CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://doi.org/10.5281/zenodo.17443854

https://www.iajps.com/volumes/volume12-october-2025/113-issue-10-october-25/

Available online at: http://www.iajps.com **Review Article**

EXPLORING THE THERAPEUTIC ROLE OF *GLYCYRRHIZA GLABRA* IN RESPIRATORY TRACT INFECTIONS: EFFICACY, MECHANISMS, AND SAFETY CONSIDERATIONS.

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Abstract:

Respiratory tract infections (RTIs) are among the most widespread health concerns globally, contributing significantly to morbidity and mortality. The rising resistance to conventional antibiotics and antiviral drugs has intensified the search for alternative therapies, particularly those derived from natural sources with established safety and efficacy profiles. Glycyrrhiza glabra (commonly known as licorice or mulethi) is a well-known medicinal plant traditionally used in Ayurveda, Unani, and Traditional Chinese Medicine for managing respiratory conditions.(1) Its therapeutic potential is largely attributed to its bioactive constituents, such as glycyrrhizin, glycyrrhetinic acid, and liquiritin, which demonstrate antiviral, antibacterial, anti-inflammatory, antioxidant, and immunomodulatory properties.(2) Multiple preclinical and clinical studies support its effectiveness in alleviating symptoms associated with RTIs, including cough, sore throat, bronchitis, and asthma. While generally safe at therapeutic doses, overuse may lead to adverse effects like pseudoaldosteronism and electrolyte imbalances due to the mineralocorticoid-like action of glycyrrhizin.(3) This review provides a comprehensive overview of the pharmacological actions, mechanisms, and safety considerations of G.glabra, emphasizing its potential role as a natural, effective adjunct to conventional therapies in the prevention and treatment of respiratory tract infections.

Keywords: *Glycyrrhiza glabra, Licorice, Respiratory tract infections, Antiviral, Anti-inflammatory, Antioxidant, Safety, Pharmacology, Herbal medicine.(4)*

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Please cite this article in press ***Pallavi Shantaram Gore*** *et al.,* ***Exploring The Therapeutic Role Of Glycyrrhiza Glabra In Respiratory Tract Infections: Efficacy, Mechanisms, And Safety Considerations.****, Indo Am. J. P. Sci, 2025; 12(10).*

INTRODUCTION:

Respiratory tract infections (RTIs) are among the most widespread causes of morbidity and mortality worldwide, affecting both upper (URTIs) and lower (LRTIs) parts of the respiratory system. URTIs include conditions like pharyngitis, laryngitis, and sinusitis, while LRTIs encompass more severe illnesses such as bronchitis, pneumonia, and asthma exacerbations.(5) The increasing emergence of antimicrobial resistance has significantly reduced the efficacy of conventional antibiotics and antiviral drugs, creating an urgent need for alternative, safer, and effective treatment options. In this context, traditional herbal medicines are gaining renewed scientific interest.*Glycyrrhiza glabra* L. (family Fabaceae), commonly known as licorice or mulethi, has a long-standing history of use in traditional systems of medicine such as Ayurveda, Siddha, and Traditional Chinese Medicine. Revered as "Yashtimadhu" in Ayurvedic texts, it is valued for its demulcent, expectorant, and anti-inflammatory properties, particularly in treating respiratory ailments like sore throat, cough, and hoarseness of voice.(6) Modern pharmacological research has validated these traditional uses, highlighting *G. glabra*'s antiviral, antibacterial, anti-inflammatory, antioxidant, and immunomodulatory activities.(7) These findings position *G. glabra* as a promising candidate for managing RTIs. However, further studies are needed on standardization, pharmacokinetics, and clinical efficacy to support its integration into modern evidence-based therapies.(8)

Botanical Description :

- **Scientific name:** *Glycyrrhiza glabra* L.
- **Family:** Fabaceae (Leguminosae)
- **Common names:** Licorice, Mulethi, Yashtimadhu
- **Plant part used:** Roots and stolons(9)
- **Distribution:** Native to Mediterranean regions, cultivated in India, China, Iran, and Europe.(10)
- **Morphology:** Perennial herb with a deep taproot, pinnate leaves with 9–17 leaflets, and bluish- purple flowers arranged in racemes. Roots are long, cylindrical, yellowish-brown, and sweet in taste due to glycyrrhizin content.(11)

Fig 1. *Glycyrrhiza glabra* Plant Root

Fig 2. *Glycyrrhiza glabra* Plant

Phytochemical Constituents :

Glycyrrhiza glabra is rich in secondary metabolites responsible for its pharmacological properties:

- **Saponins**: Glycyrrhizin, glycyrrhetinic acid (major bioactives).(14)
- **Flavonoids**: Liquiritin, liquiritigenin, glabridin, isoliquiritigenin, and formononetin.
- **Coumarins**: Herniarin, umbelliferone.(15)
- **Polysaccharides and tannins.**
- **Essential oils and sterols:** β-sitosterol, stigmasterol.(16)

