# Gastroretentive Delivery of Herbal Anti-Ulcer Agents: Design Strategies and Therapeutic Potential

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***Abstract*—Acid-related disorders such as hyperacidity, peptic ulcer disease, and gastroesophageal reflux disease (GERD) continue to affect a large portion of the population. Although conventional antacids and proton pump inhibitors are widely used, their prolonged use is often associated with limitations such as frequent dosing, reduced patient compliance, and potential adverse effects. Herbal anti-ulcer agents have gained attention due to their gastroprotective, antioxidant, and mucosal healing properties; however, their clinical effectiveness is often limited by insufficient gastric residence time (12,14,16). Gastroretentive drug delivery systems have emerged as a promising approach to enhance the therapeutic performance of drugs intended for local action in the stomach (1,2,8,15). This review focuses on the gastroretentive delivery of herbal anti-ulcer agents and discusses various formulation strategies including floating systems, mucoadhesive systems, in-situ gelling systems, and swellable matrices (4,17). In addition, commonly used herbal drugs, natural polymers, evaluation parameters, advantages, and formulation challenges are highlighted. The integration of herbal therapeutics with gastroretentive delivery platforms may offer a safer and more effective approach for the management of acid-related disorders (6,7).**

***Index Terms*—Gastroretentive drug delivery systems, Herbal anti-ulcer agents, Hyperacidity, Floating drug delivery, Mucoadhesive systems, Gastric retention**

## I. INTRODUCTION

Acid-related disorders such as hyperacidity, peptic ulcer disease, and gastroesophageal reflux disease (GERD) are among the most common gastrointestinal problems affecting people of all age groups. These conditions mainly arise due to excessive secretion of gastric acid, impaired mucosal defense, stress, irregular dietary habits, and prolonged use of non-steroidal anti-inflammatory drugs. If left untreated, chronic acid-related disorders may lead to complications such as gastric erosion, ulceration, and bleeding (2,11,14).

Conventional pharmacological treatment for hyperacidity and ulcer includes antacids, $H_2$-receptor antagonists, and proton pump inhibitors. Although these therapies are effective in reducing gastric acid secretion, their long-term use has been associated with several limitations, including frequent dosing, reduced patient compliance, and adverse effects such as nutrient malabsorption and rebound acidity. In addition, many conventional dosage forms exhibit short gastric residence time, which reduces their effectiveness for drugs intended to act locally in the stomach (1,9).

Herbal anti-ulcer agents have gained increasing attention as safer alternatives for the management of acid-related disorders. Medicinal plants such as Glycyrrhiza glabra, Aloe vera, Emblica officinalis, Ocimum sanctum, and Curcuma longa have been reported to possess gastroprotective, antioxidant, anti-inflammatory, and mucosal healing properties. Despite their therapeutic potential, the clinical effectiveness of herbal drugs is often limited by poor bioavailability, instability in gastric conditions, and rapid gastric emptying.

Gastroretentive drug delivery systems (GRDDS) have emerged as a promising approach to overcome these limitations by prolonging the residence time of drugs in the stomach. These systems are designed to remain in the gastric environment for an extended period, thereby enhancing local drug concentration and improving therapeutic efficacy. Various gastroretentive approaches, including floating systems, mucoadhesive systems, in-situ gelling systems, and swellable formulations, have been explored to achieve prolonged gastric retention (2,4,8).

The combination of herbal anti-ulcer agents with gastroretentive drug delivery systems offers a rational and effective strategy for the management of acid-related disorders. Such systems not only improve gastric retention but also enhance mucosal protection while minimizing systemic side effects. Therefore, the present review focuses on gastroretentive delivery of herbal anti-ulcer agents, highlighting formulation strategies, therapeutic benefits, challenges, and future prospects in the treatment of hyperacidity and related gastric disorders.

