WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

An Overview on Gastroretentive Drug Delivery System (GRDDS)

Badadare Rajashri*., JunghareShekhar, Gaikwad Sonal

Department of Pharmaceutics, College of Pharmacy, Medha
rajbadadare@gmail.com

ABSTRACT:

GRDDs are a type of drug delivery device that directs drug release to specific areas in the upper GI tract for local or systemic impact. For a long time, gastrointestinal retentive dosage forms (GRDFs) have been used to improve therapy with a variety of important drugs. By releasing medications locally, GRDFs considerably improve stomach pharmacotherapy, resulting in high drug concentrations at the gastric mucosa that may be maintained for longer periods of time. GRDFs allow for the prolonged and continuous release of a drug to the upper part of the Gastrointestinal tract (GIT), significantly increasing the duration of drug release and improving bioavailability of drugs with a narrow therapeutic window, thereby extending the dosing interval and improving patient compliance. The goal of this work is to briefly outline gastro retentive drug delivery (GRDD), elements associated to GRDD, its benefits and drawbacks, and the importance of GRDD over traditional drug delivery methods.

Keyword: Gastroretention, Conventional drug delivery, Current trends, GRDDS, GRDDF.

1.Introduction:

In the realm of oral medication delivery, the gastro-retentive drug delivery system (GRDDS) has recently gained a lot of attention. It is a common way of maintaining the dose form in the stomach for a long period and slowly releasing the medicine, which can address many of the issues with standard oral delivery, such as insufficient bioavailability. (1) Drug absorption in the gastrointestinal system is a highly variable process influenced by parameters such as stomach emptying, gastrointestinal transit time for dosage forms, drug release from dosage forms, and drug absorption site. (2) Gastroretentive drug delivery systems (GRDDS) are a novel technique to the oral controlled-release delivery of a variety of medicines. (3) The oral route of drug administration is the most extensively used and accessible. All controlled release strategies have limited utility if the systems cannot remain in close proximity to the absorption site. (4) One of the fundamental drawbacks of oral controlled medication delivery is that not all drug candidates are absorbed uniformly throughout the GIT. (5) A gastro retentive drug delivery system is a controlled-release medication administration system that can be retained in the stomach. They can help with the optimization of oral controlled delivery of pharmaceuticals with a "absorption window," releasing the medication for a long time prior to the absorption window, ensuring excellent bioavailability. Gastric emptying occurs in both fasting and fed situations. However, the migratory patterns in the two states are not the same. According to gastric emptying studies, orally administered controlled release dosage forms have two challenges: a short stomach residence time and an unpredictable gastric emptying rate. (4)
An Ideal drug delivery system should possess two main properties:
1) For the course of the treatment, it should be a single dose.
2) The active medicine should be delivered directly to the site of action.(6)

1.1 Anatomy of the stomach

The gastro intestinal tract can be divided into three main regions

a) Stomach
b) Small intestine- duodenum, jejunum, and ileum
c) Large intestine

The gastrointestinal tract (GIT) is a muscular tube that connects the mouth to the anus. It measures around 9 meters in length. The physiological processes of digestion, absorption, secretion, motility, and excretion all help the body absorb nutrients and eliminate waste. The oblique muscles, which branch over the fundus and higher portions of the gastric body and are found in the proximal section of the stomach, are made up of three layers of muscle. The fundus, the body, and the pylorus are the three sections of the stomach. The stomach is a triangular-shaped organ located on the abdomen's upper left side. The stomach's primary function is to store food for a short period of time, pulverize it, and gently release it into the duodenum.

.

1.2 Physiology of the stomach

The stomach is an extended section of the digestive tract that lies between the oesophagus and the small intestine. When the stomach is empty, the mucosa and submucosa are pushed up into rugae, which are folds in the mucosa and submucosa. There are four types of secretory epithelial cells that coat the stomach and spread into gastric pits and glands. Alkaline mucus is secreted by mucous cells.

1) Parietal cells – secrete HCL
2) Chief cells- secrete pepsin
3) G cells- secrete hormone gastrin.

