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Review Article **Pharmacy**

A Comprehensive Review on Floating Drug Delivery System

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Abstract

Out of all the several types of gastro-retentive drug delivery systems, floating drug delivery is thought to be the most efficient and effective system. Enhancing the bioavailability of medications with a stomach absorption window is mostly dependent on two key parameters: short gastric residence times (GRT) and variable gastric emptying times (GET). The floating drug delivery method is a low-density system that can be either non-effervescent or effervescent, but it must have enough buoyancy to pass over the contents of the stomach and stay buoyant there for an extended period of time without slowing down the stomach's rate of emptying. Drugs that are unstable in the lower intestine environment, have a limited absorption window in the upper gastrointestinal tract, are lowly soluble at higher pH levels, and are active locally can be delivered via the floating drug delivery system approach. The physiological and formulation factors influencing stomach retention time are included in the latest advancements in floating drugs delivery systems. Bringing together the most recent research on classification, factors influencing the stomach residence time of floating drug delivery system, and the benefits and drawbacks of application mechanisms of action is the fundamental objective of crafting this review study.

Keywords: Floating Drug Delivery Systems (FDDS), Gastric Residence Time, Gastric Emptying Time, Buoyancy.

INTRODUCTION

The oral route drug administration gained its popularities due to some of the unique features includes the reasonable cost of therapy, ease of administration, better patient compliance and acceptability, good range of available dosage form [1, 2]. Despite certain diversity, the oral route of drug delivery has several limitations to deliver the drug in the upper part of GIT [3]. Development of oral Controlled release dosage forms that capable to deliver the drug at a predetermined rate for a prolonged period of time. Floating drug delivery systems (FDDS) is one, amongst the several approaches that are most probably employed in prolongation of the gastric residence times (GRT) [4, 5].

The theory behind floating systems, which Davis discovered in 1968, is that because they are less dense and have a higher buoyancy to float above the gastric juices in the stomach and support prolonged activity [6]. Floating drug delivery systems can prolong the half-life of short-lived biological pharmaceuticals, enhancing their effectiveness and reducing the need for frequent dosage. In addition to helping to improve absorption, floating drugs delivery methods strike to extend the dosage form's time in the gastrointestinal tract [7]. Specifically, these mechanisms are better adapted to drugs with a specific absorption location in the upper region of the small intestine and greater solubility in acidic environments [8]. Certain drugs—namely, those that operate locally in the stomach, are absorbed exclusively there, have a limited window of absorption, are poorly soluble at an alkaline pH, and are unstable in the intestinal or colonic environment—are particularly interesting candidates for floating drug delivery [9].

A more recent development in pharmaceutical technology, FDDS is a family of gastro-retentive drug delivery systems that offers a number of benefits over traditional drug means of administration. They are acknowledged as a crucial tool for obtaining sufficient medication bioavailability and stomach retention. FDDS are buoyant enough to float over the contents of the stomach and stay buoyant there for an extended amount

of time without slowing down the rate at which the stomach empties. The medicine is gradually removed from the system at the desired pace while it is floating on the stomach content. The stomach is cleared of any leftover medication after the substance has been released. As a result, the variations in the plasma drug concentration are better controlled and the GRT is raised [10].

Since the floating sustained release dosage forms are able to maintain their low apparent density while the polymer hydrates and forms a gel-like barrier at the outer surface, they are known as "hydrodynamically balanced systems" (HBS) and display most of the properties of hydrophilic matrices. The drug is gradually released from the enlarged matrix, much like in regular hydrophilic matrices. These forms are expected to remain buoyant (3–4 h) in the gastric contents without affecting the intrinsic rate of emptying because their bulk density is lower than that of the gastric contents [11].

