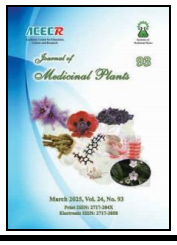
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Review Article

Barberry (*Berberis* L.) as a functional food and therapeutic agent in traditional persian medicine and modern phytotherapy: a narrative review

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ABSTRACT

Background: Barberry (*Berberis* L.) is a well-known fruit traditionally used in various ethnomedical systems, including Ayurveda and Traditional Persian Medicine (TPM), for its nutritionaland therapeutic properties. **Objective:** This study aims to provide a comprehensive overview of the traditional medicinal uses, phytochemical composition, and pharmacological effects of barberry. **Method:** A systematic review was conducted by examining traditional Persian medicine texts and electronic literature on traditional medicine. Additionally, electronic databases were searched for scholarly articles focusing on the pharmacological activities and phytochemical components of barberry. **Results:** Phytochemical analysis revealed the presence of essential oils, micronutrients, macronutrients, phytosterols, and various phenolic compounds. Pharmacological studies demonstrate that barberry possesses diverse biological activities, including anti-cancer, antioxidant, cardiometabolic protective, antimicrobial, hepatoprotective, anti-inflammatory, anxiolytic, nootropic, and neuroprotective effects. **Conclusion:** Although barberry shows promising therapeutic potential, further clinical trials and meta-analyses are required to confirm its efficacy in medical applications.

1. Introduction

Nutraceuticals are described as foods or food components that possess medicinal effects and can significantly contribute to promoting health, preventing disease, or aiding in treatment. In recent decades, these compounds have garnered considerable attention due to their safety, nutritional value, and therapeutic potential [1] Nutraceuticals can be classified according to their chemical compositions, which include terpenoids, phenolic compounds, fatty acids and structural lipids, carbohydrates, amino acid-based substances, and minerals [2] Fruits, considered as nutraceuticals, are nutritious and health-promoting foods widely utilized for their healing effects. They have numerous beneficial components, such as proteins, carbohydrates, and fats. Additionally, fruits are rich in essential

Abbreviations: TPM, Traditional Persian Medicine

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minerals, vitamins, dietary fiber, nutrients, and antioxidants, all of which contribute to their medicinal benefits [3].

Berberis species are primarily consumed fresh or dried and are commonly used in juice production. [4] In Iran, the fruits are known as Zereshk, and frequently utilized in cooking and jam production. The substantial demand for barberries has led to an annual production of approximately 22,000 tons of fresh, edible, seedless barberries [5] These fruits are widely processed into various products, including beverages, syrups, candies, and other confectionery items that are particularly popular in Iran. Furthermore, both the leaves and fruits of barberries are utilized in manufacturing teas and food flavorings. Barberry is highly valued for its nutritional significance; not only the fruit, but also various parts of the plant, including the roots, bark, and leaves, are key components in herbal remedies within Indian, Persian, and Chinese traditional system of medicine, with a history spanning at least 3,000 years[6] Currently, the flowers of this species are widely used among Tibetan-speaking populations in regions such as Litang, China. [7].

A study was undertaken to assess the efficacy of cold-pressed filtered oil extracted from *Berberis* seeds in delaying the oxidation of soybean oil, in comparison to commercially available antioxidants. The results demonstrated that *Berberis* seed oil provided oxidative stability to soybean oil comparable to that of commercial antioxidants [8]. The antioxidant and antibacterial activities of barberry water extract suggest its potential application as a preservative in the food industry [9].

The genus *Berberis* is native to temperate and subtropical regions across Asia, Europe, Africa, North America, and South America. Various species of *Berberis* can be found in many regions globally, including Iran. Iran is the largest producer of *Berberis* sp. fruit, with approximately 11,000 hectares of land under cultivation. The country produces over 10,000 tons of dried *Berberis* fruit annually. Within Iran, Southern Khorasan is a major producer of *Berberis* sp., with more than 97% of the cultivation occurring in Ghaenat County, Southern Khorasan Province. This region is responsible for 95% of the total *Berberis* fruit production in Iran. Different species of *Berberis* are cultivated worldwide for specific purposes, while *Berberis* sp. being particularly well-known and widely used in cooking, often prepared with rice (either seedless or red)[10].

