A Review on Natural Antioxidants

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ABSTRASCT

Natural antioxidants are widely distributed in food and medicinal plants . These natural antioxidant especially polyphenols and carotenoids exhibit a wide range of biological effects including anti-inflammatory ,anti-aging ,anti-atherosclerosis and anticancer.The effective extraction and proper assessment of antioxidants from food and medicinal plant are crucial to explore the potential antioxidants source and promte the applications in functional foods,pharmaceutical and food additives .The present paper provides the comprehensive information on the green extraction technologies of natural antioxidants ,assessment of antioxidants activity at chemical and cellular based levels and their main resources from food and medicinal plants.

keywords: Antioxidants ,extraction,assessment,resource.

Introduction

Plants such as shrubs, herbs, or trees in parts or in whole were used in the treatment and management of various diseases, and disorders can be dated long back. Natural phytochemicals present at low levels in fruits, vegetables, herbs, and spices offer many health benefits, but these compounds may not be effective or safe when consumed at higher dose [1]. The presence of free radicals in biological materials was discovered less than 50 years ago [2].

Pollutants, ionizing radiation or UV light, smoking, exposure of biological systems to xenobiotics, and development of certain pathological conditions lead to oxidative stress, thereby increases production of oxy radicals [3]. Cell damage caused by free radicals appears to be a major contributor in aging and degenerative diseases such as cancer, cardiovascular disease, cataracts, rheumatoid arthritis, and brain dysfunction.

Free radicals have been implicated in the pathogenesis of at least 50 diseases. Fortunately, free radical formation is controlled naturally by various beneficial compounds and antioxidants, and its availability is limited that this dam- age can become cumulative and debilitating. Antioxidants are capable of stabilizing, deactivating, or scavenging free radicals before they attack cells.

Sources and origin of antioxidants: Antioxidants are abundant in fruits and vegetables, as well as in other foods including nuts, grains, and some meats, poultry, and fish. β-Carotene is found in many foods, including sweet potatoes, carrots, cantaloupe, squash, apricots, pumpkin, and mangoes. Lutein, best known for its association with healthy eyes, is abundant in green, leafy vegetables such as collard greens, spinach, and kale. Lycopene is a potent antioxidant found in tomatoes, watermelon, guava, papaya, apricots, pink grapefruit, blood oranges, and other foods. Estimates suggest 85% of American dietary intake of lycopene comes from tomatoes and tomato products.

List of some reactive oxygen species:

Reactive Species	**oxygen**		**Remarks**
Superoxide	$O^{*}2$	10^{-6} s	Generated in mitochondria, in cardiovascular system, and others
Hydroxyl radicle	$^{*}OH$	10^{-9} s	Very highly reactive, generated during iron overload and such conditions in our body
Hydrogen peroxide	H2O2	Stable	Formed in our body by many reactions and yields potent species like. OH
Peroxyl radical	ROO*	S	Reactive and formed from lipids, proteins, DNA, sugars, etc.during oxidative damage
Organic hydroxide	ROOH	Stable	Reactive with transient metal ions to yield reactive species
Singlet oxygen	O2	10^{-6} s	Highly reactive, formed during photosensation and chemical reactions.
Ozone	O3	S	Present as an atmospheric pollutant can react with various molecules

Reactive Species	Nitrogen		Remarks
Nitric oxide	NO*	S	Neurotransmitter and blood pressure regulator can yield potent oxidants during pathological status
Peroxy nitrile	−ONOO	10−3 s	Formed from nitric oxide and superoxide and highly reactive
Peroxynitrous acid	ONOOH	Fairly stable	Protonated from of ONOOH
Nitrogen dioxide	NO2	S	Formed during atmospheric pollution

Definition: Antioxidants can be defined as substances whose presence in relatively low concentrations significantly inhibits the role of oxidation of the targets. Due to continuous generation of partially reduced forms of oxygen by constitutive meta- bolic pathways, a number of protective antioxidant enzymes, such as superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GSHPx), glutathione reductase (GSHRx), glutathione-S-transferase (GST), and nonenzymatic antioxi- dants, have involved to deal with toxic species. Oxidation is a chemical reaction that transfers electrons from a substance to an oxidizing agent. Oxidation reactions can produce free radicals, which start chain reactions that damage cells. Antioxidants terminate these chain reactions by removing free radical intermediates and inhibit other oxidation reactions by being oxidized themselves. Antioxidants are often reducing agents such as thiols, ascorbic acid, or polyphenols.

