REVIEW ARTICLE

Recent Advances in Gastroretentive Drug Delivery Systems: A Review

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Abstract

Many advances have been achieved in the study and development of oral drug delivery system in recent years. The conception of novel drug delivery system originated to address a specific issue linked to the physicochemical characteristics of drug molecules and associated formulations. The goal of this study is to synthesize new research on gastroretentive drug delivery systems to provide an update on pharmacological techniques employed in improving gastric residence time. Gastroretentive floating drug delivery systems, swelling and expanding systems, polymeric bioadhesive systems, modified-form systems, high density systems, and other delayed gastric emptying devices are now employed. These technologies are quite useful in resolving various issues that arise during the development of various dosage forms. Because of the short residence period, oral absorption of medicines with a limited absorption of drugs inside the upper intestinal wall results in low bioavailability with traditional dose forms. Controlled drug delivery systems with an extended residence period in the stomach can be employed to circumvent this constraint and boost the bioavailability of these medications. A gastric retention drug delivery device can be used to extend medication residence period in the upper gastrointestinal tract. This review article focuses on the most recent advances in expandable technological advancement in floating drug delivery systems, with a particular emphasis on the primary mechanism of floatation and the benefits of achieving gastric retention, as well as a brief collection of various polymers used in floating drug delivery systems.

Key words: Buoyancy, controlled release, floating duration/gastric residence time, floating lag time, gastroretentive drug delivery systems, natural gum, bioadhesive system, swelling index

INTRODUCTION

Oral administration is the most convenient and preferred method of drug delivery to the systemic circulation and has also dominated many other drug delivery systems for human administration due to the numerous advantages such as ease of administration, formulation flexibility, cost-effectiveness, ease of storage and transport, and high patient compliance. The effective oral drug delivery technique is dependent on a number of elements, including stomach emptying, gastrointestinal (GI) transit duration of the dosage form, drug release from the dosage form, and drug absorption site.[1-3]

The capacity to extend and manage the emptying time of dosage forms is a key feature for dosage forms that linger inside the stomach for such a longer amount of time than standard dosage forms. Due to peristaltic movement as a result, medications from the upper section of the GI tract (GIT) are not fully absorbed. To address this constraint, the development of such oral gastroretentive sustained or controlled release formulation is an attempt to slowly release the medication at the upper GIT to implement good drug concentration in systemic circulation for an extended period of time.[3] There are several challenges to build controlled release devices for improved absorption and bioavailability.[4]

Gastroretentive drug delivery system (GRDDS) is viable for medicines with low absorption in the lower GIT, is extremely unstable and poorly soluble at alkaline pH, has such a short half-life, and has local efficacy in the upper gut

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Received: 26-04-2022
Revised: 15-07-2022
Accepted: 28-07-2022

for helicobacter pylori eradication.[5-17] Several formulation techniques, including several super porous hydrogel, bio/mucoadhesive, raft-forming, magnetic, ion-exchange, expandable, and low- and high-density systems, have been employed to create effective controlled release GRDDS.

Polymer types (non-ionic, cationic, and anionic polymers), polymer compositions in dosage form, viscosity grade, polymer molecular weight, and drug solubility are all formulation-related parameters that might impact the quality of the gastroretentive dosage form.[9] Furthermore, the physicochemical character of excipients is crucial in a variety of GRDDS. For example, in effervescent floating systems, excipient density and effervescent agent composition are significant considerations. To generate a highly porous hydrogel, high swelling excipients such as cross-povidone and sodium carboxymethylcellulose are required.[18] Similarly, process factors such as compression pressure during tableting might depend on the quality of the gastroretentive dosage form.

The primary goal of this study is to give information on numerous GRDDS which have been created to date, and also the physiological condition of the stomach, potential pharmacological candidates for GRDDS, variables affecting GRDDS, and GRDDS *in vitro* or *in vivo* characterization.

APPROACHES TO INCREASE GASTRIC RESIDENCE TIME INCLUDE

- High-density systems
- Bioadhesive or mucoadhesive systems
- Swelling and expanding systems
- Superporous hydrogels
- Ion exchange resins
- Bioadhesive liposomal systems
- Raft-forming systems
- Gas-generating systems
- Low-density systems (Floating systems/ Hydrodynamically balanced systems).

PHYSIOLOGY OF STOMACH

The stomach plays an important part in the GRDDS; hence, a complete understanding of the anatomy and physiology of the stomach area is required for the effective creation of the gastroretentive dosage form. The stomach is anatomically divided into two parts: The proximal stomach, which also includes the fundus and body, and the distal stomach, which includes the antrum and pylorus, as shown in Figure 1. The stomach's primary function is to briefly hold food, grind it, and then gently release it into duodenum. The fundus and body largely serve as repositories for undigested food, while the antrum functions as a pump to aid in stomach emptying through a pushing action.

