IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, August 2024

A Review of Modern Developments in Gastroretentive Drug Delivery Methods

Syeda Sadia[1], Dr. Rakesh K. Jat[2], Dr. Padmalatha Malthar[3]
Department of Pharmacy[1,2,3]
Shri Jagdishprasad Jhabarmal Tibrewala University, Jhunjhunu Rajasthan, India

Abstract: *Research and development of oral medication delivery systems have made great strides in the last several years. A problem with the physicochemical properties of medicinal molecules and their formulations prompted the idea of a new drug delivery technology. This work aims to update the pharmacological strategies applied in enhancing stomach residence time by synthesizing fresh research on gastro retentive drug delivery systems. Various devices that delay stomach emptying are now in use, including systems that enlarge and contract, systems that use polymeric bio adhesives, systems with changed forms, systems with high densities, and gastro retentive floating drug delivery systems. These technologies prove to be highly beneficial in addressing a multitude of problems that crop up when different dosage forms are being developed. Low bioavailability is a consequence of conventional dosage forms due to the brief residence time, oral absorption of medications, and restricted absorption of narcotics inside the upper intestinal wall. To get over this limitation and increase the bioavailability of these drugs, people can use controlled drug delivery systems that stay in the stomach for a long time. To prolong the time that medication stays in the esophagus and stomach, a gastric retention drug delivery device can be utilized. This article provides a concise overview of the different polymers utilized in floating drug delivery systems, focuses on the latest developments in expandable technology for these systems, and discusses the advantages of gastric retention and the main mechanism of floating*

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

I. INTRODUCTION

Drugs are most effectively delivered to the systemic circulation through oral administration because of its numerous benefits, including its low cost, high patient regulation, ease of storage and transportation, and formulation adaptability. Ingestion has also took over numerous additional drug delivery systems for humans. The time it takes for the medication to travel through the gastrointestinal tract (GI tract), the rate of drug dissolution from the dosage form, the location of the drug being absorbed, and how quickly the stomach empties are all factors that determine the efficacy of oral drug delivery techniques.

dose forms that remain in the stomach for a longer period of time than regular dose forms need the ability to prolong and control the absorption time. Consequently, drugs originating in the GIT are incompletely absorbed because of peristaltic contractions. To overcome this limitation, researchers have been working on oral gastroretentive prolonged or controlled-release pills that slowly dissolve the medicine at the upper gastrointestinal tract (GIT) in an effort to maintain a high level of drug in the bloodstream for a longer duration. Developing controlled-releasing devices to increase bioavailability and assimilation is not an easy task.

With its short half-life, local potency in the upper gut for helicobacter pylori eradication, and very unstable and poorly soluble at alkaline pH, gastroretentive drug delivery systems (GRDDS) are a potential option for medications with reduced absorption in the lower GIT. Various formulation approaches have been utilized to develop regulated GRDDS, such as as raft-forming, magnetic, ion-exchange, convertible, bio/mucoadhesive, and low- and high-density solutions.

Several formulation-related factors might affect the quality of the gastroretentive dosage form. These include the types of polymers used (non-ionic, cationic, and anionic), the composition of the polymers in the dosage form, the viscosity grade, the molecular makeup of the polymers, and the solubility of the medication. Excipients' physicochemical

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, August 2024

properties are also important in several GRDDS. Considerations such as excipient thickness and explosive agent composition are crucial in effervescent floating infrastructure, for instance. Excipients with a high swelling potential, like sodium carboxymethyl cellulose and cross-povidone, are necessary to create a hydrogel with a large number of pores. The substance of the gastroretentive dosage form may also affect process parameters like compression pressure during pilling.

The main objective of this research is to provide details about the many GRDDS that have been developed so far, as well as the stomach's physiological state, possible pharmacological possibilities for GRDDS, factors that influence GRDDS, and the analysis of GRDDS in vitro or in vivo.

Methods to lengthen gastric residence time encompass

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

II. PHYSIOLOGY OF STOMACH

Since the stomach is involved in the GRDDS, it is necessary to have a thorough knowledge of the stomach's structure and physiology in order to effectively create the gastro retentive dosage form. Figure 1 shows the anatomical division of the stomach into two sections: the proximal section, which comprises the body and fundus, and the distal section, which comprises the antrum and pylorus. The principal role of the stomach is to absorb food, break it down, and then transfer it into the duodenum with little pressure. Undigested food is mainly stored in the fundus and body, and the antrum helps empty the stomach by acting as a pump.

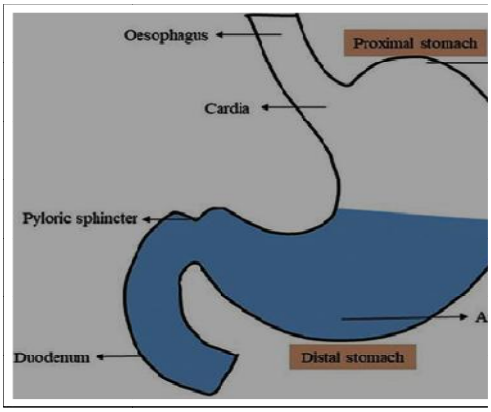

Figure 1: Schematic view on the anatomy of stomach

Table 1 displays the many stages of the migrating myoelectric complex (MMC), which is the name given to the pattern of motion in the stomach. While both the fed and fasted states do empty the stomach, the fundamental pattern of gastric emptying is very different. During the fasting state, the small intestine and stomach undergo a sequence of electrical events called interdigestive cycles every 90 to 120 minutes. Approximately 19 mm of pylorus diameter expansion occurs throughout the interdigestive phase. Consequently, particles smaller than the pyloric sphincter's diameter can easily discharge from the pylorus toward the duodenum amid the inter-digestive phase.

