



## FREE RADICALS, ANTIOXIDANTS AND FUNCTIONAL FOODS: IMPACT ON HUMAN HEALTH

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### Abstract

Free radicals are unstable atoms that can harm cells and have a role in ageing and a number of disorders. In addition to being created by the body naturally, they can also be absorbed from outside sources like cigarette smoke and pollution. Many chronic health issues, including cancer, cataracts, inflammatory and cardiovascular diseases, are partly caused by the damage caused by free radicals. Antioxidants stop radicals from forming, which stops tissue damage caused by free radicals. Our body produces reactive oxygen species (ROS), reactive nitrogen species, and free radicals when it is exposed to varied physiochemical situations, pathological states, or other endogenous systems. Correct physiological function requires a balance between antioxidants and free radicals. Oxidative stress is the result of free radicals surpassing the body's capacity to control them. Because functional foods suppress acetylcholinesterase, they may be able to treat dementia and Alzheimer's disease. Similarly, treatments based on the presence of antioxidants, herbs, and spices may also be beneficial.

**Keywords:** Free radicals, antioxidants, oxidative stress, dementia and Alzheimer's disease.

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### Introduction

The recent growth in the knowledge of free radicals and reactive oxygen species (ROS) in biology is producing a medical revolution that promises a new age of health and disease management. It is ironic that oxygen, an element indispensable for life, under certain situations has deleterious effects on the human body [1, 2]. Most of the potentially harmful effects of oxygen are due to the formation and activity of a number of chemical compounds, known as ROS, which have a tendency to donate oxygen to other substances. Free radicals and antioxidants have become commonly used terms in modern discussions of disease mechanisms [3].

#### 1. Free Radicals:

A free radical can be defined as any molecular species capable of independent existence that contains an unpaired electron in an atomic orbital. The presence of an unpaired electron results in certain common properties that are shared by most radicals. Many radicals are unstable and highly reactive. They can either donate an electron to or accept an electron from other molecules, therefore behaving as oxidants or reductants. The most important oxygen-containing free radicals in many disease states are hydroxyl radical, superoxide anion radical, hydrogen peroxide, oxygen singlet, hypochlorite, nitric oxide radical, and peroxy nitrite radical [4]. These are highly reactive species, capable in the nucleus, and in the membranes of cells of damaging biologically relevant molecules such as DNA, proteins, carbohydrates, and lipids. Free radicals attack important macro molecules leading to cell damage and homeostatic disruption. Targets of free radicals include all kinds of molecules in the body. Among them, lipids, nucleic acids, and proteins are the major targets.

Sources of free radical

- Internal sources
- External source
- Physiological Factors

#### Internal sources

These can be enzymatic reactions, which serve as a source of free radicals. These include those reactions involved in the respiratory chain, in phagocytosis, in prostaglandin synthesis and in the cytochrome P450 system. Some internal sources of

generation of free radicals are mitochondria, xanthine oxidase, phagocytes, and reactions involving iron and other transition metals, peroxisomes, Arachidonate pathways, exercise, ischemia/reperfusion, and inflammation.

#### **External sources**

These include non-enzymatic reactions of the oxygen with organic compounds. Free radicals also arise in reactions, which are initiated by ionizing radiations. Some external sources of free radicals are cigarette smoke, environmental pollutant, radiations, ultraviolet light, ozone, certain drugs, pesticides, anesthetics and industrial solvents.

#### **Physiological Factors**

Mental status like stress, emotion, etc., and disease conditions are also responsible for the formation of free radicals.

Types of free radicals

- Hydroperoxyl radical
- Superoxide radical
- Hydrogen peroxide
- Triplet oxygen
- Active oxygen

#### **Hydroperoxyl radical**

The hydroperoxyl radical, also known as the perhydroxyl radical, is the protonated form of superoxide with the chemical formula HO<sub>2</sub>. Hydroperoxyl is formed through the transfer of a proton to an oxygen atom. HO<sub>2</sub> can act as an oxidant in a number of biologically important reactions, such as the abstraction of hydrogen atoms from tocopherol and polyunsaturated fatty acids in the lipid bilayer. As such, it may be an important initiator of lipid peroxidation.