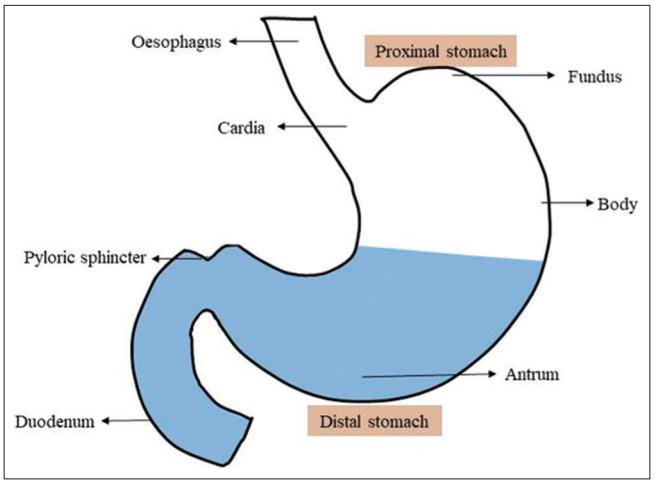

Figure 1: Schematic view on the anatomy of stomach

The stomach's movement pattern is known as the migrating myoelectric complex (MMC); Table 1 shows the several stages of the MMC. Stomach emptying happens in both fed and fasted states; however, the basic pattern of gastric emptying differs greatly between the two. In the fasting state, an interdigestive series of electrical events cycles through the stomach and small intestine every 90–120 min. During in the interdigestive phase, the pylorus expands to roughly 19 mm in diameter. As a result, during the inter-digestive phase, particles smaller than the diameter of the pyloric sphincter can readily evacuate from the pylorus toward the duodenum.

Therefore, in the fed state, motor activity begins 5–10 min after a meal is consumed and continues for as long as the food stays in the stomach, which can cause a delay in gastric emptying.

MAIN TYPES OF GASTRORETENTIVE DRUG DELIVERY SYSTEMS

Gastroretentive delivery systems are intended to be kept in the stomach for an extended period of time and release their active components, allowing for sustained and prolonged medication input to the upper section of the GIT. This technique has gotten a lot of interest in recent decades because of its potential use to improve the oral administration of several key medications whose longer retention in the upper GIT can really considerably increase of their own oral bioavailability and/or therapeutic success. The following types of gastroretentive delivery systems exist:

A. Bioadhesive drug delivery system (BDDS)
B. Expandable drug delivery system
C. Floating drug delivery system and
D. High density
E. Bioadhesive systems.

The term "mucoadhesion" refers to an interaction between both the mucin layer that lines the whole GIT and a

Table 1: Four phases of the migrating myoelectric complex[17,18]

S. No.	PHASE	COMMENTS	DURATION
1.	Phase 1	Quiet phase with sporadic contractions.	30–60 min
2	Phase 2	Intermittent action potentials and contractions that grow in intensity and frequency as the phase proceeds.	20–40 min
3.	Phase 3	Short bursts of big and regular contractions. This is known as the "housekeeper wave" because it allows all undigested debris to be washed out from the stomach and into the small intestine.	10–20 min
4.	Phase 4	Occurs in a brief transitional phase between Phases 3 and 1 of two consecutive cycles.	0–5 min

bioadhesive polymer. BDDSs are utilized as a delivery device within in the lumen to increase medication absorption in a site-specific manner. This method employs bioadhesive polymers that can stick to the stomach epithelial surface. As a result, they lengthen the stomach retention duration.[19,20] Bioadhesion can be explained by.[21,22]

- The absorption theory
- The electron theory
- The wetting theory
- The diffusion theory.

BDDSs are utilized like a delivery device within the lumen to increase medication absorption in a site-specific way [Figure 2]. This method employs bioadhesive polymers that can stick to the stomach epithelial surface. Bioadhesive systems stick to stomach epithelial cells or mucous, improving the closeness and length of contact between the GRDDS and also the biological membrane. Polycarbophil, carbopol, lectins, chitosan, gliadin, and alginate are some of the most promising excipients which have been routinely employed in these systems.

Bioadhesive systems adhere to such gastric epithelial cell surface or mucin and may be used to lengthen the gastric residency time of drug delivery systems in the stomach by enhancing the closeness and duration of drug interaction with the biological membrane. Mucin's surface epithelium adhesive qualities have long been identified and used in the creation of GRDDS mainly based on bioadhesive polymers. The capacity of a medicament to adhere to the mucous layer allows for a longer residence period in a specific organ site, resulting in a better effect in terms of local action or systemic effect.

Bio-adhesive liposomal systems

Mucoadhesive liposomal systems are created by coating a polymer with a medication that is poorly absorbed. Liposomes are often covered with muco-adhesive polymers such as chitosan, carbopol, carboxymethyl chitin, and carboxymethyl chitosan. The increased gastric retention time (GRT) of the dose forms is due to the liposomes' mucoadhesion.[23,24]

SWELLING AND EXPANDABLE SYSTEMS

Expandable gastric retentive delivery systems are readily ingested and expand to a considerably bigger size and shape in the stomach due to swelling or unfolding systems and processes that extend their gastric retention period.[8] Following medication release, their diameters are reduced due to subsequent evacuation from the stomach. The combination of considerable size and high stiffness of the dose forms to withstand peristalsis and mechanical contractility of the stomach improves GI retentivity. Narrow absorption window medicines formulated in such systems have superior *in vivo* absorption characteristics.

