A Review on Floting Drug Delivery System: An Innovative Strategy for Prolong Gastric Residence Time

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***Abstract*—Some drugs do not dissolve well in the intestine because of its alkaline pH. As a result, when these drugs are given in normal tablet or capsule form, they pass quickly through the stomach, leading to low bioavailability. Similarly, drugs that are meant to act locally in the stomach also get cleared too fast and do not stay long enough to work effectively. Because of this, patients may need to take the medicine more frequently. To overcome these issues, researchers have developed systems that allow the drug to stay in the stomach for a longer time. One such approach is the Floating Drug Delivery System (FDDS). These systems are designed with low density, allowing them to float on the stomach contents without affecting the normal gastric emptying process. While floating, the drug is slowly released at a controlled rate, which helps maintain steady drug levels in the blood and reduces fluctuations. This review focuses on the formulation, advantages, limitations, and evaluation methods of gastro-retentive floating drug delivery systems, highlighting how they offer improvements over conventional oral dosage forms**

***Index Terms*—Floating Drug Delivery System (FDDS), Gastro-retentive Drug Delivery System (GRDDS), Gastric Retention, Gastric Residence Time (GRT), and Plasma Drug Concentration.**

I. INTRODUCTION

In oral drug delivery, gastro-retentive drug delivery systems (GRDDS) have become an important area of research. These systems help the dosage form stay in the stomach for a longer time and release the drug slowly. This method can help solve problems seen in normal oral drug delivery, such as low bioavailability. (Mandal U k et.al 2016). Drug absorption in the digestive system can vary a lot. It depends on factors like how fast the stomach empties, how long the medicine stays in the digestive tract, how quickly it is released from the dosage form, and where the drug gets absorbed. (Gastric et.al 2021) Gastroretentive drug delivery systems (GRDDS) are a new method used in oral controlledrelease medicines. They help the drug stay in the stomach longer and release slowly for better treatment. ‖ (vrettos NN.et.al 2021) The oral route is the most commonly used and easiest way to take medicine. However, controlled-release drug delivery systems are not fully effective if they cannot stay near the area where the drug needs to be absorbed (sciences B et.al 2019) "One major limitation of oral controlled drug delivery is that many medicines are not absorbed evenly throughout the digestive system.‖(Bomma R.et.al 2013) A gastro-retentive drug delivery system is a special type of controlled-release system that stays in the stomach for a longer time. It helps improve drug absorption by slowly releasing the medicine before it reaches its main absorption area, which results in better bioavailability. Gastric emptying happens in both fasting and fed states, but the movement pattern is different in each condition. Studies show that oral controlledrelease dosage forms face two major challenges: short time in the stomach and unpredictable stomach emptying, which affects consistent drug absorption. (Sciences B et.al2019

II. NEED FOR GRDDS

Some medicines like beta-blockers, certain NSAIDs, and insulin are good candidates for delayed-release dosage forms. These drugs work better when they are released slowly and stay longer in the stomach. Many

medicines are absorbed only at specific sites in the gastrointestinal tract, so controlled release helps ensure that the maximum amount of the drug reaches the right location. Because of this, the pharmaceutical industry is now focusing on developing drug delivery systems that provide site-specific and controlled drug release. (Gupta and Pandey et al 2018)

III. ADVANTAGES OF GRDDS

Gastro-retentive drug delivery systems offer several important benefits:

1. They are useful in treating diseases like peptic ulcers because the drug stays longer in the stomach.
2. They are ideal for drugs with a narrow therapeutic index and help reduce how many doses a patient need.
3. They help improve the bioavailability of certain drugs.
4. They are suitable for medicines that break down or become unstable in intestinal fluids.
5. They provide controlled or sustained release of the drug, helping maintain the required drug level in the body for a longer time. (Panday A et .al 2012)

