Chapter

Use of Selected Antioxidant-Rich Spices and Herbs in Foods

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Abstract

Free radicals are chemicals that play a role in the etiopathogenesis of ischemia–reperfusion injury. To prevent or reduce this damage, many protective or therapeutic antioxidants are used effectively in alternative medicine. These antioxidants include immunological or pharmacological agents, vitamins, food and herbal products, and spices. Herbs and spices have been used for a long time as coloring or preservative agents by adding to the content of foods, and at the same time to increase the nutritional value of foods. More recently, the nutritional effects of herbs and spices have become more perceived and the area of interest for these products has increased. Concordantly, the biological contents of herbs and spices have begun to be studied in more detailed way at the cellular and molecular level. Sample plants are classified according to different chemical families, with the diet. Therefore, they have different levels of antioxidant capacity. These products also have potent anti-inflammatory, antihypertensive, glucoregulatory, antithrombotic, anticarcinogenic and so forth effects. These properties are used in the treatment of some chronic diseases. In this review, the antioxidant properties of various herbs and spices used to add flavor to foods or to extend their shelf life have been examined in the light of large-scale nutritional epidemiological studies, in vitro cellular/animal studies and clinical trials.

Keywords: antioxidant, food, herb, plant, review, spice, supplement

1. Introduction

It is known that cell or tissue damage is related to free reactive oxygen radicals (ROS; reactive oxygen species) and associated nitrogen degradation products [1–5]. These radicals are high-energy molecules that have free electrons in their outer orbits, and can easily interact with other molecules and cause DNA damage. These molecules are continuously produced in the human body secondary to some detoxification processes, phagocytosis and energy production. Although the healthy human body has the capacity to neutralize these radicals, the balances may change in the direction of increasing the ROS ratio and reducing the antioxidant capacity due to the reasons such as environmental conditions and diet, so oxidative stress develops [6]. There are many different types of ROS, and many cellular and organ system level pathologies occur in the body depending on these products [2, 7, 8]. Various antioxidant compounds are used in medicine to prevent these pathologies [1, 2, 9, 10]. These compositions include various immunological and pharmacological agents, vitamins, fruits, vegetables, food supplements, herbal products, or spices [1, 2, 4, 11].

Many types of herbs and spices have generally safe ingredients for human health and their benefits have been known for a long time [10–13]. These benefits include facilitation of digestion, anti-inflammatory, antirheumatic, antisclerotic, antimalarial, antimicrobial, antiviral, immunomodulatory, antiallergic, antiaging, antidiabetic, radioprotective, antioxidant, and antiproliferative/anticarcinogenic effects [4, 9–20]. Because of these benefits, they are used in many acute and chronic diseases (diabetes, dyslipidemia, hypertension, cancer, cardiovascular and neurodegenerative disease, liver cirrhosis, arthritis, asthma, obesity, metabolic syndrome, etc.) [9, 10, 12–14, 19, 21, 22]. In addition, herbs and spices are used in order to increase the nutritional value, flavor and aroma of foods, have protective properties during storage and extend the shelf life of foods [3, 5, 9, 11–14, 21, 23–26]. Thanks to the spices added to foods, the lipids in the food are protected against oxidative deterioration and the formation of oxidant substances is delayed.

Antioxidant materials can be classified under two main headings, which are synthetic and natural [5, 12]. Synthetic antioxidants are widely used in the market. However, it has been determined that these synthetic products have harmful effects on human health in the long term, and cause teratogenic/carcinogenic effects. Therefore, consumers prefer foods that contain natural antioxidant agents. Concordantly, over time, herbs and spices with natural antioxidant properties were replaced by synthetic products [4]. These so-called "natural antioxidants" are claimed to be more effective than synthetic ones. The origins and uses of natural antioxidants are diverse. In this review, the main properties of herbs and spices with known antioxidant properties are studied to be presented.

2. General properties of herbs and spices with natural antioxidant effects

Many bioactive foodstuffs originate from herbs [2]. These substances are generally called as "phytochemicals" [2, 5]. Most of these phytochemicals are redox active molecules so that they have antioxidant features [2].

Many herbs and spices with antioxidant effects are from the *"labiatae (lamiaceae)"* family. Most of the herbs in this family have been used in traditional treatments to cure various diseases from ancient times until today. Besides, it has areas of use in the food, cosmetics and perfumery industries [27].

Herbs and spices contain organic sulfur, tannin, alkaloid, phenolic diterpene, diketone, polyphenol, polyphenylpropanoid, vitamin, flavonoid and anthocyanin compounds, and they have a protective effect against oxidizing agents [12–14, 27–29]. It is stated that this protective effect is mostly related to the "flavonoid" and "phenolic" content of the herbs and spices [3, 4, 9, 12, 13].

It has been suggested that being fed with a flavonoid-containing diet efficiently reduces the risk of chronic diseases [9, 10, 21]. These effects of flavonoids have been reported to be related to oxidative stress defense at the molecular level [9, 30–32]. Flavonoids scavenge and neutralize free radicals [32]. Numerous articles have been published on this subject, especially in the last two decades. In these studies, very detailed investigations have been made especially on the structures and biological activities of flavonoids [4, 9, 21, 33–35].

Phenolic compounds act with redox reactions [32]. The ratio of phenolic component is an important variable on the antioxidant activity of the product [3–5, 9, 10, 12, 26].

It has been reported that the antioxidant capacity of these products is approximately 10 times higher than that of fresh fruits and vegetables [9, 32]. Parallel to the progress made by modern medicine in the last decade, studies to determine the bioactive components in herbs have gained momentum. Although the chemical structures of most herbal components have been described in detail, tests and molecular studies on their bioactive roles are still ongoing [9, 21, 36–39].

3. Antioxidant-affected plants

In the **Figure 1**, natural herbs with potent antioxidant features and which are most commonly used are listed.

3.1 Rosemary (*Rosemarinus officinalis*)

This plant, in the "*lamiaceae/labiatae*" family, is a polyphenol-containing plant with small pointed leaves, which grows particularly in the Mediterranean region [9, 12–14, 21, 27, 40]. The plant can reach 1–2 meters in height. It has an aromatic structure and does not shed its leaves in winter. Especially in spring, white-blue flowers bloom with leaves [14, 27]. Its leaves taste bitter [27]. It is used in making salads or tea [40].

