Chapter

Antioxidants Obtained from the Natural Sources: Importance in Human Health

Sushil S. Burle, Krishna R. Gupta, Swati N. Lade, Shyam W. Rangari and Milind J. Umekar

Abstract

Now a day the interest in natural and synthetic antioxidants is increasing very rapidly in functional food ingredients and dietary supplements. The differences between the number of free radicals and antioxidants are the main cause of the oxidative damage of lipids, proteins, and DNA. In this chapter, we are summarising the natural antioxidants which have been obtained from plants, animals, or microbial sources. Flavonoids are the most comprehensive antioxidant compounds which are obtained from natural sources. These flavonoids are reactive toward many radicals which are studied by many researchers under various experimental conditions and their structural activity relationships have been recognised. This chapter includes the various types of antioxidants obtained from natural sources and their impact on human health as pharmaceutical, nutraceutical, and phytoceuticals as well as their use in the treatment of various diseases along with the mechanism of action.

Keywords: free radical, natural antioxidants, phytoceuticals

1. Introduction

The antioxidant is defined as the any substance at very low concentration compared with that of an oxidizable substrate significantly which delays or inhibits oxidation of the substrate. According to the Halliwell and Gutteridge the antioxidants are the substance that prevents oxidative damage to a target molecules [1]. The antioxidant act as a oxidation inhibitors at very low concentration when people are using them to prevent the health damages ours due to the polluted plants and various factors which causes the illness in human beings [2]. For the survival of human beings the oxygen plays very important role under some situation it shows the deleterious effects on the human body. The negative effects of oxygen are due to the formation and activity of number of chemical compounds it knows as the reactive oxygen species (ROS). These ROS is collectively including both oxygen radicals and several non-radical oxidising agents that mostly take part in the intitation or propagation of chain reaction [3]. The reactive species are free radicals that represent a class of highly reactive intermediate chemical entities whose reactivity is derived from the presences

of unpaired electron in the chemical formula structure. There are the two main major group in the living cells: enzymatic and non enzymatic antioxidants these enzymatic are again further divided into the primary and secondary enzymatic. The primary is composed of three important enzymes which prevents the formation and neutralisation of the free radicals by donating two electrons to reduces the peroxidase by forming selenols and also eliminates peroxidase as potential substrate for the fenton reaction catalase which turns hydrogen peroxide into water and molecular oxygen one of the most important and efficient antioxidants known today which turns hydrogen peroxide into water and molecular oxygen—one of the most important and efficient antioxidants known today, when just one molecule of catalase converts 6 billion molecules of hydrogen peroxide. The superoxide dismutase which changes the superoxide anions into hydrogen peroxide which is act as catalase.

1.1 Antioxidant

The antioxidant is the substances that prevent the oxidative damage in the body all the cell in the body requires the oxygen (O_2) for energy production and naturally produced free radical as a byproduct which causes damage. Antioxidants act as "free radical scavengers" and repair the damage done by free radicals. This term was used in late nineteen and early twenty centuries. The antioxidant molecules are capable of preventing the oxidation of other molecules. These are obtained from both naturally as well as synthetic source [4].

1.1.1 Types of antioxidant

Antioxidants are classified in two ways depending on their solubility one is hydrophilic which is soluble in water and other hydrophobic which is water-insoluble but soluble in lipids. The water-soluble antioxidant reacts with oxidant present in cell cytosol and blood plasma. On the other hand, the hydrophobic antioxidant prevents the cell membrane from lipid peroxidation. Traditionally these antioxidants are of two classes' primary or chain-breaking antioxidant and secondary or preventative antioxidant [5, 6].

Mechanisms of primary antioxidant as follows

$$L\bullet + AH \rightarrow LH + A\bullet \quad (1)$$

$$LO\bullet + AH \rightarrow LOH + A\bullet \quad (2)$$

$$LOO\bullet + AH \rightarrow LOOH + A\bullet \quad (3)$$

$$A\bullet + A\bullet \rightarrow AA \quad (4)$$

Where L• is a lipid radical, AH• inhibited antioxidant (**Figure 1**).

1.1.2 Use of Antioxidant

- They prevent the oxidative degradation of polymers like plastics, adhesives, and rubber which causes the loss of strength and flexibility in these materials [7].

- It used in neurodegenerative diseases like Parkinsonism, Alzheimer and amyotrophic sclerosis diseases treatment.