IV. DISADVANTAGES OF SEDDS

1. Drugs that are unstable in strong acidic conditions, have poor solubility in stomach acid, or may irritate the stomach lining cannot be used in GRDDS.
2. Floating Drug Delivery Systems (FDDS) need a sufficient amount of fluid in the stomach to float properly and work effectively. This means the patient must drink plenty of water when taking these dosage forms. (Vyas and Joseph et.al 2009)
3. Drugs with poor solubility in acidic stomach conditions (example: Phenytoin).
4. Drugs that break down or become unstable in acidic environments (example: Erythromycin).
5. Drugs that may irritate the stomach or cause gastric damage when released slowly (examples: Aspirin and other NSAIDs) (maryam kouchaka et.al 2004)

V. ANATOMY STOMACH

The success of GRDDS depends on understanding how the stomach works and how food leaves it. The human stomach has three main parts: the fundus, body, an antrum pylorus). After eating, the stomach volume is around 1.5 liters, but during fasting it can shrink to about 250–500 Ml. (Klausnar et.al 2003) The fundus and body of the stomach mainly help in holding the food and pushing any undigested material forward. The antrum acts like a mixer and grinder, and also works as a pump to push food out of the stomach. The pylorus controls the opening between the stomach and the duodenum, helping regulate how long food stays in the stomach. It's also important to know that the movement of the stomach changes depending on whether it is in the fasting state or the fed state. (Laulichat B et.al 2010) The stomach moves in a repeated cycle of activity and rest. Each cycle lasts about 90–120 minutes and is divided into four phases (Talukdar et.al 2004

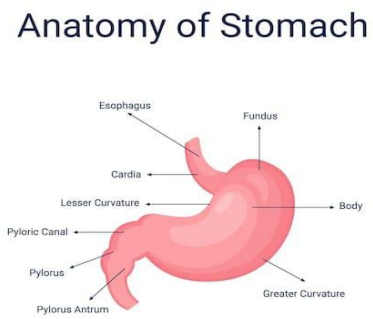

Fig. no.1 Anatomy of stomacho

VI. FACTOR AFFECTING GASTRIC RETENTION

1 Density: For a drug to stay longer in the stomach, its density should be lower than the stomach contents (around 1.004 g/ml) so it can float easily.

2. Size: The larger the dosage form, the longer it stays in the stomach. Tablets with a size greater than 7.5 mm remain longer than those around 9.9 mm. (Khosala et.al 1990)

3. Dosage Form Shape: The shape and size of the dosage form affect how long it stays in the stomach. Larger and round forms usually remain in the stomach longer. Compared to single-unit forms, multi-unit dosage forms provide a more controlled and predictable drug release. They are also safer because even if one unit fails or contains incompatible substances, the overall performance is not affected.

4. Fed or Unfed State: The stomach behaves differently depending on whether you have eaten or not. In a fasting state, strong muscle movements called the Migrating Myoelectric Complex (MMC) occur every 1.5 to 2 hours. These movements push any undigested material out of the stomach, which can reduce the gastric retention time (GRT) of the dosage form if given during this cycle. In contrast, when food is present (fed state), the MMC is delayed, and the GRT becomes longer, allowing the dosage form to stay in the stomach for more time. (Deshpandae et.al 1996)

5. Nature of Meal: Eating certain foods like indigestible polymers or fatty acid salts can change the stomach's normal movement. This slows down gastric emptying and allows the drug to stay longer in the stomach.

6. Caloric Content: Meals that are high in protein and fat can significantly increase gastric retention time (GRT), sometimes extending it by 4–10 hours.

7. Meal Frequency: Eating meals frequently slows down the strong stomach movements (MMC). When multiple meals are eaten close together, the gastric retention time increases more than with a single meal sometimes extending retention for over 400 minutes (Abrahammson and oth et.al 1992)

8. Gender: Gastric retention time (GRT) is affected by gender. On average, men have a shorter GRT (about 3–4 hours), while women of the same age and race have a longer GRT (about 4–6 hours). (Hermansson (et.al 1994)

9. Age: People aged 70 years or older tend to have a longer gastric retention time (GRT). 10. Drug interactions: Some medicines, such as opioids (like codeine) and anticholinergic drugs (like atropine and propantheline), can slow stomach movement and increase GIT (kaus et al 1984)

