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Short Review Article

Antioxidants: A Masterpiece of Mother Nature to Prevent Illness

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Abstract:

Reactive oxygen and nitrogen species, generated in usual biochemical reactions with increased exposure to the environment can cause an imbalance in homeostatic process between oxidants and antioxidants leading to oxidative stress. Oxidative stress is primarily responsible for a wide array of human diseases such as neurodegenerative disorders (Alzheimer's disease, Parkinson's disease), diabetes, cancers, and rheumatoid arthritis. Therefore, a subtle balance between oxidation and antioxidation is an essential requirement in order to maintain a healthy biological system. Antioxidants, widely distributed among plants and animals are substances which can significantly prevent or inhibit the oxidative damage to cells. COVID-19 is a major threat to the entire world and the need to boost one's immunity is crucial. This can be achieved by consuming antioxidants. Thus, this article attempts to delineate different types of antioxidants, their sources in Mother Nature, the need of antioxidants to maintain good health and their mode of action along with mechanisms.

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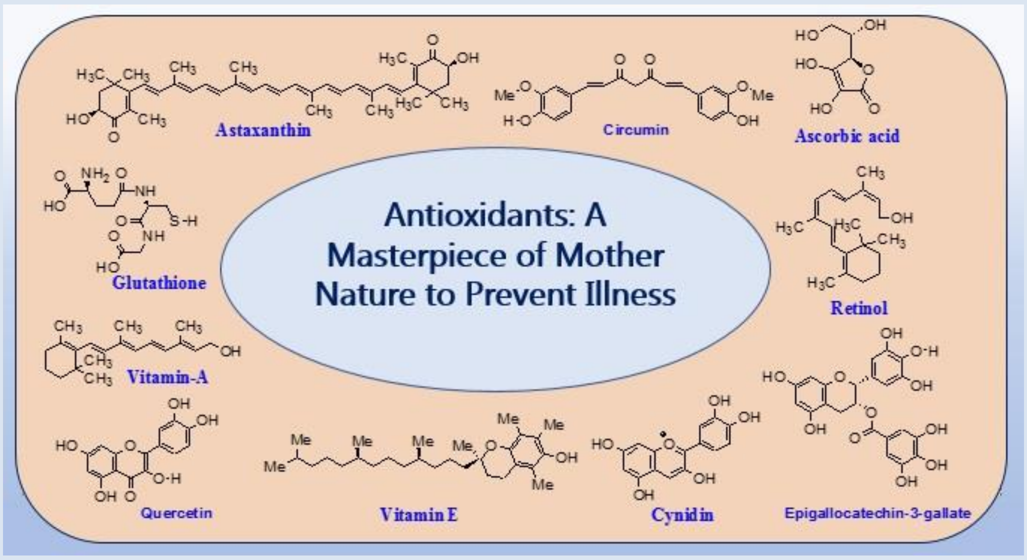
Keywords: Antioxidants; Bioflavonoids; Carotenoids; Curcumin; Glutathione; Vitamins; Oxidative stress.

Graphical Abstract:



Biography:

Amrit Krishna Mitra Dr. Amrit Krishna Mitra is presently an Assistant Professor (West Bengal Education Service Gr: A) and Head of the Department of Chemistry, Government General Degree College–Singur, West Bengal, India. He acquired his Honours degree in Chemistry from St. Xavier's College, Calcutta under University of Calcutta, India and his Master's degree from Indian Institute of Technology, Kharagpur. He was awarded Ph.D. in Organic Chemistry by the University of Calcutta, India. His area of research is based on 'Synthesis and Photophysical Studies of Heterocyclic Compounds'. He has published several research papers in various journals of international repute. He has also penned a book and several book chapters. He is very much involved in various activities related to 'Chemistry Education'.

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1. Introduction

Recently, human beings are imprisoned in an environment where uncertainty, unknown fear and misbelief pervade the air. The COVID-19 (Corona Virus Disease-2019) pandemic is racing across the globe. Researchers are working hard to develop new techniques to understand the mechanism of infection, virulence, pharmacology and evaluate potential therapeutics and vaccines to combat coronavirus. Researchers all over the world are working hard to discover new drugs against coronavirus. Apart from the hazards of COVID-19, for the past few decades, the human civilisation has also been threatened by heart diseases, diabetes, different cancers, Alzheimer's disease, Parkinson's disease, renal disease, diseases due to cellular mutations and many other such ailments. In short, there is no scarcity of diseases in the modern world although technology has made a breakthrough in every branch of medicine. In this research study, we shall discuss in detail the benefits of antioxidants, one of the biggest gifts of mother nature that can be used to minimise our health problems.

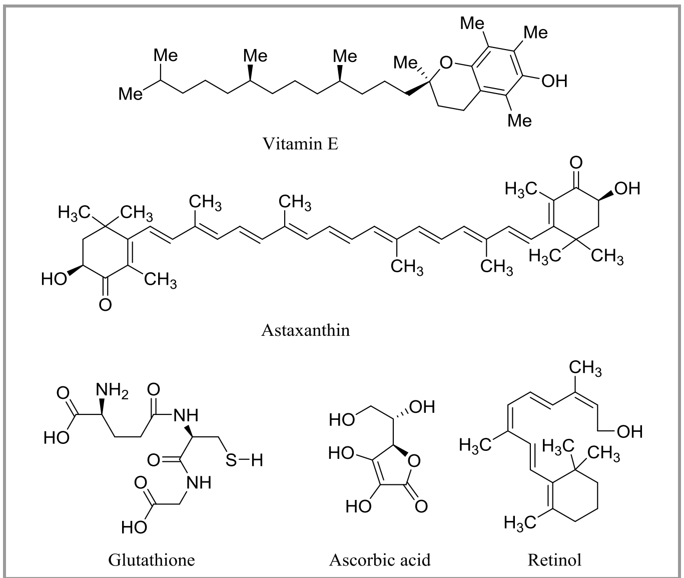
As molecular oxygen is essential for human life, cells can also be damaged when certain chemical processes generate oxygen free radicals. Free radicals can cause "oxidative stress," a process that can trigger cell damage [1-3]. Oxidative stress is involved in the onset of many diseases including cancer, arteriosclerosis, cardiovascular diseases, diabetes, Alzheimer's disease, Parkinson's disease and eye diseases such as cataracts and age-related macular degeneration. In the broader sense, oxidation is a type of chemical reaction that can generate free radicals, leading to chain reactions that may damage and affect cells [4,5]. An antioxidant is a molecule that slows down the oxidation of other molecules. Antioxidants, found in nature and in the body, function as protective agents against oxygen free radicals thereby preventing some types of cell damage. Mother Nature has infused antioxidants in many kinds of food, including fruit and vegetables. Among the best known antioxidants are vitamins C and E, beta-carotene, selenium, ubiquinone (Q10) and the flavonoids found in apples, onions and tea. Antioxidants act *via* several chemical mechanisms like single electron transfer, hydrogen atom transfer and the ability to chelate transition metals [6,7].

2. Types and benefits of antioxidants

The benefits of antioxidants are incredibly significant to good health. The human body naturally produces lots of free radicals during its various physiological processes [5-7]. If free radicals are not treated at the right time, they can cause multiple illnesses and chronic diseases as discussed earlier. Here we shall discuss the role of antioxidants in counteracting the damaging effects of free radicals [8]. However, most of the times, free radicals far outnumber the naturally occurring antioxidants. To maintain the subtle balance, a continual supply of external sources of antioxidants is necessary in order to obtain the maximum benefits of antioxidants. The way antioxidants benefit the body is by neutralizing and removing the free radicals from the bloodstream [8, 9].

