GOLDENSEAL

(Hydrastis canadensis)

Family: Ranunculaceae,
Synonyms: Puccoon root, Yellowroot,[1] eye balm, eye root, Goldsiegel, Ground Raspberry, Indian Plant, Indian tumeric, jaundice root, orange root, sceau d'or, turmeric root, warnera, wild curcuma, yellow Indian paint, yellow paint,[2,3] Kanadische Gelbwurzel, guldsegl.[4]

Key Clinical Points

- Goldenseal is a popular component of herbal remedies for upper respiratory, eye, and skin infections.
- Although multiple organisms are sensitive to goldenseal constituents *in vitro*, few published clinical studies support its use.
- Avoid goldenseal during pregnancy and lactation, with gastrointestinal inflammation, and with proinflammatory disorders.

Key Constituents and pharmacology

The root is used medicinally. Goldenseal characteristically contains the isoquinoline alkaloids: berberine, hydrastine, canadine, berberastine, hydrastinine tetrahydroberberastine, and canalidine.[5] A related compound, 8-oxotetrahydrothalifendine was identified in one study.[6] Berberine behaves as a quaternary base and dissolves slowly in water.[7] Hydrastine is insoluble in water, but freely soluble in alcohol and acetone.[7]

Research into the toxicology and pharmacology of goldenseal has focused on berberine and hydrastine.[8] Berberine is a constituent of the roots of several species of plants, including *Hydrastis canadensis,* though hydrastine is found only in *Hydrastis canadensis* and *Berberis laurina.*[7] Berberine is thought to be antimicrobial, antidiarrheal, antiarrhythmic, a positive inotrope, cytotoxic, choleretic, mydriatic, anticariogenic, and hypoglycemic.[4] Hydrastine is thought to be choleretic, sedative, antibacterial, and vasoconstrictive.[4] The National Toxicology Program is currently investigating the toxicology of goldenseal root powder.[9,10] To support the effort, Weber et al. has developed a rapid ambient extraction method to assay goldenseal root powder and determine its purity.[5]

No developmental toxicity was noted in rats fed goldenseal powder at up to 7738 mg/kg/day (300 times the standard human dose).[9] In rats fed about 47 times the usual human dose of 26 mg/kg, maternal liver weights increased, but there were no adverse fetal effects.[10] Carcinogenicity studies are ongoing. The oral LD_{50} for berberine in mice is 329 mg/kg; the subcutaneous LD_{50} in mice is 18 mg/kg; the intraperitoneal LD_{50} for berberine sulfate is 24.3 mg/kg in mice and 500mg/kg in rats.[7] The IM LD_{50} of berberine sulfate in rats is 14.5mg/kg.[7] The LD_{50} of berberine in humans is thought to be 27.5 mg/kg.[2] The intraperitoneal LD_{50} for rats of hydrastine is 104 mg/kg.[7] An LD_{50} of 1620 was reported for goldenseal root extract.[4]
Animal studies suggesting improved cardiac function in rats with induced left ventricular hypertrophy treated with berberine must be interpreted with caution because the dose of berberine was not reported.[11]

Human studies of berberine have revealed evidence of absorption through the skin.[7] Berberine is absorbed slowly orally; it achieves peak plasma concentrations in 4 hours and takes 8 hours to clear[7]. Berberine is excreted in the urine.[8] No pharmacokinetic data is available for hydrastine or goldenseal root powder. The following biological activities are cited for berberine in humans: 1) blocking α_1 and α_2 receptors in smooth muscle, 2) blocks potassium channels in the heart and reduces ventricular tachycardia, 3) inhibits intestinal ion secretion and toxin formation in the gut and 4) increases bile secretion.[4,8]

Multiple bacteria and fungi, along with selected protozoa and chlamydia are susceptible to berberine *in vitro*[4].

Pharmacology (cont.)