#### **Superoxide radical**

Superoxide can act either as oxidant or reductant, it can oxidize sulphur, ascorbic acid or NADPH and it can reduce Cytochrome C and metal ions. A dismutation reaction leading to the formation of hydrogen peroxide and oxygen can occur spontaneously or is catalyzed by enzyme superoxide dismutase. In its protonated form (pKa 4.8), superoxide forms and perhydroxyl radical, which is powerful oxidant.

#### **Hydrogen peroxide**

The univalent reduction of superoxide produces hydrogen peroxide, which is not a free radical because all its electrons are paired. It readily permeates through the membranes and is therefore not compartmentalized in the cell. The main damages caused by this are breaking up of DNA, resulting in single strand breaks and formation of DNA protein crosslink. Numerous enzymes (peroxidases) use hydrogen peroxide as a substrate in oxidation reactions involving the synthesis of complex organic molecules [9].

Singlet oxygen: It is not a free radical but it can be formed in some radical reactions and can trigger off others. This arises from hydrogen peroxide molecules. Singlet oxygen on decomposition generates superoxide and hydroxyl radicals.

#### **Triplet oxygen**

Triplet oxygen can react with elements and ions to form oxides, but usually not with organic compounds, which are in singlet state. However, it reacts easily with free radical molecules produced by the action of other active radicals, radiations, ultra violet light,

and heat or by complex formation with oxygen and transition metal to produce active peroxide radicals and trigger auto-oxidation of unsaturated fatty acids and others.

Damages caused by free radicals

If free radicals are not inactivated, their chemical reactivity can damage all cellular macro molecules including proteins, carbohydrates, lipids and nucleic acids. Their destructive effect on protein may play a role in the causation of diseases, like cataracts [6]. Free radical damage to DNA is also implicated in the causation of cancer and its effect on LDL cholesterol is very likely responsible for heart disease. Free radicals are also responsible for ageing.

Oxidative damages to proteins: Oxidative attack on proteins results in site-specific amino acid modification, fragmentation of the peptide chain, aggregation of cross linked reaction products, altered electrical charges and increased susceptibility to proteolysis [7].

#### **Oxidative DNA damage**

Activated oxygen and agents that generate oxygen free radicals, such as ionizing radiations, induce numerous lesions in DNA that causes deletion, mutations and other lethal genetic effects. Characterization of this damage to DNA has indicated that both sugar and base moieties are susceptible to oxidation, causing base degradation, single strand breakage and cross links to proteins.

#### **Production of free radicals in the human body**

Free radicals and other ROS are derived either from normal essential metabolic processes in the human body or from external sources such as exposure to X-rays, ozone, cigarette smoking, air pollutants, and industrial chemicals. Free radical formation occurs continuously in the cells as a consequence of both enzymatic and non-enzymatic reactions. Enzymatic reactions, which serve as source of free radicals, include those involved in the respiratory chain, in phagocytosis, in

prostaglandin synthesis, and in the cytochrome P-450 system. Free radicals can also be formed in non-enzymatic reactions of oxygen with organic compounds as well as those initiated by ionizing reactions.

Some internally generated sources of free radicals are [8].