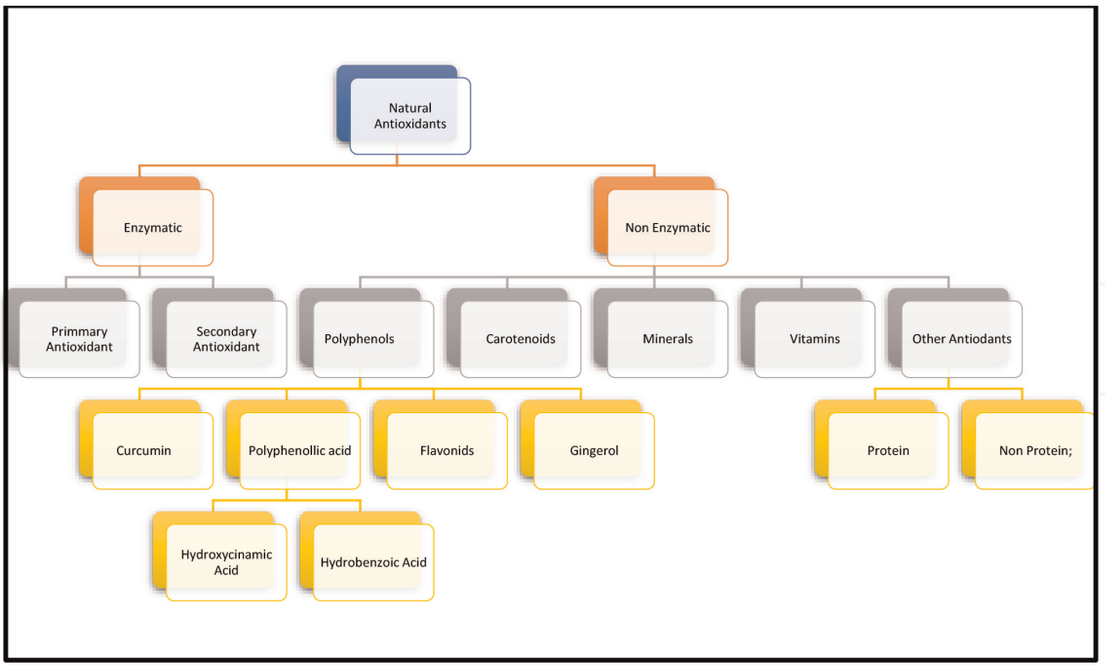

Figure 1.
Classification of antioxidants found in natural sources.

- They are used in the treatment of various brain injury, sodium thiopental, superoxide dismutase mimetic and propofol is used for the treatment of reperfusion injury and trauma.

- Vitamins like E and C also used as an antioxidant out of which Vit. E it helps for the protection of cells and tissues from lipid peroxidative damage caused due to free radicals While Vit. C used as a supplement by inactivating free radicals produced through normal cellular activity and stressors

- An antioxidant like ascorbic acid, carotenoids, amino acids, peptides, flavonoids and other phenolic compounds might also play an important role in physiological and dietary antioxidants.

2. Free radicals

These are highly reactive chemical species. These reactive oxygen species generated in phagocytosis, mitochondrial respiratory chain, fertilisation, and arachidonic acid metabolism. These free radicals are a species which contains an unpaired electron in an atomic orbital. They either donate an electron or extract an electron from other molecules. [8] Chain reactions of these radicals are dividing into three parts viz., Initiation, Propagation, and Termination.

In initiation reaction a net increase in the number of free radicals, while in propagation reaction are those reactions involving free radicals in which the total number of free radicals are same. Further in termination reaction, the net reduction in the number of free radicals takes place. Two free radicals combine to form a more stable species.

2.1 Types of free radicals

As a free radical originated from oxygen atom hence it is called as a reactive oxygen species (ROS) this ROS include a superoxide (O_2^-), Hydroxyl (OH), hydrogen peroxide (H_2O_2), peroxyl (ROO), nitric oxide (NO) and alkoxy (RO) until completely reduced to water. The large no superoxides are produced in mitochondrial and microsomal electron chain. On the other hand, the cytochrome oxidase is retained by the moderately reduced oxygen intermediated bound to its active site. All other elements of mitochondrial respiratory chain transfer the electron directly to oxygen and not preserve the reduced oxygen intermediate in the active site [9].

2.1.1 Super oxide ion

This is an oxygen molecule which contains extra electron. This free radical causes damage to DNA, Mitochondria. The body can neutralise the superoxide radical by producing Superoxide dismutase.

2.1.2 Hydroxyl radical

It produced by the reduction of an oxygen molecule in electron transport chain. These hydroxyls radical are highly reactive in nature and cannot eliminate by an enzymatic reaction. As it is more reactive it damages most of the organic molecules like DNA, Lipid, Carbohydrate, and proteins.

2.1.3 Nitrogen species

These are also called reactive nitrogen species. The metals like copper and iron have many numbers of unpaired electrons which can also act as free radicals. These metals have not strong affinity of the electron but can effortlessly accept and donate electrons.

2.1.4 Oxygen radical

The radical are mostly formed by the immune system. These generally cause the oxidation of cholesterol and LDL.

2.2 Free radical and biology

It helps for intracellular killing of bacteria by phagocyte cells such as macrophages and granulocytes.

Superoxide and Hydroxyl radical are most important radical due to their reactivity. These radicals take part in unwanted side reaction this side reaction results in cell damage. As it concentration increase it may lead to cell injury and finally death of the cell. This action is responsible for various disease conditions like myocardial infarction, stroke, cancer, diabetes etc. Few symptoms of ageing like atherosclerosis are also recognised to free radical-induced oxidation of numerous chemicals. Apart from this disease it may also involve in Parkinson's disease, senile deafness caused due to drugs, Alzheimer disease, and schizophrenia [10].