Hence, gastric emptying can be delayed in the fed state because motor activity starts 5-10 minutes after food is taken and continuing for as long as the food remains in the stomach.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, August 2024

Different Gastroenterological Drug Delivery Methods

For continuous and extended pharmaceutical input to the upper region of the GIT, gastro retentive delivery systems are designed to remain in the stomach for a longer period of time and discharge their active ingredients. A number of important medications have shown promise for enhanced oral delivery using this method in recent years. This is due to the fact that these drugs have a longer retention time in the upper gastrointestinal tract, which may substantially enhance their oral bioavailability and therapeutic efficacy. A variety of gastro retentive delivery methods are available, including:

- Bioadhesive drug delivery system (BDDS)
- Expandable drug delivery system
- Floating drug delivery system and
- High density
- Bioadhesive systems.

Table 1: Four phases of the migrating myoelectric complex

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

By "mucoadhesion," we mean the interaction among a bio adhesive polymer and the mucin layer that lines the whole gastrointestinal tract. In order to improve the site-specific absorbed by medication, BDDSs are used as delivery devices within the lumen. Bio adhesive polymers are used in this technique so that they can adhere to the surface of the stomach's epithelial cells. Consequently, they make the stomach retention last longer. Bio adhesion can be described by.

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

Figure 2 shows how BDDSs are used as a delivery device inside the lumen to enhance site-specific medicine uptake. Bio adhesive polymers are used in this technique so that they can adhere to the surface of the stomach's epithelial cells. By attaching to the stomach's epithelial cells or mucus, bio adhesive systems increase the GRDDS's proximity to and duration of interaction with the biological membrane. Excipients such as polycarbophil, carbopol, lectins, chitosan, gliadin, and alginate have been commonly used in these systems.

To increase the amount of time that drugs stay in the stomach, bio adhesive systems stick to the surface of gastric epithelial cells or mucin, bringing the drugs closer to the biological membrane and allowing them to interact with it for longer. The sticky properties of mucin's surface epithelium have been known for a long time and have been utilized in the production of GRDDS, which primarily consist of bio adhesive polymers. An improved local action or systemic impact can be achieved when a medicine has the ability to stick to the mucous layer, which prolongs its residence length in a particular organ site.

Bio-adhesive liposomal systems

Coating a polymer with an inadequately absorbed medicine yields mucoadhesive liposomal systems. Chocopolymer, carboxymethyl chitin, chitosan, and carbopol are examples of muco-adhesive polymers that are frequently used to coat liposomes. Liposome mucoadhesion is responsible for the dosage forms' prolonged gastric retention time (GRT).

III. SWELLING AND EXPANDABLE SYSTEMS

Easily ingestible, expandable gastric retentive delivery systems undergo swelling or unfolded mechanisms that lengthen their gastric retention duration, causing them to grow in size and shape in the stomach. Due to subsequent evacuation from the stomach, their diameters are lowered following medication release. Dose forms enhance GI retentivity due to

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, August 2024

their large size and high stiffness, which allows them to endure peristalsis and physiological contractility of the stomach. The in vivo absorption properties of medicines produced in these systems are superior because of their narrow absorption window.

They are unable to get out the pylorus because their system's expansion function is enlarged. This causes the dosage form to remain in the stomach for an extremely extended period of time. The reason these systems are called "plug type systems" is that when their increased diameter is 12-18 mm, they tend to stay blocked at the pyloric sphincter. Gastric retention and controlled drug delivery into the stomach are the goals of the formulation. Several hours after ingestion, such polymeric matrices remain in the gastrointestinal tract. A steady equilibrium among swelling size and endurance is maintained by the degree of cross-linking within the polymeric strands. A system's physical integrity can be preserved for a long period with a high degree of cross-linking since it slows down its expansion ability. In Figure 3, we can see a schematic representation of the expanding drug delivery system in action.

IV. DRUGS DELIVERY SYSTEMS THAT FLOAT

Floating delivery systems are able to float in the stomach for an extended period of time without impacting the rate of gastric emptying because their bulk density is lower than that of gastric fluids. While floating on the stomach contents, the drug is gradually let go from the system at the needed rate. After the drug is released, any residual system is removed from the stomach. Consequently, greater control over changes in drug levels in the blood and an increase in stomach retention length are achieved. The following categories make up floating medication delivery systems:

