Food Applications of Berberis Plants

Subjects: Food Science & Technology

Contributor: Adedayo Ademiluyi

The genus Berberis includes about 500 different species and commonly grown in Europe, the United States, South Asia, and some northern areas of Iran and Pakistan. Leaves and fruits can be prepared as food flavorings, juices, and teas. Phytochemical analysis of these species has reported alkaloids, tannins, phenolic compounds and oleanolic acid, among others. Moreover, p-cymene, limonene and ocimene as major compounds in essential oils were found by gas chromatography. Berberis is an important group of the plants having enormous potential in the food and pharmaceutical industry, since they possess several properties, including antioxidant, antimicrobial, anticancer activities.

Keywords: Berberis ; food preservative ; alkaloid ; antioxidant ; human health

1. Introduction

Berberis species. are shrubs in the family *Berberidaceae*, native to central and southern Europe, western Asia, as well as northwest Africa [1]. About 500 species of these plants are found in most areas of central and southern Europe, the north-eastern region of United States, and Asia (including the northern area of Pakistan [2] and Iran [3]). The genus *Berberis* consists of spiny deciduous evergreen shrubs which are characterized by yellow wood and flowers [2], dimorphic long and short shoots (1–2 mm). Some *Berberis* fruits are small oblong berries 7–10 mm long and 3–5 mm broad and turn blue or red upon ripening during the late summer or autumn [1].

Berberis spp. are mainly consumed fresh, dried or used in juice production [4]. The fruits are very popular, known as *zereshk* in Iran where they are commonly used for cooking and in jam production, thus, encouraging the production of fresh edible seedless barberries fruits reaching about 22,000 tons per annum [5]. The fruits are also processed into beverages, drinks, syrups, candy and other confectionary products which are popular Iran. Furthermore, the leaves and fruits have also found applications in the production of food flavorings and teas. *Berberis* are popular due to their nutritional importance; however, they have found most usefulness in folk and traditional medicine where various parts, including roots, bark, leaves and fruits serve as major ingredients of herbal remedies in Ayurvedic, Iranian and Chinese medicine dating back at least 3000 years [6]. Currently, this species flower is popularly used amongst Tibetan speaking population in areas, such as Litang, China [7].

The effect of cold-pressed filtered oil of *Berberis* spp. seeds in delaying soybean oil oxidation in comparison to commercial antioxidants were carried out, and the study reported that *Berberis* oil contributed to oxidative stability of soybean oil comparably to commercial antioxidants [8]. Antioxidant and antibacterial activity of water extract of barberry has suggested their possible application as preservatives in food industries [9].

Isoquinoline alkaloids are the major bioactive constituents in *Berberis* [10]. Protoberberines and bisbenzyl-isoquinoline alkaloids, such as berbamine, tetrandrine and chondocurine, which have been known for their anti-inflammatory and immunosuppressive properties, have been detected by phytochemical analysis of the root and stem back extracts of *B. vulgaris*. Berberine (an isoquinoline alkaloid) and berbamine are the most abundant phytochemicals of *Berberis* species [2]. The fruits contain a high amount of alkaloids, tannins, phenolic compounds and oleanolic acid [3][11], gum, pectin, oleoresins, organic acids, anthocyanins and carotenoids. In addition, palmitine [10], stigmasterol and its glycoside [12] have all been detected in various species of the *Berberis* plant.

Some *Berberis* fruits have been employed in the treatment of guts [13] kidney stones [14] and liver [15] and gall bladder [10] conditions. The root bark and stem of the *Berberis* have found usage as a diuretic, febrifuge, cathartic and antiseptic. Furthermore, preparations of the stem and root bark have been used to treat mouth and stomach ulcers [16]. Several parts of the plant have been reported to possess astringent and antiseptic properties, while the stem bark and flowers were found to be anti-rheumatic [17]. The alkaloid rich root bark of the plant has also been used as purgative and treatment for both diarrhea and rheumatism [18]. The berberine-rich rhizomes of *Berberis* species possess marked antibacterial and

antitumor properties, with reported efficacies in treatment of various eye conditions [10][19]. Furthermore, the anti-inflammatory activity of berberine has been extensively studied amongst other pharmacological actions [10][20].

Berberine sulphate which is an alkaloid extracted from the roots and bark of various *Berberis* spp. Have been reported to possess antibacterial, antifungal and antiprotozoal activities. Reported the bacteriostatic activity of berberine against streptococci, and that the sub-minimum inhibitory concentrations (MICs) of the compound blocked the adherence of streptococci to host cells, immobilized fibronectin, and hexadecane in epithelial cells [21]. Furthermore, blood glucose and lipid regulatory properties of *Berberis* have been demonstrated [3][22][23][24]; and this was due to berberine-induced improvement in insulin sensitivity through regulation of adipokine secretion [25][26][27]. Effectiveness of *Berberis* species in the maintenance of heart health has been demonstrated in their ability to improve hypertension, ischemic heart disease, cardiac arrhythmias and cardiomyopathy [2][28].

The health-promoting effect of *Berberis* spp. cannot be overemphasized, as well as its popularity; however, this is restricted to central and southern Europe, western Asia, as well as northwest Africa. Hence, efforts should be geared towards making the *Berberis* plant also available to other regions of the world. Furthermore, most studies on *Berberis* spp. have been on berberine; therefore, efforts should be made towards researching possible therapeutic benefits of all other important phytoconstituents of the plant. Furthermore, the synergistic or additive effect of these phytoconstituents should be studied so as to elucidate the complex molecular interaction amongst various phytochemicals leading to the observed therapeutic properties. In addition, the modulatory effect of the plant/plant materials on gene expression should be prioritized.

2. *Berberis* Plants Essential Oils and Phytochemical Composition

Essential oils (EO) are volatile, complex natural compounds, which formed in aromatic plants as secondary metabolites. They are used in pharmaceutical, agricultural, and food industries, as well as are associated with antibacterial, anti-inflammatory, antioxidant, and insecticidal potential [29][30][31].

The gas chromatography coupled to mass spectrometry (GC-MS) analysis of various parts of *B. vulgaris* revealed that benzaldehyde, benzyl alcohol, 1-hexanol and I-2-hexenal [32] were major compounds of the EOs from fruit, while *p*-cymene, limonene and ocimene were identified as major compounds of the EOs (Figure 1) from leaves and flowers [33].

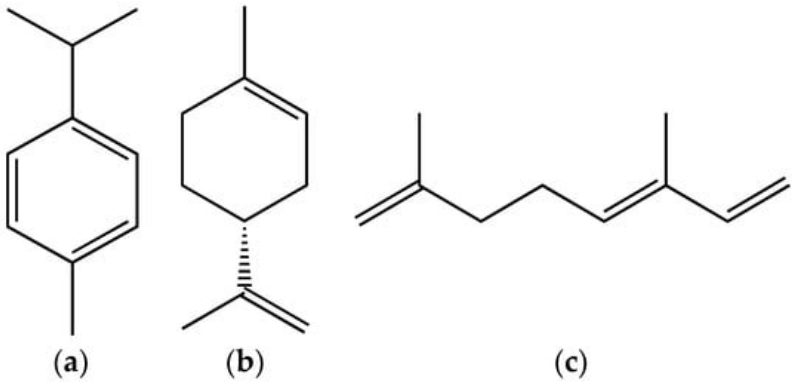


Figure 1. Major compounds of the essential oils (EOs) of *Berberis vulgaris* leaves and flowers. (**a**) *p*-cymene; (**b**) limonene; (**c**) ocimene.

