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A review on pharmacological activities and traditional uses of *Glycyrrhiza glabra* (licorice)

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Abstract
In recent years, there has been a notable increase in consumer interest in natural medicines and principles, driven by the perception of their safety. Concurrently, industries are showing a growing demand for plants traditionally used in medicine, seeking to incorporate them into various products like foods, nutraceuticals, cosmetics, and pharmaceuticals. *Glycyrrhiza glabra* Linn., has been esteemed for its medicinal properties since ancient times. It contains several phytocompounds, including glycyrrhizin, 18 β-glycyrrhetinic acid, glabrin A and B, and isoflavones, which exhibit diverse pharmacological activities such as antibacterial, anti-inflammatory, antiviral, antioxidant, and antidiabetic effects. While some toxicological studies have raised concerns, this review aims to comprehensively examine the composition and biological activities of *G. glabra*. The goal is to explore its therapeutic potential and address future challenges, with the aim of utilizing it in the formulation of new products to enhance human well-being.

Keywords: *Glycyrrhiza glabra*, pharmacology, hepatoprotective, traditional use

Introduction
Nature has long provided us with a wealth of therapeutic compounds, including medicinal plants rich in valuable phytochemicals. Among these is licorice, scientifically termed *Glycyrrhiza glabra*, belonging to the Leguminosae family. *G. glabra*, commonly known as licorice, is a prominent herb in Ayurvedic medicine and is widely used. This medicinal plant is native to various regions in Asia and can also be found in parts of Europe [1]. The species *G. glabra* is widely distributed and can be found in various regions including Italy, Spain, Turkey, the Caucasus, western China, and Central Asia. On the other hand, G. uralensis is primarily found in Central Asia extending to China and Mongolia [2, 3]. Licorice is cultivated commercially in several countries including India, China, Italy, Spain, Greece, Iran, Iraq, Turkmenistan, France, Syria, England, Azerbaijan, the United States, and Afghanistan. It holds immense commercial value globally due to its diverse applications in industries such as tobacco, cosmetics, food, and pharmaceuticals [4]. Isoliquiritigenin (ISL), extracted from licorice root, possesses a chalcone structure and demonstrates potent anticancer properties. Additionally, Glycyrrhizin, glycyrrhizinic acid, isoliquiritin, and glycyrrhizic acid are other major chemicals found in this plant. These compounds exhibit a range of beneficial properties including anti-atherogenic, anti-cancer, anti-diabetic, anti-microbial, antispasmodic, anti-inflammatory, and anti-asthmatic effects [5].

(Source: Gardening Know How, Carmen Hauser & Wikipedia)

Scientific Classification

- Kingdom: Plantae
- Division: Angiospermae
- Class: Dicotyledoneae
- Order: Rosales
- Family: Leguminosae
- Genus: *Glycyrrhiza*
- Species: *Glabra* Linn
- Binomial Name: *Glycyrrhiza glabra* Linn

Vernacular names [6]

- Sanskrit: Yashti-madhu, madhuka
- Bengali: Jashtimadhu, jaishbomodhu
- Gujarat: Jethimadhu
- Hindi: Jothi-madh, mulaithi
- Kannada: Yastimadhuka, atimaddhura
- Malayalam: Iratimadhuram
- Marathi: Jeshtamadha
- Oriya: Jatimadhu
- Tamil: Atimaduram
- Telugu: *Atimadhuranu, yashtimadhukam*
- English: Licorice, liquorices, sweet wood
- Arab: Aslussiesa
- Persia: Ausareha mahaka
- France: Boisdoux
- Germany: Sussholz

Morphology

Leaves - Leaves of this plant are compound, with an odd number of leaflets arranged alternately along the stem. Each leaf typically has 4-7 pairs of oblongs, elliptical, or lanceolate leaflets that are covered in soft hairs on their undersides.

Fruit- The fruit is a flattened legume or pod, measuring up to 1.5 cm in length. It stands erect, is smooth, and exhibits a somewhat reticulated pattern on its surface. Inside, it usually contains 3-5 brown, kidney-shaped seeds [7].

Flowers - The flowers are slender and arranged in axillary spikes, with colors ranging from lavender to violet. The calyx, which surrounds the flower, is short and bell-shaped, with lanceolate tips and covered in glandular hairs [8].

