



AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: <http://www.ajptr.com/>

Floating Drug Delivery System: A Brief Review

Haridwar Lodh^{1*}, Sheeba FR¹, Prabhat Kumar Chourasia¹, Harshitha Arun Pardhe¹
1. Department of Pharmaceutics, Mallige Collage of Pharmacy, Bangalore -560090, Karnataka, India.

ABSTRACT

Scientific and technological developments in the research and development of new drug delivery systems have been made in recent years by resolving physiological disorders, such as short gastric residence periods and unpredictable gastric emptying times. Dosage forms that can be hold within the stomach are called as Gastro-retentive Dosage Forms (GRDF). Multiple methods used in the prolongation of gastric residence time are floating drug delivery system, swelling and expanding system, polymeric bio-adhesive system, high density system and other delayed gastric emptying system. Medication-based disease treatment is entering a new era in which a increasing range of innovative drug delivery technologies are being used and are available for clinical use. Floating Drug Delivery Systems (FDDS) is one of the gastro-retentive dosage forms used to achieve extended duration of gastric residency. The aim of writing this review on floating drug delivery systems (FDDS) was to compile the recent literature with particular focus on the main floating mechanism to achieve gastric retention. Sustained oral release of gastrointestinal dosage types provides many benefits for drugs with absorption from the upper sections of the gastrointestinal tract and those that function locally throughout the stomach. This review includes the physiology, factors controlling gastric retention time, excipient variables influencing gastric retention, approaches to designing single-unit, hydro-dynamically balanced system and multi-unit floating structure, and aspects of their classification, formulation and evaluation are discussed in detail, and few applications of these systems.

Keywords: Gastro retentive system, Floating drug delivery system, Classification, Methods, Evaluation.

*Corresponding Author Email: haridwar462@gmail.com

Received 24 June 2020, Accepted 08 July 2020

Please cite this article as: Lodh H *et al.*, Floating Drug Delivery System: A Brief Review. American Journal of PharmTech Research 2020.

INTRODUCTION

Drug delivery system represents pure crude form of the drugs either in solid, liquid or semi-solid form, which should be therapeutically efficient, safe and stable enough to deliver a required amount of the drug to the specified site in the body to reach instantly, to achieve the correct concentration and then retain the adapted concentration. Many of the drug delivery systems commercialized are oral drug delivery systems.¹ Due to low treatment costs, increased patient compliance and ease of administration oral drug delivery is mostly preferred. Despite of multiple benefits, the frequency of dosing of a medication should be increased as it gets easily emptied from the stomach.²

To overcome these barriers, the delivery of drugs must provide prolonged duration of gastric residence. Gastro retention contributes to an increase in bioavailability, an improvement in the duration of drug release, minimizes drug waste and improves drug solubility that is less soluble in a high environmental pH.³ Many drugs released in the stomach have the greatest therapeutic impact as they are continuously delayed and controlled in release. This type of drug delivery method would have comparatively less side effect and would eliminate the need for repeated dosages.⁴ In pharmaceutical dosage, the formulation of drugs in multilayered / bi-layered tablets is a innovative approach for providing the loading dose and maintenance dose in a tablet. This design allows for the preparation of extended release with an immediate release quantity of drug in one layer and an extended release proportion in the second, thereby retaining a prolonged blood level. The immediate release section will disintegrate rapidly after absorption, by supplying the initial dose of medication for immediate action where the matrix layer remains intact as it passes through the intestine most of the time, thus gradually dissolving from its exposed phases in this path, which helps to retain the blood level that was initially reached.⁵

Typically, conventional controlled-release dosage forms prolong the release of drugs and do not have a rapid onset of action after oral usage. Accordingly, the layered tablets provide a pharmacokinetic benefit over conventional controlled release dosage forms as the drug is rapidly released from the rapid release layer leading to a rapid increase in drug plasma concentration accompanied by a continued release of the drug from the sustained release layer.⁶

Drug Suitable for Gastro retentive Drug Delivery System:⁷

- The Drugs which are locally active in the stomach like Antacids, Misoprostol, etc.
- Drugs showing narrow absorption window in Gastro intestinal tract e.g. Riboflavin, Furosemide, etc.
- Drugs showing instability in the colonic environment e.g. Ranitidine HCl, Captopril, etc.

- Drugs which are effective against normal colonic microbes e.g. antibiotics against *Helicobacter pylori*.
- Drugs which have low solubility at high pH values e.g. Chlordiazepoxide, Diazepam, etc.

Drugs Unsuitable for Gastroretentive Drug Delivery System:⁷

- Drugs which have very limited solubility in the acid medium e.g. Phenytoin, etc.
- Drugs enduring instability in the gastric environmental conditions e.g. Erythromycin, etc.
- The Drugs which are mainly employed for their selective release in the colon e.g. 5-amino salicylic acid and corticosteroids, etc.

CLASSIFICATION OF GRDDS: ⁸⁻¹²

Dosage forms that can be hold within the stomach are called as Gastroretentive Dosage Forms (GRDF).

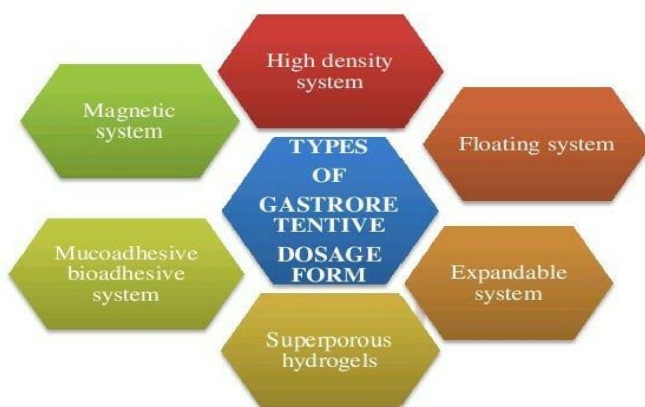


Figure 1: Types of Gastroretentive Dosage Form.¹²

High Density System:

These GRDF type have a density of $\sim 3 \text{ g / cm}^3$, and are retained in the stomach rugae. These systems can be maintained in the lower part of the stomach above a maximum threshold density of $2.4\text{-}2.8 \text{ g / cm}^3$. The major limitation of it is that they are technically difficult to manufacture with a large amount of drug product.

