REVIEW ARTICLE

Gastro Retentive Drug Delivery System: Latest Approach towards Novel Drug Delivery

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Received: 24th October, 2023; Revised: 12th November, 2023; Accepted: 30th November, 2023; Available Online: 25th December, 2023

ABSTRACT

Various efforts have been undertaken to enhance the bioavailability and clinical performance of oral drug formulations. In pursuit of improving the therapeutic effectiveness of medications that are susceptible to degradation in alkaline pH environments, possess a limited window for absorption within the stomach, and readily dissolve under acidic conditions, a diverse range of gastro-retentive drug delivery systems (GRDDS) have been innovatively designed and developed. As a result, the stomach's physiological state and the various factors that influence GRDDS will be discussed. As a rule, this survey will enlighten and coordinate enumerating scientists in arranging, plan, and planning the GRDDS.

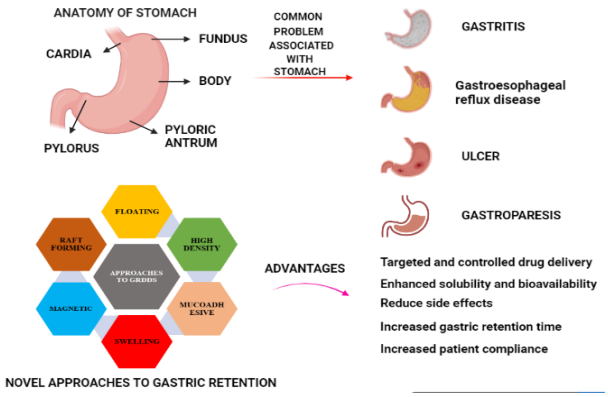
Keywords: Gastroretentive drug delivery systems, Gastric retention time, GI absorption window, Polymer gastric retention time, Bioadhesive, Bioavailability.

International Journal of Pharmaceutical Quality Assurance (2023); DOI: 10.25258/ijpqa.14.4.66

How to cite this article: Prasad D, Parashar T, Khaudiyal S, Semwal A, Jakhmola V. Gastro Retentive Drug Delivery System: Latest Approach towards Novel Drug Delivery. International Journal of Pharmaceutical Quality Assurance. 2023;14(4):1256-1263.

Source of support: Nil.

Conflict of interest: None



Graphical representation

INTRODUCTION

The GRDDS is a controlled drug delivery system that aims to improve clinical effectiveness and minimize toxicity by providing a coordinated and predetermined release rate of drugs. It represents a departure from conventional drug delivery systems and offers distinct advantages, particularly in addressing the limitations of oral drug delivery.[1] One of the major challenges in oral drug delivery is the low bioavailability and poor permeability of certain drugs, often due to their limited solubility. However, GRDDS has been shown to overcome these drawbacks and enhance the therapeutic efficacy of orally administered drugs. By prolonging the retention time of the dosage form in the gastrointestinal tract, it ensures more efficient drug absorption and distribution.[2] The gastro-retentive approach is primarily employed for orally administered drugs and leverages the increased gastro-retentivity of the dosage form. This means that the drug delivery system is designed to remain in the stomach for an extended period, allowing for controlled drug release and absorption. It achieves this through various mechanisms, such as buoyancy, bio-adhesion, swelling, or expansion. By maintaining the drug within the stomach, the GRDDS offers several advantages.[3] Firstly, it enhances the bioavailability of drugs with poor solubility or low permeability by facilitating their prolonged exposure to the absorbing surfaces in the gastrointestinal tract. Secondly, it enables localized drug delivery to specific regions within the gastrointestinal tract, which can be beneficial for drugs targeting specific sites or diseases. Additionally, it reduces the frequency of drug administration, improves patient compliance, and minimizes potential side effects.[4] The development and optimization of GRDDS involve a thorough understanding of the physicochemical and biological parameters related to the drug, as well as the design and formulation of the drug delivery system. Pharmaceutical scientists worldwide have been actively involved in researching and developing innovative

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approaches to create effective and safe gastro-retentive drug delivery systems.[5] Overall, the GRDDS represents a promising advancement in drug delivery technology, offering the potential for improved clinical outcomes and reduced toxicity. Its ability to overcome the limitations of conventional oral drug delivery systems makes it an important area of research and development in the field of pharmaceutical sciences.[6]

Benefits

- Enhance the therapeutic efficacy and bioavailability.
- Change in portion size.
- Improved drug solubility for drugs like domperidone, which are not particularly soluble in a pH environment.
- decreased drug waste.
- Designated drug conveyance to the small digestive system and stomach.[7]