This plant is used as an antioxidant and preservative, especially in the food industry [12, 14, 27, 41–43]. In addition, it can be consumed in the form of soap, perfume and lotion [27]. Its use for food preservation is for the lipid component in food. When used as a food preservative, it has been determined that rosemary does not spoil the organoleptic contents of foods [12].

There are studies indicating that the antioxidant capacity of rosemary is closely related to the techniques in production [44]. It has been reported that the antioxidant effect of rosemary depends primarily on its type, harvest time, type of treatment, environmental and ecological characteristics of the environment it grows [27]. The way rosemary is given is also an important parameter in its effectiveness. It has been reported that the encapsulated form of rosemary essential oil exhibited more antimicrobial effects compared to the standard essential oil form [12].

Carnosol, carnosic acid, phenolic diterpene, phenolic acid, rosmanol, epirosmanol, rosmarinic acid, caffeic acid ester, tosemaridiphenol, 3- (3,4 dihydroxyphenyl) lactic acid, flavonoids (apigenin, diosmin, luteolin), tannins provide antioxidant properties to the plant [9, 11–13, 27, 40, 45]. Rosemary also contains essential oils (cineole, pinene, camphor) [13]. The dominant components in its structure are

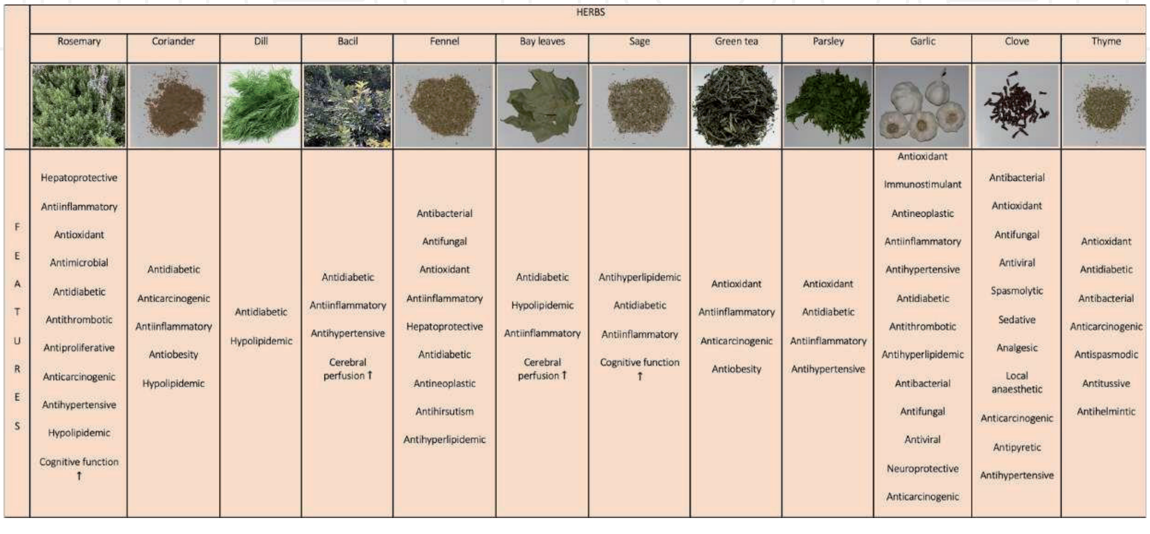

Figure 1.
Natural herbs with potent antioxidant features and which are most commonly used.

rosmarinic and carnosic acid [12, 13, 27]. Carnosic acid and carnosol are responsible for 90% of the antioxidant effect. These components reduce cell membrane damage by 40–50%. Both components also reduce DNA damage due to dietary oxidant agents [13]. The antioxidant activity of carnosic acid has been compared with synthetic antioxidants such as butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA) and tertiary butyl hydroquinone (TBHQ), and it has been proved that carnosic acid has a stronger antioxidant effect than these molecules [12].

There are many studies on rosemary in the literature. Akgül et al. determined that rosemary is among the most powerful antioxidants [46]. It has been stated that rosemary extract increases the antioxidant status and defense of aged rats [13]. Similarly, in another study, the antioxidant effect of 32 different plants and spices on lard was investigated, and rosemary was detected to be among the most important antioxidants [47]. In another study in which 15 different types of spices were tried in sausages, it was observed that one of the products with the most important antioxidant effect was rosemary [48]. In a study examining the effect of rosemary on foods prepared with some fish species, it was observed that rosemary significantly reduced the level of malondialdehyde in fish-containing foods. In a study on the oxidative stability of ground sardines, rosemary extract was determined to have an antioxidative effect over a 5-month period [27]. Rıznar et al. examined the antioxidant activity at 3 different temperatures (4, 12, 25 °C) by adding rosemary extract to chicken sausages, and observed high antioxidant effects during storage at all temperatures [49]. Lopez-Bote et al. indicated that rosemary extract is highly effective in preventing lipid peroxidation in chicken meat stored at −20 ° C for 6 days [50]. In a study of alloxan-induced diabetic rats, intraperitoneal injection of rosemary for 7 days decreased in blood glucose levels [40]. In a similar study, after administration of 100 mg/kg rosemary extract in diabetic rat models, a significant decrease in blood glucose level and an increase in serum insulin concentration were achieved [13].

The properties of rosemary include hepatoprotective, antiangiogenic, anti-inflammatory, antioxidant, antimicrobial, antidiabetic, antihypertensive, antithrombotic, antiproliferative, and anticarcinogenic effects [4, 13, 14, 40]. Its anti-inflammatory effect is thought to be because of decreased macrophage viability, inducible nitric oxide synthase (iNOS) protein expression and nitric oxide (NO) production. Rosemary can also contribute to the treatment of hypertension. Increased urinary volume and excretion of sodium, potassium, and chloride were found in healthy rats given rosemary extract daily for 7 days orally [40]. It also improves endothelial function with its antithrombotic effect [13]. Carnocic acid has an inhibitory effect on liver fibrosis [14]. Rosemary extract has been determined to have detoxifying properties on toxic chemical-related liver damage and cirrhosis in experimental animal models. In the experiments performed in mice, it was observed that fatty liver associated with obesity was decreased by giving 200 mg/kg of rosemary leaves after the diet with high fat content [13]. Another effect of rosemary is that it is hypolipidemic. In a study conducted on obese rats, it was evaluated that feeding a rosemary-rich diet for 64 days caused a decrease in body weight [40]. Rosemary extract reduces low density lipoprotein (LDL) cholesterol oxidation. In cell culture tests, it has been detected to reduce lipid peroxidation by 38–89% under oxidative stress. In a randomized clinical study conducted with rosemary inhalation in 140 subjects, it was observed that cognitive assessment and self-assessment mood scale levels and cognitive functions increased. In vivo and in vitro studies, rosemary extract has been reduced oxidative damage in fat cells on the skin surface. Rosemary is therefore a potential candidate for skin treatment. However, clinical studies with large series are needed on this subject [13]. Amoah et al. reported that this ingredient is also used in the treatment of atopic dermatitis and seasonal allergic rhinoconjunctivitis [51].

