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REVIEW

THE BERBERIS STORY: *BERBERIS VULGARIS* IN THERAPEUTICS

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ABSTRACT

Barberry has played a prominent role in herbal healing for more than 2,500 years. *Berberis vulgaris* is a common garden bush, native to Europe and the British Isles, naturalized in North America, seems to have history as old as human race. Anthropologists believe in a ritual practice or sacred object, especially by Native Americans that it works as a supernatural power or as preventive or remedy of illness.

It is a deciduous shrub having yellow flowers and scarlet colored fruit in the form of berries. Twenty two alkaloids have been reported so far from root, stem leaves and fruit of this plant, which are of medicinal importance. As a herbal remedy it has no match in serving human race since ancient times. It is the most widely used drug in Homeopathic system of medicine for kidney pain and for removal of kidney stones. In this article, we present countless blessings of nature encountered through this herb which are worthy of recording.

Keywords: Berbery, *berberis, berberis vulgaris.*

INTRODUCTION

The history of berberis vulgaris might be as old as barbarians but it is rather a sophisticated plant and is serving human in one way or the other. The Italians call the barberry Holy Thorn, because it is thought to have formed part of the Crown of Thorns.

There is accumulating evidence suggesting medicinal plants are unlimited reservoirs of drugs. The amazing structural diversity among their active components make them a useful source of novel therapeutic compounds. Researchers with interest in natural products have intensified their efforts towards scientific evaluation of traditional medicines.

Berberis is the Arabic name of the fruit that signify a shell and many authors believe that the name is derived from this word because the leaves are glossy like the inside of an oyster shell. The name berbery seems to have been first applied to this fruit by Averroes (an Arabic writer on medicines) is not only a food, a food additive, a herb but also a homeopathic remedy for countless illness (the research in this respect is still going on all over the world). As Eastern and Bulgarian folk medicine it is used in rheumatic and other chronic inflammatory disorders (Ivanovska and Philipov, 1996) and as an ayurvadic medicine in India. The anticancer property of berberis vulgaris is known and the research in this regard is still in progress. Barberry became unpopular with farmers when it was discovered to be a host plant for the wheat rust fungus that decimated crops in the 19th century.

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The Plant

Berberis vulgaris is the most significant European representative of Barberdaceae (Webb and Akeroyd, 1993). The common name Barberry includes *Berberis repens*, *Berberis aqilfolia*, *Berberis nervosa*, *Berberis pinnata*, and other Berberis species, which are used interchangeably with *Berberis vulgaris.* Also known as European barberry, jaundice berry, pepperidge, pepperidge bush, sowberry, Barberry, berberis, Daruharidra, Daruhaldi, Kingor, Barberry etc. The plant prefers light (sandy), medium (loamy) and heavy (clay) soils and can grow in heavy clay and nutritionally poor soils. The plant prefers acid, while can also grow in neutral and basic (alkaline) soils. It can grow in semi-shade (light woodland) or no shade. It requires dry or moist soil. It is a thorned, deciduous shrub growing up to 3 meters (10 feet) in height, common to most areas of Central and Southern Europe and the Northeastern regions of the United States. It is generally distributed over the greater part of Europe, Northern Africa and temperate Asia. As an ornamental shrub, it is fairly common in gardens. A closely related species, Oregon grape *(Berberis aquifolium),* is native to North America. It grows well in dry, sunny locations, flowers (fig. 1) appear in mid-spring to early summer and produces a fruit (Fructis Berberidis) that can be harvested in early autumn or fall.

The leaves of the barren shoots are alternate, they become transformed in spines the succeeding year. The secondary leaves are in fascicles from the axil of these spines and are simple, oval, tapering at the base into a short foot-stalk, the margins finely serrate, with the teeth terminating in small spines. The stem is branched, smooth, grooved

and brittle. The stems, growing from 3 to 8 feet high, are reddish when young but turn dirty gray with age. Roots are deciduous and are grey or brown in color. The root is usually 1/5 inch thick. The bark has bitter taste and slight odour. Barberry has yellow, unpleasant smelling flowers. Flowers are small, pale yellow and sassile with broad stigma. The petals are entire; the stamens irritable, springing violently against the stigma when touched. Flowers are arranged in pendulous racemes that form hanging clusters.