Stomach Physiology

Understanding the anatomy and physiology of the stomach is indeed crucial in the development and functioning of the GRDDS. The stomach can be divided into two distinct anatomical sections: the proximal (upper) and distal (lower) stomach.[8] The proximal stomach consists of the body and fundus, which serve as reservoirs for undigested food. The distal stomach comprises the antrum and pylorus. The antrum plays a vital role in propelling the gastric contents and acts as a pump to facilitate gastric emptying.[9] The pylorus is the muscular valve located at the distal end of the stomach, which controls the flow of partially digested food (chyme) into the small intestine. Gastric emptying can occur regardless of whether the individual is in a fasted or fed state, although there are significant differences in the pattern of emptying between these conditions.[10] In the fed state, the ingestion of food triggers motor activity in the stomach. This activity usually begins around 5 to 10 minutes after food intake and continues until the food has emptied from the stomach. The antrum's pumping action and coordinated muscular contractions facilitate the movement of chyme towards the pylorus, promoting gastric emptying.[11] During the fasting state, there are multiple sequential electrical events that occur in both the stomach and small intestine at intervals of approximately 90 to 120 minutes. These electrical events are known as the migrating motor complex (MMC) and serve to sweep residual undigested material through the gastrointestinal tract.[12] The MMC activity may delay the emptying of the stomach and result in the retention of chyme in the stomach for a longer duration. In the context of GRDDS, understanding the dynamics of gastric emptying and the patterns of gastrointestinal motility during fasting and fed states is essential.[13] This knowledge helps in designing drug delivery systems that can achieve the desired gastro-retentive properties. By formulating dosage forms with specific characteristics such as buoyancy, bio-adhesion, or controlled release, the GRDDS can prolong the residence time of drugs in the stomach, improve drug absorption, and enhance therapeutic outcomes.

Strategies of GRDDS

Strategies utilized for prolongation of GRT are mentioned below

- Pharmacological approach
- Physiological approach
- Pharmaceutical approach[9]

The various pharmaceutical approaches utilized in gastro-retentive drug delivery system[7]

- High-density system,
- Ion-exchange resin system,
- Magnetic systems,
- Mucoadhesive system,
- Expandable system
- Low-density system,
- Super porous hydrogel system,
- Raft forming system,
- Microballoons/Hollow microspheres,
- Micro porous compartment system,

Aspects of GRDDS that are affected by various factors

The success and performance of GRDDS can be influenced by several factors, including pharmaceutical, physiological, and patient-related factors. These factors have been extensively studied in surveys and research to understand their impact on gastro-retentive dosage forms.[14]

Pharmaceutical Factors

Drug Solubility

The solubility of the drug can affect the formulation of gastro-retentive dosage forms. Poorly soluble drugs may require specific formulation techniques to enhance their dissolution and absorption.

Drug stability

The stability of the drug within the dosage form and during gastric retention is crucial. The formulation should protect the drug from degradation or chemical reactions in the stomach.[15]

Drug release rate

Controlling the release rate of the drug from the dosage form is essential to achieve the desired therapeutic effect. Various formulation techniques, such as controlled release matrices or coatings, are employed to regulate drug release.

Formulation design

The choice of excipients, polymers, and additives in the formulation can significantly impact the gastro-retentive properties of the dosage form. These components determine factors such as buoyancy, bio adhesion, or swelling behavior.[16]

Physiological Factors

Gastric emptying

The rate of gastric emptying can affect the residence time of the dosage form in the stomach. Factors such as food intake, gastrointestinal motility, and gastric pH can influence gastric emptying and consequently affect the performance of the GRDDS.

Gastrointestinal transit

The transit time of the dosage form through the gastrointestinal tract can impact drug absorption. Factors like motility, pH, and interactions with other components of the gastrointestinal system can influence drug release and absorption.[17]

Patient-related Factors

Age and gender

Age and gender can affect gastrointestinal physiology and transit time, which may impact the performance of gastro-retentive dosage forms.

Disease conditions

Certain disease conditions, such as gastroparesis or gastrointestinal disorders, can alter gastric motility and emptying, potentially affecting the performance of GRDDS.

Patient compliance

Patient-related factors, such as the ability to follow dosing instructions, adherence to medication, and acceptance of the dosage form, can impact the effectiveness of the GRDDS. In-depth surveys and studies have examined these factors to understand their influence on gastro-retentive dosage forms. By considering and optimizing these factors during the formulation and design of GRDDS, pharmaceutical scientists aim to enhance the clinical efficacy, safety, and patient acceptance of these novel drug delivery systems.[18]

Current trends in the delivery of pharmaceutical drugs to GRDDS

The increased gastric residence time (GRT) is a key objective in the development of GRDDS. Various approaches have been devised to enhance the gastro-retentivity of dosage forms, either indirectly or directly.[19] Let's discuss each of these approaches:

Buoyancy-based systems

Floating Systems: These systems are designed to float on the gastric fluid, thereby prolonging the GRT. They contain low-density materials or incorporate gas-generating agents that create buoyancy, keeping the dosage form afloat in the stomach.[20]

Examples: Floating tablets, capsules, or multiparticulate systems, such as floating microspheres or floating pellets.

