Journal of Biomedical and Pharmaceutical Research
Available Online at www.jbpr.in
CODEN: - JBPRAU (Source: - American Chemical Society)
NLM (National Library of Medicine): ID: (101671502)
Index Copernicus Value 2023: 85.86
Volume 14, Issue 6; 2025, 116-128

ISSN (Online): 2279-0594
ISSN (Print): 2589-8752

Review Article

Gastro-Retentive Drug Delivery Systems: A Comprehensive Scientific Review

Anand J.Purohit*[1], Sheelpriya Walde[2], Raksha A. Purohit[3]
[1]Researcher, Gurunanak College of Pharmacy, Nagpur
[2]Professor, Gurunanak College of Pharmacy, Nagpur
[3]Researcher, Department of Pharmaceutical Sciences - RTMNU, Nagpur

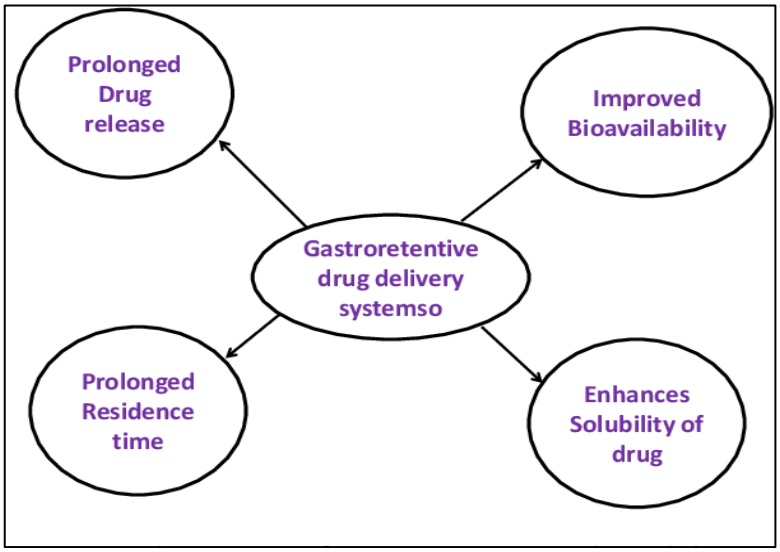
Article Info: Received: 15-09-2025 / Revised: 27-10-2025 / Accepted: 26-11-2025
Corresponding Author: Mr. Anand J.Purohit
DOI: https://doi.org/10.32553/jbpr.v14i6.1393
Conflict of interest statement: No conflict of interest

Abstract:
Gastro-retentive drug delivery systems (GRDDS) are innovative oral formulations designed to enhance the bioavailability and therapeutic efficacy of drugs with narrow absorption windows in the upper gastrointestinal tract. By prolonging gastric residence time, GRDDS enable sustained drug release, reduce dosing frequency, and improve patient compliance. Several strategies, including floating, bioadhesive, swelling, and high-density systems, have been developed to achieve effective gastro-retention. This review summarizes the physiological factors influencing gastric retention, various formulation approaches, and key evaluation techniques. It further discusses clinical applications, recent technological advances, and challenges associated with GRDDS. A critical analysis of their advantages and limitations is presented, along with insights into future directions, highlighting the role of novel polymers, nanotechnology, and 3D printing in overcoming existing barriers and translating GRDDS into successful clinical products.
Keywords: Gastro-retentive drug delivery systems, gastric retention, floating systems, bioadhesive systems, controlled release, oral bioavailability, sustained drug release, nanotechnology.

1. Introduction

Oral drug delivery is the most preferred and widely accepted route of administration owing to its non-invasive nature, cost-effectiveness, and suitability for large-scale manufacturing. Despite these advantages, conventional oral dosage forms are often limited by unpredictable gastric emptying, variable gastrointestinal transit times, and reduced bioavailability, especially for drugs that are absorbed primarily in the stomach or upper small intestine. Compounds with a narrow absorption window (e.g., riboflavin, levodopa, furosemide) or those unstable in the alkaline environment of the intestine exhibit suboptimal therapeutic efficacy when delivered through standard formulations. (Mishra, et al, 2024)

The stomach, characterized by its acidic pH and variable motility patterns, presents both opportunities and challenges for drug delivery. Gastric emptying typically occurs within 2–3 hours in the fasted state and 4–6 hours in the fed state, limiting the residence time of conventional dosage forms. Consequently, many drugs pass beyond their optimal absorption site before being fully absorbed, resulting in decreased systemic availability. To overcome this drawback, gastro-retentive drug delivery systems (GRDDS) have been developed to prolong gastric retention, enabling sustained release and improved absorption. (Miyazaki, S., et al, 1988).



Gastro-retention offers significant benefits in the following contexts:

- **Drugs with local gastric action** (e.g., antacids, antibiotics for *Helicobacter pylori*).
- **Drugs with narrow absorption windows** (e.g., riboflavin, metformin, levodopa).
- **Drugs poorly soluble in alkaline pH** (e.g., diazepam, ferrous salts).
- **Peptides and unstable compounds** that degrade in the intestinal or colonic environment.
- In addition to improving therapeutic efficacy, GRDDS reduce dosing frequency, enhance patient compliance, and maintain steady plasma drug concentrations. Several gastro-retentive strategies—including floating systems, bioadhesive systems, swelling/expandable systems, and high-density systems—have been explored, each employing distinct mechanisms to extend gastric residence. With ongoing advancements in polymer science, nanotechnology, and 3D printing, GRDDS continue to evolve as a promising platform for controlled and targeted drug delivery. (Patel D., et al.2007).

