BARBERRY

Berberis vulgaris L.

Family

Berberidaceae, a family of 19 genera of flowering plants commonly called the barberry family. The common name barberry includes *B. repens, B. aqilfolia, B. nervosa, B. pinnata* and other Berberis species, which are used interchangeably with *B. vulgaris*. Many species of Berberis are used for their herbal qualities which are quite similar among species. For example, *B. aristata*, or *B. daruharidra*, is a well-known and versatile herb in Ayurveda, several species of barberry are used in Chinese medicine, and *B. aquifolium*, the Oregon grape, is native to North America, where it has a long history of use in herbalism.[1,2,3]

Parts Used

Bark

Description

Barberry is native to Europe, the British Isles, northwest Africa and western Asia. It was introduced to America during the 17th century where it is now naturalised. This species currently has a limited naturalised distribution in Australia. It is sparingly naturalised on the southern tablelands of New South Wales and is possibly also naturalised in Tasmania. Barberry is regarded as an environmental weed in the southern highlands of New South Wales and as a sleeper weed (non-native plants that have naturalised but have not yet reached their potential to form large and widespread populations in Australia) in other parts of south-eastern Australia. Barberry is an attractive, deciduous, thorny shrub that can reach four metres in height. Its branches arch downwards, and come into contact with the ground, where it takes root and produces new shoots (suckers) providing a dense habitat

that is invaluable as wildlife-friendly hedging and screening, often used as a windbreak. It has small, leathery, serrated oval leaves and abundant hanging small, yellow flowers which are attractive but have an unpleasant odour and turn into a scarlet red, oblong fruit. The sharply acidic berries are edible and are eaten in many countries as a tart and refreshing fruit. Iran is the largest producer of *B. vulgaris* fruit in the world, with 11,000 hectares of land under cultivation. Over 10,000 tons of dried *B. vulgaris* fruit are produced in Iran per year. Consequently many clinical and laboratory studies originate from here. The Persian name for barberry is *zereshk*. It is mainly used as a food cooked with rice. *B. integerrima*, also referred to as black barberry and wild barberry, is used mainly for juice extraction in food industrises.[4,5,6]

Sustainability

According to the International Union for Conservation of Nature and Natural Resources Red List of Threatened Plants status, barberry is classified as Least Concern in Europe due to its widespread distribution, presumed stable populations and no major threats. Barberry can become invasive so it is important to control its growth and ensure that it does not escape the garden into natural habitats where it crowds-out and displaces beneficial native plants. Barberry is an alternate host for a potentially damaging stem rust disease of wheat crops making it unpopular with farmers after it decimated crops in the 19th century.[7]

Barberry is an excellent substitute for golden seal (*Hydrastis canadensis*). Like golden seal barberry has significant amounts of the isoquinoline alkaloid berberine, which gives it a similar action, although it is lacking hydrastine. Golden seal has become overharvested and is listed on the CITES Appendix II meaning that trade is controlled to avoid utilisation that could threaten the survival of this plant. When golden seal is available its price from sustainable sources steadily increases. These environmental issues, and the fact that it is expensive, mean that practitioners have been searching for substitutes. For this reason, barberry is used as a substitute for golden seal.

Traditional and empirical use

Barberry has played a prominent role in herbal healing for more than 2500 years and has a rich history of use in traditional eastern and western herbalism. Almost every civilization has used barberry in one way or another. The ancient Egyptians used it with fennel seed to prevent plagues. India's Ayurveda healers used it for dysentery, skin inflammations, high blood pressure and abnormal uterine bleeding. American Indians used barberry to improve appetite, an action that was soon picked up by early American settlers. It was also reportedly used for treating stomach problems such as ulcers and heartburn. Barberry is a powerful herb that has been widely used as a cholagogue to treat liver and gallbladder ailments. This was the result of herbalists during the early Middle Ages being guided by the doctrine of signatures, the belief that a plant's physical appearance reveals its therapeutic benefits. Barberry has yellow flowers and its roots produce a yellow dye. It was these features that were linked to the yellowing of the skin and eyes of jaundice, a symptom of liver disease, and which earned the plant the name jaundice berry.[8,9]

In addition to using barberry for liver and gallbladder problems, traditional Russian healers recommended it for inflammations, high blood pressure and abnormal uterine bleeding. Avicenna, in his Canon of Medicine which is one of the most influential medical books in history, writes of barberry being markedly cooling and drying. He says "it is very strong for eradicating the yellow bile and for swellings and pimples. It strengthens the stomach and liver and quenches the thirst." Harvey Wickes Felter (author of the Eclectic Materia Medica (1895) and co-author of King's American Dispensatory (1854)) writes: "Barberry acts much like [golden seal] and could be employed for many of the uses of that scarce and high-priced drug so far as the berberine effects are required. The fluid preparations are asserted to act more kindly and more efficiently than berberine itself…It is decidedly tonic and if pushed, purgative. Used short of its cathartic action it is of value in non-obstructive jaundice and in gastric and intestinal dyspepsia. In renal catarrh, occasioned by the presence of calculi, small doses

may be given when there is burning and soreness and excess of mucus in the urinary tract."[10]