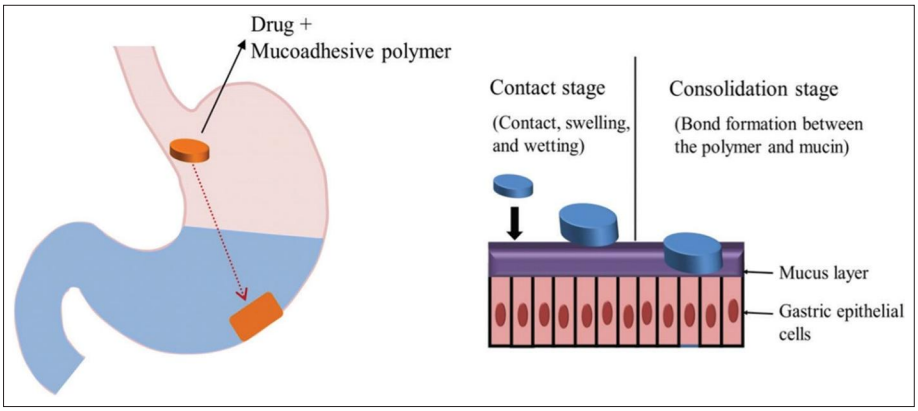

Figure 2: Mucoadhesive GRDDS (a) general representation of mucoadhesive systems and (b) mechanism of mucoadhesive system

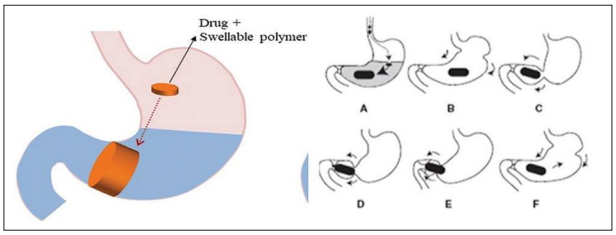

Figure 3: (a and b) GRDDS stands for an expanding medication delivery system and is based on systems that can be expanded. along with (A) a dramatic expansion of the device upon coming into touch with gastric fluids (up to several hundred times its initial volume), (B-D) the hydrogel is propelled towards the pylorus by the gastric contraction, (E) the gastric contraction passes over the hydrogel's surface, and (F) it is reintroduced into the stomach's body.

- Non-effervescent and
- Gas-generating system.
- Non-effervescent system

When you swallow, this kind of system swells out of control, absorbing all of the stomach acid to the point where it can't leave the stomach. A method for making these dosage forms involves mixing the drug with a gel. The gel will

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, August 2024

expand when it comes into touch with stomach fluid following oral delivery, but it will keep the corresponding shape and bulk density below one inside the outer gelatinous layer. These dosage forms float because the stretched polymer contains air. The most common excipients used in these systems include hydropropyl methyl cellulose (HPMC), carbopol, agar, sodium alginate, polyethylene oxide, polycarbonates, polyacrylate polymers, and polyvinyl acetate. Various types of non-effervescent systems (a-c) are discussed in the sections that proceed.

Colloidal gel barrier system

This method involves the use of a pharmaceutical that contains hydrocolloids, which are able to create gels, in order to maintain the medication's buoyancy in the stomach. A number of matrix-forming polymers, including polyacrylate, polystyrene, and polycarbophil, as well as cellulose-type hydrocolloids (HPMC, hydroxypropyl cellulose, and hydroxy-ethyl cellulose) and polysaccharides are present in this system at high concentrations. Hydrocolloids in this system hydrate when they come into contact with stomach fluid, creating a colloid gel barrier across their surfaces and causing their densities to drop below one. A colloidal gel barrier system is schematically shown in Figure 4.

Microporous compartment system

To use this technique, a microporous compartment with porous walls on both the top and bottom is used, as shown in Figure 5, to encase a medication reservoir. Because of the stomach's flotation chamber, which contains trapped air, the delivery system is able to float above the gastric contents. By passing the medication through the beginning, gastric juice can breakdown it and then carry it into the intestines for continued absorption.

Alginate beads

Floating dosage forms with several units have been developed using dried calcium alginate complex. Calcium alginate precipitates when sodium alginate solution is dropped into aqueous calcium chloride solution, creating 2.5 mm diameter spherical beads. The beads are subsequently separated, quickly frozen in liquid nitrogen, and freeze-dried for 24 hours at -40°C. This process creates a porous structure that can sustain a floating force for over 12 hours. The process of making alginate beads is illustrated schematically in Figure 5. The schematic diagram for the manufacture of alginate beads is shown in Figure 6.

Hollow microspheres/micro-ballons

Kawashima et al. developed a novel emulsion solvent diffusion method to produce hollow microspheres encased in an outer polymer shell that contained medicinal compounds. An agitated solution of poly vinyl alcohol that has been thermally controlled at 40°C was used to combine the medicine with an enteric acrylic polymer ethanol/dichloromethane solution. Evaporation of dichloromethane, which happens in the polymer's internal cavity with the drug, establishes the gas phase in the dispersed polymer droplet. The micro-balloon remained in a state of near-constant motion over an acidic-solving environment that contained surfactant for over twelve hours. Various effervescent systems (a-c) are discussed in the sections that proceed.