Table 1: Challenges in Conventional Oral Drug Delivery vs. Role of GRDDS

Challenges in Oral Drug Delivery	How GRDDS Overcomes Them
Rapid gastric emptying → short residence time of dosage form	Prolonged gastric retention via floating, swelling, bioadhesion, or high-density mechanisms
Variable absorption in different regions of GIT	Maintains drug release in the stomach and upper intestine (site-specific absorption)
Reduced bioavailability of drugs with narrow absorption window	Improves bioavailability by retaining drug in absorption window for longer
Instability of drugs in alkaline pH of intestine	Protects drugs by retaining them in acidic gastric environment
Frequent dosing required for short half-life drugs	Sustained and controlled release reduces dosing frequency
Fluctuation in plasma drug levels	Provides more consistent and predictable plasma concentration

2. Physiological Considerations for GRDDS

- The performance of gastro-retentive drug delivery systems (GRDDS) is strongly influenced by the complex physiological environment of the stomach.

Several factors determine the gastric residence time of a dosage form and, consequently, its effectiveness in sustaining drug release. (Andrew, A. 2022)

- **Gastric Motility and Emptying:** Gastric motility is regulated by the migrating myoelectric complex (MMC), which consists of cyclic phases of contraction and relaxation. In the fasted state, gastric emptying occurs more rapidly, whereas in the fed state, the process is slower, providing a longer retention window for GRDDS.
- **Gastric pH:** The pH of the stomach ranges from 1.5–2.5 in the fasted state and rises to 3–6 in the fed state. This variation significantly influences drug solubility, stability, and the performance of pH-sensitive polymers used in gastro-retentive formulations.
- **Gastric Volume and Fluid Content:** The gastric fluid volume is typically 25–50 mL in the fasted state but increases substantially after food intake. The presence of fluid facilitates the swelling of expandable systems and enhances buoyancy of floating dosage forms.
- **Size and Shape of Dosage Form:** The geometry of the dosage form affects retention; larger formulations (>10 mm) and specific shapes such as tetrahedrons and rings are more resistant to gastric emptying compared to smaller or irregular shapes.
- **Density of Dosage Form:** The relative density of a dosage form is crucial for its mechanism of retention. Formulations with density less than 1.0 g/cm³ exhibit floating behavior, whereas those with density greater than 2.5 g/cm³ sink to the bottom of the stomach, both strategies aiding prolonged retention.
- **Patient-Related Factors:** Individual characteristics such as age, gender, body posture, and pathological conditions (e.g., gastroparesis, Crohn's disease, or peptic ulcer disease) can significantly affect gastric motility and, hence, the performance of GRDDS.

Table 2: Physiological Factors Affecting Gastro-Retention and GRDDS Performance

Factor	Description	Effect on GRDDS Performance
Gastric Motility (MMC cycle)	Alternating contraction and relaxation in fasted and fed states	Strong MMC in fasted state → rapid emptying; Fed state → delayed emptying, improves GRDDS retention
Gastric pH	1.5–2.5 (fasted), 3–6 (fed)	Influences drug solubility/stability; acidic pH favors weakly basic drugs
Gastric Volume & Fluid Content	25–50 mL (fasted), increases post-prandially	Adequate fluid aids swelling/floatation; insufficient fluid may reduce effectiveness
Food Effect	High-fat and high-calorie meals delay emptying; liquids accelerate emptying	Fed state prolongs retention; fasting reduces retention
Dosage Form Size & Shape	Small (<2 mm) pass quickly; Large (>10 mm) retained longer; Shape influences retention	Ring/tetrahedron shapes show better retention than cylindrical/spherical
Dosage Form Density	<1.0 g/cm³ → floating; >2.5 g/cm³ → sinking	Determines gastric residence mechanism (floating or sinking systems)

Patient-Related Factors	Age, gender, disease state (e.g., diabetes, gastroparesis)	Can accelerate or delay gastric emptying; influences GRDDS performance
Factor	**Description**	**Effect on GRDDS Performance**
Gastric Motility (MMC cycle)	Alternating contraction and relaxation in fasted and fed states	Strong MMC in fasted state → rapid emptying; Fed state → delayed emptying, improves GRDDS retention

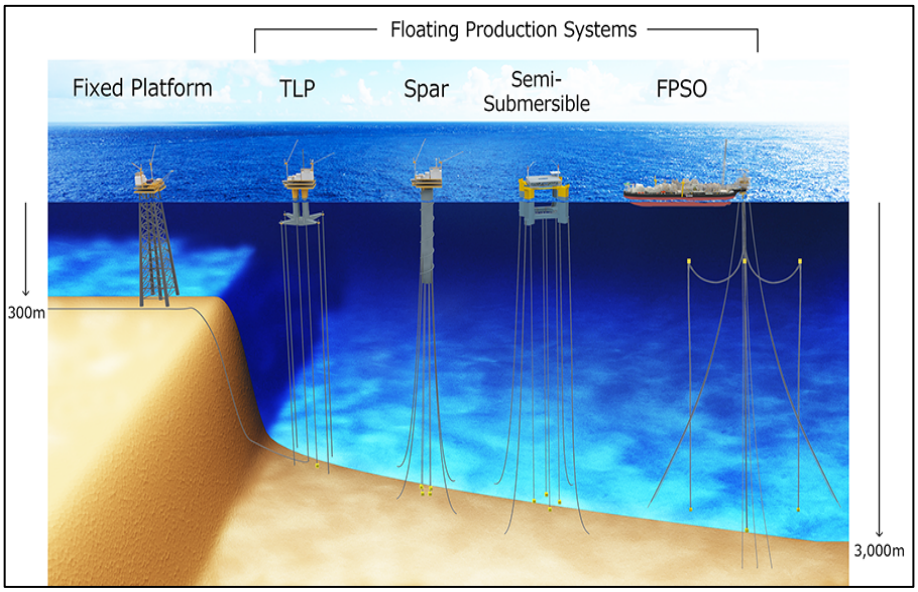
Approaches in GRDDS

Several formulation strategies have been developed to achieve gastric retention, each employing distinct mechanisms to overcome rapid gastric emptying. The major approaches are as follows:

