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THE PRESENT AND FUTURE PERSPECTIVES IN GASTRO RETENTIVE DRUG DELIVERY SYSTEMS (GRDDS)

Sante Rohini U.*[1], Fugate Ajay[1], Punam Londhe[1] and Swati Jadhav[1]

[1]Department of Pharmaceutics Shivlingeshwar College of Pharmacy, Almala Dist. Latur-413520, Maharashtra (MH), India.

***Corresponding Author: Sante Rohini U.**

Department of Pharmaceutics Shivlingeshwar College of Pharmacy, Almala Dist. Latur-413520, Maharashtra (MH), India.

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ABSTRACT

One novel approach in this area is GRDDS (Gastro Retentive Drug Delivery System). Gastroretentive drug delivery systems (GRDDs) are designed to prolong the residence time of a drug in the stomach. This can be beneficial for drugs that are destroyed by stomach acid or that need to be delivered in a sustained-release manner. GRDDs are a promising new technology for improving the delivery of drugs to the gastrointestinal tract. They have the potential to improve the efficacy and safety of drugs, and to reduce the number of side effects. In recent decades, many efforts have been made in order to improve drug bioavailability after oral administration. Gastroretentive drug delivery systems are a good example; they emerged to enhance the bioavailability and effectiveness of drugs with a narrow absorption window in the upper gastrointestinal tract and/or to promote local activity in the stomach and duodenum. Several strategies are used to increase the gastric residence time, namely bio adhesive or mucoadhesive systems, expandable systems, high-density systems, floating systems, super porous hydrogels and magnetic systems. The frequency of drug administration depends on its half-life, or means residence time (MRT), and its therapeutic index. GRDDs are a promising new technology for improving the delivery of drugs to the gastrointestinal tract. They have the potential to improve the efficacy and safety of drugs, and to reduce the number of side effects.

KEYWORDS: Gastro retentive drug delivery system (GRDDs); CR; Conventional Drug Dosage Form; Bioavailability; Gastric Retention Time, Narrow absorption window, Raft forming system.

1. INTRODUCTION

The verbal organization course has continuously expected a part of noticeable quality in treatment due to its well-established focal points. A few components make this course ideal to patients, and these definitions are too less costly, simple to transport and store, adaptable in terms of the constituents, and prepared to administer.[1] However, verbal organization faces a few physiological limitations due to the heterogeneity of the gastrointestinal framework. In expansion, a few factors alter all through the gastrointestinal tractandgreatly impact sedate assimilation. Among these components, the commensal vegetation, gastrointestinal travel time, enzymatic movement and surface region are the foremost important.[2] Customary frameworks are not sufficient to overcome all the troubles forced by the gastrointestinal tract. For occurrence, they are unseemly for drugs that are specially retained within the upper part of the stomach related framework since routine details don't have the capacity to confront gastric purging; subsequently, they cannot be discharged within the colon where they remain amid the ultimate period of their discharge time. Hence, the inadequate discharge of drugs and the concomitant diminishment of measurements viability are results of the inadequacy of the ordinary frameworks to be held at the stomachlevel.[3] In arrange to overcome these misfortunes, innovative analysts have created pharmaceutical frameworks that control medicate discharge and the home time, a few of which are as of now accessible on the advertise. The disappointment in gastric maintenance with customary frameworks has driven to the advancement of verbal gastroretentive frameworks. Such conveyance frameworks were outlined to be held within the upper gastrointestinal tract for a delayed period of time, amid which they discharge the medicate on a controlled premise. The amplified contact of gastroretentive frameworks with the retaining film permits an increment in sedate bioavailability.[4] Extra focal points of these frameworks include.[5] (i) an enhancement in helpful viability, (ii) a decrease in medicate misfortune, (iii) an increment in medicate dissolvability in cases with moo solvency in a tall pH environment, and (iv) benefits due to the conveyance of drugs that act locally within the stomach and duodenum.

A few procedures have been studied to define effective controlled medicate conveyance systems that increment the gastric home time such as bioadhesive or mucoadhesive frameworks, expandable frameworks, high-density frameworks, drifting frameworks, superporous hydrogels, and attractive frameworks.[6] This audit compiles significant data around the drugs that can advantage from gastroretention techniques, the variables that impact their gastric maintenance time, the component of activity of gastroretention, as well as their introduction as single and different unit frameworks.

Short-half-life drugs and simple assimilation from the GIT are rapidly expelled from the systemic circulation. To guarantee suitable restorative action, these drugs must be dosed regularly. The advancement of verbal maintained controlled release details endeavours to overcome this confinement by steadily discharging the medicine into the GIT whereas protecting drugs concentration that's productive within the systemic circulation for a longer length of time. Using such sedate conveyance would remain within the stomach after verbal organization and discharge the medicine in a controlled way, allowing the sedate to be ceaselessly provided to its retention locales within the GIT.[7] GRDD gadgets offer assistance with drug absorption over the predetermined period of time by remaining for a longer period of time in the stomach than routine site-specific medicate conveyance systems. The taking after moves forward as a result:

The bioavailability, diminish medicate squander, improves the solvency of medicines which are less solvent in situations with tall pH levels (such as feebly essential medicines like domperidone and papaverine), it moreover makes a difference in getting sedate deliveryloacally to the stomach and proximal little digestive system. When making a site-specific orally given controlled discharge measurement frame, it is alluring to set up longer gastro home term by means of sedate conveyance. Furthermore, drawn out gastric maintenance of the restorative moiety can offer a number of preferences for the nearby and drawn-out conveyance of drugs to the stomach and proximalsmall digestive system to treat certain disarranges, counting:

Moved forward bioavailability, progressed helpful viability, Conceivable dosage decrease, Progresses the drug solubility, which is less solvent in tall pH environment for case, pitifully essential drugs like Domperidone, papaverine, etc., Reduce drug squander, offer assistance in accomplishing neighbourhood medicate conveyance to the stomach and proximal small intestine. For nearby activity within the upper section of the little digestive tract, such as the treatment of peptic ulcers, delayed gastric retention time within the stomach may be advantageous.[8] Verbal dosage details for stomach maintenance have gotten expanding intrigued in later years due to their restorative advantage in allowing control over the timing and location of medicine discharge. Numerous drugs classified as once-a day conveyance have illustrated on dose frame travel time.[9] As a result, a framework intended for amplified stomach maintenance will expand the time accessible for sedate assimilation within the little digestive system. The instrument of strong dosage shapes controlled gastric maintenance may incorporate Buoyancy, Sedimentation, Extension, Adjusted shape frameworks or by the simultaneous administration of pharmacological operators that delay gastric purging.

Floating systems

These frameworks are made of materials that are less thick than gastric liquid, so they coast on best of the liquid and are not easily emptied by peristalsis.

Mucoadhesive systems

These frameworks follow to the lining of the stomach, making it more difficult for them to be moved by peristalsis.

Magnetic systems: These frameworks contain attractive particles that can be controlled by an outside attractive field. This can be utilized to keep the framework in a particular area within the stomach.

Expandable systems: These systems extend in the stomach, making it more troublesome for them to be emptied.[1-3]

1.1 ADVANTAGES OF GRDDS

1. Conveyance of pharmaceutical to the little digestive system with a constrained window of assimilation.
2. More prominent time went through within the stomach may be beneficial for neighbourhoods' action within the upper little digestive system.
3. Way better bioavailability (Cadwell,1988)
4. Persistent compliance, progressed helpful viability, decrease measurements recurrence, and focused on treatment for neighbourhood activity in upper GI tract are all benefits.
5. Enhancements in medicine bioavailability, restorative adequacy, and taken a toll- viable measurements.
6. Diminish the probability of anti-microbial resistance by killing swings and balancing out restorative dosages all through time.
7. For pharmaceutical with a brief half – life, advanced discharge comes about in flip – tumble pharmaceutics, which guarantees quiet compliance with lower measurement recurrence.
8. They give assurance from the gastric maintenance time (GRT).
9. Stomach purging period (GET). Due to its lower bulk thickness than stomach liquids, the framework keeps up its buoyancy.
10. These are successful in treating issues with the stomach and small digestive system. It is accepted that this is often since gastro – retentive pharmaceutical conveyance keeps up medicate

discharge and so makes neighbourhood treatment accessible in these organs.