## II. METHODOLOGY

### 2.1 Literature Search Strategy

A comprehensive literature search was carried out to collect relevant studies related to herbal anti-ulcer agents and gastroretentive drug delivery systems. Scientific databases including Google Scholar, PubMed, ScienceDirect, and SpringerLink were systematically searched. Keywords such as herbal anti-ulcer agents, gastroretentive drug delivery systems, floating drug delivery, mucoadhesive systems, in-situ gelling systems, and acid-related disorders were used either alone or in combination. The search was limited to articles published in the English language.

### 2.2 Inclusion and Exclusion Criteria

Studies were selected based on their relevance to the scope of the review. Research articles and review papers reporting the anti-ulcer, anti-acidity, or gastroprotective activity of herbal drugs, as well as studies focusing on gastroretentive formulation approaches, were included. Preference was given to articles published within the last 10 years; however, older studies of significant scientific importance were also considered. Articles unrelated to gastric disorders, non-herbal formulations, conference abstracts, and non-peer-reviewed sources were excluded from the review.

### 2.3 Selection of Herbal Anti-Ulcer Agents

Herbal drugs were selected based on their documented traditional use and scientific evidence supporting their anti-ulcer or gastroprotective activity. Medicinal plants with reported mechanisms such as acid neutralization, enhancement of mucosal defense, antioxidant activity, and inhibition of gastric acid secretion were prioritized. Information related to active phytoconstituents, pharmacological activity, and therapeutic relevance was collected from selected studies.

### 2.4 Review of Gastroretentive Drug Delivery Systems

Relevant literature describing various gastroretentive drug delivery approaches was reviewed in detail. Formulation strategies such as floating drug delivery systems, mucoadhesive systems, in-situ gelling systems, and swellable or expandable systems were analyzed. Emphasis was placed on studies involving natural polymers and herbal drugs intended for local gastric action.

### 2.5 Data Extraction and Analysis

Data from the selected studies were carefully reviewed and extracted, including details on formulation design, polymers used, evaluation parameters, and reported therapeutic outcomes. The collected information was qualitatively analyzed and systematically organized to highlight current trends, advantages, limitations, and future scope of herbal gastroretentive formulations in the management of acid-related disorders.

## III. HERBAL ANTI-ULCER AGENTS

Medicinal plants have been traditionally used for the treatment of gastric disorders due to their ability to protect the gastric mucosa and reduce ulcer formation. Several herbal drugs exhibit anti-ulcer activity through mechanisms such as inhibition of gastric acid secretion, enhancement of mucus production, antioxidant action, and promotion of mucosal healing. These properties make herbal agents' suitable candidates for gastroretentive drug delivery systems intended for local action in the stomach (12,14,16).

Various herbal anti-ulcer agents have been scientifically evaluated using different experimental ulcer models. The therapeutic activity of these plants is mainly attributed to the presence of bioactive phytoconstituents such as flavonoids, saponins, tannins, polysaccharides, and phenolic compounds. A brief description of commonly reported herbal anti-ulcer agents, along with their active constituents and mechanisms of action, is summarized in Table 1.

| Herbal drug | Biological source | Major active constituents | Mechanism of anti-ulcer action |
|---|---|---|---|
| Glycyrrhiza glabra (6,14) | Roots | Glycyrrhizin, flavoniods | Enhances mucus secretion, inhibits gastric acid, promotes mucosal healing |
| Aloe vera | Leaves | Polysaccharides, anthraquinones | Cytoprotective action, increases mucus production |
| Ocium sanctum | Leaves | Eugenol, flavonoids | Reduces gastric acid secretion, anti-inflammatory effect |
| Emblica officinalis | Fruits | Ascorbic acid, tannins | Antioxidant activity, strengthens gastric mucosal defense |
| Curcuma longa | Rhizomes | Curcumin | Antioxidant, inhibits inflammation, promotes ulcer healing |
| Azadirachta indica | Leaves | Nimbidin, flavonoids | Antisecretory and cytoprotective activity |
| Plantago ovata | Seeds | Mucilage | Forms protective layer over mucosa |
| Zingiber officinale | Rhizomes | Gingerols, shogaols | Reduces gastric irritation, antioxidant effect |

