Available online on http://www.ijhacr.com

International Journal of Health Advancement and Clinical Research (tz) 2024; 2(4); 01-06

Review Article

Gastroretentive Floating Drug Delivery Systems: Pioneering Innovations for Sustained Drug Release

Mohit Yadav [1], Mayank Bansal [2], Anupam [3]

[1]Research Scholar, Department of Pharmaceutics, Jaipur College of Pharmacy, Jaipur.
[2] Professor & Principal, Department of Pharmaceutics, Jaipur College of Pharmacy, Jaipur.
[3] Assistant Manager, Quality Assurance, Amol Pharmaceuticals Pvt. Ltd., Jaipur.

Received: 02-10-2024 / Revised: 02-11-2024 / Accepted: 03-12-2024
Corresponding author: Mohit Yadav
Conflict of interest: Nil

Abstract:

Gastroretentive drug delivery systems (GRDDS) have gained significant attention in pharmaceutical research due to their ability to prolong gastric residence time, thereby enhancing drug bioavailability and therapeutic efficacy. Floating drug delivery systems (FDDS), a prominent category of GRDDS, utilize buoyancy to remain afloat on gastric fluids, ensuring that the drug is released at a controlled rate. These systems are particularly advantageous for drugs with a narrow absorption window in the upper gastrointestinal tract, those unstable in the intestinal pH, or with poor solubility in alkaline conditions. This review discusses the principles, classification of GRDDS, advantages, limitations, mechanism of drug release and factors affecting gastric retention. Additionally, the applications of FDDS in treating various diseases are highlighted.

Keywords: GRDDS, FDDS, buoyancy, poor solubility, mechanism of drug release.

Introduction

Although the oral route is the most common and ideal way to distribute drugs, despite having good in vitro release patterns, medication absorption is inadequate and extremely varied in individuals. The physiological variability, including gastrointestinal transit and GRT, is the main issue; the latter is crucial to the total transit of the dose forms. The oral controlled release system's GRT is always less than 12 hours. These factors result in the creation of a medication delivery system that will stay in the stomach for a lengthy and consistent period of time. [1]

Gastroretentive Floating Drug Delivery Systems (FDDS) are innovative drug delivery technologies designed to prolong the retention of dosage forms in the stomach, enhancing drug bioavailability and therapeutic efficacy. These systems rely on buoyancy to float on gastric fluids, ensuring controlled and sustained drug release at the site of absorption. FDDS are particularly useful for drugs with a narrow absorption window in the upper gastrointestinal tract, those that are unstable in intestinal pH, or poorly soluble in alkaline conditions. [2]

Common types include effervescent systems that generate gas to aid buoyancy and non-effervescent systems using gel-forming polymers like hydroxypropyl methylcellulose (HPMC). The advantages of FDDS include enhanced bioavailability, reduced dosing frequency, and improved patient compliance. However, challenges such as dependence on gastric motility and food intake, as well as formulation

complexity, persist. Recent advances include dual-mechanism systems and nanotechnology integration to improve performance. FDDS hold immense promise in treating diseases like gastric ulcers, diabetes, and hypertension, making them a vital innovation in drug delivery systems. [3,4]

Advantages of Gastroretentive Drug Delivery Systems (GRDDS)

- **Enhanced Bioavailability:** Prolonged gastric retention allows drugs with narrow absorption windows in the upper gastrointestinal tract to be absorbed more efficiently.
- **Controlled Drug Release:** Provides sustained and controlled release of drugs, leading to better therapeutic outcomes.
- **Improved Solubility:** Beneficial for drugs that are more soluble in acidic environments, as they remain in the stomach longer.
- **Localized Drug Delivery:** Enables site-specific delivery of drugs for treating gastric diseases like ulcers or infections caused by Helicobacter pylori. [5]
- **Reduced Dosing Frequency:** Maintains effective drug levels for extended periods, improving patient compliance.
- **Reduced Fluctuations in Drug Levels:** Minimizes peaks and troughs in plasma drug concentrations, leading to a steady therapeutic effect.
- **Economic Benefits:** Decreases the need for higher doses and frequent administration, potentially reducing treatment costs. [5,6]