This system's expansion mechanism is swollen to the point that they cannot escape the pylorus. As a result, the dosage form is kept inside the stomach for such a long time. These systems are known as "plug type systems" because they have a propensity to remain blocked at the pyloric sphincter when their enlarged diameter exceeds 12–18 mm. The formulation is intended for gastric retention and regulated medication distribution into the stomach cavity. Even when fed, such polymeric matrices can be found in the GI cavity for several hours. The degree of cross-linking between the polymeric chains maintains a balance between the magnitude and duration of swelling. A high degree of cross-linking slows the swelling ability of a system, allowing it to keep its physical integrity for an extended length of time. The principle of the expandable drug delivery device was illustrated schematically [Figure 3].

FLOATING DRUG DELIVERY SYSTEMS

Floating delivery systems have a lower bulk density than gastric fluids and hence remains buoyant in the stomach for a longer length of time without influencing gastric emptying rate. The drug is slowly released at the required rate from the system whereas the system is floating on the gastric contents; following drug release, the remaining system is evacuated from the stomach. As a result, the stomach retention duration is increased, and the variations in plasma drug concentration are better controlled. Floating drug delivery system can be divided into:

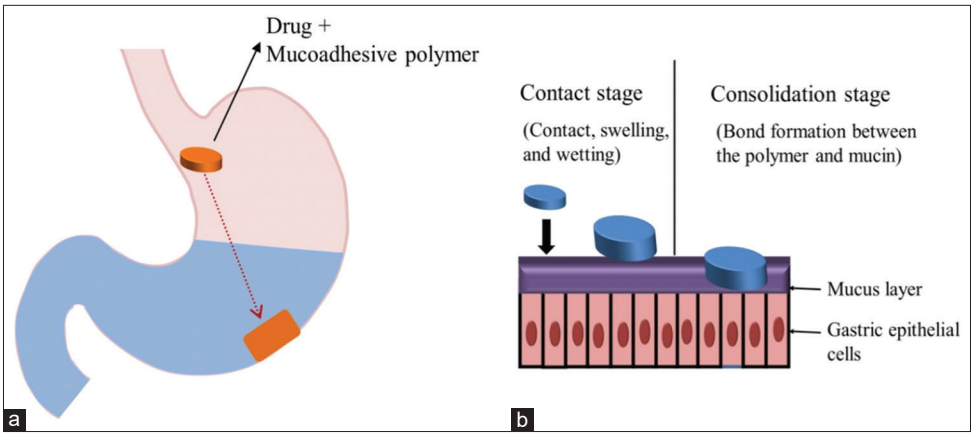

Figure 2: Mucoadhesive GRDDS (a) general representation of mucoadhesive systems and (b) mechanism of mucoadhesive system

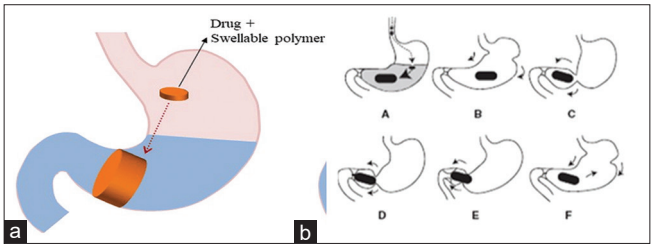

Figure 3: (a and b) GRDDS based on expandable systems and represents expandable drug delivery system. and (A) the device significantly swells on contact with gastric fluids (to a few hundred times of the original volume), (B-D) the gastric contraction pushes the hydrogel to the pylorus, (E) the gastric contraction slips over the surface of the hydrogel, and (F) the hydrogel is pushed back into the body of the stomach

i. Non-effervescent and
ii. Gas-generating system.[25]

Non-effervescent system

This sort of system expands uncontrollably after swallowing, absorbing gastric juice to the point that it stops it from exiting the stomach. One way for creating such dosage forms is to combine the medication with a gel, which expands when it comes into contact with stomach fluid after just oral administration and retains relative shape integrity and also a bulk density of less than one inside the outer gelatinous barrier. The air contained by the expanded polymer gives these dosage forms buoyancy.[26] Hydroxypropyl methyl cellulose (HPMC), polyacrylate polymers, polyvinyl acetate, carbopol, agar, sodium alginate, calcium chloride, polyethylene oxide, and polycarbonates are the most often utilized excipients in these systems. The following sections address several forms of non-effervescent systems (a-c).

Colloidal gel barrier system

A medication containing gel-forming hydrocolloids is used in this technique to keep the medicine buoyant on the stomach content. This system contains a high concentration of one or more gel-forming, highly soluble cellulose-type hydrocolloids, such as hydroxypropyl cellulose, hydroxyethyl cellulose, HPMC, polysaccharides, and matrix-forming polymers such as polycarbophil, polyacrylate, and polystyrene. When the system's hydrocolloid comes in touch with gastric fluid, it hydrates and generates the colloid gel barrier around in its surface and density falls below one. Figure 4 depicts the schematic diagram of a colloidal gel barrier system.

Microporous compartment system

This method works by encapsulating a drug reservoir inside of the microporous compartment having pores on the top and bottom walls [Figure 5]. The flotation chamber holding entrapped air in the stomach actually causes the delivery system to float above the gastric content. Gastric fluid enters through the opening, dissolves the medicine, and transports the dissolved drug across the whole intestine for continuous absorption.