VII. APPROACHES OF GRDDS

1. Floating Drug Delivery System (FDDS): Floating drug delivery systems are one of the most effective gastro-retentive systems used to increase the time a drug stays in the stomach. This helps improve the drug's absorption and overall effectiveness. These systems are especially useful for drugs that are absorbed only in the stomach or the upper part of the small intestine. FDDS can float on gastric fluids because their density is lower than the stomach contents. Due to this buoyancy, they remain in the stomach for a longer period without affecting the normal gastric emptying process. As the system floats, it slowly releases the drug in a controlled and predictable manner. After the drug is fully released, the remaining system eventually passes out of the stomach naturally (singh BN et.al 2003)

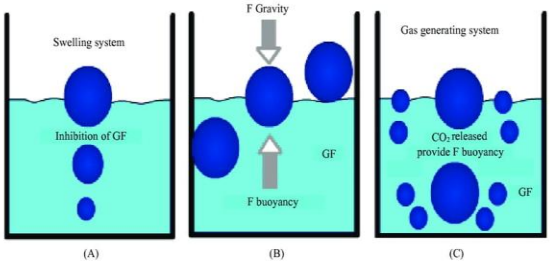

Fig. no.2 Floating drug delivery sysrem

I Effervescent System

An effervescent system is a type of drug delivery method that helps the medicine float in the stomach. It contains gas (like air, CO_2, or an inert gas) or can form gas when needed. Sometimes, organic solvents such as ether or cyclopentane evaporate and release gas, or organic acids react with carbonate or bicarbonate salts to produce CO_2. This gas helps the system float and stay in the stomach longer, allowing better drug absorption. The system has a soft, hollow structure that can expand or shrink, and after some time, it naturally collapses and leaves the stomach.

A. Gas-Generating System:

In this method, the dosage form produces gas to help it float in the stomach. When bicarbonates or carbonates react with acids (either the stomach's natural acid or an added acid like citric or tartaric acid), they release carbon dioxide (CO_2). Studies show that the best ratio for gas generation is 0.76 parts citric acid to 1 part sodium bicarbonate. Another approach

uses a matrix that holds a liquid, which turns into gas at body temperature, helping the system float. These techniques can be used in both single-unit and multiple-unit dosage forms. (Alzehar w etal 2016)

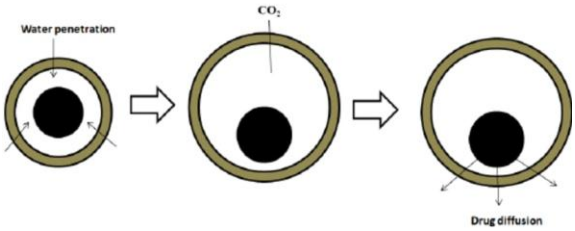

Fig. no.3 Gas-Generating system

B. Volatile Liquid-Containing System

This system consists of two chambers separated by a movable, leak-proof barrier. The first chamber holds the drug, while the second chamber contains a volatile liquid. When the system enters the stomach, the body temperature causes the volatile liquid (like ether or cyclopentane) to evaporate and form gas. This gas inflates the chamber, allowing the system to float and stay longer in the stomach (increasing gastric retention time). To make sure the device doesn't stay in the stomach permanently it includes a biodegradable plug made of materials like polyethylene or polyvinyl alcohol. Over time, this plug slowly dissolves, releases the gas, and causes the system to collapse and exit the stomach naturally. As the device remains inflated, the drug is continuously released into the stomach fluid. (Bardennot et.al 2006

II. Non-Effervescent System:

In non-effervescent floating drug delivery systems, tablets or capsules are made using a high amount (20–75% w/w) of gel-forming an swellable polymers such as HPMC, sodium carboxymethyl cellulose, hydroxyethyl cellulose hydroxypropy cellulose, and other polysaccharides. Polymers like polycarbophil, polyacrylates, and polystyrene are also used. When these dosage forms come in contact with stomach fluid, the polymers absorb water and form a thick gel layer around the tablet. This gel layer controls how quickly fluid enters the system and how slowly the drug is released. As the outer part of the tablet dissolves, more gel forms underneath to maintain the barrier. The swollen polymer traps air inside, lowering the system's density and helping it float in the stomach for a longer time. These principles are used to design intragastric floating systems. (Whitehead et.al1996)