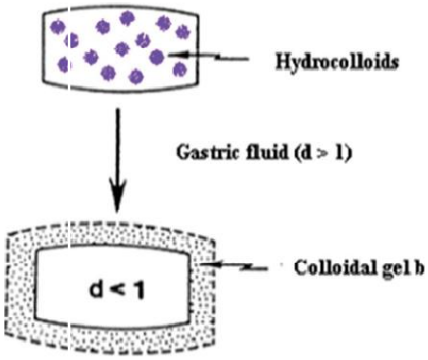

Figure 4: Colloidal gel barrier system

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, August 2024

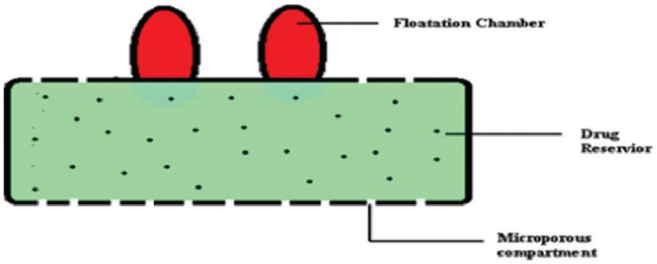

Figure 5: Microporous compartment system

Gas-generating systems/effervescent systems

The effervescent parts, such as sodium bicarbonate, citric acid, or tartaric acid, and swellable polymers, such as methocel, comprise the matrices of these buoyant systems. Chitosan is one example of a polysaccharide. The product floats to the top of the stomach because the system is so ready to receive carbon dioxide. She has recorded a variety of methods and materials, including a combination of sodium bicarbonate and sodium alginate, floating minicapsules with a core of lactose, polyvinylpyrrolidone, and sodium bicarbonate coated with hydrophobic polyethylene glycol, and floating systems that utilize ion exchange resin technology. The interior of these tiny capsules is hollow, and they also have a coating. Granules encased in high-performance microcapsules (HPC) composed of sodium bicarbonate, lactose, and a binder form the core's central component. Put some pepstatin on top of the HPMC layer. After releasing carbon dioxide into the stomach's fluid, the system floats and remains there for a long time. Figure 7 shows a simplified diagram of a floating system's function.

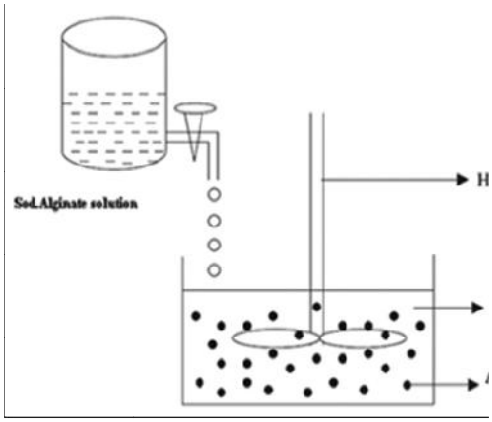

Figure 6: Schematic diagram for preparation of alginate beads

IV. RAFT FORMING SYSTEMS

Many people are interested in using raft forming systems to treat gastrointestinal infections and disorders by delivering medicine. Patients suffering from gastroesophageal reflux illness have found relief with floating rafts. A raft is formed when a viscous cohesive gel is mixed with stomach fluids; when the gel grows, it forms an ongoing layer with each segment of the liquid. This raft floats on the contents of people's stomachs due to the low bulk density that results from CO2 generation. In order to make the system more water-soluble and easier to dissolve in the stomach juices, it is common practice to incorporate a gel-forming agent and carbonates that are actually accountable for carbon dioxide production, as well as alkaline bicarbonates. The process for the formation of rafts by antacids was detailed by Fabregas et al. By floating on top of the stomach fluids and acting as a barrier within the stomach and the esophagus, a foamy sodium alginate gel (raft) prevents the reflux of gastric contents (i.e., gastric acid) into the oesophagus. A GRDDS that uses raft-forming systems is illustrated schematically in Figure 8.

HIGH DENSITY SYSTEMS

Pellets small enough to fit in the pyloric region—the lowest part of the upright stomach—have been retained by sedimentation. This mechanism is employed when the pellets are in an upright position. Peristalsis in the stomach can

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, August 2024

also be tolerated by dense pellets (about 3 g/cm3) that become entangled in rugae. The typical gastrointestinal transit time can be extended from 5.8 to 25 hours using pellets. A few examples of frequently used excipients are iron powder, zinc oxide, titanium dioxide, and barium sulfate. With these materials, density can be raised by 1.5-2.4 g/cm3. A high density system-based GRDDS is schematically shown in Figure 9.

