

# Mucoadhesive Buccal Drug Delivery Systems of Glycyrrhiza glabra (Liquorice) for Sustained Anti-Ulcer Therapy: A Comprehensive Review

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**Abstract**—Peptic ulcer disease is still a common gastrointestinal condition with high recurrence rates and drawbacks to traditional treatments, such as frequent dosage, systemic adverse effects, and decreased bioavailability because of first-pass metabolism. These difficulties call for the creation of sophisticated medication delivery methods that can enhance patient compliance and offer long-lasting therapeutic efficacy. Mucoadhesive buccal drug delivery systems have shown promise in this regard, providing regulated drug release, extended residence time, and avoidance of hepatic metabolism. The well-known medicinal herb Glycyrrhiza glabra, or liquorice, has strong gastroprotective properties that are ascribed to its bioactive components, which include glycyrrhizin, flavonoids, and saponins. Through a variety of mechanisms, such as cytoprotection, anti-inflammatory action, and antioxidant activity, these substances have anti-ulcer benefits. Liquorice improves stability, bioavailability, and sustained release properties in mucoadhesive buccal formulations, increasing their therapeutic potential.

The scientific underpinnings of mucoadhesion, formulation techniques, and design factors for buccal drug delivery systems are highlighted in this review, along with their therapeutic efficacy in the treatment of ulcers. Future prospects for clinical translation and commercialization are also covered, along with current research and scale-up issues and emerging trends like smart polymers and nano-enabled systems. All things considered, liquorice-based mucoadhesive buccal systems are an innovative and successful method of long-term anti-ulcer therapy with great potential for incorporation into contemporary healthcare.

**Index Terms**—Mucoadhesion, Liquorice, Glycyrrhiza glabra, Peptic ulcer.

## I. INTRODUCTION CLINICAL NEED AND THERAPEUTIC GAP

Helicobacter pylori infection, long-term NSAID usage, and excessive stomach acid output are all linked to peptic ulcer disease, which is still a major global health concern.[1] Even though traditional treatments like proton pump inhibitors and antibiotics are readily available, their efficacy is frequently constrained by systemic adverse effects, frequent dosing, low patient compliance, and decreased bioavailability because of first-pass metabolism.[2]

These drawbacks emphasize the necessity of continuous drug delivery methods that can offer enhanced efficacy and extended therapeutic action.[3] Mucoadhesive buccal drug delivery devices have become a viable alternative in this regard, providing controlled release, increased drug residence time, and avoidance of hepatic metabolism. Furthermore, Glycyrrhiza glabra (liquorice), a well-known gastroprotective substance, has gained attention due to the growing interest in herbal treatments. This makes it a perfect candidate for integration into cutting-edge transmucosal delivery platforms for efficient and long-lasting anti-ulcer therapy.[4]

## II. RATIONALE FOR BUCCAL MUCOADHESIVE DELIVERY

By avoiding first-pass metabolism, the buccal route provides a clear benefit over traditional oral delivery, increasing drug bioavailability and guaranteeing a quicker and more reliable therapeutic effect. By extending the dosage form's residence time at the site of absorption and enabling continuous and regulated

drug release, the use of mucoadhesive polymers enhances this strategy even further.[5] This approach works especially well for herbal active ingredients like Glycyrrhiza glabra (liquorice), whose bioactive components would otherwise degrade or be poorly absorbed in the digestive system.[6] Adhesion to the

mucosal surface, gradual hydration and swelling of the polymer matrix, and controlled drug diffusion across the buccal mucosa are all part of the conceptual framework of buccal mucoadhesive systems, which eventually contribute to longer anti-ulcer activity and better therapeutic results.[7]

