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REVIEW ARTICLE

A NEW AGE FOR OAK, BIOLOGICAL ACTIVITY AND THE MIRACULOUS HEALING PROPERTIES

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Summary

Background and Purpose: Different oak species (*Quercus* spp.) are widely distributed in Asia, Africa, Europe, and North America. The oak plant and its fruit hull have considerable antiinflammatory, antimicrobial, and antioxidant effects with important potential to be applied in wound healing products.
Methods: The systematic review of documents and manuscripts from clinical trials, and scientific societies has been carried out. The surveys of interest were indexed in "PubMed", "Web of Science", "SciFinder", and "Elsevier". As a research strategy to carry out this review, two reviewers were responsible for searching the publications. Relevant literature has been obtained using the keywords "antimicrobial activity", "antioxidant activity", "flavonoids", "oak", "oak fruit", "phytochemicals", "tannins", and "natural components". The selection criterion was to include research papers on the most important topics, using *in vitro* or *in vivo* studies.
Results: The most important *Quercus* species are *Quercus infectoria*, *Quercus ilex*, *Quercus cerris*, *Quercus brantii*, *Quercus virgiliana*, *Quercus suber*, *Quercus rotundifolia*, and *Quercus robur*. Important chemical components in lipophilic compounds are aliphatic alcohols such as octacosanol, hexacosanol, tetracosanol, and docosanol; fatty acids such as oleic acid and α linolenic acid; tannins such as castalagin, pedunculagin, and diagalloyl hexose; terpenoids such as cornin, agnuside, lamioside, and gibberellin A4 glucosylester; tocopherols such as α-tocopherol, β-tocopherol, and γ-tocopherol. The most important chemical constituents in its hydrophilic compounds are flavonoids, phenolic acids, tannin, amino acids, peptides, and analogues, carbohydrates and carbohydrate conjugates, and other phenolic compounds. Acorns are affordable and easily accessible raw material known in different cultures and regions which can be used in medicine, pharmacology, and food industry. Acorns are rich in many bioactive components with importance in food products with high health-promoting activities. Different parts of oak, especially its bark can be used as an antiseptic and hemostatic, which makes it appropriate to cure gastropathies, and toothache with beneficial activities as healing agents in burn.

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Conclusions: The general conclusion is that different parts of oak can be used more widely as an important ingredient in drugs, supplements, and functional foods.

Key words: antimicrobial activity; antioxidant activity; flavonoids; oak; oak fruit; phytochemicals; tannins

Introduction and background

There are more than 500 extant species of oak (*Quercus* spp.) are extensively found across the world (1-3), with great economical and ecological importance (4,5). *Quercus* (oak) belongs to the family Fagaceae, and the genus evolved at nearly 56 million years ago, and it shows significant adaptability in response to cold, drought, and different environmental stress (6-12). In many areas, indigenous peoples use different species to treat gastrointestinal tract disorders such as hemorrhoids and diarrhea and as antiseptics (13). The oak fruit, known acorn, is housed in a cup called gland, and the leaves are commonly egg-shaped, uniform with a serrated margin, dense florets on the leaves, with stellate-shaped, and yellow fur on the back (14-16). Oak forests have an important role in storing atmospheric CO_2 in terrestrial ecosystems, both production of organic components with long C residence times, and accumulation of biomass, which can mitigate global climate change (17-21). Oak seedling growth negatively correlated with diversity of plant pathogenic fungi (22). Oak is commonly more shade-tolerant compared to pine, and is likely more late-successional (23-26).