2.2.1 Sources of free radicals

The free radicals are the byproduct of cellular processes and these are produced from metal cofactors by spontaneous catalyzation. Nowadays the environmental sources act as a measured source of free radicals as the radiation is increasing largely around the city are also responsible for the radiation sources includes the mobile phone, X-ray, computer and television set etc. apart from this mental stress is also one of the sources of free radical generation [11].

3. Oxidation

The utilisation of oxygen for generation of energy by metabolism of food nutrients is most important part for survival of all living beings. This oxygen is extremely reactive atom which is useful for the destruction of singlet oxygen, hydroperoxyl radical, superoxide radical, organic peroxides, nitric oxide, peroxynitrite and triplet oxygen. The oxygen which is consumed during the breathing it produces free radical production and apart from this environmental factors such as smoke, pollutants, and certain chemicals also contribute to their formation. This leads to the starting of chain reactions in cells and it can cause damage or death to the cell [12]. The Mechanisms with antioxidant properties were purposefully included to fatty meals in order to disrupt chain processes by substituting free radical intermediates and inhibiting other oxidation reactions. Antioxidants, such as ascorbic acid, thols, and polyphenols, help to neutralise free radicals by oxidising themselves and acting as reducing agents. In the packaged food, the antioxidant is added separately to prevent the generation of free radicals and to ensure food safety.

The various properties of radicals like accepting or donating an electron from other molecules which leads to the stabilising the free radical at the beginning but stats to produces another process which leads to the damage of biological molecules like Proteins Carbohydrates lipids and DNA which leads to the homeostatic disruption [13].

3.1 Concept of oxidative stress

The Oxidative stress explain the relation between the disease and free radicals. The normal healthy human body, generates the pro-oxidants in the form of reactive nitrogen species and reactive oxygen species and reactive nitrogen species are useful for the maintains of all antioxidant level. This delicately maintained balance is shifted in favour of pro-oxidants whenever it is exposed to various environmental, physico-chemical, and pathological agents such as cigarette smoking, atmospheric pollutants, radiation UV rays, toxic chemicals, overnutrition, and advanced glycation end products (AGEs) in diabetes. It has been linked to the genesis of over 100 human illnesses as well as the ageing process [5].

3.2 Molecular damage induced by free radicals

Various biological molecules present in our body are attacked by the various free radicals which leads to the impairment of cell functions and damaged the molecules produces the diseased states.

3.3 Lipids and lipid peroxidation

The lipids present in membrane are highly susceptible to free radical damage when this lipid reacted with free radicals can undergo highly damaging chain reaction of lipid peroxidation leading to both direct and indirect effects. The lipid peroxidation mediated by the free radical process in this the intitation caused by the species attack which abstract a hydrogen atom from the methylene group which leave an unpaired electron on the carbon atom. Molecular rearrangement stabilises the resulting carbon radical to form a conjugated diene, which can then combine with an oxygen molecule to form a lipid peroxyl radical. These radicals can then extract hydrogen atoms from additional lipid molecules to generate lipid hydroperoxides, further propagating lipid peroxidation. A variety of responses can end the peroxidation process. The most important one involves the reactivity of LOO• or lipid radical (L•) with an antioxidant molecule such as vitamin E or -tocopherol (-TOH), resulting in a more stable tocopherol phenoxyl radical that is not engaged in further chain reactions. Other cellular antioxidants, such as vitamin C or GSH.

Many toxicologically interesting chemicals are produced during the lipid peroxidation process, including malondialdehyde, 4-hydroxynonenal, and other 2-alkenals. Isoprostanes are unique products of arachidonic acid lipid peroxidation, and procedures such as mass spectrometry and ELISA-assay kits have recently become available to identify isoprostanes [14, 15].

3.4 Proteins

Protein oxidation by ROS/RNS can result in the formation of both stable and reactive molecules, such as protein hydroperoxides, which can generate additional radicals when they interact with transition metal ions.

Although the majority of oxidised proteins that are functionally inactive are quickly removed, some can accumulate over time and contribute to the damage associated with ageing as well as a variety of diseases. Lipofuscin, a peroxidized lipid and protein aggregation, forms in the lysosomes of aged cells and Alzheimer's disease brain cells [16].

3.5 Carbohydrates

Many toxicologically interesting chemicals are produced during the lipid peroxidation process, including malondialdehyde, 4-hydroxynonenal, and other 2-alkenals. Isoprostanes are unique products of arachidonic acid lipid peroxidation, and procedures such as mass spectrometry and ELISA-assay kits have recently become available to identify isoprostanes [13].

3.6 DNA

The interaction of DNA with ROS or RNS causes oxidative damage to the DNA. •OH, eaq-, and H• free radicals react with DNA by adding to bases or removing hydrogen atoms from the sugar moiety. •OH attacks the C4—C5 double bond of pyrimidine, resulting in a variety of oxidative pyrimidine damage products such as thymine glycol, uracil glycol, urea residue, 5-hydroxydeoxyuridine, 5-hydroxydeoxycytidine, hydantoin, and others. Similarly, when •OH reacts with purines, it produces 8-hydroxydeoxyguanosine (8-OHdG), 8-hydroxydeoxyadenosine,

formamidopyrimidines, and other unidentified purine oxidative products. Several repair pathways are involved in the repair of DNA damage [9, 17]. 8-OHdG has been linked to cancer and is regarded as a trustworthy marker for oxidative DNA damage.