Types of antioxidants:

Antioxidants are grouped into two:

1. Primary or natural antioxidants
2. Secondary or synthetic antioxidant

Primary or natural antioxidants: They are the chain breaking antioxidants which react with lipid radicals and convert them into more stable products. They are mainly phenolic in structures and include the following [5]:

a. A**ntioxidant minerals**: These are cofactor of antioxidants enzymes. Their absence will definitely affect metabolism of many macromolecules such as carbohydrates. Examples include selenium, copper, iron, etc.

b. Antioxidant vitamins: They are needed for most body metabolic functions. They include vitamin C, vitamin E, and vitamin B.

c. Phytochemicals: These are phenolic compounds that are neither vitamins nor minerals.

These include:

Flavonoids: These are phenolic compounds that give vegetables fruits, grains, seeds leaves, flowers, and bark their colours. Catechins are the most active antioxidants in green and black tea and sesamol. Carotenoids are fat soluble colour in fruits and vegetables. Zeaxanthin is high in spinach and other dark greens.

Secondary or synthetic antioxidants: These are phenolic compounds that perform the function of capturing free radicals and stopping the chain reactions; the compound includes [5]:

a. Butylated hydroxyanisole (BHA)

b. Butylated hydroxytoluene (BHT)

c. Propyl gallate (PG) and metal chela0ng agent (EDTA)

d. Tertiary butylhydroquinone (TBHQ)

e. Nordihydroguaiaretic acid (NDGA).

Classification:

Enzymatic antioxidants:

1.Primary antioxidants, for example, SOD, catalase, glutathione peroxidase

2.Secondary enzymes, for example, glutathione reductase, glucose-6-phos- phate dehydrogenase.

Nonenzymatic antioxidants:

1.Minerals, for example, zinc, selenium

2.Vitamins, for example, vitamin A, vitamin C, vitamin E

3.Carotenoids, for example, β-carotene, lycopene, lutein, zeaxanthin

4.Low-molecular weight an0oxidants, for example, glutathione, uric acid

5.Organosulfur compounds, for example, allium, allyl sulfide, indoles

6.Antioxidant cofactors

7.Polyphenols.

5.1 Enzymatic antioxidants

Copper/zinc and manganese dependent:

a. Superoxide dismutase (SOD): SOD is a group of endogenously produced metalloenzymes with various prosthetic groups present both in prokaryotes and eukaryotes [6]. Three main classes of them differ in their amino acid sequence structure and metallic factors as follows:

1.Cu-Zinc SOD in the cytoplasm with two sub-units and sensitivity to cyanide and hydrogen peroxide.
2.Mn SOD in the mitochondrial matrix and in prokaryotes and is insensitive to cyanide.

3.Fe SOD, usually found in prokaryotes and in the chloroplasts of some plants. It is not sensitive to cyanide but is inhibited by hydrogen peroxide.

4.Al SOD has recently reported [7].

Catalase: H_2O_2 is also metabolized by catalase (CAD), a heme protein with an extremely high turnover rate

$$2H_2O_2 \rightarrow 2H_2O + O_2$$

SOD protects from senescence, aging, ischemic tissue damage, lipid peroxidation, protein denaturation, and radiation damage.

b. Glutathione peroxidase: Glutathione carries out the reduction of H_2O_2 which is enzymatic reaction catalysed by GPx, found in vacuole, cystol, and extracellular space. The enzyme has substrate specificity.

Peroxidases are involved in (1) biotic and abiotic stresses, (2) lignin and suberin synthesis, and (3) disease and pathogen response [8].

$$2\ GSH+H2O2 \rightarrow GSSG+2H2O$$

Consequence of H2O2 accumulation in glucose-6-phosphate dehydrogenase deficiency due to malarial drug primaquine results in haemolytic anemia due to oxidative stress.

c. Glutathione reductase: Glutathione keeps cysteine thiol groups in the reduced state. If two thiol groups become oxidized, they can be reduced nonenzymatically by glutathione. GSSG is reduced by NADPH-dependent enzyme glutathione reductase.

$$6GSSG + NADPH + H \rightarrow 2GSH + NADP+$$

d. Glutathione: Glutathione is a tripeptide that is present in high concentrations in most eukaryotic cells and reacts with free radicals. It directly quenches lipid peroxides. Vitamin C and glutathione work interactively [9].