In *The Complete Herbal*, originally published in 1653, Culpeper attributes the barberry shrub to Mars (in relation to medical astrology) and recommends its use to purge the body from *choler*, which was one of the four bodily humours associated with bile and anger in medieval science and medicine. Interestingly, Culpeper writes that the fruits are equally as good to use as the bark, but simply have a better taste.[11]

Herbalist Richard Whelan says "a person who has not been able to pull themselves out of a chronic illness because they are encumbered, congested, bogged down by tiredness and toxicity, can be the ones who benefit the most from such a medicine as barberry, because it is a superb liver tonic." It can be taken in the spring months as a blood-purifier to wake-up the body and move-out accumulated metabolic waste and stagnation from the winter. He combines it with dandelion root (*Taraxacum officinale*) and burdock (*Arctium lappa*) for deep blood cleansing programs and with liquorice (*Glycyrrhiza glabra*) to cleanse and tone the bowel. For a strong liver program he uses it with celandine (*Chelidonium majus*) and a small amount of poke root (*Phytolacca americana*). Combining it with red clover (*Trifolium pratense*) and clivers (*Galium aparine*) is a good lymphatic system cleanser for problems such as swollen glands, eruptive skin or sore joints.[12]

Constituents

Isoquinoline alkaloids (acanthine, berbamine, berberine, columbamine, jatrorrhizine, lambertine, magnoflorine, palmatine, thaliemidine), flavonoids (chrysanthemin, delphinidin, pelargonin, petunidin), tannins, phenolic compounds, triterpenes (lupeol, oleanolic acid), sterols (stigmasterol, stigmasterol glucoside), flavanols.

Actions

Anti-inflammatory, antioxidant, hypotensive, hepatoprotective, hepatic, cholagogue, choleretic, antiemetic, mild laxative, bitter, anthelmintic, vermifuge, antimicrobial, antipyretic, antirheumatic, depurative, immunomodulant.

Pharmacological activity

Traditionally different parts of barberry are used in cases of an enlarged liver, jaundice, acne and other conditions. Unfortunately it is not always clear in the literature what parts are used. The studies presented here are limited to the use of *B. vulgaris* stem bark extract, rather than fruit or root bark studies, unless otherwise stated. Most clinical trials use isolated alkaloids from the *Berberis* species, particularly berberine which has well documented pharmacological actions followed by berbamine, both being strongly antimicrobial in preclinical studies. The berberine doses used in many clinical trials is higher than what could be achieved in using liquid herbal extracts. Some of the other alkaloids have hypotensive and antineoplastic activity *in vitro*. There are very few human clinical trials that use extracts from *B. vulgaris*. While there are a growing number of clinical trials with different kinds of barberry products, the number of participants is still very small. A large number of studies in the literature are cell culture or animal studies which confirm the actions and traditional use. These have not been included given that they would need to be replicated in humans in order to draw meaningful conclusions. The indications are based on traditional use.[13]

Hepatic Activity

A study investigating the potential of barberry to induce changes in liver enzymes levels to treat non-alcoholic fatty liver disease (NAFLD) found a significant decrease in the liver enzymes, triglycerides, weight and cholesterol after using the extract. This clinical trial was conducted on 80 patients, including 32 males and 48 females, who were randomly assigned into two groups of case and control. All the patients had ultrasound evidence of lipid accumulation in the liver and increases in liver enzymes. The case group received two capsules (750mg) containing barberry extract every day for three months, while the control group was treated with placebo. NAFLD is the most prevalent liver disorder in western countries and an important cause of liver cirrhosis, as well as liver failure. It is one of the most prevalent causes for increases in liver enzymes and has a close relationship with obesity, dyslipidaemia, hypertension and type 2 diabetes. The researchers said further studies, with larger sample sizes, will identify the accurate dose

as well as duration of consumption for this extract, to recommend in the treatment of patients with NAFLD.[14]

Antimicrobial Activity

Research shows that full-spectrum extracts of barberry are more antimicrobial than pure berberine extracts reiterating the power of herbal synergy and full-spectrum plant medicine. It is well-known that berberine has antibacterial effects against strains of methicillin-resistant *Staphylococcus aureus*. However, recent studies have shown a synergistic effect of the many compounds present in barberry. A recent study showed that whole barberry extract was more effective against *S. aureus* than berberine alone because several barberry species have an inhibiting effect on multidrug resistance pumps, which protect microbial cells from antimicrobials. In this way the barberry extract was preventing bacteria from pumping berberine out of their cells, enhancing the antimicrobial effects.[15]

