

GLYCYRRHIZA GLABRA (LIQUORICE): A COMPREHENSIVE REVIEW OF ITS PHYTOCHEMISTRY, TRADITIONAL USES AND PHARMACOLOGICAL ACTIVITIES

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ABSTRACT

Glycyrrhiza glabra L., commonly known as liquorice or licorice, is an important medicinal plant belonging to the family Fabaceae and has been used traditionally for centuries in various systems of medicine. The therapeutic potential of liquorice is largely attributed to its diverse phytochemical constituents, particularly triterpenoid saponins, flavonoids, isoflavonoids, chalcones, phenolic compounds and polysaccharides. Glycyrrhizin, glycyrrhetic acid, liquiritin, liquiritigenin, isoliquiritigenin, glabridin and glabrene are among the major bioactive constituents associated with its pharmacological effects. Increasing experimental evidence suggests that *G. glabra* possesses a broad spectrum of pharmacological activities, including anti-inflammatory, antioxidant, antiviral, antimicrobial, hepatoprotective, anticancer, cardiovascular, neuroprotective, gastroprotective, antidiabetic, antifibrotic and immunomodulatory activities. Several of these effects are associated with modulation of oxidative stress, inflammatory mediators, nuclear factor-kappa B (NF-κB), nuclear factor erythroid 2-related factor 2 (Nrf2), apoptotic signalling and other cellular pathways. Liquorice-derived compounds have also attracted attention as potential therapeutic leads for hepatic, respiratory, infectious, gastrointestinal and inflammatory disorders. However, the pharmacological evidence remains predominantly preclinical, and considerable variation exists with respect to plant part, extract composition, dose, standardization and experimental model. In addition, excessive or prolonged exposure to glycyrrhizin and glycyrrhetic acid may produce mineralocorticoid-like adverse effects, including sodium retention, hypokalemia, hypertension and edema. This review summarizes the phytochemical composition, traditional medicinal applications and major pharmacological activities of *G. glabra*, with emphasis on the proposed mechanisms of action and its potential for future therapeutic development.

KEYWORDS: *Glycyrrhiza glabra*; liquorice; glycyrrhizin; glycyrrhetic acid; flavonoids; phytoconstituents; pharmacological activities; medicinal plant.

1. INTRODUCTION

Medicinal plants have played an important role in traditional healthcare systems and continue to serve as valuable sources of bioactive molecules for modern drug discovery. The therapeutic importance of medicinal plants is largely associated with the presence of structurally diverse secondary metabolites capable of influencing multiple biological pathways. Among these plants, *Glycyrrhiza glabra* L., commonly known as liquorice, is a well-known medicinal plant with a long history of traditional use.

G. glabra belongs to the family Fabaceae and is widely distributed across Asia and Europe. The medicinally important material mainly consists of the roots, rhizomes, rootlets and stolons. Traditionally, liquorice has been used for cough, sore throat, gastrointestinal disorders, inflammation, liver disorders and other ailments. The plant is also recognized for its demulcent, anti-inflammatory, antitussive and antiulcer properties.

The pharmacological effects of *G. glabra* are associated with a complex phytochemical profile. Triterpenoid saponins, particularly glycyrrhizin and its metabolite glycyrrhetic acid, represent important constituents. Liquorice also contains flavonoids such as liquiritin, liquiritigenin, isoliquiritin and isoliquiritigenin, together with isoflavonoids including glabridin and glabrene. These compounds have been investigated for antioxidant, anti-inflammatory, antiviral, hepatoprotective and other biological effects.

Growing experimental evidence indicates that liquorice possesses a broad pharmacological spectrum rather than a single therapeutic action. Its constituents may influence oxidative stress, inflammatory signalling, apoptosis,

immune responses and other molecular mechanisms. Consequently, *G. glabra* has attracted increasing interest as a source of pharmacologically active compounds and potential therapeutic leads.