Nonenzymatic antioxidants:

These are biological molecules that can act as antioxidants by either quenching a free radical directly or indirectly by promoting a process responsible for radical scavenging indirectly [10].

a. Selenium: Selenium is a mineral and a component of antioxidant enzymes. Rice

and wheat are the major dietary sources of selenium. The amount of selenium in soil, which varies by region, determines the amount of selenium in the foods grown in that soil. Animals that eat grains or plants grown in selenium- rich soil have higher levels of selenium in their muscle. Brazil nuts also contain large quantities of selenium.

b. **Transferrin:** Transferrin is a major iron transporting protein in the body. It is normally 20–30% loaded.

c. Lactoferrin: Lactoferrin is a milk protein similar to transferrin that helps in iron

binding.

d .**Ceruloplasmin:** Ceruloplasmin catalyses the oxidation of Fe^{++} to Fe^{+++}, while oxygen is reduced to water.

e. Vitamin A: Vitamin A is found in three main forms: retinol (vitamin A1), 3,4-didehydroretinol (vitamin A2), and 3-hydroxyretinol (vitamin A3). Foods rich in vitamin A include liver, sweet potatoes, carrots, milk, egg yolks, and mozzarella cheese.

f. Vitamin C (ascorbic acid): In the aqueous phase, ascorbic acid may reduce reactive oxygen metabolites directly, with the concurrent formation of dehy- droascorbate and/or indirectly by the regeneration of tocopherol from the tocopherol radical [11]. Vitamin C can be found in high abundance in many fruits and vegetables and is also found in cereals, beef, poultry, and fish.

g. Vitamin E: Vitamin E, also known as alpha-tocopherol, is found in almonds and

oils, including wheat germ, safflower, corn, and soybean oils, and is also found in mangoes, nuts, broccoli, and other foods [12]. It reacts with reactive oxygen metabolites, yielding lipid hydroperoxide, which can be removed by the activity of the phospholipase-GSPHx system.

h. β-Carotene: β-Carotene is a lipid-soluble precursor of vitamin A. It functions synergistically with tocopherol to prevent lipid peroxidation.

Ubiquinol-10: It is a reduced form of coenzyme Q10, present in lipoprotein at relatiely low concentrations. It probably regenerates tocopherol from the tocopheroxyl radical and increases its an0oxidant efficiency. Plant-derived antioxidants.

To protect the cells and organ systems of the body against ROS, humans have evolved a highly sophisticated and complex antioxidant protection system. It involves a variety of components, both endogenous in origin, that function interactively and synergistically to neutralize free radicals [13].

These components include:

Nutrient-derived antioxidants like ascorbic acid, tocopherols and carotenoids, and other low-molecular weight compounds such as GSH and lipoic acid.

Antioxidant enzymes, for example, SOD, GSHPx and GSH reductase, which catalyse free radical quenching reactions. Metal-binding proteins such as ferritin, lactoferrin, albumin, and ceruloplasmin that sequester free iron and copper ions as these ions are capable of catalysing oxidative reactions.

Numerous other antioxidant phytonutrients present in a wide variety of plant foods.

Antioxidant operation and mechanism

The word antioxidant is used in a general sense to refer to any type of chemical agent which inhibits attack by oxygen or ozone [14]. As applied to vegetable oils, antioxidants are compounds which interrupt the oxidation process by preferentially reacting with the fat radical to form a stable radical which does not quickly react with oxygen [15]. Antioxidants function either by inhibiting the formation of free alkyl radicals in the initiation step or by interrupting the propagation of the free radical chain. In truncating the propagation step, the antioxidants function as hydrogen donors. Generally, the most popular antioxidants are hydroxyphenol compounds with various ring substitutions. The antioxidant radical is stabilized with its local electrons delocalized; hence antioxidant free radicals do not readily initiate other free radicals. They even react with lipid free radicals to form stable and complex compounds. In investigating phenolic antioxidants, it is found that their antioxidative capabilities bear a relationship to the number of phenol groups occupying 1,2
or 1,4 positions in an aromatic ring as well as to the volume and electronic characteristics of the ring substituents present [16]. In elucidation of the mechanism of oxidative inhibition, it is established that antioxidants function as oxygen interceptors in the oxidative process thereby breaking the chain reaction that perpetuates the process [17]. The general scheme is presented below:

$$R+AH \rightarrow RH+A$$

$$RO+AH \rightarrow ROH+A$$

$$ROO+AH \rightarrow ROOH+A$$
$$R+A \rightarrow RA$$

$$8RO+A \rightarrow ROAROO+A \rightarrow ROOA$$

$$\text{Antioxidant} + O2 \rightarrow \text{Oxidized antioxidant}$$

Certain metallic ions such as copper and iron act as prooxidants, catalysing the oxidation process. Such metal ions can be sequestered or chelated by certain organic acids. They effectively contribute to lower transition metal activity. Examples of such compounds are citric acid, phosphoric acid, and some of their derivatives.