Floating system classification

GRDDS can be classified into two types based on the mechanism of achieving gastro retentivity: effervescent systems and non-effervescent systems.[21] Let's discuss each type:

Effervescent systems

Effervescent systems rely on the generation of carbon dioxide gas within the stomach to achieve gastroretentivity. These systems contain effervescent agents that react with gastric fluid to produce bubbles of gas, leading to buoyancy and prolonged gastric residence time.[22] The gas bubbles help to keep the dosage form afloat in the stomach, allowing for controlled drug release. As the effervescent reaction occurs, the dosage form gradually disintegrates, releasing the drug.[20]

Table 1: Different theories of the Mucoadhesive system

S. No.	*Theories*	*Mechanisms*
1	Wet ability	The adhesion is reduced by the muco-adhesive's contact angle with the surface. Therefore, the contact angle must be minimal for optimal performance.
2	Diffusion	The interpenetration of the mucin chain and polymer choose the level of bond. The mucoadhesive increases in proportion to the polymer's interpretation.
3	Fracture	The amount of mechanical force required to separate the adhered surface is the foundation of this theory.
4	Adsorption	Mucoadhesion is caused by a variety of primary and secondary forces, including hydrogen bonds, ionic bonds, and covalent bonds.
5	Electronic	based on the idea that the biological layer and the mucoadhesive layer have opposite charges, which results in their attraction and the subsequent mucoadhesion.[42-44]

Non-effervescent Systems

Non-effervescent systems achieve gastro retentivity through mechanisms other than gas generation. These systems employ various approaches like buoyancy, bio-adhesion, swelling, or geometrical factors to prolong the gastric residence time.[23]

Both effervescent and non-effervescent systems aim to enhance the gastro-retentive properties of the dosage form and overcome the limitations of conventional oral drug delivery systems.[24] By prolonging the gastric residence time, these systems improve drug absorption, increase bioavailability, and optimize therapeutic outcomes. The choice between effervescent and non-effervescent systems depends on factors such as drug characteristics, desired release profile, and the specific mechanism required to achieve gastro-retentivity.[25]

High-density systems

The high-density system is a type of GRDDS where the pharmaceutical formulation has a density higher than that of the gastric fluid. The objective of this approach is to extend the transit time of the dosage form in the stomach, thereby delaying its passage to the small intestine, where most drug absorption takes place. By increasing the density of the dosage form, it becomes less buoyant and tends to sink in the gastric fluid instead of being rapidly emptied from the stomach. This prolonged gastric retention allows for a slower release and absorption of the drug, resulting in a delayed response and potentially extending the duration of therapeutic effect.[26]

The high-density system can be achieved by incorporating high-density materials or using specific formulation techniques that increase the overall density of the dosage form. This can be advantageous for drugs that require a sustained release or a delayed onset of action.

Expandable systems

Indeed, expandable systems, also known as plug-type systems, are another type of GRDDS. In these systems, the drug formulation is designed to exhibit delayed gastrointestinal transit by expanding in volume and shape. Initially, these systems were widely used in veterinary applications before their clinical significance in humans was established.[27]

The expandable systems utilize various mechanisms to achieve expansion, such as swelling, unfolding, or unfolding triggered by factors like pH, temperature, or enzymes present in the gastrointestinal tract. These mechanisms allow the dosage form to change its shape or increase in size, prolonging its gastric residence time.[28]

Overall, expandable systems represent a unique approach in GRDDS, allowing for delayed gastrointestinal transit and controlled drug release. By meeting the specific pharmaceutical requirements mentioned, these systems hold potential for improving drug delivery and therapeutic outcomes.

Superporous hydrogel system

The superporous hydrogel system is indeed one of the promising types of GRDDS. Hydrogels are crosslinked polymeric structures composed of acidic, basic, or neutral monomers.

Superporous hydrogels are utilized in GRDDS because of their ability to absorb and retain a large amount of water. When they come into contact with gastric fluid, they rapidly absorb water and swell to a significant extent. This swelling behavior allows them to remain in the stomach for an extended period, leading to prolonged drug release.[29]

Superporous hydrogels can exhibit significant swelling ratios, often swelling over 250 times their initial volume. Continued research and development in super porous hydrogel systems offer promising opportunities for the design of advanced gastro-retentive drug delivery systems, enhancing drug bioavailability, patient compliance, and overall treatment outcomes.[30]

Magnetic system

Magnetic systems are employed in GRDDS to increase the residence time in the gastrointestinal tract. These systems utilize magnets to control and enhance the retention of the developed pharmaceutical formulation within the stomach.