3.7 Significance of antioxidants in relation to disease

Zinc is a trace element that functions as a cofactor for approximately 200 human enzymes, including the cytoplasmic antioxidant Cu-Zn SOD, an isoenzyme of SOD found mostly in the cytosol. Selenium, a trace element, also serves as a cofactor for glutathione peroxidase. Vitamin E and tocotrienols (produced from palm oil) are powerful lipid-soluble antioxidants that act as a "chain breaker" during lipid peroxidation in cell membranes and other lipid particles like LDL [18, 19].

Vitamin E is considered the "gold standard antioxidant" against which other antioxidant-containing compounds are tested, particularly in terms of biological activity and therapeutic importance. The recommended daily intake varies from 400 to 800 IU. Ascorbic acid (vitamin C) is a free radical scavenger that is water soluble. The daily suggested dose is 60 mg. Aside from these carotenoids, other carotenoids such as beta-carotene, lycopene, lutein, and others function as important antioxidants, quenching 1O2 and ROO•. Flavonoids, which are typically present in plants as colouring pigments, can act as powerful antioxidants at varying concentrations [5, 18, 19].

3.8 Antioxidants and human disease prevention

Several epidemiological studies have discovered an inverse association between established antioxidants/phytonutrient levels in tissue/blood samples and the occurrence of cardiovascular disease, cancer, or mortality from these diseases. A recent meta-analysis, however, reveals that supplementing with largely single antioxidants may not be as beneficial. A point of view that contradicts preclinical and epidemiological data on the use of antioxidant-rich foods. Based on the majority of epidemiological and casecontrol studies, recommendations for daily dietary intake of several well-known antioxidants, such as vitamin E and C, as well as others, were produced. Because of dietary variances, antioxidant requirements in India differ from those in industrialised western nations. There are also a variety of antioxidant-rich dietary supplements that have been studied for effectiveness. Many laboratories in India are researching the antioxidant impact of plant chemicals, primarily sourced from natural sources, that can protect against such damage. Carotenoids, curcumin from turmeric, flavonoids, caffeine (found in coffee, tea, and other beverages), orientin, vicenin, glabridin, glycyrrhizin, emblicanin, punigluconin, pedunculagin, 2-hydroxy-4-methoxy benzoic acid, dehydrozingerone, picroliv, withaferin, yakuchinone, gingerol, chlorogenic acid, van (a water-soluble analogue of chlorophyll) [20].

3.9 Newer therapeutic approaches using antioxidants

Over the last three decades, antioxidant-based drugs/formulations for the prevention and treatment of complicated illnesses such as atherosclerosis, stroke, diabetes, Alzheimer's disease (AD), Parkinson's disease, cancer, and others have emerged. The significance of dietary antioxidants in the prevention of numerous human illnesses, including cancer, atherosclerosis, stroke, rheumatoid arthritis, neurodegeneration, and diabetes, has been substantially influenced by free radical theory. Dietary

antioxidants may offer intriguing therapeutic potential in delaying the onset of Alzheimer's disease and its associated consequences in the elderly population. There are two neuroprotective clinical studies with antioxidants available: the Deprenyl and tocopherol antioxidant treatment of Parkinson's research. India can manufacture world-class products by combining traditional knowledge and contemporary science. As a result, it has launched a fast-track effort to develop novel pharmaceuticals by expanding on established therapies and examining the country's various plant and microbial sources. This initiative is not only the world's largest undertaking of its sort in terms of scale, variety, and access to talent and resources, but it is also unique [21].

3.10 Ayurveda, antioxidants and therapeutics

Ayurvedic medications are often tailored to an individual's constitution using a unique holistic approach. Ayurvedic Indian and traditional Chinese systems are living 'great traditions,' and they play major roles in the bioprospecting of novel medications from medicinal plants, which are also high in antioxiodants. According to current estimates, around 80% of people in underdeveloped nations still rely on traditional medicine, which is mostly focused on diverse kinds of plants and animals, for their main treatment. Ayurveda is one of the most ancient and still extensively practised systems in India.

4. Sources of antioxidants, phytonutrients and functional foods

Natural substances, particularly those originating from food sources, contain a considerable amount of antioxidants. Some drinks, such as tea, are also high in antioxidants. A increasing amount of research shows that moderate tea drinking may protect against several types of cancer, cardiovascular disease, kidney stone development, bacterial infections, and dental cavities. Tea is notably high in catechins, the most abundant of which is epigallocatechin gallate (EGCG) [9, 15].

4.1 Indian medicinal plants

Aside from food sources, Indian medicinal plants contain antioxidants, such as: (with common/ayurvedic names in brackets) *Aegle marmelos* (Bengal quince, Bel), *Allium cepa* (Onion), *Allium sativum* (Garlic, Lahsuna), *Aloe vera* (Indian aloe, Ghritkumari), Amomum subulatum (Greater cardamom, Bari elachi), *Asparagus racemosus* (Shatavari), *Azadirachta indica* (Neem, Nimba) [15].

