



Comprehensive Review of *Hydrastis Canadensis* (Goldenseal): Botany, Phytochemistry, Pharmacology, Health Benefits.

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ABSTRACT:

Background: Goldenseal, or *Hydrastis canadensis* Linn, is a medicinal plant that is likely used as a dietary supplement and in a number of traditional medical systems. This herbaceous perennial plant belongs to the Ranunculaceae family. Native Americans long utilised it as a colouring vehicle and as a medicinal cure for diseases, such as ulcers, cancer, wounds, digestive issues, and skin and eye ailments.

Methods: A library, Google Scholar, Pubmed, and Web of Science have all been used to gather literature. Current data on goldenseal's phytoconstituents, pharmacological activity, active chemicals, and health advantages are included in this review.

Result: The three main alkaloids found in *Hydrastis canadensis* roots and rhizomes are canadine, berberine and hydrastine. Several fungal metabolites, flavonoids and by-products of phenolic acid have also been found in addition to these. Considerable antitumor and antimetastatic activity, antioxidant, anti-inflammatory and properties, cardiovascular protective benefits, neuroprotective, insulin resistance- improving action, and chronic disease management have all been demonstrated by berberine.

Conclusion: The medicinal properties, botanical description, and health advantages are identified. In this review the traditional uses of the goldenseal plant is identified. The material in this article will be helpful for both present and future research, and more conventional clinical trials are required before the plant may be employed as a medicinal agent.

Keywords: *goldenseal, phytoconstituents Berberine, flavonoids, health benefits*

1. INTRODUCTION

The perennial plant goldenseal (*Hydrastis canadensis* L., Ranunculaceae) is an origin to North America's lush forests. Native Americans has utilised the roots to cure wounds, local inflammation, fever, diarrhoea, and indigestion, among other ailments. Goldenseal is now used topically to treat mild inflammatory disorders of the mouth, skin, and eyes. Powdered goldenseal root's strong bitterness is caused by alkaloids consisting hydrastine and berberine, which have been linked to the plant's extensive antibacterial qualities. Goldenseal contains a number of alkaloids that have shown strong antibacterial activity.[1-2]

Goldenseal rhizome extract in different forms has been used for centuries in both traditional and conventional medicine to treat a variety of illnesses, such as gastritis, ulcers, intestinal catarrh, muscular weakness, urinary disorders, nervous prostration, constipation, hepatic congestion, dysmenorrhea, blood stasis, infections of the skin, mouth, and eyes, upper respiratory disorders, diarrhoea, cancer, and more. [3-5]. Many alkaloids, including hydrastine, palmatine, canadine, berberine, and hydrastinine, as well as a smaller amount of flavonoids, including sideroxylin, 8-desmethyl-sideroxylen, 6-desmethyl-sideroxylin, and others, as well as organic acids, including neochlorogenic acid and chlorogenic acid, are also present in the rhizome of this plant. The fifth In modern medicine, berberine, the most potent of these medicinally active ingredients, is used to treat a variety of ailments, including infections, cardiovascular, dyslipidaemia and diabetes.[6]

2. BOTANICAL DESCRIPTION OF GOLDENSEAL

Early spring brings the pubescent, cylindrical stems of mature goldenseal plants, which grow up to 12 inches tall. With a number of tiny scales at the base, the stem is purplish above and bright yellow below ground. There are two terminal palmate leaves with five to seven lobes on each forked stalk. With leaves that are 3 to 8 inches long and 3 to 12 inches wide. In this plant, one leaf is usually larger than the other. Both leaves are dark green with serrated edges and noticeable veining. Plants that are weak or immature produce a stem with a single leaf and no flowers.[30].

Flower: The flowers are greenish white with clusters of white stamens and are hermaphrodite, meaning they contain both male and female organs.

Fruit: The fruit of goldenseal ripens in July and August which turns red, resembling a giant raspberry, hence the popular name "ground raspberry." There are 10 to 20 tiny, firm, glossy black seeds in each berry, and birds and other animals spread them.

Root: Horizontal rhizomes that are 1/2 to 3/4 inches broad and many frootlets that are fibrous constitutes the root system. The term "goldenseal" refers to the roots' vivid yellow hue as well as the round scars. Many stages of the goldenseal life cycle are clearly described by the fact that roots mature mostly after 4 to 5 years and then start to die.