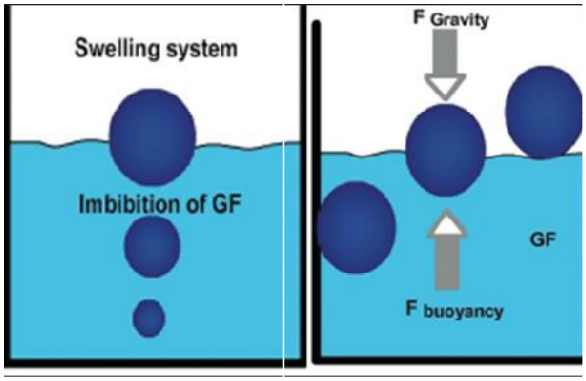

Figure 7: Mechanism of floating systems

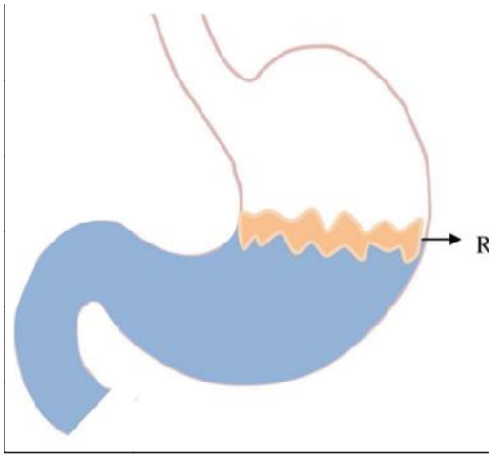

Figure 8: GRDDS based on raft-forming systems

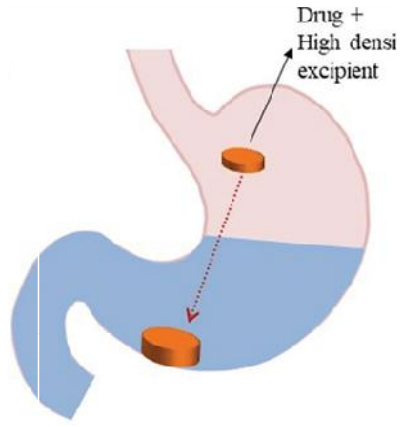

Figure 9: GRDDS based on high-density systems

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, August 2024

V. MULTIPLE UNIT TYPE FLOATING SYSTEM

Two layers of a multi-unit floating system encase the "seeds," or sustained-release tablets. A layer of swellable membrane makes up the outside, and a layer of effervescent chemicals makes up the inside. This device instantly dives when covered in a liquid that dissolves at body temperature, causing the pills to inflate and float as a result of their reduced density. Carbon dioxide production and internal trapping are associated with the decreased system density.

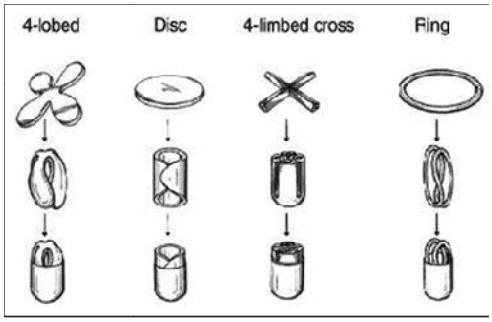

Figure 10: GRDDS based on expandable system

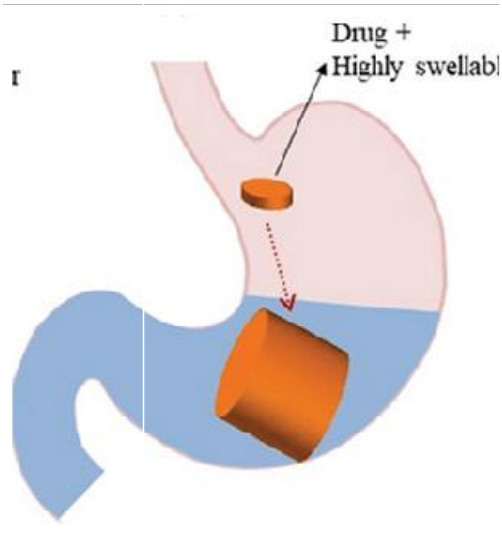

Figure 11: GRDDS based on super porous hydrogels systems

SYSTEMS THAT GROW AND SPLAT

Another type of dosage form that becomes trapped in the pylorus after swallowing is the swelling and expansion system. Consequently, the dosage form stays in the stomach for a long time. A "plug type system" is one that is also typically logged at the pyloric sphincter. When the drug delivery system comes into contact with stomach fluid, the polymer absorbs water and expands, which might cause swelling and controlled release of the drug. The hydrophilic polymer network swells substantially due to the presence of certain crosslinks.

The accumulation prevents the stomach from being "nourished" and permits gastric retention, which in turn blocks housekeeping waves. Hydrogels in the shape of swelling balloons and medicinal polymer sheets are examples of such delivery technologies. To get the most out of it and minimize the bad, you need to find a happy medium between the swelling rate, amount, and rate of polymer decomposition. Listed under "Non-effervescent systems" are their details.

These systems can multiply and stay in the stomach for long times. These typically come in a foldable and small dose form, like a capsule. Because the dosage form expands and the capsule shell breaks down in the stomach, the medication is unable to pass through the digestive system. Using the right polymer allows for controlled and sustained medication delivery. The schematic diagram of an extensible systems-based GRRDS is shown in Figure 10.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, August 2024

SUPER POROUS HYDROGELS SYSTEMS

This method for enhancing GRT involves rapidly absorbing water via capillary wetting via numerous interconnected open holes, causing super porosity hydrogels with typical pore sizes more than 100 micrometers to expand to equilibrium size in under a minute. In order to endure the pressure from the stomach contracting, they are mechanically strong and expand to a significant size (swelling ratio: 100 or above). Coprocessing with the hydrophilic particle material croscarmellose sodium achieves this. This produces "ultra-porous hydrogel composites," a type of material with a dispersed phase within a continuous polymer matrix, throughout the production process.

The very porous hydrogel hybrids spend over twenty-four hours in the gastrointestinal tract. Incorporating a hydrophilic or water dispersible polymer that can be cross-linked after the super porous hydrogel is created allows for the creation of "super porous hydrogel hybrids," a product of recent advances in the field. Sodium alginate, pectin, and chitosan are some instances of polysaccharides that can be used as hybrid agents. Figure 11 shows a simplified diagram of a GRRDS that uses technologies on the basis of ultra-porous hydrogels.

