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# Antioxidants and Natural Compounds

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## Abstract

Oxidative stress happens in body when the production of oxidants exceeds the antioxidant capacity of body system and plays a role in pathogenesis of several chronic diseases such as diabetes, cardiovascular diseases, stock, and renal failure. Tea, sesame seed, and burdock root (*Arctium lappa* L.) may improve oxidative stress and suppress the side effects of diabetes, rheumatoid arthritis and osteoarthritis. Total extract of black tea and its fractions can increase antioxidants such as Super oxide Dismotase (SOD), Glutathione Peroxides (GPX) and total antioxidants and can decrease oxidants like malondialdehyde (MDA). So, these herbal compounds can improve oxidative stress in diabetes rats. The injection of total extract and 20% fraction of black tea had positive effect on blood lipid profile in diabetic rats. Sesame seeds improved the antioxidants capacity in arthritis; therefore, decreased pain. Burdock root, in arthritis patients improved the antioxidants capacity and decreased the intensity of the pain. It can be concluded that the positive effects of these herbal components are due to the presence of antioxidants. The aim of this chapter is to review the antioxidant capacity of tea, sesame seed, and burdock root as well as to discuss their biological effects in human being.

**Keywords:** antioxidants, food, natural compounds, oxidative stress

## 1. Introduction

Oxidative stress occurs in the body when the production of oxidants exceeds the antioxidant capacity of the body system and plays a role in the pathogenesis of several chronic diseases

such as diabetes, cardiovascular diseases, stroke, and renal failure. Using antioxidants, for instance, vitamin E, vitamin C, and flavanones, can improve antioxidant capacity in the body. Degenerative diseases such as cardiovascular diseases, diabetes, stroke, cancers, and renal disorders are global health problems and it can be predicted that lack of control and attention will involve a lot of costs. Lack of physical activity, nonhealthy diet patterns, and eating salty fast foods are the main causes of these chronic diseases; while change in life style, eating healthy foods like fruits and vegetables can prevent chronic diseases. Herbal extracts and drinks were used to prevent or control diseases from ancient times. Several investigations' results show that there are several components such as flavanones, isoflavanones, and other antioxidants in herbal components that can improve antioxidants in blood and, so, can prevent chronic diseases. Tea, sesame seed, and burdock root (*Arctium lappa* L.) are the important and effective herbal components in this regard. Our results in Tabriz University of Medical Sciences showed the effectiveness of herbal components in improving oxidative stress and suppressing the side effects of diabetes, rheumatoid arthritis, and osteoarthritis. The results indicate that total extract of black tea and its fractions can increase antioxidants such as Super Oxide Dismutase (SOD), Glutathione Peroxides (GPX) and total antioxidants and can decrease oxidants like malondialdehyde (MDA). So, these herbal compounds can improve oxidative stress in diabetes rats. In a study by Alipour *et al.* [1], it has been concluded that injection of total extract and 20% fraction of black tea had positive effect on blood lipid profile in diabetic rats. In one study, using sesame seeds in arthritis improved the antioxidant capacity; therefore, it decreased pain in the mentioned patients. Burdock root, in arthritis patients, improved the antioxidant capacity and decreased the intensity of the pain. It can be concluded that the positive effects of these herbal components are due to the presence of antioxidants. The aim of this chapter is to review the antioxidant capacity of tea, sesame seed, and burdock root, as well as to discuss their biological effects in human beings.

## 2. Oxidative stress

When the production of free radical moieties exceeds the antioxidant capacity of a cellular system, oxidative stress takes place. Radicals will attack and damage proteins, lipids, and nucleic acids if cellular antioxidants do not remove them. The oxidized or nitrosylated products of free radical attack may decrease biological activity, leading to loss of energy metabolism, cell signaling, transport, and other major functions. These altered products also lead to proteosome degradation and further decrease cellular function, resulting in cell death through necrotic or apoptotic mechanisms [2].

