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# *GLYCYRRHIZA GLABRA* L.: AN OVERVIEW OF ITS PHARMACOLOGICAL SIGNIFICANCE

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## ABSTRACT

*Glycyrrhiza glabra* L., commonly known as licorice, is an important medicinal plant widely recognized for its traditional therapeutic applications and diverse pharmacological properties. Its roots have been used as medicine for centuries in Indian, Chinese, Greek, and other traditional systems to treat respiratory, gastrointestinal, inflammatory, and hepatic disorders. The present review provides a comprehensive overview of the botanical characteristics, traditional uses, phytochemical constituents, and pharmacological activities of *G. glabra*, highlighting its potential applications in healthcare and pharmaceutical research. The plant contains numerous bioactive compounds, including glycyrrhizin, glycyrrhetinic acid, glabridin, licochalcones, flavonoids, phenolic compounds, saponins, and terpenoids, which contribute to its diverse biological activities. Reported pharmacological properties include antioxidant, antibacterial, antifungal, antiviral, hepatoprotective, antidiabetic, anti-inflammatory, hypolipidemic, gastroprotective, anticancer, antimalarial, antithrombotic, immunostimulatory, skin-lightening, and hair-growth-promoting effects. Despite promising findings, further investigations are required to establish the clinical efficacy, pharmacokinetics, safety, and optimal therapeutic dosages of its bioactive constituents. Overall, *G. glabra* represents a valuable source of pharmacologically active natural compounds and offers considerable potential for the development of evidence-based herbal formulations and novel therapeutic agents.

## 1. INTRODUCTION

Medicinal plants have been an essential component of human civilization since ancient times, long before written history existed. In addition to using plants for food, fire, clothing, and shelter, early people also recognised and used them for their medical qualities.[1] As people relied on natural surroundings for remedies, medicinal plants were the first and most reliable therapeutic agents for the treatment of many illnesses, because they contain various bioactive substances having direct or indirect therapeutic benefits.[2]

People have used herbal remedies to cure illnesses and promote health for more than 3,000 years. Over the past two centuries, their uses had expanded significantly, due to increasing recognition of their efficacy and safety.[3] Currently, more than 50,000 plant species, representing over one-tenth of the world's flora, are extensively utilized in pharmaceutical and cosmetic industries.[2] Additionally, the World Health Organization (WHO) estimates that around 80% of the world's population receives primary care from plant-based medications, highlighting the ongoing importance of medicinal plants in both conventional and modern healthcare systems.[4]

*Glycyrrhiza glabra* (Family - Fabaceae) commonly known as licorice, is one of the most popular medicinal plants, widespread throughout the world, primarily in Asia, along with other parts of the world i.e. Europe, Africa, and Australia.[5] This plant has been traditionally employed in medicine for various purposes, including treating cough, bronchitis, arthritis cold, as an expectorant, and serving as an anti-inflammatory, hepatoprotective, and antidiabetic.[6, 7]

Regardless a range of reported pharmacological activities, some activities have not been yet comprehensively explored. This lack of in-depth research highlights a notable gap in the current knowledge and emphasizes the need for further inspection into the various pharmacological activities of plant and its inherent health-promoting effects. The currentreview provides an extensive overview of *G. glabra*, mainly pharmacologically important constituents and their pharmacological activities.

## 2. BOTANICAL DESCRIPTION

*G. glabra*, is a perennial herbaceous shrub attaining a height between 1 to 2.5 meters.[8] The root system includes a main root and subsidiary roots that give rise to long horizontal woody stolons, which are harvested as licorice. These roots have a fibrous texture, yellowish interior, a distinctive aroma, and a sweet taste.[1] The leaves are pinnately compound with 4 to 7 pairs of oblongs, elliptical, or lanceolate leaflets. The plant produces narrow, papilionaceous, bisexual, lavender to violet flowers arranged in axillary spikes. The fruits are flattened legume or pod, usually containing 2 to 5 brown, kidney-shaped seeds.[9]

Kingdom: Plantae
Division: Tracheophyta
Class: Magnoliopsida
Order: Fabales
Family: Fabaceae
Sub-family: Faboideae
Tribe: Glycyrrhizeae
Genus: *Glycyrrhiza*
Species: *glabra*



