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## Gastroretentive Floating Drug Delivery System (GFDDS): A Review



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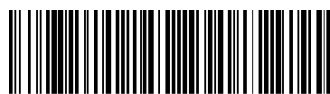
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### ABSTRACT

This review paper emphasis on the truthful facts upon floating drug delivery system in an empirical manner. A floating drug delivery system (FDDS) has become a versatile way to overcome the various issue in the delivery of drugs. Gastric Emptying is not predictable in case there are physio-coherent issues and different variables like the presence of food. Medications having a short half-life are wiped out quickly from the bloodstream. Floating drug delivery system has been majorly classified into two types- a) Non-effervescent system b) effervescent system. The Non-effervescent system comprises of different 4 subtypes whereas the Effervescent system 2. The success of GRDDS depends on the comprehension of stomach physiology and related gastric exhausting cycle. Various factors affect the action of FDDS such as size, shape, fed/unfed conditions, etc. FDDS has numerous advantages with some limited disadvantages. In conclusion, FDDS has become the most prominent dosage of medicines to enhance absorption and bioavailability. It may be pharmacologically potent and cost-effective to facilitate the use among low-income societies.



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## INTRODUCTION

A floating drug delivery system (FDDS) has become a versatile way to overcome the various issue in the delivery of drugs. The oral delivery of medications with a restricted absorption window in the gastrointestinal tract (GIT) is regularly restricted by poor bioavailability with conventional dosage forms because of fragmented medication delivery and short home time at the site of absorption. Some floating drug delivery systems (FDDS) have shown the ability to oblige these varieties without influencing drug discharge (Kotreka and Adeyeye, 2011). Gastric Emptying is not predictable in case there are physio-coherent issues and different variables like the presence of food. Medications having a short half-life are wiped out quickly from the bloodstream. This has prompted the advancement of oral gastro-retentive measurement structures. Gastro-maintenance is fundamental for drugs that are retained from the stomach, medicates that are poorly soluble or debased by the higher pH of the digestive tract, and medications with retention which can be modified by changes in gastric emptying time (Shaha et al. 2009). Oral dosage forms have been created from the recent a very long time because of their huge helpful benefits like the simplicity of administration, patient compliance, and adaptability in the formulation. These days, the pattern is going towards the readiness of a novel controlled drug delivery system, in which the active drug can be controlled for a longer period (Meka et al. 2014).

The oral delivery of drugs with a thin ingestion window in the gastrointestinal tract (GIT) is regularly restricted by poor bioavailability with traditional dose frames because of deficient medication delivery and short residence time at the site of assimilation. To defeat this disadvantage and to boost the oral ingestion of these medications, gastroretentive systems like mucoadhesive, high-thickness, expandable, and drifting (floating) systems have been created (Kotreka and Adeyeye, 2011).

Floating drug delivery system has been majorly classified into two types-

A. Non-effervescent system

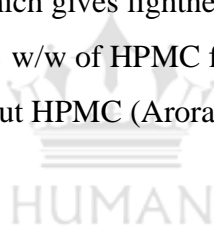
B. Effervescent system

### **A. Non-effervescent system**

It includes the blending of the medication with a gel, which grows at the point when interacts with gastric liquid and keeps general uprightness of shape and a mass thickness of short of

what one inside the external coagulated obstruction. The air caught by the enlarged polymer gives lightness to these measurement structures. The most generally utilized excipients in these systems incorporate hydroxypropyl methylcellulose (HPMC), polyacrylate polymers, polyvinyl acetic acid derivatives, carbopol agar, sodium alginate, polycarbonates, etc. (Dubey and Verma, 2013).

The multi-particulate coating supply kinds of delivery systems might contain twofold or triple layers. The triple-layered tablets might be ready, which contains enlarged capable gas-creating layer, a feasible methodology was used in the improvement of gliding or pulsatile drug delivery system depending on the covered bubbly center. The dosage form had two layers, the first layer comprised of medication, cellulose acetic acid derivation, or HPMC as a supported delivery center, and the second layer comprised of bubbly specialists, PEG 4000 and lactose or microcrystalline cellulose as filler. Sodium bicarbonate and citrus extract were utilized as effervescent specialists in a proportion of 1:0. in the centralization of 30 - 50 % of the w/w of the center. The carbon dioxide is created upon contact with the medium and gets captured in the polymeric network, which gives lightness to the structure of the measurement. It was seen that expansion of 10 - 20% w/w of HPMC fundamentally hindered drug discharge contrasted with the dosage form without HPMC (Arora et al. 2005).