1.3 Gastric motility and gastric empty rate

The gastrointestinal motility and secretion patterns differ between the fasted and fed states. The bioavailability of an orally given drug is affected by the status of food. In the fasting condition, it is distinguished by an interdigestive series of electric events known as the inter digestive myoelectric cycle or migratingmotor complex. It goes through four stages

Phase1. With only intermittent contractions, it's a pretty inactive 40-60 minute time.

Phase2. Phase 2 has a similar duration to phase 1 and includes an increasing amount of contractions.

Phase3. Strong peristaltic contractions occur once the base of the pylorus is opened, clearing the stomach of any leftover material.

Phase4. This is a shorter period of transition between phase 3's powerful activity and phase 1's powerful action. The cycle repeats every two hours until the meal is consumed and fed, or motility begins (7)

1.4Advantages of Gastro-Retentive Drug Delivery Systems

1) Drugs that are absorbed largely through the stomach, such as ferrous salts and antacids, benefit from gastroretentive systems.
2) Drugs that are intended for local action in the stomach benefit from gastro retentive systems. Antacids, for example.
3) Poor absorption is expected when there is a lot of digestive motility and a short transit time, as in certain types of diarrhea. In such cases, it may be advantageous to keep the medicine in the stomach to elicit a better response.
4) By reducing dosing frequency, GRDDS enhances patient compliance.
5) Variations in bioavailability due to fluctuations in plasma drug concentration are avoided, and a desired plasma drug concentration is maintained through continuous drug release.
6) Drugs with a short half-life can have a greater therapeutic effect.
7) GRDDS can be used to develop drugs that are pH unstable in the intestine.
8) Increased absorption of medications that are only soluble in the stomach.
9) Dose dumping is not a concern.
10) Gastric discomfort is avoided due to the sustained release effect and consistent drug release through the delivery method.
11) The use of prolonged release gastro retentive dosage forms, such as tablets or capsules, will cause the medicine to dissolve in the gastric fluid, making it available for absorption in the small intestine after the stomach contents have been emptied. It is thus expected that a drug will be fully absorbed from dosage forms if it remains in solution form, even at the alkaline pH of the intestine (8) 12) Gastroretentive dosage forms are designed to be retained in the gastric region for a long time and release incorporated drug candidates, allowing for sustained and prolonged drug input to the upper part of the GIT and thus ensuring optimal bioavailability. As a result, they not only extend dosing intervals but also improve patient compliance beyond what is now possible with controlled release dosage forms. (9) 13) Gastro retentive medication administration can reduce the body's counter-activity, resulting in increased drug efficacy.
14) Drugs that release slowly and at a controlled rate to reduce mucosal irritation.
(15) Because the technique allows for controlled rates of fluctuation, a greater range of receptor activation selectivity is available. (11)

1.5 Disadvantages of Gastro-Retentive Drug Delivery Systems

1. Incompatible with medications having low acid solubility. Phenytoin, for example.
2. Incompatible with medications that need to be stored in an acidic environment. E.g.Erythromycin.
3. Slow-release drugs that irritate or induce stomach lesions. Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) are examples.
4. Drugs that preferentially absorb in the colon Corticosteroid, for example. (4)
5.Increased formulation costs.
6. In the event of toxicity, poisoning, or hypersensitive reaction, retrieving the medicine is difficult.(12)
7.Difficulty in obtaining the desired outcome, as well as the issue of dose dumping (13)
Drug delivery systems that are gastroretentive vs. traditional drug delivery systems (14)

Table -1

Sr. No.		Conventional DDs	GRDDs
1	Toxicity	High risk of toxicity	Low risk of toxicity
2	Patient compliance	Less	Improves patient compliance
3	Drug with narrow absorption window in small intestine	Not suitable	Suitable
4	Drug act locally in stomach	Not much advantageous	Very much advantageous
5	Drugs having rapid absorption through GIT	Not much advantageous	Very much advantageous
6	Drug which degrades in the colon	Not much advantageous	Very much advantageous
7	Drugs which are poorly soluble at an alkaline pH	Not much advantageous	Very much advantageous
8	Dose dumping	High risk of dose dumping	No risk of dose dumping