When the skin is exposed to high levels of ultraviolet light, photo-oxidative damage is induced due to the generation of diverse types of reactive species of oxygen in the forms of singlet oxygen (capable of catalysing the production of free radicals), superoxide radicals and peroxide radicals [10]. These are chiefly responsible for the damage of cellular lipids, proteins and DNA thereby causing erythema (sunburn), premature aging of the skin, photodermatoses and skin cancers [11]. To protect the skin from the harmful reactive species of oxygen, astaxanthin, in combination with vitamin E can be used as a highly powerful antioxidant. Astaxanthin, a naturally occurring carotenoid, usually found in marine organisms such as microalgae, salmon, trout, krill, shrimp, crayfish and crustaceans, is the single most powerful quencher of singlet oxygen [11,12]. This is approximately ten times stronger than other carotenoids including beta-carotene and even up to 500 times stronger than alpha tocopherol (vitamin E)! Spirulina (a biomass of cyanobacteria (blue-green algae) that can be consumed by humans), on the other hand, contains a variety of antioxidants and other substances that are beneficial in enhancing immunity [12,13]. In this aspect, it is worth mentioning that both astaxanthin and spirulina have been proven to improve the non-specific and specific immune system. Both of these have a significant contribution to protect cell membranes and cellular DNA from mutation [13]. Antioxidants containing thiols and ascorbic acid (vitamin C) are also of immense significance as they can terminate the chain reactions once initiated by the free radicals [14]. In the context of today's polluted world, increasing one's antioxidant intake is indispensable for optimum health. This is primarily because the body just can't keep up with antioxidant production [15]. A significant amount of these antioxidants comes from one's daily diet in the forms of vitamins, minerals, phytochemicals and enzymes. If one is able to increase one's antioxidant intake, it can help by providing added protection for the body against mood disorders, eye problems, heart problems, memory problems and immune system problems [16]. Most of the times, chemical compounds present in foods and body tissues have beneficial health effects though instances are there when chemicals are externally added to prevent further oxidation [13,14].

To maintain the balance of the oxidative state, plants and animals preserve complex systems of overlapping antioxidants, such as glutathione and enzymes (e.g., catalase and superoxide dismutase) produced internally or by the dietary antioxidants: vitamin A, vitamin C and vitamin E (Scheme 1).



Scheme 1. Representative structures of a few common antioxidants.

Vitamin C (ascorbic acid), an important dietary antioxidant is required for collagen synthesis by acting as a cofactor for non-heme iron α-ketoglutarate-dependent dioxygenases such as prolyl 4-hydroxylase [1,13]. The synthesis of collagen is important primarily due to the maintenance of normal vascular function. Vitamin C stimulates the synthesis of all types of collagen by donating electrons that are needed for the hydroxylation of proline and lysine in procollagen by specific hydroxylase enzymes. It is also worthwhile to mention that vitamin C, under normal physiological concentrations can protect cells against oxidative damage caused by ROS [4,6]. Vitamin E (α-tocopherol), on the other hand, comprises a family of hydrocarbons which are characterised by a chromanol ring with a phytol side chain referred to as tocopherols and tocotrienols. It is a lipid soluble antioxidant, functions by scavenging hydroperoxyl radicals in lipid milieu. Vitamin A, a fat-soluble vitamin, an important component to human health [9]. Vitamin A comes from two sources. One group is retinoids, comes from animal sources and it includes retinol. Carotenoids form the other group that comes from plants and it includes beta-carotene. In the intestine or liver, the body converts provitamin A carotenoids into vitamin A (retinol). Glutathione, an important antioxidant, capable of preventing damages to important cellular components caused by ROS is present in plants, animals, fungi and bacteria [13].

3. Antioxidants usually found in food items

No food compounds have been proven with antioxidant efficacy *in vivo* other than for dietary antioxidant vitamins – vitamin A, vitamin C and vitamin E [14,17]. Recently, the regulatory agencies like the Food and Drug Administration of the United States and the European Food Safety Authority have published guidelines prohibiting food product labels to claim an inferred antioxidant benefit when no such physiological confirmation is present. Plenty of food items contain high amount of polyphenols. Polyphenols can be categorised into: a) Isoflavones (soy beans, tofu, lentils, peas and milk), b) Flavonols (citrus fruits, red wine, onions and apples), c) Catechins (tea, green tea, cocoa, dark chocolate), d) Anthocyanins (berries, red wine) and e) Chlorogenic acid (instant and brewed coffee). Spices like cinnamon, clove, turmeric, cumin, parsley, curry powder, mustard seed, ginger, pepper, chilli powder, paprika, garlic, coriander, onion and cardamom are high in polyphenols (confirmed from *in vitro* studies). Sage, marjoram, thyme, tarragon, savory, oregano, peppermint, basil and dill weed are the herbs contain significantly high amount of polyphenols. Polyphenol content is significantly high in pigmented fruits like cranberries, plums, blueberries, raspberries, strawberries, blackberries, figs, blackcurrants, cherries, grape juice, guava, oranges, mango and pomegranate juice [16]. However, polyphenols have antioxidant properties only in test tube studies [18]. Many studies have revealed that after digestion dietary polyphenols have very little or no direct antioxidant food value as they are feebly absorbed (less than ~4.5%) as observed in *in vivo* studies. Generally, the catechol group present in many polyphenols, acts as an electron acceptor thereby showing the antioxidant activity. However, within the human body, this catechol group undergoes extensive metabolism by catechol-*O*-methyl transferase, consequently no longer capable of performing the role of an electron acceptor [19]. High antioxidant content is also observed in avocados, asparagus, broccoli, artichokes, cabbage, beetroot, spinach and in typical nuts (walnuts, pecans, almonds, pistachio, hazelnuts, cashew nuts and macadamia nuts) [10].

4. Mechanistic action of antioxidants

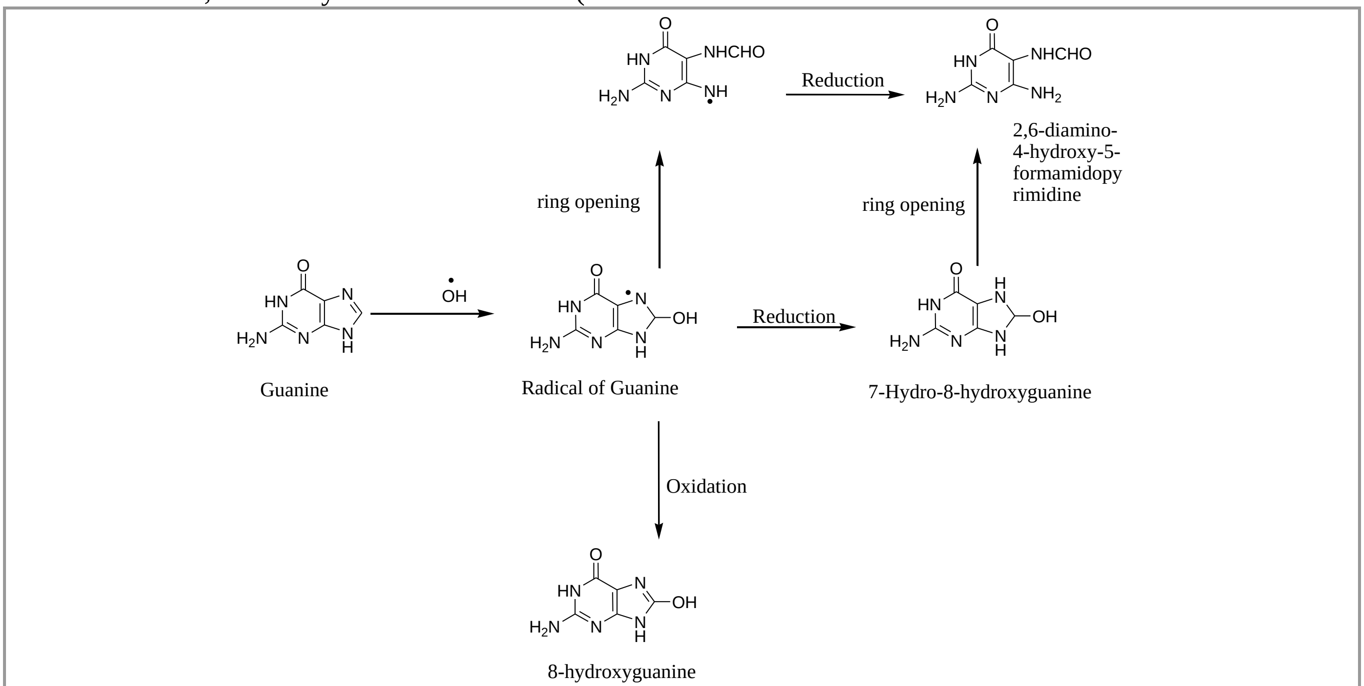
From the point of view of fundamental school level chemistry knowledge, we understand that electrons are paired in their respective molecular orbitals within the stable neutral molecules thereby imparting maximum natural stability. Hence, if there are electrons in an orbital which are unpaired, highly reactive species are generated that become quite eager to trap an electron from any other molecule in order to compensate its deficiency of electron. In free radicals, oxygen belongs to a triplet state as it possesses two unpaired electrons. In biological systems, the reaction rate of triplet oxygen is extremely sluggish [20]. However, often it can turn to severely toxic units as it metabolically transforms into one or more highly reactive intermediates which are capable of reacting with cellular components [20,21].