Alginate beads

Dried calcium alginate complex has been used to create multi-unit floating dosage forms.[27] Dropping sodium alginate solution in to the aqueous solution of calcium chloride causes calcium alginate precipitation, resulting in spherical beads of approximately 2.5 mm in diameter. The beads are then separated, snap-frozen in liquid nitrogen, and freeze-dried for 24 h at −40°C, resulting in the production of a porous system capable of maintaining a floating force for more than 12 h. Figure 5 depicts a schematic diagram for the manufacture of alginate beads. Figure 6 depicts the schematic diagram for preparation of alginate beads

Hollow microspheres/micro-ballons

Hollow microspheres loaded with medicine in their outer polymer shell were created by Kawashima *et al*.[28] using a new emulsion solvent diffusion process. The medication and an enteric acrylic polymer ethanol/dichloromethane

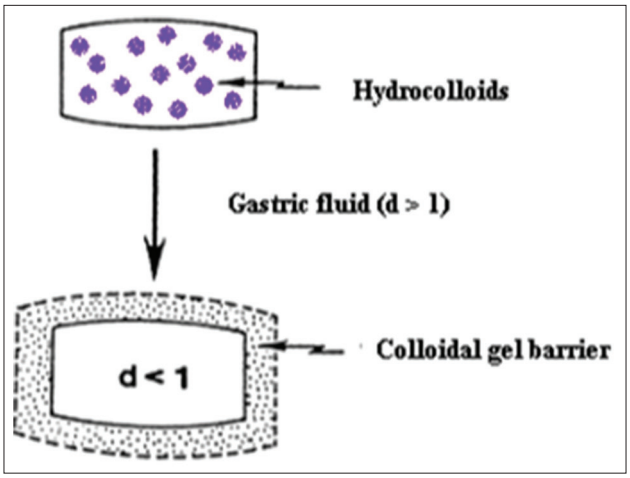

Figure 4: Colloidal gel barrier system

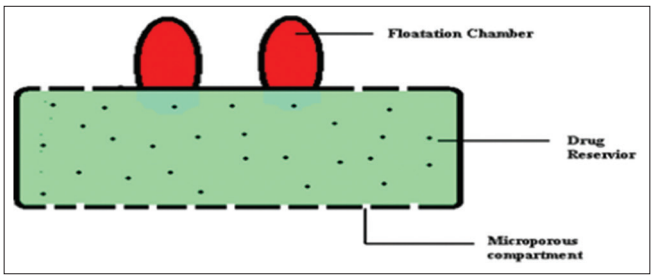

Figure 5: Microporous compartment system

solution were placed into such an agitated solution of poly vinyl alcohol that is been thermally regulated at 40°C. The gas phase is established in the dispersed polymer droplet by the evaporation of dichloromethane actually formed in the polymer's interior cavity with drug. For more than 12 h, the micro-balloon floated pretty much continuously over the surface of an acidic dissolving environment containing surfactant. The following sections address several types of effervescent systems (a-c).

Gas-generating systems/effervescent systems

These buoyant systems make use of matrices made of swellable polymers like methocel, polysaccharides like chitosan, and effervescent components (e.g., sodium bicarbonate, citric acid, or tartaric acid). The system is so well-prepared that as it enters the stomach, carbon dioxide is released, causing the formulation to float.[29,30] Among her, reported approaches and materials are a mixture of sodium alginate and sodium bicarbonate, multiple unit floating pills that generate carbon dioxide when ingested, floating minicapsules with such a core of sodium bicarbonate, lactose, and polyvinylpyrrolidone coated with HPMC, and floating systems based on ion exchange resin technology. These small capsules have a central core as well as a covering. The center core is made up of a granule covered with HPMC that is made up of sodium bicarbonate, lactose, and a binder. The top of the HPMC layer is covered with pepstatin. Because of CO_2 release into gastric

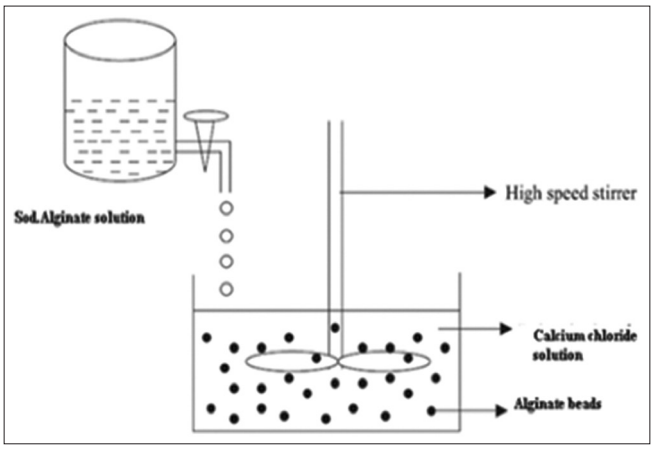

Figure 6: Schematic diagram for preparation of alginate beads

fluid, the system floats and stays inside the stomach for an extended amount of time.[31] Figure 7 depicts the schematic diagram of a mechanisms of floating systems.