The magnetic system consists of two main components: an internal magnet incorporated into the drug dosage form and an extracorporeal magnet placed externally over the stomach region.[31] The magnetic attraction between the internal and external magnets allows for precise positioning and retention of the dosage form within the stomach.[32]

However, it is important to note that the use of magnetic systems in GRDDS is still an area of active research, and further studies are required to optimize their design, evaluate their safety, and assess their clinical effectiveness. Nonetheless, magnetic systems hold promise as a targeted approach for gastro-retentive drug delivery, offering opportunities for improved drug delivery strategies and therapeutic outcomes.[33]

System of ion-exchange resin

The experimental work conducted by Saunders and Srivastava in 1950 was significant in demonstrating the potential of ion-exchange resins for developing formulations with sustained drug release. They proposed the use of ion-exchange resins as effective chemical carriers in drug delivery systems, based on their experiments involving the uptake and release of alkaloids by the resin.[34]

Ion-exchange resins possess the property of hosting a drug and releasing it in the gastrointestinal tract (GIT) in the presence of other ions or pH changes in the surrounding environment. This property makes them suitable candidates for GRDDS.[35] When formulated with a drug, the resin particles are ingested along with the drug particles by the gastric mucosa. They can then be either eliminated through biological breakdown or excreted with the faces.[36]

Further research and development in this field continue to explore the potential of ion-exchange resins and coatings to improve drug delivery systems and enhance therapeutic outcomes.[31]

Raft-forming System

The raft-forming system in GRDDS utilizes effervescent agents and polymers that form gels. When these components interact, they generate carbon dioxide, resulting in the formation of a raft-like structure in the stomach. This raft is resistant to peristaltic movement, making it difficult for it to enter the small intestine.[37]

The mechanism of action of the raft-forming system is similar to that of the floating system. It remains in the stomach, gradually releasing the drug. However, the raft-forming system offers limited mechanical strength and can be easily disrupted by vigorous gastric motility.[38]

It is important to note that the success of the raft-forming system relies on the appropriate selection of effervescent agents and polymers to achieve the desired raft formation and drug release profile. The choice of components and formulation parameters should be carefully optimized to ensure optimal performance and therapeutic efficacy.[39]

Mucoadhesive system

In GRDDS, both synthetic and natural polymers are used as mucoadhesive agents. These polymers possess the ability to adhere to the mucosal surface of the stomach, thereby enhancing the GRT of the medication. By binding to the epithelial layer of the stomach, these polymers prolong the contact between the drug and the absorption site.[40]

Various theories have been proposed to explain the mechanism of mucoadhesion, including wettability, diffusion, adsorption, electronic, and fracture theories (Table 1). These theories aim to elucidate the specific molecular interactions that occur between the mucoadhesive polymer and the mucosal surface, leading to the adhesive properties.[41]

Micro balloons/Hollow microspheres

Microballoons, in combination with other polymers, are utilized to increase the gastric residence time (GRT) of the

dosage form. Various polymers such as cellulose acetate, calcium alginate, polycarbonate, low methoxylated pectin, and Eudragit S, among others, are used to construct the micro balloons. The micro balloons filled with surfactants demonstrate continuous floating behavior for more than 12 hours on the surface of the acidic dissolution medium.[45]

By employing these micro balloons or floating beads, a gastric residence time of more than 5.5 hours can be achieved. This extended retention time in the stomach can improve the controlled release of drugs and enhance their therapeutic efficacy.

Evaluation Parameters of GRDDS

In vivo evaluation parameters of GRDDS

Animal models and human research are essential to validate the efficacy of GRDDS *in-vivo*. In these studies, the bioavailability of the developed pharmaceutical formulation and the GRT are evaluated.

Various imaging techniques are employed to assess the in vivo performance of GRDDS. These include gastroscopy, radiology, scintigraphy (including gamma scintigraphy), and magnetic resonance imaging (MRI). Each method provides valuable insights into the behavior and location of the dosage forms within the GIT.[46]

Gamma scintigraphy has been particularly useful in studying GRDDS. It allows for the assessment of parameters such as location, size, and movement of the dosage forms throughout the GIT. This method utilizes small doses of radiation, which have a favorable safety profile, to track and visualize the behavior of the dosage forms.

Gastroscopy, a procedure in which a flexible tube with a camera is inserted into the stomach, is also employed to locate and examine GRDDS in vivo. It allows for direct visualization and assessment of the dosage forms in the stomach.[47]

MRI is another effective method for evaluating GRDDS in live animals and human subjects. By utilizing a strong magnetic field, MRI provides detailed imaging of anatomical structures and enables visualization of the location and residence time of ingested medication forms.[46]

Through the combination of these imaging techniques and in vivo studies, researchers can gather valuable data on the performance and behavior of GRDDS, confirming their efficacy and optimizing their formulation parameters.