To prevent oxidative damages, the antioxidant compounds react in single electron transfer mechanisms with free radicals in vivo/in vitro. In this section, the mechanistic action of the natural antioxidant compounds will be discussed as it is very important to understand the reaction mechanism of antioxidants with free radicals. Reactive oxygen species (ROS) and reactive nitrogen species (RNS) are generated in usual biochemical reactions with increased exposure to the environment [22]. These are responsible for the oxidative stress in different pathophysiological conditions which in turn liable for alterations of cellular constituents of our body and results in various disease states. There are certain compounds acting as antioxidants to enhance cellular defence mechanism to reduce the oxidative stress [1]. Depending on their activities we can categorize antioxidants as enzymatic and non-enzymatic antioxidants. The function of enzymatic antioxidants involves catalyzing the break down and removal of free radicals. These are also involved in the conversions of oxidative products into hydrogen peroxide. Hydrogen peroxide is then converted to water in the presence of cofactors such as copper, zinc, manganese and iron *via* a multi-step process. On the other hand, non-enzymatic antioxidants (classic examples involve vitamin C, vitamin E, plant polyphenol, carotenoids and glutathione) involve in the process by interrupting free radical chain reactions [18,23,24]. ROS are generated on activation of NADPH oxidase with fast uptake of oxygen. Initially, superoxide anion radical (O_2^{-}) is generated which is then converted to hydrogen peroxide by SOD (superoxide dismutase) [22].

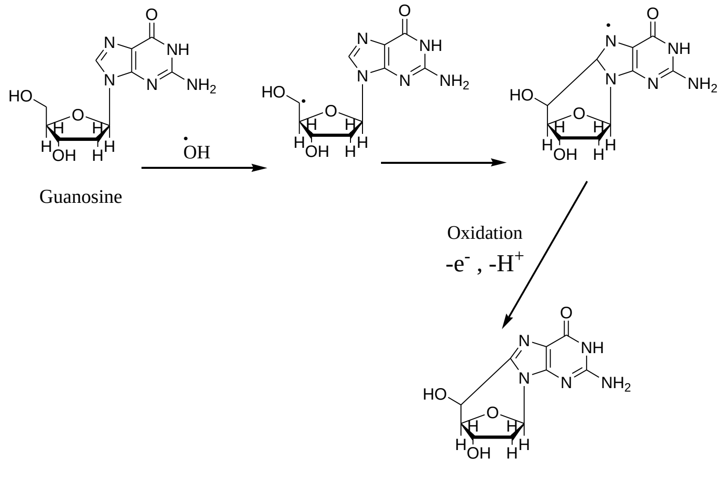
On the other hand, RNS such as nitric oxide ($NO^{\cdot}$), are generated by the enzyme nitric oxide synthase from arginine. Evidently, an inducible nitric oxide synthase (iNOS) is competent of constantly producing a huge quantity of $NO^{\cdot}$. This $NO^{\cdot}$ acts as an $O_2^{\cdot}$−quencher as $NO^{\cdot}$ and O_2^{-} can react to produce peroxynitrite (ONOO−), a very strong oxidant. Neither $NO^{\cdot}$ nor $O_2^{\cdot -}$ can be considered to be a strong oxidant. However, peroxynitrite is a strong and versatile oxidant that can attack a broad array of biological targets. The resultant peroxynitrite reacts with the residues of aromatic amino acid present in the enzyme resulted in nitration of the aromatic amino acids and enzyme inactivation [25-27].

Several research reports clearly reveal that oxygen metabolism generates $^{\cdot}OH$, O_2^{-} and the non-radical H_2O_2 and among these $^{\cdot}OH$ is extremely reactive and it reacts with biological molecules such as DNAs, proteins and lipids, which results in huge to moderate chemical alterations of these molecules (Scheme 2, Scheme 3) [28,29].

In DNA, the hydroxyl radical forms an adduct on reacting at the C-8 position of guanine. The resulting radical (C-8-hydroxy-adduct radical of guanine), on



Scheme 2. Reaction of hydroxyl radical with guanine [18].



Scheme 3. Reaction of the hydroxyl radical with sugar moiety of DNA [18].

oxidation is then converted to 8-hydroxyguanine whereas reduction followed by ring opening leads to the formation of 2,6-diamino-4-hydroxy-5-formamidopyrimidine. The same product is obtained from C-8-hydroxy-adduct radical of guanine by an initial ring opening followed by reduction (Scheme 2).

A similar type of reaction of hydroxyl radical is also observed with the other DNA bases resulting in impaired dsDNA. Again it has been shown in Scheme 3, in DNA, the hydroxy radical abstracts a hydrogen atom, present at C-5' carbon of the sugar moiety and the resulting radical then combines with the C-8 carbon of the purine ring system *via* intramolecular cyclization resulting in the formation of 8,5'-cyclo-2'-deoxyguanosine.

Activated oxygen species and metal ions such as Fe^{2+} and Cu^{2+} come together to damage the proteins oxidatively. Lysine, proline, arginine and histidine are extremely sensitive towards such oxidative damage. Recent studies have revealed that a wide array of residue modifications can take place obviously including the formation of peroxides and carbonyls and usually oxidative damage to tissue indicates in the increased amount of oxidized protein [23]. The defence mechanism of the body is then activated against ROS by the utilization of enzymatic antioxidant mechanisms and reduction of the levels of lipid hydroperoxide and H_2O_2. These enzymatic antioxidants inhibit lipid peroxidation and maintain the structure and function of cell membranes. Classic examples include superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GSHPx) and peroxiredoxin I–IV (I–IV) [30].

SOD's are situated in the cytosol and mitochondria and they catalytically convert the O_2^- into oxygen and H_2O_2 in company of the metal ion cofactors such as copper (Cu), zinc (Zn) or manganese (Mn). Now, the enzyme CAT that is frequently present in the peroxisome, converts H_2O_2 to water and oxygen. On the other hand, GSHPx are usually found both in the cytoplasm and extracellularly in almost every human tissue and they are capable of converting H_2O_2 into water [30,31]. There is no scarcity of research articles and reviews that reveal the enzymatic antioxidants and their mechanisms [10,18,23].

