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Floating Drug Delivery Systems (FDDS) Review

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Abstract: *This review on floating drug delivery systems (FDDS) was written with the intention of gathering the most recent research with a particular focus on the main mechanism of flotation to induce stomach retention. The most current advancements in FDDS are reviewed in depth, along with the physiological factors and formulation factors impacting stomach retention, design strategies for single-unit and multiple-unit floating systems, and their classification and formulation characteristics. The techniques used in vitro, the in vivo tests used to gauge the effectiveness and use of floating systems, and the applications of these systems are all summarized in this paper. These systems are helpful for a number of issues that arise during the creation of a pharmaceutical dosage form.*

Keywords: Floating drug delivery system, Sustained release, controlled release, Floating tablet, Evaluation, Application, Gastro-retentive drug delivery system

I. INTRODUCTION

The oral route is increasingly being employed to deliver therapeutic drugs since it is simple to administer and has a cheap cost, which results in high patient compliance. Oral medication delivery methods make up more than half of all drug delivery systems on the market.

Low-density systems that are buoyant enough to float over the contents of the stomach and stay there without slowing down the gastric emptying rate are known as floating systems or hydrodynamically regulated systems. The medicine is slowly withdrawn from the system at the desired rate while the body is floating on the contents of the stomach. The stomach's residual system is emptied after the medication has been released. As a result, GRT increases.

II. CLASSIFICATION OF FLOATING DRUG DELIVERY SYSTEM

A. Single Unit Floating Dosage Systems
a) Effervescent Systems (Gas-generating Systems)
b) Non-effervescent Systems

B. Multiple Unit Floating Dosage System
a) Effervescent Systems (Gas-generating Systems)
b) Non-effervescent Systems
c) Hollow Microsphere

C. Raft Forming System

A. Single Unit Floating Dosage Systems

Single-unit dose forms are simpler to make, but suffer from all or no stomach emptying because of this.

A substantial amount of medicine delivered at one specific region in the gastrointestinal tract can result in high variability in bioavailability and local pain due to the danger of losing their effects too early.

a) Effervescent Systems. (Gas-generating Systems)

In order to create these matrix forms of systems, swelling polymers like chitosan and methylcellulose as well as a number of effervescent substances like salt are used.Citric acid, tartaric acid, and bicarbonate. They are designed so that when CO2 comes into contact with acidic gastric contents, it is generated and lodges in swelling hydrocolloids, giving dosage types buoyancy.

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b) Non-effervescent Systems

Polysaccharides, hydrocolloids, and matrix-forming polymers are used in non-effervescent floating dosage forms, including asTo create a gel-forming or swelling cellulose type, polyacrylate, polycarbonate, polystyrene, and polymethacrylate were combined. The medicine and the hydrocolloid-forming gel are fully mixed using a straightforward procedure in the formulation process. After oral administration, this dosage form swells when in contact with gastric juices and reaches a bulk density of 1. The dose shape is buoyant due to the air that has been trapped inside the inflated matrix. This results in the formation of a swelled, gel-like structure that serves as a reservoir and permits the gelatinous mass to release the medicine over time. The most prevalent excipients used in pharmaceutical products are hydroxypropyl methyl cellulose (HPMC), polyvinyl acetate, polyacrylate polymers, sodium alginate, carbopol, agar, polyethylene oxide, and polycarbonate.

B. Multiple Unit Floating Dosage System

Given that there are both intra- and inter-subject variances, several unit dose forms may be a desirable alternative. Both the risk of dose dumping and the in-medication absorption are decreased. Concepts like a multiple unit system of air compartments, hollow microspheres generated using the emulsion solvent diffusion method, and beads made using the emulsion gelation process were used to build a number of multiple unit floating systems. Using effervescent and swellable polymers is another method for organizing multiple unit FDDS.

a) Effervescent Systems (Gas-generating Systems)