Turkish *B. crataegina* fruit berry has 22 volatile compounds which are aldehydes had the highest concentration (5382 µg/kg), followed by alcohols (2487 µg/kg) and lactone (2422 µg/kg).

Major volatile compounds of the *B. crataegina* fruit are *y*-butyrolactone, 3-hexanal and 2,6-dimethylphenol. Moreover, the olfactometric analysis of dry *B. crataegina* resulted eight aroma active compounds [34].

EOs of the roots of *B. integerrima* were analyzed by using modified microwave-assisted hydrodistillation (MAHD). Chemical diversity of 10 and 18 compounds were obtained from MAHD, MAHD with modified anyl, and with modified phenyl magnetic nanoparticles, the yields of the EOs were 0.16, 0.61 and 0.71 *w/w* %, respectively. Hexadecanoic acid was identified as a major compound for MAHD and modified MAHD methods [35].

Moreover, the GC/MS study on hexane extracts of the *B. aetnensis* and *B. libanotica* roots was showed that *B. aetnensis* have twenty-six and *B. libanotica* have thirty-seven non-polar compounds. Stigmasterol (Figure 2) is the major compound

of both species [36].

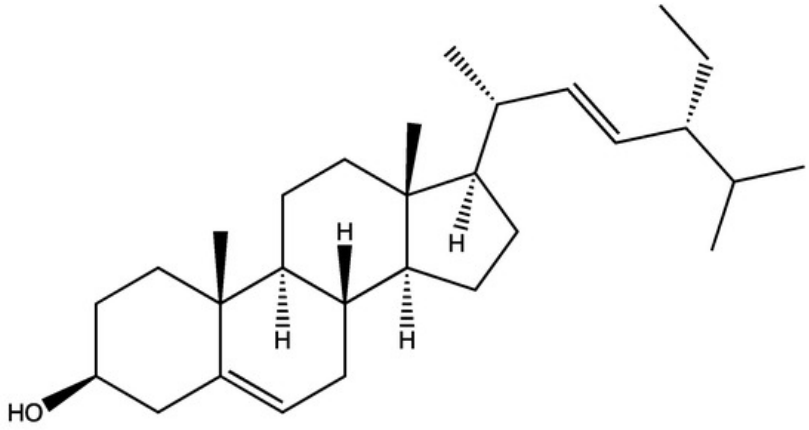
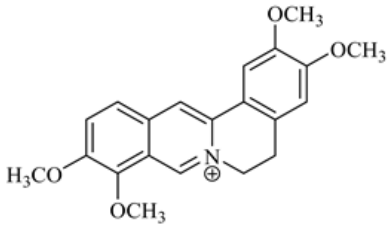
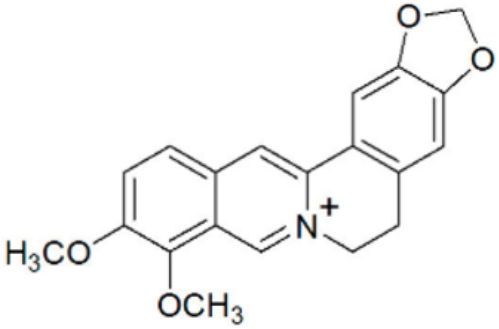
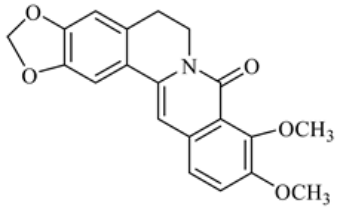
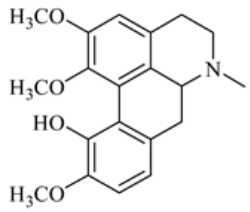
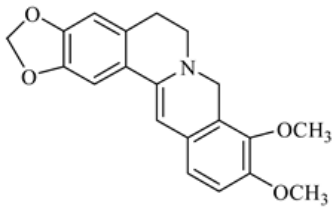
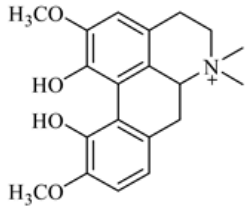
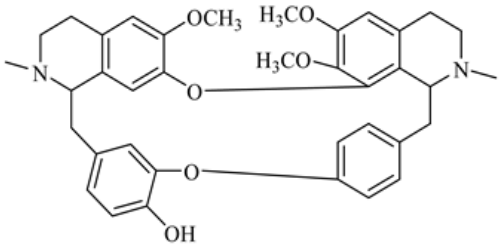
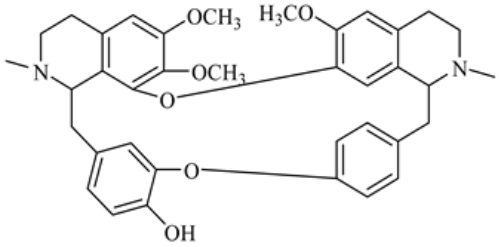
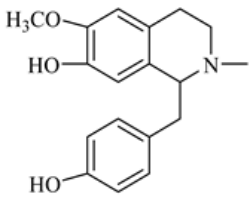
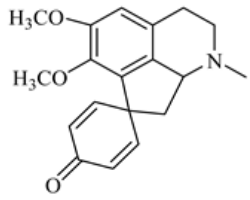


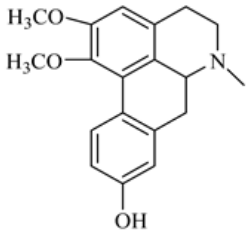
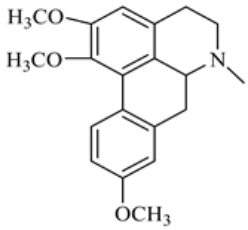
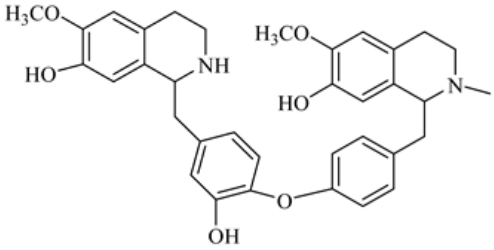
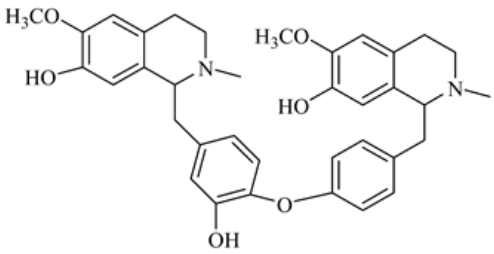
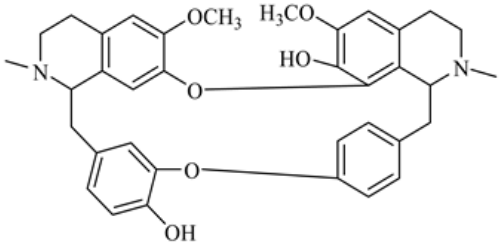
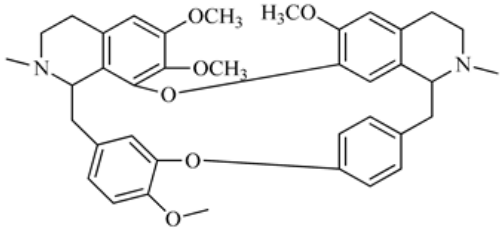
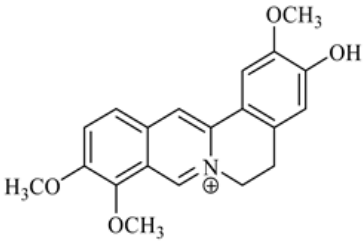
Figure 2. Stigmasterol.