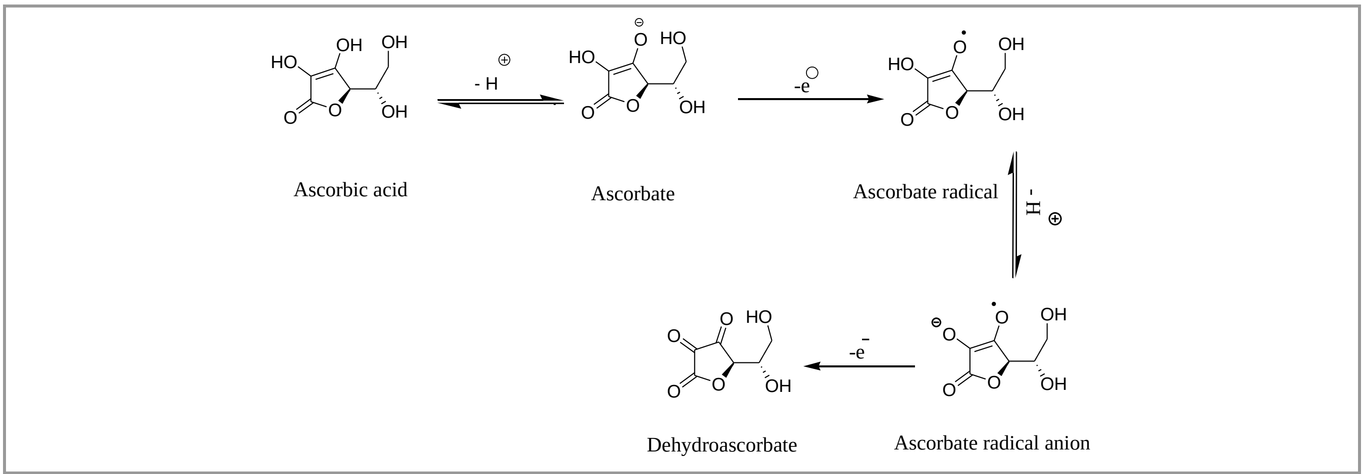
4.1. Panacean quality of vitamins

Vitamin E (α-tocopherol) functions as a 'chain breaker' during lipid peroxidation in cell membranes. This is an efficient lipid soluble antioxidant that exhibits antioxidant effects by scavenging lipid peroxyl radicals in vivo as well as in vitro systems [17]. However, vitamin E is not an efficient scavenger of ˙OH and alkoxyl radicals (˙OR) in vivo.

Vitamin C (ascorbic acid), a dibasic acid containing an enediol group primarily assembled into a five-membered lactone ring. Vitamin C is a water-soluble free radical scavenger and it gets converted to the ascorbate radical by donating an electron to the lipid radical in order to cease the lipid peroxidation chain reaction (Scheme 4).

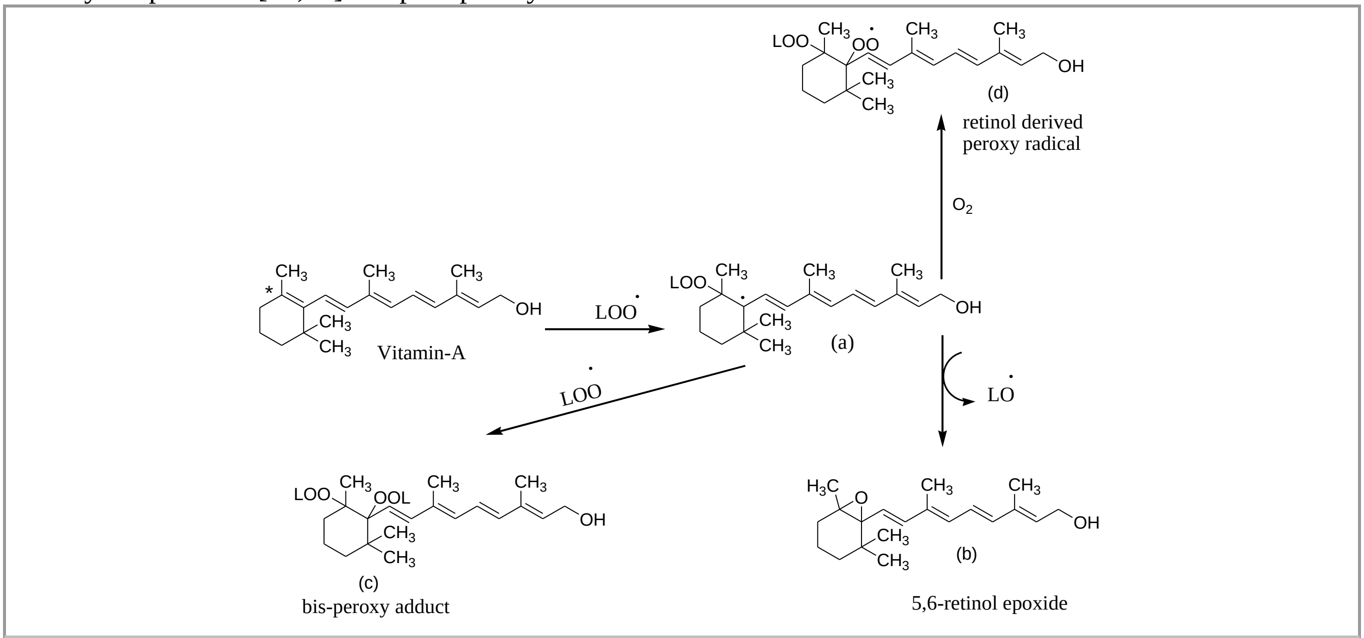
Electrochemical studies have clearly indicated that a reversible redox couple is formed between ascorbic acid and dehydroascorbic acid. It is quite evident from the above mechanism that the pairs of ascorbate radicals react rapidly to produce one molecule of ascorbate along with another molecule of dehydroascorbate. Since dehydroascorbate does not show any antioxidant capacity, it gets converted back into the ascorbate by the addition of two electrons with the help of oxidoreductase [32-34]. Dehydroascorbic acid, the oxidized form, can be reduced back to ascorbic acid by glutathione (GSH).

Monaghan and Schmitt were the persons who first described antioxidant potential of vitamin A and its protecting behaviour of lipids against rancidity [35].



Scheme 4. Radical scavenging mechanism of Ascorbic acid.

