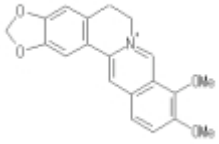
Berberine



While some complementary and alternative techniques have been studied scientifically, high-quality data regarding safety, effectiveness, and mechanism of action are limited or controversial for most therapies. Whenever possible, it is recommended that practitioners be licensed by a recognized professional organization that adheres to clearly published standards. In addition, before starting a new technique or engaging a practitioner, it is recommended that patients speak with their primary healthcare provider(s). Potential benefits, risks (including financial costs), and alternatives should be carefully considered. The below monograph is designed to provide historical background and an overview of clinically-oriented research, and neither advocates for or against the use of a particular therapy.

Related Terms:

- Acetone, berberine, barberry, benzophenanthridine alkaloid, berberin, berberin hydrochloride, berberine alkaloid, berberine bisulfate, berberine chloride, berberine complex, berberine hydrochloride, berberine iodide, berberine sulfate, berberine tannate, *Berberis aquifolium*, *Berberis aristata*, *Berberis vulgaris*, *Coptis chinensis*, coptis, goldenthread, goldenseal, *Hydrastis canadensis*, jiang tang san, Oregon grape, protoberberine, protoberberinium salts, tree turmeric.

BACKGROUND

- Berberine is a bitter-tasting, yellow, plant alkaloid with a long history of medicinal use in Chinese and Ayurvedic medicine. Berberine is present in the roots, rhizomes and stem bark of various plants including *Hydrastis canadensis* (goldenseal), *Coptis chinensis* (coptis or goldenthread), *Berberis aquifolium* (Oregon grape), *Berberis vulgaris* (barberry), and *Berberis aristata* (tree turmeric). Berberine has also been used historically as a dye, due to its yellow color.
- Clinical trials have been conducted using berberine. There is some evidence to support its use in the treatment of trachomas (eye infections), bacterial diarrhea, and leishmaniasis (parasitic disease). Berberine has also shown antimicrobial activity against bacteria, viruses, fungi, protozoans, helminths (worms), and chlamydia (STD). Future clinical research is warranted in these areas, as well as cardiovascular disease, skin disorders, and liver disorders.
- Berberine has been shown to be safe in the majority of clinical trials. However, there is a potential for interaction between berberine and many prescription medications, and berberine should not be used by pregnant or breastfeeding women, due to potential for adverse effects in the newborn.

SCIENTIFIC EVIDENCE

Uses *These uses have been tested in humans or animals. Safety and effectiveness have not always been proven. Some of these conditions are potentially serious, and should be evaluated by a qualified healthcare provider.*	Grade*
Heart failure	

Preliminary research suggests that berberine, in addition to a standard prescription drug regimen for chronic congestive heart failure (CHF), may improve quality of life and heart function, and improve mortality. Further research is necessary before a firm conclusion can be drawn in this area.	B
Chloroquine-resistant malaria One trial has assessed the use of berberine in combination with pyrimethamine in the treatment of chloroquine-resistant malaria. Well-designed clinical trials are still required in this field.	C
Diabetes (type 2) Historically, berberine has been suggested to aid in glycemic regulation. The safety and effectiveness of berberine for this indication remains unclear. More research is needed in this area.	C
Glaucoma Preliminary study of berberine does not appear to reduce intraocular pressure in patients with glaucoma. The safety and effectiveness of berberine for this indication remains unclear. Additional study is needed in this area.	C
H. pylori infection Berberine has been compared with antibacterial drugs and ranitidine in stimulation of ulcer healing and *Helicobacter pylori* clearance. Berberine was suggested to be less effective at ulcer healing than ranitidine, but potentially more effective at *Helicobacter pylori* clearance. Additional study is needed in this area.	C
Hypercholesterolemia (high cholesterol) Berberine may reduce triglycerides, serum cholesterol, and LDL cholesterol. Higher quality trials are needed before berberine's cholesterol-lowering effect can be established.	C
Infectious diarrhea Berberine has been evaluated as a treatment for infectious diarrhea, including choleric diarrhea, although the data is conflicting. Therefore, there is currently insufficient evidence regarding the efficacy of berberine in the management of infectious diarrhea.	C