Components of Floating Drug Delivery Systems (FDDS)

Following components are used in the formulation of FDDS:

- **Hydrocolloids:** Hydrocolloids are synthetic, anionic or nonionic slightly modified cellulose derivatives e.g. - acacia, pectin, agar, gelatin, bentonite etc [12].
- **Polymers:** Polymers like HPMC K4M, HPMC K15M, HPMC K100M, polyethylene glycol, polycarbonate, sodium alginate, PVA, PVP, eudragit, carbopol, methyl methacrylate, acrylic polymers are mostly used for the development of floating drug delivery [13, 14].
- **Effervescent Agent:** Sodium bicarbonate, citric acid, tartaric acid, nitroglycerin, Di-sodium glycine carbonate etc. are used as an effervescent agent in the preparation of effervescent based floating formulation [15].
- **Inert Fatty Materials:** Fatty materials have a specific gravity less than one which decreases the hydrophilic property and hence increased buoyancy. E.g. Beeswax, fatty acid, long-chain alcohol, mineral oil [15].
- **Release Rate Modifier:** The release rate of the formulation can be modified by using excipients like lactose, mannitol [12-15].
- **Release Rate Retardants:** They decrease the solubility hence retard the release rate of medicaments. E.g.- dicalcium phosphate, talc, Mg stearate [12].
- **Buoyancy Increasing Agent:** Materials like ethyl cellulose which has a low bulk density less than one can be used for increasing the buoyancy of the formulation. It may be present with 80% of the weight [12].
- **Low-density material:** They are used if necessary to decrease the weight of the formulation for them to float e.g.- Polypropylene foam powder.
- **Miscellaneous:** Adjuvant like preservatives, stabilizers, lubricants, binders, etc can be used in the formulation as per requirements.

Need for Floating Drug Delivery Systems [16]

- ✓ The pharmaceutical industry frequently uses conventional oral administration to treat illnesses. However, there are a number of problems with traditional delivery, the main one being non-site specificity.
- ✓ Certain medications only absorb at a particular location. They demand a release at a specified location or one that ensures the maximum quantity of medicine reaches the designated location.
- ✓ The pharmaceutical industry is currently concentrating on these medications that need to be site-specific.
- ✓ One site-specific method for delivering medications to the stomach or intestines is gastro-retentive delivery. The medication is taken by keeping the dosage form in the stomach, and it is then released gradually into the stomach, duodenum, or intestine at a designated location.

Drug Candidates Suitable for FDDS:

- Drugs that have narrow absorption window in GIT (e.g. Theophylline, L-DOPA, para-aminobenzoic acid, Furosemide, Riboflavin, Methotrexate) [17].
- Drugs those are locally active in the stomach (e.g. Anti-ulcer medications, Misroprostol, Antacids) [18].
- Drugs those are unstable in the intestinal or colonic environment (e.g. Captopril, Ranitidine HCl, Metronidazole, Metformin HCL) [19].
- Drugs that disturb normal colonic microbes (e.g. antibiotics used for the eradication of Helicobacter pylori, such as tetracycline, clarithromycin, amoxicillin) [20].
- Drugs that exhibit low solubility at high pH values (e.g. diazepam, chlordiazepoxide, verapamil HCL, Furosemide). [21]

Drugs Unsuitable for Floating Drug Delivery System [22]

- Drugs having limited solubility in the acid medium e.g. Diphenylhydantoin, 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. Mesalamine, 5-amino salicylic acid and corticosteroids, etc.

Classification of Floating Drug Delivery System:

Based on the buoyancy mechanism floating systems are classified as follows

- Effervescent systems
- Non effervescent systems

Effervescent Systems

Effervescent systems are matrix types of systems made with a variety of effervescent substances, including sodium bicarbonate, citric acid, and tartaric acid, together with swelling polymers like chitosan and methylcellulose. They are designed so that when they come into contact with acidic stomach contents, CO2 is released and lodges in swelling hydrocolloids, giving dosage forms buoyancy [23]. This system is further divided into two categories: gas generating system and volatile liquid containing system.

Gas generating System

In order to retain drugs, this system primarily uses agents that release carbon dioxide. The primary purpose of agents like sodium bicarbonate, citric acid, tartaric acid, and chitosan is to produce carbon dioxide, which lowers the drug's density and causes it to float in the stomach. This floating aids in the drug's longer-term retention [24].