In traditional sciences in both Eastern and Western cultures, remedies which include *Quercus* sp. galls have been used to treat different inflammatory conditions, including dysentery (27-32), and diarrhea, toothaches, stomach aches, postpartum care, tooth decay in combating oxidative stress-related diseases and metabolic abnormalities (33,34). In the Mediterranean region, cork oak (*Quercus suber*) woodlands are classified as high nature value farming systems with high socio economic and conservation value (35-42). The growing demand for natural ingredients by consumers, and the number of health conditions related to the consumption of plant-based extracts have caused in a significant increase in the investigation of effectiveness produced bioactive extracts from natural sources (43-47). Plants and herbs used as raw materials to obtain bioactive components for the treatment of various health conditions in traditional and pharmacy medicine (48-50). Common oak (*Quercus robur* L.) is one of the main hardwood species in North America and Europe. Its bark has been found important because of possessing the high amounts of phenolic compounds, which have been associated to a number of bioactive ingredients, such as anti inflammatory, anticancer, antimicrobial, and antioxidant activities (51-64).

Both drought and heat stress have triggered forest dieback episodes, influencing oak forests, especially in hotspots of climate change (65), earlywood anatomy can serve as an important early warning signal of oak decline (65). Drought can negatively influence secondary growth, especially at the vascular cambium, and transcriptional analysis showed a global downregulation of genes associated to cell differentiation, division, and cell wall biogenesis in inner bark, phellem, and xylem under water deficit conditions (66). Hotter drought and rising temperatures predispose some of the oak species to die-off, growth decline, and high mortality rates (67). Zukowska *et al*. (68) reported that oak seed germination does not appear to be related to genetic variation, and oak is known as the moisture-driven ecosystem (69). Drought tolerance differences in oaks species are primarily connected with the taproot and the foliage, but not with the stem, and it is related to the recovery capacity of physiological performance following severe water stress (70,71). Oak growth reduced in response to dry-warm winter-spring and summer conditions (72). Rubio-Cuadrado *et al*. (73) found that *Q. pyrenaica* showed the lowest tolerance and highest soil water requirements, one evergreen oak, which is *Q. suber* showed the most tolerance to drought, and *Q. faginea* revealed intermediate tolerance. Other parameters which can influence oak decline are genetic predisposition, defoliation, droughts, and soil pathogens (74-76). The most important species in North America, Asia and Europe are *Quercus arizonica*, *Quercus robur*, and *Quercus ilex*. *In vivo* and *in vitro* analyses revealed the potential of oak extracts especially for antitumoral, anti inflammatory, antioxidant, and antimicrobial effects (77,78). Acorn have been traditionally applied as a natural remedy for different ailments, such as blood pressure and diarrhea, as well as production of herbal medicines such as vanogl tablet, phytovan tablet, coated tablets of veinovital, and vinagol ointments (79). This article aims to study the importance of Oak in food, nutritional and medicinal sciences, and give primarily and basic knowledge of oak in pharmacological sciences with considering different chemical components.