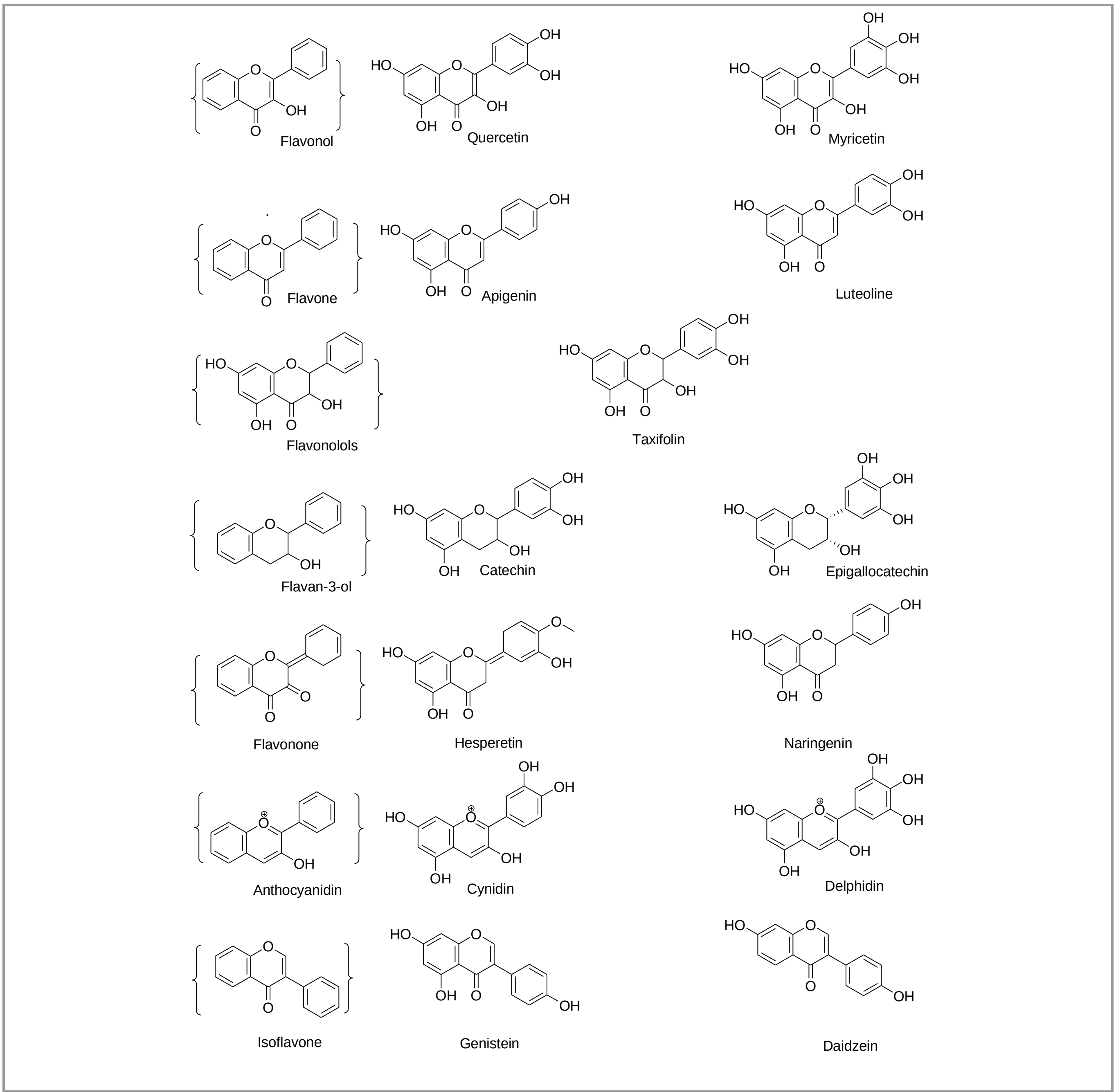
Study has been performed on vitamin A in relation to protect human LDL against copper-stimulated oxidation. Oxidation of the polyunsaturated fatty acid (PUFA) generates a fatty acid radical (L˙) (where, LH is the target PUFA), which rapidly adds oxygen to form a fatty acid peroxyl radical (LOO˙). The peroxyl radicals are the carriers of the chain reactions and they can further oxidize PUFA molecules to initiate new chain reactions, producing lipid hydroperoxides (LOOH). In the mechanism below (Scheme 5), vitamin A's radical scavenging pathway has been briefly explained [36,37]. Lipid peroxyl radicals (LOO·) undergo radical addition on the unsaturated carbon atom (marked *) of vitamin A. The resulting carbon radical (a) thus generated can react in multiple ways. It can either attack the oxygen centre of -OOL moiety in an intramolecular fashion to form 5,6-retinol epoxide (b) or it can combine with another lipid peroxyl radical (LOO·) to generate bis-peroxyl product (c). Another possibility of the carbon radical is that the carbon radical can combine with atmospheric oxygen to form retinol derived peroxyl radical (d).



Scheme 5. Radical scavenging mechanism of vitamin A [18, 37].

4.2. Antioxidant Activities of Bioflavonoid

Bioflavonoids, fundamentally a class of natural benzo-γ-pyran derivatives have the general structure of a 15-carbon skeleton consisting of two phenyl rings and a heterocyclic ring [38]. Bioflavonoids possess important antioxidant activities and they can be classified into: flavone (e.g. apigenin, luteoline), flavonol (e.g. quercetin, myricetin), flavonolols (e.g. taxifolin), flavan-3-ols (e.g. catechin, epigallocatechin), flavonone (e.g. hesperetin, naringenin), anthocyanidin (e.g. cynidin, delphidin), isoflavone (e.g. genistein, daidzein) [39-41] (Representative structures are given in Scheme 6).

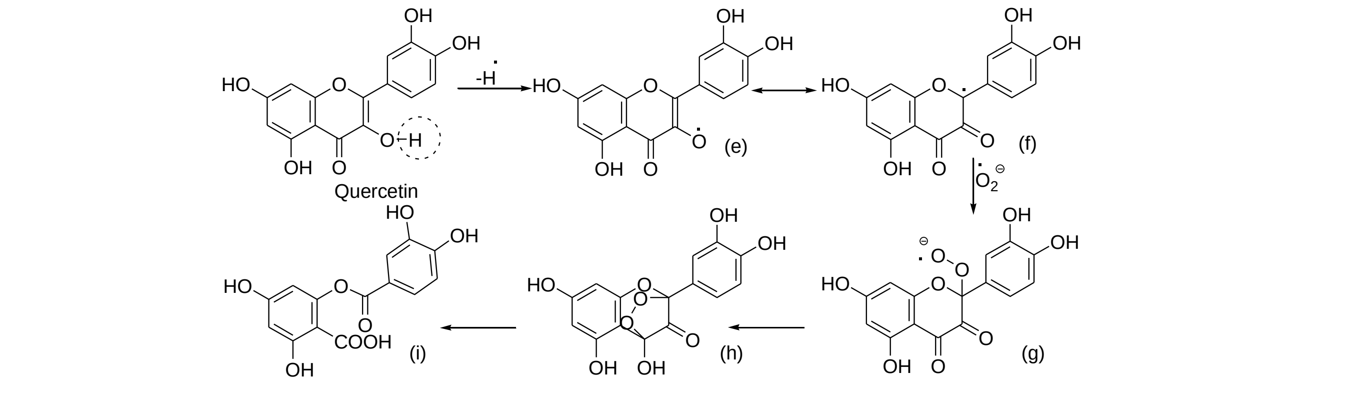


Scheme 6. Representative structures of a few bioflavonoids.