A multi-unit system was created, consisting of a calcium Alginate core and a calcium alginate/PVA membrane Separated by an air compartment. The PVA leaches out in the Presence of water and increases the permeability of the Membrane, preserving the integrity of the air compartment. The increase in molecular weight and PVA concentration has Resulted in the improvement of the system's floating Properties. The technique of freeze-drying for the Preparation of floating calcium alginate beads is also Mentioned. Sodium alginate solution, due to the formation of Calcium alginate, is applied drop wise into the aqueous Solution of calcium chloride, allowing the droplet surface to Instantly gel. The beads obtained are freeze-dried, leading to A porous structure that assists in floating. The researchers Explored the behavior of radiolabeled floating beads and Used gamma scintigraphy in contrast with non-floating Beads in human volunteers. For floating beads, prolonged Gastric residence time was observed in excess of 5.5 h. With An overall emptying time of 1 hr, the non-floating beads had A shorter residence time

b) Non-effervescent Systems

Compared to effervescent systems, effervescent multiple unit systems have received less research.the written word. The idea of developing such an indomethacin-containing technique employing chitosan as the polymeric excipient has, however, only been somewhat explored by researchers. Indomethacin-containing multiple HBS units are listed as a type of extrusion-prepared medication. A mixture of the medication, acetic acid, and chitosan is extruded via the blade, and the extrudate is then chopped and dried. The required drug release may be obtained in the acidic media where chitosan hydrates and floats by altering the drug-polymer ratio

c) Hollow Microsphere

A unique emulsion technique was used to create hollow microspheres with pharmaceuticals inside of their outer polymer shelf. Liquid diffusion Enteric acrylic polymer was added to a thermally regulated, agitated Poly Vinyl Alcohol (PVA) solution at 400C along with the drug's ethanol/dichloromethane solution. Dichloromethane, which was produced in the drug polymer microsphere's internal cavity and dispersed polymer droplet, evaporates to create the gas phase. Over the course of more than 12 hours, the micro-balloon floated continually over the top of a surfactant that contained acidic dissolving media. Due to the hollow core of the microsphere, which has several unit system advantages as well as improved floating characteristics, hollow microspheres are one of the most promising buoyant structures

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C) Raft Forming System

Here, a gel-forming solution (such as a sodium alginate solution containing carbonate or bicarbonate) expands and creates aWhen in contact with stomach juice that contains entrapped CO2 bubbles, a thick cohesive gel form. In order to reduce gastric acidity, antacids like calcium carbonate or aluminum hydroxide are frequently employed in formulations. As raft forming systems provide a covering on top of stomach fluids, they are also utilized to treat gastro-esophageal reflux. One of the mechanisms involved in raft formation is the development of a viscous cohesive gel in contact with stomach fluid, where the liquid swells in each portion, forming a continuous layer known as a raft. Because to its low density and carbon dioxide generation, this raft floats on stomach juices

III. BASIC GIT PHYSIOLOGY

The stomach is anatomically separated into the Fundus, Body, and Antrum sections (pylorus). The body and fundus-made proximal portion function as aWhereas the antrum is the primary location for mixing motions and serves as a pump for stomach emptying by thrusting actions, the reservoir for undigested materials is located there.3 Both when one is fasting and when one is eaten, the stomach empties. Interdigestive myoelectric cycle, also known as migrating myoelectric cycle (MMC), is a series of electrical events that occur during the fasting state and cycle through the stomach and intestine every two to three hours. MMC is further broken down into four phases.

Following the consumption of a mixed meal, the contraction pattern switches from a fasted to a fed condition, which is also known as digestive motility. Pattern.

Phase 1 (Basic phase) lasts between 30 and 60 minutes with infrequent contractions.

Phase 2 (Prebirth phase) lasts 20 to 40 seconds. Minutes with sporadic contractions and action potential.

Phase 3 (Burst phase) lasts for 10 to 20 minutes and is characterized by brief, strong, and regular contractions.

Phase 4 lasts between phase 2 and cycle 1 of the next two cycles, lasting 0 to 5 minutes.