4.2 Synthetic antioxidants

Due to availability and Importance, synthetic antioxidants are commonly employed as food additives to prevent rancidification. In edible vegetable oil and cosmetics, synthetic antioxidants such as butylated hydroxyanisole, tertiary butyl hydroquinone, 2,4,5-trihydroxybutyrophenone, octyl gallate, propyl gallate, 4-hexylresorcinol and nordihydroguaiaretic acid and are utilised [22, 23]. As synthetic phenolic antioxidants, propyl gallate and butylated hydroxyanisole shown greater chemical activity in reducing chain start of unsaturated fatty acid oxidation. Although antioxidants are effective in protecting product quality during food distribution, excessive amounts of antioxidants added to food may generate toxicities or

mutagenicities, putting people's health at risk. The antioxidant will be chosen based on the kind of fat and oil in the diet. Butylated hydroxyanisole and butylated hydroxytoluene dissolve in most fats and oils, however they work best in animal fats. When consumed in conjunction with other meals, it has a more favourable impact than when used alone. Propyl gallate, on the other hand, which is not easily soluble, is more effective in vegetable oils than butylated hydroxyanisole and butylated hydroxytoluene, tertiary butyl hydroquinone is the most efficient antioxidant for slowing oxidation in unsaturated fats such as vegetable oils. Lower quantities of tertiary butyl hydroquinone can achieve oxidative stability than other synthetic antioxidants [24].

4.3 Natural and synthetic antioxidants

Natural and synthetic antioxidants are utilised as food additives in the food business to help extend the shelf life and appearance of various foods. Synthetic phenolic antioxidants (butylated hydroxyanisole, propyl gallate and butylated hydroxytoluene [BHT]) substantially suppress oxidation; for example, chelating compounds like Metals can be bound by ethylene diamine tetraacetic acid (EDTA), reducing their contribution to the process. Antioxidants are also naturally contained in many foods and are essential for human health. They contain vitamins C and E, which may be found in fruits and vegetables and seeds and nuts, respectively. Antioxidants can be found in vitamins (ascorbic acid and -tocopherol), herbs and spices (rosemary, thyme, oregano, sage, basil, pepper, clove, cinnamon, and nutmeg), and plant extracts (tea and grapeseed). While synthetic antioxidants (such as butylated hydroxytoluene and butylated hydroxyanisole) are commonly used to protect the quality of ready-to-eat food items, public concern about their safety has prompted the food industry to explore natural antioxidants. Some people's health issues have been induced by synthetic antioxidants. Butylated hydroxyanisole, butylated hydroxytoluene, and tertiary butyl hydroquinone appear to be the most troublesome antioxidants, with gallates coming in second position and having been utilised in food items with certain limits since the late 1950s. TBHQ is a relatively recent addition to the list of antioxidants permitted in food; it was approved for use as an antioxidant in food in Europe in 2004. Butylated hydroxyanisole, butylated hydroxytoluene, and tertiary butyl hydroquinone are typically found in meals containing oil and fat. Their activity is comparable to that of Vitamin E, which is utilised as an alternative antioxidant in some of the same products. These antioxidants may exist alone in a diet, but they are frequently combined with other molecules that have antioxidant action, such as phosphoric acid, propyl gallate, citric acid, and ascorbic acid [17, 25].

4.4 Health concerns of synthetic antioxidants

While the bulk of studies have been conducted on animals, there is still a substantial body of research that has discovered issues with synthetic antioxidants in humans [26–28]. The **Table 1** below covers some of the human health concerns associated with butylated hydroxyanisole, butylated hydroxytoluene, and tertiary butyl hydroquinone. In one study, seven people reported symptoms such as vasomotor rhinitis, headache, flushing, asthma, conjunctival suffusion, dull retrosternal (behind the breastbone) pain radiating to the back, diaphoresis (excessive sweating), or somnolence after being exposed to butylated hydroxyanisole and butylated hydroxytoluene (sleepiness). In a subsequent trial looking for cross-reactivity with aspirin, they

Rhinitis
Angioedema
Asthma
Dermatitis
Eye Problems
Joints paints

Table 1.
Effect of butylated hydroxy anisole, butylated hydroxytoluene, and tertiary butyl hydroquinone on human health.

discovered twenty-one patients who were intolerant to butylated hydroxyanisole and butylated hydroxytoluene. A handful of persons have developed dermatitis after being exposed to these synthetic antioxidants [29]. In one investigation, tertiary butyl hydroquinone in a hair colour produced contact dermatitis, and cross sensitization with butylated hydroxyanisole and butylated hydroxytoluene was seen. According to the US Department of Health and Human Services' Carcinogens report, butylated hydroxyanisole is "reasonably expected to be a human carcinogen based on substantial evidence of carcinogenicity in experimental animals." There is also worry that "butylated hydroxytoluene. May change to other carcinogenic chemicals in the human body." One conversion product of butylated hydroxytoluene (the hydroperoxide form, for example) has been demonstrated to disrupt chemical signals conveyed from cell to cell.