11. This approach offers a deliberate, controlled component for sedate conveyance that diminish the probability of sedate overexposure at the debilitated location.

1.2 DISADVANTAGES

1) When it comes to drugs that shouldn't be used in an acidic environment, GRDDS is inappropriate.
2) It is not suitable for drugs that are best absorbed in the lower part of the GIT.
3) The difficulty in achieving the desired result and the problem with dosage dumping.
4) Inadequate in vivo and in vitro connection.
5) The formulation is expensive.

2) Drug Conditions Suitable for gastroretention

Selecting drugs for Gastroretentive Drug Delivery Systems (GRDDs) involves considering various factors to ensure that the chosen drug is suitable for such a delivery approach. The key drug selection criteria for GRDDS:

- **Poor Solubility and Low Permeability:** GRDDs are particularly useful for drugs with poor solubility and low permeability in the gastrointestinal tract. These drugs often have limited absorption in the upper GI tract, and prolonging their residence time can enhance bioavailability.
- **Narrow Absorption Window:** Drugs with a narrow absorption window in the stomach or upper small intestine can benefit from GRDDS. These systems can ensure that the drug remains in the absorption site for an extended period, increasing the chances of absorption.
- **Reliant on pH Absorption:** Some medications have stability or solubility that varies with pH. To ensure the best possible absorption, GRDDS can be made to release the medication in reaction to the stomach's pH.
- **High First-Pass Metabolism:** Gastroretentive delivery may be advantageous for medications undergoing substantial first-pass metabolism in the liver. The medication can initially avoid the liver by staying exposed in the stomach for a longer period of time, which lowers metabolism and increases systemic bioavailability.
- **Local Action in the Stomach:** Antacids and medications for the treatment of peptic ulcers and gastroesophageal reflux disease (GERD) are examples of pharmaceuticals with a local action in the stomach that are appropriate candidates for GRDDS.
- **Food Interactions:** Certain medications may react negatively to changes in stomach pH or interact with meals.
- GRDDS can be made to minimize food interactions or to regulate the drug's release when food is present.[3]
- **Chronic illnesses:** GRDDS may benefit from medications used to treat chronic illnesses like diabetes or hypertension when ongoing therapeutic levels are required.
- **Drug Stability:** It's critical that a medication remain stable in the gastrointestinal tract. Until the medicine is released at the desired site of absorption, it should stay stable within the GRDDS.
- **Toxicity and Side consequences:** When choosing candidates for GRDDS, it's critical to take into account any possible toxic consequences or adverse medication reactions. Extended drug exposure in the upper gastrointestinal system or stomach shouldn't make a substance more hazardous.[10–11]

These same standards apply to the medicine of choice, and the GRDDS formulation complies with legal regulations and specifications for drug delivery systems.

Table 01: Examples of Drug and GRDDS Drug selection criterion.

Drug Selection Criteria	Example Drugs selected
Solubility	Poorly soluble in the small intestine but soluble in the stomach: Ranitidine, Metformin
Stability	Stable in the acidic environment of the stomach: Ranitidine, Sucralfate
Absorption	Absorbed in the stomach or upper small intestine: Ranitidine, Ondansetron
Pharmacokinetics	Has a long half-life so that it can be released over an extended period of time: Metformin, Ondansetron
Safety	Safe to be released in the stomach: Ranitidine, Sucralfate
Tolerability	Well-tolerated by patients: Ranitidine, Ondansetron

A thorough assessment of these factors should be part of the medication selection process for GRDDS in order to ascertain the viability and possible advantages of this drug delivery strategy. Furthermore, in the development phase, cooperation with regulatory specialists, formulation specialists, and pharmaceutical scientists is crucial. Drugs with a short half-life are frequently delivered via GRDDS since this keeps the drug level in the bloodstream consistent.[12]

3) NEED FOR GRDDS

There are several reasons why a drug might need to be delivered in a gastroretentive drug delivery system (GRDDs).

The most common reasons include as following:
A medicine may need to be administered via a gastroretentive drug delivery system (GRDD) for a number of reasons. Among the most frequent causes are the following:

a) **To improve the bioavailability of the drug**: Certain medications are better absorbed in the stomach than in the small intestine where they are less well absorbed. By retaining these medications in the stomach for an extended amount of time, GRDDs can aid in boosting their bioavailability.
b) **To provide a sustained release of the drug**: GRDDs can be made to release the medication gradually, which can aid in preserving a steady concentration of the medication in the blood. For medications that must be taken once day or more, this can be advantageous.
c) **To protect the drug from stomach acid:** Certain medications are acid sensitive and risk being ruined if not shielded. By reducing the length of time these medications are in the stomach or by covering them in a layer that shields them from the acid, GRDDs can aid in their protection.
d) **To target the drug to the stomach:** For some medications to work, the stomach must receive them. By decreasing the likelihood of these medications being absorbed in the small intestine, GRDDS can aid in directing them toward the stomach.[13]

4. Physiology of stomach

The medicine, the patient, and the doctor's preferences will all determine whether or not GRDDS is specifically required. The unique properties of the medication, the therapeutic indication, the patient's preferences, and regulatory concerns all influence the necessity or prerequisites for GRDDS. Researchers and pharmaceutical companies frequently evaluate these variables to decide if creating a gastroprotective drug delivery system is advantageous and warranted for a specific medication. The GRDDs is a multi-phase drug delivery and elimination process.

GRDDs motility pattern are depicted in Table 02, with a description provided below.

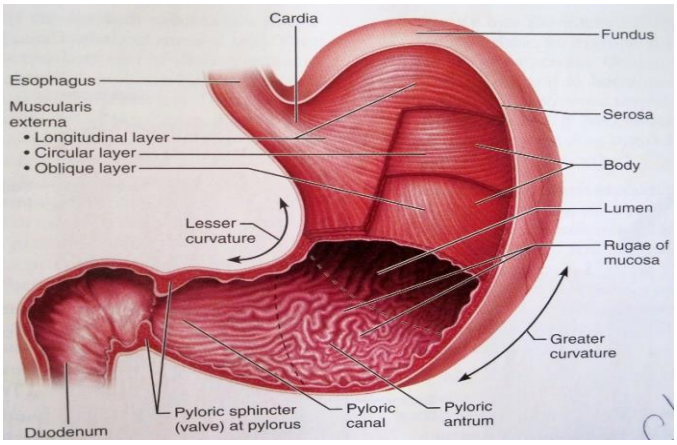

Fig.1: Motility Pattern.

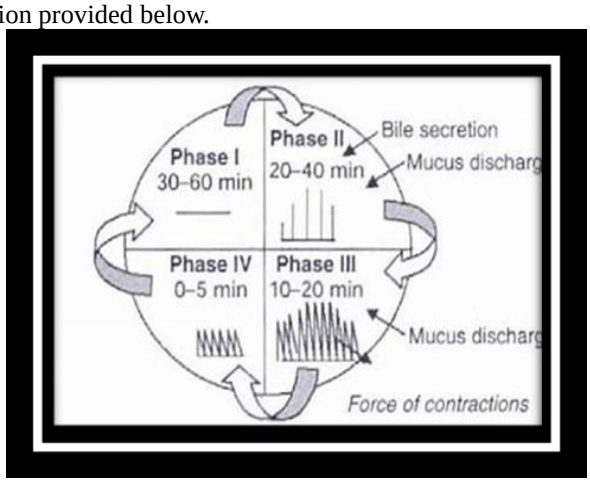

Fig.2: Git Phases.

