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Gastro Retentive Drug Delivery System: A Review

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ABSTRACT:
The aim of a gastro-retentive drug delivery system (GRDDS) is to target site-specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effects by maintaining the dose form in the stomach for a prolonged amount of time. The goal of this strategy is to extend the gastric residency period, which is crucial for medications that need to be released specifically in the upper intestine or stomach to improve absorption. GRDDS are especially helpful for medications with shorter half-lives, unstable or poorly soluble at alkaline pH, or poor absorption in the lower gastrointestinal tract. To accomplish the necessary retention time and release pattern, the system can be constructed employing a variety of cutting-edge techniques, such as floating, bioadhesive, expandable, or magnetic systems. Recent years have seen a huge increase in the use gastro-retentive drug delivery system (GRDDS) for oral medication delivery. Effective GRDDS have been designed using variety of creative techniques such as widely adopted floating drug delivery system (FDDS). GRDDS offers several benefits such as delivering medications with limited absorption window, enhancing pharmacological effects, reducing dosage frequency, improving bioavailability and having longer residence time in the stomach for local action like treating peptic ulcer disease. This paper aims to provide a quick overview of gastro retentive drug delivery (GRDD), including its need, advantages, disadvantages, factors affecting, approach and also its applications.

KEYWORDS: Gastroretentive, GRDDS, bioadhesive, bioavailability, gastrointestinal tract, floating drug delivery system.

INTRODUCTON:

The most efficient and approved method of delivering a drug to the systemic circulation is oral administration. The pharmaceutical industry has recently shown a growing interest in oral controlled release drug delivery due to its potential to improve therapeutic benefits such patient compliance, dose administration convenience, and formulation flexibility. Medications with a brief half-life and easy absorption from the gastrointestinal tract (GIT) are rapidly removed from the systemic circulation. It takes frequent doses of these medications to produce therapeutic activity. In an attempt to get around these limitations, oral sustained controlled release formulations were developed, which release the drug gradually into the gastrointestinal tract while maintaining an effective drug concentration in the systemic circulation for a considerable amount of time.Such a drug delivery would be retained in the stomach following oral administration and release the medication in a regulated manner to allow the drug to be given constantly to its absorption site in the gastro intestinal tract[1].When a medicine has an absorption window, GRDDSs can help with controlled delivery by releasing the drug continuously for a longer amount of time before it reaches the absorption site[2].When a drug is absorbed from the proximal portion

of the gastro intestinal tract (GIT), is less soluble in an alkaline pH or encounters the lower part of the GIT, it may be desirable to prolong its gastric retention in order to achieve therapeutic benefits. GRDDS improves the bioavailability, therapeutic efficacy, and potential dosage reduction of these drugs. In addition to these benefits, these systems provide pharmacokinetic benefits such as maintaining steady therapeutic levels for an extended length of time and minimizing fluctuations in the therapeutic levels[3].Medications with short half-lives and easy absorption from the GIT leave the systemic circulation quickly. It takes multiple doses of these medications to produce appropriate therapeutic action. In an attempt to overcome this limitation, oral sustained controlled release formulations were developed, which release the drug gradually into the gastrointestinal tract and maintain an effective drug concentration in the systemic circulation for a considerable amount of time.Such a drug delivery would remain in the stomach after oral administration and release the medication in a regulated manner, allowing the drug to be constantly given to its absorption sites in the GIT[4]. The process of gastric emptying of dosage forms is very variable, and the capacity to extend and regulate the emptying time is an important feature for dosage forms that stay in the stomach for longer than traditional dosage forms. Creating a regulated delivery system to improve bioavailability and absorption presents a number of challenges. The inability to contain the dose form in the intended region of the gastrointestinal tract is one of these challenges. Drug absorption from the gastrointestinal tract is a complex and multifaceted process.It is commonly known that contact time with the small intestinal mucosa affects how much a medicine is absorbed through the gastrointestinal tract. The duration of drug gastric residence is greatly extended by gastro retentive systems, which can stay in the stomach area for several hours. In addition to reducing drug waste and increasing bioavailability, prolonged stomach retention makes drugs more soluble that are less soluble in high pH conditions.It can also be used to administer local medications to the stomach and first part of the small intestine[5].Better product availability with novel therapeutic potential and significant patient benefits is made possible by gastro retention. The mechanisms of mucoadhesion, flotation, sedimentation, expansion, changed shape systems, or the concurrent administration of pharmacological drugs that delay stomach emptying can all be used to produce the regulated gastric retention of solid dosage forms[6,7,8,9].

NEED FOR GRDDS: [60]

- In the pharmaceutical industry, conventional oral administration is frequently utilized to treat illnesses. However, there were a number of issues with conventional delivery, the main one being non-site specificity.
- Some drugs only absorb where they are absorbed. They demand a release at a certain location or a release that ensures the maximum quantity of medicine reaches the designated location.
- The pharmaceutical industry is currently concentrating on these medications that need to be site-specific.
- One site-specific delivery method for administering medications to the stomach or intestine is gastro-retentive administration. It is obtained by keeping the dosage form in the stomach, and the medication is then delivered gradually to a designated location in the duodenum, stomach, or intestine.