Fig. 1: Berberis Vulgaris plant showing leaves flowers and fruit. Figure: Enlarged view of Berberis vulgaris fruits.

The fruit of Berberis (fig. 1) is long scarlet colored berries (Drofler and Roselt, 1989). Berries are oblong, slightly curved, about ½ inches long and edible. The berries become red on ripening. The taste of berries is pleasantly acidulous. The leaves are also acidic. Leaves are used to season the meat with instead of salad. Berries are sourer but less bitter than cranberries. Both the berries and the bark are used for medicinal purposes (Bergner, 1996).

Overview

Barberry has played a prominent role in herbal healing for more than 2,500 years. The ancient Egyptians used it with fennel seed to prevent plagues. India's Ayurveda healers used it for dysentery. During the early middle ages, European herbalists used it to treat liver and gallbladder ailments. Russian healers used it for inflammations, high blood pressure, and for abnormal uterine bleeding. American Indians recognize barberry as similar to Oregon grape.

It is said to make excellent preserves; was highly esteemed by the ancients, and probably would be now, if other fruits had not been cultivated to such a degree of excellence. In traditional folk medicine, barberry has been used to treat diarrhea, reduce fever, improve appetite, relieve upset stomach, and promote vigor as well as a sense of well being (Bergner, 1996). Today, it is widely used to fight the infection of the throat, urinary tract, gastrointestinal tract, lungs, yeast infection and diarrhea. Mostly the bark of the stem and root are used as medicine. Native Americans also used it as yellow dye.

In folk medicine, European barberry root bark has been used for various conditions including liver dysfunction, gallbladder disease, diarrhea, indigestion and urinary tract diseases (Foster and Tyler, 1999; Jellin *et al*., 2000 and Gruenwals, 1998). It has been applied in many cultures to treat malaria, and leishmaniasis (Jellin *et al*., 2000; Gruenwals, 1998 and Hostettmann *et al*., 1995).

American Indians used Barberry to improve appetite, a function that was soon picked up by early American settlers. It was also reportedly used for treating stomach problems such as ulcers and heartburn (Foster and Tyler, 1999), and is listed in the American Medical Ethnobotany Reference Dictionary as being effective in reducing fever (Moerman, 1977).

In short almost every civilization had used barbery in one way or the other.

What's It Made of?

The stem, root bark, and fruit of barberry contain isoquinoline alkaloids (e.g. berberine), which are the main active ingredients of barberry (Gorval and Grishkovets, 1999). The amount of berberine fractions in the stem was 2: 3 times higher than the amount in the leaves. The following alkaloids have been isolated and characterized from Berberis vulgaris species.

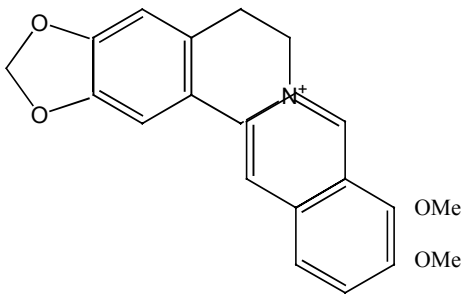
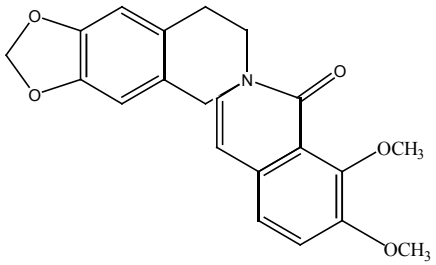