The objective of the present review is to summarize the botanical characteristics, traditional medicinal applications, major phytochemical constituents and diverse pharmacological activities of *G. glabra*, while also discussing its mechanisms, translational potential and safety considerations.

2. Botanical Profile

2.1 Taxonomy

G. glabra is a perennial herbaceous plant that may grow to approximately 1.4 m in height. It possesses compound leaves with oval leaflets, white to purplish flower clusters and flat pods. The underground system consists of an extensive root system with a main taproot and runners. The roots, rhizomes, rootlets and stolons constitute the major medicinal portions of the plant.

2.2 Distribution

G. glabra is distributed widely across Asia and Europe and has been reported from regions including Italy, Spain, Turkey, the Caucasus, western China and Central Asia. Commercial cultivation has also been reported in countries including Iran, Iraq, Turkey, Afghanistan, India, China, Spain, Italy, Greece, France, Syria, Uzbekistan, Turkmenistan, Azerbaijan, the United States and England.

2.3 Traditional Medicinal Uses

Liquorice has been traditionally used for a variety of therapeutic purposes. Different parts of the plant have been associated with different traditional applications.

Plant part	Traditional uses
Root	Cough, sore throat, hepatitis, constipation, inflammation and liver disorders
Rhizome	Respiratory disorders and digestive ailments
Stem	Sore throat and gastric ulcers
Leaves	Topical skin applications and folk remedies
Fruit	Sore throat, cough and digestive disturbances

The broad traditional use of liquorice has contributed to continued scientific interest in its phytochemistry and pharmacological properties.

3. Phytochemical Constituents

The pharmacological properties of *G. glabra* are closely associated with its diverse phytochemical composition. The major phytochemical groups include triterpenoid saponins, flavonoids, isoflavonoids, chalcones, phenolic compounds, polysaccharides, sterols, coumarins, resins and volatile constituents.

3.1 Triterpenoid Saponins

Glycyrrhizin is one of the characteristic constituents of liquorice and contributes to its characteristic sweet taste.

Glycyrrhetic acid represents the aglycone of glycyrrhizin and has also been investigated extensively for its pharmacological effects.

3.2 Flavonoids and Chalcones

Liquorice contains flavonoids such as liquiritin and liquiritigenin, together with chalcones including isoliquiritin and isoliquiritigenin. These compounds have demonstrated antioxidant and anti-inflammatory properties and have been investigated in several disease models.

3.3 Isoflavonoids

Important isoflavonoids include formononetin, glabridin and glabrene. Glabridin has received particular attention

because of its antioxidant and anti-atherogenic properties.

3.4 Other Constituents

Other reported constituents include asparagine, betaine, choline, amino acids, glucose, sucrose, starch, polysaccharides, sterols, coumarins, resins and volatile oils. Several additional flavonoids, prenylated flavonoids, chalcones and glycosides have also been reported.

The chemical composition may vary considerably depending on species, geographical origin, plant part, cultivation conditions and extraction method. Therefore, standardization of liquorice preparations is important when comparing pharmacological studies.

4. Pharmacological Activities of *Glycyrrhiza glabra*

4.1 Anti-inflammatory Activity

Anti-inflammatory activity is one of the most extensively investigated pharmacological properties of liquorice. Glycyrrhizin and liquorice-derived flavonoids can influence inflammatory mediators and signalling pathways involved in inflammatory responses.

Isoliquiritigenin has demonstrated anti-inflammatory activity through modulation of pathways including NF- κ B and Nrf2. Experimental studies have also reported reductions in inflammatory-cell infiltration and inflammatory cytokines in models of respiratory disease.

The anti-inflammatory effects of liquorice may therefore contribute to its reported activity in respiratory, hepatic, gastrointestinal and other inflammatory disorders.

4.2 Antioxidant Activity

Oxidative stress plays an important role in the pathogenesis of numerous diseases. Liquorice contains flavonoids and phenolic compounds with free-radical-scavenging and antioxidant properties.