5. Health issues related to the antioxidant

5.1 Neurodegenerative disorders

Because of the high amount of lipids, particularly polyunsaturated fatty acids, nervous tissue, including the brain, is very sensitive to free radical damage. Biochemical and histological investigations in Alzheimer's disease have revealed elevated levels of oxidative stress and membrane damage. Peroxidation of Lipids Changes in antioxidant enzyme levels in neurons of Alzheimer's disease patients, such as catalase and CuZn- and Mn-SOD, are associated with increasing stress. Protein oxidation, protein nitration, and lipid peroxidation have all increased. They are seen in neurofibrillary tangles and neuritic plaques. Increased levels of peroxidation products such as 4-hydroxynonenal (4-HNE) in the cerebral fluid of Alzheimer's disease patients suggest widespread lipid peroxidation. Iron (Fe2+) is thought to play a role in enhanced lipid peroxidation in Alzheimer's disease. Multiple pathways, including impairment of the activity of membrane ion-motive ATPases (Na+/K + -ATPase and Ca2 + -ATPase), glucose transporters, and glutamate transporters, may contribute to neuronal mortality in Alzheimer's disease. Lipid peroxidation produces the aldehyde 4-HNE, which appears to play a key role in the neurotoxic effects of amyloid [14].

5.2 Free radicals, diabetes and ages

Experimental data suggests that free radicals have a role in the establishment of diabetes and, more crucially, the development of diabetic complications [30]. The

Free radical scavengers are useful in avoiding experimental diabetes in animal models and in type 1 (IDDM) and type 2 (NIDDM) patients, as well as in lowering the severity of diabetic sequelae. Persistent hyperglycemia in diabetic individuals causes oxidative stress due to

a. glucose autooxidation;

b. non-enzymatic glycosylation;

c. the polyol pathway.

The spontaneous reduction of molecular oxygen to superoxide and hydroxyl radicals, which are extremely reactive and interact with all biomolecules, occurs during glucose auto-oxidation. In addition, they hasten the production of advanced glycation end products (AGEs). Pyrroles and imidazoles, for example, tend to accumulate in tissue. Crosslinking AGE-protein with other macromolecules in tissues causes cell and tissue function problems. The third route by which free radicals are created in tissues is the polyol pathway [31]. This route deletes 30 lots of NADPH, which reduces the production of antioxidants like glutathione. The ability of antioxidant enzymes is also diminished as a result of protein glycation. In endothelial cells, free radicals react with nitric oxide, resulting in a reduction of vasodilation function. Long-lived structural proteins, collagen and elastin, undergo non-enzymatic crosslinking throughout life and in diabetics [32]. This abnormal protein crosslinking is mediated by AGEs generated by nonenzymatic glycosylation of proteins by glucose.

5.3 Free radical damage to DNA and cancer

DNA is a common site of free radical damage. Strand breakage (single or double strand breaks), different forms of base damage giving products such as 8-hydroxyguanosine, thymine glycol, or abasic sites, damage to deoxyribose sugar, and DNA protein cross linkages are among the numerous types of damages generated. These damages can cause heritable changes in the DNA, which can lead to cancer in somatic cells or foetal abnormalities in germ cells. The interaction of free radicals with tumour suppressor genes and proto-oncogenes suggests that they have a role in the genesis of several human malignancies [9]. Cancer occurs as a result of a series of genetic alterations. Tobacco smoking and chewing, UV rays from sunshine, radiation, viruses, chemical contaminants, and other factors can all be initiating agents. Hormones are examples of promoting agents (androgens for prostate cancer, estrogens for breast cancer and ovarian cancer). Inflammation causes the production of iNOS (inducible nitric oxide synthase), as well as COX and LOX. These are capable of initiating carcinogenesis. Experimental and epidemiological evidence show that a number of dietary components can serve as antioxidants, inhibiting cancer formation and lowering cancer risk. Vitamins A, C, E, beta-carotene, and micronutrients such as antioxidants and anticarcinogens are among them [33, 34]. The recent studied the processes behind dietary phytochemical anticancer effects. Chemopreventive phytochemicals have the ability to prevent or reverse the promotion stage of multistep carcinogenesis. They can also prevent or slow the growth of precancerous cells into malignant cells. Many of the molecular changes linked with carcinogenesis occur in cell-signalling pathways that control cell proliferation and differentiation. The family of mitogen activated protein kinases is a key component of the intracellular signalling

network that maintains homeostasis (MAPKs). With the activation of the transcription factors NF-B and AP1, several intracellular signal-transduction pathways converge. These variables are prominent targets of several types of chemopreventive phytochemicals because they mediate the pleiotropic effects of both external and internal stimuli in the cellular-signalling cascades [34]. Curcumin, the active ingredient of *Curcuma longa* (Turmeric, Haldi), inhibits the production of COX2, LOX, iNOS, MMP-9, TNF, chemokines, and other cell-surface adhesion molecules, as well as cyclin D1. Human clinical studies have demonstrated that curcumin at dosages up to 10 g/day is safe and can inhibit tumour start, promotion, and metastasis. Many Long-term prospective clinical investigations are required to validate the hypothesis.