RAFT FORMING SYSTEMS

Raft forming systems have garnered a lot of attention for medication delivery in the treatment of GI infections and diseases. Gastric esophageal reflux diseases has been treated with floating rafts. The mechanism of raft creation comprises the production of viscous cohesive gel into interaction with stomach fluids, where each section of the liquid expands and forms a continuous layer known as a raft. Because of the low bulk density caused by CO_2 production, this raft floats on stomach contents. A gel forming agent and alkaline bicarbonates or carbonates actually responsible for CO_2 creation are usually included in the system components to make the system less thick and float on the stomach juices. Fabregas *et al*. described an antacid raft-forming floating mechanism. When a foamy sodium alginate gel (raft) comes into contact with such as gastric fluids, the raft floats on the gastric fluids and inhibits the reflux of gastric contents (i.e., gastric acid) into the esophagus by functioning as a barrier between the stomach and the esophagus.[32,33] Figure 8 depicts the schematic diagram of a GRDDS based on raft-forming systems.

HIGH DENSITY SYSTEMS

Sedimentation has been used as a retention mechanism for pellets tiny enough to be held in the folds of the stomach body at the pyloric region, which is the lowest section of the organ in an upright position.[34] Dense pellets (about 3 g/cm^3) caught in rugae can also endure stomach wall peristaltic motions. With pellets, the GI transit time also can be increased from 5.8 to 25 h on average. Excipients that are commonly utilized include barium sulfate, zinc oxide, titanium dioxide, and iron powder, among others. Density can be increased by up to 1.5–2.4 g/cm^3

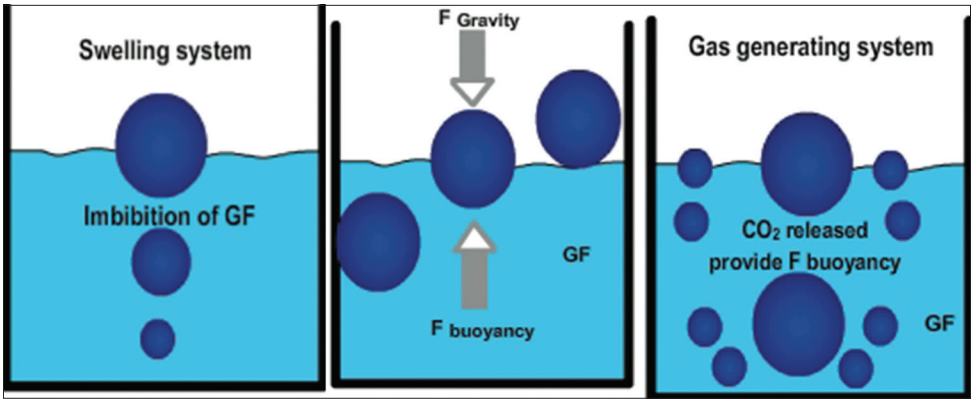

Figure 7: Mechanism of floating systems

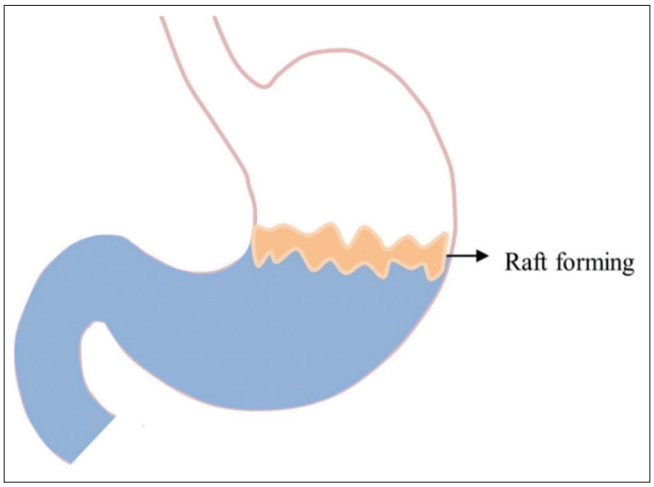

Figure 8: GRDDS based on raft-forming systems

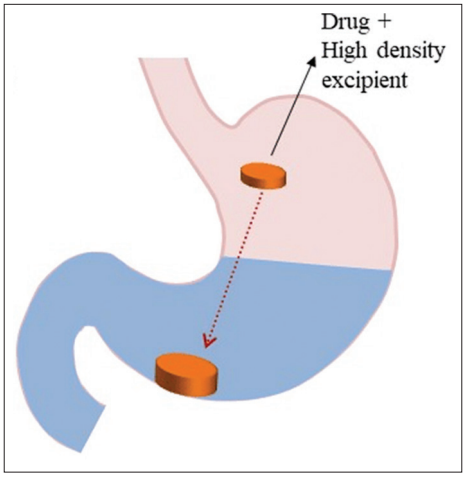

Figure 9: GRDDS based on high-density systems

with these materials. Figure 9 depicts the schematic diagram of a GRDDS based on high density systems.