Oak and Chemical Components

The production of bioactive components from oak bark has predominantly been carried out using conventional extraction methods, such as Soxhlet extraction and reflux, which commonly need extraction times of several hours as well as large volumes of solvents (80,81). Some other effective extraction technologies such as Ultrasound-Assisted Extraction (UAE), and Microwave Assisted Extraction (MAE) have been also reported as effective methods (82,83). Another important green extraction technology is Pressurized Liquid Extraction (PLE) which has been successfully used to produce bioactive components from different parts of biomass and plants (84 87). It is also found that the nutritive value of forage common in kermes oak shrublands significantly depends on the floristic constituents of plant groups as well as their phenological stage of growth, and these shrubs may support the nutrition of grazing goats during winter and spring (88). It is reported that *Quercus infectoria* oak trees have noticeable phenolic components (89). The dried bark of *Quercus petraea*, *Quercus robur*, and *Quercus pubescens* contains at least 3% tannins (90). The polyphenols found in *Quercus robur* bark include gallic acid, ellagic acid, catechin, protocatechuic, and vanillic acid (90). Acorn fruit of Persian oak (*Quercus brantii*) contains different amounts of biologically active components such as ellagic acid, gallic acid, gallvil derivatives, malic acid, tannic acid, hexa-hydroxy diphenyl, mucilage, quercin, and pectin, and all of these chemical components have antioxidant impacts (91). Its fruit is called Gland which is placed in acron cup with various amounts of starch, sugars, oil, and small amount of tannin, pentosan, and quercetin, and its tannins with antiseptic and astringent effects are the main components of Iranian oak (91). Nutritionally, acorn fruit is a source of carbohydrates mainly vitamins such as E and A, fat, protein, starch, fiber, malic acid, ellagic acid, gallic acid, different galloyl, tannic acid, unsaturated fatty acids like linoleic acid and oleic acid, and minerals such as Mg, Ca, K, and P (92). In one experiment, it is reported that *Quercus brantii* var. *Persica* various chemical components, but the most important are Terpin-4-ol, Verbenone, β-pinene, *trans*-linalool oxide, 2,3-dimethyl pyrazine, 2-acetyl pyridine, 2-methoxy pyrazine, 2-methoxy-p-cresol, Tetrahydro-linalyl acetate, 2-methoxy pyrazine, 2-methoxy-p-cresol, Tetrahydro-linalyl acetate, and β-pinene oxide (93). Tumen *et al*. (94) reported that the chemical components of Strendzha oak (*Quercus hartwissiana*) bark, sapwood, and heartwood are hexanoic acid, 4-acetyl morpholine, decanal, ethyl ester, ethylboronate, 2.4-Decadienal, 3-hydroxy-4-methoxy benzaldehyde, 2,4-di-tert-butyl phenol, γ-Gurjunene, γ-Eudosmol, α-Cadinol, Tetradecanyl ester acrylicacid, Tetradecanal, 4,6-Dimethoxysalicyladehyde, 1-Decene, Octadecane, Bis(2 methylpropyl) ester Benzenedicarboxylic acid, Nonadecane, Methyl ester hexadecenoic acid, Eicosane, Hexadecanal, Ethyl linoleate, 1-Octadecene, Heneicosane, 9,12-Octadecadienoic acid, 9-Octadecenamide, Docosane, 1,19-Eicosadiene, 1-Heptadecene, Tricosane, Methyletherbenzyl, 1-Eicosanol, Tetracosane, Octadecyl ester, Linoleicacid butyl ester, isopropyl linoleate, 1 Octadecanol, Pentacosane, γ-Sitosterol, Hexacosane, Heptacosane, Octacosane, Nonacosane, Stigmastan-3,5-dien, Triacontane, γ-Tocopherol, α-Tocopherol, Campesterol, and Spinasterone. Sohretoglu and Renda (95) showed that the most important phenolic components from *Quercus* species are Kaempferol, Kaempferol-3-O-*β*-D-glucopyranoside, Kaempferol-3-O-*β*-D galactopyranoside, Kaempferol-3-*O*-α-L-arabinopyranoside, Kaempferol-3-*O*-(6//-*O*-galloyl)-*β* D-glucopyranoside, Quercetin, Quercetin-3-*O*-*β*-D-glucopy-ranoside, Quercetin-3-*O*-*β*-D galactopyranoside, Quercetin-3-*O*-α-L-arabinofuranoside, Quercetin-3-*O*-α-L-arabinopyranoside, Isorhamnetin-3-*O*-*β*-D-glucopyranoside, Naringenin Dihydrokaempferol, Leucopelargonidin, 7-*O*-*β*-D-glucopyranoside, 6,7-Dihydroxycoumarin, 7-Hydroxy-6 methoxycoumarin, (+)-Catechin, (+)8-Chlorocatechin, (-)-Epicatechin, (+)/(-)Gallocatechin, (-) Epigallocatechin, Quercuschin, *trans*-resveratrol-3-*O*-*β*-glucopyranoside, Gallic acid, Methyl gallate, Syringic acid, Kermesoside, *m*-digallic acid, Ellagic acid, Valoneic acid bilactone monogallate, Valoneic acid bilactone digallate, Casuariin, Casuarinin, Grandinin, Castalagin, Vescalagin, Acutissimin A, Acutissimin B, Stenophynin A, Stenophynin B, Stenophyllanin A, Stenophyllanin B, Stenophyllinin A, Mongolicain B, Castavaloninic acid, Isocastavaloninic acid, Pterocarinin A, Phillyraeoidin A, Phullyraeoidin B, Phillyraeoidin C, Phillyraeoidin D, Phillyraeoidin E, Cocciferin D1, Cocciferin D2, Cocciferin D3, Cocciferin T1, Cocciferin T2, Roburin A, Roburin B, Roburin C, Roburin D, Roburin E, (+)/(-)-Lyoniresinol, (+)/(-)-5 Methoxuisolariciresinol, Olivil, and Matairesinol.