**(A) Plant Morphology**



**(B) Roots**

## 3. TRADITIONAL USES

*G. glabra* is an important herb used as medicine for thousands of years in ancient Egyptian, Greek, Roman, Indian, and Chinese traditional systems of medicine.[5] Traditionally, licorice roots have been used to manage a wide range of disorders, including asthma, paralysis, coughs, tonsillitis, sore throat, hyperdipsia, arthritis, epilepsy, fever, jaundice, pneumonia, sexual debility, stomach ulcers, rheumatism, skin diseases, acidity, leucorrhoea, haemorrhagic diseases, kidney and heart diseases.[10,11]

In Indian medicine, licorice has traditionally been used to enhance vitality and treat influenza, liver disorders, arthritis, eye diseases, and gynaecological conditions.[12]

In Traditional Chinese Medicine, it has been employed to improve strength and endurance, treat acne, epilepsy, hysteria, irritability, and to reduce the toxicity of other herbal medicines while harmonizing herbal formulations.[5]

## 4. PHYTOCHEMICAL PROFILE

*G. glabra* exhibited a wide range of active chemical components. Among the predominantly reported chemical constituents, those primarily found are alkaloids, flavonoids, phenols, tannins, saponins, terpenes, coumarins, glycosides and essential oils. Out of them, terpenoids and flavonoids are two important classes of chemical compounds that influence the medicinal effects of licorice.[13,14]