MULTIPLE UNIT TYPE FLOATING SYSTEM

The sustained release tablets, known as "seeds," are enclosed by two layers in a multiple unit types floating system. The exterior

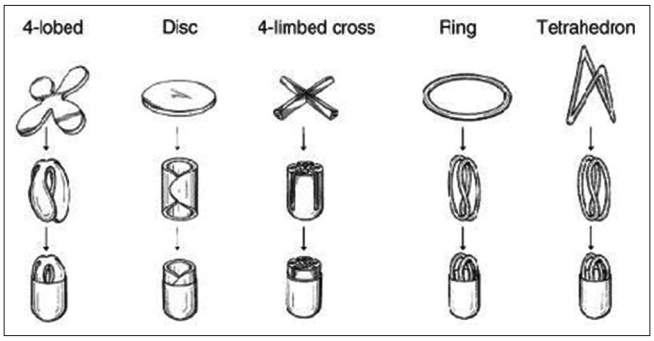

Figure 10: GRDDS based on expandable system

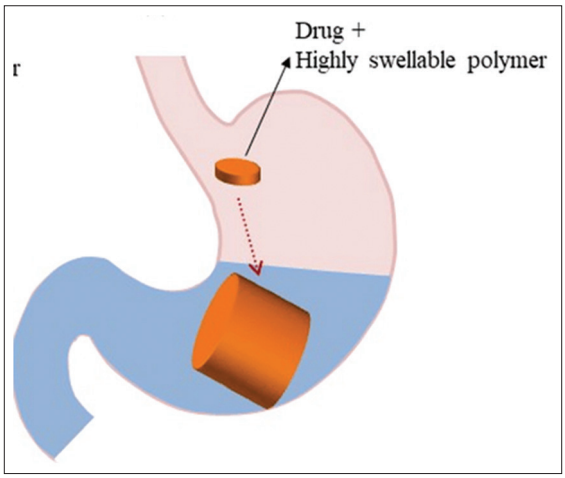

Figure 11: GRDDS based on super porous hydrogels systems

layer is made up of a swellable membrane layer, while the inner layer is made up of effervescent agents. When submerged in the dissolving liquid at body temperature, this system dips immediately and subsequently produces inflated pills that float due to their decreased density. The reduced system density is related to CO2 creation and trapping inside the system.[35]

SWELLING AND EXPANDING SYSTEMS

Swelling and expanding systems are also dose forms that enlarge after swallowing to the point that they can no longer

escape the pylorus.[36] As a result, the dose form remains inside the stomach for an extended amount of time. These systems are known as "plug type systems" because they tend to also be logged at the pyloric sphincter. Swelling and controlled drug release may occur when the drug delivery system comes into touch with stomach fluid; the polymer absorbs water and expands. The presence of specific crosslinks in the hydrophilic polymer network causes extensive swelling of the polymer.

The mass allows for gastric retention and keeps the stomach "nourished," inhibiting housekeeping waves.[8,37] Such delivery technologies include medicated polymer sheets and swelling balloon hydrogels. A balance between the pace and amount of swelling as well as the rate of polymer degradation is critical for maximizing benefit and avoiding negative consequences. They are described below (Non-effervescent systems).[38]

These systems have the ability to grow and remain in the stomach for extended periods of time. These are often designed as a capsule carrying a foldable and compact dosage form. When exposed to the stomach environment, the capsule shell disintegrates and the dose form swells, preventing it from passing through. Sustained and controlled drug delivery can be achieved by utilizing the suitable polymer. Figure 10 depicts the schematic diagram of a GRRDS based on expandable systems.

SUPER POROUS HYDROGELS SYSTEMS

Super porosity hydrogels with average pore sizes more than 100 micrometers expand to equilibrium size in less than a minute due to fast water absorption through capillary wetting through multiple interconnected open holes in this technique to improving GRT. They swell to a considerable size (swelling ratio: 100 or above) and are designed to be mechanically strong enough to withstand pressure from stomach contraction. This is accomplished by coprocessing with croscarmellose sodium, a hydrophilic particle substance. During the synthesis, this generates a dispersed phase inside the continuous polymer matrix ('ultra-porous hydrogel composites).[39]

The extremely porous hydrogel composites remain in the GIT for more than 24 h. Recent advancements in the field have resulted in "super porous hydrogel hybrids," which are made by including a hydrophilic or water dispersible polymer which can be cross-linked after the super porous hydrogel is generated. Polysaccharides such as sodium alginate, pectin, and chitosan are examples of hybrid agents. Figure 11 depicts the schematic diagram of a GRRDS based on super porous hydrogels systems.

ION EXCHANGE RESINS

A coated ion exchange resin bead formulations containing bicarbonates has been found to exhibit stomach retentive effects. Bicarbonate is added to ion exchange resins and a negatively charged medication is attached to the resin. To counteract the quick loss of carbon dioxide, the beads were encased in a semi-permeable membrane. When chloride and bicarbonate ions enter the acidic environment of the stomach, they exchange. As a result of this reaction, carbon dioxide was produced and held in the membrane, bringing beads to the top of the stomach content and generating a floating layer of resin beads as opposed to uncoated beads, which sink fast.

OSMOTIC REGULATED SYSTEMS

It consists of an osmotic pressure-controlled medication delivery system as well as an inflatable floating support enclosed in a bioerodible capsule.[40] The drug reservoir compartment and the osmotically active compartment comprise the osmotic controlled drug delivery system. The capsule swiftly degrades in the stomach, releasing the intragastric osmotically regulated medication delivery system. Inside, the inflatable support creates a flexible hollow polymeric bag containing a liquid which gasifies at body temperature to inflated the bag.