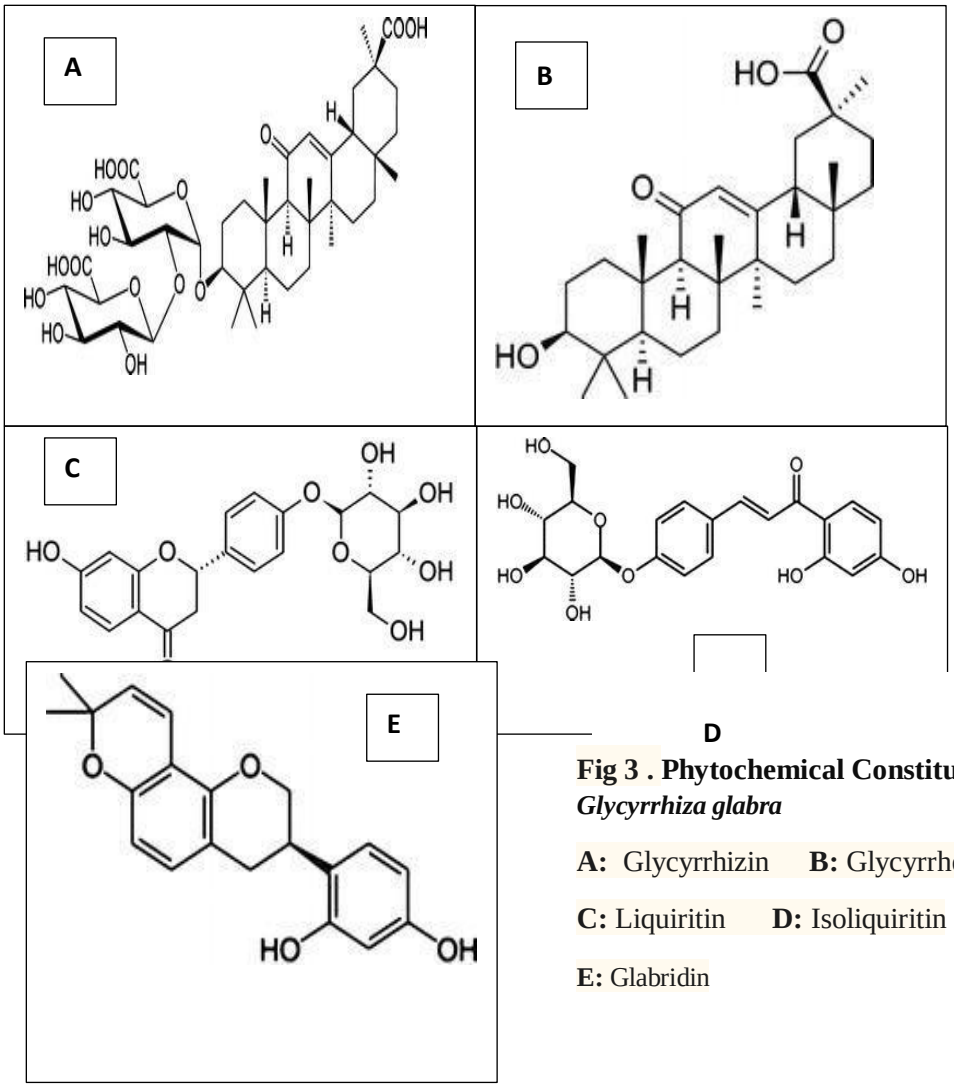

Fig 3 . Phytochemical Constituents of *Glycyrrhiza glabra*

A: Glycyrrhizin **B:** Glycyrrhetic acid

C: Liquiritin **D:** Isoliquiritin

E: Glabridin

Mechanistic Insight:

Glycyrrhizin hydrolyzes to glycyrrhetinic acid, which exhibits strong anti-inflammatory and antiviral effects by inhibiting 11β-hydroxysteroid dehydrogenase and modulating immune responses.Flavonoids act as antioxidants and synergize to reduce oxidative stress in infected tissues.(18)

Mechanism of Action in Respiratory Tract Infections :

Pharmacological Action	Mechanism / Effect	Evidence
Antiviral	Inhibits viral replication, interferes with viral attachment and penetration (notably influenza, SARS-CoV, RSV)	In vitro studies show inhibition of SARS-CoV-2 and influenza virus(19)
Antibacterial	Disrupts bacterial cell wall and inhibits biofilm formation (*S. pneumoniae*, *H. influenzae*)	MIC studies confirmed bacteriostatic effect(20)
Anti-inflammatory	Suppresses cytokine storm by inhibiting NF-κB and COX-2 pathways	Shown to reduce IL-6, TNF-α levels(21)
Expectorant / Demulcent	Soothes mucous membranes, promotes mucus secretion for easier expulsion	Traditional and experimental validation(22)
Immunomodulatory	Stimulates macrophage and lymphocyte activity, enhancing innate immunity	Demonstrated in murine models of infection(23)
Antioxidant	Neutralizes free radicals, protecting lung tissue from oxidative damage	DPPH and NO scavenging assays positive(24)