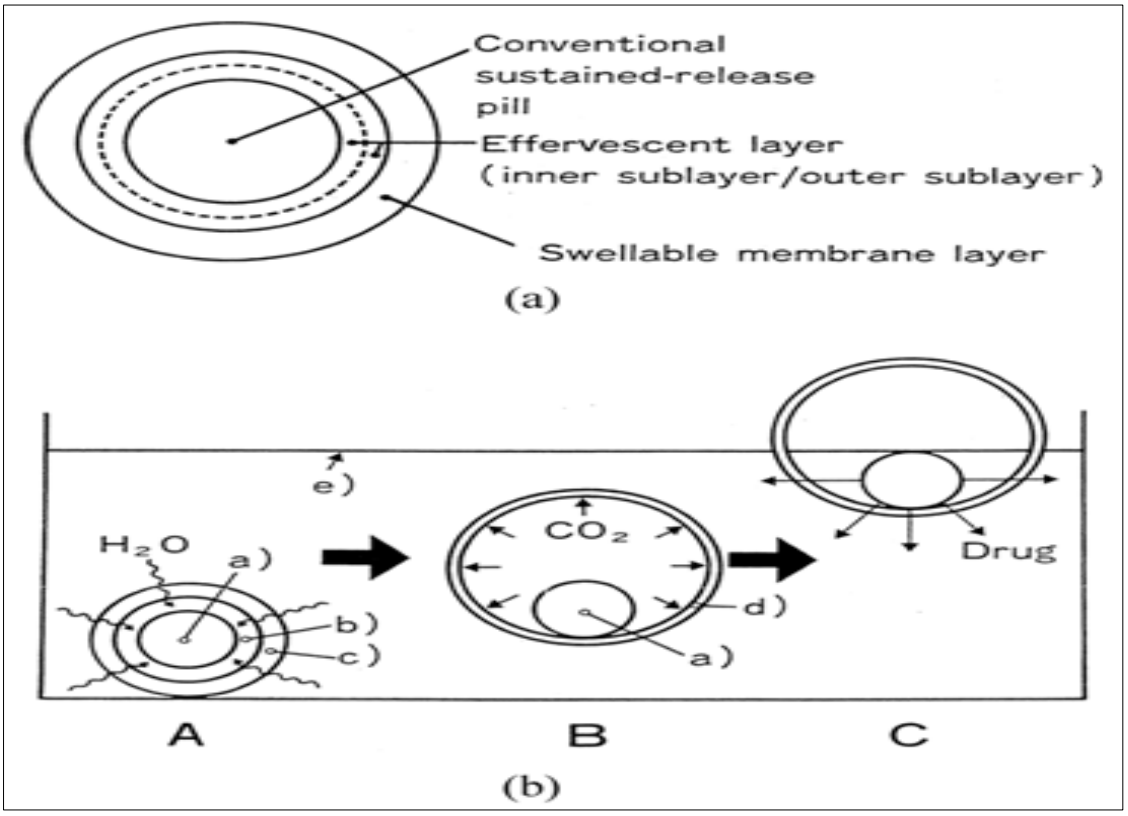

Figure 1: Stages of Floating Mechanism in Gas Generating System [Part (a) shows various layers of gas generating system are shown and in Part (b) stages of floating mechanism are depicted where (A) penetration of water; (B) generation of CO2 and floating; (C) dissolution of drug]