5.4 Mitochondria, oxidative protein damage and proteomics

Proteomic technologies' fast advancement and application to large-scale investigations of protein-protein interactions and protein expression patterns imply that these approaches are ideally suited to give the molecular insights required to completely comprehend oxidative harm caused by free radicals [35]. The very significant progress has been made in identifying specific proteins that are confined to the mitochondria throughout the previous two decades. Specifically, the 100 or more subunits that make up the five complexes of the electron transport chain (ETC). Several groups have recently begun to tackle the bigger task of establishing the content of complete mitochondrial proteomes from a variety of key model systems as well as human tissues, utilising contemporary mass spectrometry (MS)-based proteomic methods. Gibson and colleagues identified 684 distinct proteins from the combined peptide data acquired from over 100,000 mass spectra generated by MALDI-MS and high performance liquid chromatography (HPLC) MS/MS analysis using mitochondria isolated from human heart. These findings have been included into 'MitoProteome,' a publicly available database for the human heart mitochondrial proteome.

5.5 Free radicals and ageing

Ageing is caused by mitochondrial ROS generation and oxidative damage to mitochondrial DNA. Increased lipid peroxidation in cellular membranes as a result of oxidative stress results in fatty acid unsaturation. According to the most current study on 'free radicals and ageing, Caloric restriction (CR) is the only known experimental alteration that reduces the rate of mammalian ageing, and it has multiple beneficial impacts on rodent and likely human brains. Calorie-restricted mitochondria, like those seen in long-lived animal species, effectively inhibit ROS generation with pyruvate and malate at complex I. The oxygen consumption of the mitochondria stays same, while the free radical leak from the electron transport chain is reduced in CR. Many researchers discovered that increasing the number of oxidative stress defence systems may increase an organism's health span. Arking's group's work on artificial selection in flies resulted in organisms with much higher levels of oxidative stress tolerance and more efficient mitochondria. Indeed, lower ROS formation and increased ROS removal resulted in less oxidative damage and a later start of senescence in those flies. However, using genetic engineering techniques to introduce additional copies of these oxidative stress-resistance genes into mice did not result in a longer lifetime.

6. Conclusion

Natural ingredients are becoming increasingly popular these days. Food antioxidants and preservatives may cause lipid peroxidation and deterioration of taste and quality. Free radicals have been linked to the genesis of a wide range of important illnesses. They can cause several important biological molecules to lose shape and function. Such unfavourable alterations in the body might result in illness. Antioxidants can guard against the damage caused by free radicals at various levels of action. Plants' dietary and other components are rich in antioxidants. The link between free radicals, antioxidants, and the function of numerous organs and organ systems is extremely complicated, and the discovery of 'redox signalling' marks a watershed moment in this critical interaction. Recent research has focused on several ways for protecting vital tissues and organs from oxidative damage caused by free radicals. Many unique techniques have been developed, and substantial discoveries have been achieved in recent years. Natural antioxidants are abundant in the traditional Indian food, spices, and medicinal herbs. Increased consumption of foods with functional properties, such as high levels of antioxidants in functional foods, is one method that is gaining traction in advanced nations and is making an appearance in our country.

This chapter focuses on an overview of the potentials of numerous sources with appropriate antioxidant potential, as well as their influence on human health. Because 70–80% of the world's population cannot afford contemporary supplements and treatments, this chapter illustrates that individuals may priorities their food habits depending on the antioxidant capacity and cost-effectiveness of the accessible supply.

Conflict of interest

None.

Author details

Sushil S. Burle, Krishna R. Gupta*, Swati N. Lade, Shyam W. Rangari
and Milind J. Umekar
Smt. Kishoritai Bhoyar College of Pharmacy, New Kamptee, Nagpur, India

*Address all correspondence to: krg1903@gmail.com

References

[1] Hamad AMA. Some natural antioxidants sources from foods and tree barks. International Journal of Scientific and Technology Research. 2019;**8**(6):93-98

[2] Shebis Y, Iluz D, Kinel-Tahan Y, et al. Natural antioxidants: Function and sources. FNS. 2013;**04**:643-649

[3] Shiv kumar. Free radicals and antioxidant: Human and food system. Applied Science Research. 2011;**2**: 129-135

[4] Mattill HA. Antioxidants. Annual Review of Biochemistry. 1947;**16**: 177-192. DOI: 10.1146/annurev.bi.16.070147.001141

[5] Sies H. Oxidative stress: Oxidants and antioxidants. Experimental Physiology. 1997;**82**(2):291-295. DOI: 10.1113/expphysiol.1997.sp004024

[6] Madhavi DL, Deshpande SS, Salunkhe DK. Introduction. In: Food Antioxidants: Technological, Toxicological, and Health Perspectives. New York, NY: Marcel Dekker, Inc.; 1996. pp. 1-4

[7] Melton SL. Vitamin E. In: Xiong YL, Chi-Tang H, Shahidi F, editors. Quality Attributes of Muscle Foods. Boston, MA: Springer; 1999. DOI: 10.1007/978-1-4615-4731-0_3