3.2 Coriander (*Coriandrum sativum*)

It is a plant with a flavonoid structure [9]. Coriander leaves and roots are used in cooking. Especially the coriander leaf type known as "*cilantro*" is frequently used for this purpose [40].

The roots of this plant contain high levels of chlorogenic acid, caffeoyl derivatives, quercetin-3-O-rutinoside and p-coumaric acid [9, 40].

Several potential benefits of chlorogenic acid have been reported [9]. These include antidiabetic, anticarcinogenic, anti-inflammatory and antiobesity effects [9, 52, 53]. In streptozotocin-induced diabetic rats, intraperitoneal injection of coriander seed extract significantly decreased serum glucose and increased insulin secretion in pancreatic β-cells. It was also observed that lipid peroxidation and protein oxidation decreased in the subjects given coriander. Coriander roots also have a hypolipidemic effect. In a study conducted in obese and hyperlipidemic rats, it was presented that total cholesterol, LDL and triglyceride levels were reduced in the group given coriander extract orally for 30 days. Additionally, serum and erythrocyte antioxidant parameters have been detected to be increased [40].

3.3 Dill (*Anethum graveolens*)

Dill has a flavonoid structure [4, 6]. It is generally consumed during feeding with seafood [40]. Fresh dill contains high levels of flavonol glucuronides, chlorogenic acid quercetin and isorhamnetin [9, 40].

It has antidiabetic potential. Dill given orally for 15 days in diabetic rats induced by dexamethasone has been determined to cause a decrease in serum glucose and insulin levels. Dill is also hypolipidemic. In rats fed a high-fat diet for 3 weeks, daily oral dill was found to cause a decrease in blood total cholesterol, triglyceride and LDL levels after 2 weeks [40].

3.4 Bacil (*Osimum basilicum*)

It is a medium density plant with flavonoid and polyphenol content [9, 40]. Bacil leaves are used in the form of a salad or cake dressing [40].

Bacil extract contains significant rosmarinic acid and catechin [40].

In studies on bacil extract, it has been determined that bacil is highly effective in preventing metabolic syndrome. Its antidiabetic and anti-inflammatory properties are known. The bacil extract also prevents the accumulation of intracellular sorbitol by providing aldose reductase inhibition. In this way, it is suggested that it reduces vascular osmotic pressure and oxidative stress, which are among diabetic complications. Due to its dense polyphenol content, it has also been closely associated with the reduction of advanced glicosylation products that occur in oxidative stress. It is also effective in the regulation of blood pressure. It increases renal function in hypertensive rats. Subjects treated with bacil had a decrease in blood urea nitrogen concentration and a decrease in creatinine and angiotensin compared to the hypertensive control group [40]. In an experimental study in which cerebral hypoperfusion and ischemia/reperfusion damage was performed in the brain in mice, it was found that it reduced the size of cerebral infarct with its antioxidant effect, but also increased short-term memory and motor coordination [21].

3.5 Fennel

This plant species belonging to the "*foenicuum vulgare*" species and often called "fennel" belongs to the "*apiaceae*" family [14]. It is consumed in salads, sauces, bread making, together with fish products and in the form of tea [40]. This product is a type of plant that is used quite often in alternative medicine. Although it often grows in the Mediterranean, it is known that it grows in different parts of the world today [14].

It contains fenchone, estragole, anise aldehyde, trans-anethole, and essential oils [14]. This ingredient gives fennel its unique smell and taste [5]. The most concentrated flavonoid in its composition is quercetin [40].

It has antibacterial, antifungal, antioxidant, hepatoprotective, antidiabetic, antineoplastic, and anti-inflammatory effects [14, 40, 54]. Anise aldehyde content of fennel is responsible for the hepatoprotective effect [14]. The reducing effect of fennel consumption on systemic complications of diabetes is through aldose and aldehyde reductase inhibition [40]. Studies have proved that *F. vulgare* accelerates the removal of harmful waste from the body by increasing body excretion. The anticancer potential of fennel seed methanolic extract (FSME) has been observed to be due to its reduction in oxidative stress in human MCF-7 and HepG-2 cell lines [14]. Fennel bulb has an antihyperlipidemic effect. In a study conducted on mice, it was observed that 24 hours after fennel bulb administration, a decrease was achieved in total cholesterol, triglyceride, LDL and ApoB levels [40]. In the experimental study conducted on Swiss albino mice by Mohamad et al., it was reported that oxidative stress decreased in subjects who were given 100 mg/kg FSME intraperitoneally, and they were protected from Ehrlich Ascites Carcinoma (EAC) associated with ROS [55]. In another study, it has been proved that fennel extract administered orally to mice reduces arachidonic acid-related ear edema [40].

3.6 Bay leaves (*Laurus nobilis*)

Laurus nobilis is a plant that is often grown in southern Europe and used in cooking. It contains flavonoids such as quercetin, kaempferol and sesquiterpen in particular [40].

It is especially known for its antidiabetic effect. Its hypolipidemic effect has been demonstrated in several in vivo studies. Bay leaf extract has been increased glucose uptake in rat epididymal adipocytes by acting like insulin. Besides, it causes a decrease in total plasma cholesterol level in hypercholesterolemic people. It inhibits ApoA1 glycation, oxidation of LDL particles and uptake of oxidized LDL particles from macrophages, in in vitro studies. Bay leaf additionally has an anti-inflammatory effect. Bay leaf extract reduces interleukin-6 (IL-6) production and cyclooxygenase-2 (COX-2) protein expression, particularly in stimulated macrophages [40]. It has also been detected to reduce the rate of cell death and cerebral infarction after cerebral ischemia in rats [21].