A. Hydrodynamically Balanced Systems (HBS): Hydrodynamically Balanced Systems are single-unit dosage forms that use one or more gelforming (hydrophilic) polymers. The most commonly used polymer is HPMC, but others like agar, hydroxyethyl cellulose (HEC), hydroxypropyl cellulose (HPC), sodium carboxymethyl cellulose (NaCMC), and alginic acid can also be used. In this system, the drug is mixed with the polymer and usually filled into a gelatin capsule. After swallowing, the capsule dissolves quickly in the stomach fluid. Once exposed, the polymer absorbs water, swells, and forms a gel-like layer that helps the system float in the stomach. This swollen gel layer also controls the rate of drug release. As the outer layer slowly erodes, water continues to enter the inner layers, maintaining buoyancy and hydration. Sometimes fatty excipients are added to reduce water penetration and make the dosage form lighter for better floatation. However, one limitation of this system is that it works passively meaning its performance depends entirely on factors like the type and amount of polymer used and the air trapped inside after the gel layer forms. Finding the right balance between drug concentration and polymer level is essential to achieve proper floating ability and a controlled drug release profile

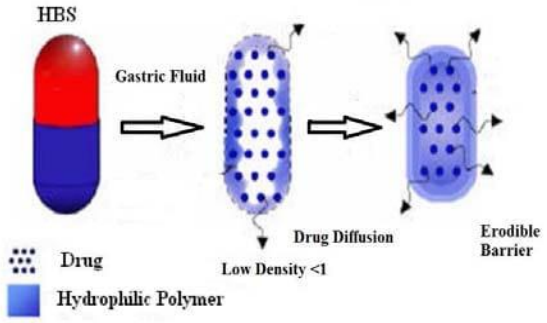

Fig.no.4 Hydrodynamically Balanced System

B. Micro porous Compartment System:

In this system, the drug is stored inside a special chamber that has tiny pores on the top and bottom. The sides of the chamber are sealed to prevent the dissolved drug from directly touching the stomach lining. Air trapped inside the chamber helps the system float on the stomach contents. When gastric fluid enters through the pores, it dissolves the drug, and the dissolved medicine slowly releases into the stomach for absorption.

C. Alginate Beads:
In this method, floating drug-loaded beads are made using calcium alginate. First, a sodium alginate solution is dropped into a calcium chloride solution, which forms small round beads (about 2.5 mm in size). After forming, the beads are separated and freeze-dried at −40°C for 24 hours, then quickly frozen in liquid nitrogen. This process creates tiny porous beads that can float in the stomach for more than 12 hours. These floating beads help increase the drug's gastric residence time, lasting more than 5.5 hours. (Kawashima et.al 1992)

D. Hollow microspheres:
Hollow microspheres, also called micro balloons, are tiny floating particles used for controlled drug delivery. They are prepared using simple methods like solvent evaporation or solvent diffusion. These microspheres contain the drug inside and are made using polymers such as cellulose acetate, calcium alginate, Eudragit S, agar, polycarbonate, and low-methoxyl pectin. The drug release and floating ability of these systems depend mainly on three factors: The amount of polymer used

- The ratio of polymer to plasticizer
- The type of solvents used in the formulation
- These hollow particles can float on acidic media containing surfactants for more than 12 hours. Because they provide good buoyancy and act as a multiple-unit system, hollow microspheres are considered one of the most effective floating drug delivery systems. (Moes et .al 1993)