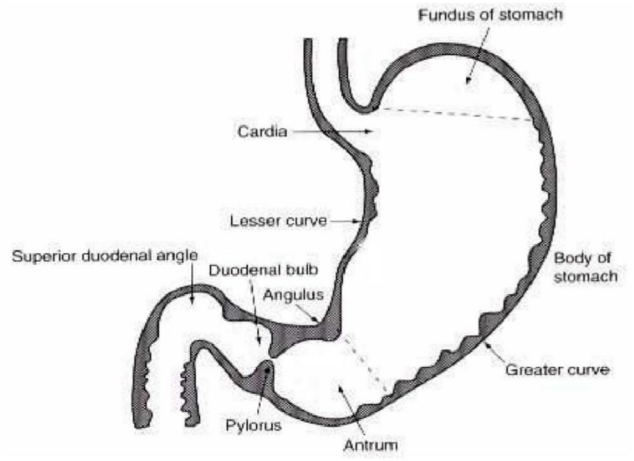

Figure 1: Anatomy of stomach

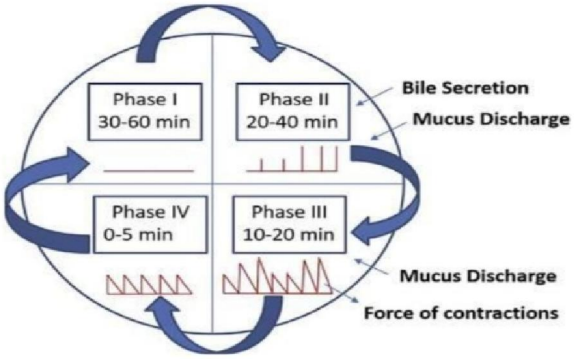

Figure 2: Gastrointestinal motility pattern

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Following the consumption of a mixed meal, the contraction pattern shifts from a fasted to a fed condition, which is also known as digestive motility. Pattern.

3.1 Mechanism of Floating Systems

There have been several attempts to prolong the retention duration by keeping the dosage form in the stomach. Among these efforts is the introduction of floating dosage. Gastric-emptying delaying devices, co-administration of gastric emptying delaying medications, mucoadhesive systems, high-density systems, changed shape systems, and forms (gas-generating systems and swelling or expanding systems).The floating dose forms are the ones that are utilized the most frequently. Floating drug delivery systems (FDDS) float in the stomach without slowing down the gastric emptying rate since their bulk density is lower than that of gastric fluids. The medicine is removed from the system slowly and at the desired pace while the body is floating on the contents of the stomach (Fig. 2). The drug's residual system is expelled from the stomach after release. As a result, the GRT is elevated, and the oscillations in plasma drug levels are better managed. Concentration

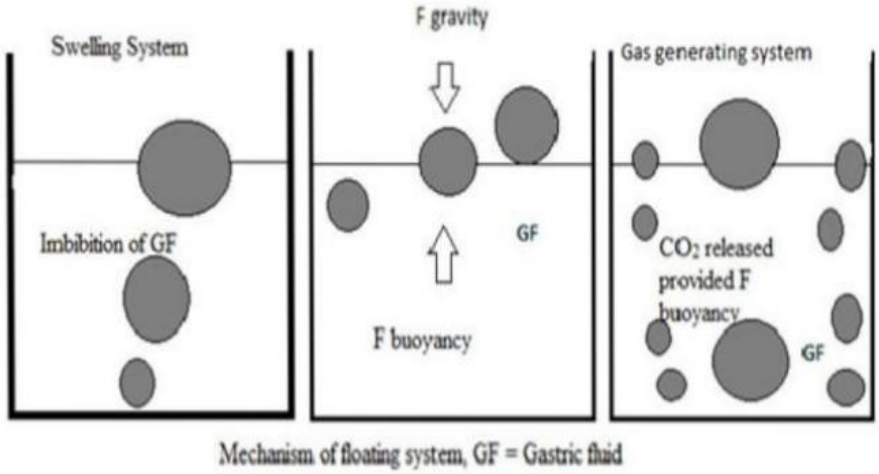

Figure 3: Mechanism of floating system.

IV. PHARMACOKINETIC AND PHARMACODYNAMIC ASPECTS OF FDDS

A. Enhanced bioavailability

Due to poor GI absorption caused by a number of factors that also contribute to poorer bioavailability, FDDS has explored the improvement in bioavailability of several medications with a limited therapeutic window. The medications that were taken into consideration had a limited window for absorption, but FDDS demonstrated the possibility of improved compound bioavailability at the required spot. In comparison to the administration of the standard formulation, the bioavailability of riboflavin and levodopa in control release (CR) floating systems is greatly improved. On the other hand, alendronate and other bisphosphonates in CR polymeric formulations are immediately absorbed from the stomach. Even though the longer stomach retention of the bisphosphonate in rats is caused by experimental or surgical methods, the amplitude of this route is still quite modest. It might bedetermined that a number of distinct mechanisms, including those involved in medication absorption and transit in the gastrointestinal system, function concurrently and affect the degree of drug absorption.

B. Enhanced first-pass biotransformation

The pre-systemic metabolism of the tested substance is analogous to increased efficacy of active transporters displaying restricted capacity activity. If the drug is given to the metabolic enzymes (cytochrome P450, in particular, CYP3A4) in a sustained way rather than via a bolus input, the risk of FDDS is significantly enhanced.

