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ADVANCEMENTS IN GASTRORETENTIVE DRUG DELIVERY SYSTEMS: ENHANCING DRUG EFFICACY THROUGH PROLONGED GASTRIC RESIDENCE

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ABSTRACT

Oral delivery is the most practical and recommended method of drug delivery due to its ease of use and patient compliance. However, challenges such as poor bioavailability and short gastrointestinal residence times can limit the effectiveness of certain medications. To address these issues, researchers have developed gastroretentive drug delivery systems (GRDDS), which extend the duration of the drug's residence time in the stomach and upper gastrointestinal tract, thereby Improving absorption and therapeutic efficacy. This review discusses various types of GRDDS, including floating, expandable, and bio adhesive systems, and their mechanisms of action. Additionally, it explores the physiological gastric retention-causing factors, the advantages and applications of GRDDS, and the future potential of these systems in improving drug delivery and patient outcomes.

Key Words: Gastroretentive drug delivery system, Gastric residence time, Floating drug delivery, Gastrointestinal tract, buoyancy system, Floating tablets, Sustained drug release, Prolonged gastric retention.

1. INTRODUCTION

Oral administration is convenient and comfortable for patients, it remains popular even with ongoing advancements in drug delivery techniques. Systems for the controlled release of pharmaceuticals are intended for oral use. The drug is released by these drug delivery systems in a regulated, predictable, and predetermined manner because of problems with stability or absorption, they are not appropriate for medications with low bioavailability[(1)]. Modern methods that are intended to prolong the duration of such medications residence in the stomach can alleviate these issues.

Gastroretentive drug delivery systems

(GRDDS) are the name given to such drug delivery systems. GRDDS work well with medications that are taken into the body through the stomach (such as albuterol)[(2)] easily affected by alkaline pH (like ranitidine and metformin)[(3)] , furosemide is not soluble in alkaline pH similar to diazepam, with limited solubility[(4)] , narrow Absorption window (such as riboflavin and levodopa)[(5)] , improved patient compliance through fewer dosing frequency, increased therapeutic efficacy of short-half-lived drugs, and medication delivery tailored to the patient's location. Some typical advantages associated with the utilization of GRDDS include continuous and controlled drug delivery in the stomach, extended drug presence at the absorption site, improved drug absorption from the gastrointestinal tract, and avoidance of drug wastage[(6)]. A variety of materials, including raft-forming materials, magnetic materials, raft-exchange resins, mucoadhesive, high-density materials, and ultra porous hydrogels, are utilized to create GRDDS [(7,8)].

Fundamental physiology of the gastrointestinal tract

The stomach consists of three anatomical regions: The fundus, corpus, and antrum (pylorus). The bottom and main part the area near the beginning of the digestive system acts as a storage area for food that has not been digested. The antrum is where most materials are located. Blending movements and driving them forward, functioning as emptying of stomach pump. Whether consuming food or dining During a fast, the stomach becomes empty. Nonetheless, there are a pair of regions with varying motility patent regulations. An intercommunication system allows individuals to connect with each other using electronic devices. There is an electrical sequence of events that happens during digestion. Fasting state; these occurrences happen in the stomach intestinal every 2-3 h[(9)]. This is commonly referred to as the interdigitate myoelectric cycle, also known as migrating myoelectric cycle and Wilson and Washington have further classified it into the following 4 phases [(10)].

- Basal phase (Phase I): Its mild contractions last for around forty to sixty minutes.
- Pre-burst phase (Phase II): It lasts for 40–60 min and is characterized by irregular contractions. As the phase progresses more quickly, frequency and intensity rise.

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- (Phase III): It experiences brief, powerful contractions that last between 4 to 6 min. The "housekeeper wave" that moves the incompletely digested contents of the stomach into the small intestine is this stage.
- (Phase IV): This phase, ranges from 0 to 5 min, happens in between the dormant phase of Phase I and the final segment of Phase III of two subsequent cycles.