- Mitochondria
- Xanthine oxidase
- Peroxisomes
- Inflammation
- Phagocytosis
- Arachidonate pathways
- Exercise
- Ischemia/reperfusion injury
- Some externally generated sources of free radicals are:
  - Cigarette smoke
  - Environmental pollutants
  - Radiation
  - Certain drugs, pesticides
  - Industrial solvents
  - Ozone

#### **Free radicals in biology**

Free radical reactions are expected to produce progressive adverse changes that accumulate with age throughout the body. Such “normal” changes with age are relatively common to all. However, superimposed on this common pattern are patterns influenced by genetics and environmental differences that modulate free radical damage. These are manifested as diseases at certain ages determined by genetic and environmental factors. Cancer and atherosclerosis, two major causes of death, are salient “free radical” diseases. Cancer initiation and promotion is associated with chromosomal defects and oncogene activation. It is possible that endogenous free radical reactions, like those initiated by ionizing radiation,

may result in tumor formation. The highly significant correlation between consumption of fats and oils and death rates from leukemia and malignant neoplasia of the breast, ovaries, and rectum among persons over 55 years may be a reflection of greater lipid peroxidation [9]. Studies on atherosclerosis reveal the probability that the disease may be due to free radical reactions involving diet-derived lipids in the arterial wall and serum to yield peroxides and other substances.

#### **Concept of Oxidative Stress**

The term is used to describe the condition of oxidative damage resulting when the critical balance between free radical generation and antioxidant defenses is unfavorable. Oxidative stress, arising as a result of an imbalance between free radical production and antioxidant defenses, is associated with damage to a wide range of molecular species including lipids, proteins, and nucleic acids. Short-term oxidative stress may occur in tissues injured by trauma, infection, heat injury, hypertoxia, toxins, and excessive exercise). These injured tissues produce increased radical generating enzymes (e.g., xanthine oxidase, lipogenase, cyclooxygenase) activation of phagocytes, release of free iron, copper ions, or a disruption of the electron transport chains of oxidative phosphorylation, producing excess ROS. The initiation, promotion, and progression of cancer, as well as the side-effects of radiation and chemotherapy, have been linked to the imbalance between ROS and the antioxidant defense system. ROS have been implicated in the induction and complications of diabetes mellitus, age-related eye disease, and neurodegenerative diseases such as Parkinson’s disease.

#### **Oxidative stress and human diseases**

A role of oxidative stress has been postulated in many conditions, including anther sclerosis, inflammatory condition, certain cancers, and the process of aging. Oxidative stress is now thought to make a significant contribution to all inflammatory diseases (arthritis, vasculitis, glomerulonephritis, lupus erythematosus, adult respiratory diseases syndrome), ischemic diseases (heart diseases, stroke, intestinal ischemia), hemochromatosis, acquired immunodeficiency syndrome, emphysema, organ transplantation, gastric ulcers, hypertension and preeclampsia, neurological disorder (Alzheimer’s disease, Parkinson’s disease, muscular dystrophy), alcoholism, smoking-related diseases, and many others [10]. An excess of oxidative stress can lead to the oxidation of lipids and proteins, which is associated with changes in their structure and functions.

#### **Cardiovascular diseases**

Heart diseases continue to be the biggest killer, responsible for about half of all the deaths. The oxidative events may affect cardiovascular diseases therefore; it has potential to provide enormous benefits to the health and lifespan. Poly unsaturated fatty acids occur as a major part of the low density lipoproteins (LDL) in blood and oxidation of these lipid components in LDL play a vital role in atherosclerosis. The three most important cell types in the vessel wall are endothelial cells; smooth

muscle cell and macrophage can release free radical, which affect lipid per oxidation. With continued high level of oxidized lipids, blood vessel damage to the reaction process continues and can lead to generation of foam cells and plaque the symptoms of atherosclerosis [11]. Oxidized LDL is atherogenic and is thought to be important in the formation of atherosclerosis plaques. Furthermore, oxidized LDL is cytotoxic and can directly damage endothelial cells. Antioxidants like B-carotene or vitamin E play a vital role in the prevention of various cardiovascular diseases.

### **Carcinogenesis**

Reactive oxygen and nitrogen species, such as super oxide anion, hydrogen peroxide, hydroxyl radical, and nitric oxide and their biological metabolites also play an important role in carcinogenesis. ROS induce DNA damage, as the reaction of free radicals with DNA includes strand break base modification and DNA protein cross-links. Numerous investigators have proposed participation of free radicals in carcinogenesis, mutation, and transformation; it is clear that their presence in biosystem could lead to mutation, transformation, and ultimately cancer.