Parasitic infection (leishmania) The benefits of berberine in the treatment of leishmaniasis are widely accepted. Berberine is thought to be equally efficacious as the standard drug treatment of cutaneous leishmaniasis, antimonite (sulfide mineral), although limited study of this treatment probably limits its widespread use. Additional study is needed to confirm these results.	C
Thrombocytopenia (low platelet count) Berberine has been shown to significantly increase platelet production in individuals with thrombocytopenia both as monotherapy and adjunctive therapy. Additional human study is needed to confirm these results.	C
Trachoma (eye disease) Berberine has been found to possess antimicrobial properties, and there is limited evidence of anti-inflammatory properties as well. Preliminary evidence suggests that berberine eye preparations may be beneficial for trachoma. However, the safety and efficacy of berberine for this indication remains unclear.	C
*Key to grades: ***A**: Strong scientific evidence for this use; **B**: Good scientific evidence for this use; **C**: Unclear scientific evidence for this use; **D**: Fair scientific evidence against this use (it may not work); **F**: Strong scientific evidence against this use (it likely does not work).	

TRADITION/THEORY

The below uses are based on tradition, scientific theories, or limited research. They often have not been thoroughly tested in humans, and safety and effectiveness have not always been proven. Some of these conditions are potentially serious, and should be evaluated by a qualified healthcare provider. There may be other proposed uses that are not listed below.

- Alcoholic liver disease, antibacterial, anticonvulsant, antifungal, anti-inflammatory, antimicrobial (typanosomes), antioxidant, antiviral, arthritis, bile secretion, burns, cancer, cardiovascular disease, dental conditions (root canal), dental hygiene, eye infections (general), fatigue, fever, headaches, high blood pressure, immunostimulant, irritable bowel syndrome (IBS), leukemia, leukopenia, liver disease (alcoholic), osteoporosis, respiratory disorders, sedative, skin infections, urinary tract infection, ventricular tachyarrhythmias, yeast infections.

DOSING

The below doses are based on scientific research, publications, traditional use, or expert opinion. Many herbs and supplements have not been thoroughly tested, and safety and effectiveness may not be proven. Brands may be made differently, with variable ingredients, even within the same brand. The below doses may not apply to all products. You should read product labels, and discuss doses with a qualified healthcare provider before starting therapy.

Adults (18 years and older)

- A wide range of doses has been studied for berberine, although no dose has been proven effective. Berberine is possibly safe when taken by mouth in doses up to 2 grams daily for eight weeks. For hypercholesterolemia (high cholesterol), 0.5 gram of berberine twice daily for three months has been used. For infectious diarrhea, berberine sulfate 400 milligrams as a single dose has been used. For thrombocytopenia, berberine bisulfate 5 milligrams, three times daily (20 minutes before meals) for 15 days has been used.
- As an injection into the vein, berberine has been infused at a rate of 0.2 milligrams/kilogram per minute for 30 minutes. Injections should only be given under the supervision of a qualified healthcare professional, including a pharmacist.
- For trachoma, 0.2% berberine eye drops have been studied for eight weeks.

Children (younger than 18 years)

- There is no proven effective dose for berberine in children. Nonetheless, berberine is possibly safe when used in otherwise healthy children, as young as two months, at recommended doses for treatment of diarrhea up to six days.

SAFETY

The U.S. Food and Drug Administration does not strictly regulate herbs and supplements. There is no guarantee of strength, purity or safety of products, and effects may vary. You should always read product labels. If you have a medical condition, or are taking other drugs, herbs, or supplements, you should speak with a qualified healthcare provider before starting a new therapy. Consult a healthcare provider immediately if you experience side effects.

Allergies

- Avoided in individuals with a known allergy or hypersensitivity to berberine, to plants that contain berberine [*Hydrastis canadensis* (goldenseal), *Coptis chinensis* (coptis or goldenthread), *Berberis aquifolium* (Oregon grape), *Berberis vulgaris* (barberry), and *Berberis aristata* (tree turmeric)], or to members of the Berberidaceae family. Allergic reactions have been reported, with symptoms of vomiting, itching, and a feeling of faintness.