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C. Improved bioavailability due to reduced P-glycoprotein (P-gp) activity in the duodenum

P-gp mRNA levels rise longitudinally along the gut, with the highest levels seen in the colon, seemingly in contradiction to the higher density of CYP3A4 at the upper section of the intestine. Consequently, floating systems may increase absorption in comparison to immediate and controlled release (CR) dose forms for medications that are P-gp substrates and do not undergo oxidative metabolism, such as Digoxin**.**

D. Reduced frequency of dosing

The results of several research show that the pharmacokinetics of medicines with relatively short biological half-lives, sluggish input from sustained release, and control release floating system flip-flops were seen. These characteristic increases patient compliance, which enhances therapy.

E. Targeted therapy for local ailments in the upper

Local therapy in the stomach and small intestine may benefit from the prolonged and sustained administration of the medicine from the floating systems to the stomach.

F. Pharmacodynamic Aspects of FDDS

Reduced fluctuations of drug concentration

Dosage formulations with instant release that need ongoing drug ingestion. When compared to the fixed system of medication administration, the floating approach results in constant blood drug concentrations within a narrower range. As a result, variations in drug effects are reduced, and undesirable effects that are concentration-dependent and linked to peak concentrations can be avoided. This characteristic is especially beneficial for medications with a limited therapeutic index.

Improved selectivity in receptor activation

It is also feasible to achieve some selectivity in the induced pharmacological action of medicines that activate distinct types of receptors at different doses by minimizing variations in drug concentration.

Reduced counter-activity of the body

In many instances, the pharmaceutical response, which interferes with the body's normal physiological functions, causes a rebound activity that reduces the effects of the drug. It has been demonstrated that slow medication absorption into the body, like in the case of FDDS, minimizes counteractivity and increases pharmacological efficacy.

Minimized adverse activity at the colon

The amount of medication that enters the colon is reduced when the drug is retained in the FDDS, particularly when it is in gastro retentive form at the stomach. As a result, the drug's negative effects in the colon may be avoided. Due to the fact that beta-lactam antibiotics can only be absorbed through the small intestine and that their presence in the colon promotes the growth of bacteria, floating formulations are necessary. [31]

V. FORMULATION OF FLOATING DOSAGE FORM

Following types of the ingredients can be incorporated in to floating Mert Thin E the Ated Dosage form

A) Hydrocolloids
B) Inert fatty materials
C) Release rate accelerants long
D) Release rate retardant in
E) Buoyancy increasing agents
F) Low density material
G) Miscellaneous

a) Hydrocolloids

Synthetics, anionic or non-ionic hydrocolloids like hydrophilic gums and modified cellulose derivatives are suitable hydrocolloids. Examples include the usage of accasia, pectin, agar, alginates, gelatin, casein, bentonite, veegum, MC, HPC, and Na CMC. The hydrocolloids require an acidic environment to hydrate, such as the pH 1.2 of gastric juice. As

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stomach fluid is introduced into the system, the formulation should be hydrodynamically balanced to have a bulk density of less than one in order to ensure buoyancy, even though the bulk density may initially be greater than one.

b) Inert fatty materials

To reduce the formulation's hydrophilic property, edible, pharmaceutical-grade fatty material with a specific gravity below one can be added thus increasing buoyancy. Examples include using fatty acids, long-chain alcohols, glycerides, and mineral oils that have been purified.

c) Release rate accelerants long

The release rate of the medicament from the formulation can be modified by including excipient like lactose and/or mannitol. These may be present from about 5-60% byWeight**.**

d) Release rate retardant

Insoluble materials like magnesium stearate, talc, and dicalcium phosphate reduce solubility and hence delay the release of medications.

e) Buoyancy increasing agents

You can employ substances like ethyl cellulose, which has a bulk density below one, to increase the formulation's buoyancy. It can be weight-adapted up to 80%.

f) Low density material

Powdered polypropylene foam

g) Miscellaneous

Adjuvants suitable for use in medicine, such as Depending on the needs, dosage forms can include preservatives, stabilizers, and lubricants. They have no negative effects on the systems' hydrodynamic equilibrium.

Advantages of floating drug delivery system:

1. Floating dosage forms, like tablets or capsules, will stay in the solution for a long time even if the intestines have an alkaline PH.
2. For medications intended for local action in the stomach, FDDS are advantageous. Such as antacids.
3. FDDS dosage forms help keep the drug in a floating state in the stomach to get a relatively better response in cases of diarrhea and vigorous gastrointestinal movement.
4. Since aspirin and other similar medications can irritate the stomach wall when they come into contact with them, FDDS formulations may be helpful for their administration.
5. Drugs absorbed through the stomach benefit from the FDDS. Such as antacids and ferrous salts.