ION EXCHANGE RESINS

Research has shown that bicarbonate-containing coated ion-exchanging resin bead compositions can retain food in the stomach. A medicine with a negative charge is attached to ion exchange resins when bicarbonate is introduced to them. The carbon dioxide beads were enclosed in a semi-permeable membrane to slow down the rate of loss. Chloride and bicarbonate ions swap places as they reach the stomach's acidic environment. In contrast to uncoated beads, which sink quickly, resin-coated beads float on top of the stomach contents and create a layer of carbon dioxide, which was created and retained in the membrane throughout the procedure.

OSMOTIC REGULATED SYSTEMS

It is composed of a bioerodible capsule with an inflatable lying encouragement and an osmotic pressure-controlled treatment delivery system. The drug reservoir and osmotically active compartments make up the osmotic controlled drug delivery system. The capsule breaks down quickly in the stomach, publishing the intragastric organically regulated medicine delivery system. Within, the inflatable support forms a fluid-filled polymeric bag that is inflated using a liquid that gasifies at body temperature.

MAGNETIC SYSTEMS

In magnetic systems, a dosage form consists of an internal magnet, excipients, and active medicinal components. Figure 12 shows the positioning of the medications with internal magnets in relation to an extracorporeal magnet placed above the stomach. The positioning and strength of the extracorporeal magnet can influence the GRT. Magnetic tablets increase both GRT and bioavailability, according to earlier studies. Human volunteers were tested with both magnetic acyclovir tablets and those that did not have a magnetic field around them, according to Groning et al. Researchers found that GRT and plasma medicine concentration were both improved when an extracorporeal magnet was present.

Bio adhesive granules comprising different types of ultra-fine ferrite have been developed and evaluated on rabbits by Ito et al. They found out that there was an outside magnetic field. They found that all grains remained in the stomach for almost 2 hours when exposed to an external magnetic field strength of 1700 G. Nevertheless, patients might not comply because it's hard to get the magnet exactly where it needs to be. The therapeutic significance of the limited studies conducted on magnetic systems is still unknown. Research into these systems in the future should, therefore, center on how useful they are in medication treatment.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, August 2024

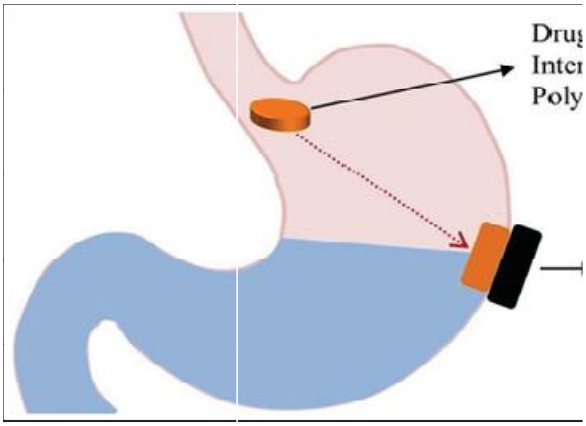

Figure 12: GRDDS based on magnetic systems

FACTORS AFFECTING GASTRORETENTION TIME OF FLOATING DRUG DELIVERY SYSTEMS

The effectiveness of gastro retentive drug formulations as a system is affected by several aspects, including:

- Formulation Factors and
- Idiosyncratic Factors.
- Formulation factors

One density-dependent dose-form buoyancy function is GRT. The rate of stomach emptying is affected by the density of a dosage form. Because it has a lower density than gastric secretions, a buoyant dosage form floats. The dosage unit stays in the stomach for a long period since it is not close to the pyloric sphincter. As long as the conditions for hydrodynamic equilibrium are met, drug flotation can continue indefinitely. There is a gradual dissolution of the active substance from dosage forms that sink to the bottom of the whole atrium due to their higher density than the stomach material.

Size

A higher GRT is associated with dosage form units with a diameter greater than 7.5 mm compared to those having a diameter of 9.9 mm. Because larger dosage forms are emptied during digestion (weak MMC) and have a more difficult time passing across the pyloric sphincter into the small intestine, their gastric retention duration is longer than that of smaller ones.

Shape of dosage form

In terms of GRT = 90-100% retention at 24 hours, tetrahedron and ring-shaped devices with flexural moduli of 48 and 22.5 kilo pounds per square inch, respectively, outperform other creations.

Periods of maximal motor activity (MMC) happen every 1.5-2 hours during fasting gastrointestinal motility. The GRT of the unit will be fairly brief if the formulation is supplied at the same time as the MMC, since the MMC sweeps undigested material from the stomach. On the other hand, in the fed condition, both MMC and GRT are considerably longer.

Viscosity grade of polymer

Drug release and floating properties of gastro retentive floating drug delivery systems (GRFDDS) are greatly affected by the viscosity of polymers and how they interact with one another. More successful in boosting floating qualities were low viscosity polymers (e.g., HPMC K100 LV) than high viscosity polymers (e.g., HPMC K4M). Additionally, the distribution rate was shown to decrease as the polymer viscosity increased.