After eating a mixed meal, the pattern of contractions changes from the fasting to the fed state. This is known as the "digestive motility pattern" at times." and it consists of ongoing contractions similar to those seen in phase II of a fast. Food particles are reduced in size by these contractions to less than 1 mm, and they are then sent in a suspension state in the direction of the pylorus. Stomach emptying proceeds more slowly during the fed state due to the delayed onset of MMC. The two main difficulties associated with oral controlled release dose forms are as follows: short gastrointestinal residence duration and unpredictable gastric emptying rate, as shown by scintigraphy studies that measure gastric emptying rates.

Numerous elements impact delivery systems' gastric residence times

When creating the gastroretentive dosage form, the parameters related to the stomach's morphology and function should be taken into account. The Particles must be between 1-2 mm in size in order to pass through the pyloric sphincter and reach the small intestine [(11)]. A patient's gender, age, sex, body mass index, type of food consumed, frequency of consumption [(12,13)], density, size, and shape of dosage forms [(14,15)], as well as medications that alter the duration of gastrointestinal transit time (e.g., prokinetic agents like metoclopramide and cisapride or anticholinergic drugs like atropine) all influence how long the delivery systems stay in the stomach[(16)].

Density

The rate at which the dose form stomach is emptied of its contents also influenced by its density. The position of the delivery system in the stomach is also influenced by density. Systems with a high level of density descend to the depths of the stomach while low-density dosage forms allow the contents of the stomach to float on the surface. For low-density systems or floating systems to stay buoyant on the stomach contents, the bulk density should not exceed 1 g/cm^3 [(17)].

Size

Dosage forms with a diameter greater than 7.5 mm showed an increased gastrointestinal transit time compared to those with a smaller diameter measuring 9.9 mm. As they pass through the digestive phase, they are emptied. The flow from the pyloric sphincter to the small intestine is blocked, so larger doses may take more time to pass through the stomach. Larger molecules have longer retention times compared to smaller ones

Shape of dosage form:

Devices with flexural moduli of 48 and 22.5 kilo pounds per in tetrahedron and ring shapes, respectively. A (KSI) square inch both have higher retention rates of 90 % to 100 % at 24 h with different forms. During periods of fasting, the migrating myoelectric complex MMC, or intense motor activity, happens every 1.5 to 2 h, which is a characteristic of the GI motility. If the timing of the formulation's administration aligns with that of the migrating myoelectric complex MMC. Very short GRT is expected for the unit, as the MMC removes undigested material from the stomach. Still, the fed condition results in a notably prolonged GRT and delayed MMC.

Polymer's Viscosity Grade:

The viscosity of polymers and their interactions possess an important impact on the floating qualities of GRFDDS and drug release. When it came to enhancing floating qualities, low viscosity polymers—like HPMC K100 LV—were shown to be more advantageous than high viscosity polymers—like HPMC K4M. Furthermore, it was noted that a rise in polymer viscosity was correlated with a decrease in the release rate.

Nature of the meal:

When indigestible polymers or fatty acid salts are consumed, the stomach's motility pattern can be altered to a fed state, which slows down the pace of gastric emptying and increases the duration of medication release.

Regularity of feeding

Because migrating myoelectric complex MMC occurs infrequently, giving meals in succession can enhance GRT by more than 400 min as compared to giving meals during a single meal.

Gender

Men have a lower average ambulatory GRT (3.4 ± 0.6 h) than women of the same age and race (4.6 ± 1.2 h) [(20)].

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Age

Elderly subjects exhibit a lower stomach emptying time compared to younger subjects. Transit times in the intestines and stomach exhibit both intra- and inter-subject variability. Elderly individuals, especially those above 70 years of age have noticeably longer GRTs.

Posture

GRT may differ depending on whether the patient is lying down or standing up and walking

Upright Position:

A vertical posture shields buoyant shapes from after-meal effects clearing as the floating structure stays on top of the stomach contents regardless of its size. Floating dosage forms are demonstrated by extended and more consistent GRTs compared to the traditional dosage from descending into the lower portion of the distal stomach where they are located pushed out of the pylorus by movements of peristalsis from the stomach

Supine Position:

There is no consistent defence in this position against abrupt and early emptying. Both floating and traditional large dose formulations had longer retention in supine patients. Between the stomach's lower and larger curvatures, the gastric retention of floating forms seems to stay buoyant. When these units travel distally, they might be carried away by the peristaltic motions that push the stomach contents in the direction of the pylorus, which would significantly lower GRT in comparison to patients who remain upright.