2.Need of gastroretentive drug delivery systems

Certain drugs taken through the gastrointestinal tract (with short half-lives) are swiftly removed from the circulatory system, necessitating continuous administration. To address this issue, innovative gastroretentive medicine delivery systems are being used. (15) (1) Oral dose forms have reduced bioavailability due to the quick gastric transition from the stomach, especially for drugs that are less soluble at an alkaline pH of the intestine. Drugs with a local action in the stomach are likewise quickly ejected and do not have enough time to remain in the stomach. As a result, the frequency of dose administration is increased in such a condition. A floating drug delivery device has been created to avoid this problem. (16) The basic idea behind the development of such a system is to preserve a desired level of medicine in blood plasma for a longer period of time while preventing the drug from disintegrating. The dose form floats in the stomach fluid and slowly releases the drug at a predetermined rate, guaranteeing consistent drug levels in the blood plasma. Because FDDS has a lower density than gastric fluid, it can float in the stomach for longer periods of time without affecting the rate at which the stomach empties. Longer stomach retention increases bioavailability, decreases drug waste, and increases the solubility of drugs that are less soluble in a high pH environment. (17)

3.Criteria for drug selection

• Acting locally in the stomach.
• Primarily absorbed in the stomach.
• Poorly soluble at alkaline pH.
• Narrow absorption window.
• Degrade in the intestines.
• Drugs absorbed from the gastrointestinal tract's proximal portion (GIT).
• Drugs that are less soluble or are degraded in the lower region of the GIT due to the alkaline pH.
• Drugs absorbed as a result of a varied stomach emptying time.
• To treat specific disorders, local or sustained medication delivery to the stomach and proximal small intestine is used.
• Particularly effective in the treatment of H. Pylori-related peptic ulcers.(18)
• Drugs that have a local effect on the stomach (e.g. misroprostol, antacids)
• Drugs have a small absorption window in the GI tract (e.g. L-DOPA, paminobenzoic acid, furosemide, riboflavin).
• Drugs that have a local effect on the stomach (e.g. misroprostol, antacids).
• Drugs have a low solubility at high pH. (e.g. diazepam, chlordiazepoxide, verapamil).
• Antibiotics including tetracycline, clarithromycin, and amoxicillin, which disrupt typical intestinal microorganisms.
• Drugs that are unstable in a colonic or intestinal environment.(19)

4.The influencing Factors for Gastric Residence Time

1) Meal Volume- If the meal is larger, the time it takes for the stomach to empty will be longer.
2) Meal contents- Fats in the meal cause increased bile secretion, which slows down stomach emptying time.
3) Meal and dose form appearance- The viscous strength of the meal delays stomach emptying time. Food that is more viscous empties more slowly than food that is less viscous.
4) Physical activity or exercise extends the time it takes for the stomach to empty.
5) Stress and worry stimulate stomach motility, whereas depression slows down the motility of aged materials.
Circadian rhythms are one of the most essential determining variables. The stomach retention period is also influenced by increased cardiac rhythms throughout the day and decreased cardiac rhythms at night.
7) The density of the gastric fluid is roughly 1.2 gm/cubic cm, according to the data. As a result, the dose form should have a lower density than that to stay buoyant for a longer period of time in the stomach.
8) If the stomach is irritated, such as with flatulence or a stomach ulcer, it has a significant impact on gastric retention because the environment of the dose form is altered.