Glabridin has been reported to protect low-density lipoprotein against lipid peroxidation, whereas isoliquiritigenin has demonstrated antioxidative activity through activation of the KEAP1/Nrf2 pathway. Enhancement of antioxidant defence may contribute to the protective effects of liquorice against oxidative cellular injury.

The antioxidant activity of *G. glabra* is particularly relevant to its hepatoprotective, cardiovascular, respiratory and cytoprotective properties.

4.3 Antiviral Activity

Liquorice and its major constituents have been investigated for antiviral activity against a range of RNA and DNA viruses. Glycyrrhizin, glycyrrhetic acid and related compounds have been studied against influenza viruses, respiratory syncytial virus, hepatitis viruses, herpes viruses, HIV and coronaviruses.

The proposed antiviral mechanisms include interference with viral attachment, uptake and penetration into host cells, inhibition of viral replication and modulation of host cellular responses.

Although these findings indicate considerable antiviral potential, much of the evidence remains experimental and requires further validation in appropriate clinical settings.

4.4 Antimicrobial and Antibacterial Activity

G. glabra exhibits antimicrobial activity against various microorganisms. Triterpenoids, flavonoids and phenolic compounds have been implicated in these effects.

The antimicrobial and anti-inflammatory properties of liquorice may act synergistically in respiratory tract infections and other inflammatory infectious conditions. Several liquorice-derived isoflavonoids and related compounds have also been investigated for antimicrobial activity.

4.5 Anti-asthmatic and Bronchodilator Activity

Liquorice-derived glycyrrhizic acid and flavonoids have been investigated for their potential anti-asthmatic effects. Isoliquiritigenin has demonstrated beneficial effects in experimental models of cigarette-smoke-induced respiratory disease, with reported reductions in inflammatory-cell infiltration and inflammatory cytokines.

A clinical study involving patients with chronic bronchial asthma has also reported bronchodilator-related effects of *G. glabra*. However, further controlled clinical investigations are necessary to establish its clinical relevance.

4.6 Anti-COPD Activity

Liquorice constituents have been investigated in chronic obstructive pulmonary disease models. Isoliquiritigenin was reported to reduce inflammatory changes in cigarette-smoke-induced COPD models and to regulate NF- κ B and Nrf2 signalling.

These findings suggest that liquorice flavonoids may provide protective effects against oxidative and inflammatory damage associated with chronic respiratory disease.

4.7 Hepatoprotective Activity

Hepatoprotection represents one of the important pharmacological activities associated with *G. glabra*. Glycyrrhizin and glycyrrhetic acid have been extensively investigated for their protective effects against hepatic injury.

Their antioxidant and anti-inflammatory properties may reduce oxidative damage, inflammation and toxic injury to hepatic cells. Glycyrrhetic acid has additionally been

investigated for its ability to inhibit bile-acid-induced necrosis and apoptosis.

Preclinical studies have reported reductions in biochemical markers of hepatic injury and oxidative stress following administration of liquorice extracts or its constituents. These observations support further investigation of *G. glabra* as a source of hepatoprotective compounds.

However, it is important to emphasize that the available evidence is predominantly preclinical and that variations in extract composition, dose, plant part and experimental model limit direct comparison between studies.

4.8 Anticancer Activity

Liquorice has attracted considerable interest for its potential anticancer properties. Glycyrrhizin, glycyrrhetic acid and flavonoids such as isoliquiritigenin and glabridin have been investigated in different cancer models.

The reported effects involve mechanisms associated with cellular proliferation, apoptosis, oxidative stress and inflammatory signalling. Liquorice-derived flavonoids may therefore represent potential sources of lead compounds for anticancer drug development.

Nevertheless, most available evidence is experimental and cannot be directly extrapolated to clinical anticancer efficacy.