Fig. 2: Berberine



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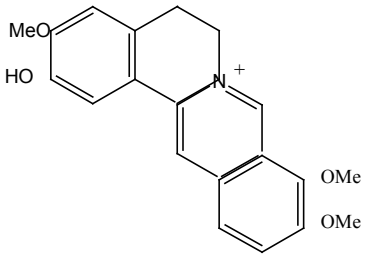

Fig. 4: Columbamine

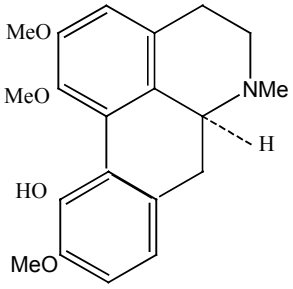

Fig. 5: Isocorydine

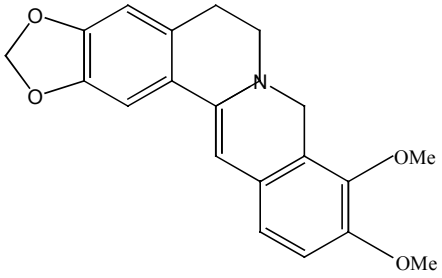

Fig. 6: Lambertine

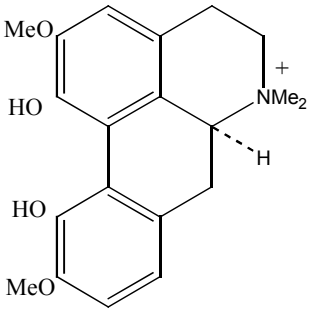

Fig. 7: Magniflorine

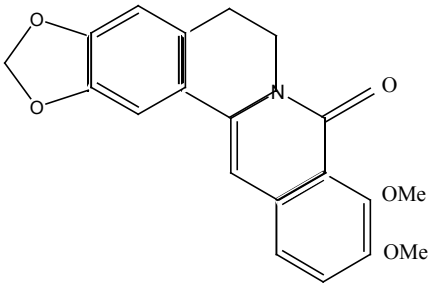

Fig. 8: Oxyberberine

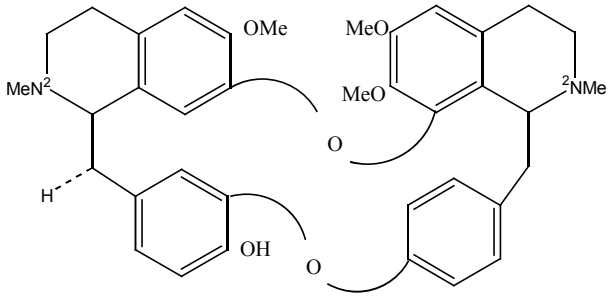

Fig. 9: Oxycanthine

The alkaloid, berberine, received the most research and widest acclaim as the active component of barberry and its relatives. It is yellow crystalline bitter alkaloid. Other constituents are oxyacanthine, berbamine and related alkaloidal matter, a little tannin, wax, resin, fat, albumin, gum and starch. Berberine and its related constituents (such as oxyacanthine) are antibacterial (Amin *et al*., 1969) have been shown to kill *amoebae* (Subbaiah *et al*., 1967) *in vitro* and inhibits the growth of many microorganisms, including fungi, protozoa, and bacteria (Hahn and Ciak, 1976; Lesnau *et al*., 1990 and Amin *et al*., 1969). Berberine inhibits bacteria from attaching human cells that helps prevent infection (Sun *et al*., 1988). This component treats diarrhea caused by bacteria, such as *E. coli* (Rabbani *et al*., 1987). Berberine also stimulates some immune system cells to function better (Kumazawa *et al*., 1984) and is an antioxidant (Wong *et al*., 1992 and Ju *et al*., 1990).

