



## REVIEW PAPER

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# Fundamentals of the use of *Berberis* as a medicinal plant

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## ABSTRACT

**Introduction.** The daily use of medicinal plants has increased in recent years. The study of drugs of natural origin as an academic discipline and its applications in healthcare has changed remarkably but still focus on the quality of products and the development of new medicines.

**Aim.** This study covers all fundamental aspects of pharmacognosy as well as topics relating to the therapeutic use of plant drugs known as phytotherapy. The purpose of the study was to review the literature about the use of *Berberis*.

**Materials and method.** We reviewed the literature regarding the use of *Berberis* published between 1933 and 2018. We found more than 500 articles studying the properties of *Berberis* for digestive disorders, antibacterial, antidiabetic, hypotensive effects, anti-inflammatory effects, cholesterol regulation, cardiovascular disease, hyperlipidemia, cerebral ischemia trauma, mental disease, Alzheimer disease and osteoporosis. Our review includes recent studies regarding chemical composition and medicinal outcomes of *Berberis*.

**Keywords.** medicinal plants, phytotherapy, *Berberis*

## Introduction

Plants have been the basic medical systems for thousands of years, particularly in China and India. Studies dealing with medicinal and other useful plants and their bioactive compounds have used many concepts and methodologies.

In the January 2018, The National Center for Biotechnology Information (NCBI) PubMed Data Base

showed that the total number of publications regarding *Berberis* and its use is 500. The healing properties of *Berberis* have been known and appreciated for thousands of years. *Berberis* occurs in central and southern Europe, northwest Africa and western Asia. The genus *Berberis* includes about 500 species worldwide such as *Berberis vulgaris*, *Berberis aristata*, *Berberis darwinii*, *Berberis*

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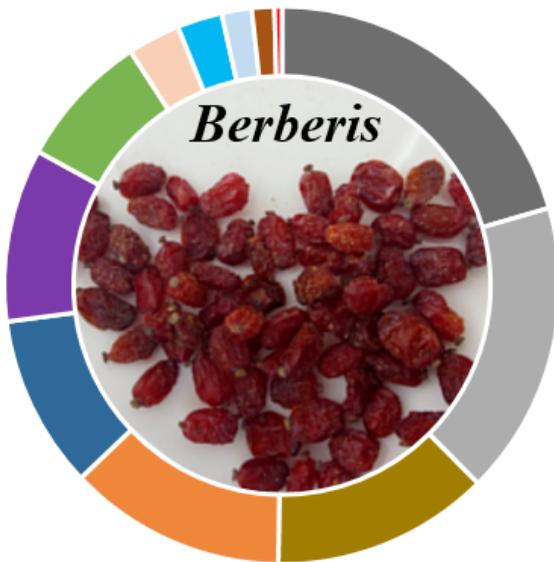
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*dictyophylla*, *Berberis julianae*, *Berberis thunbergii* and *Berberis verruculosa*.<sup>1-3</sup>



**Figure 1.** The basic applications and properties of *Berberis*.

The percent of publications pertaining to individual *Berberis* properties are as follows:

- – anti-inflammatory effects 20%,<sup>7-9</sup>
- – antibacterial 16%,<sup>10,11</sup>
- – cholesterol regulation 12%,<sup>12,13</sup>
- – digestive disorders 12%,<sup>14</sup>
- – antidiabetic 9%,<sup>2</sup>
- – cardiovascular disease 9%,<sup>15</sup>
- – anticancer 8%,<sup>16,17</sup>
- – mental disease 4%,<sup>18</sup>
- – Alzheimer disease 4%,<sup>18</sup>
- – osteoporosis 3%,<sup>18</sup>
- – hypotensive properties 2%,<sup>19</sup>
- – cerebral ischemia trauma 1%,<sup>15</sup>

In natural medicine, *Berberis* leaves are also used being harvested in May or June and dried in natural drying rooms. The *Berberis* fruit which is harvested in August or September is also used for medicinal purposes. They are dried in heated ovens, initially at a temperature of about 30 degrees Celsius, and then further dried at 50-60 degrees Celsius. *Berberis* fruits are very rich in vitamin C; therefore they have a vitaminizing effect. *Berberis* species are rich in polyphenolic constituents such as anthocyanin and have shown significant free radical-scavenging activity.<sup>4</sup> *Berberis* species are rich in polyphenolic constituents such as anthocyanin and have shown significant free radical-scavenging activity showed that leaves and fruits of *Berberis crataegina* contain predominant phenolic compounds which includes rutin and chlorogenic acid.<sup>4,5</sup> A new porphine base named O-methylcorydine-N-oxide together with berberine, palmatine, jatrorrhizine and oxyacanthine have

been isolated from *Berberis chitria*.<sup>6</sup> Berberine has antimicrobial and ameocidal properties and is used either in the form of the pure compound or as a component of plant extract. Berberine is known to be a substrate of p-glycoprotein and to affect expression of cytochrome P (CYP) 450 enzymes, 3A4 and others.