Concomitant drug administration:

The FDDS is impacted by anticholinergics (e.g., atropine and propantheline), opiates (e.g., codeine), and prokinetic drugs (e.g., metoclopramide and cisapride).

Biological factors

Gastritis, gastric ulcers, pyloric stenosis, hypothyroidism, and diabetes are among the illnesses that cause this delay in stomach emptying. Gastric emptying rate is accelerated by duodenal ulcers, hypothyroidism, and partial or complete gastrectomy [18,19].

2. SUITABILITY OF A DRUG AS "FLOATING TABLETS

- It must be Functioning within the gastrointestinal tract at a local level, similar to misoprostol, an antacid with localized activity in the stomach.
- The Drug must have value with a narrow therapeutic index, such as riboflavin, levodopa,
- p-aminobenzoic acid, and furosemide.
- Drugs including metronidazole, ranitidine, and captopril that degrade in the colon or gut.
- Medications that disrupt the natural bacteria in the colon, such as antibiotics which serve a purpose as Eradication of H. pylori bacteria using clarithromycin, tetracycline, and amoxicillin.
- Drugs such as diazepam and verapamil have lower solubility in alkaline pH levels.
- Chlordiazepoxide is a medication used for treating anxiety [21,22].

3. DRUGS THOSE ARE NOT SUITABLE FOR GRDDS

- Medications such as phenytoin that have a low solubility in acidic environment
- Medications that are not stable or break down in the stomach's acidic conditions. (e.g. erythromycin)
- Medications that are specifically designed to be released in the colon (e.g., corticosteroids) [23].

Approaches to design floating dosage forms

An approach to addressing the problem of certain persons choking or gaging when taking medication pills is the Floating Drug Delivery System. One possible solution to this problem is to give tablets with density that is below 1.0gm/ml, which will allow them to float on the surface of water. Numerous drug delivery systems have been experimented with for retaining in the stomach since that time in an effort.to improve drug absorption in the gastrointestinal tract by overcoming restrictions related to region and timing. The main reason density floats in gastric fluid and swells to large size; bio adhesive attaches to gastric mucosa; expansion or unfolding due to physical or chemical reactions; mucoadhesive interacts with mucus layer.in GRDF causing buoyancy (Floating system); dense enough. Absorption of the dosage form in the stomach; simultaneous intake of medications or additives that delay the absorption of GIT's movement, sticking to the stomach lining, and expanding to obstructiveness increasing size passage of medication form via the pyloric sphincter [24,25].

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Types of Floating Drug Delivery Systems

Varieties of Floatable Drug Delivery Systems Two different technologies have been used based on buoyancy's mechanism creation of FDDS that are:

A. Effervescent System

B. Non-Effervescent System.

A. Effervescent System

In effervescent systems, gas generating agents like sodium bicarbonate and organic acids (e.g. citric and tartaric acid) are utilized to create carbon dioxide (CO_2) gas, reducing the density of the system and causing it to float on stomach fluid. Mixing a liquid with a matrix is another option, resulting in gas that vaporizes at the same temperature as the human body.

The effervescent systems can be divided into two types:

1. Gas Generating systems
2. Volatile Liquid/Vacuum Systems

1. Gas – Generating Systems:

Intra Gastric Single Layer Floating Tablets or Hydro dynamically Balanced System (HBS): These methods combine CO2 producing agents and drugs into a matrix tablet. Their lower bulk density compared to gastric fluids makes them float in the stomach for extended periods, which in turn slows down gastric emptying. The medicine is released gradually from the floating system and then discharged from the stomach. This improves GRT and stabilizes plasma medication concentrations.

Intra Gastric Bilayer Floating Tablets:

These are also compressed tablet and containing two layers

- Immediate release layer
- Sustained release layer.

Multiple Unit type floating pills:

The "seeds" in these systems are two-layered sustained release tablets. An effervescent agent makes up the inner layer, while a swellable membrane layer makes up the outside layer. When immersed in a liquid that dissolves at body temperature, the apparatus sinks instantly and it later forms enlarged pills that resemble balloons, which float because of their decreased density. The system's creation and entrapment of CO2 is the cause of this decreased density.