### 2.1. Background

Free radicals were defined as a Pandora's Box of evils that may account for cellular damage, mutagenesis, cancer, and, last but not least, the degenerative process of biological aging [3]. Mittal and Murad [4] suggested that the superoxide anion, through its derivative, the hydroxyl radical, stimulates the activation of guanylate-cyclase and formation of the "second messenger" cGMP. Related effects were reported for the superoxide derivative hydrogen peroxide as

it was discovered that nitric oxide (NO) has independent role as a regulatory molecule in the control of smooth muscle relaxation and in the inhibition of platelet adhesion [5]. It is recognized that the production of T-cell growth factor and interleukin-2, an immunologically important T-cell protein, is increased in activated T-cells by superoxide anion or low micromolar concentrations of hydrogen peroxide. Studies have shown that the expression of the hemeoxygenase (HO-1) gene is induced by hydrogen peroxide and it has also induction effects on several genes in bacteria, as well as stimulation of the transcription factor nuclear factor κB (NF-κB) in mammalian cells. There is a large amount of proof showing that living organisms have not only adapted to an unfavorable coexistence with free radicals but also have developed mechanisms for the advantageous use of free radicals. The following includes vital physiological functions that involve free radicals or their derivatives: regulation of vascular tone, sensing of oxygen tension and regulation of functions that are controlled by oxygen concentration, improvement of signal transduction from various membrane receptors including the antigen receptor of lymphocytes, and oxidative stress responses that ensure the maintenance of redox homeostasis [5]. In consideration of the role that oxidative stress has been found to play in numerous disease conditions, the field of redox regulation is also receiving growing attention from clinical colleagues. These conditions show the biological significance of redox regulation. The balance between the advantageous and hurtful effects of free radicals is clearly an important aspect of life. The science of biological "redox regulation" is a rapidly growing area of research that has effect on various disciplines including physiology, cell biology, and clinical medicine [5].

## 2.2. Oxidative stress biomarkers

Oxidative stress biomarkers' measurement is an important step in order to understand the pathogenesis of and developing treatments for some diseases like diabetes. Measurements of the reduction of antioxidant reserves, changes in the activities of antioxidant enzymes, free radical production, and presence of protein, lipid, and DNA free radical adducts are several methods that may be accepted. As enzyme activities and cellular antioxidants are likely to display transient changes, for the purposes of clinical assessment, measurements of end products of free radical attack may be the most reliable determination of the occurrence of oxidative stress. An indication of the stress level experienced in a cell or tissue can be provided by the enzymes responsible for detoxifying free radicals or regenerating antioxidant molecules and they can be measured by in vitro activity assays; however, changes in transcription can also provide evidence of cell stress. For example in long-term diabetes, catalase, GSH reductase, GSH peroxidase, and SOD decrease in complication-prone tissue [2].

## 2.3. Plasma markers of oxidative stress

The body's total antioxidant capacity functions in order to protect cells from excess production of reactive oxygen/nitrogen species (RONS) [6]. Antioxidant capacity includes endogenous (e.g. uric acid, superoxide dismutase, catalase, glutathione peroxidase) and exogenous (e.g., carotenoids, tocopherols, ascorbate, bioflavonoids) compounds. The exogenous antioxidants

are consumed in the diet mainly from fruits and vegetables [7]. Dietary habits can alter an individual's susceptibility to oxidative damage since these exogenous compounds contribute to antioxidant capacity.

Oxidative stress can be defined by formation of RONS that exceed the body's antioxidant capacity [8]. Cellular metabolism as well as environmental (e.g., cigarette smoke, ozone, certain nutrients) and physiological (e.g., physical and mental stress) challenges can form RONS in the body. Cellular harms and disease generation that may accompany oxidative stress are related to those macromolecules (nucleic acid, protein, and lipid) that are targeted by RONS, the frequency and duration of attack, and the tissue-specific antioxidant defenses present [9]. For instance, RONS reacting with DNA can create wide strand breakage and degradation of deoxyribose, an effect caused by formation of hydroxyl radicals [10]. Over time such changes may lead to disease because of the alterations in nucleotide roots. The presence of 8-hydroxydeoxyguanosine (8-OHdG), an irregular intermediate in nucleotide metabolism, in urine and blood shows oxidative DNA damage. Biomarkers of protein oxidation represent amino acid modifications such as phenylalanine residues alteration to o-tyrosine or tyrosine to dityrosine, as well as overall modifications such as the alteration to carbonyl derivatives. Aromatic and sulfllydryl-containing residues are chiefly vulnerable to oxidation, often causing loss of catalytic or structural function in the affected proteins, makeing them susceptible to proteolytic degradation [11]. Proteins oxidation has been associated with disease like cancer, diabetes, and cardiovascular disease [12]. Lipid peroxidation has been recognized as a main mechanism of cellular damage in humans along with DNA and protein oxidation [13]. Polyunsaturated lipids are mainly vulnerable to damage in an oxidizing environment and may make lipid peroxides that can react to form malondialdehyde (MDA). MDA that can be measured in plasma is regularly used to estimate lipid-specific oxidative stress [14]. While MDA has been a practical indicator of oxidative stress for clinical studies [15], other lipid biomarkers, such as F2-isoprostanes, have gained agreement in recent years [16].