3.1 Floating Systems

Floating drug delivery systems (FDDS) are among the most widely investigated GRDDS. Their mechanism relies on reducing the dosage form's density to less than that of gastric fluid (approximately 1.004 g/cm³), enabling it to remain buoyant on the gastric contents for prolonged periods. This buoyancy delays gastric emptying and ensures extended drug release. (Fouladi, F., & Mortazavi, S. A. 2012)

- Effervescent Systems: These contain gas-generating agents such as sodium bicarbonate, citric acid, or tartaric acid, which react with gastric acid to release carbon dioxide. The generated gas gets trapped within the polymer matrix, imparting buoyancy.



Non-effervescent Systems: These employ swellable polymers such as hydroxypropyl methylcellulose (HPMC), chitosan, alginate, or carbopol. Upon hydration, the polymers form a gel barrier and decrease system density, allowing the dosage form to float.

3.2 Bioadhesive/Mucoadhesive Systems

These systems rely on adhesion to the gastric mucosa to prolong residence time. By forming strong hydrogen bonds or electrostatic interactions with mucin, the dosage form remains attached to the stomach wall even during peristalsis. Commonly used mucoadhesive polymers include carbopol, chitosan, polycarbophil, and sodium alginate. Bioadhesion not only ensures gastric retention but also provides localized drug delivery at the gastric mucosal surface. (Brody, T. 2016).

3.3 Swelling/Expandable Systems

Expandable systems are designed to swell upon contact with gastric fluid, increasing in size beyond the pyloric sphincter opening (~12–15 mm). This prevents premature transit into the small intestine. Swelling is typically achieved using superporous hydrogels, cross-linked polyacrylates, or natural polysaccharides. These materials rapidly absorb gastric fluid and expand in volume while maintaining mechanical integrity. Once drug release is complete, the system gradually degrades or disintegrates to allow safe passage. (Shaikh, S. C., et al, 2018)

3.4 High-Density Systems

Unlike floating systems, high-density dosage forms are designed with a density greater than 2.5 g/cm³. Such formulations sink to the bottom of the stomach and resist peristaltic waves that normally expel gastric contents. Excipients like barium sulfate, zinc oxide, and titanium dioxide are often used to increase density. This approach ensures prolonged gastric residence, especially in the fed state when gastric emptying is slower. (Chatterjee, B., et al, 2017)

4. Advantages of GRDDS

Gastro-retentive drug delivery systems (GRDDS) offer significant clinical and pharmaceutical benefits compared to conventional oral dosage forms. Their ability to prolong gastric residence and release drugs in a controlled manner makes them especially valuable for drugs with narrow absorption windows or localized gastric activity. (Garg, T., et al, 2014).

4.1 Enhanced Bioavailability

Several drugs, including riboflavin, furosemide, and levodopa, exhibit limited absorption in the upper small intestine. Conventional dosage forms often pass through the absorption window too quickly, leading to suboptimal systemic exposure. GRDDS overcome this limitation by retaining the drug in the stomach, thereby allowing maximum absorption and improved bioavailability. (Andrew, A., 2022).

4.2 Sustained and Controlled Release

By extending gastric residence time, GRDDS enable sustained and predictable drug release. This minimizes sharp fluctuations in plasma drug concentrations, reduces the risk of dose-dependent adverse effects, and provides a more consistent therapeutic effect. Such controlled release profiles are particularly beneficial for drugs with a narrow therapeutic index. (Raza M., et al,2022).

4.3 Reduced Dosing Frequency and Improved Patient Compliance

The prolonged release characteristics of GRDDS allow for less frequent dosing, decreasing pill burden. This enhances patient adherence, especially in chronic therapies such as hypertension, diabetes, and Parkinson's disease, where long-term compliance is essential for successful treatment outcomes.

4.4 Targeted Local Action in the Stomach

GRDDS are highly advantageous for drugs intended to act locally in the stomach. Examples include antacids, anti-ulcer agents (ranitidine, famotidine), and antibiotics for *Helicobacter pylori* eradication (e.g., amoxicillin, clarithromycin, metronidazole). Localized retention improves drug efficacy, reduces required doses, and minimizes systemic side effects.

4.5 Protection of Labile Drugs

Certain drugs are unstable or degrade rapidly in the alkaline environment of the intestine and colon. By retaining the drug within the acidic gastric milieu, GRDDS can protect acid-soluble and pH-sensitive drugs, thereby preserving stability and therapeutic activity.

4.6 Economic and Industrial Advantages

Compared to parenteral sustained-release formulations, oral GRDDS are more cost-effective, less invasive, and easier to administer. They are compatible with standard manufacturing processes, making them suitable for large-scale production and enhancing their commercial feasibility.

5. Limitations of GRDDS

Despite their numerous advantages, gastro-retentive drug delivery systems (GRDDS) face several physiological, formulation, and patient-related challenges that can limit their effectiveness and clinical applicability. (Jain, S., & Srinivasan, B. 2023)

5.1 Variable Gastric Residence Time

Gastric motility and emptying patterns vary significantly among individuals and are influenced by factors such as food intake, body posture, age, and pathological conditions. This variability can lead to unpredictable drug release and absorption, reducing the consistency of therapeutic outcomes.