Disadvantages of Gastroretentive Drug Delivery Systems (GRDDS)

- **Variable Gastric Conditions:** Effectiveness can be influenced by gastric motility, pH, and the presence of food, leading to unpredictable drug release.
- **Unsuitable for Certain Drugs:** Ineffective for drugs that are unstable in gastric fluids or absorbed in the lower gastrointestinal tract.
- **Formulation Challenges:** Designing systems with consistent floating or retention properties is complex and requires careful optimization.
- **Patient-Specific Variability:** Conditions like gastroparesis, gastric emptying disorders, or altered gastric pH can affect performance.
- **Risk of Irritation:** Prolonged gastric retention of certain drugs might irritate the stomach lining.
- **Size Constraints**: Large dosage forms may cause discomfort or difficulty swallowing.
- **High Development Costs:** Advanced materials and techniques required for formulation increase the cost of development and production. [7]

Classification of GRDF

They may be broadly classified into:

1) High density systems

2) Floating systems

3) Expandable systems

4) Superporous hydrogels

5) Mucoadhesive or bioadhesive systems

6) Magnetic systems and

7) Dual working systems.

High density systems

High-density systems in GRDDS are designed with a density greater than that of gastric fluids (approximately 2.5 g/cm^3), allowing them to sink and remain in the lower part of the stomach, especially in the antrum. These systems resist gastric emptying due to their weight, ensuring prolonged retention for drugs that require

extended release. High-density systems are particularly useful for drugs that need to be retained in the stomach for a longer duration or for localized action.

Floating systems

Floating systems in GRDDS are designed to remain buoyant on the surface of gastric fluids, ensuring prolonged retention in the stomach. These systems typically have a low density, achieved through the use of effervescent agents (which generate gas) or swellable polymers (which trap air). Floating systems enhance the bioavailability of drugs with narrow absorption windows and provide controlled, sustained drug release. They are particularly effective in the fed state when gastric motility is slower, allowing for better retention. [8]

Expandable systems

Expandable systems in GRDDS are designed to expand in size once they reach the stomach, preventing early gastric emptying. These systems typically consist of a polymeric matrix or a combination of materials that swell or unfold when in contact with gastric fluids. By expanding beyond the size of the pyloric sphincter, they remain in the stomach for prolonged periods. This mechanism ensures sustained drug release, making expandable systems ideal for drugs requiring extended gastric residence and slow absorption.

Superporous hydrogels

Superporous hydrogels in GRDDS are highly porous materials that rapidly swell upon contact with gastric fluids, enabling fast expansion and retention in the stomach. Due to their large pores, these hydrogels can absorb large amounts of water, quickly increasing their size to prevent premature gastric emptying. They provide controlled drug release by maintaining prolonged gastric retention. Superporous hydrogels are particularly useful for drugs requiring extended release or localized action in the stomach. [9]

Mucoadhesive or bioadhesive systems

Mucoadhesive or bioadhesive systems in GRDDS use polymers that adhere to the mucus layer of the gastric mucosa, ensuring prolonged contact with the stomach lining. These systems improve gastric retention by resisting premature removal through gastric motility. Bioadhesive polymers, such as chitosan or carbopol, form a bond with the mucosal surface, enhancing drug absorption and providing controlled drug release. These systems are particularly beneficial for drugs that require localized delivery or extended release in the stomach.

Magnetic systems

Magnetic systems in GRDDS incorporate magnetic materials, such as ferrites, within the dosage form. These systems are retained in the stomach by an external magnetic field, which attracts the magnetic particles, preventing early gastric emptying. The external magnet can be adjusted to maintain the position of the dosage form in the desired region of the stomach for extended retention. Magnetic systems are particularly useful for targeted drug delivery or drugs requiring prolonged residence in the stomach.