Table 1: Common Herbal Anti-Ulcer Agents and Their Mechanisms (6,7,12,14)

Relevance of Herbal Anti-ulcer Agents in Gastroretentive systems

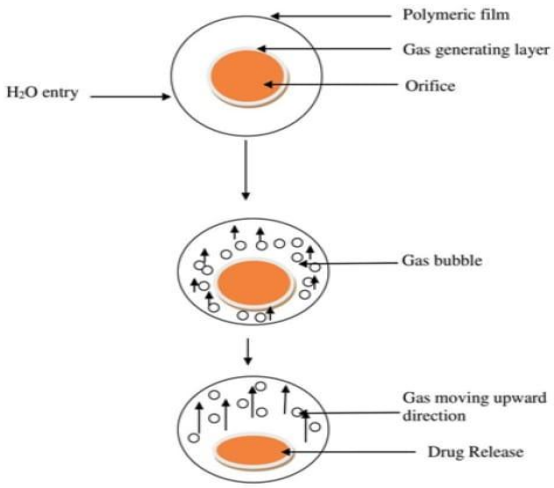
Herbal anti-ulcer agents are particularly beneficial when formulated into gastroretentive drug delivery systems, as prolonged gastric residence enhances their local therapeutic action. Natural polymers and mucilage-containing herbs further contribute to mucoadhesion and sustained release. Gastroretentive formulations of herbal drugs may reduce dosing frequency and improve patient compliance while minimizing systemic side effects.

## IV. GASTRORETENTIVE FORMULATION STRATEGIES

Gastroretentive drug delivery systems are designed to retain the dosage form in the stomach for an extended period, thereby improving the therapeutic effectiveness of drugs intended for local gastric action. Herbal anti-ulcer agents particularly benefit from gastroretentive formulations as prolonged gastric residence enhances mucosal protection and sustained drug release.

### 4.1 Floating Drug Delivery Systems

Floating drug delivery systems remain buoyant in gastric fluid due to their low density. These systems are formulated using gas-generating agents and swellable polymers, which enable the dosage form to float for a prolonged duration. Floating tablets and beads are commonly used for this purpose (2,4,8).

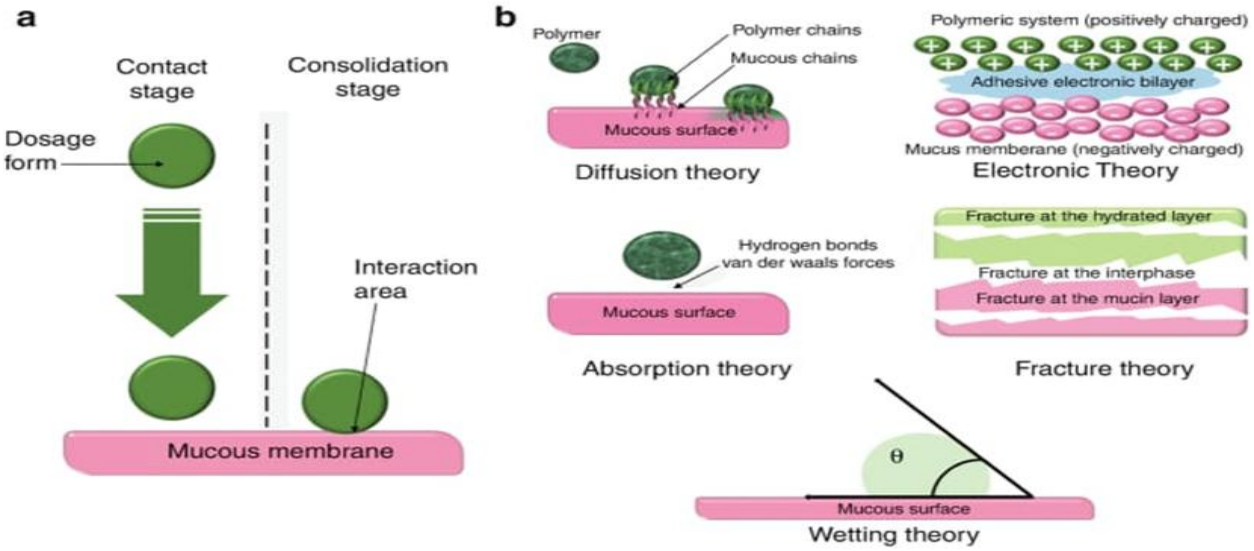



Example:

