# Golden Seal

***Hydrastis canadensis***

## Common names

Eye root, eye balm, jaundice root, orange root, yellow root, wild curcuma, Indian dye

## Family

*Ranunculaceae* (buttercup)

## Part used

Root and rhizome

## Background and traditional uses

Golden seal is a low-growing perennial herb with dark green serrated leaves and small, greenish-white flowers with rose-coloured sepals. The roots and rhizomes are a deep shade of golden yellow when cut.[1] Native to North America and Canada and used prolifically by the Cherokees,[2] golden seal was considered a cure-all by the settlers who praised its traditional use in cases of digestive complaints, women's reproductive disorders, dropsy, ulceration, eye and mouth inflammation and infection, and as a dye for textiles.[3]

Golden seal became an official and very popular pharmaceutical medicine in several countries in the early 19th century, which unfortunately led to its current status as a threatened species. Commercial golden seal products are now largely manufactured using cultivated plants, which require between three and four years to yield medicinally viable root stock, explaining the very high market price of golden seal.[4]

## Actions

**Primary:**[3,5]

- Anticatarrhal
- Antidiarrheal
- Anti-inflammatory
- Antimicrobial
- Bitter tonic
- Depurative
- Mucous membrane trophorestorative

**Secondary:**[3,5]

- Anticancer
- Antidepressant
- Antidiabetic
- Astringent
- Cardioactive
- Choleretic
- Hypercholesterolaemic
- Immune modulating
- Neuroprotective
- Oxytocic
- Vulnerary

# Applications and indications

- When used within the specified dosage range, golden seal has been used to aid in the management of diarrhoea (specifically acute infectious diarrhea), gastritis, and ulceration.[3,6,7]
- Golden seal is also used in the treatment of oedema, eye and mouth inflammation, menstrual abnormalities and irregularities and vaginitis.[3]
- Golden seal is frequently used in the treatment of colds and flus as well as to treat lung and sinus infections due to its antimicrobial and anti-inflammatory actions.[5]

# Active constituents and pharmacodynamics

While there have been at least 10 different benzylisoquinoline **alkaloids** identified in golden seal, there are four key alkaloids that have been isolated including, hydrastine, berberine, canadine and canadaline.[2] From these, the majority of empirical data compiled on golden seal has focused on the medicinal properties of isolated **berberine**, which has demonstrated antimicrobial, antibacterial, antifungal, antimycobacterial and antiprotozoal activity.[2,3] Additionally, berberine appears to inhibit intestinal ion secretion and microbe originating toxin formation, reduce cyclic adenosine monophosphate (cAMP) and activate alpha-2 adrenoreceptors that reduce intestinal activity; lending to the plant's known antidiarrhoeal effects.[3]

Other constituents found in golden seal include chlorogenic acid, meconin, lipids, sugars, starch, resin and some volatile oils.[8]

# Summary of clinical evidence

The majority of human and animal trials related to golden seal have taken place using isolated berberine.

### Diarrhoea

A double-blind, randomised, placebo-controlled trial on 400 patients with acute, watery diarrhoea divided the group into four. Patients were prescribed tetracycline (500mg), berberine hydrochloride (100mg), a combination of tetracycline (500g) and berberine hydrochloride (100mg) or placebo four times daily. Of the groups administered berberine hydrochloride, 77% experienced an average volume reduction of one litre of stool output after 24 hours of treatment.[9] In a non-controlled study, 137 children with giardiasis were prescribed oral berberine at a dose of 10mg/kg/day for 10 days. The results of the experiment showed berberine could elicit comparable benefits to quinacrin hydrochloride, furazolidine and metronidazole in the management of giardiasis.[10]

### Intestinal parasites

The potential antiparasitic properties of berberine have been shown repeatedly *in vivo*:

- Berberine sulphate has been shown to inhibit the growth of *Giardia lambda, Trichomonas vaginalis* and *Entamoeba histolytica*; inducing morphological changes in all three parasites.[11]
- Berberine has also been shown to significantly diminish the parasite load of *Leishmania donovani* in hamsters, inhibiting both endogenous and glucose stimulated respiration of amastigotes.[12]
- Berberine sulphate was shown to inhibit the intestinal secretory responses induced by *Escherichia coli* and *Vibrio cholera* by 70% *in vivo*.[13]