4.9 Cardiovascular and Anti-atherogenic Activity

Cardiovascular protective properties have also been investigated for liquorice. Glabridin and other polyphenolic constituents may protect lipoproteins from oxidative modification.

Experimental studies have evaluated antioxidant and anti-atherogenic effects of *G. glabra* root preparations. These findings suggest that liquorice constituents may influence oxidative processes associated with cardiovascular disease.

4.10 Neuroprotective Activity

Glycyrrhizin has been investigated for neuroprotective effects in experimental models. A dose-dependent neuroprotective effect of phyto-derived glycyrrhizin has been reported in a rat brain model involving norepinephrine depletion.

Liquorice constituents have also been discussed in relation to memory deficits and neurodegenerative disorders. However, additional mechanistic and clinical studies are required to establish the therapeutic relevance of these observations.

4.11 Gastroprotective and Anti-ulcer Activity

Liquorice has a long history of traditional use in gastrointestinal disorders. Its anti-inflammatory and mucosal-protective properties are considered important contributors to its gastroprotective effects.

Liquorice-derived compounds have also been investigated against *Helicobacter pylori*, suggesting that antimicrobial, anti-inflammatory and mucosal-protective mechanisms may collectively contribute to its anti-ulcer activity.

4.12 Antidiabetic and Metabolic Activity

Liquorice and its flavonoid constituents have been investigated for potential effects on glucose metabolism and metabolic disorders. The antioxidant and anti-inflammatory activities of its phytochemicals may contribute to these effects.

However, evidence for antidiabetic and metabolic effects remains largely experimental, and further well-designed clinical studies are required before therapeutic significance can be established.

4.13 Antifibrotic Activity

Liquorice constituents have been investigated for protective effects against tissue fibrosis, particularly in hepatic and respiratory conditions.

Reduction of oxidative stress and inflammatory signalling may contribute to the antifibrotic effects observed in experimental models. The interaction of liquorice constituents with pathways involved in fibrogenesis warrants further investigation.

4.14 Immunomodulatory Activity

G. glabra may influence immune responses and has been investigated for immunomodulatory effects. Glycyrrhizin can modulate inflammatory and immune responses associated with infection.

These properties may contribute to the reported protective effects of liquorice in respiratory infections and inflammatory disorders.

5. Major Bioactive Constituents and Their Pharmacological Significance

Several constituents of *G. glabra* have received particular attention because of their broad biological activities.

Constituents	Major reported pharmacological relevance
Glycyrrhizin	Anti-inflammatory, antiviral, hepatoprotective and immunomodulatory effects
18 β -Glycyrrhetic acid	Hepatoprotective, anti-inflammatory and cytoprotective effects
Glabridin	Antioxidant and anti-atherogenic effects
Liquiritigenin	Antioxidant and anti-inflammatory effects

Isoliquiritigenin	Anti-inflammatory, antioxidant and respiratory protective effects
Liquiritin	Bioactive flavonoid associated with antioxidant and other pharmacological effects
Glabrene	Bioactive isoflavonoid with reported biological activities

The multitarget nature of these constituents may partly explain the broad pharmacological spectrum of liquorice.

6. Possible Molecular Mechanisms

The pharmacological activities of *G. glabra* appear to involve multiple cellular pathways rather than a single molecular target.

Important mechanisms reported or proposed in the literature include:

- Modulation of NF- κ B-dependent inflammatory signalling
- Activation of the KEAP1/Nrf2 antioxidant pathway
- Regulation of oxidative stress and lipid peroxidation
- Modulation of apoptosis-associated proteins such as Bax/Bcl-2 and caspases
- Regulation of CYP2E1-associated toxic bioactivation
- Modulation of TGF- β 1-related fibrogenic signalling
- Regulation of inflammatory cytokines
- Modulation of cellular immune responses

The simultaneous influence of oxidative stress, inflammation, apoptosis and fibrosis pathways provides a mechanistic rationale for the broad biological effects of liquorice.