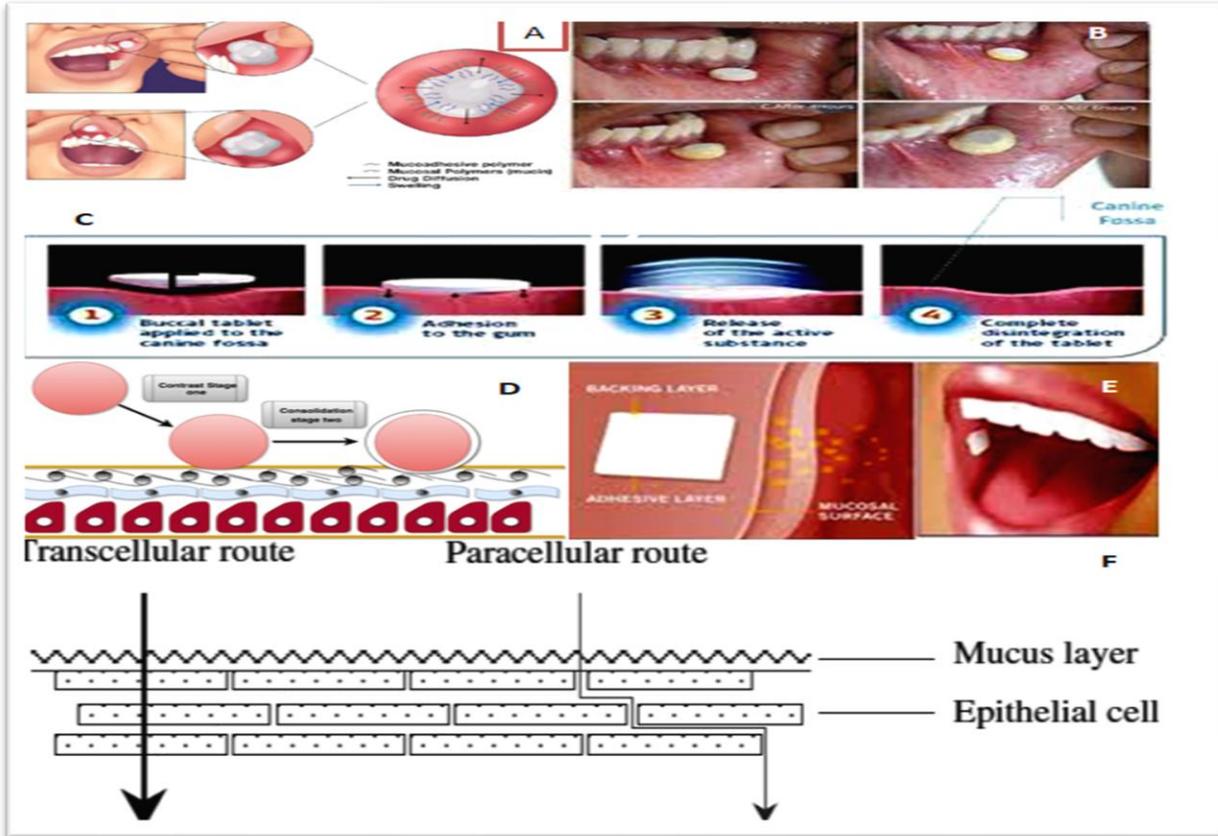


Fig.01: Graphical representation of mucoadhesive buccal drug delivery system of Glycyrrhiza glabra showing adhesion, controlled drug release, transmucosal absorption, and anti-ulcer action [32]

### III. GLYCYRRHIZA GLABRA AS A GASTROPROTECTIVE AGENT

Liquorice, or Glycyrrhiza glabra, has long been used in both traditional and contemporary herbal therapy to treat peptic and stomach ulcers due to its strong gastroprotective qualities. It is a promising option for integration into mucoadhesive buccal drug delivery systems for long-term anti-ulcer therapy because of its therapeutic efficacy, which is attributed to a combination of bioactive constituents that work in concert to protect the gastric mucosa, encourage healing, and lessen ulcer severity.[8]

#### 3.1 Ethnopharmacological Background

Traditional medical systems including Ayurveda, Traditional Chinese Medicine, and Unani medicine have long utilized liquorice to treat gastrointestinal conditions like ulcers, gastritis, and inflammation. Its importance in contemporary gastroprotective uses is supported by the fact that it has historically been prized for its calming, healing, and demulcent actions on mucosal tissues.[9]

#### 3.2 Bioactive Compounds and Their Roles

Compounds such as glycyrrhizin, flavonoids, saponins, and polyphenols are primarily responsible for Glycyrrhiza glabra's pharmacological effects. While

flavonoids have anti-inflammatory and antioxidant properties, glycyrrhizin is essential for mucosal protection and ulcer healing. Together, these substances promote tissue regeneration and strengthen stomach defense systems.[10]