Table 02: The phases and timing of GRDDS motility pattern respectively.

Phases	Description	Timing
Phase I	Liquid phase: The drug is released in the liquid phase of the stomach. This phase is typically very short, lasting only a few minutes	**Immediately after administration**
Phase II	Dispersion phase: The drug is dispersed in the stomach contents. This phase can last for several hours	**0-3 hours**
Phase III	Floating phase: The drug forms a floating layer on top of the stomach contents. This phase can last for several hours to days.	**0-24 hours**
Phase IV	Adhesion phase: The drug adheres to the lining of the stomach. This phase can last for several days to weeks.	**24-168 hours**
Phase V	Release phase: The drug is released from the dosage form and is absorbed into the bloodstream. This phase can last for several days to weeks	**24-168 hours**

5. GASTRORETENTIVE DRUG DELIVERY SYSTEMS (GRDDs) VS. CONVENTIONAL DRUG DELIVERY SYSTEMS (CRDDs)

The applications, drug release processes, and designs of gastroprotective drug delivery systems (GRDDs) and conventional drug delivery systems (CRDDs) are highly different. GRDDs are customized drug delivery devices made to extend a medication's half-life in the stomach or upper gastrointestinal tract.[14] GRDDs are primarily intended to improve drug absorption by keeping the

medicine in the stomach area for a longer amount of time. The standard pharmaceutical dosage forms that are frequently employed for medication administration are referred to as conventional drug delivery systems. These include injectables, syrups, pills, capsules, and other forms in which the medicatiousually absorbed and delivered throughout the gastrointestinal tract.

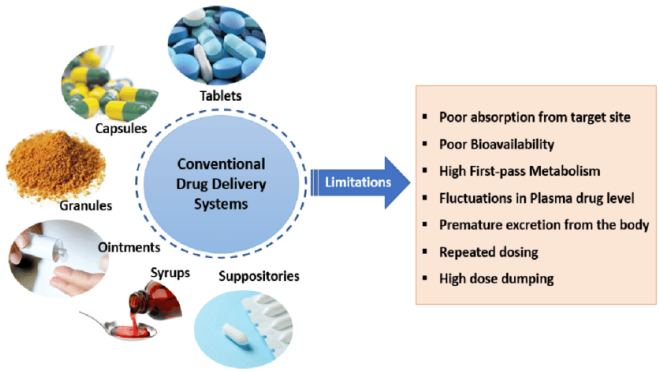

Fig.3: CRDDS.

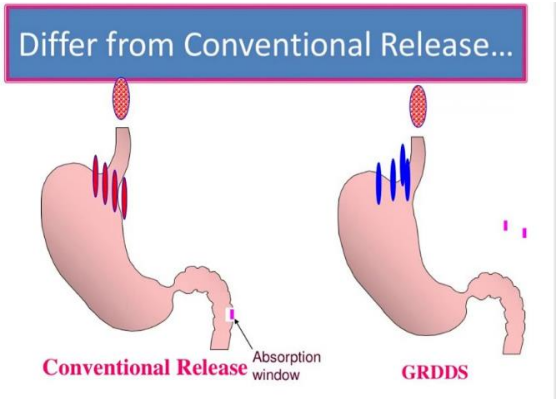

Fig .4: Crdds and Grdds Release.

Table 03 mentions the diversion in GRDDs and CRDDs as follows.

Table 03: The differences between gastroretentive drug delivery systems (GRDDs) and conventional drug delivery systems (CRDDs) in terms of features.

Features	GRDDs Description	CRDDs Description
Purpose	To prolong the residence time of a drug in the stomach.	To deliver the drug to the small intestine as quickly as possible
Mechanism	Uses various mechanisms to keep the drug in the stomach, such as floating, swelling, mucoadhesion, and magnetic targeting.	Does not use any mechanisms to keep the drug in the stomach
Drugs	Suitable for drugs that are poorly absorbed in the small intestine, sensitive to stomach acid, or need to be delivered to the stomach.	Suitable for a wider range of drugs.
Side effects	May cause nausea, vomiting, or other side effects due to the harsh environment of the stomach.	Less likely to cause side effects.
Efficiency	More efficient at delivering drugs to the stomach.	Less efficient at delivering drugs to the stomach
Patient compliance	May be more difficult for patients to take GRDDs consistently due to the need to take them with food or on an empty stomach	CRDDs are easier for patients to take consistently

A key component of gastroretentive drug delivery systems (GRDDs) is the stomach. The upper abdomen contains a muscular pouch called the stomach. It is in charge of breaking down, storing, and combining food with the digestive juices. Enzymes and hydrochloric acid are found in the stomach juices, which aid in the breakdown of food.

5.1 FACTORS AFFECTING GASTRIC RETENTION TIME OF THE GRDDS[15]

The elements listed below have an impact on GRDDS's performance and stability:

1. Density of dose form: dose forms with a density of less than stomach fluids (~1.004g/ml) frequently demonstrate good floating properties. While high-density systems require a density closer to 2.7g/ml in order to achieve adequate gastro-retention.

2. The dose form's size: Because the bigger particle size prevents the dosage form from passing through the pyloric antrum and into the intestine quickly, dosage forms with a diameter of more than 7.5mm have longer gastric retention times.

3. Dosage form shape: Tetrahedron- and ring-shaped devices exhibit superior gastroprotection in comparison to other forms.

4. Fed or unfed state: When fasting, the stomach's undigested material is frequently carried away by powerful waves of the Migrating Myoelectric Cycle (MMC). If the timing of the dose matches that of MMC, there will be less gastroretention.

5. Meal composition: Feeding indigestible polymers or fatty acid salts, such as cellulose or starch, might alter the stomach's motility pattern, delaying the MMC, slowing down the pace of gastric emptying, and prolonging the release of drugs.

6. Caloric content: A high-protein and high-fat meal can cause a 4–10 hour increases in GRT.

7. Feed frequency: Due to the low frequency of feeding, GRT can be enhanced over a period of 6 to 7 hours with continuous meals as opposed to a single meal.
8. Age: The GRT is noticeably longer in individuals over 70.
9. Gender: Compared to their age- and race-matched female counterparts (4.6h), men have a lower mean GRT (3.4h).
10. Posture: For people in the upright, ambulatory, and supine states, there was no discernible impact of posture on GRT.

6. CURRENT PHARMACEUTICALS APPROACHES OF GASTROINTESTINAL DRUG DELIVERY SYSTEM (GRDDs)

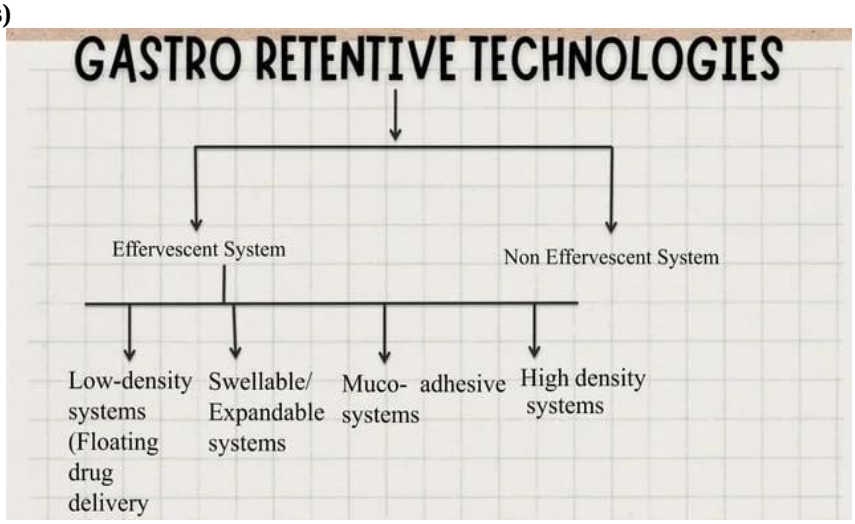

Fig.5: classification of GRDDS.

