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A Review on Gastroretentive Drug Delivery System (GRDDS)

[1]Sakshi Laxman Sonawane, [2]Assist. Prof. Jayashree Khemnar

[1]At Post Khedgoan, Tal-Dindori, Dist. Nashik, Post Code- 422205, INDIA
[2]Shree Mahavir Institute of Pharmacy Nashik. (422004)

Abstract-

The field of oral medication administration has seen tremendous growth recently thanks to the gastro-retentive drug delivery system (GRDDS). It is a widely used strategy to keep the dose form in the stomach for an extended period of time and release the medications gradually, which can address numerous issues with conventional oral delivery, including inadequate bioavailability. Different cutting-edge techniques, such as magnetic field assisted gastro retention, plug type swelling systems, muco-adhesion techniques, and floating systems with or without effervescence, are being used to facilitate the development of GRDDS. Despite the many advantages, substantial subject differences in gastrointestinal physiological condition, the effects of food, and variable rates of stomach emptying time are the difficulties that restrict the number of available GRDDS on the market. The in-vivo research done by GRDDS in the recent past is highlighted in this review paper, along with its limits and difficulties that need to be overcome in the near future.

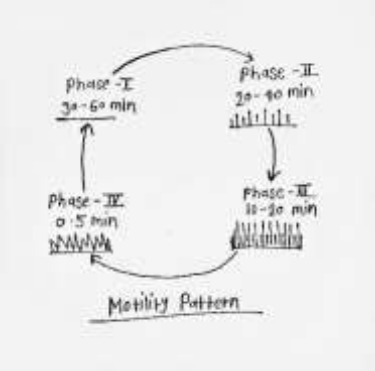
Keywords: Gastroretentive, GRDDS, Oral route. Various Approaches

1. Introduction-

Gastroretentive dose forms are a changeable process, and their capacity to extend and regulate the duration until the stomach empties is a key advantage over conventional dosage forms. Drugs' gastric residence times can be considerably extended by gastroretentive systems, which can stay in the gastric region for several hours. Prolonged stomach retention increases bioavailability, lowers drug waste, and increases solubility for medicines that are less soluble in a high pH environment.

1.1 Gastrointestinal Tract Basic Physiology:

Fundus, body, and antrum are the three anatomical divisions of the stomach (pylorus). While the antrum is the primary location for mixing movements and serves as a pump from stomach emptying by driving the actions, the proximal region made of fundus and body serves as a reservoir for undigested materials. Both when one is eating and when one is fasting, the stomach empties. However, there are two states where the patent of motility is different. An interdigitate series of electrical events that cycle through the stomach and intestine every two to three hours occur during the fasting state. This is known as the interdigitate myoelectric cycle or migrating myoelectric cycle (MMC), which is further divided into the following 4 phases as defined by Wilson and Washington.



1. Phase I (basal phase) lasts for 40 to 60 minutes and is accompanied with contractions.

2. Intermittent action potentials and contractions characterize Phase II (pre burst phase), which lasts 40 to 60 minutes. The intensity and frequency also steadily rise as the phase progresses.

3. Phase III (burst phase) lasts for 4 to 6 minutes. It consists of brief yet incredibly strong and frequent contractions. This wall has caused all of the undigested, in part.

4. Phase IV of two successive cycles lasts for 0 to 5 minutes and comes after phase III. After consuming a mixed meal, the pattern of contractions switches from that of a fasting state to that of a fed one. This pattern of continuous contractions, sometimes referred to as the digestive motility pattern, is seen throughout phase II of a fasting condition. Food particles that are driven into the pylorus in a suspension state are reduced in size (to less than 1mm) as a result of these contractions.

Gastric emptying rate slows down when MMC doesn't start acting right away in the fed state. Studies using scintigraphy to measure stomach emptying rates have shown that controlled release dose forms taken orally are primarily affected by two issues: a short gastric residence period and an unpredictably high gastric emptying rate.

1.2 Promising medication choices for gastro retention:

When medications are released in the stomach, especially when the release is prolonged and regulated, they have the greatest therapeutic impact. The amount of adverse effects associated with drugs administered in this way is reduced, and they can achieve their therapeutic goals with a low dose frequency and no recurrent dosing. Sustain release in the stomach is also helpful for therapeutic agents that the stomach does not readily absorb, as it extends the agent's contact time in the stomach or upper part of the small intestine, where absorption occurs and contact time is constrained under normal or average conditions, for example. In about 1-3 hours, food will have completed its journey through the small intestine.

Compounds with low colonic absorption but excellent absorption and upper GIT characteristics are often considered potential CRGRDF molecules. Riboflavin and levodopa, for example, have a small window of absorption in the GIT. Calcium supplements, chlordizepoxide, and cinnarizine are examples of substances that are mostly absorbed from the stomach and upper section of the GIT. Such as antacids and misoprostol, which act locally in the stomach. Such as ranitidine HCl and metronidazole, which break down in the gut. Amoxicillin trihydrate is one example of a drug that affects healthy colonic flora.