The bitter compounds in barberry, including alkaloids, stimulate digestive functions following meals. Barberry and goldenseal (Bergner, 1996) (*Hydrastis canadensis*) have very similar therapeutic uses because both contain active substances (berberine alkaloids). These substances have been shown to combat infection and bacteria, stimulate the activity of the immune system, and lower fever. Laboratory studies suggest that these substances have antimicrobial (for example, antibacterial and antiparasitic), anti-inflammatory (Ivanovska and Philipov, 1996), immune-stimulant, fever reducing, hypotensive (causing a reduction in blood pressure), and sedative, anticonvulsant, and smooth muscle effects. Smooth muscles line the gastrointestinal tract; therefore, this last

Table 1: Compounds isolated from *Berberis vulgaris*

Compound	Nature	Structure	Reference
Aromoline	alkaloid	—	(Bick *et al.,* 1953 & 1960), (Saa′ *et al.,* 1976), (Koike *et al.,* 1982), (Wu *et al.,* 1980), (Akasu *et al.,* 1976)
Berbamine	alkaloid	—	(Akasu *et al.,* 1976), (Yang *et al.,* 1960), (Gasparec *et al.,* 1968)
Berbamunine	alkaloid	—	(Yang *et al.,* 1960), (Gasparec *et al,.* 1968), (Cassels *et al.,* 1987), (Ahmed *et al.,* 1977), (Kametani *et al*., 1969), (Tses'ko *et al.,* 1974), (Martindale, 1982/1989)
Berberine	Alkaloid	Figure 2	(Yang *et al.,* 1960), (Gasparec *et al.,* 1968), (Perkin *et al.,* 1925), (Wu *et al*., 1977), (Tses'ko and Ladygina, 1974)
Berlambine	Alkaloid	Figure 3	(Yang *et al.,* 1960), (Gasparec *et al.,* 1968)
Bervulcine	Alkaloid	—	(Werner, 1963)
Chlorogenic acid	Acid phenol	—	
Columbamine	Alkaloid	Figure 4	(Pavelka and Sme′kal, 1976)
Hydroxycanthine	Alkaloid	—	(Ohmoto *et al.,* 1981), (Hagen *et al.,* 1989)
Isocorydine	Alkaloid	Figure 5	(Comin and Deulofeu, 1954), (Kuck and Faydman, 1961), (Saxena and Bhakuni, 1979), (Marsaioli *et al.,* 1979)
Jatrorrhizine	Alkaloid	—	(Yang *et al.,* 1960), (Pavelka and Sme′kal, 1976)
Lambertine	Alkaloid	Figure 6	(Chatterjee and Maiti, 1955)
Magniflorine	Alkaloid	—	(Rumbero *et al.,* 1991)
Magnoflorine	Alkaloid	Figure 7	(Ivanovska and Philipov, 1996), (Yang *et al.,* 1960), (Nakano, 1954), (Slavik and Dolejs′, 1973), (Dominguez, 1974)
Oxyberberine	Alkaloid	Figure 8	(Yang *et al.,* 1960), (Gasparec *et al.,* 1968), (Pavelka and Kovar, 1976), (Cushman and Dekow, 1979)
Oxycanthine	Alkaloid	Figure 9	(Gasparec *et al.,* 1968), (Baldas *et al.,* 1972), (Kuroda *et al.,* 1976), (Bhakuni *et al.,* 1978), (Hearth *et al.,* 1987)
Palmatine	Alkaloid	—	(Yang *et al.,* 1960), (Gasparec *et al.,* 1968), (Pavelka and Sme′kal, 1976), (Skerl and Gros, 1971)
Anthocyanin	Pigment	—	
Quercentin	Flavonoid	—	(Gasparec *et al.,* 1968), (Wu *et al.,* 1977)
Rutin	Flavonoid	—	(Gasparec *et al.,* 1968)
(-)-tejedine	Alkaloid	—	(Kametani *et al.,* 1969)
Yatrorizine	Alkaloid	—	(Gasparec *et al.,* 1968)

effect may help improve digestion and reduce stomach pain. Oxyacanthine was less effective than berberine (Ivanovska and Philipov, 1996). Common barberry leaves contain a small but diverse polysaccharide fraction which afforded an α-glucan, a β-xylan, and three neutral, and two galacturonic acid containing glucoxylans. Only the α-glucan was devoid of protein. The α-glucan is primarily (1→4)-linked, but some residues are branched through C-3 or C-6. The flowers contain sugar and an essential oil while malic acid is present in the berries.