1. High-density system: The density of the dosage form is an important factor in the formulation of the GRDDS. A high-density system's weight acts as a retention mechanism. A drug's density must be greater in the stomach than the typical stomach content (1.004 g/mL) in order for it to work better there. When a system's density equals 3 g/ml, it can be stored in the stomach and tolerate peristaltic movements throughout this time. Gastric fluid has a density of 1.004 g/ml, which is the same as that of water. They use iron powder, zinc oxide, titanium dioxide, and barium sulphate to increase the retention period.

2. floating or low-density system: This strategy involves making the dosage form less dense than the typical gastric content in order to enhance gastric residency. J. Davis introduced this technique for the first time in 1968. It is also known as hydrodynamically balanced systems. Less than 1.004 g/cm should be the bulk density for floating. Consequently, they allow a dosage form to linger in the stomach for a longer amount of time. A prolonged stomach retention period and increased medicine absorption can be achieved with these crucial tactics. Among the two types are low-density systems and floating systems.

a) Effervescent systems
b) non-effervescent systems

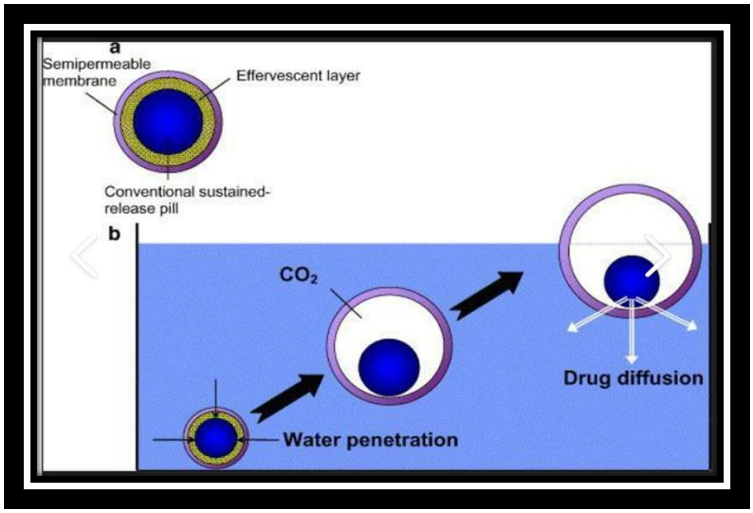

Fig. 6: Effervescent systems.

a) Effervescent systems

These formulations include release-retardant polymers, xanthan gum, eudragit L100, ethyl cellulose, and polyethylene oxide (PEO)N12K. By mixing hydrophilic polymers, the gas-producing component in that mixture increases the tablet's buoyancy in gastro floating systems.

Since no thorough investigation has been done to date, it is imperative to look at the impact of sodium bicarbonate's function in the effervescent process on the drug release kinetics of more water-soluble drugs. Typically, the gas-entrapped membrane was discovered during storage, which led to issues with sustained release and floating. Applying tale as an anti-tacking agent in conjunction with glyceryl monostearate can resolve these issues.

It is categorized into three types

(i) Gas generating systems: When the mixture is added to a beaker, it sinks and rises and floats due to the effervescent interaction between the carbonate/bicarbonate salts, citric/tartic acid, and CO2. This reaction occurs in the presence of water.

(ii) System holding volatile liquid: It consists of a liquid, such ether, in an inflatable chamber that expands the stomach chamber by producing gas at body temperature. This inflated container contains a gelatine capsule that holds a pool of drugs. The pharmaceutical reservoir and balloon are released from the capsule after ingestion. due to the incorporation of bicarbonates or carbonates and their interaction with the stomach area, which results in the production of CO2 gas bubbles.

(iii) Raft forming systems: This process creates a thick gel with trapped carbon dioxide bubbles when stomach juice reacts with carbonates or bicarbonates. Antacids such as aluminium hydroxide or calcium carbonate are commonly added to formulations to lessen gastric acidity. They create a layer on top of gastric fluids, which are commonly used in GI treatments[13] and resemble water.

b) Non-effervescent systems: Originally described by Sheth PR and Tossounlan J in 1984, the main advantages of non-effervescent systems are the stability of acid- or base-labile pharmaceuticals and the fact that gastric pH is unaffected by floating lag time. When the medication in non-effervescent floating systems comes into touch with stomach fluid, it expands. Because it maintains its shape and has a density of less than one, it floats in gastric fluid. Hydrocolloids of the swellable kind, matrix-forming polymers, or gel-forming materials are used for these kinds of floating systems [1]. An ideal dispersion of a combination of swellable and action retardant polymers, such as polyethylene oxide and xanthan gum, was used to construct the tablet. Drugs containing gel-forming agents, hydrocolloids of the swellable cellulose type, polysaccharides, and matrix-forming agents are also included in the hydrodynamically balanced system. Polymers lengthen gastrointestinal stays and improve drug absorption. Microporous compartment systems are composed of drug encapsulation reservoirs inside microporous compartment pores.

Because of the trapped air in the flotation chamber, the gadget can float over stomach contents.[15,16]

They are further classified as follows

(i). Hydrodynamically balanced systems (HBS): The main component of these devices is a drug-hydrocolloid mixture that, upon swelling, forms a gelatinous barrier upon contact with gastric juice. It floats in the stomach for a long time because its bulk density is lower than that of gastric fluid. By using HPMC, polyethylene oxide can be optimally disseminated in xanthan gum and other swellable, action-retardant polymers. Drugs containing gel-forming agents, hydrocolloids of the swellable cellulose type, polysaccharides, and matrix-forming agents are also included in the hydrodynamically balanced system. Polymers lengthen gastrointestinal stays and improve drug absorption. Microporous compartment systems are composed of drug encapsulation reservoirs inside microporous compartment pores.

(ii) Micro ballooning: Micro ballooning is the technique of progressively adding a drug-containing emulsion into a volatile solvent. When the solvent evaporates and produces gas in a dispersed polymer droplet, an inner opening form in the drug's polymer microsphere. Another term for it is the diffusion method of emulsion solvents. The kind and amount of polymer used in the formulation have an impact on how long the microspheres float.

(iii)Alginate beads: The interlocking agents in these systems are made of sodium alginate and a hydrocolloid gel-forming agent. The hydrocolloid absorbs water from the stomach juice and forms a barrier that traps air inside the polymer, causing the polymer to inflate. Consequently, the dose form starts to float, releasing the drug gradually.

3. Mucoadhesive and bioadhesive systems: The mechanism of mucoadhesive drug delivery systems involves utilizing the bio adhesion property of a particular polymer, which becomes adhesive when hydrated and permits the distribution of a medication to a particular region of the body for extended periods of time. When two materials are held together by interfacial forces, at least one of which is biological, the phenomenon known as "bio adhesion" takes place. One example of how an artificial substance and biological substrate could attach is adhesion between a polymer and a biological membrane. The term "mucoadhesion" describes a polymer that is attached to the mucin layer of mucosal tissue.