3.7 Sage (*Salvia officinalis*)

It is in the fragrant herbs class that forms the "salvia" genus from the "*lamiacea*" family. It is also known as "A*mmi majus*" and "*salvia*". It grows a lot in Asian and European countries [27]. The dried form of the leaves, which are furry and whitish, can be boiled like tea and can be used to add taste and flavor to meat dishes [27, 40].

It is dense in terms of polyphenols. It is particularly rich in phenolic and rosmarinic acid [40]. The most important phenolic components in the structure of sage, which has antioxidant effect, are carnosol, carnosic acid and rosmanol [27].

It has an antihyperlipidemic effect [40]. Fasseas et al. reported that lipid peroxidation decreased in meats treated with sage extract, but this effect may vary depending on storage temperature and time [56]. In streptozotocin-induced diabetic rats, it was observed that sage extract given intraperitoneally caused a decrease in serum glucose level after 3 hours, but it was shown that it did not cause any change in serum insulin level. However, it has been shown to contribute positively to glucose management in healthy subjects. Serum glucose levels have been decreased in healthy subjects given oral sage for 14 days. Experimental studies have been conducted on the potential anti-inflammatory effect of sage and positive results have been obtained. Inflammation at the injection site was observed to be reduced by administering sage one hour before injection of carrageenan or formalin to rats [40]. In a study conducted on people between the ages of 65 and 80 with mild or moderate Alzheimer's disease, another type of salvia called "*salvia lavandulaefolia*" was used for 4 months and significant improvement was obtained in cognitive functions. Thus, this product is thought to have the feature of increasing "speed of memory" in healthy volunteers. In a comparative study conducted between "S*alvia officinalis*" (aroma form) and "*salvia lavandulaefolia*" (oil form), it was detected that *Salvia officinalis* increased cognitive and emotional characteristics and memory quality more [21].

In a study of industrial microwave exposure of sage, it was examined that there was no change in the antioxidant properties of this plant [50].

3.8 Green tea

It is an antioxidant and anti-inflammatory product with flavonol structure [21]. It is an important component of many diets, due to its high antioxidant content [2].

Major flavonoids in green tea are monomer catechins, epigallocatechin gallate (EGCG), epigallotechin, epicatechin (EC), epicatechin-3-gallate (ECG) and epicathechin (EGC) [2, 26]. EGCG is the most active and the most concentrated component in green tea [26]. It makes up 43% of total phenol [4, 26]. Most of the stated effects of green tea are related to the EGCG component. EGCG presents its antioxidant, anti-inflammatory effect by reducing COX-2 overexpression. The polyphenol content constitutes approximately 35% of its dry weight. Compared to black tea, green tea has a higher proportion of catechins [26].

Green tea is a herb known to have positive effects on age-related chronic diseases, cardiovascular diseases, cancer, obesity, diabetes, and neurodegenerative pathologies. In many epidemiological studies, it has been suggested that green tea consumed daily reduces morbidity and mortality due to chronic diseases [26].

3.9 Parsley (*Petroselinum crispum/Petroselinum neapolitanum*)

It is an antioxidant herb with a very high flavonoid content [9, 21, 40]. It mainly contains apigenin [40].

It was observed that parsley, which was given parsley extract and administered orally to streptozotocin-induced diabetic rats for 28 days, caused a decrease in the level of glucose in the circulation. In addition, parsley also has an anti-inflammatory effect. One hour after oral administration of parsley extract in rats with paw edema induced by carrageenan, a decrease in edema was observed in the area where carrageenan injection was applied. Another benefit of parsley consumption is that it contributes to the treatment of hypertension. In a study conducted on healthy rats, it has been presented that oral administration of parsley extract leads to an increase in urinary output after 5 hours and an increase in excretion of sodium, potassium and chlorine with urine [40].

3.10 Garlic/Chive (*Allium schoenumprasum*)

It is a herb that has always had a place in traditional and modern diets [21]. Garlic, also known as "A*llium sativum*", is a plant belonging to the "*amaryllidaceae*" family that can be used prophylactically or in treatment in both the food industry and alternative medicine [14, 21].

Bioactive ingredients include organosulfide compounds such as allicin, ajoene, S-allyl-L-cysteine, dallyltrisulfide (DATS) [13]. Dallyltrisulfide (DATS), which is found in the composition of garlic, is also an important phenolic component [14].

It has various pharmacological activities accepted in the medical literature [14]. These include antioxidant, immunostimulant, antineoplastic, anti-inflammatory, antihypertensive, antithrombotic, antibacterial, antifungal and antiviral activities [13, 14, 21].

Its anti-inflammatory property is due to inhibition of nuclear factor κB (NFκB) (transcription factor regulating inflammatory response) activation, iNOS and COX-2 expression. In in vitro and in vivo animal studies, garlic has been determined to strengthen immune function, stimulate lymphocyte proliferation, increase interferon-γ (IFN-γ) release, increase macrophage phagocytosis function and natural killer (NK) cell activity [13]. Garlic has been reduced TNFα-induced ROS and NFκB activation on human umbilical vein endothelial cells. It has been proved that the anti-inflammatory effect of garlic or garlic oil derivatives is due to NO suppression in induced macrophages. However, it has reduced endotoxin-induced iNOS activity in rat intestinal mucosa and weaken monocyte chemoattractant protein-1 by IL-6 induced by macrophage-secreted factors in human preadipocytes [21].