9) The stomach retention time is also modified by medicinal medications. Drugs like atropine slow down the retention time, but prokinetics like cisapride speed up the stomach emptying.
10) Age is a key issue because as people get older, their gastric motility slows down, resulting in a longer gastro retentive period.
11) Gender plays a role as well, with women's gastric emptying times being slower than men's.(9)
12) Dimensions: Dosage form units having a diameter more than 9.5mm are said to have a higher GRT.
13) Dosage form shape: When compared to other forms, tetrahedron and ring-shaped devices with a flexural modulus of 48 and 22.5 kilopounds per square inch (KSI) have improved GRT and 90 percent to 100 percent retention at 24 hours.(20)

5.Approaches in gastro-retentive drugdelivery systems

To design a dose form that can be retained in the stomach, many technical approaches have been used. To increase the retention of an oral dose form in the upper gastrointestinal tract, these methods have been proposed. (21)

5.1 High density systems

Dosage forms with densities ranging from 1.0 to specific higher values can shorten the average GI transit time. Systems with a density of less than 3.0 g/cm3 are stored in the rugae of the stomach and can withstand peristaltic movements. Producing such dosage forms with a large amount of medication and a density of 2.4-2.8 g/cm3 is, however, technically challenging. Diluents like barium sulphate, zinc oxide, and titanium dioxide can be used to create high-density dosage forms.

.

5.2 Floating systems

Because floating drug delivery systems have a lower bulk density than gastric fluids, they can stay in the stomach for longer periods of time without affecting the rate at which the stomach empties. When the medicine is floating on the gastric contents, it is discharged in a controlled manner from the system. Once the drug is released, the stomach's residual system is emptied. The mechanism of buoyancy is used to classify floating qualities: (22)

a) Low density effervescent systems due to gas production and entrapment
b) Non-effervescent systems with low density that is either intrinsic or caused by swelling.

5.3 Effervescent floating drug delivery systems

Based on CO2 gas production, this approach develops floating drug delivery systems. It's made out of effervescent substances like sodium bicarbonate (NaHCO3) or sodium carbonate, as well as citric or tartaric acid if required. When an acidic environment comes into contact with the dosage form, a gas is released, causing the dosage form to rise and maintain its buoyancy. Due to a decrease in specific gravity, the dosage form floats on the chyme. In this sort of effervescent system, swellable and rate-controlling polymers like hypromellose and polyethylene oxide are commonly utilized. This combined method provides greater buoyancy and increased stomach retention thanks to its expanding action and low density.

a) Gas generating system:

The main process at work in this system is the production of CO2 gas as a result of the reaction between sodium bicarbonate, citric acid, and tartaric acid. The gas produced lowers the density of the system, allowing it to float on stomach fluids. CO2 is produced by salts and citric/tartaric acid, which is trapped in the system's jellified hydrocolloid layer, which lowers its specific gravity and causes it to float over the chime. The seed in this technique is a sustained release pill, which is encased by many layers. The inner layer is an effervescent layer containing sodium bicarbonate and tartaric acid. A swellable membrane layer made of PVA shellac and other materials makes up the outer layer.

b) Inflatable liquid-containing system:

These have an inflatable chamber that contains a liquid, such as ether or cyclopentane, thatgasifies at body temperature, causing the chamber to inflate in the stomach. These are floating systems with an osmotically regulated hollow deformable element. The system is divided into two chambers, the first containing the medicine and the second containing the volatile system. Non-effervescent floating drug delivery methods (23)

5.4 Non-effervescent floating drug delivery systems

Because they lessen the risk of premature stomach emptying, systems with a low starting density are favored. Inherent low density can be caused by the entrapment of air or the insertion of low-density materials such as fatty substances or oils, or foam powder. These dosage forms are buoyant due to the air trapped within the inflated polymer. Furthermore, the drug is progressively released through the gelatinous barrier by controlled diffusion.

a) Colloidal gel barrier systems

The first hydrodynamically balanced system (HBS) was invented by Sheth and Tossounian in 1975. This procedure uses a pharmaceutical that contains gel-forming hydrocolloids to keep the medicine buoyant in the stomach contents. This system consists of tablets or capsules containing a high concentration of one or more gel-forming, highly swellable cellulose hydrocolloids, such as HEC, HPMC, NaCMC, Polysacchacarides, and matrix-forming polymers, such as polycarbophil, polyacrylates, and polystyrene. The hydrocolloid in the system hydrates when it comes into contact with gastric fluid, forming a colloidal gel barrier surrounding the gel surface. This dose form is buoyant because the air retained by the expanded polymer has a density less than unity..