Estimation of antioxidants

a. Conjugated diene assay: This method allows dynamic quantification of conjugated dienes as a result of initial PUFA (polyunsaturated fatty acids) oxidation by measuring UV absorbance at 234 nm. The principle of this assay is that during linoleic acid oxidation, the double bonds are converted into conjugated double bonds, which are characterized by a strong UV absorption at 234 nm. The activity is expressed in terms of inhibitory concentration (IC50) [17, 18, 19].

b. DPPH method (1,1 diphenyl-2-picrylhydrazyl): This most widely reported DPPH assay method is based on the reduction of methanolic solution of coloured free radical DPPH by free radical scavenger. The procedure involves measurement of decrease in absorbance of DPPH at its absorption maxima of 516 nm, which is

proportional to concentration of free radical scavenger added to DPPH reagent solution. The activity is expressed as effective concentration EC50 [20].

c. Superoxide radical scavenging activity: In vitro superoxide radical scavenging activity is measured by riboflavin/ light/ NBT (Nitro blue tetrazolium) reduction. NBT method is based on generation of superoxide radical by auto-oxidation of riboflavin in presence of light. The super- oxide radical reduces NBT to a blue-coloured formazan that can be measured In nm. The capacity of extracts to inhibit the colour to 50% is measured in terms of EC50. Antioxidant activity of **Ailanthus,** flavonoids, and Triphala has been reported in terms of superoxide radical scavenging activity. The superoxide radical can also be detected by oxidation of hydroxylamine, yielding nitrite which is measured colorimetric reaction [20].

d. Hydroxyl radical scavenging activity: Generation of hydroxyl radicals using Fe3+/ascorbate/EDTA/H2O2 system using Fenton reaction. Scavenging of this hydroxyl radical in presence of antioxidant is measured. In one of the methods, the hydroxyl radicals formed by the oxidation is made to react with DMSO (dimethyl sulphoxide) to yield formaldehyde. Formaldehyde formed produces the intense yellow colour with Nash reagent (2 M ammonium acetate with 0.05 M acetic acid and 0.02 M acetyl acetone in distilled water). The intensity of yellow colour formed by that reaction is measured at 412 nm spectrophotometrically against reagent blank. The activity is expressed as % hydroxyl radical scavengering [21].

e. Nitric oxide radical inhibition activity: Nitric oxide, because of its unpaired electron, is classified as a free radical and displays important reactivities with certain types of proteins and other free radicals. In vitro inhibition of nitric oxide radical is also a measure of antioxidant activity. This method is based on the inhibition of nitric oxide radical generated from sodium nitroprusside in buffer saline and measured by Griess reagent. In presence of scavengers, the absorbance of the chromophore is evaluated at 546 nm. The activity is expressed as % reduction of nitric oxide [21].

f. Reducing power method: This method is based on the principle of increase in the absorbance of the reaction mixture, which indicates increase in the antioxidant activity. In this method, antioxidant compound forms a coloured complex with potassium ferricyanide, trichloroacetic acid, and ferric chloride, which is measured at 700 nm. Increase in absorbance of the reaction mixture indicates the reducing power of the samples [22].

g. Phosphomolybdenum method: A spectroscopic method for the quantitative determination of antioxidant capacity, through the formation of phosphomolybdenum complex. The assay is based on the reduction of Mo(VI) to Mo(V) by the sample and subsequent formation of a green phosphate Mo(V) complex at acidic pH [22].

h. Peroxynitrite radical scavenging activity: Peroxynitrite is now recognised by researchers as the culprit in many toxic reactions. Hence, an in vitro method for scavenging of peroxy radical has been developed to measure antioxidant activity. The scavenging activity is measured by monitoring the oxidation of dihydrorhodamine on a microplate fluorescence spectrophotometer at 485 nm [23].