2. Muco/Bio-adhesive System:
Bio-adhesive drug delivery systems help the medicine stay in the stomach for a longer time by sticking to the stomach lining. This makes the drug absorb better at the exact location where it is needed. These systems use special adhesive (sticky) polymers that attach to the mucus membrane of the stomach. Common polymers used include chitosan, cholestyramine, sodium alginate, polyacrylic acid, HPMC, sucralfate, tragacanth, dextrin, and polylactic acid. Although these polymers work well for sticking to the stomach lining, they have one challenge the mucus layer in the stomach is constantly renewed. Because of this, maintaining long-lasting adhesion can be difficult. (Kockisch et.al 2003) These systems are special drug delivery shapes made from plastic-like materials. They do not break apart in the stomach. Their size, shape, and flexibility help them stay in the stomach longer, allowing the medicine to be released slowly and effectively

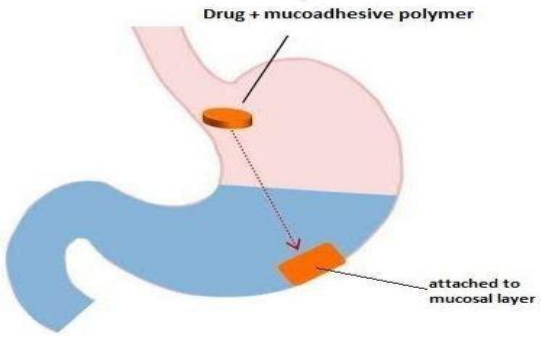

Fig.no.5 Muco/Bio-adhesive System

4. High-Density System:
High-density systems are designed to stay in the stomach for a longer time by sinking and settling in the folds of the stomach (called rugae). Since the density of stomach fluid is almost the same as water (about 1.004 g/cm³), these dosage forms are made heavier so they are not easily pushed out by stomach movement. When the pellets are heavy enough, they sink and remain in the lower part of the stomach (antrum), especially when the patient is standing. A density of around 2.5 g/cm³ is ideal to increase gastric retention time. To achieve this, drug pellets are mixed with heavy, harmless materials like barium sulfate, iron powder, zinc oxide, or titanium oxide. This increases the overall density of the dosage form to 1.5–2.4 g/cm³, which is close to the density needed for effective gastric retention. (Deshpande et.al 1997)

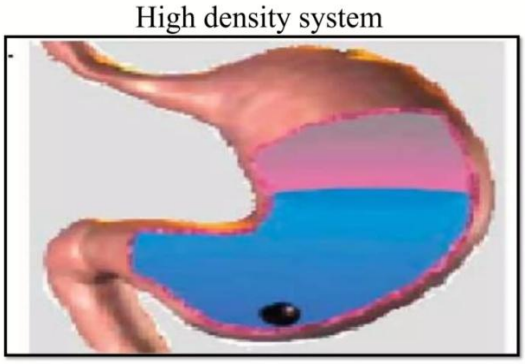

Fig.no.6 High-Density System

5. Magnetic System:
In this method, the drug dosage form contains a small magnet, and another magnet is placed on the outside of the stomach area. This external magnet helps keep the dosage form in the stomach for a longer time. Although the system works well, it may be uncomfortable for patients because the external magnet must be placed in the exact position. In animal studies (rabbits), bioadhesive granules with tiny ferrite particles were tested. After 2 hours, most of the granules stayed in the same area where they were guided by the external magnet during the first 2 minutes. (Jorgen)