5.2 Unsuitability for Certain Drugs

- Drugs unstable in acidic pH (e.g., erythromycin, omeprazole) may degrade in the stomach and are unsuitable for GRDDS.
- Drugs that cause gastric irritation (e.g., aspirin, non-steroidal anti-inflammatory drugs) may exacerbate side effects due to prolonged gastric retention.

5.3 Dose Limitation

High-dose drugs may be difficult to formulate as a single gastro-retentive unit without increasing size and risking patient discomfort. Multi-unit systems may be required, which can complicate formulation and reduce convenience.

5.4 Formulation Challenges

Developing dosage forms that reliably float, swell, or adhere under varying gastric conditions is technically demanding. Achieving reproducibility and scaling up these formulations for industrial production presents additional challenges.

5.5 Patient-Related Limitations

- GRDDS are not recommended for patients with gastrointestinal obstruction, gastroparesis, or motility disorders.
- Elderly patients or those with delayed gastric emptying may experience unpredictable gastric retention and drug absorption.

5.6 Ethical and Clinical Considerations

Certain GRDDS technologies, such as expandable or swelling systems, may cause discomfort, bloating, or even obstruction if not properly optimized. Careful design and clinical evaluation are necessary to ensure patient safety.

6. Evaluation Parameters of GRDDS

The evaluation of GRDDS is critical to ensure safety, efficacy, and performance.(Kumar V., et al. 2024). Studies are typically divided into in vitro, in vivo, and in silico methods:

6.1 In Vitro Evaluation

- **Floating Behavior**
  - *Floating Lag Time (FLT):* Time taken for dosage form to rise to the surface.
  - *Total Floating Time (TFT):* Duration of buoyancy in simulated gastric fluid.
- **Swelling Index / Water Uptake**
  - Measures the extent of polymer hydration and expansion.
- **Mucoadhesion Strength**
  - Determined by texture analyzer or detachment force studies against gastric mucosa.
- **Drug Release Studies**
  - Carried out in simulated gastric fluid (SGF, pH 1.2) to assess dissolution and sustained release kinetics.

6.2 In Vivo Evaluation

- **Radiographic Studies (X-ray/γ-scintigraphy):** Dosage forms labeled with radio-opaque markers or radionuclides are tracked for gastric retention.
- **Endoscopic Studies:** Direct visualization of dosage form behavior inside stomach.
- **Pharmacokinetic Studies:** Plasma concentration-time profile used to assess bioavailability improvement.

6.3 In Silico / Computational Studies

- **Physiologically Based Pharmacokinetic (PBPK) Modeling:** Predicts absorption and release profiles based on gastric physiology.
- **Simulation of gastric motility:** Helps optimize design before in vivo testing.

6.4 General Quality Control Parameters

Like all oral dosage forms, GRDDS must also be evaluated for:

- Hardness, friability, thickness, and weight variation (for tablets).
- Content uniformity and drug assay.

7. Recent Advances in GRDDS

Continuous innovations in material science, nanotechnology, and fabrication techniques have advanced the scope of GRDDS beyond conventional floating or bioadhesive systems. (Pushpamalar, J., et al,2021)

7.1 Nanoparticle-Loaded GRDDS

Nanoparticles incorporated within gastro-retentive matrices improve drug solubility,

stability, and absorption. For example, nanoemulsion-based floating tablets of poorly water-soluble drugs (like curcumin) have shown enhanced bioavailability.

7.2 3D Printing of GRDDS

Additive manufacturing (3D printing) enables precise control over dosage form geometry, porosity, and drug release profiles. It allows personalization of GRDDS tailored to patient-specific needs and drug pharmacokinetics.

7.3 Smart Polymers and Stimuli-Responsive Systems

Polymers sensitive to pH, temperature, or enzymatic activity can achieve "on-demand" drug release. Example: pH-sensitive hydrogels that swell in acidic gastric pH but shrink in neutral intestinal pH, ensuring site-specific action.

7.4 Combination Systems

Hybrid GRDDS combine multiple mechanisms, e.g., floating-bioadhesive systems or swelling-floatable systems, to maximize retention efficiency. These multifunctional systems overcome limitations of single-mechanism formulations.

7.5 Multi-Unit GRDDS (MUGRDDS)

Instead of a single large unit, multiple smaller gastro-retentive particles (microspheres, beads, minitablets) distribute uniformly in the stomach, reducing risk of dose-dumping and providing more consistent drug release.

7.6 Novel Carriers and Natural Polymers

Biodegradable and natural polymers (chitosan, alginate, xanthan gum) are gaining attention for their safety, biocompatibility, and sustainable production in GRDDS formulations.

8. Applications of GRDDS

GRDDS are applied across a wide spectrum of therapeutic classes:

8.1 Eradication of *Helicobacter pylori*

- Localized delivery of antibiotics such as amoxicillin, clarithromycin, and metronidazole provides high local concentrations in the gastric mucosa, improving eradication rates.(Patel K., et al, 2022).

8.2 Antihypertensive Therapy

- Drugs like propranolol, verapamil, and nifedipine show narrow absorption windows and benefit from controlled release GRDDS, ensuring steady plasma levels and improved cardiovascular outcomes.

8.3 Antidiabetic Therapy

- Metformin, the first-line drug for type 2 diabetes, shows site-specific absorption in the upper small intestine. Floating tablets of metformin improve absorption and glycemic control.