Edible uses

Fruit - raw or cooked (Hedrick, 1972; Simmons, 1972; Mabey, 1974; Chiej, 1984; Launert, 1981; Bean, 1981; Saunders, 1976 and Facciola, 1990). Rich in vitamin C (Staurt, 1979), has a very acid flavor and is mainly used in preserves (Polunin, 1969), though children and some adults like it raw when it is fully ripe. A refreshing lemon-like drink can be made from the fruit (Facciola, 1990). The fruits are about 10mm long (Huxley, 1992). Young leaves are used as flavouring or as an acid nibble (Kunkel, 1984 and Facciola, 1990). They can be used in much the same way as sorrel (Rumex acetosa). The dried young leaves and shoot tips make a refreshing tea (Launert, 1981 and Facciola, 1990).

Medicinal uses

Barberries have long been used as a herbal remedy for the treatment of a variety of complaints. The main chemical constituent berberine possesses a wide range of biochemical and pharmacological activities, viz. antidiarrheal, antiarrhythmic anti-inflammatory, fever-reducing, analgesic (pain-reducing) effects (Kupeli *et al*., 2002 and Yesilada and Kupeli, 2002) and antitumor activities (Takase *et al*., 1993; Huang *et al*., 1989; Fukuda *et al*., 1999a, 1999b). Barberry fruit may have anti-hypertensive and antihistaminic effects (Shamsa *et al*., 1999 and Fatehi-Hassanabad *et al*., 2005).

All parts of the plant can be used though the yellow root bark which is the most concentrated source of active ingredients. Extracts obtained from the roots of Berberidaceae species have been used in Eastern and

Bulgarian folk medicine in rheumatic and other chronic inflammatory disorders. The total ethanol extract (TEE) of berbrine and oxacanthine showed the heighest reducing effect when applied against acute inflammation (carrageenan- and zymosan- induced paw edema). TEE was also most effective in a chronic inflammatory model of adjuvant arthritis. The proto-berberine fractions Bv2, Bv3 and berberine suppressed a delayed type hypersensitivity (DHT) reaction.

Barberry may also be an effective treatment for diarrhea (Kaneda *et al*., 1991) (including traveler's diarrhea and diarrhea caused by food poisoning). A few studies have suggested that barberry improves symptoms faster than antibiotics (Rabbani *et al*., 1987 and Shamsa *et al*., 1999) but may be less effective than the drugs in clearing bacterial organisms out of the intestines. Because of the serious consequences associated with bacterial diarrhea, if barberry is used to ease symptoms, it is best to take the herb along with standard antibiotic therapy for this condition.

It is used in *pitta* detoxification, congestion of abdomen and in pelvic cavities. It is an excellent herb in scarlet fever, brain disorders, heat, thirst, nausea; periodic neuralgia, fevers, vomiting in pregnancy; blood purifier. Gastric and duodenal ulcers; sores. Used in diabetes. It is prescribed for renal calculi, abdominal and pelvic congestion. It acts as a G.I. stimulant and Barberry tends to dilate the blood vessels, thereby lowering blood pressure.