## 2.4. Oxidative stress and disease

Oxidative stress plays a role in several pathophysiologic conditions, for example, malignant diseases, diabetes, atherosclerosis, chronic inflammation, human immunodeficiency virus (HIV) infection, ischemia reperfusion injury, and sleep apnea. These diseases are divided into two types. In the first type, diabetes mellitus and cancer display a pro-oxidative shift in the systemic thiol/disulfide redox state and impaired glucose clearance, proposing that skeletal muscle mitochondria may be the major site of elevated reactive oxygen species (ROS) creation. These conditions may be referred to as "mitochondrial oxidative stress," which, without healing intervention may lead to massive skeletal muscle wasting, indicative of aging-related wasting. The second type refers to "inflammatory oxidative conditions," because it is usually associated with stimulation of NAD(P)H,H$^+$ oxidase activity by cytokines or other agents. In this case, changes in intracellular glutathione levels or increased ROS levels are often associated with pathological changes revealing a disregulation of signal cascades and/or gene expression, demonstrated by altered expression of cell adhesion molecules [5].

## 2.5. Oxidative stress and antioxidants

Several free radical species are produced in the body to carry out specific functions. $O_2^-$, $H_2O_2$, and NO are three free radical reactive oxygen species (ROS) that are crucial for body physiology. However, they can accelerate the process of aging, mediate cellular degeneration in disease states, and produce highly active singlet oxygen, hydroxyl radicals, and peroxy-nitrite that can attack proteins, lipids, and DNA. Antioxidants by donating at least one hydrogen atom to a free radical can result in the termination of radical chain reactions. Extra production of free radicals can cause oxidative stress. Acute hyperglycemic episodes such as an oral glucose tolerance test or a meal can increase oxidative stress in diabetic patients and decrease the antioxidant ability of plasma in both normal and diabetic subjects. Elevated basal levels of free radical production and decreased antioxidants are strengthened by elevated plasma glucose. Analysis of individual vitamin and enzyme components of the antioxidant system in man shows that the levels of vitamins A and E and catalase activity are decreased in both type 1 and 2 patients compared with controls. Whereas GSH-metabolizing enzymes are decreased in type 1 but not type 2 patients, SOD activity is lower in type 2 but not type 1 [2].

# 3. Antioxidants

## 3.1. Definition

Antioxidants are defined as any compound that can donate at least one hydrogen atom to a free radical so that it can result in the termination of radical chain reactions. A substitute type of antioxidant is defined by its ability to prevent the initiation of a free radical chain reaction rather than to terminate them. This latter type of antioxidant includes ceruloplasmin, transferrin, and albumin that are usually dependent upon the ability to bind metal ions. Cells must preserve the levels of antioxidants, often defined as antioxidant potential, through dietary uptake or de novo synthesis. Excess production of free radicals can reduce the intracellular antioxidants, resulting in oxidative stress [2].

## 3.2. Classification

Ingold [17] classified all antioxidants into two groups, namely primary or chain-breaking antioxidants, and secondary or preventive antioxidants.

### 3.2.1. Primary or chain-breaking antioxidants

Primary antioxidants can react with lipid radicals to convert them to more stable products. The major lipid radical at normal oxygen pressures is the alkylperoxy radical ROO, which is an oxidizing agent and is readily reduced to the related anion and then converted to a hydroperoxide by an electron donor, or which may be directly converted to a hydroperoxide by a hydrogen donor, AH. Alkyl radicals are in general reducing agents and are scavenged by electron acceptors. Inhibition by electron acceptors is not significant in most food systems, but

it can become important in biological tissues since the oxygen pressure is much lower in healthy tissues.

