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# GLYCYRRHIZA GLABRA FOR ULCER: A BRIEF REVIEW OF ITS THERAPEUTIC POTENTIAL: A NARRATIVE REVIEW

*Narrative Review*

**Muhammad Hamza[1]*, Muaz Ahmed[1], Hafiz Muhammad Hamza Anwar[1], Muhammad Hamid[1], Hooria Zia[2]**
[1]Department of Pharmacy, The University of Chenab, Gujrat, Punjab, Pakistan.
[2]Women Institute of Learning, Abbottabad, affiliated with The University of Peshawar, Khyber Pakhtunkhwa, Pakistan.
**Corresponding Author:** Muhammad Hamza, Department of Pharmacy, The University of Chenab, Gujrat, Punjab, Pakistan, dr.hamza.rx@gmail.com
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## ABSTRACT

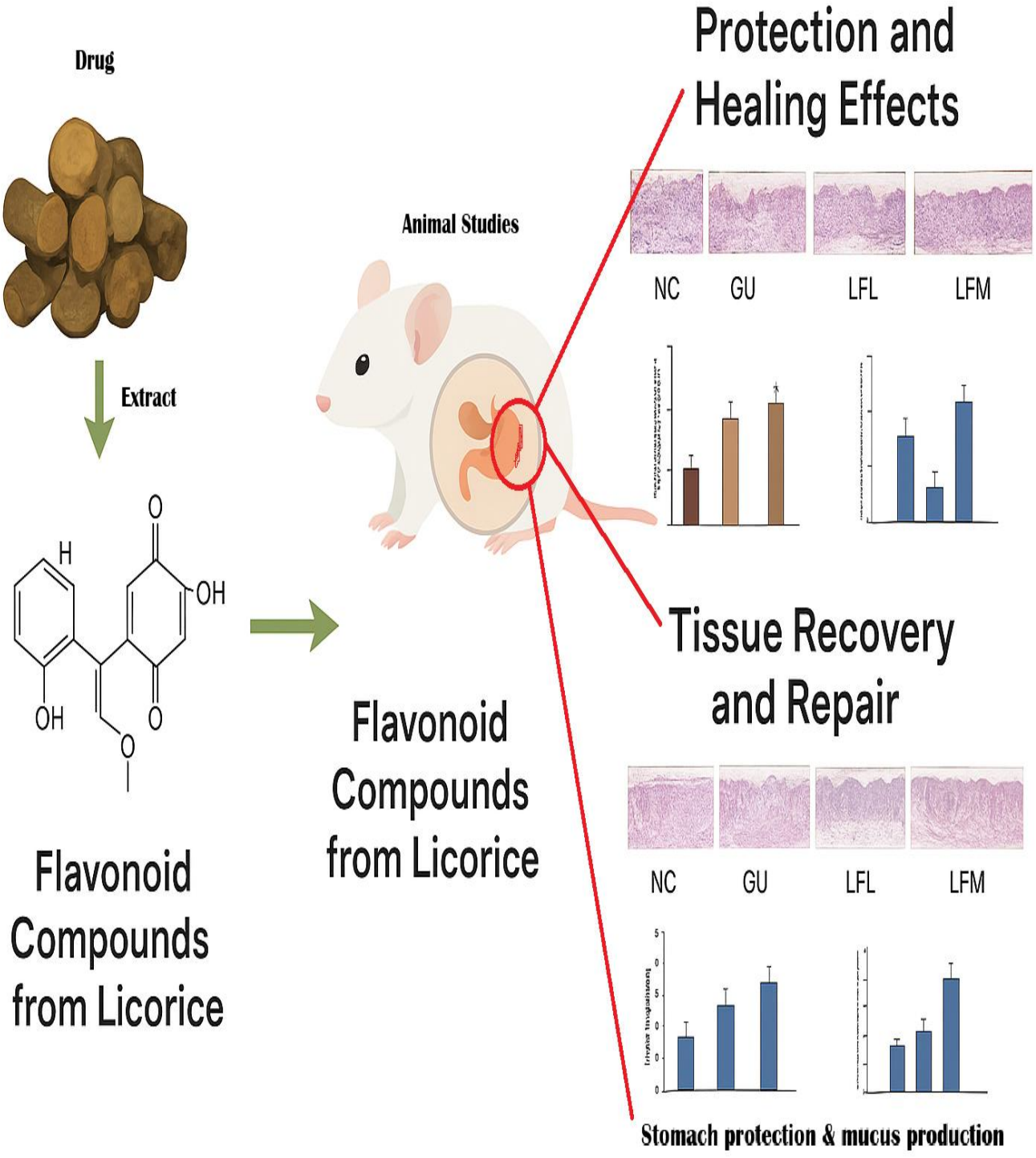
**Background:** *Glycyrrhiza glabra* (liquorice) has been widely utilized in traditional and modern medicine for its therapeutic benefits, particularly in gastrointestinal disorders. Its relevance in ulcer management has gained increasing scientific interest due to its diverse pharmacologically active constituents that demonstrate anti-inflammatory, antioxidant, and gastroprotective properties. Understanding its therapeutic potential is essential as peptic and duodenal ulcers remain significant global health concerns.