8.4 Antiulcer and Acid-Suppressing Agents

- Ranitidine, famotidine, and misoprostol benefit from gastric targeting for enhanced therapeutic activity in treating gastric ulcers.

8.5 CNS Drugs

- Levodopa (for Parkinson's disease) and gabapentin demonstrate enhanced absorption and prolonged action when formulated as GRDDS.

8.6 Nutraceuticals and Vitamins

- Drugs and nutrients like riboflavin, iron salts, and calcium supplements show improved uptake when delivered using gastro-retentive dosage forms.

9. Future Prospects of GRDDS

The field of GRDDS is evolving rapidly, and future research directions include:

9.1 Integration with Personalized Medicine

With advances in pharmacogenomics and 3D printing, GRDDS can be customized to match patient-specific needs, drug metabolism patterns, and disease progression. (Lodh H., et al, 2020).

9.2 Development of Intelligent GRDDS

Emerging research focuses on smart, stimuli-responsive GRDDS that respond to physiological triggers (e.g., pH changes, enzymes, gastric motility) for precise drug release.

9.3 Biopolymer and Green Technology Approaches

The move toward eco-friendly, sustainable polymers (e.g., plant-based gums, marine polysaccharides) will reduce toxicity and improve biocompatibility of GRDDS.

9.4 Combination with Nanotechnology

The merging of nanocarriers with gastro-retentive platforms may revolutionize the delivery of poorly soluble, unstable, or peptide drugs by protecting them in the stomach and enhancing absorption.

9.5 Clinical Translation and Regulatory Acceptance

Despite many experimental successes, only a few GRDDS have reached the market. Future focus should be on clinical trials, scale-up feasibility, and regulatory guidelines to translate laboratory concepts into viable therapies.

9.6 Expansion into New Drug Classes

GRDDS hold potential for biologics, vaccines, and gene therapy vectors, provided stability challenges in the stomach can be addressed using protective and mucoadhesive carriers.

10. Inference

Gastro-retentive drug delivery systems (GRDDS) represent one of the most promising innovations in oral controlled drug delivery, particularly for drugs with narrow absorption windows, poor solubility in alkaline pH, or those requiring localized gastric action. The diversity of approaches—floating, swelling, bioadhesive, and high-density systems—demonstrates the adaptability of GRDDS to various therapeutic needs. From the compiled evidence, it is clear that GRDDS significantly enhance bioavailability, therapeutic efficacy, and patient compliance compared to conventional dosage forms. However, physiological variability, formulation complexity, and limitations in scalability remain critical barriers to clinical translation. Recent advances such as 3D printing, stimuli-responsive polymers, and nanotechnology are bridging these gaps and expanding the applicability of GRDDS. The future of this field lies in personalized medicine, eco-friendly biomaterials, and regulatory acceptance, which together will determine the real-world success of gastro-retentive platforms. In summary, GRDDS are not just a theoretical innovation but a clinically relevant strategy with the potential to transform oral drug delivery if ongoing challenges are systematically addressed through interdisciplinary research and translational studies.

References

1. Adebisi, A., & Conway, B. R. (2011). Gastroretentive microparticles for drug delivery applications. *Journal of Microencapsulation, 28*(8), 689–708. https://doi.org/10.3109/02652048.2011.590613
2. Adibkia, K., Ghanbarzadeh, S., Mohammadi, G., et al. (2013). Gastro retentive drug delivery systems: A review. *JRPS, 2*(2), 190–204.
3. Ahmed, M. G. (2017). Development and in vitro evaluation of rosuvastatin tablets by floating drug delivery system. *Asian Journal of Pharmaceutics, 11*(2). https://doi.org/10.22377/ajp.v11i02.1262
4. Ali, M., & Manoj, Y. V. (2022). A scientific overview on gastro retentive drug delivery system. *World Journal of Pharmaceutical Research, 11*(4), 379–393. https://doi.org/10.20959/wjpr20224-23457
5. Alomar, M., Tawfiq, A. M., Hassan, N., & Palaian, S. (2020). Post-marketing surveillance of suspected adverse drug reactions through spontaneous reporting: Current status, challenges and the future. *Therapeutic Advances in Drug Safety, 11*, Article 2042098620938595. https://doi.org/10.1177/2042098620938595
6. Andrew, A. (2022). A review on raft-forming drug delivery system – Mechanism and its significance. *Australas Med J. International Journal of Pharmacognosy, 5*(6), 337–349.
7. Anothra, P., Pradhan, D., Halder, J., Ghosh, G., & Rath, G. (2023). Gastroretentive drug delivery system in cancer chemotherapy. *Current Drug Delivery, 20*(5), 483–496. https://doi.org/10.2174/1567201819666220608141124
8. Asane, G. S., Nirmal, S. A., Rasal, K. B., Naik, A. A., Mahadik, M. S., & Rao, Y. M. (2008). Polymers for mucoadhesive drug delivery system: A current status. *Drug Development and Industrial Pharmacy, 34*(11), 1246–1266.