In Ilam country of Iran, phytochemical components of Iranian oak assessed by using HS SPME (GC-MS) method, and the components were 3Z-hexenal, 2-methoxy pyrazine, 2,3-dimethyl pyrazine, tetrahydro citronellene, cyclohezyl formate, cyclohexyl formate, β-pinene, dihydroxy *trans*-linalool oxide, 3Z-hexenol acetate, 1,4-cineole, 2-acetyl pyrazine, 2-acetyl pyridine, lavender lactone, isopentyl butanoate, *trans*-linalool oxide, terpinolene, linalool, 1,3,8-p menthatriene, 2*E*-heptenyl acetate, dehydrosabina ketone, chrysanthenone, isopulegol, neo isopulegol, 2*E*,6*Z*-nonadienal, β-pinene oxide, 1,4-dimethoxy benzene, terpinen-4-ol, lavandulol, dihydrocitronellol, verbenone,

linalyl formate, exo-fenchyl acetate, pulegone, ethyl 2-octynoate, isobutyl benzoate, α-cubebene, thymol acetate, cis-mentholactone, and ethyl anthranilate (14). Shakuri *et al.* (96) reported that rosmarinic acid, rutin, salicylic acid, and gallic acid were known as the main phenolic components, and for food and pharmaceutical industries, the appropriate oak population can be selected to achieve the maximum total flavonoid content, total phenolic content, highest yield, and total tannin content. Key gallotannins reported in oak galls are 1,2,3,4,6 Pentagalloyl glucose, 1,2,4,6-Tetragalloyl glucose, Monogalloyl glucose, 1,6-Digalloyl glucose, 1,3,6-Trigalloyl glucose, and representative phenolic acids found in oak galls are ellagic acid, caffeic acid, vanillic acid, gentisic acid, and gallic acid (97). Hydrophilic constituents of mostly commonly known acorns are shown in Table 1.

Table 1- Hydrophilic components of most commonly identified in acorns (98-101).

Bioactive components	
Lipophilic compounds	
Tannins	Digalloyl hexose; Castalagin; Pedunculagin; Digalloyl-hexahydroxy-diphenoyl-glucose; Casuarictin; Trigalloyl-glucose; Tetragalloyl-pentoside; Trigalloyl-hexahydrodiphenoyl-glucose; Pentagalloyl-glucose.
Terpenoids	Cornin; Gibberellin A4 glucosylester; Agnuside; Lamioside; 7-deoxyloganin; Spruceanol; Gentiopicrin; Inumakilactone A glycoside; Schizonepetoside E.
Fatty acids	Oleic acid; α-linolenic acid.
Tocopherols	A-tocopherol; β-tocopherol; γ-tocopherol; δ-tocopherol.
Aliphatic alcohols	Docosanol; Tetracosanol; Hexacosanol; Octacosanol.
Phytosterols	Stigmasterol; Campesterol; β-sitosterol; Clerosterol.
Hydrophilic compounds	
Carbohydrates and Carbohydrates Conjugates	Fagopyritol A2; Sambacin; Icariside F2; Cyclomaltodextrin; Agarotriose.
Amino acids, Peptides, and Analogues	N-valeryl-glycine; Pyrrolidonecarboxylicacid; Blastacidin S.
Tannins	Tannic acid; Glucogalin; Eugeniin; Arecatannin B1; Procyanidin A2; Procyanidin B6; Sanguiin H1.
Phenolic Acids	Caffeic acid; Vanillic acid; Syringic acid; Ellagic acid; Chlorogenic acid; Gallic acid; p-hydroxybenzoic acid.
Flavonoids	Quercetin; Rutin; Naringin; Catechin; Gambriin A2; Dalbergioidin.
Other Phenolic Compounds	Pyrocatechol; Pyrogallol