The tree of *Berberis* is a thorny tree and its thorns are triangular. It grows at mountains and mountain slopes that are close to water, in Khorasan and Shirvan, and etc. Most of them are seedless and fresh, and in the areas of Shirvan and other areas, most of them are seeded, its stem is similar to that of jasmine, it is larger and narrower than that, its whole is whitish-yellow, its heads are complex and Its fruit is clustered and long, green in its raw state, then turns red to violet and black when ripe, it ripens in the summer, and its tree is as tall as two or three meters tall, its fruit is round. The red color is the best, in most of the compositions, it is also used in juice, paste, and extracts of the seeds, in which it is squeezed, or dried, soaked in water, rubbed and filtered [12].

Berberis spp. is known as “Zereshk” in Iran and “Ambarbaris” in TPM. It is utilized in the treatment of various conditions, including skin, liver, stomach, kidney, and eye disorders. Numerous pharmacological researches have reported beneficial effects of *Berberis*, corroborating its traditional uses.

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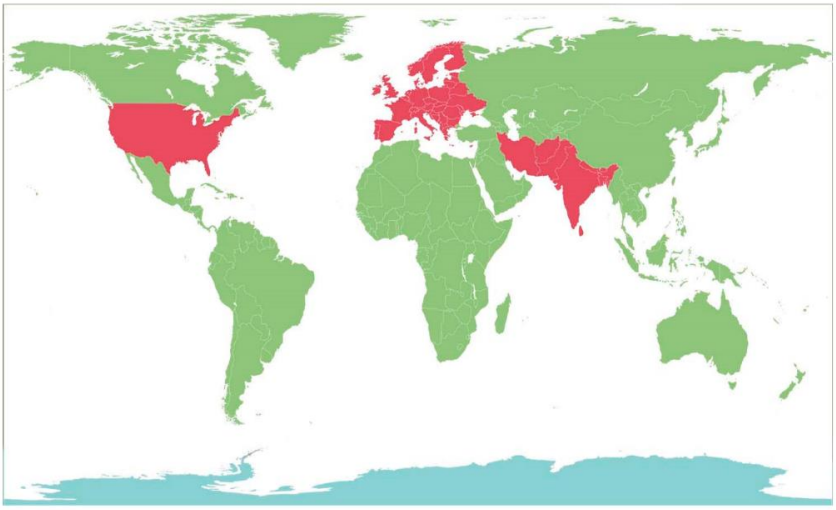


Fig. 1. The lands under cultivation of barberry in the world [11]

2. Methods

In this review, we examined prominent ancient TPM texts, including *Al-Qānūnfī al-Tibb* (The Canon of Medicine) by Avicenna, *Al-Hawi fi al-Tibb* by Rhazes, and comprehensive traditional medicine pharmacopeias such as *Makhzan al-Adviah*, *Al-Shamil fi al-Tibb*, and *Tohfah al-Momenin*. We also reviewed published literature using keywords such as "Zereshk" and "Ambarbaris" to investigate the traditional uses and medicinal properties of barberry. Additionally, we searched electronic databases, including Google Scholar, PubMed, Medline, and Elsevier, for studies on the phytochemical components, pharmacological activities, and therapeutic uses of barberry. Data collection focused on review articles and clinical trial studies, with keywords including *Berberis* sp. L., berries, barberry, Persian medicine, complementary medicine, traditional medicine, and Zereshk. The results of this review are summarized and discussed in this paper.