Swelling and Expandable System:

The expandable GRDF is typically based on three configurations, a small configuration that allows for easy oral intake; an expanded form that is accomplished in the stomach and thus preventing its passage through the pyloric sphincter and finally another small form that is achieved in the stomach when retention is no longer necessary. Swelling usually occurs due to osmosis and the unfolding is because of mechanical shape memory.

Mucoadhesive or Bioadhesive System:

These systems allow the incorporation with the bioadhesive agents that allow the system to adhere to the walls of the stomach, thus avoiding gastric emptying. Bio/Mucoadhesive systems binds to the surface of the gastric epithelial cell, or mucin, and extend the GRT by increasing the intimacy and contact duration between the dosage type and the biological membrane.

Superporous Hydrogel:

These are the swellable systems with an average pore size of $> 100\mu\text{m}$, within a minute they swell to equilibrium due to a rapid absorption of water through capillary wetting through multiple interconnected open pores. They swell to a large size and expect to provide enough mechanical strength to endure the pressure by the gastric contraction.

Magnetic System:

The magnetic dosage types contain an extra-corporal magnet and a small internal magnet that controls the gastrointestinal transit of the dosage form.

From the formulation and technological point of view Floating Drug Delivery System (FDDS) is considerably easy and logical approach in the development of GRDD.^{8,9,11}

Table 1: Comparison between Conventional drug delivery systems and GRDDS.¹²

| Sr.No. | | Conventional DDs | GRDDS |
|--------|---|---------------------------|-----------------------------|
| 1. | Toxicity | High risk of Toxicity | Low risk of toxicity |
| 2. | Patient compliance | Less | Improves patient compliance |
| 3. | Drug with narrow absorption window in Small intestine | Not suitable | Suitable |
| 4. | Drug acting locally in the stomach | Not much advantageous | Very much advantageous |
| 5. | Drugs having Rapid absorption through GIT | Not much advantageous | Very much advantageous |
| 6. | Drug which degrades in the colon | Not much advantageous | Very much Advantageous |
| 7. | Drugs which are poorly soluble at an alkaline pH | Not much advantageous | Very much advantageous |
| 8. | Dose dumping | High risk of dose dumping | No risk of dose dumping |

FLOATING DRUG DELIVERY SYSTEM:^{3,8}

FDDS or Hydro-dynamically balanced systems (HBS) are low-density systems having sufficient tendency to float over the gastric contents and remain in the stomach for an extended period of time that releases the drug component at the desired rate, while floating over the gastric contents it contributes to increased gastro-retention time and reduced fluctuation. FDDS is the mechanism of

a gastro-retentive drug delivery system which controls the pharmacokinetic release rate of a drug to a specific site to achieve its pharmacological action.

Basic Gastrointestinal Tract Physiology: ¹¹

The stomach is anatomically divided into 3 regions: fundus, body, and antrum (pylorus).

Fundus: proximal part.

Body: acts as a reservoir for undigested material,

Pylorus: it is a site for mixing of contents and act as a pump for gastric emptying by propelling actions.

Stomach Physiology:

The stomach is an expanded digestive tube section present between the oesophagus and small intestine. The stomach is contracted in the empty state, and the mucosa and sub mucosa are thrown up into distinct folds called rugae.

Below are identified the four major types of secretory epithelial cells which cover the surface of the stomach and extend into gastric pits and glands.

Mucous cells: secrete alkaline fluid.

Parietal cells: secretes a acid that is hydrochloric acid.

Chief cells: secrete pepsin, a proteolytic enzyme.

G cells: secrete the hormone gastrin.

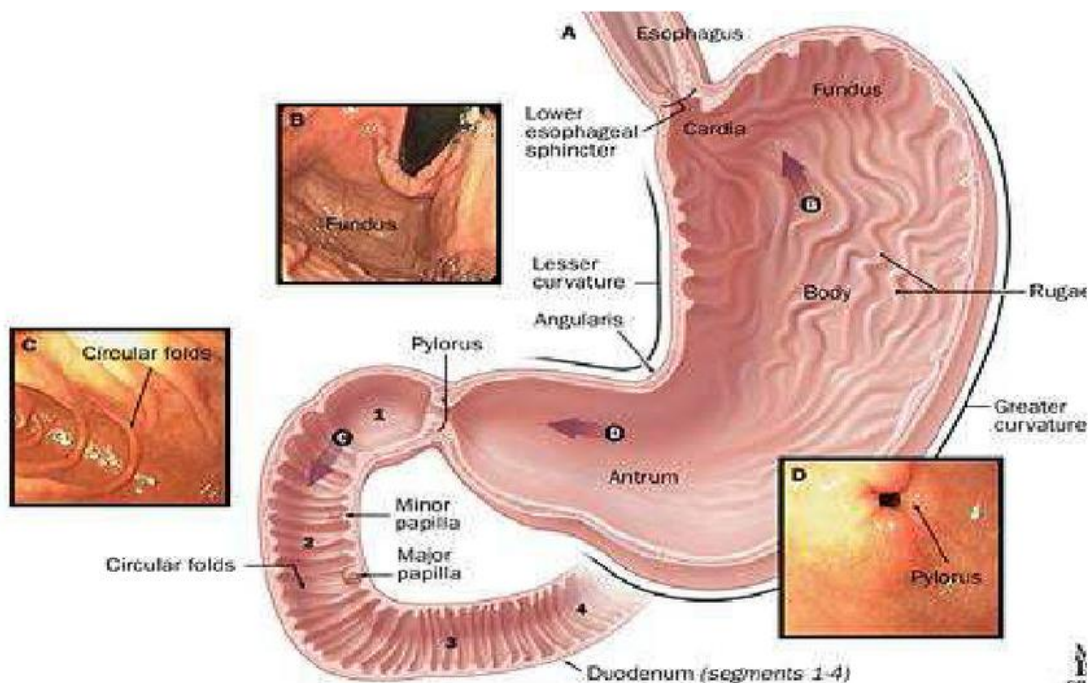


Figure 2: Physiology of stomach

Gastric motility:

Gastric motility is being controlled by a complex set of neural and hormonal signals.