In some studies, it has been observed that garlic has positive effects, especially in cardiovascular diseases [13, 14]. It is known that it slows down the atherosclerotic process, reduces the risk of heart attack and infarction, prevents fat accumulation in blood vessels, inhibits LDL cholesterol oxidation, reduces total cholesterol, increases HDL, and has positive effects on endothelial function [10, 13]. There are studies reporting the antioxidant effect of garlic, especially in elderly and hypertensive persons [10, 21]. It has reduced systolic blood pressure by 5.5% [10]. Garlik extracts have also reduced oxidative stress and contribute to vascular remodeling in rats given sucrose-containing water [21]. Other effects include decreasing blood glucose levels [10, 13, 21]. In a study conducted on rats fed with fructose for 8 weeks, it was demonstrated that the metabolic syndrome was attenuated, insulin sensitivity was increased, and oxidative stress was reduced by giving garlic homogenized with water. In addition, garlic has neuroprotective effects in Alzheimer's disease [21]. In rats, it reduces the infract size in rats following edema and ischemia/reperfusion injury after transient global brain ischemia [13, 21]. It has a learning and memory strengthening effect. Garlic has been detected to prevent Abeta-induced neurotoxicity and apoptosis and protect neurons [13]. In the absence of any stress environment, a significant increase in memory was observed in rats given garlic after 21 days of oral use [21]. It is known that garlic has beneficial effects on respiration and digestion. Garlic is also used in some skin diseases and parasitic infections. DATS, which is in the composition of garlic, has an effect that inhibits tumorigenesis. It achieves this effect through the Wnt/β-catenin signaling pathway. Thus, it is known to affect SW480 and DLD-1 colorectal cancer cells [14].

3.11 Clove (*Eugenia caryophyllata/Syzygium aromaticum*)

Clove (*Eugenia caryophyllata*) comes from the "*mirtaceae*" family, a medium-sized (8–12 m) tree that grows on the Maluku Islands in Eastern Indonesia. It consists of leaves and buds. It is a widely used herb that is often combined with foods. Cloves are generally used in meat and rice dishes. In North Indian cuisine, cloves are used in almost every side dish, often mixed with curry. Previously used only as a food preservative, this herb continues to be used increasingly due to its antioxidant properties [57].

The biocomponents of this plant, which has a dominant scent, are phenolic compounds (ferulic, caffeic, ellagic, and salicylic acids) such as flavonoids (quercetin and kaempferol), β-caryophyllene, eugenol, hydroxybenzoic acids, hydroxynamic acids and hydroxyphenyl propenes [57, 58].

Its most prominent effect as a food preservative is its antibacterial and antioxidant effect. In addition, its antifungal, antiviral, spasmolytic, sedative, analgesic, local anesthetic and anticarcinogenic effects are also important. There are literature data indicating that clove increases microcirculation, lowers body temperature, provides a hypotensive effect, and may reduce cardiovascular risks and arterial sclerosis [59]. Local anesthetic effects are among the reasons that are frequently recommended by dentists. It is thought to act by depressing nociceptors, which are sensory receptors that play a role in pain perception [60]. Clove also inhibits prostaglandin biosynthesis and the release of leukotrienes in the inflammatory pathway through its potent COX-1 and 2 inhibitory activity [61].

Clove oil has antibacterial activity thanks to its β-caryophyllene and eugenol content. Bacteria with which it is effective include campylobacter jejuni, *Escherichia coli*, salmonella enteritica, *Listeria monocytogenes* and *Staphylococcus aureus*. Antifungal effects have also been reported on *Candida albicans*, trichophyton rubrum, microsporum canis, tricophyton mentagrophytes, fusarium moniliforme, microsporum gypseum, fusarium oxysporum, epidermophyton floccosum, mucor species, microsporum gypseum and aspergillus [58, 62].

3.12 Thyme/Oregano (*Thymus vulgaris/Oreganum vulgare*)

It is a member of the "*lamiaceae*" family. Although there are many species of the thymus genus, the more common one is "T*hymus vulgaris*", native to Italy and the Western Mediterranean. Oregano grows largely in temperate regions and is rare in Africa. Different studies have concluded that the use of oregano improves stability and reduces lipid oxidation throughout the shelf life of foods (meat, meat products, milk, fish or fish products). This property makes thyme an enriched functional food source [63].

Thyme includes monoterpene polyphenols such as thymol and p-cymene, with the most particular component being carvacrol, and other monoterpenes such as -pinene, 1,8-cineol, camphor, linalool and borneol [9, 21, 63]. Flavonoid content is quite high [21]. The common feature of the thyme types widely used in the industry is that they contain essential oil and the main components of these essential oils are thymol and carvacrol. These substances are phenolic compounds that give thyme its unique scent and give it antioxidant properties [27].

Thyme is a nutritional antioxidant that stands out with its antidiabetic, antibacterial and anticarcinogenic effects. The basis of its antimicrobial activity is the free hydroxyl group, its hydrophobicity and the presence of a phenol moiety [64]. Similarly, the presence of phenol is responsible for its antispasmodic and antitussive effects. There are also both animal studies and in vitro studies on its anthelmintic effects [65]. In in vitro studies, the effect of thyme oil on antibiotic-resistant enterococcus and escherichia strains, especially staphylococcus and pseudomonas strains has been presented. It is highly effective on biofilms, and its antibacterial effects are associated with direct penetration into the cell wall and matrix [66].

4. Antioxidant-affected spices

In the **Figure 2**, natural spices with potent antioxidant features and which are most commonly used are listed.

4.1 Saffron (*Crocus*)

Saffron, also known as "*Crocus sativus*", is a spice belonging to the "*iridaceae*" family. It is also called as "red gold" since it is a very precious spice in food and medicine. It is among the most valuable spices in the world [14]. It is one of the most important phytochemical carotenoids [14, 21].

Crocin/Crocetin is the most important bioactive molecule in substance of saffron. This molecule has the effect of reducing tumor growth [14].

It has potent antioxidative and anti-inflammatory effects. It has been observed that *crocetin* significantly reduces insulin resistance, corrects hyperinsulinemia, dyslipidemia and hypertension in rats that are given fructose. It reduces the oxidative damage associated with ischemia/reperfusion in the rat hippocampus. After chronic cerebral hypoperfusion in rats, it has been determined that the extracts of *crocin* and *crocetin* increase spatial cognitive abilities. A double-blind study reported significant improvement in cognitive function in individuals with Alzhemier's disease after 16 weeks of saffron use [21].