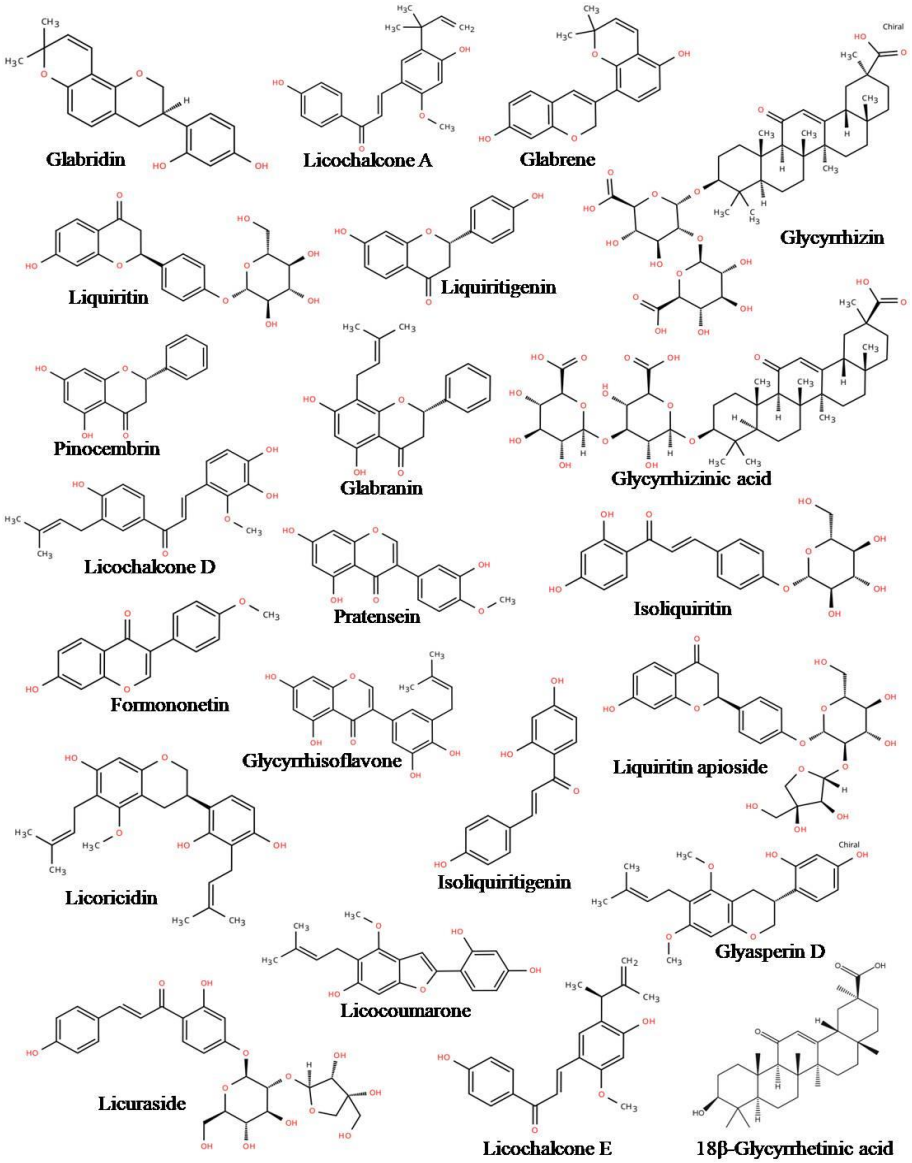



**Figure 1: Chemical structure of some common phytochemicals found in *G. glabra*.**

## 5. PHARMACOLOGICAL ACTIVITIES

### 5.1. Antioxidant Activity

Different chemical compounds isolated from licorice exhibited significant antioxidant activity. Liquorice flavonoids have exceptionally strong antioxidant activity and found 100 times stronger than that of vitamin E.[3] Earlier reports support that liquorice extract can be used to formulate cosmetic products for the protection of skin and hair against oxidative damage.[15] Ojha et al.[16] found that *G. glabra* extract exhibited protective effects against ischemia–reperfusion injury induced by left anterior descending coronary artery ligation in rats by alleviating oxidative stress and favourably regulating the cardiac function. Some flavonoids like licochalcones B and D present in *G. glabra* also exhibited strong radical scavenging activity of DPPH and showed their potency to prevent microsomal lipid peroxidation.[17]

### 5.2. Antibacterial Activity

In various studies it was found that aqueous and ethanolic extracts of liquorice possessed strong antibacterial activity against *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, and *Enterococcus faecalis*.[18] Secondary metabolites present in hydro-methanolic root extract of *G. glabra*, possess potent antibacterial activity against *S. aureus*.[19] Similarly, glabridin and glabrene compounds isolated from *G. glabra* significantly attenuated the gastritis infection caused by *Helicobacter pylori*.[20] Some notable antibacterials activity of different *G. glabra* extracts are represented in Table 1.

**Table 1: Antibacterials Activity Reported in Different *G. Glabra* Extracts.**

| Extract | Model | Inhibitory effect against bacteria | References |
|---|---|---|---|
| Aqueous and ethanolic extracts | *in vitro* | *Streptococcus pyogenes* | Fukai et al.[21]; Wang et al.[22] |
| Root extract | *in vitro* | *Mycobacterium tuberculosis* | Gupta et al. [23] |
| Ethanolic extract and tetrahydrofuran extract | *in vitro* | *S. aureus* and *E. coli* | Iqbal [24] |
| Aqueous and ethanolic extracts | *in vitro* | *S. aureus, E. coli,* and *P. aeruginosa* | Al Mousawi et al.[25] |
| Root extract | *in vitro* | *Streptococcus mutans, S. sanguis, Actinomyces viscosus, S. aureus* and *E. coli* | Sedighinia et al. [26] |

**5.3 Anti-fungal Activity**

*G. glabra* exhibited significant fungicidal activity against various phytopathogenic fungi, which has mainly been attributed due to the presence of phenolic compounds such as flavonoids, isoflavonoids and chalcones.[27] Glabridin, isolated from licorice displayed effective antifungal activity against *Sclerotinia sclerotiorum* with an $EC_{50}$ value of 6.78 µg/mL which was 8 times more potent than azoxystrobin ($EC_{50}$, 57.39 µg/mL). These findings indicated that glabridin exhibited fungicidal activitiy by inducing reactive oxygen species accumulation, the loss of mitochondrial membrane potential and cell membrane destruction.[27] Glabridin also showed resistance modifying activity against drug resistant mutants of *Candida albicans* at a minimum inhibitory concentration of 31.25-250 µg /mL.[28] In another study it was found that the methanolic extract of liquorice showed notable fungicidal activity against *Arthrinium sacchari* and *Chaetomium funicola*.[29] Furthermore, Chandra and Gunasekaran, reported the antifungal activity of crude methanolic extract of *G. glabra* against *Aspergillus niger*.[30]

**5.4. Antiviral Activity**

*G. glabra* extracts containing glycyrrhizin and 18β-glycyrrhetinic acid showed notable antiviral activity against different viruses such as *Varicella zoster*, herpes simplex, Japanese encephalitis, influenza, and vesicular stomatitis virus. These substances can reduce adhesion force and stress, limit virus gene expression and replication. Additionally, they can activate T lymphocyte proliferation, inhibit host cell apoptosis, and prevent the breakdown of the IκB enzyme, which is implicated in the spread of the cellular response to inflammation.[22] Glycyrrhizic acid can terminate the latent infection of Kaposi sarcoma-associated herpesvirus (KSHV) by downregulating the expression of latency-associated nuclear antigen (LANA) in B lymphocytes and thereby results in natural cell death of the KSHV virus.[31]