Gastric empty rate:

Gastric emptying happens during both fasting and fed conditions. An inter-digestive sequence of electrical events take place during the fasting process, which pass every 2 to 3 hours in both the stomach and intestines.

It is called the inter-digestive mylo-electric cycle or myoelectric migratory cycle (MMC), which is further divided into 4 stages.

1. **Phase I (Basal phase):** it lasts from 40 to 60 minutes with rare contractions.
2. **Phase II (Preburst phase):** lasts for 40 to 60 minutes with intermittent action potential and contractions.
3. **Phase III (burst phase):** lasts for 4 to 6 minutes, which includes intense and regular contractions for short period of time.
4. **Phase IV:** lasts for 0 to 5 minutes and occurs between phases III and I of 2 consecutive cycles.¹¹

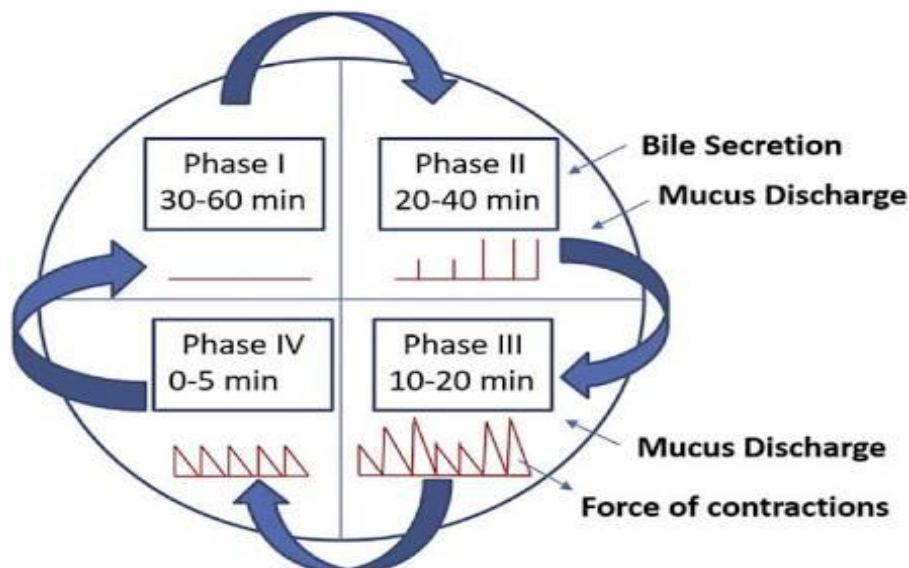


Figure 3: Motility Pattern in GIT.⁹

Factors Controlling Gastric Retention Time of a Dosage Form:¹³

- Nature of the meal
- Fed or Unfed State
- Age
- Frequency of feed
- Concomitant drug administration
- Density
- Size and Shape

- Caloric Content
- Gender
- Posture

CLASSIFICATION: ¹

A. Effervescent FDDS

1. Gas generating system
2. Volatile liquid containing system

B. Non-Effervescent FDDS

1. Colloidal gel barrier system
2. Bi-layer floating tablets
3. Microporous compartment system
4. Floating Beads/ Alginate Beads
5. Micro balloons/ Hollow Microspheres

C. Raft forming system

Effervescent FDDS

This system makes use of a floating chamber filled with water, vacuum, air, or inert gas. CO₂ which is formed as a result of an effervescent reaction between the organic acid (citric acid) and the carbonate / bicarbonate salts can be introduced into the floating chamber. Such a system uses matrix prepared with swellable polymers such as chitosan-like polysaccharides, effervescent materials such as citric acid, sodium bicarbonate, and tartaric acid, or chambers containing a liquid that gasifies at the body temperature.

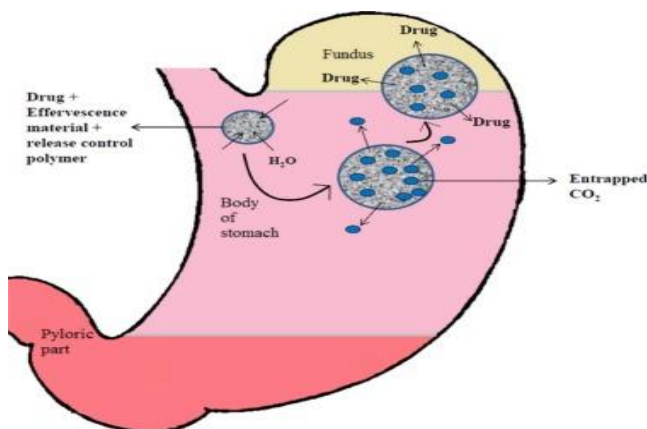


Figure 4: GRDDS based on effervescence.¹⁰

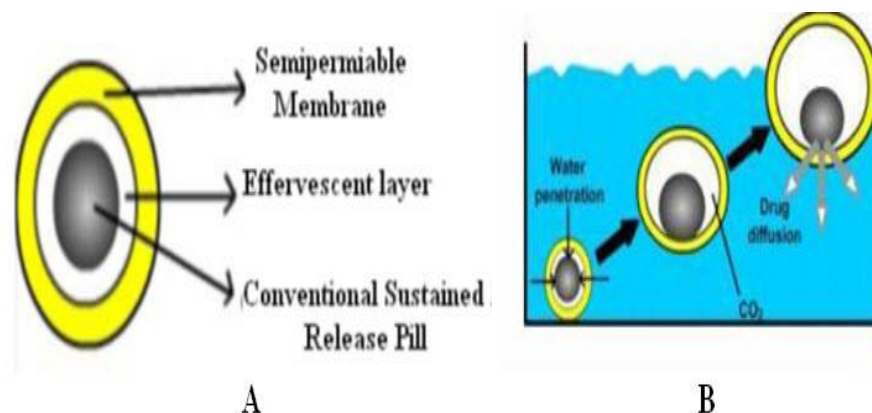


Figure 5: Multiple-unit oral drug delivery system.¹⁴

Gas generation system:

This buoyant delivery system uses effervescence reaction between citric acid / tartaric acid and carbonate / bicarbonate salts to release CO₂ which further reduces its specific gravity and makes it float over chime.