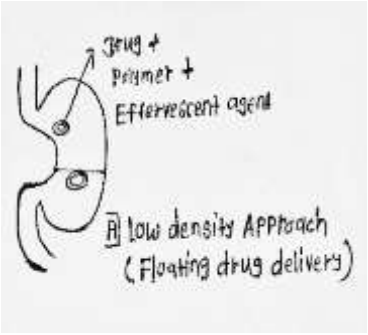
The necessity for gastro retentive dosage forms (GRDFs) has sparked significant research and development in both academia and business to create such delivery methods. Due in great part to these efforts, the following strategies were used to designate GRDFs.

2. Approaches to gastric retention

For the purpose of enhancing the GRT of a particular pharmaceutical type in the stomach, a broad variety of concepts employed a variety of techniques. Concerning these are as follows.

- **Floating drug delivery system**s

To keep pharmaceuticals in the stomach, floating drug delivery systems (FDDS) were developed. These devices are useful for medications that have poor intestinal fluid solubility and stability. Making the dose form less thick than the stomach juices allows it to float on them, which is the principle underpinning FDDS. FDDS are hydro dynamically regulated low-density systems that have enough buoyancy to float over the contents of the stomach and stay buoyant there without significantly slowing down the gastric emptying process. With the drug's release, the stomach's residual system is emptied. As a result, the stomach residence duration is prolonged and the changes in plasma drug concentration are well managed.



Increased gastrointestinal residence time for the dose form and prolonged drug release can be achieved simply and practically by using the principle of buoyant preparation. In some cases, extending a delivery system's stomach retention will result in a higher therapeutic effectiveness of the medication ingredient. Drugs with limited solubility and those that breakdown in an alkaline pH, for instance, have been proven to be effective in extending stomach retention. Additionally, prolonging gastric retention of the therapeutic moiety allows for sustained drug delivery to the stomach and proximal small intestine in the treatment of some ulcerative conditions. This has a number of benefits, including improved bioavailability and therapeutic efficacy with decreased dosing frequency.

- **Classification of floating drug delivery systems**

2.1 Effervescent system floating drug delivery system

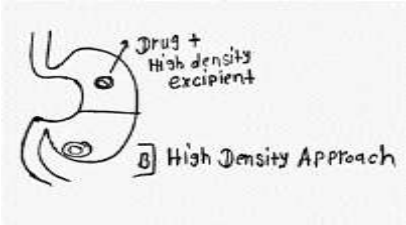
These specific drug delivery systems are composed of a matrix type, a polymer that may swell, such as methylcellulose and chitosan, as well as effervescent substances, such as sodium bicarbonate, tartaric acid, and citric acid. These are designed in a certain way so that when they come into contact with stomach juice, co2 is released and trapped in a swelling hydrocolloid, which gives the dosage form buoyancy. The swell able, asymmetric triple-layer tablet technique serves as the foundation of the delivery mechanism.

2.2 Non-Effervasant

FDDS without bubbles. In order to create floating non-effervescent matrix tablets, a direct compression technique was utilised with a variety of polymers, including Karaya gum, Chitosan, and polypropylene foam powder (Accrue® MP 1000).

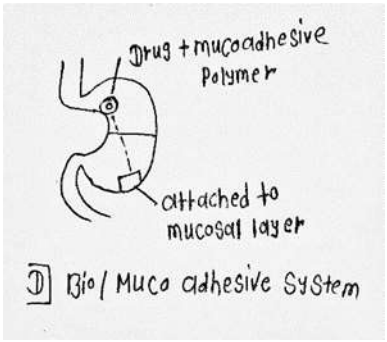
A hydrocolloid that forms a gel when in contact with stomach fluid after oral administration and maintains a bulk density of less than unity inside the outer gelatinous barrier is used to create floating dosage forms, which entail combining drugs in close proximity to the hydrocolloid. These dose forms float because of the air trapped by the inflated polymer. Additionally, the gel structure serves as a reservoir for prolonged drug release since the medication is delivered gradually by a regulated diffusion across the gelatinous barrier.

- **High Density Drug Delivery System**s



Device for delivering high doses of drugs that sink. For pellets small enough to be held in the folds of the stomach body close to the pyloric area, sedimentation has been used as a retention mechanism. Dense pellets caught in folds (around 3g/cm3) have the tendency to endure the peristaltic motions of the stomach wall. The GI transit time can be prolonged by pellets from an average of 5.8 to 25 hours, depending more on pellet density than particle diameter. Barium sulphate, zinc oxide, titanium dioxide, iron powder, and other excipients are frequently utilised. These substances raise density by up to 1.5 to 2.4 g/cm3

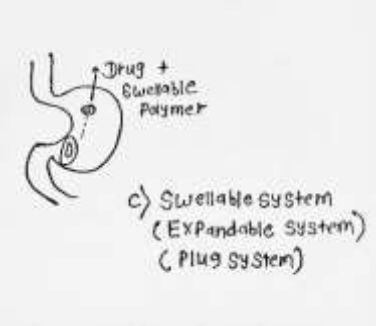
- **Bioadhesive or Mucoadhesive Drug Delivery System**



The development of bio adhesive or muco adhesive formulations was Initially done to improve GRT and regulate medication distribution for all sorts of pharmaceuticals. The process involves covering microcapsules with a bio adhesive polymer, allowing them to stick to intestinal mucosa and stay in the GI tract for a longer length of time while the active medication is released from the device matrix. Because of their well-known propensity to attach to stomach mucosa, cationic chitosan polymers can be employed to develop bio adhesive formulations that are pharmaceutically acceptable.