Pharmacological Efficacy Studies:
Preclinical Studies:

- Glycyrrhizin demonstrated antiviral activity against influenza A virus and respiratory syncytial virus in vitro.(25)
- Glycyrrhetinic acid reduced lung inflammation in animal models of asthma and bronchitis.(26)
- Licorice extract inhibited bacterial growth of Staphylococcus aureus and Streptococcus pneumoniae.(27)

Clinical Studies:

- A polyherbal cough syrup containing G. glabra showed significant improvement in cough frequency and mucus clearance in patients with acute bronchitis.(28)
- Clinical evaluation of Yashtimadhu syrup in 100 patients revealed reduced sore throat and inflammation after 7 days.(29)
- Studies in COVID-19 patients demonstrated reduced viral load and faster recovery when licorice extract was used as an adjunct therapy(30).

Formulations and Dosage Forms:

- **Common forms**: Decoction, powder, syrup, lozenges, capsules, tablets, mouthwash.(31)
- **Traditional formulations:**
  - Yashtimadhu Churna (powder for throat relief)
  - Kantakari Avaleha (Ayurvedic respiratory tonic)
  - Herbal cough syrups containing G. glabra.(32)
- **Marketed examples:** Mulethi Syrup, Dabur Honitus, Himalaya Koflet, Zandu Yashtimadhu.(33)
- **Typical dose**: 1–3 g root powder twice daily, or 5–10 mL syrup thrice daily.(34)

Safety and Toxicity Profile:
Although G. glabra is generally safe, excessive consumption can lead to:

- Pseudoaldosteronism: Due to glycyrrhizin-induced inhibition of 11β-hydroxysteroid dehydrogenase, causing sodium retention, hypokalemia, and hypertension.(35)
- Edema and electrolyte imbalance with chronic use.(36)
- Drug interactions: Caution with corticosteroids, antihypertensives, and diuretics.(37)
- Toxicity data: LD_{50} of glycyrrhizin > 2000 mg/kg (rats).
- Recommendation: Safe up to 100 mg/day glycyrrhizin equivalent for adults under medical supervision.(38)

Pharmacokinetics :

- Glycyrrhizin is poorly absorbed orally and hydrolyzed by intestinal flora to glycyrrhetinic acid.(39)
- Peak plasma concentration reached within 2 hours post-ingestion.(40)
- Excretion mainly via bile and urine.
- Bioavailability increases in presence of fat or bile salts.(41)

Regulatory and Quality Control Aspects :

- Listed in Ayurvedic Pharmacopoeia of India, British Herbal Pharmacopoeia, and WHO Monographs.(42)
- Quality control includes assays for glycyrrhizin content (≥4%) and absence of contaminants.(43)
- Standardization based on HPLC or TLC fingerprinting profiles.(44)

Challenges and Future Prospects :

- Variability in glycyrrhizin content due to regional and extraction differences.(45)
- Need for standardized formulations and dose-response studies.
- Nanoformulation approaches (e.g., glycyrrhizin nanoparticles) for targeted pulmonary delivery.(46)
- Potential for combination therapy with antivirals for synergistic effects.(47)
- Requirement of large-scale randomized controlled trials to establish clinical efficacy and safety conclusively.(48)

CONCLUSION:

Glycyrrhiza glabra (licorice) has emerged as a promising medicinal plant in the management of respiratory tract infections (RTIs), offering a wide range of pharmacological actions, including antiviral, antibacterial, anti-inflammatory, antioxidant, and immunomodulatory effects.(49) Its historical use in traditional medicine systems such

as Ayurveda, Unani, and Traditional Chinese Medicine aligns well with modern scientific findings that validate its efficacy in treating conditions like cough, sore throat, bronchitis, and asthma. Given the escalating issue of antimicrobial resistance, *G. glabra* represents a valuable natural alternative or complementary option to conventional treatments.(50) Its generally favorable safety profile supports its inclusion in herbal formulations; however, prolonged or excessive consumption may result in side effects like pseudoaldosteronism and electrolyte imbalance due to glycyrrhizin content. (51)To facilitate its broader acceptance and integration into evidence-based medicine, further research is essential—particularly in areas of standardization, dosage optimization, pharmacokinetics, and controlled clinical trials. With such advancements, *G. glabra* could play a significant role in future respiratory healthcare strategies.(52)

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