**Objective:** This narrative review aims to synthesize contemporary evidence on the efficacy, safety, and mechanisms of action of *Glycyrrhiza glabra* in the prevention and management of gastric and duodenal ulcers.

**Main Discussion Points:** Twenty relevant publications retrieved from Google Scholar, PubMed, and Scopus were analyzed to explore the plant's pharmacological activities. Key bioactive compounds, particularly flavonoids and glycyrrhizin derivatives, contribute to mucosal protection, enhanced prostaglandin synthesis, and reduction of gastric acid secretion. Preclinical studies consistently indicate ulcer-healing effects through improved mucus production and attenuation of oxidative stress. Early clinical findings suggest symptomatic improvement when used in recommended doses, although variability in formulations and limited human data remain notable challenges.

**Conclusion:** Existing evidence indicates that *Glycyrrhiza glabra* holds substantial promise as a complementary gastroprotective agent, but further high-quality clinical research is needed to determine optimal dosing, safety thresholds, and standardized formulations for therapeutic use.

**Keywords:** *Glycyrrhiza glabra*; liquorice; peptic ulcer; duodenal ulcer; gastroprotection; herbal ulcer therapy.



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## INTRODUCTION

Glycyrrhiza glabra, commonly known as liquorice and referred to as Mulethi in traditional Tibb medicine, has long been valued for its therapeutic properties, particularly in disorders of the gastrointestinal tract. As a herbaceous perennial belonging to the Fabaceae family, its roots yield a sweet, aromatic extract enriched with bioactive constituents such as glycyrrhizin, flavonoids, and isoflavonoids, all of which have been recognized for their protective and healing effects on gastric mucosa (1). This plant has been used for centuries across Asia, North Africa, and Southern Europe, yet recent scientific interest has renewed focus on its potential as a complementary or alternative therapy for ulcerative disorders. Peptic, gastric, and duodenal ulcers continue to impose a substantial global burden, largely driven by modern dietary patterns, stress, infection with Helicobacter pylori, and widespread use of non-steroidal anti-inflammatory drugs (NSAIDs) (2). Conventional pharmacological therapies, most notably proton pump inhibitors such as omeprazole, remain the cornerstone of management; however, concerns over long-term adverse effects and recurrence rates have encouraged exploration of safer, plant-based alternatives (3). Glycyrrhiza glabra has emerged prominently in this context, with preclinical and clinical research demonstrating its mucosal-protective, anti-inflammatory, and antimicrobial activities—particularly its ability to inhibit H. pylori colonization and support mucosal regeneration (4). Deglycyrrhizinated liquorice (DGL), a modified formulation with reduced glycyrrhizin content, has further expanded therapeutic possibilities by retaining anti-ulcer efficacy while minimizing the risk of mineralocorticoid-related side effects (5). Despite promising evidence, gaps remain regarding the standardization of liquorice preparations, optimal dosing strategies, and comparative effectiveness with established ulcer therapies. Growing interest in integrative medicine and the need for safer long-term treatment options underscore the importance of consolidating current knowledge. Therefore, this review aims to synthesize recent scientific findings on the phytochemistry, mechanisms of action, preclinical models, and clinical applications of Glycyrrhiza glabra in ulcer management, providing a clear and updated understanding of its therapeutic potential. The objective is to critically evaluate contemporary evidence on its anti-ulcer effects, role against Helicobacter pylori, and safety profile to guide its rational use in clinical practice.