There are several ways to provide mucoadhesive drug delivery systems

- Delivery mechanism for buccal
- System of oral delivery
- Delivery method via vagina
- Delivery mechanism for rectal
- Nasal delivery method
- Delivery mechanism for eyes

Usually, bioadhesive or mucoadhesive polymers are used for this. Natural polymers like sodium alginate, gelatine, guar gum, etc., as well as semisynthetic polymers like HPMC, lectins, Carbopol, and sodium carboxymethyl cellulose, are widely used for mucoadhesion. In the adhesion process, receptor contacts, bonding, or hydration are all important.[19]

4. Swelling system: Because these systems are larger than the pyloric sphincter, they swell when they come into contact with stomach fluid. They consequently remain stuck in the stomach. These are also known as "plug type systems. "Medication release can be controlled and delayed using the appropriate excipient. The key factor that determines the polymer's swelling ability is the degree of cross-linking within the hydrophilic polymer network. Significant swelling and rapid polymer breakdown occur when there is insufficient cross-linking, whereas a high degree of cross-linking preserves the system.[20]

5. Superporous hydrogels: A superporous hydrogel is a three-dimensional network of hydrophilic polymers that contain numerous super-sized pores. It is by capillary wetting through networked open pores that superporous hydrogels swell. To make superporous hydrogels, a few ingredients—initiators and cross-linkers, for example—are used to initiate the cross-linking process. Other ingredients included foam stabilizers, foaming agents, and foaming aids.

6. Magnetic system: This method applies a strong magnet with a potent magnetic field to the body surface to control the movement of a gastroretentive formulation with a small internal magnet. Several studies demonstrate the benefits of the system; nevertheless, in order for the system to function well, the magnet position needs to be selected extremely precisely.

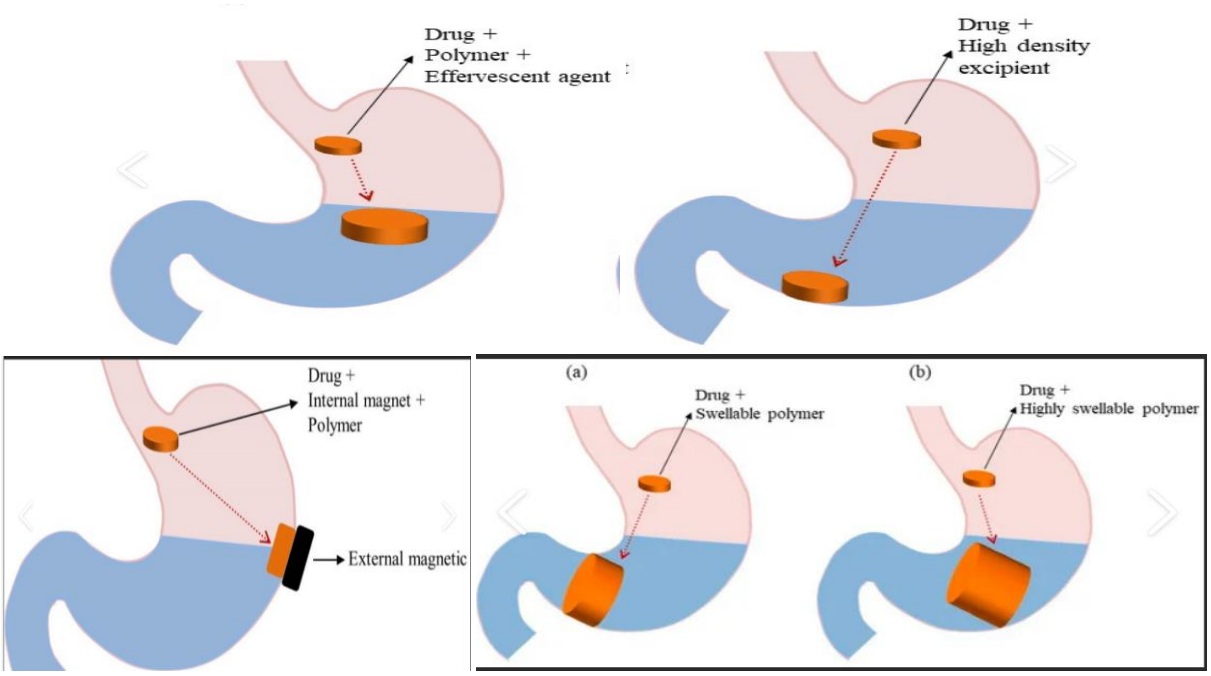

Fig. 7: GRDDS System.

Techniques for Getting the Gastro-Retentive Multiparticulates System Ready.

1. Method of Solvent Evaporation

Solvent diffusion and evaporation techniques can be employed to create the hollow inner core of a floating multiparticulates dosage form. The polymer solution, which has been dissolved in an organic solvent, contains either dissolved or dispersed medication. The medication solution is then emulsified into an aqueous phase with the appropriate component (surfactants/polymer) to produce an oil in water emulsion. The organic solvent is removed from the mixture either by stirring continuously or by increasing the temperature while applying pressure once a stable emulsion has formed.[25, 26] When the solvent is removed from the oil/water interface of droplets, polymer precipitation occurs, creating cavities and hollowing them out to give them their floating characteristics. Polymers like cellulose acetate, chitosan, Eudragit, Acrycoat, Methocil, polyacrylates, polyvinyl acetate, Carbopol, agar, polyethylene oxide, and

polycarbonates have all been researched in order to produce such systems.[18]

2. The Method of Ionotropic Gelation: The ability of poly electrolytes to cross link and form beads in the presence of opposing ions is what supports ionotropic gelation. With the usage of alginates, gellan gum, chitosan, and carboxymethyl cellulose for medicine and cell encapsulation, the ionotropic gelation approach has gained popularity.[28] Natural poly electrolytes have some anions in their chemical structure, despite the fact that they cover the drug core and slow down the rate of release. These anions interact with polyvalent cations to form meshwork structures and adhere mostly to anion blocks, which facilitates gelation. The hydrogel beads are produced by dropping a drug-loaded polymeric solution into an aqueous solution containing polyvalent cations.[29]

3. Diffusion of Emulsion Solvent Method: In comparison to the aqueous solvent, the drug and organic solvent have a better affinity when using the emulsion solvent diffusion method. The drug dissolves in the organic solvent, which is miscible, and the solution is then distributed in the aqueous solvent to form emulsion droplets. The aqueous phase diffuses into the droplets that crystallize the drug, while the organic solvent gradually diffuses out of the emulsion droplets into the surrounding aqueous phase.

4. A New Approach to Foam Powder: Additionally, a novel in vitro drug delivery technique utilizing low-density foam powder for multi-particulate gastroretentive therapy has been demonstrated and evaluated.[30] An oil-in-water solvent extraction/evaporation method was used to make floating microparticles utilizing polypropylene foam powder, Eudragit RS, ethyl cellulose, or poly (methyl methacrylate), and verapamil hydrochloride (as the model drug). The drug and the polymer that regulated the release rate were dissolved in methylene chloride. The powdered polypropylene foam was then dissolved within this organic phase. To enable the formation of microparticles, the resulting suspension was further emulsified in an external aqueous poly (vinyl alcohol) solution and agitated. Because the microparticles were very porous and irregular in shape, they were sieved, cleaned with water, and dried in a desiccator. Crucially, the drug encapsulation efficiency was high and almost unaffected by the predicted loading of the system. In every instance, good invitro floating behaviour was observed. The compositions under examination yielded very diverse release patterns. Subsequent investigations cantered on devising an enhanced manufacturing process for this kind of low density, foam-derived, buoyant microparticle and showcasing the system's in vitro capabilities.[31] The novel preparation method that has been suggested has a number of benefits, such as short processing times, the ability to avoid damaging organic solvents, low temperature exposure of the materials, and high encapsulation efficiencies. The process of creating floating microparticles involved soaking microporous foam particles in an organic drug and polymer solution, then drying them off.[32] The majority of the time, good in-vitro floating behaviour was seen, and by varying the drug loading and kind of second polymer, a variety of drug release patterns could be produced.[43]

5. The Melt Granulation Method Using a technique called melt granulation, granules are created by using a solid binder that melts during the process, or a molten binder. This is sometimes referred to as thermoplastic granulation or melt agglomeration.