Nature of meal

Slowing gastric emptying and extending medicine release can be achieved by feeding indigestible polymers or fatty acid salts, which can alter the stomach's motility characteristic to a fed state. What kind of food you eat, how much of it, its viscosity, and any medications you take at the same time all have an impact on how quickly your stomach empties? The rate of emptying is largely dictated by the number of calories in the food. It doesn't care if the calorie content is the same for proteins, lipids, and carbohydrates.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, August 2024

When the stomach's acidity, osmolarity, and calorific value are all elevated, gastric emptying takes longer. When food is present, the duration of stomach residency increases, leading to a higher breakdown of the dose form of the drug at even the most advantageous site of absorption. A GRT of 4-10 hours has previously been seen after a meal rich in lipids and proteins.

Frequency of feed

The GRT can be improved by over 400 minutes when fed numerous meals instead of just one, thanks to the low frequency of MMC.

Idiosyncratic factors

An idiosyncrasy is a hereditary chemical abnormality. The medication causes the out-of-the-ordinary response because it interacts with a personal characteristic that is absent in most people. This kind of reaction can only occur in people who share a certain gene. Another factor that could decide it is -

Gender

The pace of gastric emptying is slower in women than in men. Their mean ambulatory GRT during meals (3.40.4 h) is shorter than that of age- and race-matched females (4.61.2 h), regardless of weight, height, or body surface area. Regardless of body surface area, weight, or height, the mean ambulatory GRT for men is lower (3.4 0.6 h) than for age- and race-matched females (4.6 1.2 h).

Age

The time it takes for the stomach to empty is shorter in the elderly compared to the younger participants. Transit times through the intestines and stomach can vary greatly, both within and between individuals. The GRT is significantly longer in the elderly, especially those over the age of 70. The GRT is significantly longer in the elderly, especially those over the age of 70.

Posture

The patient's supine and upright ambulatory phases may have different GRT.

Upright position

Floating forms, no matter how big or small, remain above the contents of the stomach when upright, therefore they are unable to empty themselves after a meal. While conventional dosage forms sink to the distal stomach's base and are emptied into the stomach through the pylorus by astral peristaltic motions, floating prescription forms have longer and more repeatable GRTs.

Supine position

When it comes to early and uneven emptying, this position offers no reliable protection. Patients lying on their backs reported longer retention times for both the conventional and floating large dosage formulations. The gastric retention of buoyant forms tends to stay buoyant regardless of the degree to which the stomach curves.

Peristalttic motions, which push the fluids of the stomach into the pylorus, may also wash away these units as they move distally, leading to a significant decrease in GRT in comparison to those who are upright.

Concomitant intake of drugs

Some medications can hinder the action of GRFDDS. These include prokinetics (such as cisapride and metoclopramide), anticholinergics (such as atropine or propantheline), and opiates (such as codeine). Gastric motility-reducing drugs, when used together, can prolong the time it takes for the stomach to empty.

Biological factors

Diabetes, hypothyroidism, gastric ulcers, gastroenteritis, and gastric stenosis all impede stomach emptying. Hypothyroidism, duodenal ulcers, partial or total gastrectomy, and gastric bypass all raise the gastric evacuation rate.

ADVANTAGES OF GRFDDS

There are a number of benefits to increasing the GRT using either method, including:

- The stomach wall becomes irritated when acidic pharmaceutical chemicals, such aspirin, come into contact with it. Therefore, aspirin and similar drugs may be best administered with HBS formulation.
- Medications that have a local effect in the stomach benefit from floating systems. For instance, antacids.
- Antacids and ferrous salts, which are absorbed through the stomach, benefit from the GRFDDS. Increased GRT and dosage form residence time at the site of absorption lead to better medicine absorption.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, August 2024

- Strict control over drug governance: Mucosal irritation is reduced by releasing drugs slowly and regulated. Proper local therapeutic levels are achieved via controlled and progressive pharmaceutical administration to the stomach, hence limiting systemic exposure to the drug. This lessens the medication's negative effects in the bloodstream. It is also possible to reduce dosage frequency with a site-directed delivery device due to the enhanced GI availability.
- Extended administration: Medications released in floating dose forms, pills, or capsules dissolve in gastric juice. They would dissolve in the stomach acid and be ready for absorption in the small intestine once the stomach was empty. It is presumed that floating dosage forms will allow for full absorption of medicines if they remain in solution form even when exposed to the stomach's alkaline pH.
- There are some possible advantages to using floating dose forms as a continuous release approach. An efficient method exists to increase the absolute bioavailability of drugs whose bioavailability is low due to the fact that absorption is limited to the upper gastrointestinal tract.
- It is also anticipated that floating dosage forms including SR characteristics will reduce transit variability. It also has the potential to provide a useful method for treating duodenal and gastric cancer.

DISADVANTAGES/LIMITATIONS OF GRFDDS

- Medications that have problems dissolving or remaining stable in the gastrointestinal tract are not suitable for use with a floating device.
- A large quantity of stomach fluid is necessary for these medicine delivery systems to float and function properly.
- The best options are drugs that can be absorbed in the stomach.
- The systemic bioavailability of drugs like nifedipine, which is absorbed extensively throughout the gastrointestinal system and passes through a lot of first-pass metabolism, can be reduced if stomach emptying is delayed, so these drugs would not be good choices for increasing GRT. Additionally, GRFDDS is not always an appropriate choice for drugs that aggravate the stomach mucosa.
- Mix the dosage form with 200–250 milliliters of water and drink the whole glass.
- when compared to conventional medicine dose forms absorbed by the gastrointestinal tract (GIT), these technologies offer no significant benefits.
- A restricted pyloric aperture (mean resting pyloric diameter 12.8 ± 7.0 mm), gastropathy, bowel obstruction, intestinal adhesion, or the use of large single-unit dose forms could lead to the long-term retention of stiff large-sized forms.