Antioxidants can decrease oxidative stress induced carcinogenesis by a direct scavenging of ROS and/or by inhibiting cell proliferation secondary to the protein phosphorylation. B-carotene may be protective against cancer through its antioxidant function, because oxidative products can cause genetic damage. Immuno enhancement of B-carotene may contribute to cancer protection. B-carotene may also have anticarcinogenic effect by altering the liver metabolism effects of carcinogens. Vitamin C may be helpful in preventing cancer. The possible mechanisms by which vitamin C may affect carcinogenesis include antioxidant effects, blocking of formation of nitrosamines, enhancement of the immune response, and acceleration of detoxification of liver enzymes. Vitamin E, an important antioxidant, plays a role in immunocompetence by increasing humoral antibody protection, resistance to bacterial infections, cell-mediated immunity, the T-lymphocytes tumor necrosis factor production, inhibition of mutagen formation, repair of membranes in DNA, and blocking micro cell line formation.

### **Free radical and aging**

The human body is in constant battle to keep from aging. Research suggests that free radical damage to cells leads to the pathological changes associated with aging. An increasing number of diseases or disorders, as well as aging process itself, demonstrate link either directly or indirectly to these reactive and potentially destructive molecules. The major mechanism of aging attributes to DNA or the accumulation of cellular and functional damage. Reduction of free radicals or decreasing their rate of production may delay aging [12]. Some of the nutritional antioxidants will retard the aging process and prevent disease. Based on these studies, it appears that increased oxidative stress commonly occurs during the aging process, and antioxidant status may significantly influence the effects of oxidative damage associated with advancing age. Research suggests that free radicals have a significant influence on aging, that free radical damage can be controlled with adequate antioxidant defense, and that optimal intake of antioxidant nutrient may contribute to enhanced quality of life. Recent research indicates that antioxidant may even positively influence life span.

### **Antioxidants**

An antioxidant is a molecule stable enough to donate an electron to a rampaging free radical and neutralize it, thus reducing its capacity to damage. These antioxidants delay or inhibit cellular damage mainly through their free radical scavenging property. These low-molecular-weight antioxidants can safely interact with free radicals and terminate the chain reaction before vital molecules are damaged. Some of such antioxidants, including glutathione, ubiquinol, and uric acid, are produced during normal metabolism in the body. Other lighter antioxidants are found in the diet. Although there are several enzymes system within the body that scavenge free radicals, the principle micronutrient (vitamins) antioxidants are vitamin E ( $\alpha$ -tocopherol), vitamin C (ascorbic acid), and B-carotene. The body cannot manufacture these micronutrients, so they must be supplied in the diet.

### **Mechanism of action of antioxidants**

Two principle mechanisms of action have been proposed for antioxidants. The first is a chain-breaking mechanism by which the primary antioxidant donates an electron to the free radical present in the systems. The second mechanism involves removal of ROS/reactive nitrogen species initiators (secondary antioxidants) by quenching chain-initiating catalyst (14). Antioxidants may exert their effect on biological systems by different mechanisms including electron donation, metal ion chelation, co-antioxidants, or by gene expression regulation.

Levels of antioxidant action. The antioxidants acting in the defense systems act at different levels such as preventive, radical scavenging, repair and de novo, and the fourth line of defense, i.e., the adaptation. The first line of defense is the preventive antioxidants, which suppress the formation of free radicals. Although the precise mechanism and site of radical formation in vivo are not well elucidated yet, the metal-induced decompositions of hydroperoxides and hydrogen peroxide must be one of the important sources [12]. To suppress such reactions, some antioxidants reduce hydroperoxides and hydrogen peroxide before hand to alcohols and water, respectively, without generation of free radicals and some proteins sequester metal ions.