3. Results

3.1. Pharmacological properties

The primary compounds found in *B. vulgaris* include lupeol, oleanolic acid, stigmasterol, stigmasterolglucoside, berberamine, palmatine, berberine, oxyberberine, columbamine, isocorydine, lambertine, magniflorine, and oxycanthine. Barberry, which is rich in nutrients, contains various beneficial phytochemicals that may aid in managing diabetes, treating diarrhea, maintaining dental health, and combating acne. Additionally, it exhibits anti-cancer properties and is considered a valuable addition to the diet [13]. Research has demonstrated various effects of *Berberis* and its isoquinoline alkaloids, particularly berberine. Studies have confirmed that the primary constituents of this plant are isoquinoline alkaloids, including berberine, berbamine, and palmatine. Among these, berberine is one of the most extensively studied naturally occurring protoberberine alkaloids. In addition to being found in *Berberis* (barberry), berberine is present in many other plants and is used in the treatment of various diseases [14].

3.2. Modern phytotherapy

Berberine demonstrates significant therapeutic effects on five metabolic diseases: diabetes, obesity, non-alcoholic fatty liver disease (NAFLD), hyperlipidemia, and gout

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[15]. The effect of *Berberis* on glycemic index is proven. It can decrease insulin levels [16] A pooled analysis indicated that *B. vulgaris* L. had significant effects on various metabolic indices, including total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), fasting blood sugar (FBS), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) in patients. Reviews revealed a strong correlation between barberry consumption and decreased serum LDL-C levels in the intervention group compared to the control. *Berberis* markedly lowered serum levels of TC and TG, with patients treated with barberry exhibiting notably reduce serum TG levels compared to those receiving a placebo. Additionally, barberry demonstrated therapeutic effects on serum HDL-C levels in patients with metabolic syndrome. Systematic reviews have substantiated the protective effects of barberry on serum fasting blood sugar levels. However, *Berberis* does not appear to have a significant impact on ALT activity, although all studies reported a reduction in serum AST activity following treatment with barberry [17] The effects of *Berberis* have been evaluated in the reviews presented in the tables below [17].

Numerous studies have demonstrated that both *Berberis* sp. and berberine possess significant anti-inflammatory, antioxidant, and immunomodulatory properties. These substances can prevent the output of pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α), interleukins 1β (IL-1β), 6 (IL-6), and 17 (IL-17), while simultaneously enhancing the presentation of anti-inflammatory cytokines such as interleukin-10 (IL-10) and transforming growth factor-β (TGF-β) across various cell types and tissues. Additionally, *Berberis* and berberine are effective in combating free radicals, increasing antioxidant enzyme levels, including superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), and reducing lipid peroxidation and DNA damage. They have been reported to exert beneficial effects across a range of inflammatory, oxidative, and immune-related conditions, including diabetes, obesity, cardiovascular diseases, neurodegenerative disorders, autoimmune diseases, allergic conditions, and infections [18] malic acid which is a substant that could be used to juvenile the skin, is present in *B. vulgaris* ingredients, also is vitamin E and vitamin C. [19] Berberine and *Berberis* root extracts have been shown to significantly reduce the total nucleic acid content in three species of *Leishmania*, suggesting their potential as effective agents for antileishmanial chemotherapy [20].

3.3. Traditional uses of barberry in TPM textbooks

In traditional Persian medicine, the root's skin of *B. vulgaris* plant is called as "*Arghis*" which is useful in treating ophthalmic disorders and gastrointestinal diseases. Research has provided compelling evidence that berberine is a promising candidate for the treatment of dry eye [22] Additionally, the root of this plant is recognized as a promising source with significant chemopreventive potential for preventing colorectal cancer, owing to its antioxidant, anti-inflammatory, and antiproliferative properties [23] *Berberis* root extract can modulate glucose metabolism and lipid profiles in patients with type 2 diabetes [24].

Studies have demonstrated that daily consumption of barberry juice for 8 weeks significantly reduces both systemic and diastolic blood pressure [25].

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Berberis sp. leaf and root extracts contain potent compounds with strong antibacterial and antifungal properties, making them effective against a wide range of microorganisms. These extracts have demonstrated efficacy in combating human multi-resistant pathogens [26].