Side Effects and Warnings

- Berberine has been reported to cause nausea, vomiting, hypertension (high blood pressure), respiratory failure and paresthesias (abnormal sensations such as numbness or tingling); however, clinical evidence of such adverse effects is not prominent in the literature. Rare adverse effects including headache, skin irritation, facial flushing, headache, bradycardia (slowed heart rate) have also been reported with the use of berberine. Use cautiously when taking berberine for longer than eight weeks due to theoretical changes in bacterial gut flora.
- Use cautiously in individuals with diabetes, as both human and animal studies indicate that berberine may decrease blood sugar levels. Also use cautiously in individuals with hypotension (low blood pressure), as berberine may have antihypertensive effects.
- Patients with cardiovascular disease should also use caution as berberine has been associated with the development of ventricular arrhythmias in subjects with congestive heart failure.
- Although not well studied in humans, berberine may also theoretically cause delays in small intestinal transit time or increase the risk of bleeding.
- Berberine may cause abortion, eye or kidney irritation, nephritis (inflamed kidneys), dyspnea (difficulty breathing), flu-like symptoms, giddiness, lethargy, or liver toxicity.

- Patients with leukopenia (abnormally low white blood cell count) should use cautiously due to the potential for development of leukopenia symptoms.
- When injected under the skin, berberine may cause hyperpigmentation in the arm. Use berberine cautiously in individuals with high exposure to sunlight or artificial light due to potential for adverse phototoxic reactions.
- Avoid in newborns due to potential for increase in free bilirubin, jaundice, and development of kernicterus (brain damage caused by severe newborn jaundice). Use berberine cautiously in children due to a lack of safety information.

Pregnancy and Breastfeeding

- Berberine is not recommended in pregnant or breastfeeding women due to a lack of available scientific evidence. Although not well studied in humans, berberine has been suggested to have anti-fertility, abortifacient (abortion inducing), and uterine stimulant activity.
- Berberine may cause kernicterus (brain damage) when used in newborn jaundiced babies, such as bilirubin encephalopathy (degenerative brain disease).

INTERACTIONS

Most herbs and supplements have not been thoroughly tested for interactions with other herbs, supplements, drugs, or foods. The interactions listed below are based on reports in scientific publications, laboratory experiments, or traditional use. You should always read product labels. If you have a medical condition, or are taking other drugs, herbs, or supplements, you should speak with a qualified healthcare provider before starting a new therapy.

Interactions with Drugs

- Berberine may counter or prevent irregular heartbeat. Caution is advised when taking berberine with other agents that alter heart rate.
- Berberine may decrease the efficacy of tetracycline; in theory, berberine may decrease the efficacy of other agents with antibacterial activity.
- Berberine bisulfate may stimulate platelet formation, and berberine may have an antiheparin action. Thus, berberine may interact with certain drugs that increase the risk of bleeding, and reduce their effectiveness. Some examples include aspirin, anticoagulants ("blood thinners") such as warfarin (Coumadin®) or heparin, anti-platelet drugs such as clopidogrel (Plavix®), and non-steroidal anti-inflammatory drugs (NSAIDS) such as ibuprofen (Motrin®, Advil®) or naproxen (Naprosyn®, Aleve®). However, berberine may be hepatoprotective (liver protective) when administered before toxic doses of acetaminophen.
- Berberine may lower blood sugar levels. Caution is advised when using medications that may also lower blood sugar. Patients taking drugs for diabetes by mouth or insulin should be monitored closely by a qualified healthcare professional, including a pharmacist. Medication adjustments may be necessary.
- Berberine may decrease total and LDL cholesterol, as well as triglycerides. Caution is advised in patients taking any cholesterol-lowering agents.
- There may be additive hypotensive (blood pressure lowering) effects and bradycardia (slowed heart rate) when combining berberine with agents that lower blood pressure. Caution is advised.
- Berberine may modulate the expression and function of PGP-170 in hepatoma cells. In theory, berberine may interact with antineoplastic agents.