It is worth noting that ethical considerations and regulatory guidelines must be followed when conducting animal and human studies to ensure the safety and well-being of the subjects involved.[48]

In-vitro evaluation parameters of GRDDS

In vitro evaluations of GRDDS can provide valuable insights and help predict their in vivo behavior. Several parameters can be assessed to evaluate the floating behavior of low-density systems, including total floating length and floating lag time. These measurements help determine the ability of the dosage form to float and remain buoyant in the gastric fluid. The floating force of a floating tablet can also be measured to assess its floating capacity. This parameter quantifies the force required to displace the dosage form from the surface of the dissolution medium, indicating its ability to resist sinking and maintain buoyancy.[49]

Additionally, dissolution studies can be conducted over an extended period, typically around 8 hours, to evaluate other important parameters of the polymeric dosage form. These include the swelling rate, gel strength, and water uptake capacity. These parameters provide insights into the drug release behavior, floating mechanism, and gel strength of the formulation.[50]

By comprehensively evaluating these *in-vitro* parameters, researchers can gain a better understanding of the performance and characteristics of the GRDDS, aiding in the prediction of its behavior *in-vivo.* These evaluations contribute to optimizing the formulation and ensuring the desired drug release profile, floating ability, and gel strength of the dosage form.

Future prospective

In-vitro evaluations of GRDDS can provide valuable insights and help predict their *in-vivo* behavior. Several parameters can be assessed to evaluate the floating behavior of low-density systems, including total floating length and floating lag time.[51] These measurements help determine the ability of the dosage form to float and remain buoyant in the gastric fluid.

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The performance and properties of the GRDDS can be better understood by researchers by thoroughly examining these *in-vitro* parameters, assisting in the prediction of its behavior *in-vivo*. These evaluations contribute to optimizing the formulation and ensuring the desired drug release profile, floating ability, and gel strength of the dosage form.[53]

CONCLUSION

The development of a comprehensive understanding of the stomach's anatomy and physiology is essential for GRDDS. Factors such as gastric emptying, motility patterns and pH variations in different regions of the stomach play a significant role in determining the performance of GRDDS.

In the literature, various types of GRDDS have been explored to improve drug delivery and overcome the limitations of conventional dosage forms. Bio/mucoadhesive systems, both low density and high density, are designed to adhere to the gastric mucosa, prolonging the residence time and enhancing drug absorption. These systems utilize polymers

with mucoadhesive properties to achieve effective adhesion to the mucosal surface.

Magnetic systems involve the use of extracorporeal magnets to position and control drug delivery in the stomach. The internal magnet within the formulation interacts with the external magnet, allowing for precise localization and retention in the desired region of the stomach.

Other GRDDS approaches, such as floating systems, expandable systems, and super porous hydrogels, have also been investigated. Floating systems aim to float on the gastric contents, thereby prolonging the gastric residence time. Expandable systems expand in volume or shape to prevent passage through the pyloric sphincter and prolong gastric retention. Super porous hydrogels possess a high capacity for water absorption, leading to significant swelling and retention in the stomach.

These various GRDDS approaches offer different advantages and mechanisms to achieve extended gastric retention and enhanced drug delivery. By considering the specific needs of the drug and the target therapeutic outcome, researchers can select and design the most suiGRDDS to optimize drug delivery and improve therapeutic efficacy.