### **Enzymatic**

#### **1. Types of antioxidants**

Cells are protected against oxidative stress by an interacting network of antioxidant enzymes. Here, the superoxide released by processes such as oxidative phosphorylation is first converted to hydrogen peroxide and then further reduced to give water. This detoxification pathway is the result of multiple enzymes, with superoxide dismutases catalyzing the first step

and then catalases and various peroxidases removing hydrogen peroxide [15].

#### **Superoxide dismutase**

Superoxide dismutases (SODs) are a class of closely related enzymes that catalyze the breakdown of the superoxide anion into oxygen and hydrogen peroxide. SOD enzymes are present in almost all aerobic cells and in extracellular fluids. There are three major families of superoxide dismutase, depending on the metal cofactor: Cu/Zn (which binds both copper and zinc), Fe and Mn types (which bind either iron or manganese), and finally the Ni type which binds nickel. In higher plants, SOD isozymes have been localized in different cell compartments.

#### **Catalase**

Catalase is a common enzyme found in nearly all living organisms, which are exposed to oxygen, where it functions to catalyze the decomposition of hydrogen peroxide to water and oxygen. Hydrogen peroxide is a harmful by-product of many normal metabolic processes: to prevent damage, it must be quickly converted into other, less dangerous substances [16]. To this end, catalase is frequently used by cells to rapidly catalyze the decomposition of hydrogen peroxide into less reactive gaseous oxygen and water molecules. All known animals use catalase in every organ, with particularly high concentrations occurring in the liver. Glutathione systems. The glutathione system includes glutathione, glutathione reductase, glutathione peroxidases, and glutathione S-transferases. This system is found in animals, plants, and microorganisms. Glutathione peroxidase is an enzyme containing four selenium cofactors that catalyze the breakdown of hydrogen peroxide and organic hydroperoxides [11]. There are at least four different glutathione peroxidase isozymes in animals. Glutathione peroxidase 1 is the most abundant and is a very efficient scavenger of hydrogen peroxide, while glutathione peroxidase 4 is most active with lipid hydroperoxides. The glutathione S-transferases show high activity with lipid peroxides. These enzymes are at particularly high levels in the liver and also serve in detoxification metabolism.

#### **Nonenzymatic**

##### **Ascorbic acid:**

Vitamin C or ascorbic acid is a monosaccharide antioxidant found in both animals and plants. As it cannot be synthesized in humans and must be obtained from the diet, it is a vitamin. Most other animals are able to produce this compound in their bodies and do not require it in their diets. In cells, it is maintained in its reduced form by reaction with glutathione, which can be catalyzed by protein disulfide isomerase and glutaredoxins [16]. Ascorbic acid is a reducing agent and can reduce and there by neutralize ROS such as hydrogen peroxide. In addition to its direct antioxidant effects, ascorbic acid is also a substrate for the antioxidant enzyme ascorbate peroxidase, a function that is particularly important in stress resistance in plants.

##### **Glutathione**

Glutathione is a cysteine-containing peptide found in most forms of aerobic life. It is not required in the diet and is instead synthesized in cells from its constituent amino acids.

Glutathione has antioxidant properties since the thiol group in its cysteine moiety is a reducing agent and can be reversibly oxidized and reduced [10]. In cells, glutathione is maintained in the reduced form by the enzyme glutathione reductase and in turn reduces other metabolites and enzyme systems as well as reacting directly with oxidants. Due to its high concentration and central role in maintaining the cell's redox state, glutathione is one of the most important cellular antioxidants. In some organisms, glutathione is replaced by other thiols, such as by mycothiol in the actinomycetes, or by trypanothione in the kinetoplastids.