https://doi.org/10.1080/03639040802026012

9. Brody, T. (2016). Food and dietary supplement package labeling-guidance from FDA's warning letters and Title 21 of the Code of Federal Regulations. *Comprehensive Reviews in Food Science and Food Safety, 15*(1), 92–129. https://doi.org/10.1111/1541-4337.12172
10. Shaikh, S. C., Sanap, D., Bhusari, D. V., Jain, S., Kochar, P. P., & Sanchati, V. N. (2018). Formulation and evaluation of ibuprofen gastro-retentive floating tablets. *Universal Journal of Pharmaceutical Research, 3*(4). https://doi.org/10.22270/ujpr.v3i4.178
11. Chatterjee, B., Amalina, N., SenGupta, P., et al. (2017). Mucoadhesive polymers and their mode of action: A recent update. *Journal of Applied Pharmaceutical Sciences, 7*(5), 195–203.
12. Chaudhari, K. D., Nimbalwar, M. G., Singhal, N. S., Panchale, W. A., & Jagdish, V. (2021). Formulation and application of gastro-retentive floating drug delivery system. *GSC Advanced Research and Reviews, 7*(1), 35–44. https://doi.org/10.30574/gscarr.2021.7.1.0070
13. Chawla, G., & Bansal, A. (2003). A means to address regional variability in intestinal drug absorption. *Pharmaceutical Technology, 27*(2), 50–68.
14. Chen, H., Pan, L., Zhang, C., Liu, L., Tu, B., Liu, E., & Huang, Y. (2024). Gastroretentive raft forming system for enhancing therapeutic effect of drug-loaded hollow mesoporous silica on gastric ulcers. *Advanced Healthcare Materials, 13*(22), Article e2400566. https://doi.org/10.1002/adhm.202400566
15. Chow, S.-C., & Pong, A. (1998). An overview of the regulatory approval process in drug development. *Drug Information Journal, 32*(1_suppl), 1175S–1185S. https://doi.org/10.1177/00928615980320S102
16. Crowley, M. M., Zhang, F., Repka, M. A., Thumma, S., Upadhye, S. B., Battu, S. K., McGinity, J. W., & Martin, C. (2007). Pharmaceutical applications of hot-melt extrusion: Part I. *Drug Development and Industrial Pharmacy, 33*(9), 909–926. https://doi.org/10.1080/03639040701498759
17. Fouladi, F., & Mortazavi, S. A. (2012). Preparation and in-vitro evaluation of gastro retentive bupropion hydrochloride tablets. *Tropical Journal of Pharmaceutical Research, 11*(3), 351–359. https://doi.org/10.4314/tjpr.v11i3.3
18. Garg, T., Kumar, A., Rath, G., & Goyal, A. K. (2014). Gastro retentive drug delivery systems for therapeutic management of peptic ulcer. *Critical Reviews in Therapeutic Drug Carrier Systems, 31*(6), 531–557. https://doi.org/10.1615/CritRevTherDrugCarrierSyst.2014011104
19. Gunda, R. K. (2015). Design, formulation and evaluation of atenolol gastro retentive floating tablets. *Asian Journal of Pharmaceutics, 9*(4), S34–S42. https://doi.org/10.22377/ajp.v9i4.484
20. Hatwar, P. R., Bakal, R. L., Dere, M. D., et al. (2023). A review on: Gastro-retentive drug delivery system. *WJPR, 12*(12), 277–290.
21. Jain, K. K. (2002). Personalized medicine. *Current Opinion in Molecular Therapeutics, 4*(6), 548–558.
22. Jain, S., & Srinivasan, B. (2023). An insight on the strategical approach of gastro-retentive drug delivery systems, 3(2).
23. Jakasaniya, P., Patel, J., Dudhat, K., & Mori, D. (2024). Formulation and optimization of gastro-retentive in situ gel of antiepileptic agent by using a Box-Behnken factorial design. *Proceedings of the Indian National Science Academy*, 1–4. https://doi.org/10.1007/s43538-024-00343-5
24. Javaid, M. U., ul Ain, Q., Tahir, U., et al. (2017). A summarized review about natural polymers' role in floating drug delivery systems and in-vivo evaluation studies.

International Current Pharmaceutical Journal, 6(4), 23–26.
25. Jeganath, S. (2022). Recent approaches of gastro retentive drug delivery system – A review. *Asian Journal of Pharmacy, 16*(1). https://doi.org/10.3390/pharmaceutics11040193
26. Kantak, M. N., Kumar, L., Bhide, P. J., & Shirodkar, R. K. (2023). Oral gastroretentive film of lacidipine for the treatment of gastroparesis. *Assay and Drug Development Technologies, 21*(3), 97–109. https://doi.org/10.1089/adt.2022.091
27. Kavitha, K., Kumar, M. R., & Singh, S. J. (2011). Novel mucoadhesive polymers: A review. *Journal of Applied Pharmaceutical Sciences*, 37–42.
28. Khalaf, M. M., Alinejad, S. S., Sajad, O., et al. (2023). e1–e19. *Journal of Population Therapeutics and Clinical Pharmacology, 30*(5). https://doi.org/10.47750/jptcp.2023.30.05.001
29. Klausner, E. A., Lavy, E., Friedman, M., & Hoffman, A. (2003). Expandable gastroretentive dosage forms. *Journal of Controlled Release, 90*(2), 143–162. https://doi.org/10.1016/s0168-3659(03)00203-7
30. Kumar, S., Das, M., Gupta, K. S., Kumar, R., et al. (2013). Design, development, optimization and evaluation of gastro-retentive floating tablets of atenolol. *Der Pharmacia Lettre, 5*(3), 436–456.
31. Kumar, V., Somkuwar, S., & Singhai, A. K. (2024). A recent update on gastro-retentive drug delivery systems. *GSCBPS, 27*(1), 125–144.
32. Lee, B.-J., & Min, G.-H. (1995). Preparation and release characteristics of polymer-reinforced and coated alginate beads. *Archives of Pharmacal Research, 18*(3), 183–188. https://doi.org/10.1007/BF02979193
33. Liao, D.-H., Zhao, J.-B., & Gregersen, H. (2009). Gastrointestinal tract modelling in health and disease. *World Journal of Gastroenterology, 15*(2), 169–176. https://doi.org/10.3748/wjg.15.169
34. Lodh, H., Sheeba, F. R., Chourasia, P. K., Pardhe, H. A., & Pallavi, N. (2020). Floating drug delivery system: A brief review. *Asian Journal of Pharmacy and Technology, 10*(4), 255–264. https://doi.org/10.5958/2231-5713.2020.00043.4
35. Mishra S, Shukla P, Tiwari R. Exploring the Potential of Gastro Retentive Drug Delivery Systems: An Insightful Perspective. Int. J. Pharm. Investigation. 2025;15(3):313-24.
36. Mahmoud, D. B., & Schulz-Siegmund, M. (2023). Utilizing 4D printing to design smart gastroretentive, esophageal and intravesical drug delivery systems. *Advanced Healthcare Materials, 12*(10), Article e2202631. https://doi.org/10.1002/adhm.202202631
37. Maniruzzaman, M., Boateng, J. S., Snowden, M. J., & Douroumis, D. (2012). A review of hot-melt extrusion: Process technology to pharmaceutical products. *ISRN Pharmaceutics, 2012*(1), Article 436763. https://doi.org/10.5402/2012/436763
38. Mayur, C., Senthilkumaran, K., & Hemant, G. (2013). Super porous hydrogels: A recent advancement in gastro-retentive drug delivery system. *Indonesian Journal of Pharmacy, 24*(1), 1–3.
39. Meenakshi, P., & Naazneen, S. (2013). Gastro retentive drug delivery system—a novel approach for the management of diabetes mellitus. *Inventi Rapid NDDS, 2*, 1–7.
40. Miyazaki, S., Yamaguchi, H., Yokouchi, C., Takada, M., & Hou, W. M. (1988). Sustained-release and intragastric-floating granules of indomethacin using chitosan in rabbits. *Chemical & Pharmaceutical Bulletin, 36*(10), 4033–4038. https://doi.org/10.1248/cpb.36.4033
41. Mora-Castaño, G., Domínguez-Robles, J., Himawan, A., et al. (2024). Current trends in 3D printed gastro-retentive floating drug delivery systems: A comprehensive review.