PHYSIOLOGY OF GIT:

The muscular, hollow, and dilated alimentary canal includes the stomach. It can be found beneath the diaphragm. The stomach's functions include briefly holding food, grinding it, and then gradually releasing the ground food. The stomach is the most significant location for the synthesis of enzymes due to its

limited surface area and extremely tiny absorption. In the small intestine, it creates a barrier. The volume consumed, a person's posture, and their skeletal make-up can all influence how their stomach is positioned. As seen in Figure 1, the stomach is divided into three sections: the fundus, body, and pylorus/antrum. The proximal portion, which consists of the body and fundus, is allocated for undigested material. The principal location for mixing motion is the antrum or pylorus, which propels motions to form a gastric pump for emptying. The process of stomach emptying happens while fasting. An electrical sequence of interstitial events happens when a person is starving. It passes through the stomach and intestines for a few hours. This is referred to as the migrating myoelectric cycle (MMC) or the inter-digestive myoelectric cycle[51,52].

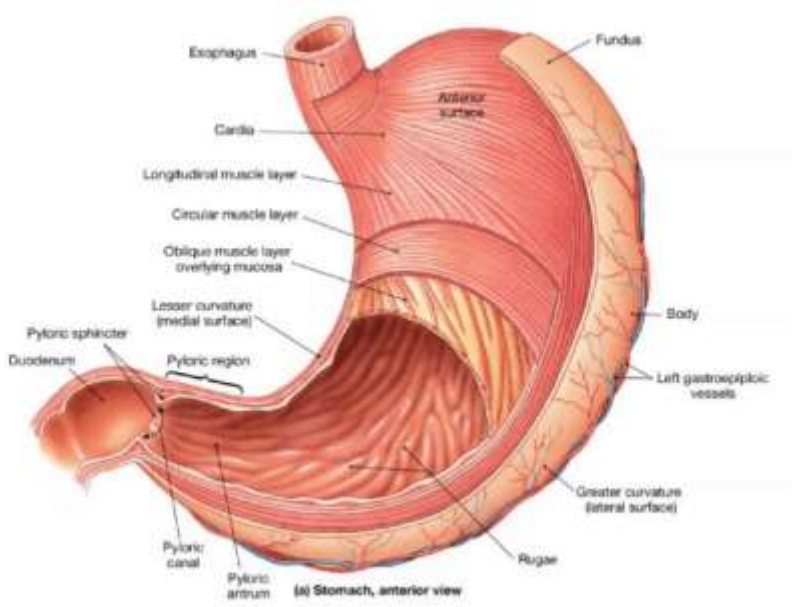

Figure 1: Anatomy of Stomach.

Gastric motility:

The stomach motility is regulated by neural and hormonal indications. The parasympathetic and sympathetic nervous systems are governed by the nervous system. Many hormones are involved in influencing gastric motility; for instance, "cholecystokinin and gastrin are used to relax the stomach and enhances the contractions of distal stomach." The smooth muscle cells are integrated through stomach motility for both stimulatory and inhibitory impulses. Liquid passes through the pylorus, but solids need to have a diameter of one to two millimeters in order to pass the stomach. It is crucial to consider the in vivo stomach volume of drug distribution in dose form. The stomach's resting capacity is 25–50 ml. The GI pH in the drug delivery system has a significant impact on drug absorption. The pH ranges for fed and fasting conditions are 2.0–6.0 and 1.2–2.0, respectively[53,54].

Gastric emptying rate:

Gastric emptying takes place in both fed and fasting states. One can divide it into two phases. An inter-digestive sequence of electrical processes takes place during the fasting stage. It is referred to as the migrating myoelectric cycle (MMC) and may go through the gastrointestinal tract every two to three hours. It is separated into four further phases: -

Phase I: (Basal phase): It may remain upright for 40–60 minutes, occasionally contracting. **Phase II**: The preburst phase, lasting between forty and sixty minutes. It is typified by contractions and

an erratic action potential. The phase moves forward and the intensity rises with increasing frequency.

Phase III: (Burst phase), lasting four to six minutes at most. The small intestine receives the partially digested food after leaving the stomach. For brief intervals, there are waves of strong, regular contractions. It's also known as the "housekeeper wave."

Phase IV: Occurs between Phases III and I and lasts for 0 to 5 minutes. The contraction pattern shifts from the fasted to the fed condition when a meal is consumed. This pattern is known as the digestive motility pattern. In Phase II, it consists of constant contractions. It causes food particles to shrink by up to 1 mm and is discharged in suspension form into the pylorus. The delayed fed state start of MMC causes the rate of stomach emptying to decrease. [55-58]