b) Microporous Compartment System

This method is based on the encapsulation of a drug reservoir inside a microporous compartment having openings along the top and bottom walls. The peripheral walls of the drug reservoir compartment are completely sealed to keep undissolved medication from coming into touch with the gastric mucosal surface. Because the stomach's flotation chamber contains trapped air, the delivery system floats above the contents. Gastric fluid enters through the apertures, dissolves the medicine, and continuously carries the dissolved drug across the intestine for absorption.

c) Alginate beads

Calcium alginate that has been freeze-dried has been utilized to make floating dosage forms containing numerous units. Calcium alginate precipitates

when a sodium alginate solution is dropped into an aqueous solution of calcium chloride, resulting in spherical beads with a diameter of roughly 2.5 mm. The beads are then snapped apart and frozen in liquid nitrogen before being freeze dried at -40° for 24 hours, resulting in a porous structure with up to 12 hours of floating force. (24)

d) Raft forming systems

The major mechanism involved in raft formation is the formation of a viscous cohesive gel in contact with stomach contents, where each segment of the liquid expands to form a continuous layer called a raft. Gelation begins with the formation of double helical junction zones, which are followed by the aggregation of double helical segments, which are then cationcomplexed and hydrogen bonded to form three-dimensional networks. Because of the buoyancy induced by CO2 production, the raft floats and acts as a barrier to prevent stomach contents like HCl and enzymes from refluxing into the esophagus. (22)

6. Current trends and advancements

6.1 Dual working systems

These systems operate on the principles of floating and bioadhesion or swelling and bioadhesion. FDDS are designed to float on the gastric liquid when the stomach is full after a meal. As the stomach empties and the tablet reaches the pylorus, the buoyancy of the dose form may be reduced. The dosage form may then pass via the pylorus and into the small intestine. As a result, an FDDS' stomach buoyancy may be limited to only 3–4 hours. Floating gadgets also don't always get the medicine to where it's supposed to go. When a bioadhesive drug delivery system is fully loaded and the semiliquid contents are swirling around due to peristalsis, the system is very likely to dislodge from the stomach mucosa wall. The limitations of bioadhesive, swelling, and floating systems would be addressed by a dual-functioning system, which would have a significant impact on the drug's therapeutic efficacy. Sonar et al. (2007) developed a bilayer and floating-bioadhesive drug delivery system with a unique mix of flotation and bioadhesion to prolong stomach residency using rosiglitazone maleate as a model medication. The release of rosiglitazone maleate from the tablets was preceded by the matrix first-order release of rosiglitazone maleate from the tablets.

6.2Floating-pulsatile systems

Pulsatile drug delivery techniques release the drug swiftly and completely after a predetermined lag period. However, such systems are always fraught with risk; because to lag time, they may expel from the body without releasing therapeutic content. To overcome this constraint, floating pulsatile devices have become increasingly popular for a range of pharmaceutical regimens in recent years. Zou et al. (2008) developed a floating-pulsatile verapamil HCL drug delivery system in a study. In a dry-coated tablet, a drug-containing core is followed by a buoyant layer comprised of Methocel K4M, carbopol 934P, and sodium bicarbonate, which is covered with a hydrophilic erodible polymer. A dissolving, pharmacokinetic, and gamma-scintigraphic research were all performed on the generated formulations. The created system persisted in gastric fluid and resulted in controlled medication release, according to the findings.