Root - The root system consists of a main root approximately 1.5 cm long, which gives rise to subsidiary roots about 1.25 cm long. From these roots, horizontal woody stolons emerge, which can extend up to 8 meters in length. When dried and cut, these roots, along with the stolons, are commercially known as licorice. The root pieces may be found either peeled or unpeeled. When broken, they reveal a fibrous texture, with a yellowish interior possessing a distinctive odor and sweet taste [9].

Phytochemistry/chemistry

The roots of *Glycyrrhiza glabra* contain a multitude of components, with a water-soluble, biologically active complex making up 40–50% of the total dry weight. This complex includes triterpenes, saponins, flavonoids, polysaccharides, pectins, simple sugars, amino acids, mineral salts, asparagines, bitters, essential oils, estrogen, gums, mucilage (from the rhizome), proteins, resins, starches, sterols, volatile oils, tannins, glycosides, and numerous other substances [10, 11]. Glycyrrhizin A triterpenoid compound is responsible for the sweet taste of licorice root. This compound is a blend of potassium-calcium-magnesium salts of glycyrrhizic acid, which typically ranges from 2% to 25%. Glycyrrhizic acid, a natural saponin, comprises a hydrophilic section consisting of two molecules of glucuronic acid, along with a hydrophobic fragment known as glycyrrhetic acid. The yellow color of licorice is attributed to its flavonoid content, which includes liquiritin, isoliquiritin is a type of chalcone, and other compounds. Licorice also contains isoflavones like glabridin and hispaglabridins A and B [12, 13].

Pharmacological activity

1. Anti-inflammatory activity

Glycyrrhetinic acid found in licorice extract exhibits anti-inflammatory properties akin to glucocorticoids and mineralocorticoids. For over 2000 years, it's been recognized that licorice root extract (*Glycyrrhiza*) aids in healing stomach and mouth ulcers. Research indicates that glycyrrhizic acid, a component of licorice, suppresses various inflammatory factors. It hampers cyclooxygenase activity and the formation of prostaglandins, and it indirectly impedes platelet aggregation [14].

2. Anti-ulcer activity

The antiulcer effect of glycyrrhizinic acid, a major compound in licorice, is attributed to its ability to increase the local concentration of prostaglandins in the stomach. These prostaglandins facilitate mucous secretion and cell proliferation, aiding in the healing process. In a previously reported study involving *Extractum liquiritiae* (EL), glycyrrhizic acid, glycyrrhetinic acid, and a novel lipophilic derivative of glycyrrhetinic acid monoglucuronide (GAMG), acetylated GAMG (aGAMG), demonstrated activity against 29 strains of Helicobacter pylori. The potent invitro activity of glycyrrhizic acid against H. pylori suggests its potential benefits in treating peptic ulcers [15].

3. Anti-bacterial Activity

Secondary metabolites found in the hydro-methanolic root extract of *Glycyrrhiza glabra*, such as saponins, alkaloids, and flavonoids, exhibit strong antibacterial effects against Staphylococcus aureus. Furthermore, several studies on both aqueous and ethanolic extracts of licorice have demonstrated their inhibitory activity against cultures of Staphylococcus aureus and Streptococcus pyogenes [16].

4. Anti-diabetic activity

In a prior investigation it was observed that the ethyl acetate extract of licorice demonstrated notable binding activity to PPAR-γ (peroxisome proliferator-activated receptors), which act as transcription factors governing the expression of genes related to glucose and lipid metabolism. This extract was also found to effectively reduce blood glucose levels in diabetic mice lacking PPAR-γ [17].

5. Hepatoprotective activity

Glycyrrhizin has been shown to cause a significant decrease in serum aminotransferases and to enhance liver histology. Additionally, it has been suggested that prolonged use of glycyrrhizin can help prevent the onset of hepatocellular carcinoma in individuals with chronic hepatitis C. *In vitro* research has also indicated that glycyrrhizin alters intracellular transport and inhibits the production of hepatitis B virus surface antigen (HBsAg) [18].

6. Anti-tussive and Antidemulcent activity

Liquorice powder and extract have proven effective in treating sore throat, cough, and bronchial catarrh. Research suggests that liquorice can be as effective as codeine for sore

throat relief, reducing irritation, and promoting expectoration. Carbenoxolone, a semi-synthetic compound derived from *Glycyrrhiza*, stimulates the secretion of gastric mucus. Glycyrrhizin is credited with the demulcent action of liquorice. Additionally, liquiritin apioside, an active compound found in the methanolic extract of liquorice, has been observed to inhibit cough induced by capsaicin [19].