Pharmaceutical and Health Benefits

Around 70% water and ethanolic extracts from three main oak species, namely *Q. aliena*, *Q. serrata*, and *Q. dentata* showed high anti-glycation and antioxidant potential (102), and according to the reports, the flavonoid (taxifolin, isorhamnetin, kaempferol, myricetin, quercetin), procyanidin, ellagic acid, ellagitannins, and phenolic acids are the major phenolic compounds (103,104). The bioactive components of oaks include moderately or polar components such as phenolic acids, flavonoid glycosides, flavonoids, tannins, ellagic acid, and nonpolar compounds such as sterols, fatty acids, and terpenoids (105,106). Different sources have informed that oak trees are an important source of bioactive components that have been used for their biological activities such as alkaloids, saponins, polysaccharides, peptides, phytosterols, triterpenoids, flavonoids, and tannins (107-109). Some biological activities of different components from *Quercus* species are polydatin for dermatological disorders, (-)-8-Chlorocatechin for antidiabetic, Tiliroside for antidiabetic, epicatechin for antioxidant, Quercetin-3-O-(2//-O-galloyl)-*β* galactopyranoside, Betulin for anticancer activities, Roburgenic acid with cytotoxicity activity, A (-)-Epicatechin and B-Procyanidin B3 with anti-inflammatory activity (13). Its fruits can be introduced as an important source of indigestible fibers because of the existence of considerable amounts of polysaccharides, and fiber in the oak structure (13). According to Persian traditional medicine, oak is dry-natured and war which is used as bread and food; brewed

oak is used for anemia, gastric ulcer, gastric pain, rickets, and hemorrhoids with analgesic and sedative agent (108,109). Both English oak (*Quercus robur* L.) roots secretes mucilage, and the mucilage reduced the growth of the rhizobacterium, and its mucilage polysaccharides consists of 12% glucuronic acid, 7% xylose, 11% arabinose, 16% mannose, and 54% galactose with no detectable galacturonic acid and glucose (110); furthermore, English oak mucilage can suppress bacterial growth because of its antimicrobial components, and promote carbon sequestration (110). The bark of *Quercus alba* L. can be used as hemostatic, venotonic, and astringent, and the acron of *Quercus acutissima* Carr. Can be applied for treatment of obesity, laryngopharyngitis diseases, labor pains, stomatitis, colitis, furuncles, diarrhea, and astrictiona (111,112). The leaves of *Quercus brantii* Lindi can be used in treatment of chronic skin diseases such the varicose veins and eczema, its bark can be used for treatment of internal enzymes, diarrhea, stomach pain, indigestion, rickets, anemia, and tuberculosis, its acorn can be used for treatment of tuberculosis, and its gall can be applied for cure of bleeding stopper, astringent, and stomach tonic (113,114). The bark and acorn of *Quercus cerris* L. can be used for treatment of throat inflammation, female disorders, diaphoretic, psoriasis, intestinal inflammation, ointment for wounds, and fodder (115-117); moreover leaves, gall and acorn of *Quercus coccifera* L. can be used for treatment of cough, vaginal diseases, dermatitis, hypertension, diarrhea, gingivitis, metritis, wild vegetables and fodder (118,119).