### 1. Chemical Composition of Glycyrrhiza glabra

Glycyrrhiza glabra contains a diverse and chemically rich profile, with its root serving as the primary medicinal component due to its dense concentration of bioactive molecules. Approximately 40–50% of the total dry weight of the root consists of pharmacologically active compounds that contribute to its therapeutic efficacy (6). These include triterpenoid saponins, flavonoids, isoflavonoids, polysaccharides, sterols, amino acids, and mineral salts, collectively forming a complex network of substances responsible for its anti-ulcer, anti-inflammatory, antioxidant, and antimicrobial properties. The chemical diversity of the plant supports its broad pharmacological actions across gastrointestinal, respiratory, and metabolic systems.

### 2. Traditional uses

Historically, liquorice has been deeply embedded in traditional medical systems, including Ayurveda, Unani Tibb, and Chinese and Tibetan medicine. Its documented use extends back to 2800 B.C. in Chinese pharmacopoeia, while ancient Egyptians valued it for its soothing and healing properties, evidenced by its presence in the tomb of Pharaoh Tutankhamun (7). Across cultures, it was used for respiratory and throat ailments, serving as an expectorant, demulcent, and flavouring agent in decoctions. Prior to the formal description of its gastrointestinal benefits in the mid-20th century, liquorice was primarily prescribed for bronchial inflammation, digestive discomfort (8), hyperdipsia, epilepsy, fever, tremors, rheumatism, and various inflammatory skin disorders. Its broad traditional use provides a historical foundation for contemporary pharmacologic exploration, linking ancient ethnomedicine to modern gastroenterology.

### 3. Major bioactive compounds effective for ulcer treatment

Among the numerous constituents of G. glabra, glycyrrhizin stands out as the principal compound, comprising nearly 10% of the dry root weight and imparting the characteristic sweet taste of liquorice (1). Its derivative, glycyrrhetinic acid, plays a central role in modulating enzymes responsible for prostaglandin metabolism, leading to enhanced prostaglandin availability, increased gastric mucus secretion, and prolonged surface epithelial cell survival (6,9). Flavonoids such as liquiritin, isoliquiritin, glabridin, and hispaglabridin A possess strong antioxidant properties (8) and contribute to ulcer prevention by mitigating oxidative stress and supporting mucosal integrity. Together, these compounds form the mechanistic basis for the plant's well-established anti-ulcer activity.

### 4. Analysis of major phytochemicals

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Beyond glycyrrhizin and flavonoids, Glycyrrhiza glabra contains an extensive profile of phytochemicals, including essential oils, amino acids, resins, pectins, sterols, carbohydrates, and simple sugars like glucose and sucrose (8,9). Its essential oil fraction contains volatile constituents such as pentanol, linalool oxide, geraniol, α-terpineol, and hexanol, contributing to both therapeutic effects and aroma. Organic acids—including acetic, citric, malic, tartaric, and fumaric acids—further enhance the plant's medicinal properties by supporting anti-inflammatory and antioxidant pathways. The synergistic effect of these molecules reinforces the plant's therapeutic versatility and strengthens its pharmacological influence across different ulcer models.

**5. Structural characteristics of tonstituents**

The structural complexity of the active components strongly determines their biological roles. Glycyrrhizin, composed of one glycyrrhetinic acid molecule linked with two molecules of glucuronic acid, allows site-specific interaction with gastric epithelial enzymes and receptors, enhancing its mucosal protective activity (6). The flavonoid class in liquorice includes a variety of molecular subclasses, such as flavanones, chalcones, flavanonols, and isoflavonoids (8,10). The glycosides of liquiritigenin and isoliquiritigenin are particularly significant due to their potent antioxidant capacity, which reduces cell injury and prolongs epithelial survival (6,9). Glabridin, a key isoflavonoid, contributes additional antioxidant strength, amplifying the gastroprotective potential of the plant (10). These structural nuances help explain the biochemical diversity and therapeutic specificity observed in liquorice-based treatments.