- Berberine and berberine sulfate have anti-inflammatory effects and may interact with COX-2 inhibitors. COX-2 inhibitor drugs include celecoxib (Celebrex®) and rofecoxib (Vioxx®).
- Berberine may elevate the blood concentration of cyclosporin A. Caution is advised.
- Berberine may interfere with the way the body processes certain drugs using the liver's "cytochrome P450" enzyme system. As a result, the levels of these drugs may be increased in the blood, and may cause increased effects or potentially serious adverse reactions. Patients using any medications should check the package insert, and speak with a qualified healthcare professional, including a pharmacist, about possible interactions.
- Although not well studied in humans, there may be a potential for synergism between berberine chloride and fluconazole. Berberine and L-phenylephrine may have additive effects when administered concurrently. Furthermore, berberine may reverse the secretory properties of neostigmine (Prostigmin®).
- Berberine and 1,3-bis (2-chloroethyl)-1-nitosurea (BCNU) may have additive effects.
- Berberine may increase sensitization to acetylcholine's hypotensive (blood pressure lowering) effects.
- P-glycoprotein may contribute to the poor intestinal absorption of berberine.
- It is been purported that berberine may have sedative effects. Although human study is lacking, caution is advised.
- Berberine may competitively inhibit the binding of yohimbine to platelets. Patients taking yohimbine should consult with a qualified healthcare professional, including a pharmacist, to check for interactions.

Interactions with Herbs and Dietary Supplements

- Berberine may counter or prevent irregular heartbeat. Caution is advised when taking berberine with other herbs that alter heart rate.
- Berberine may decrease the efficacy of tetracycline; thus, in theory, berberine may decrease the efficacy of herbs with antibacterial activity.
- Berberine bisulfate may stimulate platelet formation, and berberine may have an antiheparin action. Thus, berberine may interact with certain herbs that increase the risk of bleeding and reduce their effectiveness. Multiple cases of bleeding have been reported with the use of *Ginkgo biloba*, and fewer cases with garlic and saw palmetto. Numerous other agents may theoretically increase the risk of bleeding, although this has not been proven in most cases.
- There may be additive hypotensive (blood pressure lowering) effects and bradycardia (slowed heart rate) when combining berberine with herbs that lower blood pressure. Caution is advised.
- Berberine may lower blood sugar levels. Caution is advised when using herbs or supplements that may also lower blood sugar. Blood glucose levels may require monitoring, and doses may need adjustment.
- Berberine may decrease total and LDL cholesterol, as well as triglycerides. Caution is advised in patients taking herbs or supplements with cholesterol-lowering effects, such as red yeast rice.
- Concomitant use of berberine-containing herbs may increase the risk of berberine toxicity. Berberine-containing herbs include: bloodroot, goldenseal, celandine, Chinese goldthread, goldthread, Oregon grape (*Mahonia* species), amur cork tree, and Chinese corktree.
- Berberine may interfere with the way the body processes certain herbs or supplements using

the liver's "cytochrome P450" enzyme system. As a result, the levels of other herbs or supplements may become too high in the blood. It may also alter the effects that other herbs or supplements possibly have on the P450 system.

- Although not well studied in humans, berberine may have sedative effects.
- Based on clinical study, tyramine-containing foods, such as wine, cheese, and chocolate, may have an interaction with berberine due to berberine's effect on decreasing levels of tyramine.
- Berberine may competitively inhibit the binding of yohimbine to platelets. In addition, due to the antifertililty properties of berberine, use of yohimbe for fertility may not be effective.
- Berberine may decrease the metabolism of vitamin B; therefore, the concomitant use of berberine with vitamin B should be avoided.

AUTHOR INFORMATION

- This information is based on a systematic review of scientific literature edited and peer-reviewed by contributors to the Natural Standard Research Collaboration (www.naturalstandard.com).

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Natural Standard developed the above evidence-based information based on a thorough systematic review of the available scientific articles. For comprehensive information about alternative and complementary therapies on the professional level, go to www.naturalstandard.com. Selected references are listed below.

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