##### **Melatonin**

Melatonin, also known chemically as N-acetyl-5-methoxytryptamine, is a naturally occurring hormone found in animals and in some other living organisms, including algae. Melatonin is a powerful antioxidant that can easily cross cell membranes and the blood-brain barrier. Unlike other antioxidants, melatonin does not undergo redox cycling, which is the ability of a molecule to undergo repeated reduction and oxidation [16]. Melatonin, once oxidized, cannot be reduced to its former state because it forms several stable end-products upon reacting with free radicals. Therefore, it has been referred to as a terminal (or suicidal) antioxidant.

##### **Tocopherols and tocotrienols (Vitamin E)**

Vitamin E is the collective name for a set of eight related tocopherols and tocotrienols, which are fat-soluble vitamins with antioxidant properties. Of these,  $\alpha$ -tocopherol has been most studied as it has the highest bioavailability, with the body preferentially absorbing and metabolizing this form. It has been claimed that the  $\alpha$ -tocopherol form is the most important lipid-soluble antioxidant, and that it protects membranes from oxidation by reacting with lipid radicals produced in the lipid peroxidation chain reaction [9]. This removes the free radical intermediates and prevents the propagation reaction from continuing. This reaction produces oxidized  $\alpha$ -tocopheroxyl radicals that can be recycled back to the active reduced form through reduction by other antioxidants, such as ascorbate, retinol, or ubiquinol.

##### **Uric acid**

Uric acid accounts for roughly half the antioxidant ability of plasma. In fact, uric acid may have substituted for ascorbate in human evolution. However, like ascorbate, uric acid can also mediate the production of active oxygen species [8].

### **Factors Related to Feeding of the Older Person**

The impact of dietary nutrients on the health of persons of all ages is complex and multifactorial, and chemosensory, involving biology, food antioxidants, chronobiology, environment, culture, religion, eating habits, memory loss, intake of natural products and herbal remedies (such as phytoalexins, polyphenols, carotenoids, spices and aromatic herbs, alcoholic and non-alcoholic beverages), commercial and marketing hype, language, interventions (pharmacological and “non-drug”), special cuisines, nursing and domestic care (intravenous and tube feeding), primary nutrients like omega-3 fatty acids, (e.g., alpha-linolenic acid) carbohydrates (glucose-monosaccharide-energy), amino acids (tryptophan), vitamins (B12, B6, C) and trace elements. From the biosystems perspective and intervention, it is evident from many clinical trials and meta-analysis lead to the reverse engineering safety viewpoint; and as an associated (chemical structures in their own right or as a result of chemical interaction with other constituents) functional food property with health giving properties; [9] and culinary skills including the colors not only of the food/beverage but the color of the tableware such as plates, glasses, cups, and tablecloth evoking color contrasts which may be translated into “food” appeal/perception, just as we can use geometry, spatial configuration can be used to create an illusion of size of plate. Or else we may have “edible provoking” perfumes or “edible provoking” hues; perhaps these may work together or in tandem depending on neurodegeneration characteristics.

### **Food Aroma, the Brain, and Dietary Sufficiency**

Chemosensory disorders of smell, apart from a warning function, may dictate our food preference and hence our food sufficiency in the older person particularly in patients with Alzheimer's disease. The future aim should be to integrate nutritional needs of the older person and compensate for chemosensory deficits, through socioeconomic and innovative agricultural and food industry processes. The testing for smell disorders may be cross-cultural and in a cosmopolitan community may be difficult [7].

### **Food Flavor, the Brain and Dietary Sufficiency**

In this section, we discuss mechanisms related to flavor rather than dietary composition (q.v. Griffiths et al.; with more specific intervention action, for example, one broad (“mechanistic”) observation from a study of a variety of foods constituting a normal diet in Alzheimer's disease subjects, gustatory (tasting) impairment was an associative agnosia in mild Alzheimer's disease, suggesting a dissociation of olfactory and gustatory thresholds at a central level. It is generally believed that the substantial neuronal brain loss, e.g., Alzheimer's disease, affects gustatory function but perhaps not in peripheral transmission of such information from taste buds (salty, bitter, sweet, umami and sour) to gustatory nerve fibers [10]. There are chemoreceptors in the human brain for olfaction and taste and their expression is different in Parkinson's disease and dysregulation of these types of receptors in the entorhinal cortex and frontal cortex in Alzheimer's disease and response is an area in which functional foods may play a role in this pathological process.