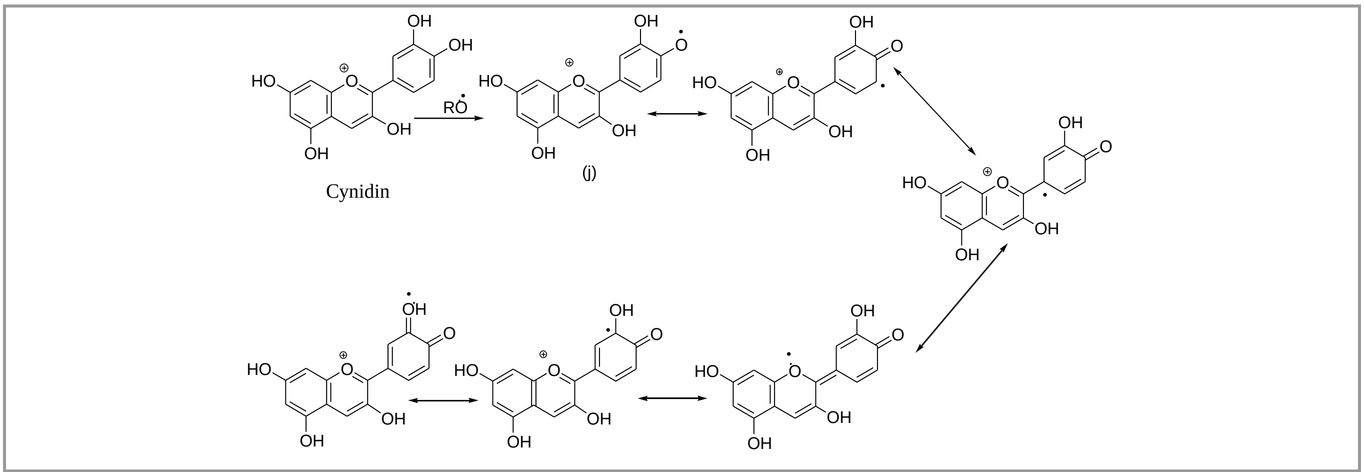
Bioflavonoids constitute the most common group of polyphenolic compounds in the human diet and they are found ubiquitously in fruits and vegetables. They show several biological effects including free radical-scavenging activity. For example, Quercetin is a flavonol, acknowledged extremely for its ability to protect DNA from oxidative damage resulting from the attack of $^{\cdot}OH$, H_2O_2 and O_2^- on the DNA oligonucleotides (Scheme 7) [42]. Quercetin releases the labile enolic hydrogen (circled) to generate radical (e). The other canonical form of radical (e) is shown here as (f). Radical (f) then combines with the superoxide anion radical to generate (g). The newly formed radical, (g), undergoes intramolecular nucleophilic addition on carbonyl carbon to form a new five membered ring, (h), which slowly breaks down to (i).

On the other hand, anthocyanidins (cynidin) releases a hydrogen radical from the marked phenolic –OH group to the foreign radical (R-O ·) to form a phenoxy radical (j) which is stabilised *via* resonance through various canonical forms thereby inactivating the foreign free radical (Scheme 8) [43].

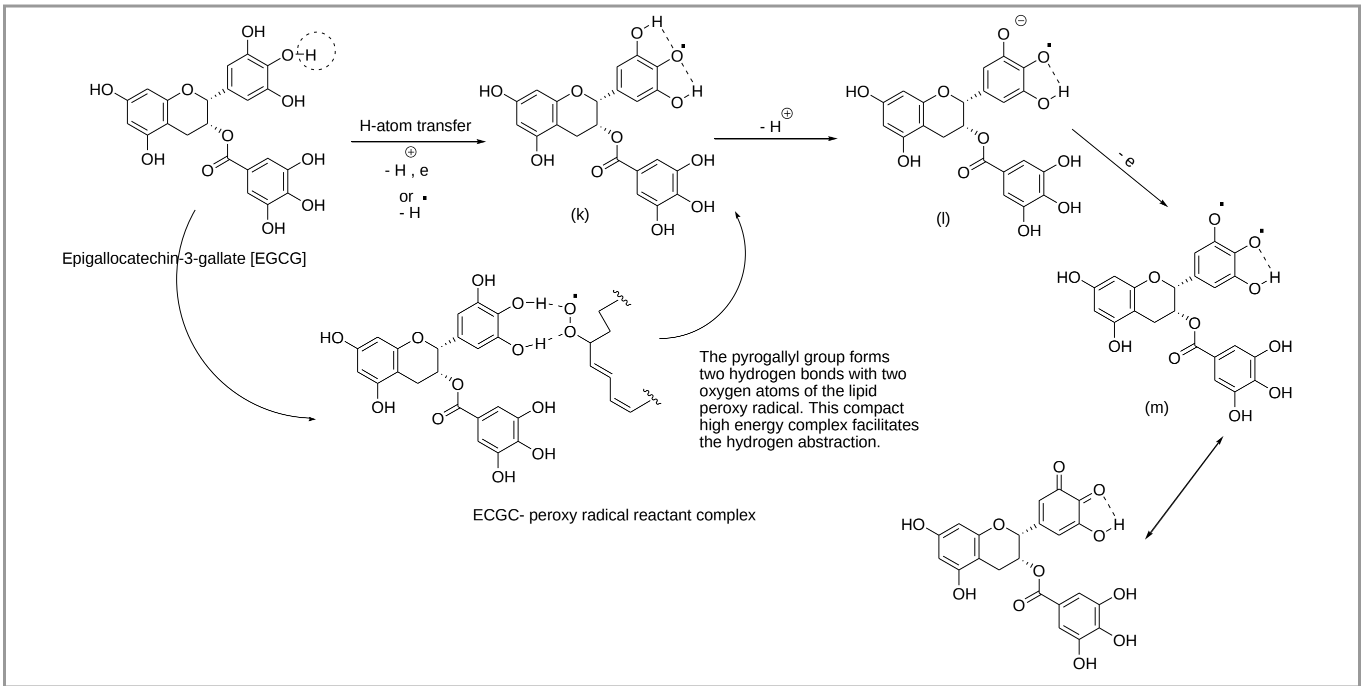
Again, Epigallocatechin gallate (EGCG), mainly found in green tea improves the cognitive function of our brain, helping in faster circulation of the blood to the brain. There are two ways in which EGCG exhibits antioxidant activity-either by the quenching of ROS or by the interruption of free radicals. The mechanism, in all probably, proceeds *via* a hydrogen-



Scheme 7. Superoxide anion radical scavenging mechanism of Quercetin [42].



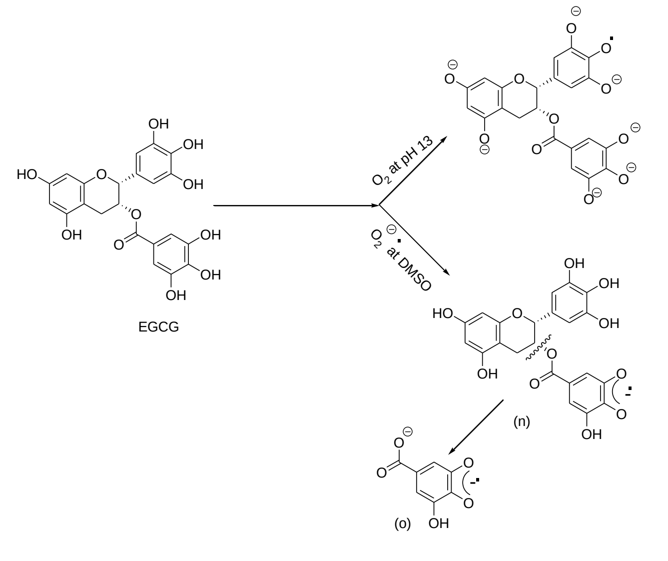
Scheme 8. Radical scavenging mechanism of cynidin.