Volatile liquid storage system:

These contain an inflatable chamber consisting of a liquid, e.g. cyclopentane, ether, which gasifies at body temperature to induce inflation of the chamber in the stomach. The system consists of two chambers the first chamber consisting of the drug, and the volatile liquid in the second chamber.

Non-Effervescent FDDS

In GI tract, the non-effervescent FDDS is based on the mechanism of polymer swelling or bioadhesion to the mucosal layer. The excipients most frequently used in non-effervescent FDDS are:

- Hydrophilic gums,
- Gel forming or highly swellable cellulose type hydrocolloids
- Polysaccharides and matrix forming materials such as polymethacrylate, polycarbonate, polystyrene, polyacrylate, as well as bioadhesive polymers such as Carbopol and Chitosan.

Colloidal gel barrier systems / Single layer floating tablets:

Such systems contain a high degree of one or more gel forming, cellulose type hydrocolloids, polysaccharides, and polymers forming matrix, which are extremely swellable.

Bi-layer floating tablets:

A bi-layer tablet comprises of two layers with first layer is the immediate release layer, which releases the initial dose from the system while the other is the sustained release layer which absorbs the gastric fluid, creating an impermeable colloidal gel barrier on its surface and retaining a bulk density of less than 1.

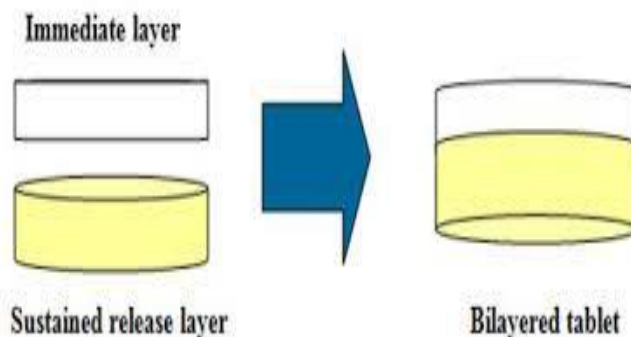


Figure 6: Bilayer tablet.¹⁵

Micro porous compartment systems:

This technology is based on a drug reservoir being encapsulated within a micro porous compartment with apertures along its top and bottom walls.

Multi particulate system: Floating beads / Alginate beads:

Multi-particulate drug delivery systems are often oral dosage types consisting of a multiplicity of small discrete units.

Micro balloons/Hollow microspheres:

Hollow microspheres, also known as micro balloons when immersed in aqueous media they were found to float *in vitro* for 12 hrs.

Raft Forming System

For the delivery of antacid and other medications for gastro-infection and gastro intestinal disorders, a Raft forming systems are mostly considered. Upon contact with gastric fluid the gel forming solution swells and creates a viscous compact gel containing an entrapped CO₂ bubbles forming raft layer on top of gastric fluid that gradually releases the drug substance into the stomach.

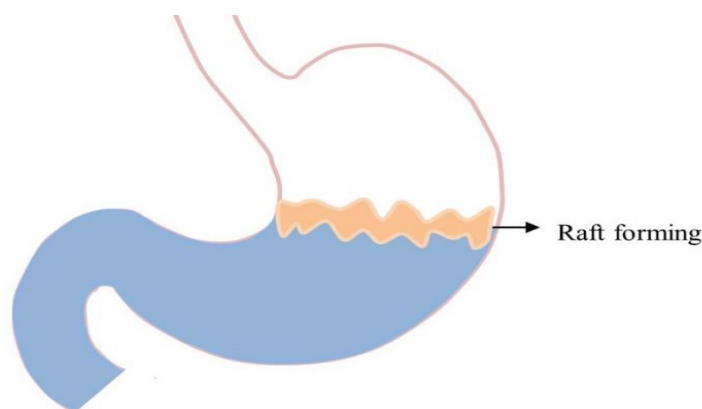


Figure 7: GRDDS based on Raft Forming System.¹⁶

Approaches to Design Floating Drug Delivery System:¹¹

For Single Unit Dosage Forms (Ex: Tablets):

A) Floating Lag Time: Time taken for the tablet to emerge onto the dissolution medium surface and is measured in seconds or minutes.

B) In-vitro drug release and floating duration: This is calculated by the use of USP II devices (paddle) stirring in simulated gastric fluid (pH 1.2 without pepsin) at a speed of 50 or 100 rpm at $37 \pm 0.20^\circ\text{C}$. The samples are then frequently collected and analyzed for the drug content.

The time (hrs) during which the tablets remain buoyant on the dissolution medium surface is the floating duration and is observed visually.

(C) In-vivo Gastro-Retention Assessment: This is done by X-ray or gamma-scintigraphic testing of the dosage form transition in GIT. The tablets are also tested for hardness, variation in the weight etc.

Hydrodynamically Balanced System:

The delivery system are designed to extend the stay of medication types in the gastro intestinal tract, and to help enhance absorption. HBS system produces drugs which have a greater solubility in acidic conditions and also have a particular absorption site in the upper part of the small intestine. For the drug to retain in stomach for an extended period of time the dosage form should have the bulk density of less than '1' and release the drug constantly from the dosage form.