FACTORS AFFECTING GASTRIC RETENTION

1. **Density:** The dose form's density should be lower (1.004g/ml) than the gastric contents' density.
2. **Size:** A dose form's duration in the stomach is longer if its diameter is greater than 7.5 mm than if it is 9.9 mm.[14].
3. **Dosage form shape:** Compared to other devices of comparable size, a diameter stayed in the stomach for a longer amount of time. When compared to single unit dosage forms, multiple unit formulations exhibit a more predictable release profile, permit a larger margin of safety against dosage form failure, and show negligible performance impairment due to the failure of units with different release profiles or containing incompatible substances.
4. **Fed or unfed state:** Strong motor activity, or the migrating myoelectric cycle (MMC), which happens every 1.5 to 2 hours, is what defines the GI motility during a fast. Undigested material is swept from the stomach by the MMC, and if the formulation's administration time aligns with the MMC, the formulation's GRT is impacted. GRT is noticeably longer and MMC is delayed in the fed condition[15].
5. **Nature of meal:** The stomach's motility pattern can be altered to a fed state by feeding indigestible polymers or fatty acid salts, which slows down the pace of gastric emptying and extends the time that drugs escape from the stomach.
6. **Caloric content:** Having a high-protein, high-fat meal can raise GRT by 4–10 hours.
7. **Meal frequency:** Due to the low frequency of MMC. Feeding increases over 400 minutes when consecutive meals are compared with a single meal[16,17].
8. **Gender:** Regardless of height, weight, or body surface area, the mean ambulatory GRT in men (3,4 hours) is lower than that of their age- and race-matched female counterparts (4,6 hours)[18].
9. **Age:** Individuals over 70 have a noticeably longer GRT.
10. **Administering drugs concurrently:** Opioids such as codeine and atropine, as well as anticholinergics like propantheline, might prolong GRT[19].

APPROACHES IN GASTRO RETENTIVE DRUG DELIVERY SYSTEM:

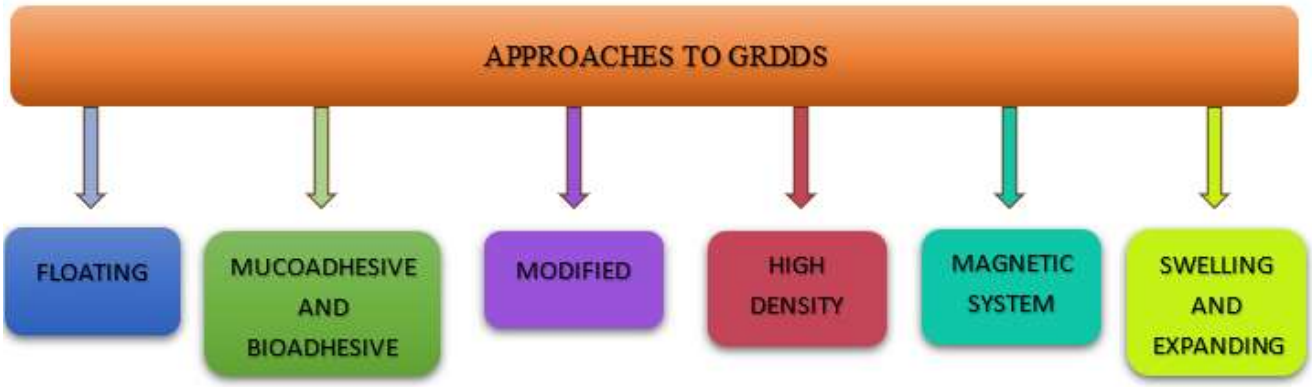

Figure 2: Approaches to GRDDS

1. Floating drug delivery system:

Among all other gastroretentive types of dosing systems, floating systems are among the most effective methods for gastric retention in order to provide improved drug bioavailability with prolonged gastric residence periods. For medications with absorption window restrictions and better outcomes of absorption window difficulties window in the stomach or upper small intestine, floating systems are appropriate drug delivery methods. These systems can stay in the stomach for long periods of time without slowing down the rate of gastric emptying because they have a lower bulk density than gastric fluids. They exhibit good gastrointestinal retention because to their effective buoyancy qualities, which allow the dosage form to release the drug gradually in a preset and regulated manner. Once the drug has completely released, the residual system is discharged from the stomach[20,21,22].

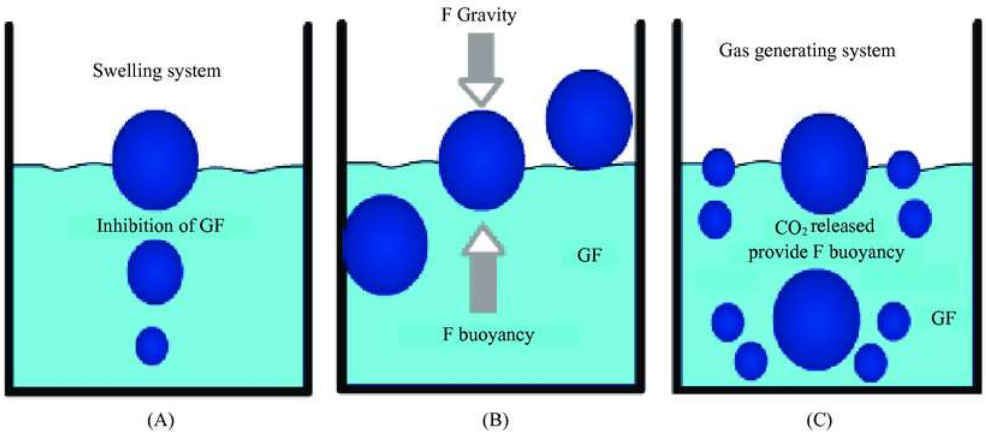

Figure 3: The floating drug delivery system's mechanism.