MAGNETIC SYSTEMS

A dosage form in magnetic systems is made up of active medicinal ingredients, excipients, and a small quantity of internal magnet. As shown in Figure 12, an extracorporeal magnet is positioned over the stomach to regulate the location of the pharmaceutical formulations containing an internal magnet. The GRT can be affected by the extracorporeal magnet's location and magnetic field intensity. The previous research has found that magnetic pills boost GRT and bioavailability.[41] Groning *et al*. studied magnetic acyclovir tablets with and without an external magnetic field in human volunteers. The scientists discovered that the presence of an extracorporeal magnet boosted GRT and plasma medication concentration.

Ito *et al*. developed bioadhesive granules containing various ultra-fine ferrite and tested them in rabbits.[42] They discovered

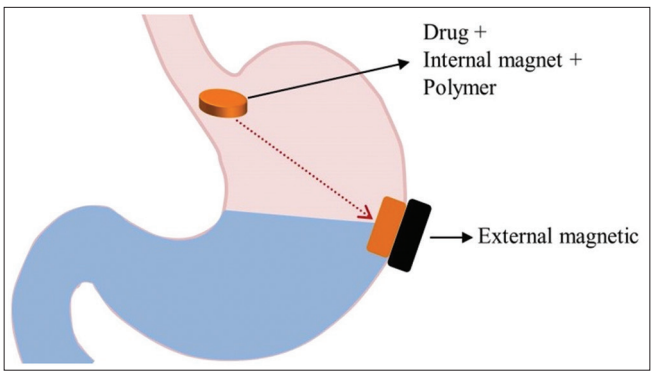

Figure 12: GRDDS based on magnetic systems

which an external magnetic field. They discovered that an external magnetic field strength of 1700 G kept all grains in the stomach for more than 2 h. However, precise placement of the magnet may be challenging, resulting in low patient compliance. Only a few investigations on magnetic systems have been undertaken, and their therapeutic importance has yet to be determined. As a result, the future research investigations on these systems must focus further on their therapeutic importance.

FACTORS AFFECTING GASTRORETENTION TIME OF FLOATING DRUG DELIVERY SYSTEMS

The various factors which influence the efficacy of gastroretentive drug formulation's as a gastroretentive systems are:

- Formulation Factors and
- Idiosyncratic Factors.[43]

Formulation factors

GRT is a dose form buoyancy function that is density dependent. The density of a dose form influences the pace of stomach emptying. A buoyant dose form floats because its density is less than that of the stomach juices. Because it is not near the pyloric sphincter, the dose unit remains in the stomach for an extended amount of time. Drug flotation is a function of time, and it can last as long as hydrodynamic equilibrium is maintained. Dosage forms with a higher density than the stomach content sink to the bottom of the whole atrium, wherein they settle and slowly release the active chemical over time.

Size

Dosage form units with such a diameter more than 7.5 mm have a higher GRT than those with a diameter of 9.9 mm. Larger dose forms have a longer gastric retention period than smaller ones because they are emptied during the digesting phase (weaker MMC) and their passage through pyloric sphincter into the small intestine is hampered.

Shape of dosage form

When compared to other designs, tetrahedron and ring shaped devices with flexural moduli of 48 and 22.5 kilo pounds per square inch exhibit greater GRT = 90–100% retention at 24 h.

Fasting GI motility is characterized by times of vigorous motor activity, or the MMC, which occur every 1.5–2 h. The MMC sweeps undigested material from of the stomach, therefore, if the formulation is administered at the same time as the MMC, the GRT of the unit will be quite brief. In the fed condition, however, MMC is significantly delayed and GRT is significantly longer.

Viscosity grade of polymer

The viscosity of polymers and their interaction have a significant impact on drug release and floating qualities of gastroretentive floating drug delivery systems (GRFDDS). Low viscosity polymers (e.g., HPMC K100 LV) were shown to be more effective in increasing floating qualities than high viscosity polymers (e.g., HPMC K4M). Furthermore, a rise in polymer viscosity resulted in a decrease in release rate.

Nature of meal

Feeding indigestible polymers or fatty acid salts can shift the stomach's motility pattern to a fed state, slowing gastric emptying and extending medication release. Stomach secretions and gastric emptying time are affected by the kind of food and its caloric content, volume, viscosity, and coadministered medicines. The pace of emptying is mostly determined by the caloric amount of the consumed meal. It makes no distinction between proteins, lipids, and carbs as long as their caloric composition is the same.

Gastric emptying is often delayed due to increased acidity, osmolarity, and calorific value. In the presence of food, gastric residence duration rises, resulting in greater drug breakdown of the dosage form at even the most favorable site of absorption. Following a meal of fats and proteins, a GRT of 4–10 h has already been documented.

Frequency of feed

Due to the low frequency of MMC, the GRT can be enhanced by nearly 400 min when multiple meals are given instead of a single meal.