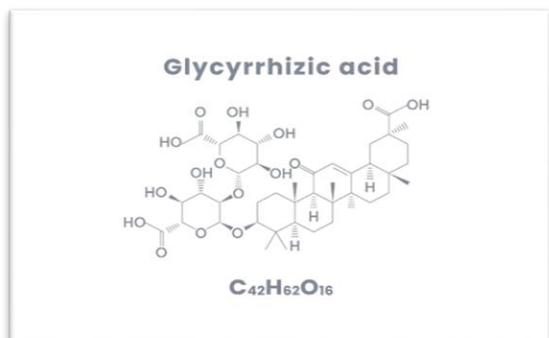


Fig.02: Major bioactive constituents of Glycyrrhiza glabra including glycyrrhizin, flavonoids, and saponins responsible for anti-ulcer activity

### 3.3 Molecular Mechanisms in Ulcer Healing

Liquorice's anti-ulcer properties involve several molecular pathways that support mucosal repair and protection. It controls inflammatory pathways by blocking pro-inflammatory mediators (anti-inflammatory signaling), increases mucus secretion and fortifies the gastrointestinal barrier (cytoprotection), and neutralizes reactive oxygen species to stop oxidative damage (free radical scavenging). Liquorice is a very powerful natural remedy for ulcers because of these combined effects.[11]

## IV. SCIENTIFIC BASIS OF MUCOADHESION IN BUCCAL SYSTEMS

A fundamental tenet of buccal drug delivery systems' efficacy is mucoadhesion, which allows the dosage form to be retained at the application site for an extended period of time. The way mucoadhesive polymers interact with the mucosal surface is described by a number of theoretical models, including as wetting, diffusion, and adsorption theories. The interaction between polymer chains and mucin glycoproteins, which results in the creation of strong adhesive connections, is essential to this process.[12]

Drug diffusion and sustained release are made easier by hydration and the ensuing swelling of the polymer matrix, which further improves close contact with the mucosa. Adhesion strength is also greatly influenced by variables such polymer content, molecular weight, flexibility, pH, and contact time. Designing successful mucoadhesive buccal systems that use Glycyrrhiza glabra for long-term anti-ulcer therapy requires an understanding of these fundamental principles.[13]

## V. DESIGN CONSIDERATIONS FOR BUCCAL TABLETS

To guarantee optimal drug distribution and therapeutic performance, a number of formulation characteristics must be carefully considered in the production of effective buccal tablets.[14] The rate and degree of absorption through the buccal mucosa are significantly influenced by drug characteristics including solubility and permeability. Mucoadhesion, swelling behavior, and controlled drug release are all influenced by the choice and structure of polymers, especially the ratio of hydrophilic to hydrophobic components.[15] In order to maximize contact with the mucosal surface and improve adherence, tablet geometry and surface area are also crucial. Diffusion, polymer erosion, and swelling-controlled systems are some of the mechanisms that control the overall drug release profile and work together to provide prolonged drug delivery. For Glycyrrhiza glabra-based mucoadhesive buccal tablets to have long-lasting anti-ulcer efficacy, certain design elements are crucial.[16]

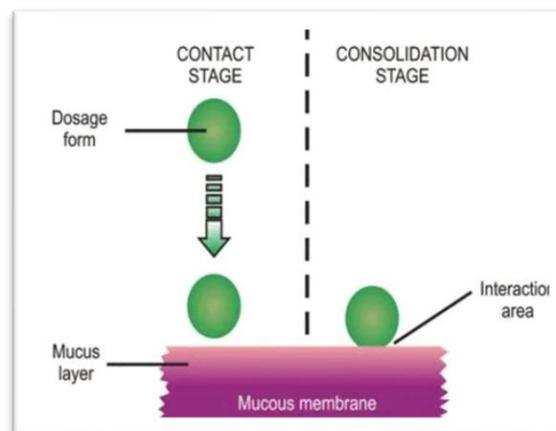


Fig.3: Mechanism of drug release from mucoadhesive buccal tablets involving swelling, diffusion, and polymer erosion [33]