The Melt Granulation Principle

Three steps are combined to form the granulation process:

a) Wetting and nucleation,

The process of wetting and nucleation

Tiny agglomerates are produced when the binder and powder bed come into contact during the nucleation process. Two mechanisms of nucleation are proposed by mSchafer and Mathiesen.

Submersion

Nucleation by immersion occurs when the molten binder droplets' size exceeds that of the tiny solid particles. As immersion continues, fine solid particles are deposited onto the surfaces of molten binder droplets.

Distribution

Using the distribution approach, a molten binding liquid is applied to the surfaces of small solid particles. The nuclei are created when the wetted particles collide. Large shearing pressures, low binder viscosity, and small binder droplet sizes are frequently favourable conditions for nucleation using the distribution technique.

b. Step of coalescence

It involves nuclei with residual surface liquid to boost the success rate of fusion nuclei.

The surface liquid provides the nuclei with their plasticity and is essential for the nuclei's surface to undergo deformation during coalescence and to aid in the rounding of granules.

c. Breakage and attrition: Granulation fragmentation events such as breakage and attrition are solidified by tray cooling to room temperature, eliminating the requirement for tumbling drying. Therefore, during the granulation phase, breaking is known to have a greater impact on the melt granulation's final properties.

The requirements for melt granulation Meltable binder concentrations of 10–30% w/w are typically used in place of fine solid particles.

The melting point of a meltable binder that is appropriate for granulation is usually between 50 and 100°C.

For the creation of immediate-release dosage forms, hydrophilic meltable binders are used, while hydrophobic meltable binders are the preferred choice for the creation of formulations with a longer release. Melting points of fine solid particles ought to be at least 20°C higher than the highest processing temperature.

6. Adhesive Polymers stability both chemically and physically. It must melt between 40 and 80°C and be solid at room temperature. Its hydrophilic-lipophilic balance (HLB) guarantees appropriate release of the active component.

Two varieties of meltable binder exist
a) Meltable hydrophilic binders
b) Meltable hydrophobic binder

Polymeric Substances Gastroprotective Formulations

1. HPMC, or hydroxypropyl methyl cellulose

The most often used hydrophilic carrier material in the production of oral controlled drug delivery systems is hydroxypropyl methylcellulose (HPMC).[28] In HPMC, also referred to as Hypromellose, a cellulose ether, one or more of the three hydroxyl groups from the cellulose glucopyranose units have been altered, forming ether linkages. As a result, it is a semisynthetic polymer made from very pure natural pulp that is etherified using a methyl chloride and propylene oxide mixture to produce a non-ionic, water-soluble cellulose ether.[29] The two brands under which the most widely used HPMC is marketed are Methocel® and Pharmacoat®.

2. Hydroxyethyl and hydroxypropyl cellulose (HEC and HPC): Because HPC has a low Tg, meaning that the formulations may be processed at a low temperature, it has been employed as the main matrix forming polymer in formulations manufactured using hot-melt extrusion and 3D printing processes. The creation of bioadhesive films has been shown to be possible with HPC.[30] After examining the impact of various additives on the bioadhesive qualities of HPC-based films, it was found that, in comparison to films containing HPC and PEG 3350, the incorporation of Carbomer 971P and a polycarbophil into HPC films greatly enhanced bio adhesion. In order to gel and thicken biostructures that are intended to deliver hydrophobic medications, hydroxyethyl cellulose (HEC) is utilized.

For instance, enalapril mucoadhesive films that exhibited controlled drug release and favourable swelling properties were produced by combining sodium carboxymethylcellulose with HEC.[31] Hydroxyethyl cellulose (HEC) has been included into multicomponent polymeric matrices to provide the necessary gastro-retentive properties, much like HPC. It has been possible to successfully make pentoxifylline effervescent floating tablets by using, for example, a polymeric matrix consisting of sodium alginate and HEC and sodium bicarbonate as a gas-forming agent.

3. Cellulose Carboxymethyl Ether (CMC): Carboxymethyl cellulose (CMC) is a water-soluble, semisynthetic, nontoxic cellulose derivative that has carboxymethyl groups (-CH2-COOH) bonded to some of the hydroxyl groups of the glucopyranose repeating units of the cellulose backbone via an ether bond. NaCMC's anionic carboxylate groups may enhance the gel-viscosity properties of non-ionic hydrocolloids like HPMC and HEC through interactions with them.[31]

4. Organic Gums: Drug release from swellable systems has been effectively controlled by the use of natural polymers as hydrocolloids in addition to synthetic cellulose ethers.[32] Natural polymers have many useful uses in biology and medicine because they have advantageous qualities including safety and biocompatibility. Together with other polysaccharides like chitosan and alginates as well as natural polymers like pectin and gelatine, natural gums such as xanthan gum, guar gum, gellan gum, and carrageenan's are natural hydrocolloids or gel-forming agents that can swell in contact with gastric fluid, maintain relative shape integrity, and have a bulk density less than the gastric content.[23,29]

5. Guar gum: is obtained from the seeds of the legume family plant Cymopsistetragonolobus. Guar gum swells quickly in the presence of water with a translucent suspension because of its dual composition, which consists of an insoluble component and an approximately 85% water-soluble portion known as guaran. Because of the mannose units, cohesive structural gels are formed when borate ions are added to hydrated guar gum.[29] In the pharmaceutical business, guar gum improves viscosity and functions as a disintegrant and binder when used in solid dosage forms.[33]

6. Carrageenan's: are high molecular weight anionic polysaccharides derived from red seaweeds in the Rhodophyceae family. They were effective as tablet excipient agents due to their great durability, good compatibility, and persistent viscoelasticity of the tablet throughout granulation and compression. Thus, carrageenan's make good excipients for formulations that operate slowly. Interestingly, it was discovered that the carrageenan's' real densities were significantly higher than those of the cellulose ethers (MC, HPMC, NaCMC's, and HPC).[33]

7. Gum Gellan: Gellan gum works as a crosslinking agent when Ca2+ ions are present, which allows for in-situ gel formation. When coupled with Ca2+ ions, gellan gum can be used as a crosslinking agent in in-situ gels.

8. Gum Xanthan: Xanthan gum is utilized in food, cosmetics, and topical and oral medication formulations due to its non-toxicity and non-irritating properties.

Its existence affects the drug release From Formulations zero-order kinetics.[34]

9. Carbomers, Carbopol, and Polycarbophyl (PCP): are examples of crosslinked polyacrylates. Carbomers are high molecular weight synthetic polyacrylic acids that are crosslinked with polyalcohol allyl ethers, such as polyallyl sucrose and pentaerythritol polyallylether. The physical structure and chemical composition, crosslink density, crosslinking type, crosslinking solvent, network electrical charge, and physical appearance of different Carbopol polymer grades affect their performance. For usage as controlled release polymers in matrix tablets, carbomers need polymer ratios between 3 and 30%. Generally speaking, Carbopol and polycarbophil hydrogels are very permeable to a variety of pharmacological compounds and can be made to "swell," releasing molecules that have been trapped thanks to their structure, which resembles a network.[35,36] By adjusting the polymer concentration, the drug release can be precisely controlled.

10. Poly (ethylene oxide) (PEO): increased molecular weight Because PEO's rate of swelling and erosion permits APIs to be released continuously, it has been employed successfully in controlled release dosage forms. increased molecular weight Because PEO may form dense polymeric networks in aqueous settings, it is viscoelastic in its inflated condition.[27] PEO is therefore useful as an addition to enhance the mechanical characteristics of extremely swellable and robust matrix tablets.