4.2 Curcumin (Turmeric/Eugenol/*Curcuma longa*)

Its use in traditional medicine, especially in dermatological diseases, in eastern societies, especially in China and India, is based on approximately 4,000 years. This product, which is accepted as a combination of plants that have a place in religious rituals in ancient times, is collected in its roots and stems and then reproduces by giving seeds again [20]. Originally, this spice, which comes from the ginger family, has been recognized to have a healing effect on many disease

	SPICES						
	Saffron	Curcumin	Cumin	Cinnamon	Ginger	Black pepper	Red chili
							
FEATURES	Antioxidant Antiinflammatory Anticarcinogenic Antidiabetic Antilipidemic Antihypertensive Cognitive function ↑	Antiinflammatory Antioxidant Antibacterial Cognitive function ↑ Antidiabetic Antiobesity Anticarcinogenic Antilipidemic	Antiinflammatory Antioxidant Hypolipidemic Antidiabetic Antibacterial Antimicrobial Hepatoprotective Nefroprotective Neuroprotective	Antioxidant Antiinflammatory Sedative Antidiabetic Antimicrobial Antibacterial Antifungal Anticarcinogenic Antilipidemic	Antioxidant Antiinflammatory Neuroprotective Antinausea Antiobesity Antilipidemic Antimicrobial	Antioxidant Antimicrobial Analgesic Antipiretic Antidepressant Antifungal Antiinflammatory Anticarcinogenic Antithyroid Antiallergic Antilipidemic	Antioxidant Antiinflammatory Anticarcinogenic Cerebral perfusion ↑ Antiplatelet Antidiabetic Antilipidemic Gastroprotective

Figure 2.
Natural spices with potent antioxidant features and which are most commonly used.

progression, although some remained only in the clinical trial phase. However, the transition from traditional medicine to modern plug was not difficult. This spice with flowers and broad leaves grows in tropical climates. Its color and taste are used by putting it in pasta, rice, vegetables, meat dishes and salads. The Food and Drug Administration (FDA) has confirmed that curcumin is a compound "generally considered safe". Curcumin has been proven to be sensitive to light, so it is recommended that biological samples containing curcumin should be protected from light [67]. Studies are underway to increase its bioavailability after oral ingestion, as its absorption from the gastrointestinal tract is poor and most of it is excreted in the feces [68].

Biologically active component of "*Curcuma longa*" is lipophilic, yellow-orange colored curcumin (diferuloylmethane). It is also referred to "Indian saffron" because of its specific color. Its antioxidant properties are due to the methoxy, phenoxy and carbon–carbon double bonds in its structure. Even though its metabolic rate and elimination are high, its bioavailability is limited. However, in the development phase of many diseases, cytokines, it plays an important role by regulating growth factors, kinases, transcription factors and enzymes. Its molecular activity on signal transduction and redox reactions has always been a curiosity. High-level methoxylation and low-level hydrogenation of curcumin content increase free radical scavenging ability [68].

Curcumin is one of the spices with the highest antioxidant and anti-inflammatory component [2, 12]. The antioxidant effect of curcumin is based on reducing TNFα and IL-1 expression and establishing balance with ROS. Curcumin, other than being beneficial for wound healing, also has an antibacterial effect by controlling the inflammatory response. Curcumin induces apoptosis of inflammatory cells and thus shortens the inflammatory phase. It accelerates healing by increasing collagen synthesis and fibroblast migration in the early phase of wound healing. However, forms suitable for topical use are not yet available. In vivo and in vitro studies on this subject continue. Therefore, it is much more effective to add oral forms of curcumin to the diet for wound healing at this stage [69]. Studies have shown that the effects of curcumin on the processes of Alzheimer's, diabetes mellitus, obesity, neurodegenerative diseases, osteoarthritis, and oncogenesis give promising results [20]. There are studies showing that curcumin reduces the proliferation and invasion of tumor cells [70]. It has been examined that curcumin is a biologically active agent that increases cancerous cell apoptosis in head–neck, pancreatic and colorectal cancer patients [70–73]. Curcumin is also a good source of ω-3 fatty acids and α-linolenic acid. It prevents atherosclerosis by reducing the level of LDL in the blood, preventing lipoperoxidation, and reducing cholesterol levels [74]. It is mostly because of this effect that it is used as a common cooking spice in developed countries where the consumption of saturated fatty acids is greatly increased. Curcumin supplementation is recommended for foods during both prevention and treatment of cardiovascular diseases in which atherosclerosis plays a major role. Curcuminoids reduced blood sugar, partly due to their effect of reducing free fatty acids, and in addition, in studies on rodent models, they prevent the reduction in antioxidant capacity caused by diabetes. As a result, it has been reported to have an antidiabetic effect in patients with insulin-resistant type-II diabetes and in in-vivo studies [75, 76].

4.3 Cumin (Cumin aldehyde/*Cuminum cyminum*)

Cumin (*Cuminum cyminum*) is a well-known culinary spice that is often used in mealtimes. It is a small herbaceous product belonging to the "*apiaceae*" family. Its oblong-shaped seeds have a strong aromatic scent and a warm bitter flavor. It is widely grown in Central Asia, Pakistan, India, Iran and China. It is traditionally used as an antiseptic agent. It is also widely used in digestive disorders such as dyspepsia and diarrhea [72].

Its bioactive components are terpenes, phenols and flavonoids. Thanks to these components, it has been proven that it has free radical scavenging and metal chelating properties [77].

It is a spice with anti-inflammatory and antioxidant properties [12]. Animal studies are available showing the hypolipidemic and antidiabetic effects of cumin [78]. Experimental studies have been conducted to support the effect of cumin on renal ischemia–reperfusion injury [79, 80]. It also has antibacterial and potent antimicrobial activity [66, 77]. Cumin seeds also have immunostimulating, gastric protective, hepatoprotective, nephroprotective, and neuroprotective activities [81].

4.4 Cinnamon (Cinnam aldehyde/*Cinnamomum zeylanicum*):

Cinnamon comes from the "*lauraceae*" family, and its leaves and shells as a spice have been in the world trade for centuries. Cinnamon is mostly obtained from the bark of the "C*innamomum zeylanicum*" tree originating from South and Southeast Asia. The most specific feature of cinnamon, which is an evergreen tree, is its aromatic scent. Cinnamon, which is also widely traded, is frequently consumed in Iran in the form of traditional tea. It is used to prevent lipid oxidation of bakery products such as cakes, so that it prevents the taste of foods [82].

The antioxidant activity is estimated to be due to the polysaccharide known as "daruchini" derived from cinnamon bark. Thanks to "arabinogalactan" and "glucan" in its structure, it loses protons and gives a radical scavenging effect [83].