## 6. PATHOPHYSIOLOGY OF PEPTIC AND DUODENAL ULCERS

Peptic and duodenal ulcers arise from disruptions in mucosal integrity caused by an imbalance between aggressive gastric factors (acid, pepsin, reactive oxygen species, and bacterial toxins) and mucosal defence mechanisms (mucus, bicarbonate, prostaglandins, and epithelial regeneration) (7,11). When damaging factors exceed protective capacities, injury extends through the muscularis mucosae, producing ulcerative lesions. Persistent inflammation, impaired blood flow, and altered epithelial cell turnover further contribute to ulcer chronicity.

### 6.1. Role of H. pylori in causing Ulcer

Helicobacter pylori remains the predominant cause of peptic ulcer disease worldwide, implicated in more than 90% of duodenal ulcers and 80% of gastric ulcers (12). The bacterium colonizes the gastric mucosa and releases virulence factors such as urease, catalase, and vacuolating cytotoxin, which promote inflammation and epithelial injury (13). By altering gastric hormone levels—raising gastrin and lowering somatostatin—H. pylori heightens acid secretion, disrupts bicarbonate production, and promotes gastric metaplasia in the duodenum (10,13). These changes create an environment conducive to ulcer formation and recurrence.

## 7. PHARMACOLOGICAL ACTIONS ON ULCER TREATMENT

Glycyrrhiza glabra's therapeutic effect in ulcer management arises from its anti-inflammatory, antioxidant, antimicrobial, and mucosal-protective activities, which operate synergistically to restore gastric integrity.

### 7.1. Anti-inflammatory effects

Glycyrrhizin and glycyrrhetinic acid inhibit key enzymes in prostaglandin metabolism, leading to higher endogenous prostaglandin levels essential for epithelial protection, mucus secretion, and cell longevity (5,9). These effects extend beyond the gastrointestinal tract, offering potential benefits in respiratory inflammation through flavonoid-mediated responses (14). The reduction of inflammatory mediators supports both ulcer healing and protection from future injury.

### 7.2. Antioxidantal properties

Flavonoids and isoflavonoids exert potent antioxidant actions by neutralizing reactive oxygen species and reducing the oxidative injury associated with ethanol-, NSAID-, and stress-induced ulcers (8). Studies demonstrate that hydroalcoholic extract of Glycyrrhiza glabra (HEGG) reduces the cell damage index in HCl/Ethanol ulcer models and provides significant mucosal protection (2,9). The antioxidant mechanisms complement prostaglandin-mediated cytoprotection, enhancing epithelial regeneration and ulcer healing.

### 7.3. Antimicrobial activity

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Liquorice exhibits strong antimicrobial activity, particularly against H. pylori, with inhibition rates reported as high as 70% compared to 45% in control groups (12,14). This suggests its potential role as an adjunct or alternative to quadruple therapy, especially in settings where antibiotic resistance or treatment intolerance occurs (4,10). Antifungal activity against Candida albicans and antibacterial activity against gram-positive organisms such as Staphylococcus aureus and Bacillus subtilis further broaden its therapeutic usefulness.

## 8. MECHANISMS OF GASTROPROTECTION

The gastroprotective action of liquorice arises from overlapping mechanisms that strengthen mucosal defences, modulate acid secretion, and accelerate healing.

### 8.1. Mucus production enhancement

Liquorice increases the number and activity of mucus-producing cells, reinforcing the gastric barrier against acid and irritants (7,11). Enhanced mucus thickness prevents proteolytic injury and supports epithelial regeneration, especially in ethanol-induced ulcer models (4).

### 8.2. Prostaglandin synthesis stimulation

Liquorice inhibits enzymes that degrade prostaglandins, allowing sustained concentrations that promote mucus secretion, regulate mucosal blood flow, and reduce inflammatory injury (5). Higher prostaglandin levels prolong epithelial survival and strengthen mucosal resistance to acid (1).

### 8.3. Gastric acid secretion inhibition and healing

Deglycyrrhizinated liquorice (DGL) promotes mucosal blood flow, inhibits gastrin release, and raises gastric pH while maintaining mucosal defence pathways (6,15). At therapeutic doses, it decreases gastric volume and significantly increases the protective pH of the mucosal layer (7). These effects work alongside antioxidant mechanisms that reduce reactive oxygen species, improving mucosal stability and healing.