Floating tablets of Glycyrrhiza glabra extract have been reported to show prolonged gastric residence time and enhanced gastroprotective activity. The sustained release of glycyrrhizin from floating tablets helps in continuous mucosal protection and reduction of gastric irritation (3,15).

### 4.2 Mucoadhesive Drug Delivery Systems

Mucoadhesive systems adhere to the gastric mucosal surface through physical and chemical interactions between the polymer and mucus layer. This adhesion delays gastric emptying and allows the drug to remain in close contact with the stomach lining. Natural polymers such as guar gum, xanthan gum, chitosan, and pectin are widely used in herbal formulations (11,13).

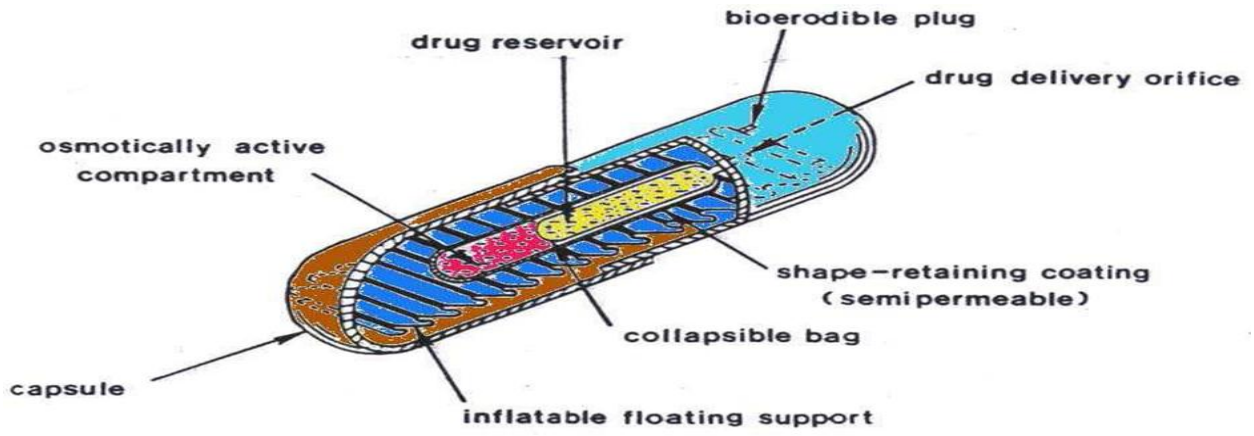



Example:
Mucoadhesive tablets containing Aloe vera gel have demonstrated prolonged gastric retention and improved ulcer healing due to sustained release and direct contact with the gastric mucosa.

4.3 In-Situ Gelling Systems
In-situ gelling systems are liquid formulations that undergo gelation after administration due to physiological conditions such as acidic pH, temperature changes, or the presence of ions. These systems are easy to administer and form a gel matrix in the stomach, which remains retained for a longer duration and releases the drug gradually (11,15). Alginate-based in-situ gelling systems are particularly effective for gastric retention. In the presence of calcium ions and acidic pH, sodium alginate forms a raft-like gel that floats on gastric contents and acts as a physical barrier against acid reflux.

Example:
An alginate-based in-situ gel containing Emblica officinalis extract forms a floating gel in the stomach, providing prolonged gastric retention and antioxidant protection to the gastric mucosa.

4.4 Swellable and Expandable Systems
Swellable gastroretentive systems are formulated using hydrophilic polymers that absorb gastric fluid and swell to a size larger than the pyloric opening. The increased size prevents premature passage of the dosage form into the intestine, thereby enhancing gastric retention. These systems gradually release the drug while maintaining their swollen structure.
Expandable systems are designed to unfold or expand after administration, further increasing gastric residence time(8,15). Such systems are especially useful for sustained drug delivery in acid-related disorders.