### **Potential Role of Functional Foods for Prevention of Neurodegeneration**

Acetylcholinesterase inhibitors are used to treat neurological disorders, including Alzheimer's disease (AD), and it has been suggested that some plant-derived dietary agents like functional foods may be target candidates for treating Alzheimer's disease. Functional foods consist of

natural or processed foods that contain known or unknown biologically active compounds and are effective for promoting health and well-being beyond dietary needs [16]. These foods provide clinically proven and documented health benefits for the prevention, management, and treatment of chronic disease. This definition of functional foods is important as it contains key words for the candidate food, e.g., “clinically proven and not speculative”, and “documented”, indicating evidence-based trials which have been properly reported in the literature; as well as relating to intact species and not ex vivo as in cell culture.

### **Herbal Antioxidants**

Garlic contains many biologically active compounds which purport to be beneficial to human health; one such garlic-preparation contains the water soluble antioxidant S-allyl mercaptocysteine (aged garlic). Chauhan has reviewed the beneficial effects of garlic and its constituents on neuronal physiology and brain function; and the potential of dietary garlic as a pharmacotherapy for Alzheimer's disease [11]. Despite these and other claims, cross-sectional studies of overall dietary patterns or specific foods (fruit and vegetables) or antioxidants or flavonoids in an older cohort using the same sample have not shown that biomarkers (C-reactive protein (CRP) and fibrinogen) of systemic inflammation relate to flavonoids or antioxidants, though a balanced or Mediterranean diet was favorable: however, the vagaries of cross-sectional studies of narrow age bands is questionable [12].

### **Food and Antioxidants**

Intervention, particularly with prodromal cognitive decline, with vitamin D which is an antioxidant and a neurosteroidal hormone with protective properties may supplement the efficacy of meantime [15]. Brain function depends on dietary nutrients, and implicit in the definition of functional foods/molecular species are target organs such as regions of the brain, with omega-3 polyunsaturated fatty acids, and B, E and D vitamins, etc. Studies of the immune system have demonstrated the role of antioxidants in balancing the free radical production that is needed for functional purposes against oxidative stress, which increases with age. Monitoring the immune system in response to antioxidant dietary intake may be another indicator of health or disease [13]. Aerobic exercise in humans has an increasing effect on superoxide dismissed levels and enhances

the antioxidant defense mechanism yielding health benefit along with risk reduction for metabolic syndrome, diabetes and cardiovascular diseases, which combined with food restriction on, for example, a balanced diet, may provide extra benefit.

### **Spices and Aromatic Herbs**

According to Griffiths et al., "A spice is a seed, fruit, root, rhizome, bark, resin, berry, bud, stigma, or vegetable substance primarily used for seasoning and provides sweet or savory flavorings, colors or preserves food, or is a medicinal product, cosmetic or simply a vegetable". Spices include coriander, fennel, mustard, cinnamon, mace, clove, saffron, ginger, asafetida, bay leaf oil, cinnamon, cloves, cumin, fenugreek, turmeric, poppy seed, pomegranate, red chili, sesame seed, and so forth [4]. Many countries have spice mixtures, e.g., chaat masala (Pakistan and India). Herbs are parts of leafy green plants used for flavoring or to garnish culinary dishes. Aromatic herbs include thyme, sage, oregano, parsley, dill, marjoram, chives, rosemary, mint, lemon grass, etc.

### **6. Selected Organs and Antioxidants**

#### **Hepatoprotective Dietary Antioxidants and Their Potential for Treating Alzheimer's Disease**

The eponym "Alzheimer's disease" introduced by Kraepelin in 1910 for the disease discovered by Alois Alzheimer in 1906 has long sought an effective treatment for the observed pathology described as senile plaques and neurofibrillary tangles found in the cerebral cortex of one Auguste Deter, a 51 year old woman from Frankfurt who in 1901 displayed characteristic symptoms of dementia.