Barberry is one of the best remedies for correcting liver function and promoting the flow of bile. When jaundice occurs due to a congested state of the liver, Barberry is also indicated. It is proved as excellent remedy for dyspepsia and functional derangement of the liver. It is an excellent herb to treat enlarged liver and spleen and regulates liver function. It destroys toxins and reduces body fat (with turmeric). It is used in all cases of jaundice, generally debility and biliousness. Berberine has been reported to interfere with normal liver function in infants, raising a concern that it might worsen jaundice (Chan, 1993). For this reason, berberine- containing plants, including barberry, goldenseal and Oregon grape should be used with caution during pregnancy and breast-feeding (Blumenthal *et al*., 1998).

A tea made from the bark of barberis is taken during the spring months as a blood purifier. A strong decoction is employed as an application to the *sores,* which sometimes afflict children's lips. The berries form an agreeable acidulous draught, useful as a refrigerant in fevers. It possesses febrifuge powers and is used as a remedy for intermittent fevers.

Berberidaceae roots have been used in European folk medicine for inflammation. Total ethanol extract inhibited induced paw edema. Berberine suppressed delayed type hypersensitivity more than oxyacanthine (Ivanovska and Philipov, 1996). It helps in regulating the digestive powers and if given in large doses it acts as a mild purgative and removes constipation. Barberry is also claimed to have anti-viral activities, and as a treatment for chronic candidiasis, indigestion and parasites (USDA, 2003).

Herbalists recommend barberry as a stimulating tonic for liver. It influences the mucosa generally, removing mucoid accumulations and controlling excess secretion. Improves appetite, digestion and assimilation. Indicated for gouty constitutions.

Berberine and its related constituents (such as oxyacanthine) are antibacterial (Amin *et al*., 1969) and have been shown to kill amoebae in a test tube study (Subbaiah and Amin, 1967). Berberine inhibits bacteria from attaching to human cells, which helps prevent infection (Sun *et al*., 1988). This compound treats diarrhea caused by bacteria, such as *E. coli* (Rabbani *et al*., 1987). Berberine also stimulates some immune system cells to function better (Kumazawa *et al*., 1984) Berbamine is another alkaloid found in barberry. It may help reduce inflammation (Wong *et al*., 1992) and is an antioxidant (Ju *et al*., 1990).

Laboratory studies have shown that berberine has some activity against *E. histolytica* in mice (Hostettman *et al*., 1995). The astringent property makes it useful against bilious disorders.

Barberis contain citric acid and malic acid and due to these possesses astringent, and anti scorbutic properties useful in inflammatory fevers, especially typhus, and scurvy, and in the form of a jelly, are very refreshing for irritable sore throat; syrup of berberis made with water is used as an excellent astringent gargle. The fresh juice of the fruit is also said to strengthen the gums and relieve pyorrhea when brushed on or applied directly to the gums. A decoction of the bark or berries has been found of service as a wash in aphthous sore mouth, and in chronic ophthalmia.

In distilled water, barbery fruit extract showed 73.62% (higher than in ethanol) free radical scavenging activity. Another study shows that it has anti-inflammatory properties, useful for treating arthritis. More work is needed in this case. It forms a good lotion for application to cutaneous eruptions and a reliable treatment for acne. It also act as a stimulant for the circulatory and respiratory systems (Blumenthal, 1998). It is used for treating pinkeye and conjunctivitis.

It acts against malaria. Pyrimethamine effect on cholroquine-resistant malaria was increased more by berberine (74%) than by tetracycline (67%) or

cotrimoxazole (48%) in a randomized clinical trial with 215 patients (Sheng *et al*., 1997).

Strong standardized extracts may cause stomach upset and should be used for no more than two weeks continuously. Other symptoms of excessive berberine intake include lethargy, nosebleed, skin, and eye and kidney irritation (Blumenthal, 1998).

Berberine chloride had a higher bacteriostatic activity against *Staphylococcus epidermidis, Neisseria meningitidis, Escherichia coli,* and other *bacteria* than did chloramphenicol.