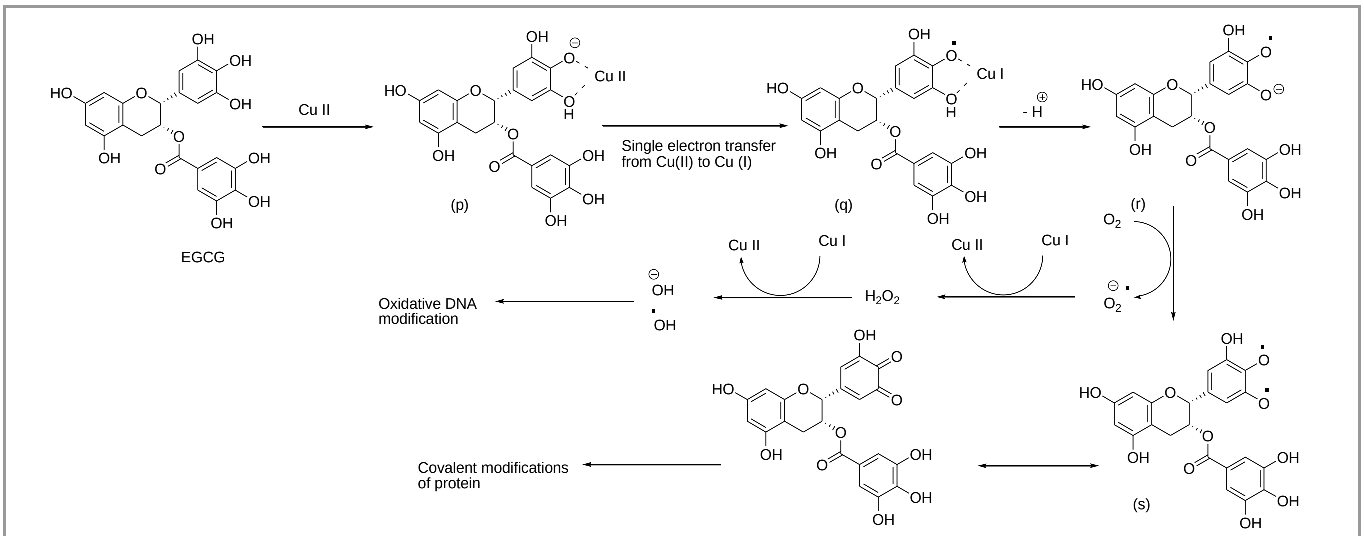
Scheme 9. EGCG antioxidant mechanism [44].

atom transfer. It must be noted that the resultant phenoxy radical is stabilized by intramolecular hydrogen bonding as shown in Scheme 9. EGCG releases the hydrogen radical (circled) and the resulting radical (k), gets stabilised through intramolecular hydrogen bonding involving two adjacent phenolic -OH group. After deprotonation, (k) gets converted to (l) which on further releasing an electron slowly gets converted (m) which is significantly stabilised by resonance.

At high pH, *in vitro* pro-oxidant effects can be enhanced by green tea polyphenols. During autoxidation in alkaline (pH 13) conditions, EGCG readily forms free radicals by radical oxidation according to findings from EPR analysis (outlined in Scheme 10). EGCG oxidation by superoxide radical anion generates the unstable radical (n), which on degradation, forms a more stable gallic radical (o). EGCG pro-oxidant reactions have been shown in Scheme 11. Copper (II) plays an instrumental role here. Initially, it forms a complex involving two oxygen atoms of mono-anion of EGCG (p). Cu (II) is then reduced to Cu (I) *via* single electron transfer alongside the formation of a radical (q) from mono anion (p). Radical (q) then undergoes deprotonation to form radical anion (r). The radical anion (r) then gets oxidised by aerial oxygen releasing an electron to form a diradical (s) which is then stabilised through resonance along with the formation of superoxide radical. Cu (I) converts superoxide radical thus getting generated in this process to hydrogen peroxide (H_2O_2) and itself gets converted to Cu (II). Hydrogen peroxide then collapses to hydroxyl radical and hydroxide anion in presence of Cu (I).



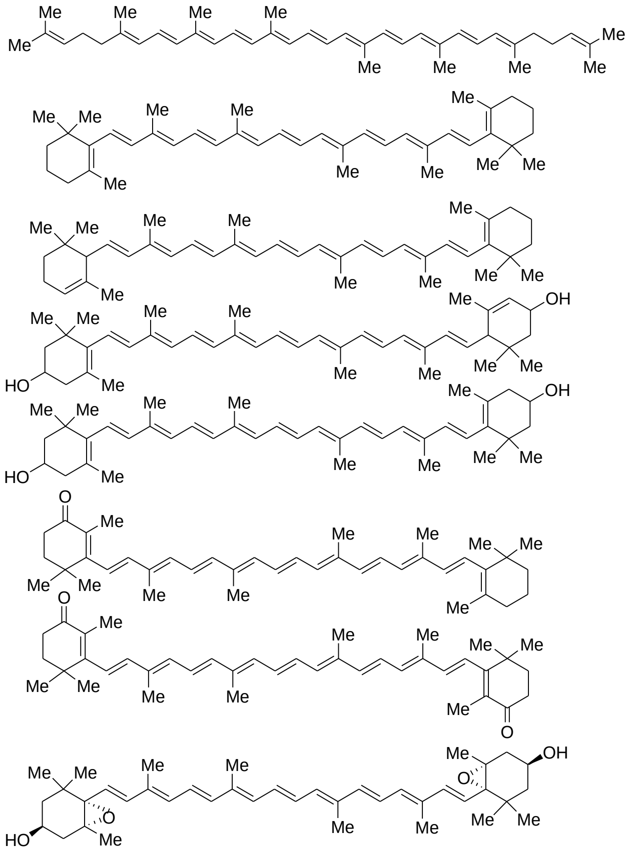
Scheme 10. EGCG autooxidation and superoxide reactions [44].



Scheme 11. EGCG pro-oxidant reactions [44].

4.3. *Carotenoids-pigmented antioxidants obtained from the plant kingdom*

Carotenoids, also known as tetraterpenoids, are naturally occurring yellow, orange and red organic pigments which are chiefly produced in the plastids of plants and algae and several bacteria and fungi. Carotenoids are large in numbers (more than 600) and they are chiefly divided into two categories, namely carotenes and xanthophylls depending on their chemical constituents. α-carotene, β-carotene and lycopene are the examples (Scheme 12) of hydrocarbon-only carotenoids and they are known as carotenes whereas oxygenated derivatives are called xanthophylls [45]. Besides these, complex xanthophylls are also observed in the forms of lutein and zeaxanthin (oxygen substituents); echinenone and canthaxanthin (keto/oxo groups); violaxanthin, antheraxanthin and neoxanthin (epoxide groups); and β-citraurin (aldehyde groups). These are the most common lipid soluble (long unsaturated alkyl chains in carotenoids are responsible for lipophilicity) phytonutrients [46]. Among more than 600 different compounds, Lycopene and β-carotene are the prominent carotenoids. A process like lipid peroxidation generates peroxyl radicals and these peroxyl radicals damage the lipids in the cell wall. Among many other ROS, peroxyl radicals are efficiently scavenged by carotenoids (reacting with them by forming resonance stabilized carbon-centred radicals) [47]. A significant number of conjugated double bonds are mainly responsible for the quenching of singlet oxygen and demonstration of antioxidant activity of Lycopene [45,48]. Reports reveal that the ability of Lycopene to quench singlet oxygen is stronger than that of β-carotene. β-Carotene, naturally occurring orange-colored carotenoid, abundantly found in the yellow-orange fruits and in dark-green leafy vegetables shows probable antioxidant property due to its chemical structure and the interaction with biological membranes [49,50].



Scheme 12. Representative structures of a few carotenoids.