Disadvantages of Floating drug delivery system:

1. These systems need a lot of fluid in the stomach to float and function well while delivering drugs.
2. Unsuitable for medications with GIT solubility or stability issues.
3. It might not be advisable to take medications like nifedipine (a calcium channel blocker), which is well absorbed throughout the GIT and goes through first-pass metabolism.
4. It is also not advisable or appropriate to take drugs that irritate the gastric mucosa.
5. Drug substances that are unstable in the stomach's acidic environment should not be incorporated into the systems.

Application of floating drug delivery system

1. Increase Bioavailability of drugs.
2. Site specific. Drug delivery systems.

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3. Sustained drug delivery.
4. Enhancement of absorption. ↑
5. Minimize adverse activity at the Calon.

Evaluation of Floating Drug Delivery System.

- **Shape of tablets:** Compressed tablets intended for FDDS are evaluated in accordance with theA magnifying glass to assess the uniformity of its shape.
- **Tablet dimensions:** According to official compendia, a calibrated Vernier calliper is used to measure the thickness and diameter of tablets in FDDS form, much like with traditional tablets. Each formulation's three pills.Are chosen at random, and each thickness is measured.
- **Determination of hardness of the tablet:** Using a hardness tester of the Monsanto type, randomly select 20 tablets from each batch of formulations should be used to determine the hardness.
- **Determination of weight variation:** Twenty randomly chosen tablets are carefully weighed, and the average tablet weight is computed. Then the departure from Calculating individual weight from the average weight
- **Determination of thickness of the tablets:** Ten tablets' individual crown to crown thickness is calculated. Each batch using slide calipers
- **Measurement of floating capacity:** Each flask carrying 400 ml of 0.1(N) HCL solutions has three tablets in it. The duration of floating and the floating lag time, which are both measured in minutes, are the amount of time that it takes for a tablet to consistently float on the water's surface. After that, the sample mean and standard deviation are computed.
- **Measurement of the density of the formulation:** The volumes and masses of the tablets are calculated in triplicate to determine their apparent densities. Using the mathematical equation for a cylinder, the volume V of the cylindrical tablets is estimated from their height h and radius r (both measured using a micrometer gauge) (V-Arch)
- **Determination of drug content in tablets:** Ten tablets are chosen at random from each batch and transferred to a 100 ml volumetric flask that has been filled with 0.1(N) HCL Stir and After setting it aside for two hours, transfer 1 ml from the volumetric flask to the test tube. After that, samples are filtered, appropriately diluted, and spectrophotometrically analyzed at an appropriate wavelength [32,33].

In vitro dissolution study

The dissolving vessel held the tablet inside. 5 ml of the sample are taken at 1-hour, 2-hour, 3-hour, 4-hour, 5-hour, 6-hour, 8-hour, 10-hour, and 12-hour intervals, or at any additional intervals as required. After each sampling, 5 ml of the dissolving media were replaced with new, bringing the total amount of dissolution fluid to 900 ml. The mean values are depicted versus time in the release studies, which used "n" tablets. Each sample is examined using a UV visible spectrophotometer at its maximum wavelength in comparison to a reagent blank, and the corresponding concentration is calculated using the associated calibration curve [34].

Buoyancy/Floating test

Measurements are made of the interval between the dosage form's introduction and the onset of buoyancy on the simulated stomach fluid as well as the interval during which the dosage form maintains buoyancy. Total floating time (TFT) refers to the total amount of time that the dosage form remains buoyant. The time it takes for the dosage form to emerge on the amedium surface is referred to as floating lag time (FLT) or buoyancy lag time (BLT) [35].

Swelling study

By observing a dose form's weight rise or water intake, swelling behaviour can be determined. The growth in tablet diameter and/or thickness over time could be used to quantify the dimensional changes. The equation's result, a percent weight gain, can be used to assess water uptake.

WU (Wt.-Wo)x100

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Where,
WU= Water uptake
Wt. = Weight of dosage form at time t.
Wo = Initial weight of dosage form [35].

VI. CONCLUSION

The process of a medicine being absorbed in the gastrointestinal tract is very varied, and increasing stomach retention of the dosage form causes the time for drug absorption to be prolonged. Gastric retention could potentially be addressed with FDDS. How many commercial

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