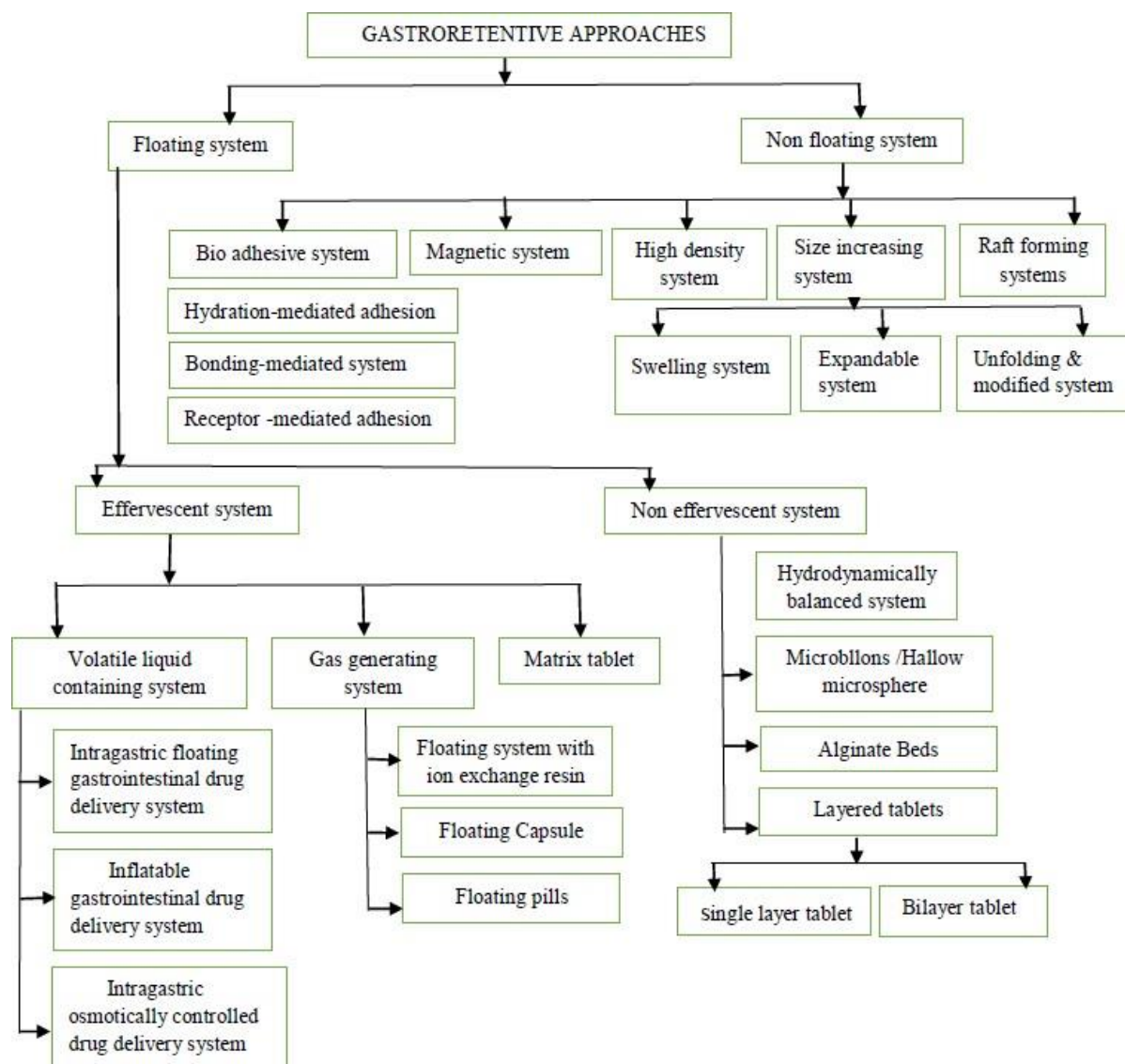


Figure No. 1: Gastro-retentive approaches

Non-effervescent system comprises of different 4 sub-systems (Birajdar et al. 2021)

- **Micro-permeable system**

In this method, medicine is put inside the permeable microcompartment along its base and top divider with pores. The air is caught by the floatation chamber and afterward, the gastric liquids begin to float.

- **Micro-balloon floating**

They are developed in light-weight, synthetic form and seem like hollow glass in existence.

- **Beds Alginate**

The calcium alginate precipitate is prepared by reducing the concentration of sodium alginate into an aqueous solution of calcium chloride. It generates a porous system, which enables it to float over the gastric juice for longer than 12 hours.