On the other hand, alkaloids (Table 1) represent the main compounds in *Berberis* species, and many of them have been identified by different spectroscopic techniques previously mentioned. The most known are berberine, berbamine, palmitine, jatrorrhizine, and isotetrandrine. They are located mainly in the cortical tissues of the roots and stems and have important biological activities. In fact, in vitro and in vivo anti-proliferative and anti-metastatic effects on various types of cancers have been reported for different alkaloids. These compounds, such as vinblastine, have already used as anticancer drugs [3].

Table 1. Alkaloids from *Berberis* species.

Chemical structure	Name	Plant
	palmatine	*B. vulgaris*
	berberine	*B. vulgaris*
	oxyberberine	*B. vulgaris*

Chemical structure	Name	Plant
	isocoridine	*B. vulgaris*
	lambertine	*B. vulgaris*
	magniflorine	*B. vulgaris*
	oxycanthine	*B. vulgaris*
	berbamine	*B. aristata*
	(+)-N-methylcoclaurine	*B. montana*
	(−)-pronuciferine	*B. montana*

Chemical structure	Name	Plant
	(+)-9-hydroxynuciferine	*B. montana*
	(+)-orientine	*B. montana*
	2-norberbamunine	*B. stoloniferais*
	berbamunine	*B. stoloniferais*
	aromoline	*B. stoloniferais*
	isotetrandrine	*B. stoloniferais*
	jatrorrhizine	*B. umbellate*

3. Food Preservative Applications of *Berberis* Plants

Food preservation is the most vital issue in food industries to ensure food safety for a longer period. Basically, the process of food preservation depends on the growth inhibition of undesirable microorganisms. Use of chemical agents with antimicrobial activity is commonly used a traditional method for food preservation [37]. However, antimicrobial agents also gain momentum, due to their fewer side effects and compatibility with the human body. Further, synthetic antimicrobials and their toxicological safety as food additives needed to be ensured by regulatory authorities. Moreover, processed foods with natural preservatives have great demand and considered safer and beneficial for public health [38]. The naturally occurring compounds demonstrated antimicrobial activity in foods as natural ingredients and can be used as additives to other foods.

Berberis is an important plants having enormous potential in the food industry. However, only a few reports are available on the direct application of these plants in food products. For example, seed oil and fruit extracts of *B. crataegina* were supplementing into chitosan matrix for preparation of a chitosan-based edible film. The films produced have been analyzed for the physiochemical and biological activities. Results showed that chitosan-fruit extract film exhibited higher thermal stability, antimicrobial, antioxidant, and anti-quorum sensing activity as compared to other films. Furthermore, the addition of *B. crataegina* seed oil and fruit extract into the chitosan film create a mark reduction in the UV-vis transmittance but improve the tensile strength. Likewise, hydrophobicity of the chitosan-seed oil film was found to be higher than chitosan-control film, while chitosan-fruit extract film displayed slightly lower hydrophobicity than chitosan film. These results indicated that chitosan-fruit extract film of *B. crataegina* fruit extract could be used as an effective ingredient for the production of the edible film with increased physicochemical and biological properties [39].

A list of the antimicrobial potential of the *Berberis* species evaluated across the globe is provided which support the use of *Berberis* species in food preservation (Table 2).

Table 2. A list of the antimicrobial potential of the *Berberis* species evaluated across the globe is provided which support the use of *Berberis* species in food preservation.

S. No.	Species	Part	Country	Extract/Model/Compound	Tested Micro-Organism	Results	Reference
1	*B. aristata*	Stem and leaves	Nepal	Hexane, Ethyl acetate, Methanol	*Staphylococcus aureus*, *Kleibsella pneumoniae*, *Salmonella typhimurium*	Against *S. aureus*: methanol significant zone of inhibition (21 mm), ethyl acetate extracts moderate activity, hexane extract of stem slightly active.	[40]

S. No.	Species	Part	Country	Extract/Model/Compound	Tested Micro-Organism	Results	Reference
2	*B. aristata,* and *B. ligulata*	Bark stem Leaves	Nepal	Ethanol	*Bacillus subtilis*, *Escherichia coli*, *Pseudomona aeruginosa*, *Salmonella. typhi*, *Salmonella dyjenteriae*, *Salmonella cholerae*	Ethanol extract of *B. aristata:* largest zone of inhibition (21 mm) against *B. subtilis* and the smallest MBC value (90 mg/mL) for *S. aureus.* Gram positive bacteria more susceptible to the ethanol extract. *B. aristata* relatively broad-spectrum antibacterial activity.	[41]
3	B. vulgaris	Stem	Iran	Ethanol	*P. aeruginosa*, *Acinetobacter baumannii*, *E. coli* and *Salmonella enteritidis*	MIC determination: stem extracts inhibit the growth of all the studied bacteria (3900 to 37,500 µg/mL) by synergistic effects with ciprofloxacin.	[42]
4	*B. asiatica*	Leaves	Uttarakhand, India	Methanol	*E. coli, Enterobacter aerogenes, Proteus vulgaris, P. aeruginosa, K. pneumoniae, B. subtilis, S. aureus*	Methanol extracts of leaves: high inhibitory potential on *S. aureus, K. pneumoniae, E. coli, B. subtilis* and *P. vulgaris* in all concentration.	[43]
5	*B. aristata, B. asiatica, B. lycium*	Stem	Bangalore, India	Methanol	*Nocardia sp.*, *S. aureus*, *S. pneumonia*, *P. aeruginosa*, *Streptococcus viridians*, *E. coli*	Sensitivity to *Nocardia* sp., *S. pneumonia* and *E. coli*.	[44]