Usage of *Berberis* can decrease signs and symptoms of opiate withdrawal syndrome [27]

It is also proven that using B. vulgaris in adults leads to reduction of the waist – hip ratio [28].

Studies have indicated that adjunctive therapy with *Berberis* shows promise in the treatment of refractory primary sclerosing cholangitis and primary biliary cholangitis [29].

Tables of Nutritional Properties of (*Berberis* L.) Fruits are designed below [30, 31].

Table 1. Minerals of *Berberis* L.

Minerals	Ppm (mean)	Minerals	Ppm (mean)
Ag	41.73	K	12111.19
Al	16.86	Li	0.32
As	3.54	Mg	1193.30
B	56.93	Mn	6.54
Ba	1.42	Na	2569.33
Bi	0.22	Ni	19.98
Ca	2744.06	P	2715.51
Co	0.26	Sr	16.17
Cr	33.21	V	0.69
Cu	4.75	Zn	7.95
Fe	323.86		

Table 2. Propertieses of *Berberis* L.

Properties	Values
Moisture (%)	71.42
Soluble dry matter (%)	19.4
Reducing sugar (%)	6.52
Ascorbic acid (mg/kg)	256.48
Total phenolics (mg/100gr)	789.32
Total anthocyanin (mg/kg)	931.05
Crude protein (%)	10.32
Crude cellolose (%)	9.42
Crude energy (kcal/gr)	69.25
Crude oil (%)	0.84
Nonsolouble HCL ash (%)	0.0018
pH	3.35
Acidity (%)	3.10
Ash (%)	1.12
Alcohol-solouble extract (%)	26.64

Table 3. Traditional uses of *Berberis* L. [32]

System	Effect	Part of plant	Preparation	Country
Cardiovascular	Antihypertensive	Stem bark	Decoction	France
Blood	Blood rectifier	Dried root	Decoction	Iran
Gastrointestinal	Choleretic	Dried entire	Infusion	Iran
	Cholagogue	Root	Fluid extract	France
	Laxative	Dried root	Decoction	Iran
		Dried entire	Infusion	Iran
		Dried root bark	Decoction	Iran
		Fruit	Decoction	Turkey
	Stomachic in severe diarrhea Hepatic	Fruit	Infusion	Turkey
		Dried fruit-root	H20 extract-root	Iran and India
	Intestinal ulcers	root	Dry powder	India
	Indigestion associated with hepatic disorders or loss of appetite hemorrhoids	Dried root	Decoction	Iran

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Table 3. Traditional uses of *Berberis* L. [32] (Continued)

System	Effect	Part of plant	Preparation	Country
Endocrine	Painful menstruation	fruit	Juice	Argentina
Immune system	Anti Inflammatory	Dried root	Decoction	Bulgaria
	Rheumatoid arthritis	Dried root	Decoction	Iran
	Anti rheumatic Gout	Flowers	Decoction	China
organisms	Antimicrobial	Root	Dried root	Bulgaria
	In typhus	Fruit	H2O extract	Iran
	In malaria	Dried root	Decoction	Iran
Central nervous system	sedative	Dried fruit and dried root	H2O extract root	Iran and Bulgaria
respiratory	Whooping cough	Fruit	Decoction	Turkey
	Cold symptoms (gargle)	Dried leaf	Infusion	Turkey
	Blood vomiting due to respiratory disorders	root	Dried root	India
skin	Irrigate wounds or in scorbutic patients	Dried leaf	Infusion	Iran
	Chewed by scorbutic to harden gums disinfectant	Leaf	External	Iran
		Root	Decoction	Iran
renal	Urinary	Root	Hot H2O	India
	Diuretic	Root	Dried root	Iran
	Kidney inflammation	Root	Dried root	Bulgaria
	nephritis	Root	Decoction	Iran

Table 4. Clinical trials of *Berberis* L.