REFERENCES

1. Bardonnet PL, Faivre V, Pugh WJ, Piffaretti JC, Falson F. Gastroretentive dosage forms: Overview and special case of Helicobacter pylori. Journal of Controlled Release. 2006 Mar 10;111(1–2):1–18.
2. Parikh DC, Amin AF. In vitro and in vivo techniques to assess the performance of gastro-retentive drug delivery systems: a review. http://dx.doi.org/101517/1742524759951 [Internet]. 2008 Sep [cited 2023 Sep 17];5(9):951–65. Available from: https://www.tandfonline.com/doi/abs/10.1517/17425247.5.9.951
3. Mehta M, Neeta, Pandey P, Mahajan S, Satija S. Gastro retentive drug delivery systems: An overview. Res J Pharm Technol [Internet]. 2018 May 30 [cited 2023 Sep 17];11(5):2157–60. Available from: https://rjptonline.org/AbstractView.aspx?PID=2018-11-5-84
4. Prajapati VD, Jani GK, Khutliwala TA, Zala BS. Raft forming system-an upcoming approach of gastroretentive drug delivery system. J Control Release [Internet]. 2013 Jun 10 [cited 2023 Sep 17];168(2):151–65. Available from: https://pubmed.ncbi.nlm.nih.gov/23500062/
5. Mandal UK, Chatterjee B, Senjoti FG. Gastro-retentive drug delivery systems and their in vivo success: A recent update. Asian J Pharm Sci. 2016 Oct 1;11(5):575–84.
6. Patil H, Tiwari R V., Repka MA. Recent advancements in mucoadhesive floating drug delivery systems: A mini-review. J Drug Deliv Sci Technol [Internet]. 2016 [cited 2023 Sep 17];31:65–71. Available from: https://www.researchgate.net/publication/287122710_Recent_Advancements_in_Mucoadhesive_Floating_Drug_Delivery_Systems_A_Mini-Review
7. Tripathi J, Thapa P, Maharjan R, Jeong SH. Current State and Future Perspectives on Gastroretentive Drug Delivery Systems. Pharmaceutics [Internet]. 2019 Apr 1 [cited 2023 Sep 17];11(4). Available from: https://pubmed.ncbi.nlm.nih.gov/31010054/
8. Hunt RH, Camilleri M, Crowe SE, El-Omar EM, Fox JG, Kuipers EJ, et al. The stomach in health and disease. Gut [Internet]. 2015 Oct 1 [cited 2023 Sep 17];64(10):1650–68. Available from: https://gut.bmj.com/content/64/10/1650
9. Davis SS. Formulation strategies for absorption windows. Drug Discov Today [Internet]. 2005 Feb 15 [cited 2023 Sep 17];10(4):249–57. Available from: https://www.researchgate.net/publication/8023871_Formulation_strategies_for_absorption_windows
10. Membrive CMB. Anatomy and physiology of the rumen. Rumenology [Internet]. 2016 Jan 1 [cited 2023 Sep 17];1–38. Available from: https://link.springer.com/chapter/10.1007/978-3-319-30533-2_1
11. Ramsay PT, Carr A. Gastric acid and digestive physiology. Surgical Clinics of North America [Internet]. 2011 Oct 1 [cited 2023 Sep 17];91(5):977–82. Available from: http://www.surgical.theclinics.com/article/S0039610911000740/fulltext
12. Khan R. Int J Pharm Bio Sci 2013 Apr; 4(2): (P) 630-646 GASTRORETENTIVE DRUG DELIVERY SYSTEM-A REVIEW. [cited 2023 Sep 17]; Available from: www.ijpbs.net
13. Jassal M, Nautiyal U, Kundlas J, Singh D. 13 A review Gastroretentive drug delivery system _grdds_. Article in Indian Journal of Pharmaceutical and Biological Research [Internet]. 2015 [cited 2023 Sep 17];3(1). Available from: www.ijpbr.in
14. Thapa P, Jeong SH. Effects of Formulation and Process Variables on Gastroretentive Floating Tablets with A High-Dose Soluble Drug and Experimental Design Approach. Pharmaceutics 2018, Vol 10, Page 161 [Internet]. 2018 Sep 17 [cited 2023 Sep 17];10(3):161. Available from: https://www.mdpi.com/1999-4923/10/3/161/htm
15. Talukder R, Fassihi R. Gastroretentive delivery systems: a mini review. Drug Dev Ind Pharm [Internet]. 2004 [cited 2023 Sep 17];30(10):1019–28. Available from: https://pubmed.ncbi.nlm.nih.gov/15595568/
16. Salessiotis N. Measurement of the diameter of the pylorus in man: Part I. Experimental project for clinical application. The American Journal of Surgery. 1972 Sep 1;124(3):331–3.
17. Bailey K. Physiological factors affecting drug toxicity. Regul Toxicol Pharmacol [Internet]. 1983 [cited 2023 Sep 17];3(4):389–98. Available from: https://pubmed.ncbi.nlm.nih.gov/6658034/
18. Parikh DC, Amin AF. In vitro and in vivo techniques to assess the performance of gastro-retentive drug delivery systems: A review. Expert Opin Drug Deliv. 2008 Sep;5(9):951–65.
19. Vrettos NN, Roberts CJ, Zhu Z. Gastroretentive Technologies in Tandem with Controlled-Release Strategies: A Potent Answer to Oral Drug Bioavailability and Patient Compliance Implications. Pharmaceutics [Internet]. 2021 Oct 1 [cited 2023 Sep 17];13(10). Available from: /pmc/articles/PMC8539558/
20. Sarmah J, Choudhury A. Formulation and Evaluation of Gastro Retentive Floating Tablets of Ritonavir. Res J Pharm Technol [Internet]. 2020 Sep 4 [cited 2023 Sep 17];13(9):4099–104. Available from: https://rjptonline.org/AbstractView.aspx?PID=2020-13-9-12
21. Pattanayak D, Arun JK, Adepu R, Shrivastava B, Hossain CM, Das S. Formulation and Evaluation of Floating and Mucoadhesive Tablets containing Repaglinide. Res J Pharm Technol [Internet]. 2020 Mar 1 [cited 2023 Sep 17];13(3):1277–84. Available from: https://www.rjptonline.org/AbstractView.aspx?PID=2020-13-3-40
22. Patel SG, Siddaiah M. Formulation and evaluation of effervescent tablets: a review. Journal of Drug Delivery and Therapeutics

[Internet]. 2018 Nov 15 [cited 2023 Sep 18];8(6):296–303. Available from: https://jddtonline.info/index.php/jddt/article/view/2021