Leaves, wood, bark and flowers of *Quercus dilatata* can be used in treatment of diarrhea, diuretic, indigestion and asthma, as well as dysentery (120-122), and seeds of *Quercus ilex* L. are useful as aesthetic hair, gingiva and tonic drink coffee (123,124). Wood, acorn, bark and leaves of *Quercus incana* Roxb. can be recommended for treatment of asthma, used as astringent diuretic and antidiarrheal agent, moreover, it is also considered as antiarthritic, antidiabetic, antipyretic and useful for gastrointestinal disorders (125,126). Gall of *Quercus infectoria-Olivier* is effective in treatment of inflammatory disorders, treatment of toothache, skin disorders, diabetes diseases, with antiseptic, antistomatitis and deodorant activity (127,128). Bark, leaves and acorn of *Quercus leucotrichophora* A. *Camus* is effective in treatment of urinary infection, astringent, stomach ache cure, diarrhea, cure toothache and piles, asthma, dysentery, and gonorrhea (129,130). It is also reported that leaves and bark of *Quercus robur* L. is essential in treatment of diarrhea and diabetes (131). Ghassemi *et al*. (132) reported that the hydroalcoholic extract of oak fruit husk disrupts liver function, and after application of 120 mg/kg/w.bt dose of the extract, the significant decrease in LDH, cholesterol, and protection occurred. Its galls can aggravate throat and lung disorders, such as cough, and as hoarseness, and can also cause dyspepsia and anemia, through the chelation of metal ions, and the inhibition of digestive enzymes by tannins (133,134). Aleppo oak (*Quercus infectoria* or *Mazu*) traditional used in Asian and Indian medicine, is beneficial in in all internal hemorrhages, with other potential impacts like local anesthetic, antimicrobial, and anti inflammatory effects (135). Herbal vaginal tablets containing ajwain and oak gall were as effectual as metronidazole vaginal tablet, as vaginitis is one of the main common diseases in women and oak gall has been used in traditional Iranian medicine for treatment of vaginitis (136). Leishmaniasis is a complicated disease caused by various species of the protozoan *Leishmania*, which is an intracellular parasite of animals and humans, and it is reported that 75 µg/ml and 221 µg/ml of oak gall extract after 24 hours might be useful, safe and effective agent for treatment of cutaneous leishmaniasis (137). Ghaffari *et al*. (138) reported the cytoprotective impacts of the inner bark of the oak tree extract in the mouse model of gastric ulcer as an increase in the mean of the mucosal gland thickness, and the decrease in the mean of the wound area was found.

A new herbal mouthwash with the combination of oak fruit husk aquatic extract as a base, *Satureja bachtiarica*, and the aquatic extract of *Zataria multiflora* is called Jaftex which is suggested for treatment of recurrent minor oral aphthous stomatitis by decreasing ulcer size, shortening the duration of the complete healing process and relieving pain (139). Alipour *et al*. (140) also emphasized on the positive impact of the combination of Persian oak husk with antibacterial and astringent properties of its tannins and *Zataria multiflora* leaves with anti bacterial characteristics related to its essential oil. Tannin content of oak husk has high astringent properties with positive effects in treatment of inflammations, ulcer, gastric, diarrhea, and hemorrhoid (141,142). Toori *et al*. (143) reported that the aqueous oak fruit extract shows high hepatoprotective activity, and it can be safely used to treat liver ailments.

The impacts of oak fruit jaft extract on gastric cancer cell lines was evaluated in one experiment, and it was found that the jaft extract could enhance the apoptosis of gastric cancer cells, which can be proposed for its hydroalcoholic extract as a suitable anticancer medication (144).

Oak (*Quercus robur*) bark extracts had variable antibacterial impacts against *Staphylococcus aureus* and *Streptococcus strains*, but no significant difference was found in activity against *Escherichia coli*, and there was also a negative correlation between antibacterial effect and solvent concentration (90).

The antifungal activity of cork oak (*Quercus suber* L.) bark extracts against *Candida albicans* strains, proving its prospective application for candidiasis treatment (145). Cork oak bark is rich in polyphenolic components, so it can show high curative and preventive properties.