7. Translational Potential and Drug Development

The pharmacological diversity of *G. glabra* provides considerable potential for development of phytotherapeutic products and lead molecules. Important constituents including glycyrrhizin, 18 β -glycyrrhetic acid, glabridin, liquiritigenin, isoliquiritigenin and magnesium isoglycyrrhizinate have demonstrated activity against multiple biological targets.

In hepatic disorders, reported mechanisms include Nrf2-mediated antioxidant defence, NF- κ B-dependent inflammatory signalling, modulation of apoptosis, CYP2E1-associated toxic bioactivation and TGF- β 1-related fibrogenesis.

Magnesium isoglycyrrhizinate represents an example of derivative-based development intended to retain hepatoprotective activity while improving tolerability.

However, translation from experimental findings to clinically validated therapy remains incomplete. Differences in extract composition, plant part, standardization, dosage, route of administration and clinical endpoints make comparison between studies difficult.

Future drug-development strategies should emphasize:

1. Botanical authentication and quality control.
2. Standardization of extracts.
3. Identification and validation of active constituents.
4. Pharmacokinetic and bioavailability studies.
5. Dose-response investigations.
6. Toxicological evaluation.
7. Drug-interaction studies.
8. Well-designed randomized controlled clinical trials.
9. Development of standardized pharmaceutical derivatives.

8. Research Gaps and Future Perspectives

Although *G. glabra* has demonstrated a broad spectrum of pharmacological activities, several research gaps remain.

First, greater emphasis should be placed on standardization of extracts and phytochemical characterization. The pharmacological activity of a plant extract may vary depending on geographical origin, plant part, extraction method and chemical composition.

Second, the relationship between individual phytoconstituents and observed pharmacological effects requires further investigation. Identification of specific active molecules followed by mechanistic validation could facilitate the development of defined therapeutic candidates.

Third, pharmacokinetic and bioavailability studies are required to determine absorption, metabolism, distribution and elimination of important liquorice constituents.

Fourth, although antioxidant and anti-inflammatory mechanisms have been extensively proposed, additional studies using molecular, cellular and validated animal models are necessary to establish causal mechanisms.

Finally, clinical trials using standardized *G. glabra* preparations are required to determine efficacy, safety, appropriate dose and treatment duration in specific diseases. Disease-specific clinical investigations should be considered for hepatic, respiratory, gastrointestinal, inflammatory and infectious disorders.

10. CONCLUSION

Glycyrrhiza glabra L. is an important medicinal plant with a rich phytochemical profile and a broad spectrum of pharmacological activities. Its major constituents, particularly glycyrrhizin, 18 β -glycyrrhetic acid, glabridin, liquiritigenin and isoliquiritigenin, have demonstrated antioxidant, anti-inflammatory, antiviral,

hepatoprotective, anticancer, cardiovascular, neuroprotective, gastroprotective, antifibrotic and immunomodulatory effects in experimental studies.

The pharmacological effects of liquorice appear to involve multiple mechanisms, including regulation of oxidative stress, activation of antioxidant defence systems, modulation of inflammatory signalling, inhibition of apoptosis and regulation of fibrotic pathways. This multitarget activity makes *G. glabra* an attractive source of pharmacologically active natural products.

However, the current evidence base remains predominantly preclinical. Differences in plant material, extraction procedures, phytochemical composition, dosage and experimental models make direct comparison between studies challenging. Furthermore, the mineralocorticoid-like adverse effects associated with excessive glycyrrhizin exposure highlight the importance of safety evaluation and standardization.

Overall, *G. glabra* represents a promising medicinal plant and a valuable source of bioactive compounds. Future research should focus on standardized extracts, identification of validated active constituents, pharmacokinetic characterization, mechanistic studies, toxicity evaluation and well-designed clinical trials. Such investigations may facilitate the transition of liquorice from a traditionally used medicinal plant to a scientifically standardized and clinically useful phytotherapeutic or source of novel drug leads.

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