First author of clinical trial	Year	Subject	Participants	Results
H.Emamat (25)	2020	8 weeks of Barberry juice usage	40 men and women with cardiovascular d. and hypertensions	Decrease in SBP, DBP, MAP And plasma lipids
T. Kermani (33)	2020	3 weeks of barberry tablets usage	60 patients with metabolic syndrome	Decrease in SBP and waist circumference and hematocrit and serum cholesterols
H. Emamat (34)	2020	8 weeks of dried barberry usage	84 hypertensive patients	Improvement in flow mediated dilation and decrease in inflammatory biomarkers

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Table 4. Clinical trials of *Berberis* L. (Continued)

First author of clinical trial	Year	Subject	Participants	Results
F. Dabaghzadeh (27)	2023	4 weeks of barberry 'root capsules usage	52 opiate addicts	Improvement in signs and symptoms of opiate withdrawal syndrome
H. Rostami (35)	2023	3 months of barberry's root capsules usage	140 patients with Schizophrenia	no significant Effect of Barberry Root (*Berberis* sp.) on the Prevention of Metabolic Syndrome Caused by Atypical Antipsychotic Drugs
Z. Naghibi (29)	2021	3 months of additional therapy with barberry's oxymel	30 patients with biliary diseases	Improve in serum level of AST, ALT, Total Bil, direct B. PT, INR
Kashkooli (17)	2015	12 weeks consumption of barberry capsules	80 patients with non-alcoholic fatty liver disease	Decrease in Triglycerides, total cholesterols, AST And ALT serum level
Lazavi (36)	2018	8 weeks of barberry juice usage	46 patients with type 2 diabetes	Decrease in FBS total cholesterols and triglycerides serum levels
Rashidi (37)	2018	4 weeks of barberry root capsules consumption	80 patients with type 2 diabetes	Decrese in FBS, ALT, AST serum levels
Shidfar (38)	2012	12 weeks Barberry extract capsules usage	42 patients with type 2 diabetes	Decrease in LDL, TG, TC and FBS serum level
Tahmasebi (24)	2019	6 weeks usage of hydro alcoholic root extract	107 patients with type 2 diabetes	Increase in HDL and decrease in FBS, Total cholesterols and LDL serum level

4. Discussion

Berberis L. (barberry) demonstrates significant therapeutic potential, supported by both traditional Persian medicine and modern phytotherapy. Its wide range of pharmacological activities, including anti-inflammatory, antioxidant, cardiometabolic protective, and antimicrobial properties, make it a valuable functional food for promoting public health.

Safety and Side Effects: Despite its promising health benefits, the safety profile of *Berberis* sp. must be carefully considered. Studies have reported potential side effects, including gastrointestinal discomfort and possible interactions with certain medications, particularly in pregnant women and individuals with chronic conditions. Therefore, clinical guidelines on safe dosage and long-term effects should be established [14, 39].

Traditional vs. Modern Applications: In traditional Persian medicine, barberry is consumed in forms such as decoctions, infusions, and syrups for treating liver, gastrointestinal, and cardiovascular conditions. Modern applications include standardized extracts and capsule supplements, which provide more controlled dosages and targeted therapeutic effects [23, 24].

Impact on Public Health: Barberry's anti-inflammatory, lipid-lowering, and glucose-regulating effects position it as a functional food with the potential to mitigate chronic diseases like diabetes, obesity, and cardiovascular disorders. Incorporating barberry into diets could support public health initiatives aimed at

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reducing the prevalence of metabolic syndromes [17, 25].

Conclusion

Further clinical trials and meta-analyses are essential to confirm the efficacy and safety of *Berberis* sp. Standardizing extracts, determining optimal dosages, and evaluating long-term effects are crucial next steps. Moreover, research should explore barberry's potential in novel therapeutic areas and drug development [18].

In conclusion, *Berberis* sp. offers significant promise as a functional food and therapeutic agent. However, rigorous scientific validation through clinical studies is necessary to fully realize its potential in modern healthcare.

Author contributions

Research conception and design: AGH and MB. Data collection: AGH and MB. Review and editing: HMK and AHJ. All authors contributed to the article and approved the submitted version.

Conflicts of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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