2. Volatile Liquid / Vacuum Containing Systems

Using a chamber filled with a liquid, such ether or cyclopentane, which gasifies at body temperature and inflates the chamber in the stomach, one may maintain the gastric resistance (GRT) of a drug delivery system. A bio erodible plug (such as PVA or polyethylene) that dissolves gradually and permits the inflatable chamber to release gas and collapse after a set amount of time may be included in the device. This would enable the inflatable systems to be spontaneously ejected from the stomach.

Vacuum Containing Systems consists of

- Intragastric Floating Gastrointestinal Drug Delivery System
- Inflatable Gastrointestinal Delivery Systems.
- Intragastric Osmotically Controlled Drug Delivery System:

Intragastric Floating Gastrointestinal Drug Delivery System

The flotation chamber in these systems allowing them to remain buoyant in the stomach It can be filled with either vacuum, harmless gas, or air. The drug reservoir is contained within small porous chamber.

Inflatable Gastrointestinal Delivery Systems:

These systems use an inflatable chamber filled with liquid ether that gasifies at body temperature, causing it to inflate in the stomach. To create these systems, a drug reservoir, such as a polymeric matrix, is loaded into an inflated chamber and encapsulated in a gelatine capsule. After oral administration, the capsule dissolves and releases the drug reservoir and inflated chamber. The Chamber automatically inflates and stores the drug reservoir in the stomach. The drug is continuously released from the reservoir to the gastric fluid

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Intragastric Osmotically Controlled Drug Delivery System:

It includes a capsule that is biodegradable and contains a floating support filled with air, as well as a drug delivery system controlled by osmotic pressure. When the capsule disintegrates in the stomach, the intragastric drug delivery device with osmotic control is activated. The interior inflatable support forms a pliable, empty polymeric pouch that expands as a liquid inside turns into gas at body temperature. The osmotic pressure-controlled drug delivery device consists of two components: the osmotically active compartment and the drug reservoir compartment. A collapsible bag that responds to pressure has a medication delivery opening which does not allow liquid or vapor to pass through, and it contains the drug reservoir compartment. The semi-permeable membrane surrounds the osmotically active chamber, which contains an osmotically active salt. The semipermeable membrane in the stomach absorbs water from the GI fluid constantly, causing the dissolution of the osmotically active salt in the osmotically active compartment. This leads to the development of an osmotic pressure that acts on the flexible bag, causing the drug reservoir section to reduce in volume and stimulate the release of a drug solution through the outlet for delivery. A bio erodible plug is incorporated into the floating support to slowly degrade and reduce the support. After releasing the air, the drug delivery device is removed from the stomach.

B. Non effervescent systems:

The Non-effervescent FDDS works by swelling the polymer or adhering to the mucosal layer in the GI tract. Gel-forming or highly swellable cellulose-type hydrocolloids, polysaccharides, and matrix-forming materials like polycarbonate, polyacrylate, polymethacrylate, and polystyrene are commonly utilized excipients in non-effervescent FDDS. Additionally, bio adhesive polymers such as chitosan and Carbopol are also frequently used.

Single Layer Floating Tablets:

The process of formulating the medication involves blending the drugs closely with a hydrocolloid that forms a gel when exposed to stomach acid, leading to expansion and maintaining a density lower than one. The inflated polymer traps air, giving buoyancy to the dosage forms.

Bilayer Floating Tablets:

A tablet with two layers consists of an immediate release layer where the initial dose is released and a sustained release layer that absorbs gastric fluid and creates a barrier of impermeable colloidal gel on its surface. This helps the tablet float in the stomach by keeping its density below one.

Alginate Beads:

Freeze-dried calcium alginate was utilized to produce multiple-unit floating dosage forms. In order to create round beads measuring approximately 2.5 mm in diameter, gently release a sodium alginate mixture into a water-based calcium chloride solution. Calcium alginate solidifies, creating a porous arrangement capable of maintaining buoyancy for as long as 12 h. Solid beads had a shorter residence period compared to floating beads, lasting less than 5.5 h.