Its aqueous extract because of its high antioxidant activity could decrease malondialdehyde, serum carbonyl protein, and enhanced superoxide dismutase activity efficiently reduced serum oxidative stress (OS) and increased serum antioxidant activity in patients with β-thalassemia major (146,147). Quercus given as an adjuvant therapy to standard iron chelators may promote the OS measurements obtained in the patients which can be introduced as a liver protector (147). The roots of *Q. ilex* were macerated with methanol to achieve phenolic fractions which are able to show genoprotective and antioxidant effects (78). It is discovered that the amounts of flavonoids were higher in oaks compare to beech trees, and although, beech extract has shown higher antioxidant activity compare to oak extract, but the antioxidant activity of acetone extract of the oak bar was considerable (148). Sheikhi *et al*. (149) found that the extracts of oak tree an important natural antioxidant and antibacterial inhibitors include good potentials to incorporate into films of packaging to extend food shelf-life, and addition of oak tree extracts enhanced redness, and reduced yellowness and lightness parameters. It is reported that high dose and low dose of *Quercus brantii* extract can be used to protect the male reproductive system of mice against Pb-induced oxidative stress (150). Paray *et al*. (151) reported that oak leaf extract has bacterial and *in vitro* antioxidants activities, stimulates immune responses and plasma antioxidant in common carp, and partially mitigates stress responses in common carp.

It is reported that oak jaft (*Quercus Persica*) extract had shown high inhibitory effect on *Shigella flexneri* which is a species of Gram-negative bacteria in the genus *Shigella* that can cause diarrhea in humans (152,153). Kocazorbaz *et al*. (119) reported that antimicrobial activity of the aqueous leaf extract of kermes oak (*Quercus coccifera* L.) against different pathogens such as *Candida albicans*, *Listeria monocytogenes*, *Salmonella typhimurium*, *Salmonella enteritidis*, *Staphylococcus epidermidis*, *Enterococcus faecium*, *Staphylococcus aureus*, and *Escherichia coli*. In one experiment, it is reported that total flavonoid and phenolic contents of ethanolic extract of *Quercus branti* var. *persica* and *Quercus castaneifolia* var. *castaneifolia* as well as caffeic, gallic, and cholorogenic acids showed high bactericidal and inhibitory effects against *Escherichia coli*, *Bacillus cereus*, *Salmonella typhi*, and *Micrococcus luteus* (154,155). Bajalan *et al.* (97) reported that the extract of *Quercus persica* fruits showed antibacterial effects against *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli*, and *Klebsiella pneumonia*. Zarei *et al*. (156) also showed that the alcoholic extract of Iranian oak fruit had significant effects on gram negative bacteria such as *S. typhi*, *K. pneumoniae*, and *E. coli*, and gram-positive bacteria such as *S. cerevisiae*, and *S. aureus*. Sadeghian *et al*. (157) reported that *Q. brantii* have high antimicrobial activity against gastrointestinal bacterial pathogen, and in their research, the effect of ethanolic extract on *Escherichia coli* was significant, and according to the extract components by gas chromatography, phenolic and tannins components could be responsible for the antimicrobial activities. Tanase *et al*. (158) reported that the Northern red oak (*Quercus rubra* L.) has shown antimicrobial and antioxidant properties, as the antioxidant activity was assessed by two complementary methods namely ABTS and DPPH, and antimicrobial activity was evaluated against three *Candida* and five bacteria species, especially against *Staphylococcus aureus*, and *Candida parapsilopsis*, moreover, in their experiment its bark extracts were rich in tannins.

Application of oak fruit husk can improve the patients, symptoms by shortening the duration of the complete healing process, relieving pain, and decreasing size, which can be recommended as an important alternative treatment factor for recurrent aphthous stomatitis (91). Its bark has high importance as hemostatic, antiseptic, to cure gastropathies, and toothache, and also used as pacifying agents in inflammation and as healing agents in burn (159,160). Persian oak (*Quercus brantii* Lindl.) has been used for a long time in treatment of inflammatory and gastric ulcers by various tribes in south western Iran, and its hydro-alcoholic extract of Persian oak seed is effective in experimentally healing rat ulcers, and its tannins extracted have shown disinfectant and contractive effects (161).