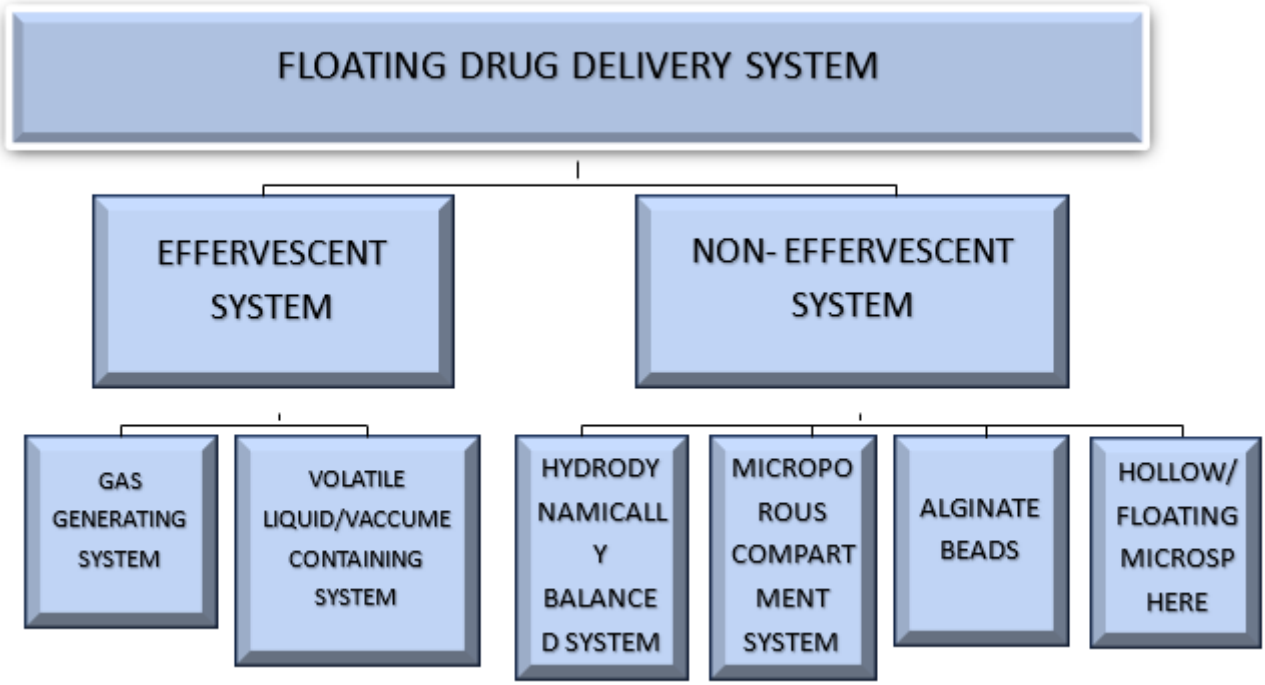

Figure 4: Classification of floating system

I. Effervescent system:

Floatation of a medication system in the stomach filled with vacuum, air, or an inert gas. Organic solvents, such as ether or cyclopentane, can volatilize and release gas into the floating chamber. Alternatively, gas can be created when organic acids react effervescently with carbonate-bicarbonate salts, producing CO2. With the help of these devices, thin floatable systems can be spontaneously expelled from the stomach. The hollow, malleable unit in them can be stretched or contracted, and it will return to its collapsed state after a certain length of time.

A. Gas generating system:

Another method for achieving floatability is the creation of gas bubbles. When carbonates or bicarbonates are combined with acid—either the stomach's natural acid or one that has been coformulated as citric or tartaric acid—CO2 can be produced in the process. It is reported that a stoichiometric ratio of 0.76:1 is ideal for gas formation when it comes to citric acid and sodium bicarbonate. Using a matrix that has liquids trapped in it, which turns into a gas at body temperature, is an alternative. These methods have been applied to both single and multi-unit systems.

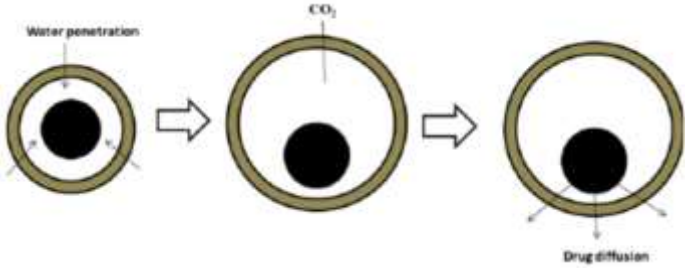

Figure 5: Gas generating system[31]

B. Volatile liquid containing system:

This kind of system has two chambers divided by a moveable, impermeable bladder that responds to pressure. The medicine is in the first chamber, while the volatile liquid is in the second. To maintain the GRT of a drug delivery system, an inflatable chamber can be filled with a liquid (such as ether or cyclopentane) that gasifies at body temperature and causes the stomach chamber to inflate.In order to allow the inflatable systems to be automatically expelled from the stomach, the device may also include a bio erodible plug composed of polyethylene, polyvinyl alcohol, etc. that gradually dissolves and causes the inflatable chamber to release gas and collapse after a set amount of time. The medication is constantly released from the reservoir into the stomach fluid as the device inflates[32].