A double-blind clinical trial evaluating the clinical effects of a dental gel containing barberry extract found that it effectively controlled microbial plaque and gingivitis in school aged children. In the study 45 boys, aged 11 to 12 years, were divided into three groups. The first group used barberry gel and the second group used placebo gel without an active ingredient. The third group used Colgate antiplaque toothpaste in order to draw a comparison to any possible antimicrobial effects of the barberry extract. The results showed that there was significant difference between barberry and placebo groups and between placebo and Colgate groups. The difference between barberry and Colgate groups was not significant.[16]

The use of barberry for skin conditions, which has been widely described, seems to be confirmed by an interesting, yet small, clinical study that looked into consumption of fresh berry juice and its effects on acne lesions in a group of 38 patients with mild to moderate acne. The researchers attribute the anti-inflammatory effects to the alkaloid berberine, however, this is controversial as some authors say there is no berberine in the fruit. It is more likely to be attributed to the antioxidant properties of phenolic compounds found in the fruits. These compounds help prevent lipid peroxidation and oxidative stress, believed to be involved in inflammatory reactions in acne. The stem bark also contains antioxidants.[17]

Diabetic Activity

A significant number of clinical studies have looked into the antidiabetic effects of the alkaloid berberine. However only a few clinical trials using the fruit extract, rather than the stem extract, have assessed the effects of barberry extract on diabetic patients. In these studies the researchers concluded that barberry fruit can have a positive effect on glycaemic control and total antioxidant capacity in patients with type 2 diabetes.[18]

Indications

- Liver dysfunction, sluggish liver, promoting the flow of bile, hepatitis, jaundice (when there is no obstruction of the bile ducts), biliousness, inflammation of the gallbladder, gallstones, cirrhosis of the liver, autism, autism spectrum disorders and attention deficit hyperactivity disorder where liver support is required.
- Acute gastrointestinal infection with non-viral diarrhoea, digestive stimulant, irritable bowel syndrome, diarrhoea including traveller's diarrhoea, chronic diarrhoea and dysentery, peptic ulcer, constipation (in larger doses), haemorrhoids (due to the secondary effects of vascular congestion), dyspepsia, gastritis, parasitic infection or giardiasis
- Malaria, leishmaniasis (a protozoan infection) including topically
- Adjuvant therapy for type 2 diabetes, insulin resistance, metabolic syndrome, hyperglycaemia
- Debility during convalescence, history of dietary or alcohol abuse or excessive exposure to drugs, chemicals or industrial pollutants, loss of appetite
- Autoimmune diseases such as rheumatoid arthritis, possibly prophylactically for cancer
- Urinary tract infections
- Skin inflammation, such as acne and mild eczema, including topically
- Prevention of hypertension, tachyarrhythmia, to lower peripheral vascular resistance, heart disease, including arrhythmia.
- Topically as a gargle to relieve mild mouth ulcers

Energetics

Bitter, cooling.[19]

Use in Pregnancy

Contraindicated during pregnancy, due to its uterine stimulant properties that may cause uterine contractions and trigger miscarriage, lactation and in neonatal jaundice.[20]

Contraindications and Cautions

Do not take excessive doses or give to jaundiced neonates. Caution may be warranted in patients with gallstones due to the potential for impacted gallstones and obstructed bile ducts.[21]

Drug Interactions

Avoid combining with cyclosporin (an immunosuppressant medication) because of theoretical increased risk of drug toxicity. The constituent berberine has been reported to significantly increase drug serum levels in renal-transplant patients.

Caution with the combined use of anticoagulant/antiplatelet drugs due to theoretical risk of increased bleeding based on preclinical trials on the constituent berberine. This has not been demonstrated in human studies.

Caution with the combined use of antidiabetic drugs due to theoretical additive effects such as increased risk of hypoglycaemia. This is based on the constituent berberine which may lower blood glucose levels.

Caution with the combined use of central nervous system depressant drugs (such as benzodiazepines, barbiturates, certain sleep medicines and antihistamines some known as Valium, Xanax, Prozac, Rohypnol and Zoloft) due to increased risks of sedative effects. This theoretical risk of excessive drowsiness is based on animal research on the constituent berberine.

Caution with combined use of cytochrome P450 (CYP) enzymes substrates due to theoretical risk of drug toxicity. CYP enzymes metabolise about 60% of prescription drugs, with CYP3A4 being responsible for about half of that. This is based on preclinical evidence on the constituent berberine. More data is needed to determine the significance of this interaction.

Monitor with the combined use of anticholinergic drugs (including antihistamines and tricyclic antidepressants) due to a theoretical risk of increased adverse and additive effects based on *in vitro* evidence.

Monitor for hypotension with the combined use of antihypertensive drugs due to theoretical additive effects, although this may not be clinically significant. This is based on evidence for the constituent berberine.

Monitor with the combined use of cholinergic drugs (such as donepezil and tacrine used for Alzheimer's disease) due to a decreased drug effect based on *in vitro* evidence although the clinical significance of this interaction is unknown.[22]

Administration and Dosage

Liquid Extract:	1:1
Alcohol:	25%
Weekly Dosage:	20 to 60mL[23]

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