S. No.	Species	Part	Country	Extract/Model/Compound	Tested Micro-Organism	Results	Reference
6	*B. glaucocarpa*	Root wood	Pakistan	Ethanol	SMRSA, EMRSA, *Mycobacterium marinum*, *E. coli*, *Trypanosoma brucei*	Berberine (MIC = 12.5 and 25 µg/mL), berberine chloroform (MIC = 25 and 12.5 µg/mL) and syringaresinol (12.5 µg/mL): very active against SMRSA, *M. marinum* and *T. brucei.*	[45]
7	*B. vulgaris*	Stem bark	Romania	Ethanol	*Botrytis cinerea*	*B*. *vulgaris* bark extract, berberine, and fluconazole significantly inhibited growth of *B. cinerea.*	[46]
8	*B. vulgaris*			Ethanol	*S. aureus*, *Staphylococcus epidermidis*, *K. pneumoniae*, *B. subtilis*, *E. coli*, *Aspergillus niger*, *Trichoderma*, *Alternaria solanai*	20 mm zone of inhibition against *E. coli.* Good activity against *B. Subtilis,* moderate against *Trichoderma,* insignificant against other stains.	[47]
9	*B. vulgaris* and its active constituent, berberine	Root	Egypt	Ethanolic extract	*Candida albicans*, *E. coli*	*Berberis* ethanolic extract and berberine standard can inhibit *C. albicans* and *E. coli* growth.	[48]
10	*B. vulgaris*	Fruit	Pakistan	Distilled water	*S. aureus*, *Proteus*, *S. typhi, Salmonella paratyphi A*, *Salmonella paratyphi B, K. pneumoniae*, *E. coli*, *P. aeruginosa*	Antibacterial activity against all tested pathogens.	[49]

S. No.	Species	Part	Country	Extract/Model/Compound	Tested Micro-Organism	Results	Reference
11	*B. thunbergii*	Fruit	Hungary	Juice; water extract and - methanol extract	*B. subtilis*, *Bacillus cereus* var. *mycoides*, *E. coli, Serratia marcescens*	Juice, water extract and methanol extract showed activity against all bacteria.	[50]
12	*B. calliobotrys*	Stems and branches	Pakistan	Methanol	*B. subtilis*, *P. aeruginosa*, *S. aureus* fungal strains namely *C. albicans*, *Penicillium notatum*	The methanol extract, ethyl acetate and n-butanol fractions: maximum zone of inhibition against all bacterial strains especially *S. aureus* and antifungal effects.	[51]
13	*B. lycium*	Roots	Libya	Distilled water, ethanol, isopropanol and methanol	*Pseudomonas* sp., *E. coli*, *Streptococcus* sp., *Staphylococcus* sp.	Methanolic displayed maximum inhibitory zone (16 mm), isopropanol extract (13 mm) and ethanol extract (12 mm). The aqueous extract exhibited the least inhibitory zone (10 mm). The methanolic extract: maximum inhibitory zone (12 mm), *Pseudomonas* (11 mm) and *Staphylococcus* (10 mm).	[52]

S. No.	Species	Part	Country	Extract/Model/Compound	Tested Micro-Organism	Results	Reference
14	*B. hispanica*	Root Bark	Marocco	Ethanolic extract	*Mycobactérium smegmatis, Mycobacterium aurum*	The ethanolic extract from root bark displayed an important antimycobacterial activity. The inhibition zones for *M. aurum A+* were significantly larger than those for *M. smegmatis* MC2.	[53]
15	*B. ruscifolia*	-	Argentina	Acetone, chloroform-methanol (1:1) and methanol	*E. coli*, *P. aeruginosa*, *Listeria monocytogenes*, *S. aureus*	All extracts exhibited antibacterial activity with MIC varying from 16 to 2 mg/mL. The highest inhibition with acetonic and chloroform-methanolic extracts of species against *S. aureus* (MIC = 2 mg/mL). Methanolic extracts *B. ruscifolia* showed no antibacterial activity against all tested bacteria.	[54]
16	*B. aristata*	Stem bark	India	Ethanol and aqueous extracts	*Shigella flexneri*, *Shigella sonnei*, *Shigella dysenteriae*, *Shigella boydii*	Extracts of *B. aristata*: antibacterial activity against four strains of *Shigella* (8 and 23 mm).	[55]

S. No.	Species	Part	Country	Extract/Model/Compound	Tested Micro-Organism	Results	Reference
17	*B. aristata, B. asiatica, B. chitria* and *B. lycium*	Root and stem	India	Ethanol	*Micrococcus luteus*, *B. subtilis*, *B. cereus*, *Enterobacter aerogenus*, *E. coli*, *K. pneumoniae*, *Proteus mirabilis*, *P. aeruginosa*, *S. aureus, S. typhimurium*, *Streptococcus pneumonia*, Fungal strains *Aspergillus nidulans*, *C. albicans*, *Aspergillus terreus*, *Trichophyton rubrum, Cistus albidus*, *Aspergillus flavus*, *A. niger*	*B. lycium*, *B. aristata* and *B. asiatica* root extract showed significant antifungal activity against *A. terreus* and *A. flavus*. *B. aristata* root and *B. lycium* (stem) extracts gave very low MIC values (0.31 µg/mL) as compared to other tested species.	[56]
18	*B. Lycium*	Root	Pakistan	Ethanol, petroleum ether	*S. aureus*, *S. epidermidis*, *B. subtilis*, *S. typhi, E. coli, C. albicans*	The ethanolic and aqueous crud root extract: most effective antifungal and antibacterial agents.	[57]
19	*B. integerrima* Syn: *B. densiflora*	Roots	Iran	Methanol	*Brucella abortus*	MIC and MBC results, jatrorhizine exhibited higher antibacterial activity with MIC (0.78 µg/mL) and MBC (1.56 µg/mL) compared with the standard (streptomycin, 10 µg/mL).	[58]

S. No.	Species	Part	Country	Extract/Model/Compound	Tested Micro-Organism	Results	Reference
20	*B. lycium*	Roots	Pakistan	Hydric extract	*E. coli*, *Pseudomonas*, *Staphylococcus*, *Proteus*	Significant activity against *E. coli* and Proteus (80 to 100%), while it demonstrated a good activity against *Pseudomonas* and *Staphylococcus* (60 to 70%).	[59]
21	*B. aristata*	Bark and leaves	India	Methanol, ethanol and hexane	*B. subtilis, Agrobacterium tumefaciens*, *E. coli*, *Xanthomonas. Phaseoli, Erwinia chrysanthemi*	All the extracts of tested plants showed variable activity against all the tested bacterial strains. Methanol extract revealed highest antibacterial activity (11 mm) recorded against *E. chrysanthemi*. Hexane extract: totally inactive against all the tested strains.	[60]
22	*B. aristata*	Roots	India	Aqueous and alcohol extracts	*S. aureus*, *B. subtilis*, *E. coli, S. typhimurium*	Alcoholic and aqueous extract showed antimicrobial activity against four tested bacteria. *B. aristata* exhibited highest zone of inhibition for *B. subtilis* followed by *S. aureus*, *E. coli* and *S. typhimurium.*	[61]