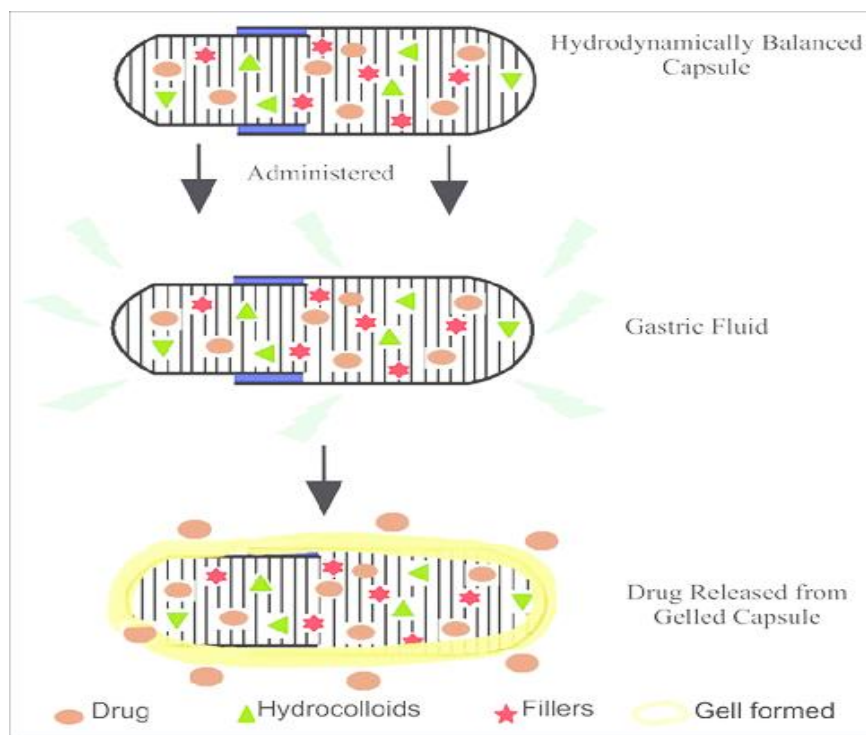


Figure 8: Working principle of Hydrodynamically Balanced System.¹⁷

For Multiple Unit Dosage Forms (Ex: Microspheres):

A) Morphological and dimensional analysis, using electron microscopy (SEM) scanning. An optical microscope can also be used to determine the dimension.

B) In-vitro floating potential (Buoyancy level): A known quantity of microspheres is distributed over the surface of a USP (Type II) dissolution system filled with 900ml 0.1 N HCl containing 0.002 level v / v Tween 80 and agitated at 100 rpm for 12 h. After 12 hours, the floating layer and settled layers are separated, then dried in a dessicator and are weighed.

The buoyancy is calculated from the following formula.

$$\text{Buoyancy (\%)} = \frac{W_f}{(W_f + W_s)} \times 100$$

Where,

W_f and W_s are the weights of floating and settled microspheres, respectively.

Drug-excipient (DE) interactions: This is usually done by using FTIR. The appearance of a new peak, and/or disappearance of original drug or excipient peak indicates the Drug-excipient interaction.

Methods of Developing Floating Drug Delivery System:¹⁸⁻²¹

• Direct compression technique:

It means compressing tablets directly from powder content without altering the substance's physical structure itself. Dicalcium trihydrate phosphate, tricalcium phosphate, etc. are the most widely used carriers.

• Effervescent Technique:

An effervescent reaction between organic acid (citric acid) and bicarbonate salts will fill the floating chamber of the drug delivery system with inert gas (CO₂).

• Wet granulation technique:

Involves wet powder massaging, milling or drying. Wet granulation shapes the granules by binding the powders together with an adhesive rather than compacting them.

• Ionotropic Gelation Technique:

Gelation of anionic polysaccharide sodium alginate, the primary polymer of natural origin, was accomplished with opposite charged calcium ions (counter-ions) with the objective of forming instantaneous micro particles.

• Solvent evaporation technique:

Continuous phase ability is inadequate to remove the entire amount of liquid dispersal solvent. Solvent evaporates from the dispersal surface to receive hardened microspheres.

• Spray Drying Technique:

Involves dispersing the core layer into the liquefied coating content and spraying the core coating mixture into the environment so that the coating is solidified by rapidly evaporating in which the coating material is solubilized.

• **Melt Solidification Technique:**

This method involves emulsifying the molten mass in the aqueous phase followed by cooling it to solidify. Lipids, waxes, polyethylene glycol, etc. are the carriers used for this technique.

• **Melt Granulation Technique:**

This is the method that agglomerates the pharmaceutical powders using a meltable binder and does not use water or organic solvents for granulation.

Excipients Incorporated in Different Floating Dosage Form:²²

- **Effervescent Agents:** E.g. citric acid, tartaric acid, sodium bicarbonate, Di-SGC (Disodium glycine carbonate), CG (Citroglycine).
- **Release rate Retardants:** Some substances such as, Talc, Dicalcium phosphate, Magnesium stearate are used for retarding the release rate.
- **Inert Fatty Materials:** E.g. Long chain fatty alcohols, Beeswax, Fatty acids, Gelucires 39/01 and 43/01.
- **Release rate Accelerants:** E.g. Mannitol, lactose, etc.
- **Hydrocolloids:** E.g. Acacia, β -cyclodextrin, Gelatin, Alginates, Pectin, HPMC, carbopol etc.
- **Buoyancy increasing Agents:** E.g. Ethyl Cellulose and Polypropylene Foam Powder (Accurel MP 1000).