- **Barrier colloidal gel**

This system involves the hydro-colloidal gel shape that enables the medications to swim (float) in gastric fluid for a longer period.

## **B. Effervescent System**

The effervescent system incorporates utilization of gas-producing specialists, carbonates (for example Sodium bicarbonate), and other natural acids (e.g. citrus extract and tartaric corrosive) present in the detailing to create carbon dioxide Gas-producing Systems) gas, consequently diminishing the thickness of the system and making it float on the gastric liquid. An option is the joining of a framework containing a piece of fluid, which produces gas that dissipates at the internal heat level (Rajak et al. 2011).

The effervescent system is further classified in two ways as below

1. Gas Generating system
2. Volatile liquid/ Vacuum system

### **1. Gas Generating System**

#### **i. Hydrodynamically Balanced System (HBS)**

These are prepared by intimately blending the CO<sub>2</sub>-producing agents and the medication inside the matrix tablet. These have a high thickness lower than gastric liquids and, in this way, stay floating in the stomach unattractive the gastric emptying rate for a delayed period. The medication is gradually delivered at an ideal rate for a delayed period. The medication is gradually delivered at an ideal rate from the system and is expelled from the stomach. This prompts an increment in the gastro retentive time and a superior command over a change in plasma drug fixation (Rajak et al. 2011).

## **ii. Intra Gastric Bilayer Floating Tablets**

This involves the controlled release of pills as seeds covered by two layers. The inner layer contains the effervescent system whereas the outer layer is made up of swellable agents. When the system is soaked in the dissolution medium, pills sink and form swollen pills like balloons and float (swim) due to lower density. This lower density develops due to the production and entrapment of CO<sub>2</sub> within the system (Revathi and Raju, 2012).

## **iii. Ion Exchange Resins Beads**

Ion exchange resins beads can be loaded with bicarbonate and covered with a semipermeable film. These beads display delayed gastric residence because of the arrival of carbon dioxide which is caught inside the covering of the dots. Notwithstanding the bicarbonate, a model medication, theophylline, has additionally been stacked onto the tar. This system gives a controlled arrival of medication, intervened by the covering, and has likely applications as a controlled delivery gastric retentive system (Atyabi et al. 1996).

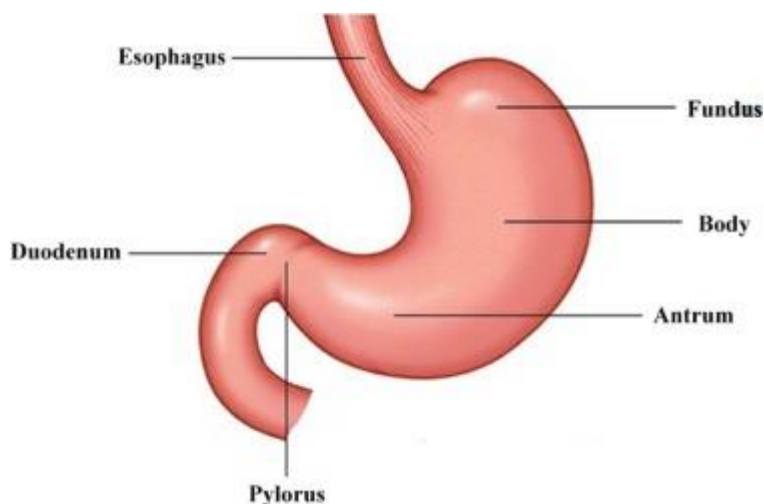
## **2. Volatile liquid/ Vacuum system**

This is an osmotically controlled floating system wherein a gadget contained an empty deformable unit in a convertible fell structure. Lodging would be connected to its deformable unit and inside partitioned into a first and second chamber isolated by an impermeable, pressure touchy versatile unit. The primary chamber generally contains a functioning medication, while the second an unpredictable fluid, for example, cyclopentane or ether gets disintegrated at a physiological temperature to create a gas, empowering the medication supply to coast. The unit gets ousted from the stomach, with the assistance of bioerodible attachment that permitted the fume to get away (Niharika et al. 2018).

## **Stomach's physiology**

The success of GRDDS depends on the comprehension of stomach physiology and related gastric exhausting cycle. Fundamentally the human stomach is made out of three physical areas: fundus, body, and antrum (pylorus), as portrayed beneath. After supper, the normal volume of a stomach is about 1.5 L, which fluctuates from 250 to 500 ml during the between stomach related stages. The part made of the fundus and the body goes about as a supply of any undigested material, while the antrum proceeds as the chief site for the blending activity. Being the lower part, the antrum functions as a siphon for gastric discharging by an impelling

activity. Pylorus acts to isolate the stomach from the duodenum and assumes a significant part in the gastric home season of the ingested materials. Gastric motility (contraction) is the way that passes the food from the esophagus to the colon via the stomach (Mandal et al. 2016).