23. Devendiran B, Mothilal M, Damodharan N. Floating drug delivery an emerging technology with promising market value. Res J Pharm Technol. 2020;13(6):3014–20.
24. Gupta H, Bhandari D, Sharma A. Recent trends in oral drug delivery: a review. Recent Pat Drug Deliv Formul [Internet]. 2009 May 30 [cited 2023 Sep 18];3(2):162–73. Available from: https://pubmed.ncbi.nlm.nih.gov/19519576/
25. Baumgartner S, Kristl J, Vrečer F, Vodopivec P, Zorko B. Optimisation of floating matrix tablets and evaluation of their gastric residence time. Int J Pharm [Internet]. 2000 Feb 15 [cited 2023 Sep 18];195(1–2):125–35. Available from: https://pubmed.ncbi.nlm.nih.gov/10675690/
26. Jiménez-Martínez I, Quirino-Barreda T, Villafuerte-Robles L. Sustained delivery of captopril from floating matrix tablets. Int J Pharm [Internet]. 2008 Oct 1 [cited 2023 Sep 18];362(1–2):37–43. Available from: https://pubmed.ncbi.nlm.nih.gov/18588962/
27. Sawanny R, Sharma A, Jain S, Mukherjee S, Khamkat P. Gastro Retentive Drug Delivery System: Latest Approach towards Novel Drug Delivery. Res J Pharm Technol [Internet]. 2023 Jan 27 [cited 2023 Sep 18];16(1):453–8. Available from: https://rjptonline.org/AbstractView.aspx?PID=2023-16-1-77
28. Sawanny R, Sharma A, Jain S, Mukherjee S, Khamkat P. Gastro Retentive Drug Delivery System: Latest Approach towards Novel Drug Delivery. Res J Pharm Technol [Internet]. 2023 Jan 27 [cited 2023 Sep 18];16(1):453–8. Available from: https://rjptonline.org/AbstractView.aspx?PID=2023-16-1-77
29. Teaima M, Abdelmonem R, Saady M, El-Nabarawi M, Shoman NA. COMPREHENSIVE OVERVIEW ON RECENT UPDATES OF GASTRORETENTIVE RAFT-FORMING SYSTEMS. International Journal of Applied Pharmaceutics [Internet]. 2022 May 7 [cited 2023 Sep 18];14(3):40–8. Available from: https://journals.innovareacademics.in/index.php/ijap/article/view/44098/26445
30. Park H, Park K, Kim D. Preparation and swelling behavior of chitosan-based superporous hydrogels for gastric retention application. 2005 [cited 2023 Sep 18]; Available from: www.interscience.wiley.com
31. Lopes CM, Bettencourt C, Rossi A, Buttini F, Barata P. Overview on gastroretentive drug delivery systems for improving drug bioavailability. Int J Pharm [Internet]. 2016 [cited 2023 Sep 18];510:144–58. Available from: http://dx.doi.org/10.1016/j.ijpharm.2016.05.016
32. Ito R, Machida Y, Sannan T, Nagai T. Magnetic granules: a novel system for specific drug delivery to esophageal mucosa in oral administration. Int J Pharm. 1990 Jun 11;61(1–2):109–17.
33. Bardonnet PL, Faivre V, Pugh WJ, Piffaretti JC, Falson F. Gastroretentive dosage forms: overview and special case of Helicobacter pylori. J Control Release [Internet]. 2006 Mar 10 [cited 2023 Sep 18];111(1–2):1–18. Available from: https://pubmed.ncbi.nlm.nih.gov/16403588/
34. Klausner EA, Lavy E, Friedman M, Hoffman A. Expandable gastroretentive dosage forms. Journal of Controlled Release [Internet]. 2003 Jun 24 [cited 2023 Sep 18];90(2):143–62. Available from: https://pubmed.ncbi.nlm.nih.gov/12810298/
35. Garg R, Gupta G. Progress in Controlled Gastroretentive Delivery Systems. Tropical Journal of Pharmaceutical Research [Internet]. 2008 Sep 11 [cited 2023 Sep 18];7(3). Available from: https://www.researchgate.net/publication/43561071_Progress_in_Controlled_Gastroretentive_Delivery_Systems
36. Anand V, Kandarapu R, Garg S. Ion-exchange resins: carrying drug delivery forward. Drug Discov Today [Internet]. 2001 Sep 1 [cited 2023 Sep 18];6(17):905–14. Available from: https://pubmed.ncbi.nlm.nih.gov/11522519/
37. Prajapati VD, Jani GK, Khutliwala TA, Zala BS. Raft forming system—An upcoming approach of gastroretentive drug delivery system. Journal of Controlled Release. 2013 Jun 10;168(2):151–65.
38. Niranjanbhai BD, Mahendrakumar N, Surendran CS, Um U. ADVANCES IN GRDDS: RAFT FORMING SYSTEM A REVIEW. Journal of Drug Delivery and Therapeutics [Internet]. 2012 Sep 15 [cited 2023 Sep 18];2(5):123. Available from: https://jddtonline.info/index.php/jddt/article/view/228
39. Shree D, Patra CN, Sahoo BM. Fabrication and Applications of Raft-Forming System - An Emerging Trend in Gastro-retentive Drug Delivery System. Nanoscience & Nanotechnology-Asia. 2022 Jul 7;12(3).
40. Md S, Ahuja A, Khar RK, Baboota S, Chuttani K, Mishra AK, et al. Gastroretentive drug delivery system of acyclovir-loaded alginate mucoadhesive microspheres: Formulation and evaluation. http://dx.doi.org/103109/107175442010536270 [Internet]. 2011 May [cited 2023 Sep 18];18(4):255–64. Available from: https://www.tandfonline.com/doi/abs/10.3109/10717544.2010.536270
41. Patil H, Tiwari R V., Repka MA. Recent advancements in mucoadhesive floating drug delivery systems: A mini-review. J Drug Deliv Sci Technol. 2016 Feb 1;31:65–71.
42. Lopes CM, Bettencourt C, Rossi A, Buttini F, Barata P. Overview on gastroretentive drug delivery systems for improving drug bioavailability. Int J Pharm. 2016 Aug 20;510(1):144-58. doi: 10.1016/j.ijpharm.2016.05.016. Epub 2016 May 9. PMID: 27173823.
43. Chatterjee, Bappaditya & Amalina, N. & Sengupta, Pinaki & Mandal, Uttam. (2017). Mucoadhesive Polymers and Their Mode of Action: A Recent Update. Journal of Applied Pharmaceutical Science. 7. 195-203. 10.7324/JAPS.2017.70533.
44. Mahajan P, Kaur A, Aggarwal G, Harikumar SL. (2013). Mucoadhesive Drug Delivery System: A Review. *International Journal of Drug Development and Research*, 5.
45. Vrettos NN, Roberts CJ, Zhu Z. Gastroretentive Technologies in Tandem with Controlled-Release Strategies: A Potent Answer to Oral Drug Bioavailability and Patient Compliance Implications. Pharmaceutics 2021, Vol 13, Page 1591 [Internet]. 2021 Sep 30 [cited 2023 Sep 18];13(10):1591. Available from: https://www.mdpi.com/1999-4923/13/10/1591/htm
46. Parashar T, Kalra K, Kalra JM, Singh N, Saha S, Singh A, et al. Formulation and In-vitro Evaluation of Bilayer Tablet of Olmesartan Medoxomil for Biphasic Drug Release. International Journal of Pharmaceutical Quality Assurance. 2023 Apr 1;14(2):388–92.
47. Kim S, Hwang KM, Park YS, Nguyen TT, Park ES. Preparation and evaluation of non-effervescent gastroretentive tablets containing pregabalin for once-daily administration and dose proportional pharmacokinetics. Int J Pharm [Internet]. 2018 Oct 25 [cited 2023 Sep 18];550(1–2):160–9. Available from: https://pubmed.ncbi.nlm.nih.gov/30138708/
48. Tripathi J, Thapa P, Maharjan R, Jeong SH. Current State and Future Perspectives on Gastroretentive Drug Delivery Systems.