## VI. FORMULATION APPROACHES FOR LIQUORICE-BASED SYSTEMS

Depending on the intended therapeutic result, both monoherbal and polyherbal approaches can be used in the formulation of liquorice-based buccal systems. Polyherbal techniques seek to create synergistic benefits by mixing *Glycyrrhiza glabra* with complementary herbs that have anti-ulcer, anti-inflammatory, or antioxidant characteristics, whereas monoherbal formulations concentrate on the unique activity of the plant.[17] To guarantee compatibility with herbal components and to preserve stability, mucoadhesion, and controlled medication release, careful excipient selection is crucial. Furthermore, sophisticated optimization methods like factorial design and Design of Experiments (DoE) are frequently used to methodically assess formulation variables and provide an optimized product with improved efficacy and repeatability for long-term anti-ulcer therapy.[18]

## VII. THERAPEUTIC PERFORMANCE AND ANTI-ULCER EFFICACY

Mucoadhesive buccal systems' therapeutic success is strongly correlated with their capacity to deliver controlled and prolonged drug release, which improves anti-ulcer efficacy.[19] These technologies establish a clear mechanistic link between the delivery mechanism and therapeutic outcomes by ensuring continuous medication absorption and increased bioavailability through prolonged interaction with the buccal mucosa.[20] Sustained release formulations improve patient compliance and efficacy by minimizing medication concentration changes and reducing dose frequency as compared to standard dosing.[21] This leads to better mucosal protection, faster healing rates, and fewer ulcer recurrences. Furthermore, because of their combination cytoprotective, anti-inflammatory, and antioxidant actions, liquorice-based buccal systems show great promise when compared to conventional anti-ulcer medications.[22]

## VIII. CHALLENGES IN DEVELOPMENT AND SCALE-UP

*Glycyrrhiza glabra*-based mucoadhesive buccal systems confront a number of significant obstacles in their development and large-scale manufacture, which may affect the consistency of the final product and its therapeutic efficacy. Due to variations in the phytochemical content resulting from variations in plant source, cultivation, and processing techniques, standardization of herbal extracts continues to be a significant concern.[23] Because herbal components may be susceptible to environmental elements including moisture, temperature, and light, ensuring stability and a sufficient shelf-life can be difficult.[24] Additionally, careful process optimization is necessary due to manufacturing constraints, such as retaining mucoadhesive characteristics during scale-up and providing uniform medication distribution. Development is made more difficult by quality control problems, which call for careful assessment of raw ingredients, intermediates, and finished formulations to guarantee safety, effectiveness, and regulatory compliance.[25]

## IX. EMERGING TRENDS AND RESEARCH OPPORTUNITIES

*Glycyrrhiza glabra*-based mucoadhesive buccal systems can now be more effective thanks to recent developments in medication delivery.[26] Drug solubility, permeability, and targeted delivery are improved by nano-enabled methods such buccal tablets loaded with nanoparticles and nanoemulsion inclusion.[27] Further enabling controlled medication release in response to physiological parameters like pH and temperature is the development of smart polymers and stimuli-responsive devices.[28] Furthermore, the use of AI in formulation design is becoming more popular as a way to optimize variables, forecast results, and shorten trial times. Another new idea is personalized herbal treatments, which aims to improve therapeutic efficacy and patient compliance in anti-ulcer medication by customizing formulations according to each patient's needs and biological responses.[29]

## X. FUTURE OUTLOOK: FROM BENCH TO BEDSIDE

Glycyrrhiza glabra-based mucoadhesive buccal systems have great potential for clinical use if important issues like scalability and commercial viability are successfully resolved. These systems have a great chance of being incorporated into standard ulcer care due to the increased public desire for herbal and non-invasive treatments.[30] Clinical uptake of herbal medications may be further aided by developments in formulation technologies and regulatory assistance. Furthermore, the growing demand for plant-based medicines around the world offers significant market expansion prospects, establishing liquorice-based buccal delivery systems as a practical and cutting-edge strategy for anti-ulcer treatment in the future.[31]

## XI. CONCLUSION

Combining cutting-edge drug delivery technologies with herbal pharmacology is a promising approach to better peptic ulcer treatment. Significant benefits of mucoadhesive buccal drug delivery systems include increased bioavailability, extended drug residence duration, and long-lasting therapeutic effects. Liquorice, or Glycyrrhiza glabra, is a powerful natural anti-ulcer agent having a variety of pharmacological effects. Its tremendous promise in future anti-ulcer therapy is highlighted by the fact that its inclusion into buccal mucoadhesive formulations not only overcomes the limits of current therapies but also offers a fresh and successful way for prolonged ulcer care.

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