S. No.	Species	Part	Country	Extract/Model/Compound	Tested Micro-Organism	Results	Reference
23	*B. microphylla*	Leaves, stems and roots	Chile	Methanol	*E. coli*, *S. typhimurium*, *L. monocytogenes*, *E. aerogenes*, *S. aureus, B. cereus*, *S. epidermidis* and *B. subtilis*	All extract possesses significant antibacterial activity against Gram-positive bacteria but not against Gram-negative bacteria.	[62]
24	*B. lycium*	Root bark	Pakistan		*E. coli*, *K. pneumoniae*, *P. aeruginosa*, *S. aureus*, *B. subtilis*	Silver nanoparticles were very active against Gram-negative and Gram-positive bacteria Aqueous bark extract (10 µg/mL) possess highest activity against *E. coli* and *P. aeruginosa.*	[63]
25	*B. vulgaris*	Fruit	Iran		*L. monocytogenes*	Average diagonal of growing area in disk diffusion test for species: 12 mm and MIC was 125 µg/mL and MBC of *B. vulgaris* was 500 µg/mL.	[64]
26	*B. aristata*	Stem bark	Alcohol	In vivo in an animal model using Sprague Dawley rats	Carbapenem-resistant *E. coli*	An aquo-alcoholic extract of the species: effectively manage peritonitis induced by Carbapenem-resistant *E. coli* in a rat model at a single post-exposure prophylactic dose of 0.5 mg/kg body weight.	[65]

S. No.	Species	Part	Country	Extract/Model/Compound	Tested Micro-Organism	Results	Reference
27	*B. aristata*	Roots	India	Aqueous and alcoholic extract of fresh roots, as well as aqueous extract of dried roots	*S. aureus*, *S. epidermidis*, *Streptococcus pyogenes*, *Streptococcus viridans*, *Enterococcus faecalis*, *B. subtilis*, *B. cereus*, *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *P. vulgaris*, *P. mirabilis*, *S. typhi*, *S. paratyphi A*, *S. typhimurium*, *S. dysenteriae* type 1, *Vibrio cholerae*	All three extracts displayed wide antibacterial activity against Gram-positive bacteria. Among the Gram-negative bacteria tested, the antibacterial activity was limited to *E. coli*, *S. typhimurium, S. dysenteriae* type 1 and *V. cholerae*. All extracts also possess antifungal activity against the fungal species tested, except *Candida krusei*.	[66]
28	*B. aristata*	Root Stem Leaf	Pakistan		*E. coli*, *S. typhi*, *S. aureus*, *Shigella, Citrobacter*, *P. vulgaris*,*Enterobacter, Streptococcus pyrogenes*, *V. cholera, Klebsiella* spp., *A. niger*, *Cladosporium*, *Rhizoctonia*, *Alternaria*, *Trichoderma*, *Penicillium*, *Curvularia*, *Paecilomyces* and *Rhizopus*	The extracts significantly inhibited the growth of the studied microbes, except *A. niger*, *Curvularia*, *Paecilomyces* and *Rhizopus*.	[67]

S. No.	Species	Part	Country	Extract/Model/Compound	Tested Micro-Organism	Results	Reference
						All the strains of *V. cholerae* are susceptible. All the *Salmonella* sp., *Pseudomonas* sp., and some of the E. *coli* strains are highly resistant, except some strains of *E. coli* as AL26, and *Shigella* sp. are susceptible. All *Xanthomonas* sp. were highly susceptible.	
29	*B. aristata*		India	Berberine sulfate	*V. cholerae*, *S. aureus*	showed antifungal action against *C. albicans*, *Candida tropicalis*, *Trichophyton mentagrophytes*, *Microsporum gypseum*, *Cryptococcus neoformans* and *Sporothrix schenckii*. *Mycobacterium tuberculosis* var. *hominis* $H_{37}RV$ and *Entamoeba histolytica*.	[68]

References

1. Minaiyan, M.; Ghannadi, A.; Mahzouni, P.; Jaffari-Shirazi, E. Comparative study of berberis vulgaris fruit extract and berberine chloride effects on acetic acid-induced colitis in rats. Iran. J. Pharm. Res. 2011, 10, 97–104.
2. Mokhber-Dezfuli, N.; Saeidnia, S.; Gohari, A.; Kurepaz-Mahmoodabadi, M. Phytochemistry and Pharmacology of Berberis Species. Pharmacogn. Rev. 2014, 8, 8.
3. Rahimi-Madiseh, M.; Lorigoini, Z.; Zamani-Gharaghoshi, H.; Rafieian-Kopaei, M. Berberis vulgaris: Specifications and traditional uses. Iran. J. Basic Med. Sci. 2017, 20, 569–587.
4. Farhadi Chitgar, M.; Aalami, M.; Maghsoudlou, Y.; Milani, E. Comparative Study on the Effect of Heat Treatment and Sonication on the Quality of Barberry (Berberis Vulgaris) Juice. J. Food Process. Preserv. 2017, 41, e12956.
5. Aghbashlo, M.; Kianmehr, M.H.; Hassan-Beygi, S.R. Specific heat and thermal conductivity of berberis fruit (Berberis vulgaris). Am. J. Agric. Biol. Sci. 2008, 3, 330–336.
6. Birdsall, T.C.; Kelly, G.S. Berberine: Therapeutic potential of an alkaloid found in several medicinal plants. Altern. Med. Rev. 1997, 2, 94–103.
7. Kang, J.; Kang, Y.; Ji, X.; Guo, Q.; Jacques, G.; Pietras, M.; Łuczaj, N.; Li, D.; Łuczaj, Ł. Wild food plants and fungi used in the mycophilous Tibetan community of Zhagana (Tewo County, Gansu, China). J. Ethnobiol. Ethnomed. 2016, 12, 21.
8. Tavakoli, A.; Sahari, M.A.; Barzegar, M. Antioxidant activity of Berberis integerrima seed oil as a natural antioxidant on the oxidative stability of soybean oil. Int. J. Food Prop. 2018, 20, S2914–S2925.
9. Aliakbarlu, J.; Mohammadi, S.; Khalili, S. A Study on Antioxidant Potency and Antibacterial Activity of Water Extracts of Some Spices Widely Consumed in Iranian Diet. J. Food Biochem. 2013, 38, 159–166.
10. Srivastava, S.; Srivastava, M.; Misra, A.; Pandey, G.; Rawat, A. A review on biological and chemical diversity in Berberis (Berberidaceae). EXCLI J. 2015, 14, 247–267.
11. Kafi, M.; Balandary, A.; Rashed-Mohasel, M.H.; Koochaki, A.; Molafilabi, A. Berberis: Production and Processing; Zaban va adab Press: City, Iran, 2002; ISBN 9789290814993.
12. Saied, S.; Begum, S. Phytochemical studies of Berberis vulgaris. Chem. Nat. Compd. 2004, 40, 137–140.
13. Yazdani, A.; Poorbaghi, S.L.; Habibi, H.; Nazifi, S.; Rahmani Far, F.; Sepehrimanesh, M. Dietary Berberis vulgaris extract enhances intestinal mucosa morphology in the broiler chicken (Gallus gallus). Comp. Clin. Path. 2013, 22, 611–615.
14. Bashir, S.; Gilani, A.H.; Siddiqui, A.A.; Pervez, S.; Khan, S.R.; Sarfaraz, N.J.; Shah, A.J. Berberis vulgaris root bark extract prevents hyperoxaluria induced urolithiasis in rats. Phyther. Res. 2010, 24, 1250–1255.
15. Hermenean, A.; Popescu, C.; Ardelean, A.; Stan, M.; Hadaruga, N.; Mihali, C.V.; Costache, M.; Dinischiotu, A. Hepatoprotective effects of Berberis vulgaris L. extract/β cyclodextrin on carbon tetrachloride-induced acute toxicity in mice. Int. J. Mol. Sci. 2012, 13, 9014–9034.
16. Amjad, M.S.; Arshad, M.; Qureshi, R. Ethnobotanical inventory and folk uses of indigenous plants from Pir Nasoora National Park, Azad Jammu and Kashmir. Asian Pac. J. Trop. Biomed. 2015, 5, 234–241.
17. Altundag, E.; Ozturk, M. Ethnomedicinal studies on the plant resources of east Anatolia, Turkey. Procedia Soc. Behav. Sci. 2011, 19, 756–777.
18. Javadzadeh, S.; Fallah, S. Therapeutic application of different parts of Berberis vulgaris. Int. J. Agric. Crop Sci. 2012, 4, 404–408.
19. Phillips, R.; Foy, N. Herbs; Pan Books Ltd.: London, UK, 2002; ISBN 0-330-30725-8.