II. Non effervescent system[33]:

High concentrations (20–75% w/w) of gel-forming, highly swellable, cellulosic hydrocolloids (such as sodium carboxymethyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, and hydroxypropyl methylcellulose (HPMC)), polysaccharides, or matrix-forming polymers (such as polycarbophil, polyacrylates, and polystyrene) are incorporated into tablets or capsules in non effervescent systems. These gel formers, polysaccharides, and polymers hydrate when they come into contact with stomach fluid, creating a colloidal gel barrier that regulates the rate at which fluid enters the device and the release of medication that follows. The gel layer is preserved by the hydrocolloid layer next to it, which hydrates when the dosage form's outer surface dissolves. The inflated polymer traps air, which reduces the dosage form's density and gives it buoyancy. The following methods were applied in the creation of intragastric floating systems.

A. Hydrodynamically Balanced Systems

These are single-unit dosage forms that comprise one or more hydrophilic polymers that form gels. The most often used excipient is HPMC, however other options include agar, HEC, HPC, NaCMC, and alginic acid. The medication is combined with the polymer and often given as a gelatin capsule. The capsules disintegrate quickly in the stomach juice, and a floating mass is created when the surface polymer swells and gets hydrated. The creation of a hydrated barrier at the surface regulates drug release. Water can seep into the inner layer of the surface due to continuous surface erosion, which keeps the surface buoyant and hydrated. Fatty excipients limit water penetration and provide low density formulations, which lessen erosion. The primary disadvantage is the operation's passivity. It is dependent upon the properties and quantity of polymer, as well as the air sealed in the dry mass center after the gelatinous surface layer has hydrated. The balance of drug loading and the impact of the polymer on the release profile are key factors in effective medication delivery.

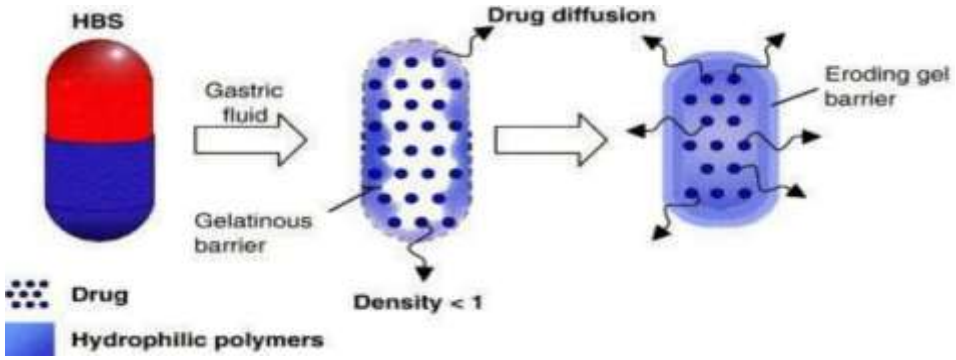

Figure 6: Hydrodynamically balanced systems

B. Microporous Compartment System

The foundation of this technique is the encapsulation of a medication reservoir within a microporous chamber that has pores across the length of its top and bottom walls. The drug reservoir compartment's periphery walls are tightly sealed to shield the undissolved drug from coming into direct touch with the stomach surface. Because of the confined air in the flotation chamber, the delivery system floats over the stomach's gastric contents. The medicine is dissolved when gastric fluid enters through the aperture and is then continuously transported across the gut for absorption.

C. Alginate Beads

Freeze-dried calcium alginate has been utilized to make floating dosage forms with multiple units. By dropping sodium alginate solution into an aqueous calcium chloride solution, calcium alginate precipitates, forming spherical beads with a diameter of around 2.5 mm. Following the separation of the beads, they are freeze-dried at -40ºC for 24 hours then snap-frozen in liquid nitrogen. By doing this, a porous structure that can support a floating force for longer than twelve hours is created.The floating beads provided a longer residence period of over 5.5 hours[34].

D. Hollow Microspheres[35].

The GRT of the dosage form was extended by using a straightforward solvent evaporation or solvent diffusion approach to create micro balloons or hollow microspheres filled with medication in their other polymer shelf. Polycarbonate, cellulose acetate, calcium alginate, Eudragit S, agar, low methoxylated pectin, and other common polymers are employed to create these systems. Three factors affect drug release and buoyancy from dosage forms: the amount of polymers, the plasticizer polymer ratio, and the formulation solvent. For more than 12 hours, these tiny balloons remained suspended above the surface of an acidic dissolving medium that contained surfactant. Since hollow microspheres combine the benefits of multiple-unit systems with good floating properties, they are currently regarded as one of the most promising buoyant systems.