Seed: In August, as the fruit ripens, seeds are spontaneously sown and sprout the next spring. It produces a tiny radicle and two cotyledons in its first year of growth. Plants produce the stem with a single palmate leaf. A forked stem with two leaves and a bloom is produced when the plant reaches adult stage in its third or fourth year.[31].

Distribution:

The understory plant known as goldenseal grows in patches along the banks of streams, on hill slopes, and in rich open forests. Its native range extends from New York, Ontario, Georgia Tennessee, Canada. It was once common in West Virginia, Ohio, Kentucky, but in recent decades, its population has been drastically declining.[29]

Common names of Hydrastis Canadensis :

Eyeroot, eyebalm ground raspberry, Golden seal, yellow pucoon, Indian dye, jaundice root, orange root, turmeric, eyebalm, eyeroot.



Figure 1. Hydrastis canadensis: Flower and early Leaves [33]

Table 1. Taxonomical Classification of Goldenseal [32]

Taxonomic Rank	Nomenclature
Kingdom	Plantae
Class	Magnoliopsida
Order	Ranunculales
Family	Ranunculaceae
Subfamily	Hydrastidoideae
Genus	Hydrastis

3. PHYTOCHEMISTRY

Alkaloid phytochemicals are abundant in goldenseal plants. The chemical components of the various plant sections have been the subject of several investigations. Berberine, canadine and hydrastine are the three major alkaloids found in hydrastis canadensis roots and rhizomes. In addition, a number of flavonoids, phenolic acid derivatives, and fungal metabolites have been documented [7]. Many alkaloids, such as berberine, hydrastine, palmatine, canadine, and hydrastinine, as well as trace amounts of flavonoids (such as sideroxylin, 8desmethyl-sideroxylen, 6-desmethyl-sideroxylin, etc.), phenolic acids, sterol, and other substances, are found in rhizomes, which are the most chemically studied parts of plants.[8] The alkaloids hydrastine (1.5–4%) and berberine (0.5–6%) are primary major active ingredients in goldenseal. The alkaloids canadine, berberastine, hydrastinidine, and isohydrastidine are

found in smaller concentrations in the plant. Additional components include of sugars, resin, lipids starch, chlorogenic acid, meconin, and small amounts of volatile oil.[9]

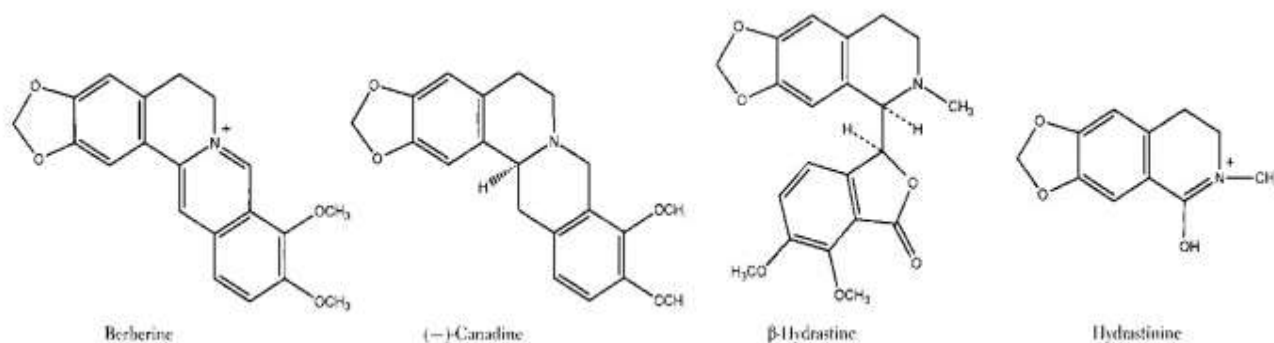


Figure 2. Structure of major alkaloids of Hydrastis Canadensis [33]