*Berberis* leaves are used mainly for colds and for general strengthening of the body; in addition, the *Berberis* fruits have antipyretic effects. In folk medicine, *Berberis* has been used among others, for liver disease and other digestive ailments, e.g. digestive disorders or lack of appetite. *Berberis* has a diuretic effect, therefore it is recommended to use it during any problems with the urinary tract. The properties and basic applications of *Berberis* species are presented in Figure 1.

### Chemical composition of *Berberis*

The main ingredient of *Berberis* are berberine and berbamine.<sup>20</sup> The chemical composition of *Berberis* include alkaloids, tannins and phenolic compounds. The triterpene lupeol, separated from fruits, and oleanolic acid, isolated from ethanolic extracts. Sterols stigmasterol, obtained from hexane extracts, and stigmasterol glucoside from ethyl acetate extracts. Alkaloids include berberamine and palmatine.<sup>20</sup> Other important alkaloids are oxyberberine, columbamine, isocorydine, lambertine, magniflorine and bisbenzisoquinolines such as oxycanthine were reported to have been extracted from *Berberis* plants.<sup>20</sup> Leaves, bark and roots contain isoquinoline-derived alkaloids such as berberine, jatririzine, palmatine, and magnoflorin. Berberine is the main alkaloid, its content in leaves and root barberry is estimated at 1.5-2%. In addition, the leaves, bark and *Berberis* roots contain tannins, resin and wax. The fruits of *Berberis* contain pectin and organic acids, among others ascorbic (vitamin C, about 1.5%), whereas apples contain about 6% and lemons from 2 to 4%.<sup>21</sup> In addition, the fruit contains sugars (glucose, fructose) and a set of bioactive components that support the action of ascorbic acid. A dozen polyphenolic compounds (anthocyanins and flavonoids, including rutoside) and other plant dyes, i.e. beta-carotene and provitamin A that support visual processes and are helpful in dermatological diseases are also found. The red color of berries is provided by anthocyanin compounds and lutein, which, along with vitamin A, support the functioning of the eye.<sup>21</sup>

Below is a graph (Figure 3) showing an increase in the number of *Berberis* publications from 1933 to present.

*Berberis* has yellow flowers that bloom in May and June. In early autumn, it yields fruit as hard, oblong red fruits that appear on the twigs. The fruit has a sour and tart flavor. *Berberis* covers about 500 species, the most popular being grown, for example, in north-eastern re-



Figure 2. Dry fruits of *Berberis*

gions of Iran. The cultivation of *Berberis* in South Khorasana dates back two hundred years. Mokhber-Dezfuli et al. in their work described the phytochemical and pharmacological activity of various species.<sup>22</sup> Whereas Srivastava et al. summarized the taxonomic, ethno-botanical, pharmacognostic, photochemical and pharmacological properties of many *Berberis* species.<sup>23</sup> The research team of Bhardwaj & Kaushik stated that due to the fact that when collecting plants, the whole plant is dug together with roots it is necessary to look at how root properties compare to leaves and fruit as the main compounds exhibiting beneficial properties exist in dif-

ferent plant parts.<sup>24</sup> Therapeutic uses have a long tradition in Asia in Chinese medicine and Ayurvedic medicine, where the bark and root of *Berberis* has been used for several thousand years. The main goal is to support the functioning of the intestines and liver as well as alleviate skin problems, cleanse the body and strengthen immunity. In natural medicine, barberry is widely used. It has a high content of vitamin C, so it is used for colds and fever as well as prophylactic. In addition, it positively affects our nervous system, used in neuroses and problems with insomnia. In addition, it has a beneficial effect on the level of concentration and a positive mood. In addition, it is used in people who are overweight, due to the fact that fruit tea has a positive effect on metabolism, additionally has a diuretic and slightly laxative effect. *Berberis* extracts show positive effects in applications for diarrhea, intestinal cramps and other gastrointestinal bowel disorders.<sup>25</sup> Another property of *Berberis* is antibacterial activity. Bark and root infusion is used for bacterial infections, due to their high content of berberine which has antibacterial properties. Bakht et al., in studies from 2017, evaluated the antibacterial activity of *Berberis* extract against gram-positive, gram-negative bacteria and fungi. Different fractions showed different degrees of antimicrobial activity.<sup>26</sup> A decoction of *Berberis* leaves has a positive effect on rheumatic pains and neuralgia. Thanks to its bactericidal properties, barberry has also found its use in cosmet-