S. No.	Species	Part	Country	Extract/Model/Compound	Tested Micro-Organism	Results	Reference
30	*B. heterophylla*	Leaves, stems and roots by different berberine	Argentina	Berberine	*S. aureus*, *E. faecali*, *P. aeruginosa*, *E. coli*, *C. albicans*, *Candida glabrata*, *Candida tropicalis*, *Candida lusitaniae*, *C. krusei*, *Candida parapsilosis*	The aqueous extracts of *B. heterophylla* do not possess significant antimicrobial activity. Berberine displayed a significant antibacterial and antifungal activity against *S. aureus* and different *Candida* spp., some of them obtained from the clinical isolated.	[69]
31	*aquifolium*	Branches and leaves	Korea	Berberine	*Bacillus atrophaeus*, *Kocuria rhizophila*, *M. luteus*, *S. epidermidis*, *B. subtilis subsp. spizizenii*, *K. pneumoniae*, *Enterobacter cloacae*, *Salmonella enterica subsp.*	No significant activity against gram-negative bacteria.	[70]

20. Kuo, C.-L.; Chi, C.-W.; Liu, T.-Y. The anti-inflammatory potential of berberine in vitro and in vivo. Cancer Lett. 2004, 203, 127–137.
21. Sun, D.; Courtney, H.S.; Beachey, E.H. Berberine sulfate blocks adherence of Streptococcus pyogenes to epithelial cells, fibronectin, and hexadecane. Antimicrob. Agents Chemother. 1988, 32, 1370–1374.
22. Hajzadeh, M.A.R.; Rajaei, Z.; Shafiee, S.; Alavinejhad, A.; Samarghandian, S.; Ahmadi, M. Effect of barberry fruit (Berberis Vulgaris) on serum glucose and lipids in streptozotocin-diabetic rats. Pharmacologyonline 2011, 1, 809–817.
23. Meliani, N.; Dib, M.E.A.; Allali, H.; Tabti, B. Hypoglycaemic effect of Berberis vulgaris L. in normal and streptozotocin-induced diabetic rats. Asian Pac. J. Trop. Biomed. 2011, 1, 468–471.
24. Zhou, X.; Chan, S.W.; Tseng, H.L.; Deng, Y.; Hoi, P.M.; Choi, P.S.; Or, P.M.Y.; Yang, J.M.; Lam, F.F.Y.; Lee, S.M.Y.; et al. Danshensu is the major marker for the antioxidant and vasorelaxation effects of Danshen (Salvia miltiorrhiza) water-extracts produced by different heat water-extractions. Phytomedicine 2012, 19, 1263–1269.
25. Zhu, X.; Bian, H.; Gao, X. The Potential Mechanisms of Berberine in the Treatment of Nonalcoholic Fatty Liver Disease. Molecules 2016, 21, 1336.
26. Yang, J.; Yin, J.; Gao, H.; Xu, L.; Wang, Y.; Xu, L.; Li, M. Berberine Improves Insulin Sensitivity by Inhibiting Fat Store and Adjusting Adipokines Profile in Human Preadipocytes and Metabolic Syndrome Patients. Evid.-Based Complement. Altern. Med. 2012, 2012, 363845.
27. Zhang, Y.; Ye, J. Mitochondrial inhibitor as a new class of insulin sensitizer. Acta Pharm. Sin. B 2012, 2, 341–349.
28. Imenshahidi, M.; Hosseinzadeh, H. Berberis Vulgaris and Berberine: An Update Review. Phyther. Res. 2016, 30, 1745–1764.
29. Imanshahidi, M.; Hosseinzadeh, H. Pharmacological and therapeutic effects of Berberis vulgaris and its active constituent, berberine. Phyther. Res. 2008, 22, 999–1012.
30. Alemardan, A.; Asadi, W.; Rezaei, M.; Tabrizi, L.; Mohammadi, S. Cultivation of Iranian seedless barberry (Berberis integerrima 'Bidaneh'): A medicinal shrub. Ind. Crops Prod. 2013, 50, 276–287.
31. Potdar, D.; Hirwani, R.R.; Dhulap, S. Phyto-chemical and pharmacological applications of Berberis aristata. Fitoterapia 2012, 83, 817–830.
32. Dolezal, M.; Velisek, J.; Famfulikova, P. Chemical composition of less-known wild fruits. In Proceedings of the EUROFOODCHEM XI Meeting, Norwich, UK, 26–28 September 2001; Volume 269, pp. 241–244.
33. Hamedi, A.; Moheimani, S.M.; Sakhteman, A.; Etemadfard, H.; Moein, M. An Overview on Indications and Chemical Composition of Aromatic Waters (Hydrosols) as Functional Beverages in Persian Nutrition Culture and Folk Medicine for Hyperlipidemia and Cardiovascular Conditions. J. Evid.-Based Complement. Altern. Med. 2017, 22, 544–561.
34. Sonmezdag, A.S.; Kelebek, H.; Selli, S. Volatile and key odourant compounds of Turkish Berberis crataegina fruit using GC-MS-Olfactometry. Nat. Prod. Res. 2018, 32, 777–781.
35. Hashemi-Moghaddam, H.; Mohammadhosseini, M.; Azizi, Z. Impact of amine- and phenyl-functionalized magnetic nanoparticles impacts on microwave-assisted extraction of essential oils from root of Berberis integerrima Bunge. J. Appl. Res. Med. Aromat. Plants 2018, 10, 1–8.
36. Bonesi, M.; Loizzo, M.R.; Conforti, F.; Passalacqua, N.G.; Saab, A.; Menichini, F.; Tundis, R. Berberis aetnensis and B. libanotica: A comparative study on the chemical composition, inhibitory effect on key enzymes linked to Alzheimer's disease and antioxidant activity. J. Pharm. Pharmacol. 2013, 65, 1726–1735.
37. Jay, J. Modern Food Microbiology; Aspen Publishers Inc.: Gaithersburg, MD, USA, 1998; ISBN 978-0-387-23180-8.
38. Pszczola, D.E. Emerging ingredients: Believe it or not! Food Technol. 1999, 53, 98–100.
39. Kaya, M.; Ravikumar, P.; Ilk, S.; Mujtaba, M.; Akyuz, L.; Labidi, J.; Salaberria, A.M.; Cakmak, Y.S.; Erkul, S.K. Production and characterization of chitosan based edible films from Berberis crataegina's fruit extract and seed oil. Innov. Food Sci. Emerg. Technol. 2018, 45, 287–297.
40. Thusa, R.; Mulmi, S. Analysis of Phytoconstituents and Biological Activities of Different Parts of Mahonia nepalensis and Berberis aristata. Nepal J. Biotechnol. 2017, 5, 5–13.
41. Pokhrel, N.R.; Adhikari, R.P.; Baral, M.P. In Vitro screening and evaluation of antimicrobial activities of some medicinal plants of Nepal. Nepal J. Sci. Technol. 2003, 5, 1.
42. Ebrahimi, A.; Chavoushpour, M.; Mahzoonieh, M.R.; Lotfalian, S. Antibacterial activity and ciprofloxacin-potentiation property of Berberis vulgaris asperma stem extracts on pathogenic bacteria. J. HerbMed Pharmacol. 2016, 5, 112–115.
43. Singh, S.K.; Vishnoi, R.; Dhingra, G.K.; Kishor, K. Antibacterial activity of leaf extracts of some selected traditional medicinal plants of Uttarakhand, North East India. J. Appl. Nat. Sci. 2012, 4, 47–50.