Idiosyncratic factors

Idiosyncrasy is a chemical anomaly that is genetically determined. The medicine interacts with a unique attribute of the individual that is not present in the majority of individuals, resulting in the unusual reaction. Individuals with a specific genotype are only susceptible to this sort of response. It may also be determined by -

Gender

Women have a slower rate of stomach emptying than males. Regardless of weight, height, or body surface, the mean ambulatory GRT in meals (3.40.4 h) is shorter than that of their age and race matched female counterparts (4.61.2 h). Males have a lower mean ambulatory GRT (3.4 0.6 h) than their age and race matched female counterparts (4.6 1.2 h), independent of weight, height, or body surface.

Age

In senior people, stomach emptying time is shorter than in younger subjects. There are also intra- and inter-subject differences in stomach and intestinal transit time. Elderly

persons, particularly those above the age of 70, have much longer GRT. Elderly persons, particularly those above the age of 70, have much longer GRT.

Posture

GRT might differ between the patient's supine and upright ambulatory phases.

Upright position

An upright position prevents floating forms from postprandial emptying because of floating form, regardless of size, stays above the stomach contents. Floating dose forms have longer and more reproducible GRTs, whereas traditional dosage forms sink to the bottom section of the distal stomach and are evacuated in through the pylorus by astral peristaltic motions.

Supine position

This stance provides no consistent defense against early and inconsistent emptying. Large dose forms (both the conventional and floating) had extended retention in supine patients. Floating forms' gastric retention tends to remain buoyant anywhere between lesser and greater curvature of the stomach.

Moving distally, these units also may be washed away by peristaltic motions that force stomach contents toward the pylorus, resulting in a substantial drop in GRT when compared to upright participants.

Concomitant intake of drugs

Prokinetic drugs (e.g., metoclopramide and cisapride), anticholinergics (e.g., atropine or propantheline), and opiates (e.g., codeine) may impair GRFDDS function. Coadministration of GI motility-reducing medications can lengthen gastric emptying time.

Biological factors

Gastric emptying is slowed by diseases such as gastroenteritis, gastric ulcer, pyloric stenosis, diabetes, and hypothyroidism. Gastric emptying rate is increased by partial or complete gastrectomy, duodenal ulcer, and hypothyroidism.

ADVANTAGES OF GRFDDS

Increasing the GRT with either of the approaches offers several advantages such as:

1. When acidic medication compounds, such as aspirin, come into touch with the stomach wall, they induce irritation. As a result, HBS formulation may be very beneficial for administering aspirin and other comparable medications.
2. Floating systems are beneficial for medications with local action in the stomach. Antacids, for example.
3. The GRFDDS is beneficial for medications absorbed through the stomach, such as ferrous salts and antacids. Improved medication absorption as a result of higher GRT and the dosage form spending more time at the absorption site.
4. Drug administration under strict control: Drugs are released slowly and at a regulated pace, reducing mucosal irritation. Controlled and gradual medication administration to the stomach gives adequate local therapeutic levels while limiting systemic exposure to the drug. This lowers the adverse effects of the medication in the bloodstream. Furthermore, the increased GI availability provided by a site-directed administration device may minimize dose frequency.
5. Prolonged administration: The release of floating dosage forms, tablets, or capsules will result in medication disintegration in the stomach juice. They would dissolve in the gastric juice and be generally available for absorption in the small intestine when the stomach contents were emptied. If a medicine remains in solution form even at the alkaline pH of the gut, it is assumed that it will be fully absorbed from floating dosage forms.
6. Floating dosage forms, as sustained release methods, provide a number of potential benefits. Drugs with low bioavailability because absorption is restricted to the upper GI tract can be administered effectively, enhancing absorption and boosting absolute bioavailability.
7. Floating dose forms with SR features are also predicted to minimize transit variability. Furthermore, it may give a good technique for the treatment of gastric and duodenal cancer.

DISADVANTAGES/LIMITATIONS OF GRFDDS

1. A floating device is not practicable for medications with solubility or stability issues in the GI tract.
2. For medication delivery to float and perform well, these systems require a high amount of fluid in the stomach.
3. Drugs with an absorption window in the stomach are only regarded better choices.
4. Drugs such as nifedipine, which is highly absorbed throughout the GI system and also undergoes extensive first-pass metabolism, also may not be appropriate candidates for boosting GRT since delaying stomach emptying may result in lower systemic bioavailability. There are also restrictions to the use of GRFDDS for medications that irritate the stomach mucosa.
5. Take the dose form with a full glass of water (200–250 ml).
6. These technologies provide no substantial advantages over traditional medication dose forms that are absorbed throughout GIT.
7. The use of big single-unit dosage forms might result in the permanent retention of stiff large-sized single-unit forms, particularly in patients with bowel obstruction,

intestinal adhesion, gastropathy, or a restricted pyloric aperture (mean resting pyloric diameter 12.8 ± 7.0 mm).

CONCLUSION

Gastroretentive drug delivery systems are the best choice for delivering medications with a small absorption window near the GI area. A variety of medication delivery systems are being developed these days with the goal of delivering the medicine in the stomach area or upper part of GIT so that whatever drug that is released can be absorbed improving the bioavailability of the drug.

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Source of Support: Nil. **Conflicts of Interest:** None declared.