6.3 Floating osmotic systems

A floating osmotic drug delivery device uses the idea of osmotic pressure to float on the stomach fluid. An osmotic core (containing the drug reservoir, osmotic agents, and other excipients), a shape-retaining semipermeable membrane, and a gas-generating and gel-forming outer compression coating make up these systems. To deliver the medication, an opening is bored through both outer layers. CO2 is formed initially when this system comes into touch with gastric fluid following administration due to the presence of a gas generating agent, and this gas entraps within the bed of swelling gel, causing the system to become buoyant due to decreased density. The drug is subsequently delivered entirely by the osmotic pressure generated inside the osmotic core. A saturated solution of medicine is formed initially by the passage of fluid across the semi-permeable membrane, followed by drug expulsion from the orifice due to osmotic pressure within the osmotic core. The advantage of floating osmotic drug delivery systems is that they can administer medications regardless of physiological circumstances like stomach fluid pH. (25)

7.Marketed formulations of GRDDS(26)

Brand name	Drug	Company,Country	Remarks
Citran OD®	Ciprofloxacin (1 g)	Ranbaxy, India	Gas generating floating tablets
Madopar®	Levodopa (100 mg)	Roche products, USA	Floating controlled release capsule
Valrelease®	Diazepam (15 mg)	Hoffmann LaRoche, USA	Floating capsule
Topalkan®	Al-Mg antacid Pierre	Fabre Drug, France	Floating liquid alginate preparation
Oflin OD®	Ofloxacin (400 mg)	Ranbaxy, India	Gas generating floating tablet
Conviron	Ferrous sulphate	Ranbaxy, India	Colloidal gel forming FDDS
Cytotec®	Misoprostol (100 µg/200 µg)	Pharmacia, India	Bilayer floating capsule

8.Evaluation Parameters of GRDDS

8.1 In Vitro Evaluation Parameters

In vitro GRDDS performance can be utilized to forecast in vivo performance. Tensile strength of gastroretentive tablets, weight variation, friability, drug content, content uniformity, and in vitro drug release are all common evaluation procedures. The floating behavior of low-density systems has been studied using floating behaviors such as floating lag time and total floating duration. Floating force is also used to assess the floating ability of the floating tablet. Furthermore, the swelling rate, water uptake capacity, and gel strength of the polymeric dosage form can be analyzed and tested for at least 8 hours using dissolution medium to ensure the floating mechanism, drug release, and gel strength of the polymeric dosage form.

The test is performed at 37 _C in a simulated gastric fluid (SGF). The time between the introduction of the dosage form and its buoyancy on the SGF (FLT) and the time the dosage form remains buoyant (TFT) were both measured. The floating strength is measured with a basket holder that is coupled to an analytical balance. The floating strength is determined by the weight reduction on the analytical balance over time.

8.1.1 Superporous hydrogel system, expandable system

The weight, diameter, and length of swollen samples are measured at a predetermined time point after placing the weighed amount of dosage form into the swelling medium (0.01N HCl).

.8.1.2 Raft-forming and Mucoadhesion systems

The consistency of the dosage form when it comes into touch with the stomach fluid is affected by the polymer's viscosity. The viscometer and texture analyzer from Brookfield/Ostwald are frequently used

8.1.3 Expandable system

The test is carried out by placing the folded dosage form into the dissolution media and evaluating its unfolding behavior at various time intervals. Ion-exchange resin system Particle size is determined using a sieve shaker, laser diffraction, and a coulter counter analyser. The ion exchange capability is determined by the functional group available for crosslinking. To determine moisture content, Karl Fischer can be utilized.