**5.5. Hepatoprotective Activity**

Glycyrrhizin isolated from licorice displayed potent Hepatoprotective activity. It has shown protective effect by inducing a significant reduction in serum aminotransferases level and improved the overall liver histology.[32] According to Huo et al. different combinations of 18α-and 18β-Glycyrrhizic acid showed hepatoprotective effects by inhibiting the production of free radicals and lipid peroxidation.[33] Furthermore, it was found that *G. glabra* showed a promising therapeutic agent for managing hepatic complications associated with diabetes mellitus. This study investigated its hepatoprotective effects in a streptozotocin induced diabetic rat model, and found that treatment with *G. glabra* significantly improved liver function in diabetic rats, as evidenced by lowering ALT, AST, and ALP levels compared to untreated diabetic rats ($p < 0.05$), suggesting hepatocyte protection through its antioxidant and anti-inflammatory properties.[34] Moreover, in vitro studies have indicated that glycyrrhizin modifies the intracellular transport and suppresses hepatitis B virus (HBV) surface antigen, thereby preventing hepatocellular cancer in patients.[35, 36] Additionally, GA also prevents the oxidative and hepatic damage caused by aflatoxins by increasing the CYP1A1 and GST (glutathione-S-transferase) activities and may also contribute to anticarcinogenic activity by metabolic deactivation of the hepatotoxin.[37]

**5.6. Anti-Hypolipidemic Effect / Anti-Dyslipidemic Effect**

In a study it was found that different extracts such as glabridin ethanolic extract, ethyl-acetate soluble, water-soluble, and hexane soluble fractions of licorice showed notable anti hypolipidemic effect. The studies revealed that the extracts reduce total serum cholesterol, triglyceride, and increased serum HDL in hamsters, fed a high-fat diet.[38]

**5.7. Antidiabetic / Hypoglycemic Activity**

Type 2 diabetes mellitus (T2DM), an insulin-resistant metabolic disorder becomes an increasingly common global health concern. Peroxisome proliferation activated receptors (PPARs), are ligand-dependent transcriptional factors that control the expression of several genes that are crucial for the metabolism of fats and glucose. Glycyrin, isolated from licorice exhibited a potent PPAR-γ ligand binding activity and therefore reduces the blood glucose level in KK-Ay (knockout diabetic mice).[39] Furthermore, in another it was found that ethyl acetate extract of licorice showed notable PPAR-γ binding activity thereby, effectively reduce blood glucose levels in diabetic mice.[40]

### 5.8. Antidemulcent and Anti-Tussive Properties

It was discovered that the liquorice powder and extract worked well for bronchial catarrh, cough, and sore throats. It has been demonstrated that liquorice relieves sore throats just as effectively as codeine. It has expectorant properties and reduces inflammation. *Glycyrrhiza* is the source of the semi-synthetic chemical carbenoxolone, which increases the production of stomach mucus. The demulcent effect of liquorice is caused by glycyrrhizin.[41]

### 5.9. Immunostimulatory Action

In a study it was found that *G. glabra* displayed promising immunostimulatory effects. It has shown an immunostimulatory effect at a concentration of 100µg/ml by increases human granulocytes' ability to produce TCD69 lymphocytes and macrophages.[31] Liquorice extract has been found to improve immunological responses in rainbow trout by increasing white blood cells, immunoglobulin, lysozyme, complement activity, and immune-related gene expression. Fish mortality was decreased and resistance to *Yersinia ruckeri* infection was enhanced by dietary supplementation, especially at 2 g $kg^{-1}$.[42]

### 5.10. Anti-inflammatory Activity

The anti-inflammatory activity of *G. glabra* and its use in the treat ment of inflammatory diseases have been documented since ancient times.[43] Shalaby et al.[44] evaluated the anti-inflammatory activity of *G. glabra* in male rats after 4 weeks of feeding. They observed a significant decrease in the total cholesterol and triglyceride levels as well as in the levels of serum liver enzymes. In another study it was found that *G. glabra* showed notable effect in treating upper respiratory tract and gastric system diseases, these pharmacological effects were due to an increase in the secretion of serotonin and prostaglandins in the stomach that led to a decrease of gastric inflammation.[45] Furthermore, Xiao et al.[46] observed that glycyrrhizin obtained from *G. glabra* showed inhibition of liver granuloma formation and the inflammatory cytokine production.