International Journal of Pharmacy, 633, Article 124543.
42. Muaddi, H., Kearse, L., & Warner, S. (2024). Multimodal approaches to patient selection for pancreas cancer surgery. *Current Oncology, 31*(4), 2260–2273. https://doi.org/10.3390/curroncol31040167
43. Mukund, J. Y., Kantilal, B. R., & Sudhakar, R. N. (2012). Floating microspheres: A review. *Brazilian Journal of Pharmaceutical Sciences, 48*(1), 17–30. https://doi.org/10.1590/S1984-82502012000100003
44. Nagariya, A. K., Meena, A. K., Jain, D., et al. (2010). Potential of natural polymer in the gastro-retentive floating drug delivery system: A review. *Journal of Pharmacy Research, 3*, 916–922.
45. Nitave, S. A., Patil, V. A., & Kagalkar, A. A. (2014). Review on gastro-retentive drug delivery system (GRDDS). *International Journal of Pharmaceutical Sciences Review and Research, 27*, 90–95.
46. Nur, A., Fiskia, E., & Tjiroso, B. (2021). Evaluation profile in vitro release gastro-retentive high-density tablet theophylline using sodium alginate and PVP. *E3S Web Conf., 328*, Article 01001.
47. Nurhalifah, N., Sundawan, P. D., Veronita, S. C., Puji Destria, S. I., Nuryamah, S., & Yuniarsih, N. (2022). Literature review article: Drug delivery system held in the stomach (Gastro retentive). *Journal of Social Research, 2*(1), 126–133. https://doi.org/10.55324/josr.v2i1.472
48. Parikh, D. C., & Amin, A. F. (2008). In vitro and in vivo techniques to assess the performance of gastro-retentive drug delivery systems: A review. *Expert Opinion on Drug Delivery, 5*(9), 951–965. https://doi.org/10.1517/17425247.5.9.951
49. Patel, D. M., Patel, N. M., Patel, V. F., & Bhatt, D. A. (2007). Floating granules of ranitidine hydrochloride-gelucire 43/01: Formulation optimization using factorial design. *AAPS PharmSciTech, 8*(2), Article 30. https://doi.org/10.1208/pt0802030
50. Patel, K., Patidar, D., & Sharma, N. (2022). A recent advantage on gastro retentive drug delivery system: An overview. *Journal of Pharmaceutical Negative Results, 13*(Suppl. 10), 4521–4529. https://doi.org/10.47750/pnr.2022.13.S10.547
51. Patel, S., Aundhia, C., Seth, A., et al. (2010). Microsponge: A novel approach in gastro-retention drug delivery system (GRDDS). *Journal of Advanced Pharmaceutical Technology and Research, 1*(3), 283–290. https://doi.org/10.4103/0110-5558.72416
52. Patil, C., Baklilwal, S., Rane, B., et al. (2011). Floating microspheres: A promising approach for gastric retention. *International Journal of Pharmaceutical Research and Development, 2*, 12.
53. Porwal, A., Dwivedi, H., & Pathak, K. (2017). Decades of research in drug targeting using gastro retentive drug delivery systems for antihypertensive therapy. *Brazilian Journal of Pharmaceutical Sciences, 53*(3), Article e00173. https://doi.org/10.1590/s2175-97902017000300173
54. Prajapati, V. D., Jani, G. K., Khutliwala, T. A., & Zala, B. S. (2013). Raft-forming system—An upcoming approach of gastro retentive drug delivery system. *Journal of Controlled Release, 168*(2), 151–165. https://doi.org/10.1016/j.jconrel.2013.02.028
55. Pushpamalar, J., Meganathan, P., Tan, H. L., Dahlan, N. A., Ooi, L.-T., Neerooa, B. N. H. M., Essa, R. Z., Shameli, K., & Teow, S.-Y. (2021). Development of a polysaccharide-based hydrogel drug delivery system (DDS): An update. *Gels, 7*(4), 153. https://doi.org/10.3390/gels7040153
56. Rajanikant, P., Nirav, P., Patel, N. M., et al. (2010). A novel approach for dissolution enhancement of ibuprofen by preparing floating granules. *International Journal of Research in Pharmacy and Science, 1*(1), 57–64.
57. Ramabargavi, J. L., Pochaiah, B., Meher, C., et al. (2013). Formulation and in vitro