**Figure No. 2: Structure of stomach**

The gastro-retentive drug delivery system is a demonstrated valuable instrument for supporting the medication discharge for the medications having great absorption through the GIT, drugs with limited therapeutic index, and low dose drugs. The gastro-retentive dosage systems have likewise been produced for antidiabetic particles and metformin hydrochloride, the primary line drug in the treatment of diabetes is commercially available in the market as prolonged-release formulations. As oral antidiabetic treatment is needed for delayed effect, the oral hypoglycemic may prompt serious effects like diabetic neuropathy, diabetic myopathy, and some more. The essential justification incidental effects are under-use of the medication particle which can be further developed utilizing gastro-retentive medication conveyance frameworks in this way limiting the incidental effects. Despite being perhaps the most effective frameworks, the business esteem gastro-retentive medication conveyance frameworks are still less than impressive (Aseem et al. 2021).

### **Conventional Vs gastro-retentive drug delivery system (Niharika et al. 2018)**

The following tables confirm the differences between conventional Vs gastro-retentive drug delivery systems

**Table No. 1: Comparison between conventional Vs gastro-retentive drug delivery system**

Parameter	Conventional drug delivery	Gastroretentive drug delivery system
Patient compliance	Low	Enhanced
Drugs with poor solubility, high pH	Not good for narrow absorption window drugs	Good for narrow absorption window drugs
Toxicity	High risk	Low risk
Action in stomach	Low	High
Dose dumping	Nil dose dumping	May occur dose dumping

**Factors affecting FDDS** (Shaha et al. 2009; Tiwari et al. 2014)

### 1. Density

The Gastric Residence Times (GRT) is directly proportional to the density of the drugs. It concentrates the action of a drug in the gastrointestinal tract for a longer period.

### 2. Shape

Ring-shaped like tetrahedrons have reported a better gastric residence time. Total 90-100 % retention was observed when compared with other shaped formulations during 24 hours.

### 3. Size

The formulations having a diameter more than 7.5 mm exhibit better gastric residence time but more than 9.9 mm demonstrated less GRT.

### 4. Nature and calories of food

Indigestible fractions of fat (fatty acids) can alter the motility/contractions of the stomach. By doing so they decrease the gastric emptying rate and prolong the action of drugs. Gastric residence time can be increased if the meal is high in proteins/calories.

### 5. Fed/unfed phenomena

In an unfed situation, gastric motility or peristaltic contractions remain high and frequently occur for 2 hours. If a drug is ingested in this condition, absorption occurs very fast. However, in the fed state, the gastric residence time becomes longer.



**Advantages of FDDS** (Tiwari et al. 2014; Dubey and Verma, 2013)

**1. Enhanced pre-systemic or first-pass metabolism**

The pre-systemic or first-pass metabolism of drugs is high when a drug is given in the dosage form of floating drugs when compared with bolus form.

**2. Prolonged drug delivery**

Drugs having a short biological half-life are incorporated into FDDS by which frequent dosing is subsided. It sustains the release of the drug and facilitates the release of the drug for a longer period.

**3. Reduced dosing frequency**

By prolonged release and action, the dosing frequency gets reduced.

**4. Targeted therapy**

A floating drug delivery system is a better way to target therapy as it may act locally in ailments in the stomach.

**5. Enhanced bioavailability**

Floating drugs have an optimistic bioavailability if compared with non-floating formulations.

**6. Receptor selectivity**

FDDS minimizes the chance of alterations of drug concentration at the receptor site. Thus, maintaining a constant concentration gradient facilitates receptor selectivity.

**7. Minimum ADR at colon**

Retention (staying) of the drug occurs at the stomach in g.i.t. thus reducing its reach and absorption in the colon. So, degradation of drugs is prevented in the colon which is sensitive for the colon.

**Disadvantages of FDDS** (Avinash et al. 2012)

- Gastric retention is facilitated by many factors including the presence of meal, pH, and peristaltic contractions. These factors are never fixed, that's why buoyancy remains unpredictable.
- Drugs irritating stomach is not suitable

- High differences in gastric emptying time
- It should not be dosed just before going to bed.

## CONCLUSION

In conclusion, FDDS has become the most prominent dosage of medicines to enhance absorption and bioavailability. It may be pharmacologically potent and cost-effective to facilitate the use among low-income societies.

## SOURCE OF FUNDING

Nil

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