.8.2 In Vivo Evaluation Parameters

To provide proof of GRDDS' in vivo efficacy, a well-designed in vivo study in an animal model or people is required. The GRT and bioavailability of a drug are determined using in vivo studies. The selection of a suitable animal model is the first step in conducting a successful in vivo investigation. Animal handling, especially for large dosage forms, might be challenging in small animals including mice, rats, guinea pigs, and rabbits. As a result, determining GRT and bioavailability continues to be difficult. Gamma scintigraphy was used to determine the location and amount of GRDDS, as well as their passage through the GIT. To transform the isotope into -emitting material, the dosage form is bombarded in a neutron source. Gamma rays are released and collected as a picture after being processed by a computer. This method can also be used to determine the dissolving and disintegration properties of a dosage form. The technique's primary benefits are its high level of safety and low radiation doses. The radiology/X-ray technique is used to assess GRT, disintegration rate, dosage form dimensions, and esophageal transit of GRDDS in a preclinical setting. The ease of usage and inexpensive cost are its key advantages over -scintigraphy. Although this treatment has been successfully used in human volunteers, dogs, and rabbits, safety concerns must be addressed because frequent x-ray exposure can cause a number of health problems. GRDDS is diagnosed and monitored via gastroscopy, a type of endoscopy. The placement of the dosage form is determined using optical fibres and a video camera in this method. Although this treatment is relevant to all types of GRDDS, it is cumbersome and may require mild or complete anaesthetic to evaluate GRDDS gastric retention. Similarly, ultrasonography is a technology used in the GRDDS. The hydrogels' intragastric position, solvent penetration into the gel, and interactions between the dosage form and the gastric mucosa during peristalsis are all determined using ultrasonic waves. MRI is another way to measure GRDDS in vivo gastric retention. This method employs magnetic fields and radiowaves to observe the entire anatomical structure as well as the position of the ingested dose form. Substances with super paramagnetic properties (e.g., ferrous oxide) are used for viewing purposes. Steingoetter et al. used this technique to investigate the in vivo gastric retention of gadolinium chelates floating tablets with Fe3O4 as a super paramagnetic agent in human volunteers, and were successful in determining intra-gastric tablet position and residence time. (27)

Future perspective

A controlled drug delivery strategy with a long residence period in the stomach can be crucial for antihypertensive medications with specific pharmacokinetic features. Among the systems developed are gastroretentive pills, capsules, microspheres, granules, and beads. Many additional systems can be investigated for the development of GRDDS of antihypertensive medicines. These could be osmotically controlled systems that allow you to test different formulation factors and designs. An unfolding bilayer system, a raft-based system, or an ion exchange resin system may be employed, depending on the physicochemical properties of the drug. Because there are few findings in the literature that offer the most promising GRDDS, the bilayer unfolding and raft forming systems must be further researched. At the same time, the foldable system's small size makes it easy to use, and once it reaches the stomach, it expands and inflates, extending gastric retention and therefore increasing bioavailability. More research is needed on this approach, which has the potential to produce positive results in the control of hypertension. The ion-exchange resin complexes, which have a large economic potential, can be made with both acidic and basic medicines. Salts of cationic and anionic exchange resins are insoluble complexes in which the medication is released as a result of the exchange of bound drug ions with ions found in body fluids, in this case stomach fluid (Guo, Chang, Hussain, 2009). However, the significance of carefully selecting ion-exchange resins and medication cannot be emphasized. Microsponges, which are based on floatation, are another important system that has been reported for its gastroretentivity. (28)