Dual working systems

Dual working systems in GRDDS combine two or more mechanisms to enhance gastric retention and controlled drug release. These systems typically integrate floating or swelling properties with bioadhesion or high-density features. For example, a dual system might include a floating core with a bioadhesive layer to prolong retention and improve drug absorption. By combining different strategies, dual working systems offer enhanced therapeutic outcomes for drugs requiring prolonged gastric residence and sustained release. [10]

Mechanism of drug release in GRDDS

he mechanism of drug release in Gastroretentive Drug Delivery Systems (GRDDS) depends on the system's design but generally involves one or a combination

of the following processes:

a) **Diffusion:** The drug diffuses through the hydrated polymer matrix or membrane of the dosage form into the gastric fluid.

b) **Erosion:** The outer layers of the dosage form gradually erode in the acidic gastric environment, releasing the drug.

c) **Swelling and Gel Formation:** Hydrophilic polymers absorb gastric fluid, swell, and form a gel barrier that controls drug diffusion and release.

d) **Effervescence:** In effervescent systems, gas generation creates pores or channels in the matrix, facilitating drug release.

e) **Floating Systems:** The buoyant nature ensures prolonged contact with the gastric mucosa, enabling continuous drug release in the stomach. [11]

Factors affecting gastric retention

Several factors influence the gastric retention of Gastroretentive Drug Delivery Systems (GRDDS):

1. Gastric Motility

Fasting State: Rapid gastric emptying occurs due to migrating myoelectric complexes (MMCs), which may expel the system.

Fed State: Gastric motility slows down, prolonging retention time, especially with high-calorie or fatty meals.

2. Gastric Volume

Larger gastric volumes (e.g., after a meal) slow gastric emptying and enhance retention.

3. Dosage Form Size

Larger systems (≥7-10 mm) are less likely to pass through the pylorus prematurely, ensuring better retention.

4. Density of the Dosage Form

Systems with densities less than gastric fluid (~1 g/cm³) float, while those with higher densities sink and may exit faster.

5. Posture

Supine or upright postures can influence retention. Upright posture enhances floating system performance.

6. Gastric pH

Variations in pH (e.g., due to disease or age) can affect drug solubility and polymer swelling, impacting retention.

7. Nature of Food

Fatty, high-calorie, or viscous meals prolong retention, while liquids or low-calorie meals accelerate emptying.

8. Physiological Conditions

Disorders like gastroparesis delay gastric emptying and enhance retention, while hypermotility reduces retention time. [12,13]

Application of GRDDS

Gastroretentive Drug Delivery Systems (GRDDS) have a wide range of applications in the treatment of various conditions, primarily where prolonged gastric retention or controlled drug release is required. Some key applications include:

Drugs with Narrow Absorption Windows: GRDDS enhances the bioavailability of drugs that are primarily absorbed in the upper gastrointestinal tract, such as certain antibiotics, antidiabetic agents, and antihypertensive drugs.

Gastric Diseases: GRDDS are used to deliver drugs locally to the stomach for treating gastric ulcers, acid reflux, and Helicobacter pylori infections. Drugs like proton pump inhibitors (PPIs) and antacids can be effectively delivered through GRDDS.

Chronic Diseases: For conditions like hypertension and diabetes, GRDDS can provide sustained release, reducing the frequency of administration and improving patient compliance.

Pain Management: GRDDS can be used

for the sustained release of analgesics, providing long-lasting pain relief with fewer side effects. [14]

Nutraceuticals: GRDDS is also utilized in the delivery of vitamins, minerals, and other nutrients, ensuring their prolonged release and absorption in the stomach.

Targeted Drug Delivery: GRDDS can be employed for targeted drug delivery in the stomach, enabling localized treatment of diseases like peptic ulcers and gastric cancers.