[8] Hemnani T, Parihar MS. Reactive oxygen species and oxidative DNA damage. Indian Journal of Physiology and Pharmacology. 1998;**42**(4):440-452

[9] Halliwell B, Gutteridge JMC. Free Radicals in Biology and Medicine. New York: Oxford University Press; 1999. pp. 1-897

[10] Tenpe CR, Aman U, Sushil B, Yeole PG. In vitro antioxidant and preliminary hepatoprotective activity of oroxylum indicum vent leaf extracts. Pharmacologyonline. 2009;**1**:35-43

[11] Gandhi V, Burle S, Kosalge S. Stem cell therapy for Parkinson's disease: A review. PharmaTutor. 2018; **6**(6):1-8

[12] Srinivasan O, Parkin KL, Fennema O, editors. Fennema's Food Chemistry. 4th ed. Boca Raton, Fla: CRC Press; 2008. p. 1144

[13] Burle S, Samanta S. Insilico design, synthesis of hybrid taurine amino acid and peptide analogues for studies on antioxidant and hepatoprotective activity. Indian Journal of Pharmaceutical Education and Research. 2017;**51**(2):S98-S109

[14] Yoshikawa T, Toyokuni S, Yamamoto Y, Naito Y, editors. Free Radicals in Chemistry Biology and Medicine. London: OICA International; 2000

[15] Devasagayam TPA, Boloor KK, Ramsarma T. Methods for estimating lipid peroxidation: Analysis of merits and demerits (minireview). Indian Journal of Biochemistry & Biophysics. 2003;**40**:300-308

[16] Stadtman ER. Protein oxidation and aging. Science. 1992;**257**(5074): 1220-1224. DOI: 10.1126/science.1355616

[17] Roman M, Jitaru P, Barbante C. Selenium biochemistry and its role for human health. Metallomics. 2014;**6**(1): 25-54

[18] Packer L, Ong ASH, editors. Biological Oxidants and Antioxidants: Molecular Mechanisms and Health Effects. Champaign: AOCS Press; 1998

[19] Kagan VE, Kisin ER, Kawai K, et al. Towards mechanism based antioxidant interventions. Annals of the New York Academy of Sciences. 2002;**959**:188-198

[20] Vivekananthan DP, Penn MS, Sapp SK, et al. Use of antioxidant vitamins for the prevention of cardiovascular disease: Metaanalysis of randomized trials. The Lancet. 2003;**361**: 2017-2023

[21] Jayaraman KS. Technology, tradition unite India's drug discovery scheme. Nature Medicine. 2003;**9**:982

[22] Guo L, Xie MY, Yan AP, Wan YQ, Wu YM. Simultaneous determination of five synthetic antioxidants in edible vegetable oil by GC–MS. Analytical and Bioanalytical Chemistry. 2006;**386**(6): 1881-1887

[23] Nazni P, Dharmaligam R. Isolation and separation of phenolic compound from coriander flowers. International Journal of Agricultural and Food Science. 2013;**4**(1):13-21

[24] Mandal S, Yadav S, Yadav S, Nema RK. Antioxidant a review. Journal of Chemical and Pharmaceutical Research. 2009;**1**(1):102-104

[25] Murthy KNC. Evaluation of antioxidant activity of pomegranate (Punicagranatum) and grapes (Vitis vinifera), [thesis] Rajeev Gandhi Univ. of Health Science, India. 2001

[26] Liu T, Stern A, Roberts LJ. The isoprostanes: Novel prostangland in-like products of the free radical catalyzed peroxidation of arachidonic acid. Journal of Biomedical Science. 1999;**6**:226-235

[27] Valko M, Leibfritz D, Moncol J, Cronin MTD, Mazur M, Telser J. Free radicals and antioxidants in normal physiological functions and human disease. The International Journal of Biochemistry and Cell Biology. 2007;**39**: 44-84

[28] Burle SS, Lade SN, Kosalge SB. Recents trends of hepatoprotective medicine. Enzyme;**1**:2

[29] Le Coz CJ, Schneider GA. Contact dermatitis from tertiary butylhydroquinone in a hair dye with cross sensitivity to BHA and BHT. Contact Dermatitis. 1987;**17**:257-258

[30] Lipinski B. Pathophysiology of oxidative stress in diabetes mellitus. Journal of Diabetes and its Complications. 2001;**15**:203-210

[31] Glugliano D, Cerriello A, Paolisso G. Diabetes mellitus, hypertension and cardiovascular disease: Which role for oxidative stress. Metabolism. 1995;**44**: 363-368

[32] Vasan S, Foiles P, Founds H. Therapeutic potential of breakers of advanced glycation end products-protein crosslinks. Archives of Biochemistry and Biophysics. 2003;**419**: 89-96

[33] Croce CM. How can we prevent cancer? Proceedings of the National Academy of Sciences of the United States of America. 2001;**98**:10986-10988

[34] Surh YJ. Cancer chemoprevention with dietary phytochemicals. Nature Reviews. Cancer. 2003;**3**:768-780

[35] Gibson BW. Exploiting proteomics in the discovery of drugs that target oxidative damage. Science. 2004;**304**: 176-177