Advantages of Floating Drug Delivery System:²³

- FDDS can remain in the stomach for several hours and thereby prolonging the gastric retention time of various drugs.
- Advantageous for drugs which are meant for local action in the stomach E.g. Antacids.
- Formulation of FDDS are useful in intestinal movement and in diarrhoea to hold the drug in floating state in the stomach in order to get comparatively better response.
- By decreasing the dosing frequency FDDS improves patient compliance.
- Treatment of gastrointestinal disorders such as gastroesophageal reflux.
- Despite of first pass effect the bioavailability since the plasma drug concentration are avoided.
- HBS/FDDS formulations may be useful for the administration of aspirin and other similar drugs since these drugs are acidic and causes irritation on the stomach wall

- Advantageous for drugs which are absorbed through the stomach E.g. Ferrous salts, Antacids.
- Delivery of the drug to the specific site.

Disadvantages of Floating Drug Delivery System:²³

- The drug substances which are unstable in the acidic environment of the stomach are not suitable candidates for integration into the systems.
- In these systems the presence of food is usually required to prolong their gastric emptying.
- It is not suitable for drugs which are having stability or solubility problem in GIT.
- The drugs which undergo first pass effect and the drugs which are significantly absorbed throughout gastrointestinal tract are only desirable candidate.
- The tendency to float depends on the hydration state of the dosage form. Intermittent water administration is useful in order to keep these tablets floating.

Evaluation of Floating Drug Delivery System²⁴⁻²⁷

Bulk Density:

It is the ratio of total mass of powder (m) to the bulk volume (Vo) of powder.

$$D_b = m/V_o$$

Tapped Density:

It is the ratio of total mass of powder (m) to the tapped volume (Vi) of powder.

$$D_t = m/V_i$$

Compressibility Index:

The flowability of powder can be evaluated via evaluating the bulk density (ρ_o) and tapped density (ρ_t) of powder and the rate at which it packed down. Compressibility index calculated by means of

$$= \frac{\rho_t - \rho_o}{\rho_t} \times 100$$

Where,

ρ_o = Bulk density g/ml,

ρ_t = Tapped density g/ml.

Hausner's Ratio: It is evaluated by means of taking Tapped density and it divided by Bulk density by the usage of following formula.

$$\text{Hausner's Ratio} = \text{Tapped density} / \text{Bulk density}$$

Table 2: Specification for Carr's index and Hausner's ratio.²⁹

| Sl. No. | Flow ability | Carr's index (%) | Hausner's ratio |
|---------|--------------|------------------|-----------------|
| 1 | Excellent | 0-10 | 1.00-1.11 |
| 2 | Good | 10-15 | 1.12-1.18 |
| 3 | Fair | 16-20 | 1.19-1.25 |
| 4 | Possible | 21-25 | 1.26-1.34 |
| 6 | Poor | 26-31 | 1.35-1.45 |

Angle of Repose:

The frictional forces in a loose powder or granules can be measured via angle of repose. This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane. The granules are allowed to flow through the funnel fixed to a stand at fixed height (h).

The angle of repose, then calculated by measuring the height and radius of the heap of granules formed.

$$\tan \theta = (h/r)$$

$$\theta = \tan^{-1} (h/r)$$

θ = angle of repose

h = height of the heap

r = radius of the heap

Table 3: The relationship between Angle of repose and powder flow.

| Angle of repose | Powder flow |
|-----------------|-------------|
| <25 | Excellent |
| 25-30 | Good |
| 30-40 | Passable |
| >40 | Very poor |

Tablet Dimensions:

Thickness and diameter were measured using a calibrated Vernier Caliper. Three tablets of each formulation have been picked randomly and thickness were measured separately.

Hardness:

Hardness shows the capability of a tablet to face up to mechanical shocks while handling. The hardness of the tablets was evaluated using Monsanto hardness tester. It was expressed in kg/cm². Three tablets have been randomly picked and hardness of the tablets was decided.

Friability test:

The friability of tablets was evaluated by using Roche Friabilator. It was expressed in percent (%). Ten tablets had been to start with weighed (W) and transferred into friabilator. The friabilator were operated at 25 rpm for 4 minutes or run as much as 100 revolutions. The tablets have been weighed again (Wo). The % friability was then calculated by using formula–

$$\%F = 100 (1-W_o/W)$$

% Friability of tablets less than 1% was considered desirable.

Tablet Density:

Tablet density was an excellent parameter for floating tablets. The tablet could float most effectively when its density turned into much less than that of gastric fluid (1.004). The density was determined by the usage of following formula.

$$V = \pi r^2 h$$

$$d = m/v$$

Where,

v = volume of tablet (cc)

r = radius of tablet (cm)

h = crown thickness of tablet (g/cc)

m = mass of tablet

Weight Variation Test:

Ten tablets were selected randomly from each batch and weighed separately to test for weight variation. A little variation was allowed in the weight of a tablet through U.S. Pharmacopoeia.

Table 4: Percentage deviation in weight variation.

| Average weight of a tablet | Percent deviation |
|-----------------------------------|--------------------------|
| 130 mg or less | 10 |
| >130mg and <324mg | 7.5 |
| 324mg or more | 5 |

Determination of Buoyancy lag time:

The buoyancy lag is the time required for tablet to come out towards surface & float. The buoyancy of tablets was studied at $37 \pm 0.5^\circ\text{C}$ in 900ml of simulated gastric fluid. The buoyancy lag time was determined by the usage of stop watch and overall floating time was observed visually.

Floating time:

Floating time was measured by the use of USP dissolution apparatus-II at 50 rpm using 900ml of 0.1N HCl and temperature was set at $37 \pm 0.5^\circ\text{C}$, throughout the study. The duration of floating (floating time) is the time the tablet floats within the dissolution medium (including floating lag time, which is the time required for the tablet to rise to the surface) is measured by visual observation.

Swelling Index:

Swelling study was carried out for the floating sustained release layer tablets. The accurately weighed tablets were placed in USP dissolution apparatus II containing 900ml of 0.1N HCl

maintained at $37 \pm 2^\circ\text{C}$ and allowed to swell up to constant weight. The tablets had been removed, blotted with filter paper, and changes in weight were determined. The experiments were performed in triplicate. The degree of swelling (Swelling index) was then determined from the formula.

$$\text{Swelling index} = \frac{(W_g - W_o)}{W_o} \times 100$$

Where,

W_o is the initial weight of tablet and W_g is the weight of tablet at equilibrium swelling in the medium.