Poorly Soluble Drugs: Drugs with poor solubility in alkaline pH can benefit from GRDDS by remaining in the stomach, where they dissolve in acidic conditions, improving their solubility and absorption. [15]

Conclusion

FDDS represents a robust approach to overcoming challenges associated with conventional oral drug delivery systems. Their ability to enhance bioavailability and control drug release positions them as a cornerstone in drug delivery innovation. However, their development is not without challenges, including formulation complexity and variable gastric conditions. Future research should focus on improving the predictability of these systems, exploring novel materials, and integrating advanced technologies to optimize their performance and expand their clinical applications.

References

1. B. M. Singh, K. H. Kim. Floating drug delivery systems: an approach to controlled drug delivery via gastric retention. J. Control. Release, 2000; 63: 235-259.
2. Singh BN, Kim KH. Floating drug delivery systems: An approach to oral controlled drug delivery via gastric retention. J Control Release 2000; 63:235 59.
3. Zaid, M., Kalam, I. and Majaz, Q., Gastro Retentive Drug Delivery System. International Journal of Research in Pharmacy and Allied Science, 2014; 3(5): 6-16.
4. Kumar, V., Somkuwar, S. and Singhai, A.K., A recent update on gastro retentive drug delivery systems. GSC Biological and Pharmaceutical Sciences,2024; 27(1): 125-144.
5. Gopalakrishnan,S.; Chenthilnathan, A. Floating Drug Delivery Systems: A Review Journal of Pharmaceutical Science and Technology. 2011; 3 (2): 548-554.
6. Jadhav, O.A., Surawase, R.K., Purkar, Y., Bhadane, S. and Shelar, S., Gastro-Retentive Drug Delivery System: A Comprehensive Review and Future Perspectives. Research Journal of Pharmaceutical Dosage Forms and Technology, 2024; 16(3): 293-298.
7. Iswariya, V.T., Anusha, S. and Laxmi, V.B.G.,. Formulation And Evaluation of Gastro Retentive Drug Delivery System of Sitagliptin. International Journal of Scientific Research in Modern Science and Technology, 2024; 3(6): 01-08.
8. Rathor, Muskan, and Anshika Garg. "Gastroretentive drug delivery system: An overview." 2024; 91-97.
9. Kriangkrai, W., Puttipipatkhachorn, S., Sriamornsak, P. and Sungthongjeen, S., Design and Evaluation of New Gel-Based Floating Matrix Tablets Utilizing the Sublimation Technique for Gastroretentive Drug Delivery. Gels, 2024; 10(9): p.581.
10. Pawar, V. K., Kansal, S., Garg, G., Awasthi, R., Singodia, D., & Kulkarni, G. T, Gastroretentive dosage forms: A review with special emphasis on floating drug delivery systems. Drug Delivery,2010; 18(2): 97–110.
11. Patel, H., Lakshmi, C.S.R., Nanaiah, K. and Chaya, H.N., 2024. Formulation and Evaluation of Gastro-retentive Drug Delivery Systems of Cinnarizine. RGUHS Journal of Pharmaceutical Sciences, 2024; 14(2: 45.
12. Shinde S, Tadwee I, Shahi S, Gastro

retentive Drug Delivery System: A Review, ijpras, 2011; 1(1): 1-13.
13. Shahwal V.k, Upadhyay A, Gastro-Retentive Floating Drug Delivery Systems, International Journal of Biomedical Research, 2011; 6: 381-390.
14. Katha, U.T.A., Sapiyan, M.S., Puad, F.N.A., Sofea, N., Aris, A.N. and bin Azhar, M.A., Optimization of non-effervescent riboflavin gastroretentive floating tablets using mixture design. Optimization, 2022; 32(3): 257-266.
15. Gupta, Y.K., Ali, M.Z., Tiwari, H. and Chandrul, K.K., 2024. Review on Gastroretentive Drug Delivery System. International Journal of Pharmacy & Life Sciences, 2024; 15(5): p16.