2. Muco/ Bio-adhesive System:

Drugs administered orally can be more efficiently absorbed at a specific place when using bioadhesive systems, which are gastroretentive dosage forms. To achieve longer gastric residence time and dosage form attachment to the stomach epithelial surface, bioadhesive polymeric materials are utilized. Different methods, based on a straightforward process wherein the dosage form adheres to the surface of the mucous membrane, enable dosage forms to exhibit bioadhesive qualities. Bioadhesive applications frequently involve the use of polymeric polymers such as chitosan, cholestyramine, sodium alginate, polyacrylic acid, hydroxypropyl methyl cellulose, sucralfate, tragacanth, dextrin, and polylactic acids. However, there are some limitations related to these polymeric materials since some of them created bioadhesive qualities efficiently, but it was difficult to sustain this adhesiveness because of the fast mucus turnover rate in the stomach tract[23,24,25].

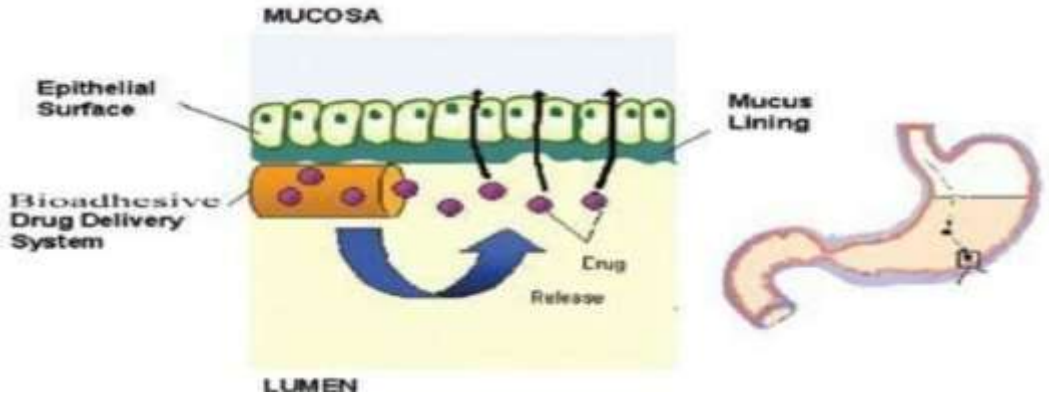

Figure 7: Bioadhesive system.

3. Modified System:

These are geometric, non-disintegrating structures that are either extruded from blends of polyethylene or molded from plastic elastomer. Depending on the size, shape, and flexural modulus of the drug delivery system, these shapes can extend the stomach retention.

4. High Density System:

Through the retention of the active drug molecule in the stomach's rugae, these systems are resistant to the stomach's peristaltic movements. The stomach content has a density of 1.004 gm/cm3, which is comparable to water. These dose forms are resistant to the stomach wall's peristaltic movements because they contain high-density pellets. However, if the patient is erect, the high density of the pellets can lead them to sink to the bottom of the stomach and become stuck in the folds of the antrum. A gastric content density of approximately 2.5 gm/cm3 is effective enough to extend the duration of the gastric stay. Combining drug-coated heavy core with inert ingredients such as barium sulphate, iron powder, zinc oxide, and titanium oxide is an efficient development strategy for creating these formulations. Following this stage, these substances cause the dosage form's density to rise to 1.5–2.4 gm/cm3, which is nearly the same as the density of the stomach contents[26-30].

Figure 8: High density system.

5. Magnetic System [36]:

The basic idea behind this strategy to improve the GRT is that the dose form has a tiny internal magnet, and there is also a magnet on the abdomen above the stomach location. The magnetic system appears to be functioning, however patient compliance may be jeopardized by the need for exact positioning of the external magnet. The technique uses bio adhesive granules containing ultra-fine ferrite on rabbits. After 2 hours, nearly all of the granules were still in the area where they had been steered by an external magnet during the first 2 minutes.

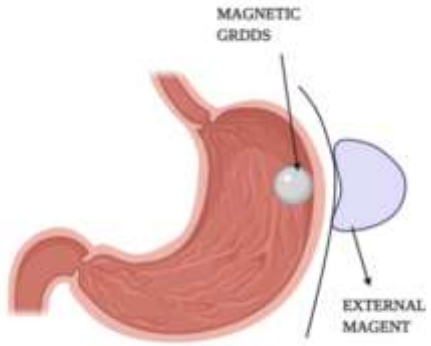

Figure 9: Magnetic system.

6. Swellable and Expandable System[37,38]:

If a dose form in the stomach is larger than the pyloric sphincter, it can endure gastric transit. Nonetheless, the dose form needs to be ingested in small enough portions and cannot obstruct the stomach either taken alone or in combination. Therefore, in order to create an extendable system that will prolong GRT, these configurations are needed:

Three configurations are available:

1. tiny for oral ingestion;
2. extended gastro retentive form; and
3. final small form that allows evacuation when the medicine is released from the device.