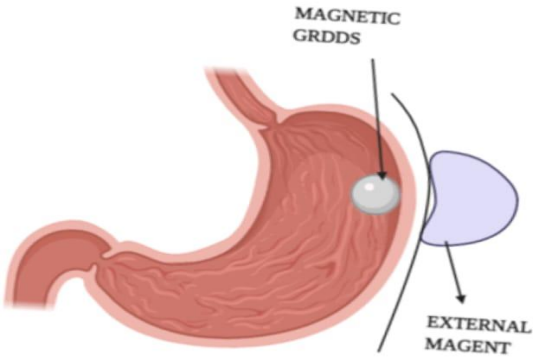

Fig. no.7 Magnetic system

6. Swellable and Expandable System: Swellable and expandable drug delivery systems are designed to stay in the stomach for a longer time by increasing their size after swallowing. When the system expands to a size larger than the pyloric sphincter, it cannot easily pass into the intestine, which helps maintain a longer gastric retention time (GRT). However, the dosage form must be swallowed easily, so it starts small and later expands in the stomach. After the drug is fully released, the system should shrink again to safely pass through the digestive tract.
These systems usually follow three stages:
1. Small size for easy swallowing
2.Expanded size inside the stomach for longer retention
3. Reduced size for safe elimination after drug release
Researchers are currently exploring expandable or unfoldable systems made using biodegradable polymers. These systems may be designed in different shapes like a ring, tetrahedron, or membrane structure and are compressed into capsules that expand once they reach the stomach. Swellable systems absorb water and increase in size due to osmotic swelling, which also helps them remain in the stomach. However, expandable systems also have some limitations, including: Difficulty storing sensitive biodegradable polymers, Limited mechanical strength to maintain expanded shape, Complex manufacturing process, Higher cost. Additionally, if these systems remain in the stomach for too long, they may cause irritation, temporary blockage, or discomfort (klusner EA et.al2002)

VIII. APPLICATION OF GRDDS

1. Site-Specific Drug Delivery Systems:
These systems are useful for medicines that need to be absorbed mainly in the stomach or the upper part of the small intestine. They release the drug slowly and in a controlled manner, ensuring the right amount reaches the target area without increasing the drug level in the whole body. This help reduce side effects and improves treatment at the required site.

2. Enhanced Bioavailability:
When riboflavin is given in a controlled-release gastroretentive system instead of a normal release form, its absorption in the body increases. This happens because the drug stays longer in the stomach and intestine, giving more time for proper absorption and improving its overall availability in the body

3. Sustained Drug Delivery:
Keeping a drug in the stomach for a long time can be challenging with normal oral controlledrelease systems. However, floating systems (HBS) help solve this by having a lower density (less than 1), which allows them to float on stomach fluids and stay there for a longer time. These systems are designed to be large enough so they cannot easily pass through the pyloric opening, helping the drug stay in the stomach and release slowly.

4. Minimized Side Effects in the Colon:
When HBS systems keep the drug in the stomach for a longer time, less medicine reaches the colon. This is useful because some drugs should not act in the colon. For example, beta-lactam antibiotics are mainly absorbed in the small intestine, and if they reach the colon, they can encourage bacteria to develop resistance. So, gastroretentiv systems help prevent unwanted drug effects in the colon

5. Absorption Enhancement:
Drugs that are only absorbed well in the upper part of the digestive system and have low bioavailability are good candidates for floating dosage forms (FDDS). By keeping the drug in the stomach for longer, these systems help improve absorption and increase the overall effectiveness of the medicine

6. Reduced Fluctuation in Drug Levels: Controlled-release systems help maintain a steady level of the drug in the blood, unlike immediate-release tablets that may cause sudden peaks and drops. This steady release reduces variations in the drug's effect and helps avoid side effects that happen when drug concentration becomes too high. (Rathod et.al 2016)

IX. FUTURE PROSPECTIVE

The future of gastroretentive drug delivery systems looks very promising. Researchers are working on new formulations that can overcome the limitations of traditional oral drug delivery. While developing these systems, it is important to consider how the drug behaves in both fed and fasted conditions, as well as its effectiveness in treating different diseases. Along with this, the possibility of scaling up the technology for large-scale production should be explored to improve its market potential and availability

X. CONCLUSION

Floating gastro-retentive drug delivery systems have many advantages compared to normal drug delivery methods. These systems offer a stable dosage form with controlled and long-lasting drug release. The idea behind hydrodynamically balanced systems helps increase the time the dosage stays in the stomach, which improves drug action. A key requirement for making floating drug delivery systems is that the dosage must have a lower density than gastric fluid so it can float. FDDS are especially useful for treating stomach-related diseases and for drugs that have a short half-life but need a longer effect. Overall, FDDS is a promising and effective approach for improving gastric retention and enhancing drug performance.

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