Drug Content:

Five tablets were chosen randomly from a batch, weighed and powdered in a mortar. An accurately weighed quantity of powdered tablets equivalent to 100 mg was taken in a standard flask and the volume was filled up to the mark with 0.1 N HCL; the solution was filtered through a 0.45 μm membrane paper. Analysis was done by the usage of spectrophotometric method.

In-vitro dissolution studies:

The release rate of floating tablets was determined by the usage of USP dissolution testing apparatus II (Paddle type). The dissolution test was carried out using 900 ml 0.1N HCL, at $37 \pm 0.5^\circ\text{C}$. A sample (5ml) of the solution was taken from the dissolution apparatus at every hour for 12 h, and the samples were replaced with fresh dissolution medium. The samples were passed via Whatman's filter paper and the absorbance of these solutions was measured.

Application of Floating Drug Delivery System:²⁸

Enhanced Bioavailability:

The bioavailability of riboflavin CR-GRDF is substantially increased compared with the administration of non GRDF CR polymeric formulations.

Sustained delivery of drugs:

Oral CR formulations experienced problems in the GIT like gastric residence time. HBS systems that can stay in the stomach for prolonged period of time and having a bulk density of less than 1 and can float on the gastric contents can usually overcome these problems.

Site specific drug delivery systems:

The controlled, gradual drug delivery to the stomach provides appropriate local therapeutic rates and reduces the systemic exposure of the drug. The dosing frequency can be decreased by extended gastric availability from a site driven drug delivery system. E.g. Furosemide and Riboflavin.

Improvement of Absorption:

Drugs with low bioavailability due to site specific absorption from the upper part of the GIT are possible candidates to be developed as floating drug delivery systems, by optimizing their absorption.

Minimized adverse reaction at the colon:

Retention of the drug in the stomach in HBS minimizes the amount of drug entering the colon. Unwanted drug activity in the colon region can thus be avoided.

Reduced drug concentration fluctuation:

Continuous input of the drug following CR-GRDF administration creates concentrations of the blood drug within a narrower range compared with types of immediate release dosage forms.

Table 5: List of Drugs formulated as single and multiple unit forms of Floating Drug Delivery System.²⁹

| | |
|--------------|--|
| Tablets | Ciprofloxacin, Chlorpheniramine maleate, Theophylline, Furosemide, Captopril, Acetylsalicylic acid, Sotalol, Nimodipine, Amoxicillin trihydrate, Verapamil HCl, Isosorbidedinitrate, Isosorbide mononitrate, Prednisolone, Acetaminophen, Ampicillin, Cinnarazine, Riboflavin 5 Phosphate, Diltiazem, Flurouracil, Piretanide. |
| Capsules | L Dopa, Benserazide, Urodeoxycholic acid, Chlordiazepoxide HCl, Furosemide, Nicardipine, Misoprostol, Diazepam, Propranolol. |
| Microspheres | Aspirin, Griseofulvin, Verapamil, p-Niroaniline, Ketoprofen, Terfenadine, Tranilast, Ibuprofen. |
| Granules | Diclofenac sodium, Prednisolone, Indomethacin |
| Films | Drug Delivery Device, Cinnarizine. |
| Powders | Several basic drugs. |

Table 6: The Marketed Products of Floating Drug Delivery System.¹³

| Brand Name | Delivery System | Drug | Company |
|--------------------------------|---|--------------------------------------|------------------------------|
| Valrelease® | Floating Capsule | Diazepam | Hoffmann-LaRoche |
| Modopar® HBS (Prolopa® HBS) | Floating, CR capsule | Benserazide and L -Dopa | Roche Products, USA |
| Liquid Gaviscon® | Effervescent floating liquid alginate preparations | Aluminium hydroxide, Mg Carbonate | Glaxo Smithkline, India |
| Topalkan® | Floating liquid alginate preparations | Al - Mg antacid | Pierre Fabre Drug, France |
| Conviron® | Colloidal gel forming FDSS | Ferrous sulphate | Ranbaxy, India |
| Cytotech® | Bilayer floating capsule | Misoprostol | Pharmacia, USA |
| Cifran OD® | Gas-generating floating form | Ciprofloxacin | Ranbaxy, India |

CONCLUSION:

Development of an efficient gastro retentive dosage form for stomach specific drug transport is an actual project. Accordingly, to produce the preferred gastro retention several strategies were used, out of which, the floating drug delivery system has emerged as the great promising approach. These systems offer the gain of better absorption of medication that are absorbed from the top part

of stomach, which enhance the bioavailability and controlled delivery of many drugs with new and vital therapeutic options. This leads to less frequent dosing and more advantageous efficiency of the treatment. Good stability and better drug release as compared to other conventional dosage form make such system greater reliable. Drug absorption in GIT is a extraordinarily variable system and prolonging GI retention of the dosage form prolongs the time of drug absorption. Floating drug delivery system guarantees to be a technique for gastric retention. Although there are wide variety of complications to be labored out to gain extended GI retention, many companies are focusing in the direction of commercializing this approach. Wide variety of industrial product and patent issued in this field are evident of it.

ACKNOWLEDGEMENT:

My sincere gratitude goes to Mrs. Sheeba FR, and friends of Mallige College of Pharmacy, Bangalore for their continuous support and guidance.