## 9. PRECLINICAL STUDIES OF ULCER MODELS

### 9.1. Ethanol-induced ulcer model

Ethanol models demonstrate the potent gastroprotective activity of HEGG, with higher doses (150–200 mg/kg) producing significant reductions in ulcer index comparable to omeprazole (2,16). The improved outcomes are attributed largely to enhanced mucus production and antioxidant activity.

**Table 1: The Effect of HEGG on Ethanol-Induced Ulcer Studies in Rats**

| Groups | Dose (mg/kg) | Ulcer Index | Preventive Index (%) |
|---|---|---|---|
| Control | – | 15.33 ± 0.19 | – |
| Omeprazole | 30 | 10.23 ± 0.78 ** | 33.26 |
| HEGG | 50 | 13.62 ± 0.25 ** | 11.15 |
| HEGG | 100 | 14.52 ± 0.67 * | 5.28 |
| HEGG | 150 | 10.09 ± 0.38 ** | 34.18 |
| HEGG | 200 | 10.33 ± 0.28 ** | 32.61 |

Note: HEGG = Hydroalcoholic Extract of Glycyrrhiza glabra

### 9.2. Stress-induced ulcer model

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In cold-restraint stress models, HEGG prevents mucosal damage through increased prostaglandin synthesis and fortified mucosal barriers (17). These findings highlight liquorice's potential to counteract ulcerogenesis resulting from physiological or emotional stress.

### 9.3. NSAID-induced ulcer model

Liquorice preparations including DGL, glycyrrhetinic acid, and liquorice-coated ibuprofen significantly reduce NSAID-induced lesions without impairing drug absorption (8). HEGG demonstrates dose-dependent protection against indomethacin ulcers, reducing ulcer indices from 32.28 ± 0.97 in controls to as low as 4.15 ± 0.33 (18).

## 10. CLINICAL EVIDENCE FOR ANTI-ULCER EFFECTS

### 10.1. Experimental studies of Liquorice on rats

Animal studies consistently show HEGG's ability to reduce ulcer severity in ethanol, stress, and indomethacin models (12). These findings confirm liquorice's capacity to enhance mucosal defence factors and limit injury progression.

### 10.2. Human trials on peptic ulcer

Clinical findings are mixed. A classical study involving 40 patients with chronic duodenal ulcers reported significant symptom reduction and eliminated the need for surgery following high-dose DGL therapy (19). In contrast, a placebo-controlled trial found no significant difference between DGL and placebo, likely due to confounding factors such as a mandated five-meal regimen that may have independently increased salivation and improved symptoms (12).

### 10.3. Animal studies

Hamster models demonstrate strong dose-dependent anti-ulcer activity, with HEGG at 200 mg/kg outperforming omeprazole in reducing ulcer index (3,19). These findings strengthen the evidence supporting liquorice as a viable anti-ulcer agent.

**Table 2: Effect of Licorice on Indomethacin-Induced Ulcer in Rats**

| Groups | Dose (mg/kg) | Ulcer Index | Preventive Index (%) |
|---|---|---|---|
| Control | – | 18.54 ± 0.14 | – |
| Cimetidine | 100 | 8.35 ± 0.63 ** | 54.96 |
| HEGG | 50 | 16.70 ± 0.11 ** | 9.92 |
| HEGG | 100 | 15.66 ± 0.47 ** | 15.53 |
| HEGG | 150 | 15.01 ± 0.38 ** | 19.03 |
| HEGG | 200 | 17.66 ± 0.40 * | 4.74 |

Note: HEGG = Hydroalcoholic Extract of Glycyrrhiza glabra

### 10.4. Dosage and administration

For peptic ulcers, DGL is typically administered as two to four 380 mg chewable tablets taken before meals for 8–16 weeks (6). Chewing is necessary to allow salivary enzymes to activate the therapeutic components, as capsule formulations show reduced efficacy.

### 10.5. Safety and toxicity

High glycyrrhizin intake (>50 g/day) may cause hypertension, hypokalemia, and cardiac events (10). DGL is considered safer and may be used in doses up to 4.5 g daily for four months (10). Caution is warranted in patients with cardiovascular, renal, or hypertensive conditions and during pregnancy.