4. TRADITIONAL USES

Appalachian culture primarily uses the root of Hydrastis canadensis as a stomachic, strengthening tonic, and source of yellow dye. When applied topically, it also helps with general ulcers and eye pain. For the purpose of treating sore throats, the powdered drug is combined with water and gargled. Oddly, it was once believed that applying it topically in a hot or warm bath would help stop smallpox scars from "pitting." Appalachian people often complain of "sour stomach" or dyspepsia, which is often linked to gum disease, dental decay, and difficulty chewing. Goldenseal, either by chewing it or making a decoction of it, is frequently used to calm unsettled stomachs. Moreover, it has been used on wounds.[26]

In addition to treating dyspepsia, goldenseal was utilised as a tonic for weakened digestive systems. It worked well as a gargle for painful mouth and throat and as a wash for irritated, sore eyes. The root was commonly used as a household bitter by mixing it with cognac or wine. As a domestic bitter, the root was added to wine or brandy.[27, 28]

5. PHARMACOLOGICAL ACTIVITIES

5.1. Anti-obesity activity

Diabetes disorders and glucose metabolism are occasionally linked to the modifying actions of substances that regulate lipid metabolism. Berberine's anti-obesity impact in an in vivo trial was demonstrated by lowering serum levels of leptin, triglycerides, insulin, as well as epididymal adipose mass, which were all caused by suppression of adipogenesis.[10] In mice's epididymal adipose tissues, it also prevented the increased levels of the proteins brought on by a fat diet. Additionally, it alleviated the fatty liver and lipid dysregulation in obese mice by activating AMPK in peripheral organs like the muscle and liver.[11]

5.2. Antibacterial activity

Historically, hydrastis canadensis rhizome extract has been used in treatment of a wide range of skin illnesses because of its potent antibacterial properties. In a number of investigations reports, the antibacterial activity was examined by calculating the minimum inhibitory concentration (MIC). Berberine, canadine, and canadine were the alkaloids that gave the plant's rhizome extract its antibacterial properties against Staphylococcus aureus, Streptococcus sanguis, S. mutans, S. pyogenes, Pseudomonas aeruginosa, and Escherichia coli. The extract's "killing time" on a low-density bacterial inoculum and its bacteriostatic and bactericidal properties in liquid bacterial growth medium were both demonstrated. In [12], the antibacterial qualities of goldenseal leaf extract were also reported; it was discovered to be noticeably more efficient than berberine alone against S. aureus that is resistant to many drugs. Within [13]

5.3. Antiviral activity

Various studies indicates that the goldenseal alkaloid berberine consists antiviral properties against a variety of viruses, such as cytomegalo, chikungunya, herpes simplex influenza, and enterovirus. In vitro tests on mouse bone marrow macrophages and human lung epithelial cells revealed that berberine had a strong growth inhibitory effect on H1N1 influenza A.[14-15]

5.4. *Anti-protozoal activity*

Along with its antibacterial, antifungal, and antiviral qualities, berberine has demonstrated substantial anti-protozoan activity against a range of protozoan parasites, such as *Blastocystis hominis*, *Entamoeba histolytica*, *Giardia lamblia*, *Trichomonas vaginalis*, and *Leishmania donovani*. Plant extracts' anthelmintic activity has been assessed for a number of purposes.[16]

5.5. *Antitumor activity*

Numerous innate compounds has been discovered to have strong anti-cancer properties. Growing potential applications of phytochemicals have revealed a novel therapeutic idea for employing them as pharmacological substitutes to treat human cancers in a medication repositioning strategy. In addition to its interaction with DNA and transcriptional control, berberine's anticancer processes also included the modulation of carcinogenesis-related gene expressions and oncogene.[17]

5.6. *Anti-arthritis activity*

Inflammatory arthritis disorders are associated with inflammation and immunomodulation. It has been demonstrated that berberine can alleviate rheumatoid arthritis brought on by collagen and Freund's complete adjuvant by regulating specific immune reactions. Berberine decreased the infiltration of inflammatory cells and synovial hyperplasia in joint tissues, per several histological analyses [19]. Gouty arthritis is largely caused by inflammation brought on by urea crystals. Berberine was found to have a protective effect against osteoarthritis development in both in vitro and in vivo tests by increasing the expression of metalloproteinase inhibitor and inhibiting NO production, IL-1 β -induced glycosaminoglycan release, and MMP-1, -3, and -13 expressions. [17]