### Anti-inflammatory and immune modulation

One study looked at the therapeutic potential of golden seal root to regulate pro-inflammatory responses and activation events.[5] One part of the study explored the innate effects of golden seal on pro-inflammatory cytokines produced by cultured macrophages on murine macrophage cultures. The other part of the study examined the ongoing modulatory effect golden seal had on lipopolysaccharide (LPS)-stimulated macrophages. Results of the study showed that golden seal had the ability to modulate macrophage responses at high concentrations, when combined with LPS stimulant. The most significant effects identified were on the reduction of IL-6, IL-10, IL-12 and TNF-alpha production. The results demonstrate the anti-inflammatory and immune modulation capacity of golden seal.[5]

### Hyperlidipaemia

In a randomised, double-blind, multicentre, placebo-controlled trial,berberine was evaluated for its used in diabetic patients with hyperlipidaemia.[14] A total of 110 patients aged between 25 and 70 years-old were included in the trial. Patients were randomised to receive either 500mg of berberine twice daily or a placebo for three months. Several dyslipidaemia markers showed significant improvements in the berberine group versus the placebo group at endpoint. Total cholesterol changed from 205±38mg/dL at baseline to 168±37mg/dL for the berberine group ($p<0.000$), while the placebo group experienced a change from 208±36 to 204±30mg/dL over the same period of time ($p<0.001$) The difference between the two groups was statistically significant ($p<0.001$). Similar results were achieved in the change of LDL (125±31 to 99±30mg/dL) and triglycerides (97±79 to 62±43mg/dL) for the berberine group at endpoint, while for the placebo group a small change was only seen in endpoint LDL (130±28 to 125±28mg/dL), and an increase was observed in endpoint triglycerides (76±36 to 79±49mg/dL).[14]

### Hypercholesterolaemia

A randomised, double-blind, placebo-controlled clinical trial evaluated the cholesterol-lowering effects of berberine in 144 subjects with low cardiovascular disease risk.[15] Following a six-month run-in period following a diet and exercise regime, subjects were randomised to 500mg twice daily of berberine for three months or placebo, followed by a two-month washout period where patient continued with only their diet and exercise regime, and ending with a reintroduction of berberine or placebo for a further three-month period. A decrease was observed for the berberine group in body weight, BMI, total cholesterols, triglycerides and LDL with an increase in HDL at the end of both three-month treatment periods. Despite a worsening of lipid profiles during the two-month washout period, test results were recovered by the reintroduction of berberine for the final three months of treatment. The improvement in all markers at the end of the study was statistically significant for berberine when compared to placebo ($p<0.05$).[15]

In another study, 32 patients with hypercholesterolaemia were administered 500mg of isolated berberine twice daily for three months.[16] At the conclusion of the trial, the participants averaged a 29% reduction in triglycerides and a 35% reduction in LDL cholesterol with unchanged HDL levels. The researchers also noted that the berberine treatment resulted in improved liver enzyme results in the majority of participants.[16]

### Type 2 diabetes

In a randomised trial, 36 patients with type 2 diabetes (T2DM) were split into two groups and administered either 500mg berberine three times daily or 500mg metformin three times daily for 13 weeks.[17] At the conclusion of the study, berberine was shown to be as effective as metformin in reducing haemoglobin A levels, fasting blood glucose levels and post-prandial blood glucose levels. A second group of 48 patients with T2DM, which was poorly controlled on their existing medication, were split into two groups with one remaining on their current regime and the other receiving 500mg of berberine three times daily for the same 13 weeks. At the conclusion of the trial, the group receiving berberine showed significant reductions in fasting and post-prandial blood glucose levels, fasting insulin, LDL cholesterol, total cholesterol and triglycerides.[17]

## Dosage summary

**Liquid extract (1:1):** 6.5-21mL weekly[18]
**Liquid extract (1:3):** 15-30mL weekly[6]
**Dried herb equivalent:** 0.5g-3g daily[6,18,19]

## Safety information

- Golden seal is contraindicated in pregnancy and breastfeeding as hydrastine has been shown to induce labour and effect bilirubin levels.[22]
- Prescribed within recommended ranges, golden seal is considered generally safe but doses supplying more than 500mg of pure berberine may result in gastrointestinal distress (nausea, vomiting, diarrhea), eye and skin irritations, dizziness, lethargy and kidney problems.[20,21]
- Due to the lack of human trials on golden seal, drug interactions are speculative. Theoretically, the herb should be prescribed with caution for individuals taking drugs metabolised by the P450 enzyme pathway as berberine has been shown to effect liver enzymes.[3]
- Caution is also advised in prescribing golden seal to patients with cardiovascular conditions, taking cardioactive medicines and with kidney diseases.[20]
- Golden seal is also suggested to be avoided in jaundiced neonates.[23]

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MM.2810 BC_0734_GOLDENSEAL_MGRAPH_220318_D6

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