A study of healthy volunteers given indinavir with and without goldenseal root powder in a crossover design showed no difference in the peak concentrations of indinavir after a single oral dose and no difference in oral clearance[12]. Goldenseal root powder increases IgM production in vivo.[13] Berberine displaced the protein binding of bilirubin a Chinese study using rats.[4] Berberine alone has weak antibiotic activity in vitro since many microorganisms actively export it from the cell. Interestingly, there is some evidence for other berberine-containing species (*Berberis fremontii*) also synthesizing an efflux pump inhibitor that potentiates the effect of berberine, a case of solid scientific evidence that the herb is superior to the isolated active principle.[14] However, it is not yet known whether goldenseal contains such an efflux pump inhibitor as well.

Herbal properties (whole herb): bitter, hepatic, alterative, anticatarrhal, anti-inflammatory, antimicrobial, laxative, emmenagogue, oxytocic.[15]

History and traditional use

Native Americans, especially the Cherokee, used goldenseal root for digestive disorders, including ulcers.[3,16] In addition, they employed goldenseal root as a yellow dye and as an eye wash and a treatment for skin disorders.[3,8] The Iroquois found it useful for diarrhea, digestion and whooping cough.[8] Goldenseal became popular among European settlers, especially in the mid-nineteenth century when it was an official herbal remedy in the United States Pharmacopeia.[3,8] By 1905, the herb was much less plentiful, partially due to over-harvesting and partially to habitat destruction.[3] Wild goldenseal is now so rear that the herb is listed in the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES).[17] Herbalists consider goldenseal an alterative, anti-catarrhal, anti-inflammatory, antiseptic, astringent, bitter tonic, laxative, and muscular stimulant.[1,3,18] They recommend goldenseal for gastritis, colitis, duodenal ulcers, loss of appetite and liver disease.[1,3,18] They discuss the astringent effect it has on mucous membranes of the upper respiratory tract (applied as a mouthwash or a snuff), the gastrointestinal (GI) tract, the bladder, and rectum (applied topically), and the skin. Goldenseal is very bitter. Bitters in herbal medicine stimulate the appetite and aid digestion and often stimulate bile secretion.[2]

Today, manufacturers of herbal products include goldenseal in preparations for upper respiratory infections, GI disorders liver disease, cancer, urinary tract infections, menorrhagia and dysmenorrhea.[2] Goldenseal is in many topical products, too, including those for sore gums, skin rashes, ulcers, wounds , and infections, itching, acne, dandruff, ringworm, and herpes.[2]

Indications supported by clinical trials

All of the clinical studies of goldenseal have focused on its constituent: berberine. Goldenseal is very popular in the US, but is little known in Europe, which may contribute to the lack of clinical research on the whole herb.[8]

Effectiveness for treating infectious diarrhea: **uncertain.**
At least 3 studies have examined the efficacy of berberine sulfate as adjunctive therapy in the treatment of cholera and *E.coli* diarrhea, as compared to treatment with tetracycline alone. Berberine significantly reduced stool volume when given with tetracycline in the *E.coli* group, but did not have any significant effects in patients with cholera.[2,8]
In a study of children with giardiasis, 90% of the children who took berberine at 10 mg/kg/day for 10 days had negative stool specimens after 10 days and 83 % had negative stools after one month. In the group treated with metronidazole, 95% had negative stools at 10 days and 90% had negative stools at 1 month[19] Lower doses of berberine or shorter durations of therapy resulted in marked reductions in efficacy.[19]

Effectiveness for treating colds and other respiratory infections: **unknown.** Researchers have not studied goldenseal for us in upper respiratory infections.

Effectiveness for masking illicit drug use in urine drug tests: **not effective.**
Two studies have demonstrated no effect of oral goldenseal on urine drug assays over water alone.[2] Subjects who drank large amounts of water had the same urine drug levels as subjects who took goldenseal capsules along with the water.

Program on Integrative Medicine, Department of Physical Medicine and Rehabilitation, School of Medicine, University of North Carolina, Chapel Hill, NC 27599-7200. http://pim.med.unc.edu/
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Traditional Use (cont):

Goldenseal is a component of products for eye infections and inflammations.[2] Goldenseal is also available as a homeopathic remedy for chronic nasal discharge and uterine hemorrhage.[8]

Preparation and dosage:

- For a tea, simmer 1tsp of dried root in 1 cup of water for 10-20 minutes and drink three times daily.[1]
- Alternatively, take 2-4 ml (about half a teaspoon of the tincture (1:10 strength in 60% alcohol)
- 0.3-1ml of the stronger fluid extract (1:1, 60% alcohol) mixed with water.[8,18]
- British sources recommend 0.7-2g of the dried root per day.[4]

As an eyewash, use a commercially-prepared 0.2% solution in sterile water: two drops in each eye, 3 times daily.[8]

Clinical Trials (cont.)