7. Anti-malarial activity

Licochalcone A, a type of chalcone found in liquorice, is accountable for its antimalarial properties. In a previously documented study, administration of oral doses of 1000 mg kg-1 of licochalcone A against *P. yoelii* in mice resulted in complete eradication of the malaria parasite [20].

8. Anti-fungal activity

Glycyrrhiza glabra exhibits potent antifungal properties. In a previous study aimed at screening for antifungal compounds from different plant sources, licorice extract containing 80% methanol (Referred to as oil-based extract of licorice, or OEL) displayed a strong fungicidal effect against Arthrinium sacchari M001 and Chaetomium funicola M002. The active compound responsible for this effect was identified as glabridin. As a result, liquorice extract holds significant promise for formulating cosmetic products with potent antiseptic properties [21].

9. Immunostimulatory activity

Studies have demonstrated that *Glycyrrhiza glabra* at a concentration of 100µg/ml exhibits immunostimulatory effects. It enhances the production of TCD69 lymphocytes and macrophages from human granulocytes. In a previously reported study, liquorice root extract was found to inhibit the increase in the level of immune complexes associated with autoimmune diseases such as systemic lupus erythematosus [22].

10. Anti-dyslipidaemia effect

In a previously reported study, researchers examined the antidyslipidaemic (anti-cholesterol) activity of an ethanolic (95%) extract derived from the root of *Glycyrrhiza glabra* and its fractions on dyslipidaemic hamsters. They found that the ethanolic extract and its fractions led to reductions in LDL-cholesterol levels of 43.9%, 31.0%, 33.4%, and 24.6%, respectively. Additionally, treatment with *Glycyrrhiza glabra* root ethanolic extract and its fractions significantly lowered LDL and VLDL (very-low-density lipoprotein) levels in hamsters fed a high-fat diet, with varying degrees of effectiveness [23].

11. Skin lightening activity

Liquorice extract is known for its efficacy as a pigment lightening agent. Glabridin, found in the hydrophobic fraction of liquorice extract, has been shown to inhibit tyrosinase activity in cultured B16 murine melanoma cells. Other active compounds in liquorice extract, such as glabrene, licochalcone A, and isoliquiritin, also contribute to the inhibition of tyrosinase activity. Additionally, liquiritin, another component of liquorice extract, disperses melanin, thereby promoting skin lightening [24].

Traditional uses: For anemia, a decoction of madhuka or its powder is often mixed with honey.

1. To promote lactation, it is mixed with cow's milk [25].
2. In cases of menorrhagia, a mixture of 10g of madhuka powder with 10 g of sugar, pounded with rice water, is commonly recommended.
3. A confection of rice milk prepared with Yashtimadhu is used for treating hoarseness of voice.
4. Charaka prescribed a combination of 10 g of madhuka powder mixed with honey, followed by intake of milk, as both an aphrodisiac and an intellect-promoting tonic [26].
5. Charaka also recommended a paste of licorice and *Picirrhiza kurroa* with sugar water as a cardio-tonic.
6. For hematemesis, Charaka prescribed a mixture of Yashtimadhu and Santalum album, powdered with milk.
7. Sushrata prescribed a paste of 10g of Yashtimadhu for intrinsic haemorrhage [27].
8. In cases of edema, a paste of licorice and Sesamum indicum, mixed with milk and butter, is used.
9. Warm clarified butter mixed with licorice is applied topically on wounds, bruises, and burns.
10. A decoction of madhuka is applied on erysipelas.
11. A decoction of the root is used as a wash for falling and greying hair [28].

Conclusion

The current global trend shows an increasing demand for phytopharmaceuticals due to concerns over the side effects associated with allopathic drugs. This trend underscores the importance of selecting plants for further phytochemical and pharmacological investigation.

The pharmacological activities discussed in this review confirm the therapeutic benefits of *Glycyrrhiza glabra*. This plant has been traditionally used for treating conditions such as asthma, bronchitis, ulcers, and inflammation. It contains essential oils, coumarins, alkaloids, and flavonoids. Extracts derived from its root are commonly found in various herbal preparations on the market today.

The presence of these chemical compounds suggests that *Glycyrrhiza glabra* could serve as a valuable starting point for the development of novel therapeutic agents in the future. Further studies are needed to fully explore its potential in preventing and treating diseases. This review provides a roadmap for future researchers to conduct investigations on this plant, with the aim of discovering new medicinally important drugs or designing innovative dosage forms of its active constituents.

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Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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