5.7. *Antioxidant activity*

Oxidative stress, which is caused by an excess of reactive oxygen species (ROS) and reactive nitrogen species (RNS), has been intimately associated with chronic inflammatory pathophysiological conditions such as obesity, diabetes, cardiovascular disease, neurodegenerative diseases, and cancer. Excess ROS and RNS can lead to oxidative damage to biological macromolecules, including proteins, DNA, and lipids. Berberine has been proven to protect against oxidative stress in a variety of organs, including the liver, adipose tissue, kidney, and pancreas.[20–21]

5.8. *Anti-platelet aggregations*

The process by which platelets group together in the blood is known as platelet aggregation, and it is one of the steps that results in the development of a thrombus clotting. Heart disease is one of the pathophysiological illnesses that are impacted by these intricate haemostatic systems. Numerous therapeutic plants and traditional medical systems have demonstrated that taking natural supplements can lower platelet aggregation. Research has indicated that berberine inhibited collagen-induced platelet aggregation.(22 Berberine was shown to inhibit platelet aggregation and reduce the generation of ROS and superoxide via altering the activities of AR, NOX, and glutathione reductase in a diabetic mouse. Berberine inhibited p38-p53 mediated BAX activation, which in turn decreased granule release, ERK phosphorylation, calcium release, and platelet stickiness factors.(20)

5.9. *Anti-aging activity*

Procollagen type I gene expression declines, matrix metalloproteinases (MMPs) are formed, and IL-6 is produced as a result of skin ageing brought on by ultraviolet (UV) radiation exposure. Berberine inhibited UV-induced MMP-1 expression in human dermal fibroblasts while increasing type I procollagen expression, according an in vitro study. Another study similarly found that berberine suppressed TPA-induced MMP-9 production and activity and decreased IL-6 expression in human keratinocytes.(24).

5.10. *Gastrointestinal effects*

According to reports, berberine has a great deal of therapeutic potential for the management of inflammatory gastrointestinal illnesses. By preventing enterobacteria from growing, berberine reduced the inflammatory reactions linked to a number of gastrointestinal inflammatory disorders. Berberine have been shown to reduce the dysfunction of the intestinal epithelial barrier in a number of chronic or acute enteropathies by blocking the HIF-1 α -mediated signals.[25]

6. TOXICITY

Hepatotoxicity

When administered in in vivo studies, higher doses of *Hydrastis Canadensis* root powder surpass liver weight within 15 days. Additionally, after receiving low to high dosages of powdered *Hydrastis canadensis* root for two years, all animals showed a dramatically elevated incidence of hepatocyte hypertrophy and cancer. "[34]

In an in vitro investigation, the genotoxic potential of *Hydrastis canadensis* extract and its main alkaloids—canadine, hydrastine, palmatine, berberine, and hydrastinine—was examined in human hepatoma HepG2 cells. The results showed that goldenseal extract, palmatine, and berberine were potent inducers of DNA damage in HepG2 cells by blocking the activities of both topoisomerase I and II.[35]

Phototoxicity

Evaluation of the phototoxic and photochemical responses is a very crucial factor for determining the therapeutic potential and action of natural substances. In medical applications such as skin lotions and eyewashes, the phototoxic and photochemical effects of goldenseal's main alkaloids, such as palmatine and berberine, have been evaluated.[36] The UVA keratinocytes had exhibited damage to DNA when exposed to both of palmatine and berberine. Moreover, berberine caused damage to hRPE cells upon exposure to visible light, while palmatine did not exhibit phototoxicity towards hRPE cells. These findings identify that eyewashes and lotions containing goldenseal should be carefully assessed for ocular phototoxicity and exposed to various light wavelengths.[37]

7. CONCLUSION

According to numerous studies, Goldenseal (*Hydrastis canadensis*) is a very attention-grabbing plant due to its high level of biological action and therapeutic uses. Its biological action is caused by active ingredients that need to be identified through further investigation. The presence of primary alkaloids gives strong antimicrobial, antimycotic, and hypoglycemic properties. The most off studies on *Hydrastis canadensis* focuses on the effects of berberine and hydrastine, which are primarily responsible for the pharmacological effects of the plant. This review briefly discussed the botany, description of plant, phytochemistry constituents, pharmacological activities. Goldenseal's use in medicine are limited to traditional remedies, which suggests that further study should be conducted to find novel pharmacological compounds with specific therapeutic actions.

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