The tannin extracted from *Q. brantii* have shown disinfectant and contractive effects, and the extracted found in seed hulls and seed have shown to have pharmacological activities such as anti bacterial (162,163), and wound-healing properties (164,165). Persian oak (*Querus brantii*) belongs to the Fagaceae family, and its applications showed high wound contraction, tensile strength, hydroxyproline, epithelialization period, and it can be suggested in wound healing ointment therapy (166). Kocazorbaz *et al.* (119) found that kermes oak (*Quercus coccifera* L.) which is an endemic plant in the Mediterranean Anatolian region such as Turkey was widely used for the treatment of different pathologies such as chronic diarrhea, hermorrhages, burns, and wounds, and its seed contain bitter tannins.

The mixture of Aleppo oak, alfalfa, ortie, and horsetail at 400 g/l concentration was effective in bleeding control, and on the basis of results the impact of mixed extract at the concentration of 400 g/l was more effective than that of 200 g/l, and according to the results, the plant extract of Aleppo oak has important influence on the bleeding control by local constriction of the bleeding site as well as influencing the blood coagulation system (167-170). In both traditional Asian and Indian medicine, Aleppo oak is important in all internal hemorrhages with other potential impacts like local anesthetic and antimicrobial activity (171-177).

Conclusion

The genus *Quercus* belongs to the family Fagaceae are widely used in traditional medicines, and they are mainly found in the basin Mediterranean such as France, Algeria, Spain, Portugal, Morocco, Tunisia, and Italy as well as Iran and North America. The Quercus species produces the acorn, a fruit, which, together with leaves and bark, has been used in folk medicine to treat different diseases. The polyphenols of oak can be used as natural antioxidants to counteract inflammatory diseases. The *Quercus* genus (oaks) comprises important plant resources which are used in different fields such as pharmaceuticals, foods, and cosmetics. Oaks fulfill various functions, contributing to charcoal and wood production, while also playing important roles in biodiversity preservation and soil conservation.

Key medicinal characteristics of oak are astringent properties, antioxidant and anti-inflammatory activities, antiseptic and antibacterial properties, and hemostatic activities. It is also beneficial in gastrointestinal health because it is used as a tea or decoction to stop diarrhea, important in oral health, and beneficial in external care as it is used in baths for hemorrhoids or to reduce inflammation. The fruit of oak trees of the genus Quercus is called acorns, which have been known to people for generations worldwide, and in ancient times, they were an important ingredient of folk medicine and culinary traditions. Acorns are known because of high mineral content, such as calcium, copper, zinc, and iron. They also contain triterpenes with anti-diabetic components, and monounsaturated fatty acids and sterols as well as phenolic components such as tocopherols with high antioxidant properties. It is clear that extracts of different parts of the oak revealed *in vivo* and *in vitro* bioactivities. More researches are needed to formulate oak-based functional foods, as well as more designed researches are needed as clinical trials to validate wound-healing, antimicrobial and antibacterial activities. Its different vegetal parts can be used as raw materials with different pharmacological benefits, however, more molecules, extraction activities and techniques should be tested, and more research is needed to study its usage in food science and to formulate oak based functional foods.

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Data Availability

No datasets were generated or analyzed during the current study.

Declarations

Author Contribution Declaration

Y.L.: writing-original draft, writing review and editing; M.Z.: writing review and editing; M.H.S.: writing review and editing; W.S.: writing review and editing. All authors have read and agreed to the published version of the manuscript. All authors contributed equally to this manuscript.

Ethical Approval

Not Applicable.

Consent to Participate

Not Applicable.

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Not Applicable.

Competing Interests

The authors declare no competing interests.

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