### 10.6. Products available in the market

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Liquorice is available in multiple formulations, including teas, candies, gels, capsules, lozenges, and patented Chinese medicinal preparations (1). DGL products are commonly marketed for digestive health, while topical preparations serve dermatological purposes.

## CRITICAL ANALYSIS AND LIMITATIONS

The existing literature examining the anti-ulcer potential of *Glycyrrhiza glabra* offers valuable insights but remains constrained by several methodological and clinical limitations that reduce the certainty of its therapeutic effectiveness. A major limitation across the evidence base is the predominance of preclinical studies, many of which rely on animal models using ethanol- or NSAID-induced ulcer paradigms. While these models provide mechanistic clarity, they do not fully replicate the chronic, multifactorial nature of human peptic ulcer disease. Moreover, many of these studies involve small sample sizes and short experimental durations, limiting statistical power and long-term extrapolation (12). Clinical trials that do exist are largely outdated or involve heterogeneous formulations such as crude extracts, hydroalcoholic preparations, and deglycyrrhizinated liquorice (DGL), making cross-study comparison difficult. Methodological biases further complicate interpretation. Several clinical studies demonstrate lack of randomization, inadequate blinding, or absence of placebo control, increasing susceptibility to performance and selection bias. Confounders such as dietary modifications, concomitant medications, and symptom-based rather than endoscopic assessment may have influenced reported improvements. Variability in extract standardization represents another significant limitation; the concentration of glycyrrhizin, flavonoids, and glycyrrhetinic acid differs markedly between preparations, impairing reproducibility and consistency across trials (13). Furthermore, older human studies often included only patients with recurrent duodenal ulcers, restricting applicability to broader populations with gastric ulcers, H. pylori–associated disease, or NSAID-related mucosal injury.

Publication bias is also evident, with most published literature reporting positive or partially favorable outcomes, whereas negative or inconclusive findings are underrepresented. Contemporary systematic reviews highlight that many liquorice-related studies remain unpublished due to insufficient effect sizes or methodological flaws (14). This selective dissemination of results exaggerates perceived efficacy and complicates evidence-based evaluation. The variability in outcome measures presents another obstacle. Studies commonly assess ulcer healing using disparate parameters, ranging from subjective symptom relief and salivary changes to ulcer indices or biochemical markers of oxidative stress. Without uniform criteria—such as standardized endoscopic scoring or validated symptom scales—comparisons across trials remain limited. Additionally, some studies fail to measure H. pylori eradication rates directly, despite its central role in ulcer pathophysiology. Generalizability of findings remains a critical concern. Most clinical studies involve small, geographically limited populations, often with unique dietary or cultural contexts that affect herbal medicine use. Variability in metabolism, genetic factors influencing glycyrrhizin sensitivity, and differences in baseline comorbidities further restrict broad clinical application (15,16). Moreover, the safety profile of liquorice is seldom assessed comprehensively; few studies evaluate glycyrrhizin-related risks such as hypertension, electrolyte imbalance, and cardiotoxicity over prolonged durations. Collectively, while existing evidence suggests that *Glycyrrhiza glabra* possesses anti-ulcer activity through anti-inflammatory, antioxidant, and antimicrobial pathways, the current body of literature remains insufficient to support definitive clinical recommendations. High-quality randomized controlled trials with standardized preparations, larger sample sizes, and longer follow-up periods are urgently needed to establish its therapeutic relevance, safety margin, and comparative efficacy alongside established ulcer treatments.

## IMPLICATIONS AND FUTURE DIRECTIONS

The current body of evidence on *Glycyrrhiza glabra* highlights an important opportunity for integrating herbal pharmacotherapy into modern ulcer management, particularly for patients seeking complementary or better-tolerated alternatives to conventional drugs. Its demonstrated anti-inflammatory, antioxidant, and antimicrobial properties suggest that liquorice-based products may serve as adjunctive therapies in mild to moderate peptic ulcer disease and in cases where NSAID-related mucosal injury or *H. pylori*–associated inflammation persists despite standard therapy (17). In clinical practice, these findings may guide physicians toward considering standardized deglycyrrhizinated liquorice (DGL) as a supportive intervention, especially for patients who experience adverse effects from proton pump inhibitors or require safer long-term mucosal protection. However, the use of such preparations must be coupled with careful monitoring of potential glycyrrhizin-related toxicities, reinforcing the importance of tailored patient education and cautious prescription practices. At a policy level, the therapeutic potential of liquorice underscores the need to establish regulatory standards for herbal extracts intended for gastrointestinal use. Currently, the absence of uniform guidelines on dosage, glycyrrhizin content, and product quality contributes to inconsistent clinical outcomes and variability in patient safety (18,19). Evidence from recent