Abts (2,2-azino-bis(3-ethyl benzothiazoline-6-sulfonic acid) diammonium salt) method: This is a measure of antioxidant activity. It also permits to distinguish between additive and synergistic effects. The assay is based on interaction between antioxidant and ABTS+ radical cation which has a characteristic colour showing maxima at 645, 734 and 815 nm [22-24]].

DMPD (N,N-dimethyl-p-phenylenediamine dihydrochloride) method: This assay is based on the reduction of buffered solution of coloured DMPD in acetate buffer and ferric chloride. The procedure involves measurement of decrease in absorbance of DMPD in presence of scavengers at its absorption maxima of 505 nm. The activity was expressed as percentage reduction of DMPD [24].

Oxygen radical absorbance capacity (ORAC):

ORAC is an exciting and revolutionary new test tube analysis that can be utilized to test "antioxidant power" of foods and other chemical substances. It calculates the ability of a product or chemical to protect against potentially damaging free radicals. This analytical procedure measures the ability of a substance to act as an antioxidant. The test is performed using Trolox (a water-soluble analogue of vitamin E) as a standard to determine the Trolox equivalent (TE). The ORAC value is then calculated from the Trolox equivalent and expressed as ORAC units or value. From this assay it shows the higher the ORAC value, the greater the "antioxidant power." In automated ORAC assay Bphycoerythrin (b-PE) was used as a target free radical damage, AAPH as a proxy radical generator and Trolox as a standard control. After the addition of AAPH to the test solution, the fluorescence is recorded, and the antioxidant activity is expressed as equivalent [25].

l. β-Carotene linoleate model:

This is one of the rapid methods to screen antioxidants, which is mainly based on the principle that linoleic acid, which is an unsaturated fatty acid, gets oxidized by "reactive oxygen species" (ROS) produced by oxygenated water. The products formed will initiate the β-carotene oxidation, which will lead to discoloration. Antioxidants decrease the extent of discoloration, which is measured at 434 nm, and the activity is measured [24].

m. TRAP method: This method is defined as total radical trapping antioxidant parameter. The fluorescence of R-phycoerythrin is quenched by ABAP (2,2′-azobis(2amidinopropane) hydrochloride) as a radical generator. The antioxidative potential is evaluated by measuring the delay in discoloration [25].

n. Cytochrome c test: Superoxide anions were assayed spectrophotometrically by a cytochrome reduction method described by McCord [6]. Xanthine oxidase converts xanthine to uric acid and yields superoxide anions which directly reduce ferricytochrome c to ferrocytochrome, having an absorbance change at 550 nm. [26]..

o. Erythrocyte ghost system: This method involves isolation of erythrocyte ghost cells and the induction of lipid peroxidation using them and the induction of tetra-butyl hydroxy peroxide (t-BHP). Thiobarbituric acid reactive substance (TBARS) produced during the reaction is measured at 535 nm [26].

p. Microsomal lipid peroxidation or thiobarbituric acid (TBA) assay: TBA test involves isolation of microsomes from rat liver and induction of lipid peroxides with ferric ions leading to the production of small amount of malondi- aldehyde (MDA). TBA reacts with MDA to form a pink chromogen, which can be detected spectrophotometrically at 532 nm [27].The potential role of antioxidants in disease.

Oxidative stress and diseases:

a. Nephrotic syndrome:

The nephrotic syndrome (NS) is defined by heavy proteinuria (urine total protein excretion greater than 3.5 g/d or total protein-creatinine ratio greater than 3.5 g/g) due to abnormal increase of glomerular permeability and following hypoalbuminemia, hyperlipidaemia, and Edema. Peroxidation of lipid membranes raises the concentration of their by-product MDA and the consequent lowering of antioxidants as a result of consumption [27]. The combined therapy of antioxidants, minerals with B complex vitamins for treatment of imbalance oxidant/ antioxidant status, hyperhomocyst anaemia, and deficiency of copper and zinc in nephrotic syndrome patients.

b. Oxidative stress and neurodegenerative diseases: The brain is exposed throughout life to OS, and certain diseases of the brain and nervous system are thought to involve free radical processes and oxidative damage, either as a primary cause or as a consequence of disease progression.

1. **Alzheimer's disease:** Alzheimer's disease (AD) is a progressive neuropsychiatric disorder of unknown etiology. It is characterized by neuronal degeneration and cognitive deterioration, especially in the elderly . OS has been implicated implicated in the pathogenesis of AD [28] by the finding of several characteristics, such as enhanced lipid peroxidation, in specific areas of the brain in post-mortem studies [28].

