioxidant agents have role in reducing agents, hydrogen donors, quenchers of singlet oxygen, delay oxidative reactions, and significantly terminate oxidative chain reactions by removing the free radical intermediates. According to different literature values Phenolic compounds are the major contributors as antioxidants and they act as shelf life of living and nonlivings things as well. Generally natural plant products are the contributing factor for terminating free radicals when they are produced on oxidation process. Therefore, the review recommends that high consumption of natural foods that are rich in antioxidants will provide more protection against toxic agents and related diseases. The very complexity in the phenolic compounds profile of these by-products has to be resolved to obtain the optimum antioxidant efficiency.

Authors' contribution

Searching the data, organization of paper and preparing the primary draft conducted by all listed authors. All authors have read, agreed and signed on submitting for publication of paper.

Conflicts of Interest

The authors declared no competing interests.

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