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pharmacognostic investigations suggests that standardized formulations with defined constituent profiles could significantly enhance therapeutic predictability (20). Therefore, the development of clinical practice guidelines addressing herbal adjuncts—particularly those based on DGL or refined extracts—may support safer integration into primary and gastroenterology care.

Despite progress, several unanswered questions remain. The long-term safety of repeated or chronic consumption, particularly concerning cardiovascular, renal, and endocrine effects associated with glycyrrhizin, requires more rigorous evaluation. The interaction of liquorice with standard therapies, including PPIs, antibiotics for *H. pylori*, and NSAIDs, has not been sufficiently explored, leaving important gaps in understanding possible synergistic or antagonistic effects. Moreover, the relative contributions of specific bioactive compounds—such as glycyrrhetinic acid, liquiritin, and glabridin—to ulcer healing are not fully delineated, limiting precision in developing optimized formulations (21). Understanding interindividual variability in metabolism and sensitivity, potentially driven by genetic or microbiome differences, also represents an important future research direction. To address these gaps, future studies should prioritize well-designed randomized controlled trials with standardized liquorice preparations, adequate sample sizes, and longer follow-up durations. Trials that incorporate objective endpoints, such as endoscopic mucosal assessment, validated symptom scales, and biomarkers of oxidative stress or inflammation, will provide greater reliability than those relying on subjective improvement alone. Comparative studies examining DGL against standard therapies—including PPIs, H2 blockers, and bismuth-containing regimens—may clarify relative effectiveness and suitability for different patient populations (22). Additionally, mechanistic studies using omics-based approaches could help identify molecular pathways influenced by liquorice constituents, thereby supporting more targeted therapeutic development. Overall, the current evidence supports cautious integration of *Glycyrrhiza glabra* into clinical practice while emphasizing the need for scientific rigor, policy standardization, and comprehensive safety evaluation. Continued progress in this field relies on collaborative research efforts that bridge pharmacology, gastroenterology, and herbal medicine to develop reliable, evidence-based strategies for ulcer care.

## CONCLUSION

The available evidence indicates that *Glycyrrhiza glabra* possesses meaningful anti-ulcer potential through its synergistic actions on mucus enhancement, prostaglandin stimulation, and gastric acid modulation, offering a multifaceted protective and healing effect on the gastrointestinal mucosa. Preclinical models and limited clinical trials consistently demonstrate beneficial outcomes, although the strength of evidence remains moderate due to gaps in large-scale, high-quality human studies. Its natural origin, favourable safety profile when used appropriately, and diverse pharmacological mechanisms make it an appealing adjunctive option in ulcer management, provided it is used under professional supervision. Clinicians may consider standardized preparations such as DGL in selected patients, while researchers should prioritize rigorous randomized controlled trials, long-term safety evaluations, and standardized dosing protocols to fully establish its therapeutic role and integrate it into evidence-based clinical practice.

### AUTHOR CONTRIBUTION

| Author | Contribution |
|---|---|
| Muhammad Hamza* | Substantial Contribution to study design, analysis, acquisition of Data<br>Manuscript Writing<br>Has given Final Approval of the version to be published |
| Muaz Ahmed | Substantial Contribution to study design, acquisition and interpretation of Data<br>Critical Review and Manuscript Writing<br>Has given Final Approval of the version to be published |
| Hafiz Muhammad Hamza Anwar | Substantial Contribution to acquisition and interpretation of Data<br>Has given Final Approval of the version to be published |
| Muhammad Hamid | Contributed to Data Collection and Analysis<br>Has given Final Approval of the version to be published |

| | |
|---|---|
| Hooria Zia | Contributed to Data Collection and Analysis<br>Has given Final Approval of the version to be published |

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