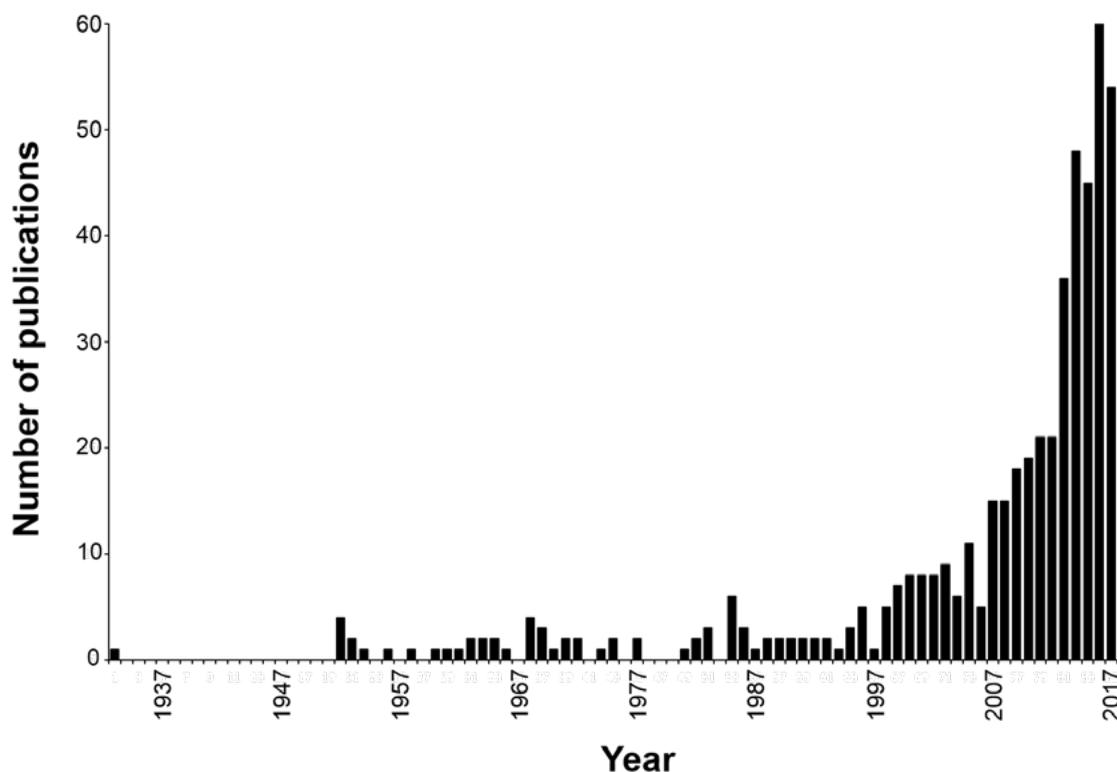


Figure 3. Number of publications on *Berberis* collected from the Library of National Center for Biotechnology Information (NCBI) PubMed Data Base over the years starting from 1933