### 3.2.2. Secondary or preventive antioxidants

Secondary antioxidants are the compounds which decelerate the degree of autoxidation of lipids by processes other than that of interrupting the autoxidation chain by changing free radicals to more stable species. These may function by several mechanisms including compounds that bind metal ions, scavenge oxygen, decompose hydroperoxide to non-radical species, absorb UV radiation, or deactivate singlet oxygen. Secondary antioxidants show antioxidant activity if a second minor component exists in the sample.

## 4. Natural antioxidants in foods

Reports in recent years both in the popular and scientific press have stressed the value and advantages of natural ingredients as food preservatives. There is an implied assumption of safety for compounds that occur naturally in foods and that have been consumed for many centuries. Natural antioxidants in foods may be from (a) endogenous compounds in one or more components of the food; (b) substances formed from reactions during processing; and (c) food additives isolated from natural sources.

Natural antioxidants may function in one or more of the following ways: (a) as reducing agents, (b) as free radical scavengers, (c) as complex of pro-oxidant metals, and (d) as quenchers of the formation of singlet oxygen. The compounds are most commonly phenolic or polyphenolic from plants sources. The most common natural antioxidants are flavonoids (flavanols, isoflavones, flavones, catechins, and flavanones), cinnamic acid derivatives, coumarins, tocopherols, and polyfunctional organic acids [18].

### 4.1. Tea antioxidants and oxidative stress

Tea (from the plant *Camellia sinensis*), consumed by over two-thirds of the world's population, is the most desirable beverage next to water. About three billion kilograms of tea are produced and consumed annually [19-21]. Thease are the enzymes in tea which catalyze oxidation. During fermentation in which tea pectins are demethylated, polyphenolic compounds are decomposed which as a result of the quinone appearance, turn into colorful agents including theaflavin and thearubigin, both of which are plentiful in black tea [22-24]. More than 600 volatile agents have been documented in tea, most of which are yellow in color and have a characteristic scent. Linalool is the chief essence in tea, others of lesser importance being dihydroactinide iolido paravinile phenol, hexenol, hexenal, aldehydes, phenyl ethyl alcohols, phenols, and geraniols [22]. According to the preparation method, the degree to which it is fermented and the steps it goes through during production, different types of tea consumed all over the world are classified into at least six categories. The less processed the tea, the greater the polyphenols content will be, which the extent of oxidation accounts for [25].

1. White tea: White tea is manufactured only from the buds or first leaves of *C. sinensis*. It is the least processed type of tea and is simply steamed and dried without a prior withering stage; therefore, the concentrations of EGCG and also methylxanthines (like caffeine) are enriched in white tea compared with green and black tea.

2. Yellow tea: It usually refers to a special tea processed in a similar way to green tea; but the drying process takes place at a slower rate. The damp tea leaves are allowed to sit and yellow. Its taste resembles that of green and white teas.

3. Green tea: To manufacture green tea, first the fresh leaves are steamed, then primary drying-rolling, rolling, and secondary drying-rolling, final drying-rolling, and at last drying are performed. No fermentation takes place in this type of tea.

4. Oolong tea: Fresh leaves undergo solar withering at the first step, then indoor withering and rolling, pan firing, rolling, mass breaking and drying are the steps taken, to produce oolong tea. In this kind of tea, partial fermentation occurs after the rolling.

5. Black tea: The manufacturing process for black tea includes withering of fresh leaves, rolling, fermenting, and drying. Thorough fermentation is done in black tea.