11. The Kollidon SR: Kollidon SR is a combination of povidone (poly (N-vinyl pyrrolidone)) and poly (vinyl acetate) (PVAc) that is primarily utilized as a matrix retarding agent. For the production of pH-independent sustained-release matrix tablets, direct compression or hot melt extrusion are the best options. PVAc is a polymeric material that creates a cohesive matrix even under low compression pressures. The water-soluble PVP in the tablets is leached out when they breakdown in stomach or intestinal fluid, creating holes that allow the active substance to gradually seep through. Because Kollidon SR doesn't include ionic groups, it is drug compound inert and retains its sustained-release characteristics in the presence of ions or salts.[38]

6.1 Assessment of the gastro-retentive dose form

1. Buoyancy lag time: It is measured to see how long it takes the dosage form to float on top of the dissolving liquid once it is submerged in it. The dissolving test may include measurements of these factors.

2. Density / Specific Gravity: Density can be computed by the displacement method with benzene serving as the displacement medium.

3. Resultant Weight: Bulk density and floating time are the two main parameters that determine buoyancy. However, as density fluctuates over time as a function of changes in the resulting weight, a single density measurement is insufficient to accurately describe buoyancy. For instance, due to gas production and entrapment, a matrix tablet containing bicarbonate and a matrixing polymer initially floats. However, after a while, a particular drug is released, and part of the matrixing polymer's outer layer may erode away, changing the dosage form's final weight.

4. Expanding networks

Swelling Index: After immersing the dosage form in a swelling solution at 37°C, it is removed from the SGF at regular intervals. Dimensional changes are quantified over time as an increase in tablet thickness or diameter.

Water Uptake: This is a measurement of the swellable matrix's swelling property that is done indirectly. Here, dose forms are taken out on a regular basis, and weight fluctuations are tracked over time.

Water uptake = WU = (Wt – Wo) * 100 / Wo

Where,

Wt = weight of dosage form at time t. Wo = initial weight of dosage form.

5. Shape and Size of Particles: Scanning electron microscopy (SEM) provides higher resolution than light microscopy (LM). Light microscopy (LM) and scanning electron microscopy (SEM) are the most widely used techniques for observing microparticles. Both are able to identify a multiparticulates form and external structure. With double-walled microspheres, coating parameters can be adjusted thanks to LM. The Multiparticulates forms can be observed and quantified microscopically both before and after coating. After particles are cross-sectioned, SEM can study double-walled systems in addition to multiarticular surfaces. The structure of multiple walled microspheres is characterized using confocal fluorescence microscopy. The Multiparticulates morphology. In addition to experimental methods, multisize Coulter counter and laser light scattering can be used to characterize the morphology, size, and shape of the Multiparticulates.

6. Entrapment Efficiency: The percentage of entrapment, or the capture efficacy of a washed multiparticulates, can be determined by letting it lyse. Next, the active components of the lysate are identified in compliance with the monograph's specifications. To determine the percentage of encapsulation efficiency, utilize the equation.

% Entrapment = Real content / Theoretical content x 100

7. Floating Inaction: The required amount of the floating microparticulate is added to 100 millilitres of the simulated gastric fluid (SGF, pH 2.0), and the mixture is stirred with a magnetic stirrer. After pipetting, the layer of buoyant microparticulate is removed by filtration. The sinking particulate layer's particles are separated by filtration. In a desiccator, the two types of particles are dried until their weight remains constant. Buoyancy is determined by weighing both microsphere fractions and

dividing the weight of the floating particles by the total weight of the sinking and floating particles.

Buoyancy (%) = Wf / Wf + Ws.

Where, Wf and Ws are the weights of the floating and settled microparticles.

8. Research on In Vitro Release: The rate at which floating microparticulate is released is measured in a dissolution instrument. To fill the basket of the dissolving rate apparatus, a weighted quantity of floating microspheres equivalent to the dosage of medication is taken. The dissolving fluid is maintained at 37 ± 0.5°C with a rotation speed that creates sink conditions during the drug release research.

9. Research on drug-excipient interactions: It can be studied using high performance liquid chromatography, differential scanning calorimetry, and FT-IR spectroscopy.

10. In vivo Assessment Exam

a. Radiology uses X-rays extensively to examine inside body systems. One popular type of radio opaque marker is bariums sulphate.

b. Similar to X-rays, chemicals that emit scintillation are integrated into dosage forms, and **scintigraphy** is then used to take pictures. 99Tc is a commonly used emission material.

c. Gastropexy Gastroscopy is the peroral endoscopy with Fiber optics or video technology. The results of stomach elongation can be visually examined with the use of gastroscopy.

d. Tracking using Magnetic Markers This technique makes use of a magnetically tagged dosage form loaded with iron powder to enable extremely sensitive bio magnetic measurement equipment to take pictures. This method's advantage is that it emits less radiation and is hence safe.

e. Ultrasonography is occasionally utilized, but not frequently as it cannot be traced to the gut.

f. Breath Test for Octanoic Acid, 13 C A component of GRDDs is 13C octanoic acid. Octanoic acid causes a chemical reaction in the stomach that releases CO2 gas, which is exhaled. The important Carbon atom that will be present in CO2 is replaced with the 13C isotope. As a result, the stomach retention period of the dose form can be defined as the amount of time that 13CO2 gas is retained in the breath. In transiting to the colon, the dosage form experiences no response and releases no CO2. As a result, this method is less costly than others.

7. Innovative Gastro Retentive Device (GRID)

With this procedure, medications can only be absorbed by the stomach or small intestine. GRID was created to enable the longer than eight-hour retention of pharmaceuticals in the stomach. Extended stomach availability enhances the absorption of prescription drugs. The pill provides both quick and prolonged release of the medication, which enhances patient compliance. manufacturing of dosage forms with a multilayer covering GRID holds its shape to allow medication to be administered in a controlled manner during periods of extreme gastrointestinal movements. Drug plasma concentrations are therefore maintained in the therapeutic range for a longer period of time when using this mode of dosing, making it suitable for usage as a "Once-a-day" strategy. With the help of this novel medication form, drug expected release can be customized to produce both instantaneous and progressive release.

Keeping the kind of drug close to the absorption site can help lower the dose and, in turn, the side effects for many oral medications.[33]

Excipients utilized in systems that float:

(1). Hydrocolloids: Materials with the capacity to form gels are referred to as hydrocolloids. It swells in contact with the contents of the stomach. Pectin, agar, sodium alginates, ethyl cellulose, and HPMC are a few examples.

(2) Release rate accelerants: These include lactose and mannitol, which speed up the pace at which drugs release.

(3) Release rate retardant: This agent works by making the drug less soluble by adding materials such calcium phosphate, magnesium striates, and tale, which delays the medication's release effect.

(4). Buoyancy-enhancing agent: To improve or increase buoyancy, use low-density materials such as ethyl cellulose. GRID device: Stine is able to absorb was created with the stomach's extended stomach in mind during absorption.

(5). Effervescent agent: These are compounds that emit carbon dioxide when they come into contact with an acidic medium. In floating systems, gas-generating substances like citric acid and sodium bicarbonate are used.

8. GRDDS'S CURRENT MARKETED BASIS STATUS

GRDDs are currently available on the market, with several of them having been approved and marketed for use in humans. Numerous medications, such as anti-inflammatory, anti-emetic, and anti-ulcer medications, are delivered by these GRDDs.

Table 04: Lists the GRDDs that are presently available for purchase, together with the diseases they are meant to treat and GRDDs are now seeing a lot of developments. Among the numerous developments are.

Disease	Drug	GRDDs Type
Gastroesophageal reflux disease (GERD)	Esomeprazole	Floating capsule
Ulcers	Ranitidine bismuth citrate	Floating tablet

Nausea and vomiting	Domperidone	Mucoadhesive tablet
Pain and inflammation	Ketoprofen	Expandable capsule
Fungal infections	Griseofulvin	Hollow microsphere [28-30]

• The creation of novel materials and polymers for the production of GRDDs. These novel materials can be engineered to possess particular characteristics like swelling, buoyancy, or mucoadhesion. Numerous novel materials and polymers are being explored for application in GRDDS. Among these materials are:
Hydrogels are water-absorbing polymers that have been cross-linked. Their purpose is to create GRDDS that float.