44. Saravanakumar, T.; Manonmani, E.; Venkatasubramanian, P.; Vasanthi, N.S. Antimicrobial potential of Daruharidra (Berberis aristata DC) against the pathogens causing eye infection. Int. J. Green Pharm. 2014, 8, 153.

45. Alamzeb, M. Bioassay guided isolation and characterization of anti-microbial and anti-trypanosomal agents from Berberis glaucocarpa Stapf. African J. Pharm. Pharmacol. 2013, 7, 2564–2570.

46. Parvu, M.; Parvu, A.E.; Craciun, C.; Barbu-Tudoran, L.; Vlase, L.; Tamas, M.; Rosca-Casian, O.; PersecA, O.; Molnar, A.M. Changes in Botrytis cinerea conidia caused by Berberis vulgaris extract. Not. Bot. Horti Agrobot. Cluj-Napoca 2010, 38, 15–20.

47. Shah, Z.; Ilyas, M.; Khan, M.; Ahmad, A.; Khan, M.; Khan, N. Antimicrobial activities of selected medicinal plants collected from Northern districts of Khyber Pakhtunkhwa, Pakistan. J. Pharm. Res. 2012, 5, 1732–1738.

48. Ghareeb, D.A.; El-Wahab, A.E.A. Biological assessment of Berberis vulgaris and its active constituent, berberine: Antibacterial, antifungal and anti-hepatitis C virus (HCV) effect. J. Med. Plants Res. 2013, 7, 1529–1536.

49. Shahid, T.; Memon, M.; Malik, R.A.; Ikram, N.; Malik, W.; Ali, A. A study of Antimicrobial Activity of Berberis vulgaris (Zirishk) Aqueous Plant Extract using Pathogenic Isolates from Patients of Islamabad and Rawalpindi. Imp. J. Interdiscip. Res. 2017, 3, 1365–1371.

50. Krisch, J.; Galgóczy, L.; Tölgyesì, M.; Papp, T.; Vágvölgyi, C. Effect of fruit juices and pomace extracts on the growth of Gram-positive and Gram-negative bacteria. Acta Biol. Szeged. 2008, 52, 267–270.

51. Rasool, S.; Khan, F.Z.; Hassan, S.U.; Ahmed, M.; Ahmed, M.; Tareen, R.B. Anticonvulsant, antimicrobial and cytotoxic activities of berberis calliobotrys aitch ex koehne (Berberidaceae). Trop. J. Pharm. Res. 2015, 14, 2031–2039.

52. Irshad, A.H.; Pervaiz, A.H.; Abrar, Y.B.; Fahelboum, I.; Awen, B.Z.S. Antibacterial activity of Berberis lycium root extract. Trakia J. Sci. 2013, 11, 88–90.

53. Haouat, A.C.; Haggoud, A.; David, S.; Ibnsouda, S.; Iraqui, M. In vitro evaluation of the antimycobacterial activity and fractionation of Berberis hispanica root bark. J. Pure Appl. Microbiol. 2014, 8, 917–925.

54. Mattana, C.M.; Satorres, S.E.; Juan, V.; Cifuente, D.; Tonn, C.; Laciar, A.L. Antibacterial activity study of single and combined extracts of Berberis ruscifolia, Baccharis sagittalis, Euphorbia dentata and Euphorbia schikendanzii, native plants from Argentina. BLACPMA 2012, 11, 428–434.

55. Joshi, P.V.; Shirkhedkar, A.A.; Prakash, K.; Maheshwari, V.L. Antidiarrheal activity, chemical and toxicity profile of Berberis aristata. Pharm. Biol. 2011, 49, 94–100.

56. Singh, M.; Srivastava, S.; Rawat, A.K.S. Antimicrobial activities of Indian Berberis species. Fitoterapia 2007, 78, 574–576.

57. Hussain, M.A.; Khan, M.Q.; Habib, T.; Hussain, N. Antimicronbial activity of the crude root extract of berberis lycium royle. Adv. Environ. Biol. 2011, 5, 585–588.

58. Azimi, G.; Hakakian, A.; Ghanadian, M.; Joumaa, A.; Alamian, S. Bioassay-directed isolation of quaternary benzylisoquinolines from Berberis integerrima with bactericidal activity against Brucella abortus. Res. Pharm. Sci. 2018, 13, 149–158.

59. Bukhari, I.; Hassan, M.; Abbasi, F.; Mujtaba, G.; Mahmood, N.; Fatima, A.; Afzal, M.; Rehman, M.; Perveen, P.; Khan, T. A study on comparative pharmacological efficacy of Berberis lycium and penicillin G. African J. Microbiol. Res. 2011, 5, 725–727.

60. Sati, S.C.; Takuli, P.; Kumar, P.; Khulbe, K. Antibacterial activity of three medicinal plants of Kumaun Himalaya against some pathogenic bacteria. Int. J. Pharma Sci. Res. 2015, 6, 1361–1368.

61. Malik, Z.; Jain, K.; Ravindran, K.; Sathiyaraj, G. In vitro antimicrobial activity and preliminary phytochemical analysis of Berberis aristata. Int. J. Ethnobiol. Ethnomed. 2017, 4, 1–6.