Therefore, the combination of a large dosage form's stiffness to endure peristalsis and the stomach's mechanical contractility improves gastro-retention. In an effort to create a GRDDS that works, researchers have recently looked into and tested expandable and unfoldable systems. Biodegradable polymers are used to create unfoldable systems. These bioerodible polymers come in many geometric shapes, such as tetrahedron, ring, or planner membrane (4-label disc or 4-limbed cross form), compressed within an extended stomach capsule. The GIT also holds onto swellable systems because of their mechanical characteristics. Usually, the swelling is caused by water absorbing osmotically. Expandable systems have several disadvantages, such as challenging storage of highly biodegradable and hydrolyzable polymers, very short mechanical shape memory for the unfolding system, difficulty in industrialization, and lack of cost effectiveness. Once more, intestinal adhesion, gastropathy, and transient blockage may result from the long-term implantation of large, inflexible, single-unit expandable drug delivery dosage forms.

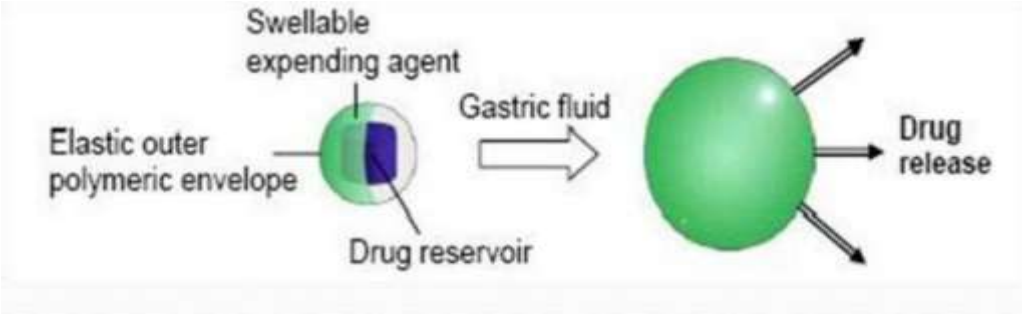

Figure 10: Swelling system

A COMPARISION OF THE CONVENTIONAL DRUG DELIVERY SYSTEM WITH THE GASTRORETENTIVE DRUG DELIVERY SYSTEM.

Sr. No	Parameters	GRDDS	Conventional DDS
1.	Patient compliance	Improve	Low
2.	Risk of Toxicity	Low risk	High risk
3.	Dose dumping	Low risk	High risk
4.	Drug having rapid absorption through GIT.	Much advantageous	Not much advantageous
5.	Drug with narrow absorption window in small intestine.	Appropriate	Not appropriate
6.	Drug which degrades in colon	Much advantageous	Not much advantageous
7.	Drugs which are poorly soluble at an alkaline pH	Much advantageous	Not much advantageous
8.	Drug acting locally in the stomach	Much advantageous	Not much advantageous

ADVANTAGES OF GRDDS [10,11,12].

1. Compared to the administration of non-gastric retentive drug delivery, the bioavailability of therapeutic agents can be markedly increased by this gastroretentive drug delivery strategy, particularly for those that are processed in the upper GIT. The amount of drug absorption is influenced by a number of interrelated elements that are connected to drug absorption and transit in the gastrointestinal tract (GIT) and work simultaneously.
2. Sustained release may cause a flip-flop in the pharmacokinetics of medications with comparatively short half-lives. Furthermore, it may facilitate improved patient compliance and a reduction in dosage frequency.
3. They also have an edge over their traditional approach since they can use it to get around the problems caused by the gastric emptying time (GET) and the gastric retention time (GRT). Because their bulk density is lower than that of the stomach fluids, these devices are projected to stay buoyant on the gastrointestinal fluid without influencing the intrinsic rate of employing.

4. By using gastroretentive drug delivery, medications from dosage forms that offer local therapy in the stomach and small intestine can be released from capsules more gradually and continuously. As a result, they are helpful in the treatment of small intestinal and stomach diseases.
5. The drug is administered cautiously and under close observation. A gastroretentive dosage form provides sufficient local action at the site of illness, hence reducing or eliminating the exposure to systemic drug. The negative consequences of side effects are decreased by this site-specific drug administration.
6. The variation in medication effects and concentrations is reduced by gastroretentive dose forms. As a result, negative effects linked to peak concentrations that are concentration-dependent can be shown. This characteristic is especially crucial for medications with limited therapeutic index.
7. medication efficiency can be increased through gastroretentive medication administration by reducing the body's counteractivity.
8. Improved selective receptor activation is made possible by a decrease in medication concentration fluctuations.
9. The extended period of time over a critical concentration made possible by the prolonged mode of drug release from gastroretentive dosages form improves the chemical results and pharmacological effects.

DISADVANTAGES OF GRDDS [13]:

1. A drawback of floating systems is that, in order to float and function well, they need a lot of fluid in the stomach. Therefore, a higher water intake is advised at this dosage.
2. When lying flat (as when you sleep), a floating dosage form could be carried away by contractile waves, if it's not too big. Therefore, the patient shouldn't take the floating dose form right before bed.
3. GRDDS cannot contain medications that cause irritation to the gastric mucosa, have stability issues in highly acidic environments, or have very low solubility in acidic environments.
4. High mucus layer turnover rate, thick mucus layer, and limits related to soluble mucus are issues with bioadhesives and mucoadhesives systems.
5. The swelling dose form needs to be able to expand quickly before leaving the stomach and reach a size greater than the pylorus aperture. It needs to be able to withstand Phase III of MMC's housekeeper waves.
6. A number of variables, including meal presence, pH, and stomach motility, might affect gastric retention. Since these elements are always changing, it is impossible to forecast the buoyancy.
7. The rapid rate of stomach mucus turnover presents the biggest obstacle for a bio adhesive system.
8. Another potential with bioadhesive drug delivery methods is esophageal binding.
9. These kinds of systems are not appropriate for drugs with GIT stability and solubility issues.