Hollow Microspheres:

Hollow microspheres were created using a distinctive technique called emulsion solvent diffusion, sometimes known as micro-Ballons, which were filled with drugs and had an exterior polymer shell. PVA was placed in a stirred liquid mixture that was kept at a controlled temperature at 400℃, together with the drug ethanol: dichloromethane solution and enteric acrylic polymer. Dichloromethane evaporation in the dispersed polymer droplet produced a gas phase that formed the internal cavity of the polymer-drug microsphere. Throughout more than 12 h in vitro, the micro-Ballons floated nonstop on the surface of an acidic dissolving liquid containing surfactants. [26]

Floating mechanism utilizing ion exchange resin

The resin beads contained bicarbonate and theophylline, which were attached to the resin. The resin beads have a semi-permeable membrane coating to inhibit quick loss of CO_2. The interaction with stomach acid leads to a reaction between bicarbonate and chloride ions, resulting in the formation of CO_2 . This trapped CO_2 within the membrane causes floating particles. Giving the system after a light, mainly liquid meal significantly increased gastric residence time compared to a control group. Furthermore, the mechanism may sustain drug release. [27]

Floating Systems

To improve the retention of drugs where Absorption occurs in the stomach or upper stomach area in small intestine, FDDS appears extremely promising. The decreased density of FDDS allows them to float above the gastric content without being impacted by the gastric emptying rate, resulting in increased bioavailability. During its prolonged stay in the upper section of the stomach, the medication is repeatedly expelled from the body. This raised the medication's plasma concentration and, thus, its bioavailability. The pyloric sphincter then pushes the remaining system into the

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small intestine. [28-31]. To maintain the system floating on the food's surface, however, a small quantity of floating power, or FT, is also needed in addition to the stomach content necessary for effective floating. The buoyancy retention principle has been used to develop a new gadget for measuring dynamic force that floats and determining the load that is produced as a result. This device operates by constant continuity computing the force, as stated in the equation below, as a function of time required to prevent an object from floating. (32)

$$FT = F_{buoyancy} - F_{gravity} = (D_f - D_o)\, V \cdot g$$

where D_o denotes the density of the item being floated, D_f is the density of the fluid, V denotes the fluid's volume, and g represents the acceleration brought on by gravity. When the F value is greater on the positive side, it indicates that the object will float properly. FDDS is able to maximize the endurance and stability of floating forces thanks to this apparatus. Preventing adverse consequences resulting from unforeseen variations in intra-gastric floating capabilities is another benefit. Swellable polymers exhibit a progressive relaxation of their cross-linked structure, leading to an increase in their total volume relative to their weight. The system floats above the stomach content as a result of the system's decreasing density. It takes a specific amount of time, known as the floating lag time, to reach this swelling condition. [32-34]

Expandable, Unfoldable and swellable systems

Expandable systems can be made larger in capacity or form to provide a longer GRT. Prior to being investigated for human usage, these technologies were created for veterinary use [35]. If a dose form is bigger than the pyloric sphincter's width, it may remain in the stomach following gastric transit. These devices are often made of hydrophilic polymers, which swell and absorb water when they come into touch with stomach fluid [36,37]. Diffusion is what causes the swelling and medication release. But caution should be exercised to ensure that the dose form is small enough to swallow and does not accumulate or induce gastric obstruction on its own. It is important to take into account their settings while creating extensible systems that extend GRT.

- A compact design intended for oral consumption.
- A larger gastroretentive version
- A compact design that enables clearance after the drug is released from the device.

To promote gastroretentive properties, dosage forms should be substantial and solid enough to survive stomach peristalsis and mechanical contractility. Recently, researchers attempted to design an effective gastroretentive drug delivery device using foldable and swellable mechanisms. Unfoldable systems are created from biodegradable polymers [36]. Bio erodible polymer capsules come in various shapes, including tetrahedrons, rings, and planner membranes (4-label discs or 4-limbed cross forms) which extend in the stomach. Because of their mechanical properties, swellable systems are also maintained in the gastrointestinal tract (GIT). The osmotic absorption of water is the usual cause of swelling, and the dose form is tiny enough to be ingested by stomach fluid. Expandable systems have some drawbacks, including the inability to store biodegradable, highly hydrolysable polymers over extended periods of time [38], the relatively limited mechanical shape memory of the unfolding system, difficulty in industrialization, and lack of cost effectiveness. Prolonged use of rigid, large-scale, expandable drug delivery dosage forms may result in transient intestine adhesions, blockages, and gastropathy [36].