Example:
Swellable matrix tablets prepared using Plantago ovata mucilage have shown effective gastric retention due to their swelling behaviour and ability to form a protective barrier over the gastric lining.

4.5 Role of Natural Polymers in Herbal Gastroretentive Formulations
Natural polymers play a crucial role in herbal gastroretentive systems by improving biocompatibility and reducing toxicity. Polymers such as sodium alginate, guar gum, xanthan gum, and chitosan not only support gastroretention but also contribute to sustained drug release and mucosal protection.

Example:
Chitosan-based mucoadhesive beads loaded with Curcuma longa extract have been reported to exhibit prolonged gastric residence and enhanced anti-ulcer activity due to improved adhesion and controlled drug release.

## V. EVALUATION PARAMETERS OF GASTRORETENTIVE DRUG DELIVERY SYSTEMS

The performance of gastroretentive drug delivery systems must be properly evaluated to confirm their ability to remain in the stomach and deliver the drug in a controlled manner. For herbal anti-ulcer formulations, evaluation mainly focuses on floating behaviour, swelling capacity, adhesion to gastric mucosa, and drug release characteristics.

5.1 Floating Lag Time
Floating lag time indicates the time required for a dosage form to rise to the surface of gastric fluid after administration. Shorter lag time is preferred, as it allows the formulation to float immediately and reduces the chance of premature gastric emptying (3,4,8).

Example:
Floating tablets prepared using Glycyrrhiza glabra extract showed rapid floating due to the presence of gas-forming agents, which helped the tablet remain buoyant soon after contact with gastric fluid.

5.2 Total Floating Time
Total floating time refers to how long the formulation remains floating on the gastric contents. Longer floating duration is beneficial for maintaining the dosage form in the stomach and ensuring sustained drug release.

Example:
In-situ gelling formulations containing Emblica officinalis extract remained buoyant for several hours, supporting prolonged gastric retention and continuous therapeutic action.

5.3 Swelling Index
Swelling index measures the extent to which a formulation absorbs gastric fluid and increases in size. Adequate swelling helps the dosage form resist gastric emptying and contributes to controlled drug release (8,15).

Example:
Matrix tablets formulated with Plantago ovata mucilage showed significant swelling, forming a soft gel-like structure that protected the gastric mucosa while retaining the formulation in the stomach.

5.4 Mucoadhesive Strength
Mucoadhesive strength determines the ability of a formulation to attach to the gastric mucosal surface. Strong adhesion improves gastric residence time and enhances localized drug action (11,13).
Example:
Mucoadhesive tablets containing Aloe vera gel exhibited good adhesion to gastric tissue, which supported prolonged contact and improved ulcer healing.

5.5 In-Vitro Drug Release Studies
Drug release studies are performed to understand the pattern and rate of drug release from the gastroretentive system in simulated gastric conditions. A sustained release profile is generally desired for anti-ulcer therapy.

Example:
Floating formulations loaded with Curcuma longa extract showed gradual release of curcumin over an extended period, which supports long-lasting gastroprotective activity.

5.6 Gel Strength (For In-Situ Gelling Systems)
Gel strength reflects the ability of the in-situ formed gel to remain intact under gastric conditions. A stable gel ensures prolonged retention and controlled drug diffusion.

Example:
Alginate-based in-situ gels containing herbal extracts formed firm gels in acidic medium and retained their structure throughout the evaluation period.

5.7 In-Vitro Buoyancy Study
Buoyancy studies are conducted to visually observe and confirm the floating behavior of the formulation in simulated gastric fluid. This test supports the results obtained from floating time measurements.

Example:
Floating beads prepared using herbal extracts showed consistent buoyancy due to efficient gas entrapment within the polymer network.

5.8 Stability Studies
Stability studies are carried out to ensure that the formulation maintains its physical characteristics and drug content during storage. These studies are essential for confirming the shelf life of herbal gastroretentive systems.