***Effectiveness for treating eye infections*: uncertain.**

Indian researchers have conducted 2 studies using berberine for treatment of trachoma. In one study, they compared 0.2% berberine chloride drops to sulfacetamide eye drops over 8 weeks of treatment or a combination of the two. The berberine groups tested negative for *C. trachomatis* at 3 weeks and had no relapse at one year.[8]

In a double-blind, placebo-controlled trial involving children with trachoma, researchers compared 0.2% berberine eye drops to berberine plus neomycin, sulfacetamide, and placebo. They saw an 84% clinical cure and a 50% microbiological cure with berberine alone. The cure rates were higher with the addition of neomycin but were lower for the sulfacetamide group.[4]

Interactions with other herbs, pharmaceuticals, disease states

Interactions with pharmaceuticals: Currently, only theoretical interactions are listed. Research on goldenseal's inhibition of cytochrome P450 3A4 enzymes is inconclusive. Physicians may wish to monitor the effects of drugs metabolized by this enzyme while their patient is taking goldenseal (including lovastatin, ketoconazole, itraconazole, fexofenadine, triazolam, etc.)

Interactions with other herbs: Avoid using with other herbs that increase stomach acid secretion, including angelica, coffee, cola, black and red pepper, cinnamon, calamus, dandelion root, devil's claw root, galangal root, gentian, ginger, guarana seeds, horseradish, ironweed, mate, mustard, tobacco, quassia, snakeroot, wormwood, and yarrow, among others.[20]

Any herb with purported immunostimulating effects should be avoided by those with any autoimmune or proinflammatory disorder, including rheumatoid arthritis and asthma.

Adverse effects/precautions/side effects/contraindications

Side effects: Goldenseal tea and tincture are very bitter and can cause nausea due to the disagreeable taste.

Adverse events: Reportedly, high doses of berberine (>500mg- corresponding to 8-100g of dried goldenseal root, depending on the amount of berberine) can cause stomach upset, nausea, vomiting, nervousness, depression, dyspnea, bradycardia, cardiac damage, hypotension, seizures, paralysis, spasms, and death. High doses of hydrastine can cause exaggerated reflexes, convulsions, paralysis, and respiratory failure.[2] For overdose, induce vomiting and intestinal emptying, instill activated charcoal and keep the patient quiet and warm. Use diazepam for spasms, correct acidosis with NaHCo3, and plasma to expand volume as necessary.[21] Irritation of the mouth has occurred with the fresh plant and vaginal ulcers have occurred with use as a douche.[2]

Precautions/contraindications: Pregnant women, nursing mothers, and jaundiced infants should avoid goldenseal.[4] Patients with acute gastrointestinal inflammation should avoid goldenseal.[20]

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Botanical characteristics

Goldenseal is a perennial herb in the buttercup family.[4] It grows to a height of 6-12 inches[22] with a spread of 6-12 inches.[23] The stem is purplish and hairy above ground and yellow below ground where it connects to the yellow rhizome.[4] The plant bears 2 rounded, hairy leaves with 5-7 double-toothed lobes[22] and single, small, inconspicuous flowers with greenish white stamens in the late spring.[23] The fruit consists of a soft red berry, somewhat like a raspberry with 10-30 black seeds.[23] The fruit ripens in midsummer.[23]

The rhizome is about 2 inches long and has many long , skinny fibrous rootlets.[23] Farmers or wild-crafters harvest the rhizome in the fall after the 3rd year if grown from division and after the 6th year if grown from seed.[23]
Goldenseal grows in the forests of the eastern United States and Canada. Once it was plentiful in the wild, but it is rare today, because of overharvesting.[3,16] Farmers use artificial shading materials to cultivate goldenseal.[23]

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