Magnetic Systems: In order to enhance gastric retention time (GRT), a dose form with a tiny magnet is inserted inside the position of the abdomen is above the stomach. The magnetic system appears to work, although precise positioning of the external magnet may hinder adherence of the patient [39].

Raft forming systems

The Basic mechanism of raft formation is the production of a cohesive gel that is viscous when it comes into contact with stomach fluids. Each part of the liquid expands to form a continuous layer known as a raft. Due to the buoyancy that CO_2 production creates, the raft floats and acts as a barrier to stop stomach contents like HCl and enzymes from refluxing into the oesophagus. In order to reduce the density of the system and enable it to float on the gastric fluids, the system typically consists of an alkaline bicarbonate or carbonate and a gel-forming agent [40].

High density systems.

These systems, which have a density of approximately 3 g/cm^3, stay within the folds of the stomach and are able to endure. Producing these mechanisms with a high drug content (> 50 %), creating peristaltic motions [41,42]. It is difficult to reach the required density of 2.4-2.8 g/cm^3. High density formulations are necessary. Substances like barium sulphate (density=4.9), zinc oxide, titanium oxide, and iron powder, can be used as diluents [43].

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Modified systems

Systems with non-disintegrating geometric shapes made from blended polyethylene or shaped with silastic elastomers extend the GRT depending on size, structure, and form the bending properties of the drug delivery device [44].

Formulation Of Floating Dosage Form [45]

Hydrocolloids

Anionic or non-ionic synthetic hydrocolloids, such as hydrophilic gums and derivatives of modified cellulose, are suitable. For example, you can utilize MC, HPC, HEC, Na CMC, agar, pectin, agar, alginate, gelatin, casein, bentonite, and veegum. The pH of the stomach fluid, which is 1.2, is the acidic medium in which the hydrocolloids must hydrate. The bulk density of the formulation could be higher than one at the beginning but in order to ensure buoyancy when gastric fluid enters the system, it must be in hydrodynamic equilibrium with a bulk density lower than one.

Inert fatty materials

Addition of edible, pharmacological inert fatty substance with a specific gravity below one can reduce the hydrophilic characteristic of the formulation and thus improve its buoyancy. Lipids contain fatty acids, long-chain alcohols, glycerides, as well as mineral oils are all viable options for use much like pure grades of beeswax.

Release rate accelerant:

By adding an excipient such as lactose or mannitol, the formulation's drug release rate can be changed. Approximately 5–60 % of the weight may contain them.

Release rate retardant:

Drug release is delayed by insoluble materials such magnesium stearate, talc, and dicalcium phosphate because they decrease the solubility of the medicament.

Buoyancy increasing agents:

To increase the formulation's buoyancy, substances with a bulk density of below one, such as ethyl cellulose, can be added. Up to 80 % of it can be adjusted based on weight.

Miscellaneous:

Preservatives, stabilizers, and lubricants are examples of pharmaceutically approved adjuvants that can be included in dosage forms based on requirements. They do not disrupt the hydrodynamic equilibrium of the systems.

***In vitro* assessment**

In vitro assessment is crucial for GRDDS in order to forecast gastric transit behaviour. The parameters listed below should be taken into consideration when creating innovative formulations for gastric retention.

The Buoyancy lag time

The floating lag time is the duration required for gastroretentive formulations to reach the surface of the dissolution medium. The testing medium consists of 900 ml of 0.1 N HCl solution at 37 °C, determined using a USP dissolution apparatus. The period needed for various dosage forms to float is referred to as floating lag time [46].

a) Floating time

This is responsible for the buoyancy of the dosage form. This test utilizes a specific dissolution Equipment for each form of medication, with 900 ml of liquid for dissolution at a temperature of 37 °C. Observation by sight decides the period of time that a dose form remains floating [47,48].

b) Specific gravity/density

Calculating specific gravity is crucial for both low- and high-density GRDDS. Displacement is a method to determine specific gravity [49].

c) Swelling index

The tablets are submerged in 0.1 N HCl at 37 °C to calculate the swelling index, and they are then periodically removed at regular intervals [50].

d) Water uptake

This study involves removing the dose form at regular intervals using a dissolving medium and determining the weight variation (51).