The constituents berberine, columbamine, and oxyacanthine show evidence of antibacterial activity, with some suggestion that berberine sulfate might be amebicidal and trypanocidal (Foster and Tyler, 1999 and Lueng and Foster, 1996). Research indicates that berberine is specifically effective against *cholera*, *giardia*, *shigella*, *salmonella* and *E. coli* (Chevallier, 2001).

Berberis vulgaris (*Berberis Vulgaris-Q)* is very useful in treatment of stones in the urinary tract. The main constituent of this stone is calcium oxalate. Recent studies show that calcium oxalate is precipitated out in the presence of berberis vulgaris and some citrus fruit juices (Das *et al*., 2004).

Isocorydine is adrenosytic, sedative and cholineragic agent shows virtually no antitussive activity.

Anti arrhythmic, antihypertensive and cardiovascular affects of the extract of berberis fruit

Berberis vulgaris fruit (barberry) is known for its antiarrhythmic and sedative effects in Iranian traditional medicine. The aqueous extract of barberry has beneficial effects on both cardiovascular and neural system suggesting a potential use for treatment of hypertension, tachycardia and some neuronal disorders, such as epilepsy and convulsion.

In a study to evaluate the cardiovascular effects of the extract of *Berberis vulgaris* fruit it is found that it has a potent hypotensive effect and was an opener of potassium channels activated by cell membrane depolarization. Experimental evidence exists for sedative effects of the *Berberis vulgaris* fruit extract (Fatehi *et al*., 2005). It has been reported that berberine blocked potassium currents in acutely isolated CA1 pyramidal neurons of rat hippocampus (Wang *et al*., 2004).

It has been shown that berbamine also prevented ventricular fibrillation probably through inhibition of sodium and calcium overload (Zhang *et al*., 1992). Augmentation of potassium currents caused by the extract may contribute to its vasodilatory and antiarrhythmic effects. There is evidence that phenolic compounds are present in barberry (Pozniakovskii *et al*., 2003). It has been shown that phenolic compounds increase potassium channels activity. Vasorelaxation induced by some polyphenolic compounds were inhibited by potassium channel blockers (Kim *et al*., 2000).

As anticancer agent

Berberis vulgaris can also act as an anticancer agent. Research in this regard is still going on. The following studies have been done in this regard which clearly indicate that berberis vulgaris can act as an anticancer agent.

Coptidis rhizoma, containing abundant berberine, is shown to inhibit the proliferation of esophageal cancer cells (Iizuka *et al*., 2000). Berberine inhibits cyclo-oxygenase-2 transcriptional activity in human colon cancer cells (Fukuda *et al*., 1999 and Lin *et al*., 1999) and preliminary studies have shown that berberine sulfate inhibits tumor promoting activity of teleocidin in two-stage chemical carcinogenesis on mouse skin (Nishino *et al*., 1986). Berberine also inhibits DNA topoisomerase I and II in biochemical system (Wang *et al*., 1996 and Kim *et al*., 1998) and in fact, several classes of compounds that inhibit eukaryotic topoisomerase I or II have antitumor activity (Liu, 1989).

Berberine has been shown to possess anti-inflammatory and antitumor properties in some *in vitro* systems. The *in vitro* treatment of androgen-insensitive (DU145 and PC-3) and androgen-sensitive (LNCaP) prostate cancer cells with berberine inhibited cell proliferation and induced cell death in a dose-dependent (10–100 μmol/L) and time-dependent (24–72 hours) manner. Treatment of non-neoplastic human prostate epithelial cells (PWR-1E) with berberine under identical conditions did not significantly affect their viability. The effectiveness of berberine in checking the growth of androgen-insensitive, as well as androgen-sensitive, prostate cancer cells without affecting the growth of normal prostate epithelial cells indicates that it may be a promising candidate for prostate cancer therapy (Sudheer *et al*., 2006).