2. **Cognitive dysfunction in the elderly:** Cognitive impairment is a common problem in the over 65-year age group, progressing to its most devastating form of clinical demen0a, usually Alzheimer's dementia, in about 5% of this population [29]. Goodwin noted a correlation between memory function and vitamin C in the blood of healthy volunteers aged 60 or over . Accordingly, Perry found a positive association of memory performance with β-carotene and vitamin C levels in plasma measured twice .

3. **Parkinson's disease:** One of the suggested causes of OS in the SNpc is the production of ROS during the normal metabolism of dopamine. In the human SNpc, the oxidation products of dopamine may polymerize to form neuromelanin, which may also be toxic . According to postmortem studies, the SNpc of PD patients shows a significant (60%) reduction in GSH and a moderate (29%) increase in oxidized glutathione (GSSG) levels [30].

4. **Huntington's disease:** Huntington's disease is an autosomal neuronal disorder characterized as a movement disorder caused by repetition of a CAG trinucleotides sequences encoding for a polyglutamine tract at the N terminus of the gene encoding a protein named huntingtin. Several post-mortem studies showed increased iron levels in the striatum of patients with Huntington's disease .

5. **Amyotrophic lateral sclerosis (ALS):** ALS is characterized by selective and

progressive degeneration of the lower motor neurons in the spinal cord and the motor neurons in the cerebral cortex, usually beginning in midlife. OS may be involved in all types of ALS [30] Levels of vitamin E and malondialdehyde (MDA), as a measure of lipid oxidation, increased overtime in mutant CuZnSOD mice, as compared to controls.

6. **Schizophrenia and tardive dyskinesia:** The presence of excess levels of ROS

has been described for both schizophrenia and neuroleptic-induced tardive dyskinesia . The contribu0on of oxidative injury to the pathophysiology of schizophrenia is indicated by the increase in lipid peroxidation products in the plasma and CSF and the altered levels of both enzymatic and nonenzymatic antioxidants in chronic naive first-episode patients.

7. **Chemically induced neurological disorders:** Several neurotoxic chemicals

have been shown to elevate the cerebral rate of ROS production in experimental animals. These include methylmercuric chloride, cadmium, toluene, and other organic solvents . All of these agents are also capable of increasing intracellular levels of calcium ions

8. Brain aging: Aging in mammalian species appears to be the result of normal developmental and metabolic processes responsible for greying of the hair, decreases in the rate of wound healing, and increases in susceptibility to disease and death. Studies have found evidence of oxidative damage to macromolecules (DNA, lipids, and proteins) especially in brains from elderly subjects, supporting the hypothesis that oxidative injury might directly cause the aging process [31].

Diabetes mellitus: Diabetes in humans is a disease associated with increased oxidative stress. The cause of this is not yet fully understood but is thought to include mitochon- drial dysfunction, direct enzyme inhibition by hyperglycaemia, auto-oxidation of glucose, and activation of NADPH oxidase. The oxidative stress manifests itself as elevated concentrations of lipid peroxidation products, erythrocyte fragility, and decreases in the antioxidant enzyme systems (CAT, GSH-PX, and SOD) [31-33].

d. Asthma: Feline asthma closely parallels human asthma, which is known to be associated with oxidative stress. Such cells generate ROS, which are involved in the pathophysiology of asthma [32].

e. Atherosclerosis: It has been known that LDL can be oxidized by many kinds of oxidants by different mechanisms and pathways. Myeloperoxidase (MPO) secreted from phago- cytes has been implicated in the pathogenesis of atherosclerosis. Reactive nitrogen species are another species, which may contribute in atherosclerosis. Nitric oxide (NO) is not a strong oxidant in itself, but it reacts rapidly with O2 to give peroxynitrite, which oxidizes LDL to an atherogenic form [33].

f. Heart failure: Accumulating evidence suggests that reactive oxygen species (ROS) play a key role in the development and progression of heart failure, regardless of the etiology.

g. Haemorrhagic shock: Acute haemorrhagic shock causes decrease in the cardiac function and contractility and is associated with an increase in oxygen free radical (OFR) producing activity of PMN leukocytes [34].

h. Ischemia–reperfusion: Reactive oxygen-derived radicals and metabolites are known to play important roles in the pathogenesis of ischemia/reperfusion and anoxia/ reoxygenation injury. Free radicals are induced by the reperfusion blood flow in addition the lack of oxygen (O2) supply to the ischemic cell.