evaluation of gastro retentive floating tablets of glipizide. *Journal of Chemical and Pharmaceutical Research, 5*(2), 82–96.
58. Rangaraj, G., Kishore, N., Dhanalekshmi, U. M., et al. (2010). Design and study of formulation variables affecting drug loading and its release from alginate beads. *Journal of Pharmaceutical Sciences and Research, 2*(2), 77.
59. Rashmitha, V., Pavani, S., & Rajani, T. (2020). An update on floating drug delivery system: A review. *International Journal of Advances in Pharmacy and Biotechnology, 6*(4), 9–18. https://doi.org/10.38111/ijapb.20200604003
60. Rathod, H. J., Mehta, D. P., & Yadav, J. S. (2016). A review on gastro-retentive drug delivery systems. *PharmaciaTutor, 4*(7), 29–40.
61. Raza, M., Jayswal, M. G., Ahmed, A., et al. (2022). A review on gastro-retentive drug delivery system. *WJP Pharm. PharmSci, 11*(9), 624–640.
62. Rohilla, A., Singh, R. K., Sharma, D., et al. (2013). Phases of clinical trials: A review. *International Journal of Pharm. Chem. Biol. Sci., 3*(3), 700.
63. Shaikh, R., Raj Singh, T. R., Garland, M. J., Woolfson, A. D., & Donnelly, R. F. (2011). Mucoadhesive drug delivery systems. *Journal of Pharmacy and Bioallied Sciences, 3*(1), 89–100. https://doi.org/10.4103/0975-7406.76478
64. Singh, R. P., & Rathore, D. S. (2012). Gastro retention: A means to address local targeting in the gastric region. *Pharmacophore, 6*, 287–300.
65. Stillhart, C., Vučićević, K., Augustijns, P., Basit, A. W., Batchelor, H., Flanagan, T. R., Gesquiere, I., Greupink, R., Keszthelyi, D., Koskinen, M., Madla, C. M., Matthys, C., Miljuš, G., Mooij, M. G., Parrott, N., Ungell, A.-L., de Wildt, S. N., Orlu, M., Klein, S., & Müllertz, A. (2020). Impact of gastrointestinal physiology on drug absorption in special populations—An UNGAP review. *European Journal of Pharmaceutical Sciences, 147*, Article 105280. https://doi.org/10.1016/j.ejps.2020.105280
66. Streubel, A., Siepmann, J., & Bodmeier, R. (2006). Gastro retentive drug delivery systems. *Expert Opinion on Drug Delivery, 3*(2), 217–233. https://doi.org/10.1517/17425247.3.2.217
67. Subedi, G., Shrestha, A. K., & Shakya, S. (2016). Study of effect of different factors in formulation of micro and nanospheres with solvent evaporation technique. *Open Pharmaceutical Sciences Journal, 3*(1), 182–195. https://doi.org/10.2174/1874844901603010182
68. Surana, A. S., & Kotecha, R. K. (2010). An overview on various approaches to oral controlled drug delivery system via gastro retention. *International Journal of Pharmaceutical Sciences Review and Research, 2*(2), 68–72.
69. Tafish, A. M., Ebraheem, A. S., El Naggar, E. E., et al. (2023). Gastro retentive drug delivery systems: A summarized overview. *ODR, 3*(1), 40–56.
70. Tariq, A., Bashir, I., Khan, K. I., et al. (2015). Structural components of gastro-retentive drug delivery systems. *American Journal of Pharmaceutical Research, 5*(4).
71. Tripathi, J., Thapa, P., Maharjan, R., & Jeong, S. H. (2019). Current state and future perspectives on gastro retentive drug delivery systems. *Pharmaceutics, 11*(4), 193. https://doi.org/10.3390/pharmaceutics11040193
72. Turac, I.-R., Porfire, A., Iurian, S., Crișan, A. G., Casian, T., Iovanov, R., & Tomuță, I. (2024). Expanding the manufacturing approaches for gastroretentive drug delivery systems with 3D printing technology. *Pharmaceutics, 16*(6), 790. https://doi.org/10.3390/pharmaceutics16060790
73. Vantimitta, S. R., & Jeganath, S. (2022). Novel approaches of gastro-retentive drug delivery system: A review. *International Journal of Health Sciences, 6*(Suppl. 1),

3464–3476. https://doi.org/10.53730/ijhs.v6nS1.5549

74. VenKateswarlu, K., & Chandrasekhar, K. B. (2016). Development and statistical optimization of sustained release gastro-retentive floating tablets of cephalexin. *Marmara Pharmaceutical Journal, 20*(2), 172–183. https://doi.org/10.12991/mpj.20162070534
75. Verma, P., Rezaei, L., Govindarajan, R., Greig, N. H., & Donovan, M. D. (2024). Gastroretentive delivery approach to address pH-dependent degradation of (+)- and (−)-