It is a spice with a pronounced antioxidant and anti-inflammatory effect [12]. It has been observed that consuming it especially in tea form is beneficial in the treatment of diseases related to oxidative stress. It has also been presented to have a sedative effect in many human studies [83]. Cinnamon, acting like insulin, increases insulin receptor kinase activity and stimulates glycogen synthase activity. Thus, it exerts antidiabetic effect [82, 84]. Spices such as cinnamon have started to be included in prescriptions as an additional treatment, due to the toxic side effects of diabetes medications and balance problems due to long-term use. In these studies, which accelerated the development of multiple antibiotic resistances, antibacterial effects on factors such as bacillus subtilis, *Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli*, salmonella typhi, *Pseudomonas aeruginosa*, *Listeria monocytogenes*, and fungal effects such as aspergillus monocytogenes, aspergillus monocytogenes are also known [85]. In addition, NF-κB, which is known to be effective in cancer development acts an anticancer by inhibiting the production of IL-1β and TNF-α. Cinnamon is beneficial in lowering triglycerides and LDL cholesterol by affecting the blood lipid profile through the poliphenols in its structure [86]. The effect of polyphenols here is achieved by inhibiting hepatic lipid peroxidation. In this way, by cleaning hydroxy and fatty acid radicals and chelates, providing the metabolic balance of fat and carbohydrates, cinnamon has turned into a functional nutrition.

4.5 Ginger (*Zingiber officinale roscoe*):

Ginger (*Zingiber officinale roscoe*) comes from the "*zingiberaceae*" family, and especially its roots are among the most widely used functional spices in the world. With a slightly bitter but strong aroma, this root can be used in powder or ground form. It can be consumed in brine, drying, canned or fresh [20].

"Oleoresin" obtained from its roots contains various bioactive molecules. Among these are terpenes, polysaccharides, lipids, but especially gingerol, physiological effects are the most intense [20, 87]. The proportion of gingerol is higher in fresh ginger than the dried form, so consuming fresh is more important for its antioxidant effect [20]. Ginger extract is also a natural and potent antioxidant compared to synthetic antioxidants, with a high Fe^{+3}-effective chelating capacity [88].

Studies mention the effects of ginger on cardioprotective, anti-inflammatory, neuroprotective, antinausea and antiobesity. Its anti-inflammatory effects have been demonstrated in the treatment of osteomyelitis, arthritis and rheumatism [89]. Ginger, which has increased glutathione levels and suppress lipid peroxidation during its anti-inflammatory effects, is widely used as a food flavor in developed countries for colds, migraine attacks and gastrointestinal disorders. Its antimicrobial effects are related to its lipophilic property, making the fungal walls and cytoplasmic membrane permeable. Antibacterial effects on species such as *Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcus pneumoniae* and haemophilus have been proved on various animal and human studies. The most stable metabolite, 6-gingerol derivative, has been observed to have an antinause effect by blocking 5-hydroxy tryptophan and serotonin-mediated vagal afferent neurons in patients used after chemotherapy, nephrectomy and cesarean operations [90, 91].

4.6 Black Pepper (*Piper nigrum*)

Black pepper is a product that belongs to the "*piparaceae*" family and is called as "P*iper nigrum*" [14]. It is obtained from the ripe fruits of *Piper nigrum* L [27]. Black pepper has a very common pharmaceutical use in the world [14]. It is cultivated in tropical regions, especially in India, Malaysia, Asia and Indonesia [12, 27]. It is among the best-selling spices on the market in some countries like India [14, 92].

Black pepper contains five phenolic acids (piperettine, piperanine, piperylin A, piperolein B and pipericine) amide with antioxidant effects [12, 13, 27]. Additionally, it contains alkamides, piptigrine, wisanine and dipiperamide [13]. These phenolic components have a damaging effect by preventing the growth of the bacterial membrane, and their antimicrobial activity occurs through this mechanism [12]. These compounds are non-greasy, odorless, tasteless and exhibit stronger antioxidant activity than α-tocopherol [27]. The composition in the form of essential oil has antimicrobial activity [12]. The quality of black pepper varies depending on piperine causing bitterness and the essential oils responsible for its aroma [12, 27]. Piperine is a green crystalline clear substance that was first isolated in 1819. This alkaloid is a compound that gives the pepper its bitterness. The nature of piperine, which is its active basic component, is known in detail, and its effectiveness in alternative medicine has been clearly proven [13, 14, 21]. Its content, piperine, is a bioactive component with known beneficial effects on human health [13, 14]. Piperine is absorbed by passive diffusion in the gastrointestinal tract and has a short clearance time [13]. In a study of industrial microwaving of black pepper, it was determined that no change was observed in the antioxidant properties of this herb [50].

It has antioxidant, antimicrobial and antipyretic properties [27]. Antidepressant, antifungal, anti-inflammatory, analgesic, anticarcinogenic, antithyroid activities are some of the important pharmacological effects of black pepper [13, 14, 93]. Its anti-inflammatory effect has been detected on rats in many experimental studies. Black pepper accelerates the digestion process, increases digestive enzymes, gastric acid and bile acid secretion, and shortens the food transit time. It has anti-depressant-like effect by regulating neurotransmitter metabolism, causing an increase in behavioral/cognitive effects [13]. Piperine significantly reduces cell death, brain edema, and post-reperfusion proinflammatory cytokines in rats. It has decreased hippocampal cell death after ethylcholine aziridinium ion administration in rats [21]. Piperine has reduced arthritis pain in animal models.

Piperine supplementation reduces muscle damage when given before and after exercise. Piperine reduces histamine release and eosinophil infiltration in animal models. However, it suppresses allergic airway inflammation and airway hypersensitivity. Piperine increases energy expenditure in animal experiments, activates the sympathetic nervous system, causes thermogenesis, increases catecholamine levels, and activates adrenal sympathetic nerves [13]. In a study, it was examined that lipid peroxidation was delayed in pork meat with the addition of black pepper [13, 94]. Piperine prevented lipid accumulation in mouse macrophages. Alternatively, it has been determined to transform into foamy cells in animal studies, which can reduce fat accumulation in the arterial wall [13].

4.7 Red Chili/Chili Pepper (*Capsicum annum*)

Red chili is a product belonging to the "*solanaceae*" family [14].