I. Lung disease: The large endothelial surface is constantly exposed to many atmospheric pollutants including tobacco smoke, fuel emissions, ozone, and nitrogen dioxide, and given the natural oxidizing nature of the atmosphere (e.g., 21% O2), the lung is always at risk of oxidative injury [35].

j. Aging: The free radical theory of aging includes phenomenological measurements of age-

associated oxidative stress, interspecies comparisons, dietary restriction, the manipulation of metabolic activity and oxygen tension, treatment with dietary and pharmacological antioxidants, in vitro senescence, classical and population genetics, molecular genetics, transgenic organisms, the study of human diseases of aging, epidemiological studies, and the ongoing elucidation of the role of active oxygen in biology.

k. Free radicals and cancer: One type of endogenous damage is that arising from intermediates of oxygen (dioxygen)-reduction oxygen free radicals, which attacks not only the bases but also the deoxyribosyl backbone of DNA. OFR are also known to attack other cellular components such as lipids, leaving behind reactive species that in turn can couple to DNA bcellula 35]

l. Inflammation: During phagocytosis, cells consume increased amount of oxygen, a process termed the respiratory burst. Activation results in increased NADPH production via the hexose monophosphate shunt, and the generation of O2, H2O2, OH and hypochlorous acid (HOCI), hypoxanthine concentration, xanthine oxidase activity, and ROS production are increased in rheumatoid arthritis..

m. Ocular disease: Oxidative stress is implicated in age-related macular degeneration and cataracts by altering various cell types in the eye either photochemically or non-photochemically. Under the action of free radicals, the crystalline proteins in the lens can cross-link and aggregate, leading to the formation of cataract.

List of different plants including their parts responsible for Antioxidant activity:

S.no	Family Name	Family	Part used	Chemical constituents responsible for antioxidant activity
1	Amaranthus paniculatus	Amaranthaceae	Leaf	Carotenoids,flavonoids, phenolic acids, and ascorbic acid.
2	Amaranthus gangeticus	Amaranthaceae	Leaf	Carotenoids,flavonoids, phenolic acids, and ascorbic acid.
3	Amaranthus blitum	Amaranthaceae	Leaf	Carotenoids,flavonoids, phenolic acids, and ascorbic acid.
4	Amaranthus	Amaranthaceae	Leaf	Carotenoids,flavonoids, phenolic acids, and ascorbic acid.
5	Amaranthus Virdis	Amaranthaceae	Leaf	Carotenoids,flavonoids, phenolic acids, and ascorbic acid.
6	Coriandrum Sativam	Umbelliferae	Leaf	S-(+)-linalool, monoterpenes, hydrocarbons, namely, α-pinene, limonene, γ-terpinene, p- cymene, borneol, citronellol, camphor, geraniol, and geraniol, acetate, heterocyclic components like pyrazine, pyridine, thiazole, furan and tetrahydrofuran derivatives,isocumarins, coriandrin, dihydrocoriandrin, coriandrons A–E, flavonoids, pthalides, neochidilide,
7	Emblica officinalis	Umbelliferae	Fruit, leaves	Vitamins, ascorbic acid, and phenolics are known as hydrophilic antioxidants,while carotenoids are known as lipophilic antioxidants
8	Digera muricata (L.)	Amaranthaceae	Leaf	Phenols, flavonoids, glycosides, tannins and terpenoids, and minimum for saponins
9	Chenopodium album L.	Amaranthaceae	Leaf	Alkaloids, apocarotenoids, flavonoids, phytoecdysteroids xyloside, limonene
10	Hibiscus cannabinus L	Malvaceae	Leaf	Tannins,saponins,polyphenolics, alkaloids,lignans, essential oils, and steroids