REFERENCE

1. Mandal UK, Chatterjee B, Senjoti FG. Gastro-retentive drug delivery systems and their in vivo success: A recent update. Asian J Pharm Sci [Internet]. 2016;11(5):575–84. Available from: http://dx.doi.org/10.1016/j.ajps.2016.04.007
2. Gastric THE, Time R, Drugs OF. International Pharmaceutical Research of Modern GASTRO RETENTIVE DRUG DELIVERY SYSTEM : A SIGNIFICANT TOOL TO INCREASE THE GASTRIC RESIDENCE TIME OF DRUGS. 2021;5(3):240–6.
3. 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;13(10).
4. Sciences B. An Overview on Gastroretentive Drug Delivery System Article ABSTRACT. 2019;2(2):1–8.
5. Bomma R, Veerabrahma K. Development, intra-gastric performance and pharmacokinetic study of gastroretentive drug delivery system for cefdinir in human volunteers. Int J Drug Deliv. 2013;5(1):63–72.
6. Makwana A, Sameja K, Parekh H, Pandya Y. Advancements in Controlled Release Gastroretentive Drug Delivery System: a Review. J Drug Deliv Ther. 2012;2(3):12–21.
7. Pund AU, Shendge RS, Pote AK. Current Approaches on Gastroretentive Drug Delivery systems. J Drug Deliv Ther. 2020;10(1):139–46.
8. Reddy B V. GASTRORETENTIVE DRUG DELIVERY SYSTEM- A REVIEW.
9. Journal I, Scientific OF. GASTRO - RETENTIVE DRUG DELIVERY SYSTEM FOR PROLONG DRUG RELEASE : A BLANKET REVIEW. 2020;9(04).
10. Sowmya B, Arvapalli S, Gupta AVSSS. World Journal of Pharmaceutical A REVIEW ON GASTRORETENTIVE DRUG DELIVERY SYSTEM. 2019;5(4):101–10.
11. Print I, Online I, Venkatesan K, Krishnaraju K, Vs S, Pichaivel M, et al. World Journal of Pharmaceutical Sciences rats. 2021;9(8):69–72.
12. Chhetri HP, Thapa P. An overview on gastroretentive drug delivery system. 2014;10(I):90–103.
13. Tomar A, Upadhyay A, Gupta SK, Kumar S. An Overview on Gastroretentive Drug Delivery System: Current Approaches and Advancements. Curr Res Pharm Sci. 2019;9(1):12–6.
14. Nautiyal U. A review : Gastroretentive drug delivery system (grdds). 2020;(June).
15. Raj Sharma A, Khan A. Gastroretentive Drug Delivery System: an Approach To Enhance Gastric Retention for Prolonged Drug Release. Int J Pharm Sci Res [Internet]. 2014;5(4):1095. Available from: http://dx.doi.org/10.13040/IJPSR.0975-8232.5
16. Rathod HJ, Mehta DP, Yadav JS. A review on Gastroretentive Drug Delivery Systems. 2016;4(7).
17. Aundhia C, Shah N, Patel S, Sen AK, Patel P. Formulation and evaluation of floating tablet of norfloxacin. Int J Pharm Res. 2020;12(06):622–7.
18. Ayre A, Dand N, Lalitha KG. Gastroretentive Floating and Mucoadhesive Drug Delivery Systems- Insights and Current Applications. 2016;11(3):89–96.
19. Siraj S, I MK, Nazim S. Various Perspectives of Gastroretentive Drug Delivery System : A Review.
20. Taneja R, Kataria MK, Bilandi A, Gupta AG, Gedar S. Floating microsphere: a potential gastroretentive drug delivery system. Pharm Glob [Internet]. 2013;4(4):1. Available from: http://pharmacie-globale.info/index.php?option=com_docman&task=doc_download&gid=328&Itemid=41
21. Malik R, Garg T, Goyal AK, Rath G. Polymeric nanofibers : Targeted gastro-retentive drug delivery systems. J Drug Target [Internet]. 2015;00(00):1–16. Available from: http://dx.doi.org/10.3109/1061186X.2014.965715
22. Patel CN. GASTRORETENTIVE DRUG DELIVERY SYSTEMS : FROM CONCEPTION TO COMMERCIAL SUCCESS. 2017;4(2).
23. Nagar P. Review Article A REVIEW ON GASTRORETENTIVE DRUG DELIVERY SYSTEM. 2016;5(4):2178–87.
24. Vasava K, Ks R, Jha LL. Review Article A REVIEW ON GASTRO RETENTIVE DRUG DELIVERY SYSTEM (GRDDS) WITH SPECIAL EMPHASIS ON FORMULATION AND DEVELOPMENT OF FLOATING MICROSPHERES. 2011;11(2):76–82.
25. Pawar VK, Kansal S, Garg G, Awasthi R, Kulkarni GT, Pawar VK, et al. Gastroretentive dosage forms : A review with special emphasis on floating drug delivery systems Gastroretentive dosage forms : A review with special emphasis on floating drug delivery systems. 2011;7544.
26. Singh R. Gastroretentive drug delivery systems : A review. 2015;9(12):405–17.
27. Tripathi J, Thapa P, Maharjan R, Jeong SH. Current State and Future Perspectives on Gastroretentive Drug Delivery Systems. 2019;
28. Porwal A, Dwivedi H, Pathak K. Decades of research in drug targeting using gastroretentive drug delivery systems for antihypertensive therapy. 2012;1–15.