"Capsaicin" is the primary bioactive substance of red chili pepper [14, 21]. Capsaicin is an alkaloid. It constitutes 50–70% of total capsaicinoids. It contains 20–25% dihydrocapsaicin and 0.2–2% capsaicinoid [10]. Among its recently discovered ingredients are capsiate and dihydrocapsiate [13].

The beneficial effects of red pepper have been documented long before. In vitro and experimental studies of red pepper and capsaicin have proved potential antioxidant and anti-inflammatory effects of it against oxidative stress in various tissues and organs [13]. This spice type has the ability to induce apoptosis in major type cancers. It has been presented that capsaicin treatment in gastic cancer cells (MGC-803) and cervical cancer cells (HeLa) prevented the G1 phase in cell cycle analysis. In an experimental study performed in athymic mice, it was indicated that tumor growth in prostate cancer cells (LNCaP) was reduced in subjects given 5 mg/kg orally [14]. In another study conducted in vitro, it has been determined that it has a protective effect on rat hippocampal neurons, reduces hippocampal death after global ischemia, decreases the size of cerebral infarction after bilateral arterial occlusion in mice, and decreases the infraction volume in neonatal rats ligated in unilateral carotid arteries after hypoxia [21]. However, capsaicin regulates energy metabolism and has beneficial effects on the cardiovascular system, with its antioxidant and antiplatelet effects. In a clinical study conducted on humans, it was determined that 5 grams of red pepper (*Capsicum frutescens*) lowered blood glucose levels and maintained healthy insulin levels. In the short-term use of red pepper, it has been observed that body mass index contributes to management, decreases energy and fat intake, increases body heat production (thermogenesis), increases body metabolic rate, decreases the conversion of fat cells to mature cells (adipogenesis) and increases fat oxidation. Capsaicin has been detected to be gastroprotective in patients with peptic ulcer disease. Capsaicin reduces acid secretion, induces alkaline mucous stimulation (particularly by affecting gastric mucosal blood flow) and contributes to ulcer healing [13].

5. Comparison of natural antioxidant-affected herbs and spices

In a study comparing antioxidant effects, it was stated that the strongest antioxidant effect was in rosemary and curcumin, followed by herbs such as cinnamon, saffron, sage, and thyme [2, 27, 46].

Shahidi et al. asserted that the antioxidant activities of clove, sage, thyme and ginger in meat oil were concentration-dependent [95]. They stated that among these substances, the most effective was clove, and the least effective spices were ginger and thyme [95].

Pizzale et al. found that, on average, the antioxidant activity of sage species (*Salvia officinalis and fruticosa*) was higher than thyme species (*Origanum onites and indercedens*) in their study [96].

Another study proved that chloroform extract of dried musk sage (*Salvia sclarea*) has higher antioxidant activity than acetone extract, and both extracts have higher total antioxidant activities than α-tocopherol [27].

Nakatani et al. determined that black pepper is more effective than synthetic antioxidants such as BHT and BHA [97].

In another study, the antioxidant properties of curcuminoids were investigated, and it was determined that the antioxidant capacity of these extracts was equivalent to ascorbic acid [98].

When evaluated in terms of the density of total phenolic compounds, it has been observed that rosemary and thyme have higher phenolic content than other herbs. Also, it was presented that fresh plants have more intense phenolic content than dried plants [9].

Correspondingly, it is thought that the most potent antioxidants are fresh rosemary and curcumin, and it may be suggested to increase the consumption of these products.

6. Antioxidant combinations

Since each spice contains a wide range of phenols, many of them can provide synergistic effects with each other. The formulations of different herbs and spices were tested in vivo and in vitro, and their antimicrobial effects were compared [12].

It is predicted that the antioxidant effect increases significantly when thyme essential oil and vitamin E are mixed in half so that there is a synergistic effect between thyme essential oil and vitamin E [27].

It has been indicated that meats are effectively protected against *Listeria monocytogenes* with the combined use of curcumin and thyme [12].

In an experimental animal study, it was observed that when capsaicin (0.015%) was given alone and in combination with curcumin, it reduced triglyceride levels by 12% and 21% in animals given a high fat diet [13].

Since piperine increases the absorption of various drug and food sources, it increases their bioavailability when used with other antioxidants. It increases the absorption of compounds such as coenzyme-Q, curcumin and polyphenol. For example, bioavailability of curcumin increases by 154% when it is given with 20 mg/kg piperine in animal studies. Piperine shows its effect by decreasing the intestinal and hepatic metabolism of curcumin. In some studies, it has been presented that piperine increases the bioavailability of resveratrol in vivo by inhibiting its metabolism. In this way, it ensures that additional resveratrol doses are not required [13].

Therefore, the combined use of herbs and spices with appropriate formulations can be recommended.

7. Conclusion

Herbs and spices used in cooking, increasing the nutritional value of foods and extending the storage time are highly interesting compounds with antioxidant properties due to their bioactive content, showing beneficial effects on human health. Interest in natural antioxidants in plants around the world is increasing day by day, with the widespread use of natural additives in the food industry. Therefore, herbs and spices have become the most important focus of research for the study of natural antioxidants.

Since ancient times, herbs and spices have been used in alternative medical treatments due to their antimicrobial, anti-inflammatory and antioxidative effects. Although the use of herbs and spices in food and treatment has been available for a long time, research on this subject is limited to the recent past. In addition to the poor antioxidant features of animal origin foods, the antioxidant power of plant-based foods is much higher.

There are over 1.000 known antioxidant phytochemicals. Although they are very small in terms of weight and volume, they have a feature of increasing the value and antioxidant content of foods. Thanks to the studies conducted on this subject, the application strategies of phytochemical antioxidants in the diet can be determined, and chronic diseases related to oxidative stress such as cancer, cardiovascular diseases, hypertension, hyperlipidemia, inflammation and diabetes can be prevented or their effects can be reduced.

Various synthetic and natural products are used in the food industry to cope with dietary oxidative stress. Hence, there is a need for optimized studies of natural antioxidant products that can be used as food preservatives in the food industry. Thus, the natural storage times and nutritional values of foods can be increased.

Conflict of interest

The authors declare that there is no conflict of interest, and there have been no sources of funding.

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