Example:
Herbal floating tablets stored under accelerated conditions showed no major changes in appearance, floating behaviour, or drug content.5.2 Participation in Antimicrobial Stewardship (AMS)

## VI. ADVANTAGES AND LIMITATIONS

6.1 Advantages of Gastroretentive Drug Delivery Systems

1 Prolonged gastric residence time allows the formulation to remain in the stomach for several hours.
2 Improved local action of herbal anti-ulcer agents due to extended contact with the gastric mucosa (2,8,15).
3 Sustained and controlled drug release helps in continuous protection of the stomach lining.
4 Reduced dosing frequency improves patient convenience and compliance (4,15).
5 Lower systemic absorption minimizes side effects associated with conventional therapies.
6 Suitable for drugs that are unstable or poorly absorbed in the intestinal environment.
7 Use of natural polymers increases safety, biocompatibility, and patient acceptability.

6.2 Limitations of Gastroretentive Drug Delivery Systems

1 Gastric emptying time varies among individuals, which may affect formulation performance (9,11).
2 Floating systems require sufficient gastric fluid; reduced fluid volume can limit buoyancy.
3 Mucoadhesive systems may lose adhesion due to continuous mucus turnover in the stomach.
4 Formulation development can be complex due to variability in herbal extracts (12,14).
5 Batch-to-batch consistency of herbal formulations can be difficult to maintain.
6 Long-term stability may be affected by moisture sensitivity and polymer–herb interactions.
7 Not suitable for drugs that irritate the gastric mucosa or are unstable in acidic conditions.

## VII. CHALLENGES

1 Variability in the composition of herbal extracts makes standardization difficult and may affect formulation reproducibility (12).
2 Ensuring uniform drug content in gastroretentive systems containing herbal drugs remains a major challenge.
3 Stability of herbal formulations can be affected by moisture, temperature, and interaction with polymers (16).
4 Selection of suitable natural polymers that provide both gastroretention and controlled release requires careful optimization.
5 Gastric physiology differs among individuals, which can influence the performance of gastroretentive systems.
6 Limited in-vivo data are available for many herbal gastroretentive formulations, restricting clinical translation.
7 Regulatory guidelines for herbal gastroretentive drug delivery systems are not well defined, creating approval challenges.

## VIII. FUTURE PROSPECTS

1 Development of standardized herbal extracts may improve batch-to-batch consistency and formulation reliability.
2 Increased use of natural and biodegradable polymers can enhance safety and patient acceptance.
3 Integration of advanced formulation techniques such as in-situ gelling and mucoadhesive systems may further improve gastric retention (8,11).
4 Application of nanotechnology in herbal gastroretentive systems could enhance bioavailability and therapeutic efficacy.
5 More in-vivo and clinical studies may help establish the effectiveness of herbal gastroretentive formulations (11,14).
6 Gastroretentive systems combining multiple mechanisms, such as floating and mucoadhesion, may offer improved performance.
7 Growing interest in herbal and patient-friendly therapies supports future development of gastroretentive systems for acid-related disorders.

## IX. CONCLUSION

Acid-related gastric disorders continue to be a major health concern, requiring effective and patient-friendly therapeutic approaches. Herbal anti-ulcer agents have gained considerable attention due to their gastroprotective action, safety profile, and long history of traditional use. However, conventional dosage forms often fail to provide prolonged gastric residence, limiting their therapeutic effectiveness. Gastroretentive drug delivery systems offer a promising strategy to overcome these limitations by enhancing gastric retention and ensuring sustained release of herbal drugs at the site of action. Formulation approaches such as floating, mucoadhesive, in-situ gelling, and swellable systems have demonstrated potential in improving treatment outcomes and patient compliance. Although challenges related to standardization, stability, and regulatory aspects remain, continued research and formulation optimization may support the successful development of herbal gastroretentive systems. Overall, the integration of herbal anti-ulcer agents with gastroretentive drug delivery represents a valuable approach for the effective management of acid-related disorders (8,11,14).

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