### 5.11. Anti-ulcer / Gastroprotective Activity

The anti-ulcer activity of *G. glabra* has been extensively investigated, particularly in treating gastrointestinal disorders. Traditionally, the licorice extracts have been widely used to treat gastric and duodenal ulcers and as an adjuvant for relieving the spasmodic pain associated with chronic gastritis.[47,48] Glycyrrhizinic acid isolated from licorice showed significant antiulcer effect by raising the local concentration of prostaglandins that promote mucous secretion and cell proliferation in the stomach.[20, 49] Additionally, liquorice has been reported to prolong the lifespan of gastric surface epithelial cells and exhibit antipepsin activity, further contributing to mucosal protection and ulcer healing.[50]

### 5.12. Anticancer Activity

Glycyrrhizic acids and 18β-glycyrrhetinic isolated from *G. glabra*, have been extensively investigated for their anticancer and antitumor activities. In a study researchers found that *G. glabra* extract containing 18β-glycyrrhetinic and glycyrrhizic acids induce mitochondrial permeability transition, leading to the apoptosis of tumour cells, thereby indicating their potential inhibitory effects on cancer cell growth.[51] According to Wang et al.[22], 18β-glycyrrhetinic acid has strong antitumor efficacy against colorectal cancer. Furthermore, Xiao et al.[46] investigated the mechanism of action of licochalcone A in human gastric cancer cells. The findings showed that licochalcone A suppresses the growth of gastric cancer cells in a dose-dependent manner by preventing cell cycle progression at the G2/M transition and causing apoptosis. In another study was also reported that the hydro methanolic root extract of *G. glabra* exhibited antimutagenic potential by suppressing micronuclei formation and chromosomal aberration in bone marrow cells of treated albino mice.[19]

### 5.13. Skin Lightening Activity

Various compounds isolated from licorice has been reported to be an effective pigment lightening agent. Pigment lightening activity is mainly attributed due to the antioxidant, anti-inflammatory and its ultraviolet (UV) protecting activity.[43] In a study, the use of liquorice mainly for skin eruptions, including dermatitis, eczema, pruritus, and cysts was also reported.[52] Glabridin isolated from liquorice extract has been shown to inhibits tyrosinase activity in cultured B16 murine melanoma cells thereby, indicating their skin lightening potential.[53] Additionally, liquiritin, another component of liquorice extract, disperses melanin, resulting in promoting skin lightening.[54]

### 5.14. Hair Growth Stimulation

Due to its significant hair growth activity, liquorice can be safely used in herbal formulations to treat many forms of alopecia. In a previously published study, liquorice hydroalcoholic extract demonstrated significant effects on promoting hair growth. It was discovered that the 2% concentration of liquorice extract showed better hair growth stimulatory effect when compared to the conventional drug (2% minoxidil).[55]

### 5.15. Antimalarial Activity

Licochalcone, a chalcone isolated from licorice, exhibited significant antimalarial action. Malarial parasites were totally eradicated by oral treatment of 1000 mg/kg, according to a previously published study.[56] Liquorice root extract in hydro-methanol and ethyl acetate demonstrated potent antiplasmodial action against the *Plasmodium. falciparum* strain with minimal toxicity to HeLa cells, according to an in vitro investigation. However, an in vivo study revealed that administering these fractions inhibits the growth of *P. berghei*.[57]

### 5.16. Antithrombotic Effect

In a previously published study, the in vivo effects of licorice extract and its combination with vitamin K and heparin were evaluated in Sprague Dawley rats. The bleeding time was found to be extended by giving licorice extract at doses of 180 mg/kg and 360 mg/kg. Blood loss was determined 60 minutes later as a function of absorbance at 540 nm due to the haemoglobin level in the water solution. All of the evidence points to *G. glabra* as an efficient anti-thrombotic agent.[58]

## 6. CONCLUSION

The present review revealed that *G. glabra* is an important medicinal plant having a rich history of traditional use and range of pharmacological activities. Its diverse phytochemical constituents like glycyrrhizin, glycyrrhetinic acid, glabridin, licochalcones etc. contribute to its antioxidant, antimicrobial, anti-inflammatory, hepatoprotective, antidiabetic, gastroprotective, antiviral, and anticancer properties. Integrating traditional medicinal knowledge with modern phytochemical, pharmacological, and clinical research may facilitate a better understanding of its therapeutic properties and limitations. Such an evidence-based approach will be essential for the safe, effective, and sustainable utilization of this plant in future healthcare and pharmaceutical applications.

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