4.4. *Curcumin, an antioxidant with multiple curative properties*

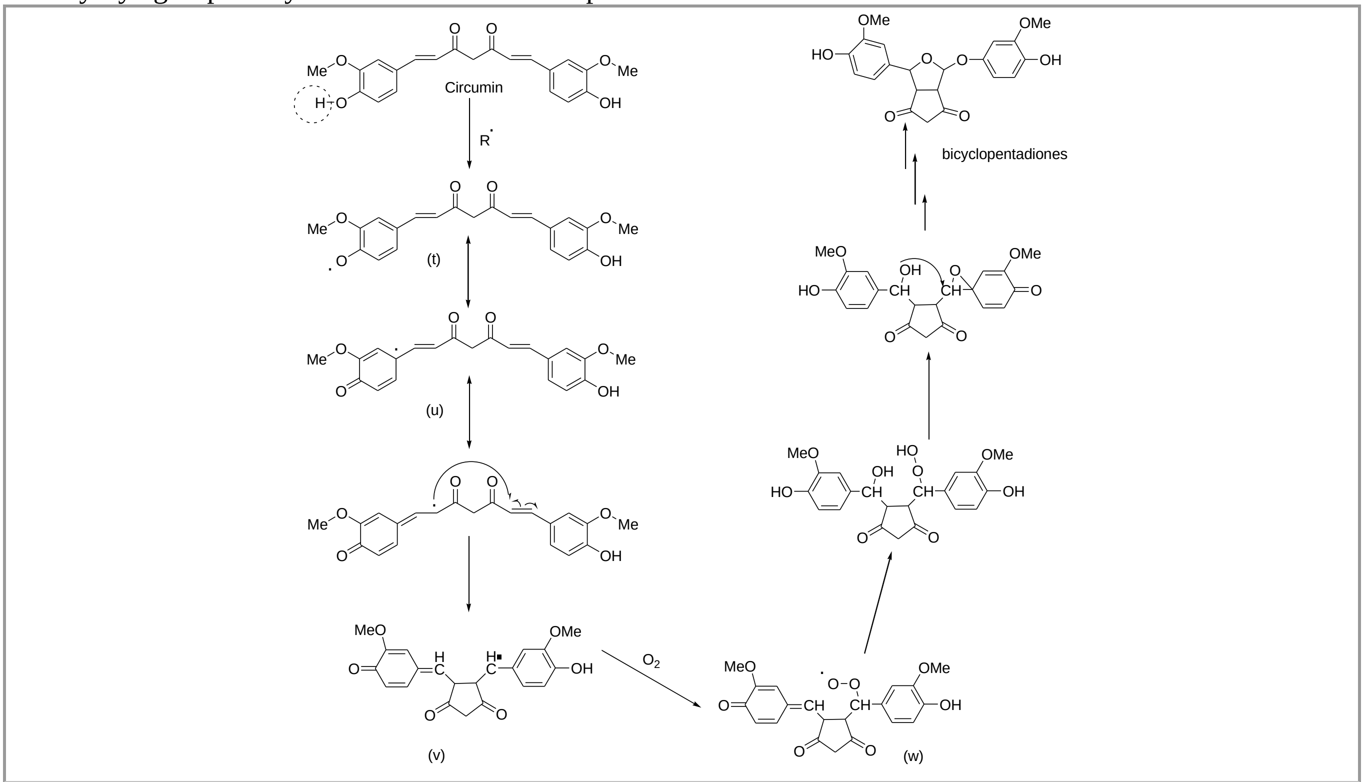
Curcumin is a bis-α, β-unsaturated β-diketone and it shows keto–enol tautomerism. Curcumin is lipid soluble and exhibits remarkable antioxidant activity [51]. The phenolic -OH group present in curcumin is chiefly accountable for the radical scavenging activity (Scheme 13) of this skeleton along with a methylene unit present in such β-diketone framework (Scheme 14) [52-54]. H-atom abstraction or transfer of electron can be performed by free radical from any of these sites. As seen in Scheme 13, one of the two phenolic hydroxyl groups (circled) releases one hydrogen radical thereby forming a phenoxyl radical (t). The other canonical form of resonance stabilised phenoxyl radical is a carbon radical (u) which then forms an intramolecular cyclization to form a new five membered ring (v) containing a β-diketone unit. The benzylic radical then combines with aerial oxygen to generate (w) which slowly gets converted to bicyclopentadiones through several steps.

Scheme 14 shows Curcumin's radical scavenging activity involving the methylenic unit present in such β-diketone framework. After abstracting a hydrogen atom from the methylenic moiety, the resulting radical (x) is extremely stabilised through resonance involving the carbonyl functionalities.

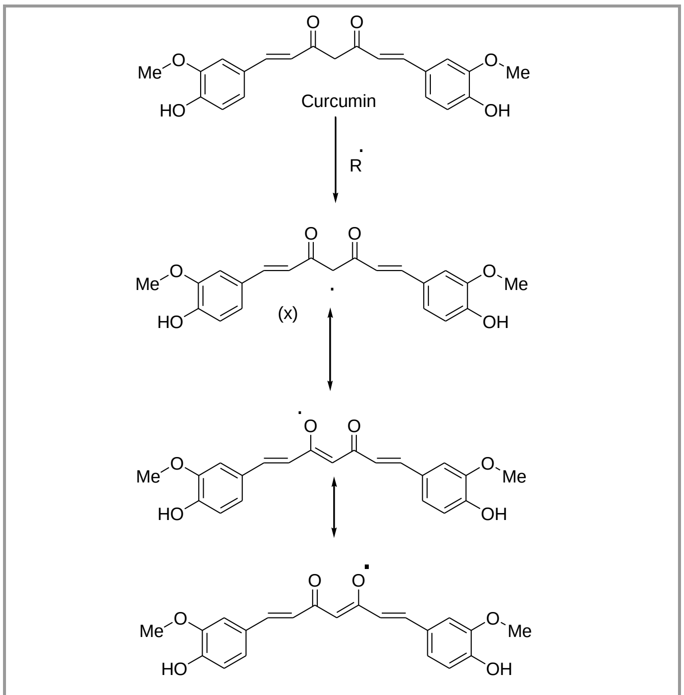
4.5. *Glutathione is also the most critical and integral part of your detoxification system*

Mark Hyman, the famous American physician and author once said the above lines to describe Glutathione. It is true that Glutathione, present in animals, plants and microorganisms, is a pivotal antioxidant in the sense that it can prevent cell damage including lipid peroxides, peroxides, free radicals and heavy metals which are generally induced by ROS [55]. ROS scavenging ability of Glutathione can be both *via* enzymatic and non-enzymatic pathways. The free thiol group present in Glutathione is responsible for its non-enzymatic antioxidant activity [56]. In addition to this, detoxification of oxidants is also possible using several enzymatic reactions involving glutathione reductase, glutathione peroxidase and glutathione-S- transferase.

Glutathione can be synthesized in the body from the amino acids such as *L*-glutamic acid, *L*-cysteine and glycine. Glutathione, a tripeptide with a gamma peptide linkage involving the carboxyl functional group of the glutamate side chain and the amino functional group of cysteine. The amino functional group of glycine forms a normal peptide linkage to the free carboxyl group of the cysteine residue. The free sulfhydryl group of cysteine unit serves as a proton donor and allows the glutathione to act as an antioxidant [57]. The sulfur atom present in the sulfhydryl group contains a vacant 3d orbital and it is present in low oxidation state allowing it to become extremely susceptible to oxidation even without the presence of the enzyme [58].



Scheme 13. Curcumin's radical scavenging activity of involving phenolic unit present [18, 53].



Scheme 14. Curcumin's radical scavenging activity involving methylenic unit present in such β-diketone framework [18,53].

5. Conclusion

Living organisms produce reactive oxygen species (ROS) by means of normal cellular metabolism. The diseases like cancer, neurodegenerative, respiratory and digestive diseases are often caused due to the overproduction of ROS. Antioxidants are believed to play a very important role in the body defence system against ROS. The concentrations of ROS, under physiological conditions are regulated in a subtle way by antioxidants. In this review, the importance of antioxidants, the types and benefits of antioxidants, their occurrence in food items, the mechanistic action of antioxidants especially vitamins, bioflavonoids, epigallocatechin gallate, carotenoids, curcumins and glutathiones have been addressed. Hence, it can be concluded that antioxidants are a powerhouse of preventive and curative compounds that can change the face of the upkeep of the human body if used wisely. Antioxidants are really a masterpiece of Mother Nature.

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Disclosure statement

The author declares that there is no conflict of interests whatsoever regarding this manuscript.

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