Water uptake (W_U) = (W_t - W_o) × 100/W_o

where Weight of the dosage form at time t, denoted as W_t, is equivalent to the initial weight of the dosage form, denoted as W_o.

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e) Weight variation

Pharmacopeia's offer many official methods for calculating weight variations. Typically, single and average weights of 20 tablets are recorded. These data are used for calculating average weight and weight variation [52,53].

f) Hardness and friability

Commonly, testers like Monsanto, Strong Cobb, and Pfizer are used to evaluate the crushing strength or hardness. A Roche friabilator is utilized for assessing tablet friability (or strength) [54,55].

g) *In vitro* dissolution tests

This test is conducted to measure drug release from GRDDS in both gastric fluid and intestinal fluid kept at 37°C at a specific time using USP dissolution type II apparatus (paddle) [55,56].

***In vivo* assessment**

a) Radiology

This method is primarily utilized for locating the position of a gastroretentive dosage form that has been filled with the presence of barium sulfate (a radio opaque marker) in the body system for the purpose of time evaluation through X-ray imaging. X-ray images are captured at various time points to document the accurate placement of the medication in the body [57,58].

b) Scintigraphy

It is used to determine the gastroretentive dosage forms *in vivo* floating behaviour, much like radiography. When using Scintigraphy utilizes 99mTc pertechnetate as the emitting substance [59,60].

c) Gastroscopy

For visual inspection of gastroretentive dose forms, gastroscopy is a commonly utilized technique. This method involves looking deeply within bodily organs including the stomach, oesophagus, and small intestine using an illuminate optical, tubular, and thin device called an "endoscope [61,62].

d) Ultrasonography

Ultrasound is a is a technique for diagnostic imaging that creates internal body images using sound waves. The primary drawback of this test is its inability to identify at the entrails [62,63].

e) 13C octanoic acid breath test

The usage of radioactive 13C octanoic acid is to evaluate medication absorption from GRDDS. When a molecule is absorbed from the duodenum and radiolabelled, the amount of octanoic acid absorbed can be connected with the amount of CO_2 exhaled during metabolism. Isotope ratio mass spectrometry was used to detect the radiolabelled CO_2 [61,62].

f) Magnetic marker monitoring

The process is safer than radiology and scintigraphy because it does not involve radiation exposure [63,64]. The dosage form is tracked in real-time in the gastrointestinal tract [65,66].

This method is primarily used to assess gastrointestinal motility and solubility of medicines. This technique involves labelling the dose form as a magnetic dipole using ferromagnetic particles and measuring the field using a bio-magnetic instrument [67,68].

Advantages and applications of gastroretentive delivery systems

Drugs are released into the targeted site of action in a regulated way via gastroretentive dosage formulations. These systems contribute to the increased bioavailability of medications, such as levodopa and riboflavin, that are processed in the upper section of the gastrointestinal tract [69,70].

By increasing GRT, gastroretentive dose forms for medications with a short half-life assist lower dosage frequency and boost patient compliance.

Additionally, they offer a consistent and extended release of medications into the stomach and intestines, which is beneficial for local treatment [71,72].

Future Potential

Recent research indicates that gastro-retentive floating medication delivery systems hold significant future potential. Prolonged stomach retention increases absorption time, benefiting therapeutic medicines with limited absorption windows and improving treatment outcomes by allowing oral medication instead of parenteral delivery.

GRDDS can maximize absorption and bioavailability for drugs with low gastrointestinal tract absorption, and offer advantages in treating gastric and duodenal cancers, formulating anti-reflux medications and creating regulated release systems for diseases like Parkinson's.

4. CONCLUSION

Gastroretentive drug delivery systems represent a promising method to overcoming the limitations of conventional oral drug delivery, enhancing therapeutic efficacy, patient compliance, and drug bioavailability. Continued research and development in this field are expected to yield innovative solutions for various medical conditions, ultimately improving patient care and treatment outcomes.

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