ics in the treatment of acne, and due to the high content of vitamin C, flavonoids and flavones, it is often used in preparations used for skin discoloration. Imenshahidi & Hosseinzadeh in 2016 presented in their work, the latest information on the pharmacological action of berberine used, inter alia, for the treatment of tumors, diabetes, cardiovascular disease, hyperlipidemia, inflammation, bacterial and viral infections, ischemic injuries, mental illness, Alzheimer's disease, and osteoporosis.<sup>27</sup> The Rahimi-Madiseh group assessed the possibility of using barberry fruits in the development of new medicines.<sup>28</sup> In the article by Imanshahidi & Hosseinzadeh the authors looked at traditional applications and pharmacological action of the active ingredient *Berberis vulgaris*.<sup>29</sup> *Berberis* has played an important role in the herbal treatment for over 2500 years. Arayne et al. presented barberry as a therapeutic agent used in homeopathic treatment of kidney pain and kidney stone removal.<sup>30</sup> In addition, these healing properties are appreciated in traditional Iranian medicine. Rahimi-Madiseh et al., based on a review of the literature, showed that *Berberis* contains a large number of positive substances that include ascorbic acid, vitamin K, several triterpenoids, more than 10 phenolic compounds, and more than 30 alkaloids. Due to these phytochemicals, its anti-cancer, anti-inflammatory, antioxidant, antidiabetic, antibacterial, analgesic and antinociceptive as well as hepatoprotective properties can be attributed.<sup>28</sup> The most important active ingredient contained in the bark and root of *Berberis* is berberine. In addition, isoquinoline alkaloids include berbamin, palmatine and magnoflorine. Together, these substances are widely used in traditional medicine. They positively affect the metabolism and the entire digestive system. They especially support the metabolism of glucose and cholesterol and the proper functioning of the liver and gall bladder. *Berberis* leaf infusion is used for digestive disorders to relieve stomach aches, nausea and overeating. In addition, it can be helpful in stopping bile production and restoring normal function.<sup>31</sup> The use of the *Berberis integerrima* extract may also have a positive effect on insulin sensitivity. Fallah and their research group tested the effect of the extract on sensitivity in insulin-resistant rats with a high fructose diet. The results of the study revealed that *Berberis integerrima* may be a candidate for protecting against type II diabetes/insulin resistance through direct insulin-like effects and an increase in adiponectin levels.<sup>32</sup> In addition to insulin sensitizing, berberine has a cholesterol-lowering effect. Guarino et al. in their studies checked the effect of berberine and silymarin on abdominal fat in patients with overweight or obesity with concurrent type II diabetes. Based on the analysis of over 100 volunteers, a clinically significant effect was demonstrated in obese people with T2DM and metabolic syndrome.<sup>33</sup> In addition, berberine has a

positive effect on the nervous system, showing sedative properties as it has been shown to minimize problems with insomnia and aid in lowering blood pressure. Fatehi et al. in their studies investigated the effect of *Berberis* extract on blood pressure in rats and the effect on potassium currents recorded from cells in the crescent and cerebellum which re-connect with the rat's brain. It has been noticed that a dose of extract of 0.05-1 mg/100 g of rat body weight exerts a positive effect. A significant reduction in mean blood pressure and heart rate was noted.<sup>34</sup> Thanks to this research, it can be concluded that barberry extract has a beneficial effect on the cardiovascular and nervous systems. The berberine present in the roots and bark is anti-inflammatory. *Berberis* berries, due to the content of pectins, also have anti-inflammatory effects. Both the roots and stem bark of *Berberis orthobotrys* have long been traditionally used to treat joint pain. The anti-arthritic potential was assessed *in vitro* using protein denaturation (bovine serum albumin and ovalbumin) and membrane stabilization methods at 12.5-800 µg/ml and *in vivo* using Freund's turpentine oil, formaldehyde and complete adjuvant models at the age of 50 at doses of 100 and 150 mg/kg. In conclusion, these results confirm traditional use of *Berberis* as a potent anti-arthritis agent will potential for the treatment of rheumatoid arthritis.<sup>35</sup> Sengupta et al. in their studies evaluated the antitumor potential of methanol extracts from the *Berberis aristata* root and *Azadirachta indica* seeds prepared by various extraction techniques in human osteosarcoma cells (HOS). *Berberis aristata* was found to be active against sensitive and drug-resistant HOS cells depending on the method of extraction.<sup>36</sup> Extracts from barberry are also used in cosmetics and for the skin in the form of ointments. Nimisha et al. in their studies investigated the effect of using a transferosomal gel with barberry extract on psoriasis. The gel contained *Berberis aristata* extracts (roots, ethanolic 70%). It has been demonstrated that the gel has anti-inflammatory and adjunctive activity against psoriasis.<sup>8</sup> Antioxidant activities of the ethanolic extracts of roots, twigs and leaves of common barberry *Berberis vulgaris* and *Berberis croatica* Horvat were studied.<sup>37</sup> The antimicrobial activity of hydroalcoholic extracts of four *Berberis* species viz. *Berberis aristata*, *Berberis asiatica*, *Berberis chitria* and *Berberis lycium* were tested against eleven bacterial and eight fungal strains. *Berberis aristata* root extract gave low MICs values against *Bacillus cereus*, *Escherichia coli*, *Staphylococcus aureus* and *Aspergillus flavus* while stem extracts gave low MICs values against *Berberis cereus* and *Streptococcus pneumoniae*.

## Conclusion

*Berberis* has pro-health effects. All components of barberry plants, apart from their flowers, are a raw material for obtaining biologically active substances with pro-

health properties. The abundance of medicinal compounds with barberry medicinal properties can be used to treat many diseases, especially those associated with inflammatory processes, and microbial etiology. Due to the fact that the substances contained in barberry are deposited in our body, it should be used very carefully, in addition, the therapy should not be prolonged.

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