VI. CONCLUSION

Medications with a narrow absorption window near the gastrointestinal area are best delivered using gastro retentive drug delivery devices. Efforts are underway to improve the bioavailability of drugs by developing various medication delivery systems that aim to administer the treatment in the stomach area or upper part of the gastrointestinal tract (GIT).

REFERENCES

[1]. Arora S, Ali J, Ahuja A, Khar RK, Baboota S. Floating drug delivery systems: A review. AAPS PharmSciTech 2005;6: E372-90.

[2]. Awasthi R, Kulkarni GT. Decades of research in drug targeting to the upper gastrointestinal tract using gastroretention technologies: Where do we stand? Drug Deliv 2016; 23:378-94.

[3]. Bechgaard H, Ladefoged K. Distribution of pellets in the gastrointestinal tract. The influence on transit time exerted by the density or diameter of pellets. J Pharm Pharmacol 1978; 30:690-2.

[4]. Chavanpatil MD, Jain P, Chaudhari S, Shear R, Vavia PR. Novel sustained release, swellable and bioadhesive gastroretentive drug delivery system for ofloxacin. Int J Pharm 2006; 316:86-92.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, August 2024

[5]. Chen J, Blevins WE, Park H, Park K. Gastric retention properties of superporous hydrogel composites. J Control Release 2000; 64:39-51.

[6]. David SS, Stockwell AF, Taylor MJ, Hardy JG, Whalley DR, Wilson CG, *et al*. The effect of density on the gastric emptying on single-and multiple-unit dosage forms. Pharm Res 1986; 3:208-13.

[7]. El-Zahaby SA, Kassem AA, El-Kamel AH. Design and evaluation of gastroretentive levofloxacin floating mini- tablets-in-capsule system for eradication of *Helicobacter pylori*. Saudi Pharm J 2014; 22:570-9.

[8]. Fabregas J, Claramunt J, Cucala J, Pous R, Siles A. *In vitro* testing of an antacid formulation with prolonged gastric residence time (AlmagateFlot-Coat). Drug Dev Ind Pharm 1994; 20:1199-212.

[9]. Harrigan RM. Drug Delivery Device for Preventing Contact of Un-dissolved Drug with the Stomach Lining. US Patent, No. 405, 5178; 1977.

[10]. Ito R, Machida Y, Sannan T, Nagai T. Magnetic granules: A novel system for specific drug delivery to esophageal mucosa in oral administration. Int J Pharm 1990; 61:109-17.

[11]. Jiménez-Martínez I, Quirino-Barreda T, Villafuerte- Robles L. Sustained delivery of captopril from floating matrix tablets. Int J Pharm 2008; 362:37-43.

[12]. Kawashima Y, Niwa T, Takeuchi H, Hino T, Itoh Y.

[13]. Kim S, Hwang KM, Park YS, Nguyen TT, Park ES. Preparation and evaluation of non-effervescent gastro-retentive tablets containing pregabalin for once-daily administration and dose proportional pharmacokinetics. Int J Pharm 2018; 550:160-9.

[14]. Lehr CM, Hass J. Development in the area of bio- adhesive drug delivery systems. Expert Opin Biol Ther 2002; 2:287-98.

[15]. Murphy CS, Pillay V, Choonara YE, Du Toit LC. Gastroretentive drug delivery systems: Current developments in novel system design and evaluation. Curr Drug Deliv 2009; 6:451-60.

[16]. Nasa P, Mahant S, Sharma D. Floating systems: A novel approach towards gastro retentive drug delivery systems. Int J Pharm Pharmsci 2010; 2:3-15.

[17]. Panda S, Sailada NS, Devi B, Pattnaik S, Maharana L. Design of floating drug delivery systems: An update on polymeric advancements with special reference from natural origin. Int J Pharm Sci Rev Res 2016; 39:125-32.

[18]. Pharmaceutics 2018; 10:161.

[19]. Ponchel G, Irache JM. Specific and non-specific bio-adhesive particulate systems for oral delivery to the gastrointestinal tract. Adv Drug Deliv Rev 1998; 34:191-219.

[20]. Rajamma AJ, Yoogesh HN, Sateesha SB. Natural gums as sustained release carriers: Development of gastroretentive drug delivery system of ziprasidone HCL. Daru 2012; 20:58.

[21]. Sarparanta MP, Bimbo LM, Mäkilä EM, Salonen JJ, Laaksonen PH, Helariutta AK, *et al*. The mucoadhesive and gastroretentive properties of hydrophobin-coated porous silicon nanoparticle oral drug delivery systems. Biomaterials 2012; 33:3353-62.

[22]. Sawicki W. Pharmacokinetics of verapamil and nor- verapamil from controlled release floating pellets in humans. Eur J Pharm Biopharm 2002; 53:29-35.

[23]. Stockwell AF, Davis SS, Walker SE. *In vitro* evaluation of alginate gel system as sustained release drug delivery system. J Control Release 1986; 3:167-75.

[24]. Thapa P, Jeong S. Effects of formulation and process variables on gastro-retentive floating tablets with a high-dose soluble drug and experimental design approach.