6. Pu-Erh: Pu-Erh reffers to old tea with extreme fermentation [22, 25-27].

Regular intake of tea is associated with low risk of certain types of cancer, coronary heart disease, atherosclerosis, stroke, reduced mutagenicity and inflammation, protection against neurodegenerative diseases, and increasing insulin sensitivity since it can improve antioxidant status in vivo conditions [28,29]. Tea is a great source of antioxidants especially flavonoids. Animal studies have strongly supported the idea of tea being an efficient suppressor of oxidative stress [30]. Several studies have shown that different types of tea are potentially effective in reducing oxidative stress and related diseases [31]. Attempts have been made to manufacture products containing tea bioactive compounds for prevention and treatment of the aforementioned diseases. To design such products, the effective compounds of tea and their safe doses must be first identified. For instance, EGCG (Epicatechingallate) has been revealed to act as a pro-oxidant when administered in high doses, leading to apoptosis. Moreover, compounds other than catechins may exert the desired effects too [32-34]. To determine the compounds acting as antioxidants in black tea, Alipour et al., in 2009 [35] performed a study in which diabetic rats were supplemented total extract of black tea and its fractions. Total extract and fractions were attained by hydromethanol method and solid phase extraction using Sep-Pak, respectively. Results of this study indicated that injection of total extract and 20% fraction of black tea decreased malondialdehyde (MDA) and increased total antioxidant, Super oxide Dismutase (SOD), Glutathione Peroxides (GPX), and Glutathione in diabetic rats. To determine the major substances in the 20% fraction, Analytical HPLC, Preparative HPLC (High Performance Liquid Chromatography), and NMR (Nuclear Magnetic Resonance) (CNMR and HNMR) were employed. Caffeine, EpicatechinGallate, Quercetin, and Kampferol were the main compounds capable of fighting oxidative stress, determined in 20% fraction of tea [31]. Caffeine is a strong antioxidant; its activity is equal to that of glutathione and exceeding that of vitamin C [36,37]. The free radical scavenging capacity of flavonoids is

due to the 3', 4' dihydroxyl and 3' hydroxy in the β ring of its structure [38]. The 20% fraction of black tea has been shown to be more effective than the other fractions, which may be explained by the high concentration of the aforementioned compounds in it and absence of polyphenol antagonists in the very extract prepared [35]. Tea polyphenols have been found to induce expression of phase II enzymes and endogenous antioxidants that protect cells from oxidative stress. Phase II enzymes have vital antioxidant properties in fighting reactive oxygen species and xenobiotics (foreign substances), including potential carcinogens. Induction of phase II detoxifying and antioxidant enzymes is mediated through cis-regulatory DNA sequences known as antioxidant-response elements (AREs) that are found in the promoter or enhancer region of the gene. The major ARE transcription factor nuclear factor E2-related factor 2 (Nrf2) is a key agent in the initiation of antioxidant and detoxifying enzymes, such as heme oxygenase-1 (HO-1), glutathione S-transferases (GSTs), and reduced nicotinamide adenine dinucleotide phosphate:quinone oxidoreductase [39]. Nrf2 binds to Kelch-like ECH-associated protein 1 (Keap1) under nonstressed conditions. Keap1 in complex with cullin3, Rocl, and E2 proteins provides ubiquitination followed by proteasomal degradation. When oxidative stress occurs, oxidation of Keap1 leads to inability to bind Nrf2 protein by forming intramolecular disulfide bonds. Then, Nrf2 migrates into the nucleus and binds a protein of Maf family (like sMaf) and CBP/p. This complex is formed on ARE promoter region of certain genes leading to transcription activation. Phosphorylation of by protein kinases which may be activated by oxidants is one way to provide Nrf2 migration in nucleus [40].

## 4.2. Sesame and oxidative stress

In recent years, there has been a growing attention paid to natural antioxidants of plants and their use is gaining importance as nutraceuticals and phytoceuticals as they have significant effect on the status of human health and disease prevention [41]. For thousands of years sesame (*Sesamum indicum L.*) is an important traditional health food that has been used to improve nutritional status and prevent various diseases in Asian countries. The results of several studies support the hypothesis that sesame seed and its lignans may have antioxidant and hypocholesterolemic effects [42-45]. Alipour et al. in 2012 [46] showed that sesame seed supplementation decreased serum TC, LDL-C, and lipid peroxidation, and increased antioxidant status in hyperlipidemic patients. A positive effect of sesame seed was seen in improving lipid profile and oxidative stress in patients with knee OA, indicating that sesame seed might be of help to reduce oxidative stress in OA patients [47]. Sesame seeds are not only rich in oil and protein, but also in lignans (e.g., sesamin and sesamolin) [48] especially phenolic lignans such as sesamol. Antioxidant effects of lignans were shown in former studies [49,50]. Furthermore, it is obvious that diets containing polyphenols and flavonoids increase catalase and SOD activity, decrease MDA and improve lipid profile [51,52]. Nakai et al. [52] revealed that sesame metabolism by CYP450 in liver results in inversion of methylene dioxyphenyl to dihydrophenyl (strong radical scavenger). Previously, scientific evidence has showed the fact that protective effects of sesame seed are because of the suppression of oxygen species production [53]. Moreover, sesame lignans have an ability to increase vitamin E levels in various tissues [54,55] and increase gamma-tocopherol levels that could lead to the suppression of different