62. Manosalva, L.; Mutis, A.; Urzúa, A.; Fajardo, V.; Quiroz, A. Antibacterial activity of alkaloid fractions from berberis microphylla G. Forst and study of synergism with ampicillin and cephalothin. Molecules 2016, 21, 76.

63. Mehmood, A.; Murtaza, G.; Bhatti, T.M.; Kausar, R.; Ahmed, M.J. Biosynthesis, characterization and antimicrobial action of silver nanoparticles from root bark extract of Berberis lycium Royle. Pak. J. Pharm. Sci. 2016, 29, 131–137.

64. Anzabi, Y. In vitro study of Berberis vulgaris, Actinidia deliciosa and Allium cepa L. antibacterial effects on Listeria monocytogenes. Crescent J. Med. Biol. Sci. 2015, 2, 111–115.

65. Thakur, P.; Chawla, R.; Narula, A.; Sharma, R.K. Protective effect of Berberis aristata against peritonitis induced by carbapenem-resistant Escherichia coli in a mammalian model. J. Glob. Antimicrob. Resist. 2017, 9, 21–29.

66. Shahid, M.; Rahim, T.; Shahzad, A.; Latif, T.A.; Fatma, T.; Rashid, M.; Raza, A.; Mustafa, S. Ethnobotanical studies on Berberis aristata DC. root extracts. African J. Biotechnol. 2009, 8, 556–563.

S. No.	Species	Part	Country	Extract/Model/Compound	Tested Micro-Organism	Results	Reference
32	*B. croatica* and *B. vulgaris*	Roots, leaves, and twigs	Croatia	Ethanol	*B. subtilis*, *S. aureus*, *E. coli*, *P. aeruginosa*, *C. albicans*	Extracts of both species: significant antibacterial activity against the Gram-positive bacteria. Root extracts of *B. croatica*: activity against *P. aeruginosa* and leaf extracts against *B. subtilis*. Neither species possessed antifungal activity. Leaf extracts of *B. croatica*: antibacterial activity against *B. subtilis*. Likewise, neither of the species extracts showed activity against *E. coli* and *C. albicans* except when were diluted. Ethanolic extracts of twigs of both species: inactive against *B. subtilis* and *S. aureus*, with the exception of *B. croatica* twig from Kiza locality.	[71]

S. No.	Species	Part	Country	Extract/Model/Compound	Tested Micro-Organism	Results	Reference
33	*B. lycium*	Roots	India	Hexane extract, Methanolic extract, aqueous extract and berberine	*K. pneumonia*, *E. coli*, *P. aeruginosa*, *S. aureus*, *B. subtilis*, *C. albicans*, *A. niger*, *Aspergillus fumigates*	Methanolic extract of species was highly effective against *E. coli*, *S. aureus*, *B. subtilis*, *C. albicans*, *A. fumigates*. Pure berberine was active against *P. aeruginosa* and *C. albicans*.	[72]
34	*B. aetnensis*	Roots	Italy	Ethanol ether and chloroform	*S. aureus*, *B. subtilis*, *E. faecalis*, *E. coli*, *P. aeruginosa*, *Stenotrophomonas maltophilia*, against 14 strains of nosocomial origin: two strains of *S. aureus* (1 Met-S, 1 Met-R); four strains of *S. epidermidis* (2 Met-S, 2 Met-R); three strains of *E. coli*; four strains of *P. aeruginosa*, *Hafnia alvei* and *C. albicans*, *C. parapsilosis*, *C. krusei*	The root and leaf extracts showed a greater activity against Gram-positive bacteria and yeasts than against Gram-negative bacteria, except for *P. aeruginosa*. The chloroform extract of leaves was more active than the ethanol.	[73]
35	*B. thunbergii, B. vulgaris*	Roots	USA		*E. coli*, *P. aeruginosa*, *S. aureus*, *S. mutans*, and *S. pyogenes*	Ethanolic extracts more active against studied bacteria, strongest activity against *S. pyogenes* and *S. aureus*.	[74]

67. Rizwan, M.; Nasir, H.; Shah, S.Z. Phytochemical and biological screening of Berberis aristata. Adv. Life Sci. 2017, 57, 1–7.
68. Amin, A.H.; Subbaiah, T.V.; Abbasi, K.M. Berberine sulfate: Antimicrobial activity, bioassay, and mode of action. Can. J. Microbiol. 1969, 15, 1067–1076.
69. Freile, M.L.; Giannini, F.; Pucci, G.; Sturniolo, A.; Rodero, L.; Pucci, O.; Balzareti, V.; Enriz, R.D. Antimicrobial activity of aqueous extracts and of berberine isolated from Berberis heterophylla. Fitoterapia 2003, 74, 702–705.
70. Hyun, T.K.; Kim, H.C.; Kim, J.S. In vitro Screening for Antioxidant, Antimicrobial, and Antidiabetic Properties of Some Korean Native Plants on Mt. Halla, Jeju Island. Indian J. Pharm. Sci. 2015, 77, 668–674.
71. Kosalec, I.; Gregurek, B.; Kremer, D.; Zovko, M.; Sanković, K.; Karlović, K. Croatian barberry (Berberis croatica Horvat): A new source of berberine—Analysis and antimicrobial activity. World J. Microbiol. Biotechnol. 2009, 25, 145–150.
72. Malik, T.A.; Kamili, A.N.; Chishti, M.Z.; Ahad, S.; Tantry, M.A.; Hussain, P.R.; Johri, R.K. Breaking the resistance of Escherichia coli: Antimicrobial activity of Berberis lycium Royle. Microb. Pathog. 2017, 102, 12–20.
73. Musumeci, R.; Speciale, A.; Costanzo, R.; Annino, A.; Ragusa, S.; Rapisarda, A.; Pappalardo, M.S.S.; Iauk, L. Berberis aetnensis C. Presl. extracts: Antimicrobial properties and interaction with ciprofloxacin. Int. J. Antimicrob. Agents 2003, 22, 48–53.
74. Villinski, J.R.; Dumas, E.R.; Chai, H.B.; Pezzuto, J.M.; Angerhofer, C.K.; Gafner, S. Antibacterial activity and alkaloid content of Berberis thunbergii, Berberis vulgaris and Hydrastis canadensis. Pharm. Biol. 2003, 41, 551–557.
75. Bereksi, M.S.; Hassaïne, H.; Bekhechi, C.; Abdelouahid, D.E. Evaluation of Antibacterial Activity of some Medicinal Plants Extracts Commonly Used in Algerian Traditional Medicine against some Pathogenic Bacteria. Pharmacogn. J. 2018, 10, 507–512.

S. No.	Species	Part	Country	Extract/Model/Compound	Tested Micro-Organism	Results	Reference
36	*B. vulgaris*	Root bark	Algeria	Methanol and water	*S. aureus*, *E. faecalis*, *E. coli*, *E. cloacae*, *K. pneumoniae*, *P. aeruginosa*	The extracts of species root barks presented a strong activity against *S. aureus* (23.0 mm), a weak activity against *E. faecalis* (13.0 mm) and no activity toward other strains.	[75]