- **Swellable Drug Delivery System**

Because of their mechanical characteristics, swellable systems are also preserved. Usually, osmotic absorption of water causes the swelling. The dosage form is tiny enough to be ingested, and when consumed, expands in the stomach to facilitate gastric retention and keep the stomach in a “fed” state, which reduces the occurrence of the housekeeping wave.



The dose form is kept in the stomach for a long time after administration of these swellable systems because their bulk hinders their passage via the pylorus. Because they frequently remain anchored at the pyloric sphincter, these systems are also referred to as "plug type" systems. Even when a person is fed, these polymeric matrices persist in the stomach for several hours. Selecting a polymer with the right molecular weight and swelling characteristics can result in sustained and regulated medication release. The polymer absorbs water and expands when it comes into touch with stomach fluid. The existence of physical-chemical crosslinks in the network of hydrophilic polymers is what causes the considerable swelling of these polymers.

3. Gastric retention-related factors the dosage form's duration

Density: The dosage form's density should be lower than the gastric contents' (1.004g/ml) density.

Size: Dosage forms larger than 7.5 mm in diameter will spend more time in the stomach. Compared to a dosage form with a 9.9mm diameter, time. Tetra hadrons, the dosage form's shape, spent more time in the stomach. Than comparable sized objects. Formulations with one or more units exhibit a greater Predictable release profile, and failure has a minimal impact on performance Among the units, permit co-administration of units containing or having a different release profile from Substances with a higher margin of safety against dosage form failure As opposed to a single unit dosage form.

Fed or unfed state- Whether you are fed or not, your motility will be characterized by bursts of intense motor activity that happen roughly every 1.5 to 2 hours when you are fasting. When the time of the formulation and the MMC coincide, the MMC removes undigested material from the stomach, and the GRT of the unit can be extremely short. However, in the fast state, the MMC is delayed, and the GRT is prolonged.

The nature of the meal—feeding the stomach with indigestible polymers or fatty acids—can alter the stomach's motility pattern, putting it un a fed condition and reducing the rate at which the stomach empties. Medication release being prolonged. A meal with a high protein and fat content can raise the calorie content-GRT by 4–10.

Frequency of feed-Due to the low frequency of MMC, when consecutive meals are given vs a single meal, the GRT can increase by almost 400 minutes.

In comparison to their age- and race-matched female counterparts, males had shorter mean ambulatory GRTs (3.4 vs. 4.6 hours), regardless of height, weight, or body surface.

Age-People beyond the age of 70 have much longer GRTs

4. Advantages

1. .Pharmaceuticals administered into the small intestine with a limited window of absorption
2. A longer stay in the stomach may be beneficial for local actions in the upper small intestine, such as the treatment of peptic ulcer disease.
3. For medications like cyclosporine, ciprofloxacin, ranitidine, amoxycillin, captopril, etc. that are quickly absorbed after release in the GI tract, improved bioavailability is anticipated.
4. Adherence to a once day therapy by the patient.
5. Greater effectiveness of treatments.
6. Lowers dosing frequency.
7. Specific therapy for conditions affecting the upper GI tract locally.
8. Contrary to the administration of non gastroretentive drug delivery, the gastroretentive drug delivery technique can greatly increase the bioavailability of therapeutic drugs, especially for those that are processed in the upper GIT.

5. Disadvantages

One drawback of floating systems is that, in order to function properly, they need a lot of fluids in the stomach. With such a dose form, increased water consumption is advised.

1. In supine position (similar to sleeping), contractile waves may sweep away floating dose form if it is not larger in size. Because of this, patients shouldn't take floating dosage forms right before night.
2. Drugs that have instability issues in highly acidic environments, have extremely low solubility's in acidic environments, or that irritate the gastric mucosa cannot be included into GRDDS.
3. The fast rate of mucus layer turnover, the thickness of the mucus layer, and limits associated with soluble mucus are issues with bio/Mucoadhesive systems.
4. A rapidly swelling dose form that can reach a size greater than the pylorus aperture is required. • Stomach retention is influenced by several elements such as gastric motility, pH, and food presence, and it must be able to withstand the housekeeping waves of Phase III of MMC. It is impossible to forecast buoyancy because these components are never constant.
5. A Bioadhesive device faces significant difficulties due to the rapid turnover of stomach mucus.
6. The use of Bioadhesive drug delivery methods has the potential to bond to the esophagus.
7. Medications that have issues with solubility and stability

Conclusion

Enhanced bioavailability and regulated medication administration are two possible benefits of gastroretentive drug delivery methods. Drug retention in the stomach may be increased by using a gastroretentive drug delivery method. Any drug delivery system's objective is to deliver a therapeutic dose of the medication to the appropriate location in the body as well as to attain and sustain the desired plasma concentration of the drug for a certain amount of time.

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