Berberine, a protoberberine group of benzyloisoquinoline alkaloids, found in *Berberis vulgaris* and in many other plants, and been used in Chinese medicine for over 5 Ka and is claimed to have a protective effect against a wide variety of diseases and may be a second-generation treatment for Alzheimer's disease due to its antioxidant properties, and suppression of hepatic oxidative stress. Caution is the watchword to avoid unsubstantiated claims, e.g., tea, that may not be evidence-based [15]. However, it has been shown to attenuate hyperphosphorylation and cytotoxicity induced by Calyculin A of the microtubule associated protein tau and retards neurofibrillary tangles and, *vide supra*, inhibits oxidative stress in Alzheimer's disease.

#### **Renoprotective Dietary Antioxidants**

Functional foods require a specific definition and food effects may vary in relation to disease e.g., Fanti et al. have noted in end-stage-renal disease that blood isoflavonoids are accumulated in line with dietary soya intake which is higher than healthy subjects with preserved kidney function, but unconjugated and sulfated levels are comparable with healthy subjects [26]. In the Women's Health Initiative Program of 96,196 women, when followed up,

and the antioxidant selenium) such mutagenesis brought about by potential mutagens in N-nitrosocompounds, fungal toxins, cooking by-products: postprandial stress caused by the latter may be ameliorated by choice of cooking oil used for frying. These studies support the potential importance of dietary supplementation demonstrated by others e.g., the early study by Mongel et al. [7].

#### **Cardiovascular Disease and Dietary Antioxidants**

Fiber is an important dietary component that may reduce the incidence of some cancers. For example, whole-grain cereals rich in antioxidants and fiber have been reported nearly twenty years ago to be protective particularly for ischemic heart disease comprising 35,000 Postmenopausal women (55–69 year) based on a 127 item food frequency questionnaire [28]. Antioxidants in total antioxidant enzymes and lipoperoxide plasma concentrations were assayed and high values of lipoperoxide related to high blood pressure in a case-control study of older person Mexicans.

#### **Breast Cancer and Dietary Antioxidants**

In a prospective Rotterdam breast cancer study of about 3200 subjects, aged 55 year and over, followed up for a median time of 17 year, and based on a food frequency questionnaire and antioxidant estimations for selenium, flavonoids, carotenoids, vitamins E, C and A, breast cancer incidence was measured and high levels of antioxidants were associated with lower risk of this cancer. Somewhat similar results were found for breast cancer patients and controls from the Cancer Institute in Chennai, India; lower antioxidants (lutein, zeaxanthin, green-yellow vegetables) being associated with more cancers (9). Functional foods designed to reduce oxidative stress were also reported for advanced breast cancer cases but the study was small and probably lacked sufficient statistical power. Similar findings for breast cancer or all-cause cancer are to be found but not exclusively so, due to possible heterogeneity of antioxidant capabilities.

### **Conclusion**

Free radicals are tiny, diffusible molecules with an unpaired electron that makes them extremely reactive (16). In living things, the electron transport chain—a system that releases energy (ATP) and allows the cell to perform regular physiological functions—needs oxygen to produce energy. Many chronic health issues, including cancer, cataracts, inflammatory and cardiovascular diseases, are partly caused by the damage caused by free radicals. By inhibiting the production of radicals, scavenging them, or encouraging their breakdown, antioxidants stop tissue damage caused by free radicals. There has been emerging evidence that synthetic antioxidants pose a risk to human health (17). Thus, in recent years, there has been a greater focus on the quest for safe, natural chemicals that have antioxidative action. Consuming antioxidants obtained from food and plants seems to be a good substitute for endogenous antioxidant defence mechanisms.

### Author contributions

All authors are contributed equally.

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### Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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