Biodegradable polymers: These are synthetic materials that the body is able to break down. They are employed in the production of GRDDs that are excreted from the body naturally without the need for surgery.

Magnetic polymers: By applying a magnetic field to particular regions of the stomach, magnetic polymers can be used to create GRDDs.

The creation of novel manufacturing processes that enable the highly accurate and repeatable production of GRDDs. For GRDDs, several novel production processes are being developed. Among these methods are:
3D printing (3DP): This technology allows for the creation of intricate structures. It is employed to create GRDDs with particular dimensions and forms.

Microencapsulation: One technology that can be used to encapsulate medications in a protective layer is microencapsulation. It's being used to create GRDDs that are shielded from the stomach's acidic environment.

The creation of fresh in vivo and in vitro techniques for GRDD assessment. The effectiveness of GRDDs can be evaluated using these techniques, which include evaluating their stomach retention time, drug release profile, and biodistribution.[31–35] A multitude of novel in vitro and in vivo techniques are being developed to assess GRDDs.

Among these techniques are:
Investigations on Gastric Emptying: These investigations quantify the speed at which medications pass through the stomach. They are employed to evaluate GRDDs' gastric retention duration.

Drug release studies: To gauge how quickly pharmaceuticals are released from GRDDs, drug release experiments are conducted. They are employed to evaluate the GRDDs' medication release characteristics.

Investigations on biodistribution: These investigations monitor how medications go throughout the body. They are employed to evaluate GRDDs' capacity for targeting.[32–33]

More patient-friendly, tailored, and effective GRDDs are now possible thanks to the advancement of these new technologies. The following are some of the widely used GRDDs products and technologies:

Gaviscon: Gaviscon is an over-the-counter (OTC) antacid that relieves acid reflux and heartburn by floating in the stomach and forming a raft there. Its purpose is to remain in the stomach and create a barrier that keeps stomach acid out.

Acuform: Ethypharm invented the patented medicine delivery system known as Acuform. It is a component of many drugs that provides for gradual and regulated drug release in the stomach. To improve stomach retention, the technology uses a swellable, hydrophilic polymer matrix.

Sustained-Release Proton Pump Inhibitors (PPIs): To treat diseases including peptic ulcers and gastroesophageal reflux disease (GERD), some proton pump inhibitors, like Dexilant (Dex lansoprazole), use GRDDS technology to give a longer release of the active ingredient.

Gastrocoat: When creating drugs to treat stomach ulcers and associated disorders, Gastrocoat—a gastroretentive drug delivery system—is utilized. It facilitates the drug's prolonged interaction with the stomach mucosa.

Swelling Systems: Pharmaceutical companies have created GRDDs based on swellable systems, in which the drug dosage form expands when it comes into touch with gastric secretions, enabling it to stay in the stomach for a longer amount of time.[34]

The medicine being administered, the intended drug release profile, and the specific requirements of the patient all play a role in the selection of GRDDs. The different commercial goods in GRDDS that are utilized with different delivery methods are listed below

Table 05: As follows.

Product Name	Dosage Form	Mechanism of Action	Indications
Esomeprazole delayed-release capsules	Capsule	Forms a gel layer in the stomach that slows down gastric emptying	Gastroesophageal reflux disease (GERD), ZollingerEllison syndrome

Lansoprazole delayed-release capsules	Capsule	Forms a gel layer in the stomach that slows down gastric emptying	GERD, Zollinger-Ellison syndrome
Pantoprazole delayed-release capsules	Capsule	Forms a gel layer in the stomach that slows down gastric emptying	GERD, Zollinger-Ellison syndrome
Rofecoxib delayedrelease tablets	Tablet	Binds to COX-2 enzymes in the stomach and inhibits the production of gastric acid	Pain relief, inflammation
Sucralfate suspension	Suspension	Forms a protective layer on the lining of the stomach that helps to prevent erosion	Duodenal ulcers, gastric ulcers
Misoprostol tablets	Tablet	Stimulates the production of mucus in the stomach and intestines that helps to protect the lining.	Prevention of NSAID induced ulcer

GRDDs are superior to traditional oral drug delivery systems in a number of ways. They can increase the bioavailability of medications with a limited absorption window or those that are unstable in the small intestine's alkaline environment. Additionally, they can be used to administer medications to the stomach for local therapy of conditions like gastritis or ulcers.[35] Furthermore, GRDDs can assist in lowering dosage frequency, which can enhance patient compliance.

8.1 FUTURE PERSPECTIVES OF GRDDS

One of the biggest problems facing the pharmaceutical business is the GRT of the typical dosage form, particularly for medications that are absorbed from the upper intestine. The disadvantages of the standard dose form will be mitigated by the development of GRDDS, while more research is required to address these issues. Numerous research on GRDDS, including those on floating, expandable, and mucoadhesive systems, have been conducted to far using the single system approach.[37] Prospects for GRDDS's future appear bright. There are several methods in which GRDDS can enhance medication delivery to the stomach with further study and advancement.

The following are the future prospects of GRDDS

Increased drug bioavailability: By keeping pharmaceuticals from being broken down by enzymes or stomach acid, GRDDS can increase the bioavailability of medications. Osmotic, mucoadhesive, and floating systems can all be used for this.

Extended drug release: By keeping the medication from being released too soon, GRDDS can be utilized to prolong the drug's release period. Osmotic or magnetic systems can be used for this.[30–38]

Targeted drug delivery: Medications can be administered to a particular area of the stomach using GRDDS. Magnetic or bioadhesive methods can be used for this.

Decreased side effects: By preventing side effects, GRDDS can help decrease the negative effects of medication.

Improved patient compliance: either by transporting them to a specific area in the stomach or preventing them from being absorbed too rapidly. Increased patient compliance can be achieved by making GRDDS easier to take and more convenient. GRDDS, for instance, can be produced as easier-to-swallow chewable pills or capsules.[33–36]

GRDDS are a cutting-edge technology that show great promise for enhancing the management of numerous illnesses. GRDDS has the potential to completely change how medications are absorbed into the stomach with more study and development. The following issues must be resolved for GRDDS to reach its full potential:

• **Stability:** In the tough environment of the stomach, GRDDS must be stable. This can be difficult because enzymes and stomach acid break down a lot of the polymers and other components used in GRDDS.

Biocompatibility: GRDDS must not damage the lining of the stomach in order to be considered biocompatible. Given how sensitive the tissue lining the stomach is, this is crucial.

Production: An economical method of manufacturing GRDDS is required. This presents a problem because GRDDS frequently call for specific tools and methods.

Clinical trials: In order to prove the safety and effectiveness of GRDDS, certain procedures must be carried out. Although it takes a lot of time and money, this procedure is necessary to guarantee that GRDDS are secure and useful for human use.[32–38]

9. CONCLUSION

The best drug delivery methods for delivering medications with a limited absorption window close to the stomach area are those that are gastro-retentive. Nowadays, an increasing number of drug delivery systems are being developed with the intention of releasing the medication in the stomach area. Even though there are several advantages to using these drug delivery modalities. Despite the literature describing several GRDDS, such as bio/mucoadhesive, magnetic,

low, and high-density systems, more investigation is still required to ascertain their therapeutic significance.

From a pharmaceutical point of view, future GRDDS techniques could have to focus on a combined strategy to enhance product quality. The right drug and excipient combinations, formulation methods, and physiological processes that take place in the GIT must all be considered. We came to the conclusion that, in light of the literature reviewed, gastro-retentive medication administration presents a number of potential benefits for drugs whose absorption results in low bioavailability. This review's conclusion included a thorough overview of GRDDS delivery, including their most current developments and commercialized goods.

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