REFERENCES:

1. Gupta P and Gnanarajan PK. Floating Drug Delivery System: A Review. *Int. J Pharm Res Rev.* 2015; 4(8): 37-44.
2. Shyama SK and Sivakumar R. Floating Drug Delivery System: An Updated Review. *Int J Curr Pharm Clinical Res.* 2014; 4(3):150-53.
3. Parmar PD, Pande S, Shah HS, Sonara SN and Patel GH. Floating Drug Delivery System: A Novel Approach to Prolong Gastric Retention. *World J Pharma Pharma Sci.* 2014; 3(4): 418-44.
4. Veerareddy PR, Bajjuri S, Sanka K, Jukanti R, Bandari S and Ajmeru RK. Formulation and Evaluation of Gastroretentive Dosage Form of Ofloxacin. *Stamford J Pharma Sci.* 2011; 4(1): 09-18.
5. Nirmal J, Saisivam S, Peddanna C, Muralidharan S, Godwinkumar S and Nagarajan M. Bi-layer tablets of Atorvastatin Calcium and Nicotinic acid; Formulation and evaluation. *Chem Pharm Bulletin.* 2008; 56(10): 1455-58.
6. Hamza Yassin El-Said and Mona HA. Design and *In Vitro* Evaluation of Novel Sustained-Release Double-Layer Tablets of Lornoxicam: Utility of Cyclodextrin and Xanthan Gum Combination. *American Assoc Pharm Scientists.* 2009; 10(4):1357-67.
7. Sarojini S and Manavalan R. An overview on various approaches to Gastroretentive dosage forms. *Int J Drug Dev Res.* 2012; 4(1): 01-13.

8. Pawar VK, Kansal S, Garg G, Awasthi R, Singodia D and Kulkarni GT. Gastroretentive dosage forms: A review with special emphasis on floating drug delivery systems. *Drug Deliv.* 2010; 18(2): 97-110.
9. Chawla G, Gupta P, Vishal K and Bansal AK. Gastroretention a Means to Address Regional Variability in Intestinal Drug Absorption. *Pharm Technol.* 2002; 27(7): 50-68.
10. Mandal UK, Chatterjee B and Faria GS. Gastro-retentive drug delivery systems and their *in vivo* success: A recent update. *Asian J Pharm Sci.* 2016; 11(5): 575-84.
11. Dixit N. Floating Drug Delivery System. *J Curr Pharm Res.* 2011; 7(1): 6-20.
12. Jassal M, Nautiyal U, Kundlas J and Singh D. A review: Gastroretentive drug delivery system (grdds). *Indian J Pharm Biol Res.* 2015; 3(1):82-92.
13. Gopalakrishnan S and Chenthilnathan A. Floating Drug Delivery Systems: A Review. *J Pharm Sci Technol.* 2011; 3(2): 548-54.
14. Rathod HJ, Mehta DP and Yadav JS. A review on Gastroretentive Drug Delivery Systems. *Pharma Tutor.* 2016; 4(7): 29-40.
15. Rajeswari S and Prasanthi T. A recent review on dual release bilayered tablets. *Crit Rev Pharm Sci.* 2016; 5(4): 1-10.
16. Tripathi J, Thapa P, Maharjan R and Jeong SH. Current State and Future Perspectives on Gastroretentive Drug Delivery Systems. *Pharmaceutics.* 2019; 11(4): 1-22.
17. Rastogi V, Kumar A, Yadav P and Hegde RR. Mathematical Optimization and Investigation on Polymeric Blend of Chitosan and Hydroxy Propyl Methyl Cellulose K4M for Sustained Release of Metronidazole. *Asian J Pharm.* 2016; 9(6): S1-S11.
18. Chien YM. *Novel Drug Delivery System*, 3rd Ed. Vol. 1. New York: Marcel Dekker 1992; 139-96.
19. Vijayasundiram K, Puratchikody A, Prasanth VV and Ravichandiran V. Enhancement of Drugs Bioavailability by Floating Drug Delivery System – A Review. *Int J Drug Deliv.* 2011; 3(1): 558-70.
20. Deshpande AA, Shah NH, Rhodes CT and Malick W. Development of a novel controlled-release system for gastric retention. *Pharm Res.* 1997; 14(1): 815-19.
21. Patel DM, Patel MJ and Patel CN. Multi Particulate System: A Novel Approach in Gastro-Retentive Drug Delivery. *Int J Ayurveda Pharm Res.* 2011; 2(4): 96-106.
22. Kaushik AY, Tiwari AK and Gaur A. Role of Excipients and polymeric advancements in preparation of floating drug delivery systems. *Int J Pharm Investig.* 2015; 5(1): 1-12.

23. Bharkatiya M, Kitawat S and Ojha A. Floating drug delivery system: A review. *J Drug Deliv Ther.* 2014; 4(2): 130-134.
24. Tomar P, Shukla V, Kharia AA and Chatterjee DP. Floating drug delivery system: an updated review. *J Med Pharm Allied Sci.* 2013; 04: 31-42.
25. Sharma N, Agarwal D, Gupta MK and Khinchi MP. A Comprehensive Review on Floating Drug Delivery System. *Int J Res Pharm Biomed Sci.* 2011; 2(2): 428-41.
26. Gadhve MV, Lende LK, Tajane TS and Gaikwad DD. Formulation and Development of Bilayer Floating Tablet of Nifedipine using surface solid dispersion technique. *Int J Adv Pharm.* 2016; 5(5): 117-26.
27. Reddy RS, Ramachandra CT, Hiregoudar S, Nidoni UK, Kammar M, and Ram J. influence of processing conditions on functional and reconstitution properties of milk powder made from Osmanabadi goat milk by spray drying. *Small Ruminant Res.* 2014; 119: 130–137.
28. Arunachalam A, Karthikeyan M, Kishore K, Prasad PH, Sethuraman S, Ashutosh kumar S and Manidipa S. Floating drug delivery systems: A review. *Int J Res Pharm Sci.* 2011; 2(1): 76-83.
29. Arora S, Ali J, Ahuja A, Khar RK and Baboota S. Floating Drug Delivery Systems: A Review. *American Assoc Pharm Scientists.* 2005; 6(3): 372-90.

AJPTR is

- Peer-reviewed
- bimonthly
- Rapid publication

Submit your manuscript at: editor@ajptr.com