One study shows that the herb might shrink some tumors. Another study indicates that berberine inhibits growth, induces G_1 arrest and apoptotic cell death of human epidermoid carcinoma A431 cells. It also provide mechanistic evidences that berberine-induced apoptosis in human epidermoid carcinoma cells is mediated through disruption of mitochondrial membrane potential and activation of caspase 3 pathway, although other pathways may have a role and that require further investigation. Moreover, further *in vivo* studies are required to determine whether berberine could be an effective chemotherapeutic agent for the prevention of non-melanoma skin cancers (Sudheer *et al*., 2006).

Available dosage formulations

Barberry is available in capsules, fluid extracts, tinctures, and as a topical ointment. Dried roots of barberry can also be used in tea. Barberry extracts are standardized to contain 8% to 12% isoquinoline alkaloids.

Related species

Berberis Canadensis is only indigenous species of the Berberis proper and very closely resembles the berberis vulgaris, but a smaller shrub, with smaller leaves, berries, and smaller and fewer flower racemes. Its locality is farther South than the introduced species, being a native of the Southern States. The acidity of the fruit and leaves and the yellow color of the wood are also observed in this species. It closely resembles the berberis in medicinal properties. Doubtless, it contains much the same principles, as the two species closely resemble each other and are used commonly for the same purpose

Precautions

The use of herbs is a time-honored approach in strengthening the body and treating disease. Herbs, however, contain active substances that can trigger side effects and that can interact with other herbs, supplements, or medications. Barberry is generally considered safe when consumed orally and appropriately for medicinal purposes, but due to its moderately toxic properties, cannot be recommended for consumption in quantities over 500 mg. Those using normal and appropriate doses of barberry do not generally report side effects. In high doses, barberry can cause nausea, vomiting, convulsions, hazardous drops in blood pressure, and depression of the heart rate and breathing. People suffering from heart disease or chronic respiratory system, should not take large doses of this herb and should use it only with the approval of doctor.

Due to the lack of reliable studies on the use of Barberry during periods of lactation, it is not recommended for use while breast-feeding (Jellin *et al*., 2000). Use only in medicinal amounts. If the herb causes dizziness or faintness, stop using the herb immediately. It is not recommended for children under 2 years of age. For older children and those above 65, a low strength is recommended.

Barberry has been classified as unsafe to take during pregnancy due to its uterine stimulant properties that may cause uterine contractions and trigger miscarriage. Berberine-containing herbs should not be used by pregnant women because berberine may increase levels of bilirubin (Chan, 1993) potentially damaging the fetus, and might also cause genetic damage(Pasqual *et al*., 1993). One study suggests that topical use of berberine could cause photosensitivity, an increased tendency to react to sun exposure (Inbaraj *et al*., 2001). Individuals who already have elevated levels of bilirubin (jaundice), or any other form of liver disease, should also avoid berberine-containing herbs. One study hints that berberine may decrease the efficacy of the drug tetracycline (Khin-Maung, 1985).

Berberine has been reported to interfere with normal liver function in infants, raising a concern that it might worsen jaundice (Chan, 1993). For this reason, berberine-containing plants, including barberry, goldenseal, and Oregon grape should be used with caution during pregnancy and breast-feeding. Strong standardized extracts may cause stomach upset and should be used for no more than two weeks continuously. Other symptoms of excessive berberine intake include lethargy, nose bleed, skin and eye irritation, and kidney irritation.

Barbery should be used only in medicinal amounts if the herb causes dizziness or faintness it should de discontinued immediately.

Possible interactions

One double-blind study found that giving 100 mg of berberine at the same time as 500 mg of tetracycline four times daily led to a reduction of the efficacy of tetracycline in people with cholera (Maung *et al*., 1985). Berberine may have decreased the absorption of tetracycline in this study. Another double-blind trial did not find that berberine interfered with tetracycline in cholera patients (Rabbani *et al*., 1987). Until more studies are completed to clarify this issue, berberine-containing herbs should not be taken simultaneously with tetracycline (Maung *et al*., 1985).

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