free radicals (those that usually increase in age-related diseases) [56]. In a study on fifty patients with knee OA, supplementation with sesame seed improved clinical signs and symptoms and indicated that sesame might be a viable adjunctive therapy in treating OA [57]. Epidemiological studies have shown that high HDL-cholesterol concentration could potentially contribute to its anti-atherogenic properties, including its ability to inhibit LDL-oxidation and protect endothelial cells from the cytotoxic effects of oxidized LDL [58]. Presently, sesame seed powder administration has shown to elevate HDL-C levels in hypercholesteremic animals [59]. Several studies reported that high antioxidant properties of sesame seed appear to be related to its lignans- sesamol, sesamolinol, pinoresinol, and sesaminol [60-64], as well as vitamin E [65]. The tocopherol of sesame seed has been shown to be mainly y-tocopherol, with only less amounts of a-tocopherol [66]. In addition, Kahae et al. [67] indicated that $\gamma$-tocopherol in sesame seed exerts vitamin E activity equal to that of $\alpha$-tocopherol through a synergistic interaction with sesame seed lignans. These compounds also have inhibitory effects on membrane lipid peroxidation, the microsomal peroxidation induced by ADP-$Fe^{3+}$/NADPH [61], and the oxidation of LDL induced by copper ions [64].

## 4.3. Burdock and oxidative stress

The examination of burdock (*Arctium lappa* L.) protective effects on oxidation of low-density lipoprotein (LDL) and nitric oxide production showed that methanolic extracts of burdock (MEB) and their major components, chlorogenic acid (CHA) and caffeic acid (CA), have antioxidant effects against oxidative damages. For many decades in Taiwan and Japan, burdock (*Arctium lappa* L.) has been consumed as a vegetable and beverage. Furthermore, burdock is also used as a folk medicine, such as a diuretic and antipyretic [68]. Analyses of its components [69], investigation of desmutagenic effect, and hepatoprotective efficacy [70] have been described. Chen (2004) [68] finds that burdock has significant free radical scavenging activity, which was mainly attributed to chlorogenicacid (CHA) and caffeic acid (CA). Duh in 1998 [71] presented that burdock, with or without heat treatment, acts as a primary and secondary antioxidant, as well as active oxygen scavenger. In addition, burdock displayed potential inhibitory action on microbial growth [72]. Although burdock showed the biological activity mentioned above, whether it has any protective effects on biomolecules and nitric oxide production remains uncertain. The protective activities of CA and CHA on LDL oxidation and nitric oxide production have been established [73,74]. Several reports showed that oxidatively damaged LDL as an atherogenic agent is clearly a main risk factor for cardiovascular disease. Thus, the bioactive activity of MEB on LDL oxidation and nitric oxide production needed to be examined. MEB inhibited oxidation of phospholipid, protein and deoxyribose, which are components of the cells. So, MEB can protect cells and tissues against oxidative damage. CA and CHA, which were major compounds present in MEB [69], showed notable inhibitory effect on oxidative damage of liposome, deoxyribose, and protein. Maghsoumi et al. in 2014 [75] suggested that *Arctium lappa L.* root tea improves inflammatory status and oxidative stress in patients with knee osteoarthritis.