Pharmaceutics [Internet]. 2019 Apr 1 [cited 2023 Sep 18];11(4). Available from: https://pubmed.ncbi.nlm.nih.gov/31010054/

49. Biradar V, Basavarajaiah JM, Win MTT, Gudugunta L, Suresh K V., Mahendra Kumar S, et al. In vitro Evaluation of Gastro Retentive Drug Delivery System of Lansoprazole. Res J Pharm Technol [Internet]. 2019 Aug 1 [cited 2023 Sep 18];12(8):3649–53. Available from: https://rjptonline.org/AbstractView.aspx?PID=2019-12-8-12
50. View of GASTRO RETENTIVE DRUG DELIVERY SYSTEM: A SIGNIFICANT TOOL TO INCREASE THE GASTRIC RESIDENCE TIME OF DRUGS | International Journal of Current Pharmaceutical Research [Internet]. [cited 2023 Sep 18]. Available from: https://journals.innovareacademics.in/index.php/ijcpr/article/view/40818/24247
51. Awasthi R, Kulkarni GT. Decades of research in drug targeting to the upper gastrointestinal tract using gastroretention technologies: where do we stand? Drug Deliv [Internet]. 2016 Feb 12 [cited 2023 Sep 18];23(2):378–94. Available from: https://www.tandfonline.com/doi/abs/10.3109/10717544.2014.936535
52. Schneider F, Koziolek M, Weitschies W. In Vitro and In Vivo Test Methods for the Evaluation of Gastroretentive Dosage Forms. Pharmaceutics [Internet]. 2019 Aug 1 [cited 2023 Sep 18];11(8). Available from: /pmc/articles/PMC6723944/
53. Tandon A, Jangra PK. Formulation and in vitro Evaluation of Lisinopril floating Gastroretentive Tablets. Res J Pharm Technol [Internet]. 2021 Jan 29 [cited 2023 Sep 18];14(1):207–13. Available from: https://rjptonline.org/AbstractView.aspx?PID=2021-14-1-36