APPLICATION OF GRDDS [59]:

1. Site Specific Drug Delivery Systems:

Drugs that are specifically absorbed from the stomach or the proximal portion of the small intestine often benefit from these systems. The medication is delivered to the stomach in a regulated, gradual manner that minimizes systemic exposure while providing sufficient local therapeutic doses. This lessens the negative impact that the medication has on blood circulation. Additionally, a site-directed administration system's

prolonged stomach availability may lessen the frequency of dose. For example, riboflavin and furosemide

2. Enhanced Bioavailability:

When riboflavin controlled release gastroretentive dosage forms are administered instead of noncontrolled release polymeric formulations, the bioavailability of the former is noticeably enhanced. Numerous processes connected to drug absorption and transit in the GIT work simultaneously to influence the extent of drug absorption.

3. Sustained Drug Delivery:

GRT in the gastrointestinal tract is an issue for oral controlled release formulations. HBS systems can help with issues where particles can float over the contents of the GI tract and stay in the stomach for extended periods of time because to their bulk density of less than 1. The systems are somewhat enormous in size, and it is not permitted to pass through the pyloric aperture.

4. Minimized adverse activity at the colon:

The quantity of medication that reaches the colon is decreased when medicine in HBS systems is retained in the stomach. Therefore, it is possible to forbid drug use that is deemed undesirable in the colon. The explanation behind the gastroretentive dosage form of beta lactam antibiotics, which are only absorbed from the small intestine and whose presence in the colon promotes the development of microorganism resistance, is provided by this pharmacodynamics feature.

5. Absorption Enhancement:

Potential candidates for FDDS formulation are medications with low bioavailability because of site-specific absorption from the upper gastrointestinal tract, which would maximize absorption.

6. Reduced fluctuations of drug concentration:

Continuous medication intake after controlled release blood medication concentrations following GRDF administration fall into a more specific range associated with instant release dosage formulations. As a result, pharmacological impact variations are lessened, and concentration-dependent side effects that are connected to peak concentrations may be avoided.

POTENTIAL DRUG CANDITATES FOR GRDDS:

1. Medications functioning locally in the stomach, such as misoprostol and antacids [39,40].
2. A medication such as furosemide that is poorly soluble at alkaline pH [41].
3. Medication used to cause intestinal degradation or instability. For example, metronidazole, ranitidine HCl [42,43].
4. Medications that cause instability in the lower GIT, such as captopril [44].
5. Medications insoluble in gastrointestinal fluids, such as Diazepam and Quinidine [45].
6. Medication that alters the usual bacteria in the colon, such as amoxicillin tirhydrate. [46].
7. Drugs such as riboflavine-5-phosphate, ofloxacin, norfloxacin, and domperidone that have a narrow period of absorption in the stomach or upper sections of the small intestine [47-50].

COMMONLY USED DRUGS IN FORMULATION OF GRDDS [61-66]:

Dosage Forms	Drugs
Floating Microspheres	Aspirin, p-nitro aniline, Terfenadine, Tranilast, Griseofulvin, Ibuprofen.

Floating Granules	Diclofenac sodium, Prednisolone, Indomethacin.
Floating Tablets	Acetaminophen, Ampicillin, trihydrate, Atenolol, Captopril, Cinnerzine, Ciprofloxacin, Diltiazem, Amoxicillin, Fluorouracil, Isosorbide dinitrate, Isosorbide mononitrate, Prednisolone, Nimodipine, Theophylline, Verapamil, Acetylsalicylic acid, p Aminobenzoic acid (PABA), Chlorpheniramine maleate, Sotalol.
Floating Capsules	Diazepam, Misoprostol, Furosemide, L-DOPA and Benserazide, Nicardipine, Chlordiazepoxide HCl, Propranolol, Pepstatin.
Powders Films	Several basic drugs, Cinnerzine.

CONCLUSION:

As our knowledge of the effects of GIT physiology on drug delivery grows, more drug delivery systems will be developed to maximize the administration of compounds that display regional diversity in drug absorption. As delivery technologies become more sophisticated, more gastro-retentive drug administration methods will be developed to maximize the delivery of compounds with long half-lives, limited bioavailability, and extensive first pass metabolism. After reviewing the literature, we concluded that gastroretentive drug delivery offers several potential advantages for drugs with low bioavailability because it maximizes absorption and improves absolute bioavailability because the upper gastrointestinal tract is the only area in which drugs can be absorbed.The patient receives maximal benefit from the gastroretentive medication delivery method, resulting in maximum patient compliance. Given the increasing effectiveness of various forms of pharmacotherapy, it is reasonable to predict that GRDD devices will become more widely used in the future to transport drugs to the systemic circulation.

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