### 4.4. Lentil and oxidative stress

Several studies have shown that legumes consumption has many effects in health improvement, control, and protection against metabolic diseases such as type 2 diabetes and CVDs [76]. Lentils (Lens culinaris), the most consumed legume grains, are good sources of dietary fiber, resistant starch, tannins, β-glucan, functional antioxidant ingredients, a wide range of phenolic acids including gallic acid, proanthcyanidins, prodelphinidin, procyanidins, catechins, epicatechin, kampferol, quercetin, cinapic acid, and apigenin [77]. Lentil contains about 28% protein on a dry weight basis [78]. The effects of lentil sprouts (LS) on glycemic parameters are associated with its fiber content. The fiber content of lentil seed is 3.7 g per 100 g; lentil seed also has low glycemic index (21/2). After germination of the lentil seeds, the amount of fiber and protein are increased [79]. The enzymatic hydrolysis of lentil proteins have resulted in bile salts binding activity and the production of hydrolysates with ACE-inhibitory activity [80, 81]. Furthermore, it has been recognized that specific fragments from legumin, vicilin, and convicilin with amino acid sequences contribute to the antioxidant and ACE-inhibitory activity of lentil hydrolysates [82]. Epidemiological studies recommend that lentils through biological activities including antioxidant, anticancer, angiotensin I-converting enzyme inhibition, reducing blood lipid, and reducing the risk of cardiovascular diseases, confer protection against chronic diseases [83,84]. Studies show that bioactive proteins of lentil decrease plasma levels of LDL-C, triglyceride content of the liver, and adipose tissue lipoprotein lipase activity; moreover, polyphenols of lentil could prevent angiotensin II-induced hypertension, and pathological changes including vascular remodeling and vascular fibrosis [85,86]. Lentils have a higher oxygen radical absorbing capacity (ORCA) value than most of the common fruits and vegetables [87]. In a study by Aslani *et al.* in 2014 [88], effects of lentil sprout (LS) consumption on glycemic parameters and anthropometric measurements in overweight and obese patients with type 2 diabetes were investigated. They found that LS consumption could have favorable effects on glycemic control in overweight and obese patients with type 2 diabetes. They showed that consumption of LS as supplementary treatment in type 2 diabetes could have favorable effects on HbA1c (Glycated hemoglobin), FBS (fasting blood glucose), QUICKI (quantitative insulin sensitivity check index), and HOMA-IR (homeostasis model assessment- Insulin resistance).

## 5. Biological effects of food antioxidants

The human organism, like that of animals, is oxygen-dependent. This suggests that oxygen, essential for life, works through a succession of mechanisms which indeed have their limits and their side effects. The survival of the species means that biochemical protection systems have developed in parallel with that promoting oxygen utilization. More generally, it may be considered that oxidation involves loss of one or more electrons that is of negative electric charges [89]. However, more complex oxidation reactions occur, with the production of toxic radicals, which, in the absence of antioxidant mechanisms, would soon destroy the vital elements of the cell [90]. The accumulation of hydroperoxides, for instance, requires the intervention of catalase, tocopherol, selenium, or reduced glutathione and its conversion

enzymes; their deficiency would promptly lead to an attack on membranes [91,92]. The multiplicity of in- vivo cellular reaction allowing aerobic life to develop implies extremely active binding as well as exchanges of oxygen molecules with other radicals. Whereas some of these metabolic sequences require radicals interacting with reactive oxygen the synthesis of prostaglandins, the metabolism of molecules with quinone structures, or the activity of macrophages, for instance these radicals may also be at the origin of chain reactions eliciting deleterious effects at the level of cell particles. The survival of tissues requires in turn that other molecules either terminate oxidative chain reactions or scavenge the excess of the generated free radicals [89].

# 6. Conclusion and future trends

There is now an agreement among scientists regarding the effect of uncontrolled oxygen radicals in the deterioration of health. Oxidative stress has been showed to play an important role in initiation and progression of disease. Thus, to prevent the very consequences of oxidative stress, it seems logical to take the necessary steps to reduce it. Antioxidants have been reported to be effective in achieving this goal. Some of these antioxidants are flavanols, isoflavones, flavones, catechins, flavanones and probiotics which are assessed for treatment and/or prevention of diseases such as diabetes [18, 93-97]. Routine methods for the determination of oxidation and peroxidation levels further need to be developed. It is recommended that well-designed, controlled clinical trials be done taking into account all the factors affecting the oxidative status of the patients and using sensitive and specific indicators of oxidative stress. By analyzing the results of studies, several nutritional factors that are effective in reducing oxidative stress markers should be recognized in order to be used as functional foods and supplements for controlling oxidative stress.

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