11	Sesbania grandiflora L	Fabaceae	Leaf	Galactomannans, linoleic acid, βsitosterol,and carbohydrates. Vitamin C, and calcium,iodine,pectin,saponins, aliphatic alcohol,leucocyanidin and cyanidin, oleanolic acid and its methyl ester and kaempferol-3-rutinoside,tannins and gum,sesbanimide
12	Portulaca oleracea L	Portulacaceae	Leaf	Omega-3 fatty acids, gallotannins,kaempferol, quercetin, apigenin,α-tocopherols, ascorbic acid and glutathione,free oxalic acids, βcarotene, omega-3 fatty acids,coumarins, flavonoids,monoterpene glycoside and anthraquinone glycosides
13	Murraya koenigii L	Rutaceae	Leaf	Alkaloid, volatile oil, glycozoline,xanthotoxin, and sesquiterpine
14	Celosia argentea	Amaranthaceae	Leaf	Alkaloids,glycosides,flavonoids, saponins,tannins, carbohydrate and essential oils,steroids, carotenoids, and anthocyanins
15	Boerhavia	Nyctaginacea Alkaloids	Leaf	Lignans(liriodendrons),ß-sitosterols and tetracosanoic
16	Eclipta alba	Asteraceae	Leaf	Coumestans, alkaloids, flavonoids,glycosides,polyacetylenes,triterpenoids,and thiophenes. Phytosterol,P-amyrin,luteolin-7-glucoside, P-lucoside of phytosterol, a glucoside of a triterpenic acid and wedelolactone.Cystine, glutamic acid, phenylalanine
17	Centella asiatica	Apiaceae	Leaf	Asiaticoside carotene,ascorbic acid, phenols, madecassic acid
18	Phyllanthus amarus	Euphorbiaceae	Leaf	Alkaloids, astragalin, brevifolin, carboxylic acids, corilagin, cymene, ellagic acid, ellagitannins, gallocatechins, geraniin, hypophyllanthin, phyllanthin, lignans, lintetralins, lupeols, methyl salicylate, phyllanthine
19	Curcuma longa	Zingiberaceae	Leaf	Ascorbic-acid rhizome,beta-carotene rhizome, caffeic-acid rhizome, curcumin rhizome, eugenol essential oil, pcoumaric-acid rhizome, protocatechuic acid leaf, syringic-acid leaf, vanillic acid in leaf, camphene, eugenol, curcumin
20	Ocimum sanctum	Labiatae	Leaf	Volatile oil, terpenoids, eugenol, thymol, estragole
21	Basella alba	Basellaceae	Leaf	High in vitamin A,vitamin C, Ca, Iron, phosphorus, vitamin B9(folic acid), calcium, magnesium, flavonoids, polyphenols
22	Mentha arvensis	Labiatae	Leaf	Flavonoids, acacetin, eriocitrin, esperidoside
23	Alternanthera sessilis	Amaranthaceae	Leaf	Carotenoids, triterpene, saponins,flavonoids, steroids, stigmasterol,β-sitosterol, glycosides,protein and amino acids, campesterol, lupeol
24	Rumex acetosa	Polygonaceae	Leaf	Oxalates, including calcium oxalate and tannins; anthracene derivatives, emodin, rhein, quinoids, and flavonoids

25	Spinacia	Amaranthaceae	Leaf	Vitamin A(especially high in lutein) vitamin C, vitamin E, vitamin K,magnesium,manganese,folate, betaine,iron,vitamin B2, calcium,potassium, vitamin B6, folic acid,copper,protein,phosphorus,zinc,niacin,selenium, and omega-3 fatty acids. Recently, opioid peptides called rubiscolins have also been found in spinach. It is a source of folic acid
26	Trianthema portulacastrum	Aizoaceae	Leaf	Tetraterpenoid 1(trianthenol)flavonoid,5,7-dihydroxy-6,8-dimethylchromone(leptorumol) Isoamericanin A

10. Conclusion:

The most important free radical in biological systems is radical derivatives of oxygen with the increasing acceptance of free radical as common place and important biochemical intermediate. Antioxidants are believed to play an important role in the body defence system against reactive oxygen species (ROS), which are the harmful by-products generated during normal cell aerobic respiration. The imbalance between ROS and antioxidant defence system increases the oxidation burden and leads to the damage of macromolecules such as carbohydrates or proteins, such processes of various diseases. To protect the cells and organ systems of the body against reactive oxygen species, humans have evolved a highly sophisticated and complex antioxidant protection system. Plants having vitamins (C, E, carotenoids, etc.), flavonoids (flavones, isoflavones, flavanones, anthocyanins, and catechins), polyphenols (ellagic acid, gallic acid, and tannins) possess remarkable antioxidant activity. Antioxidant activity is neither restricted to a particular part of plant nor the specific families. Current review reveals the different potential application of antioxidant/free radical manipulations in prevention or control of diseases. All plants discussed in this review exhibited significant, clinical, and pharmacological activity with fewer side effects.

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