Gel generating systems are of different types. Floating capsules are made by blending a solution of sodium bicarbonate and sodium alginate. When exposed to an acidic environment, the carbon dioxide that is produced becomes trapped in the hydrating gel network, causing the capsules to float. Floating pills are composed of two layers: an outside swellable polymeric membrane and an inside effervescent layer containing tartaric acid and sodium bicarbonate. To prevent sodium bicarbonate and tartaric acid from coming into physical touch, the inner layer is further separated into two sublayers. This tablet sinks to the bottom of the buffer solution at 37 °C, allowing the buffer solution to pass through the outer swellable membrane and into the effervescent layer. When sodium bicarbonates and tartaric acid mix, carbon dioxide is produced, which causes swollen pills or balloons to form. The device floats because the created carbon dioxide is trapped in the delivery system. Floating systems with ion exchange resins are formulated by using ion exchange resin that is loaded with bicarbonate by mixing the beads with sodium bicarbonate solution. In order to prevent the abrupt loss of carbon dioxide, a semi-permeable barrier was placed around these loaded beads. When the beads come into contact with the stomach contents, an exchange of bicarbonate and chloride ions occurs, producing carbon dioxide and pushing the beads toward the top of the stomach contents where they form a floating layer of resin beads that releases the medication at a predetermined time [25-27].

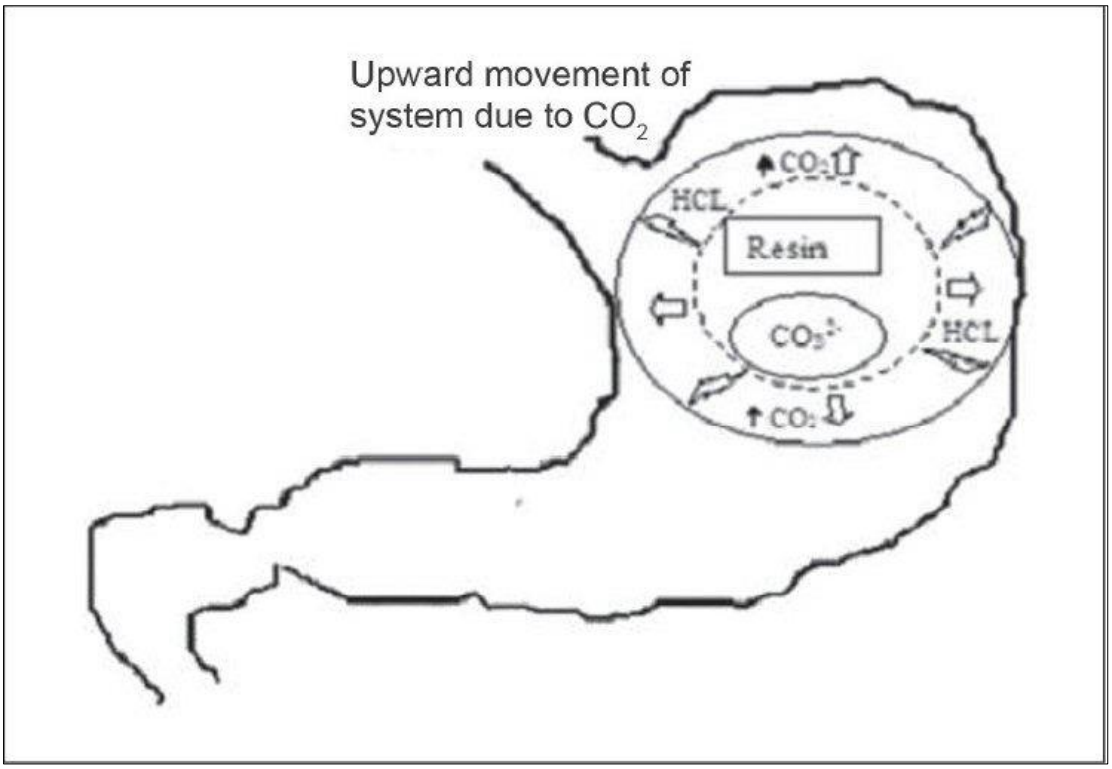

Figure 2: Floating systems with ion exchange resins

Volatile Liquid Containing System

Liquids like ether and volatile cyclopentane are used in this system. By utilizing an inflatable container filled with a liquid, this device offers gastric retention. Drugs are kept in the first compartment of the system, while volatile liquids are kept in the second compartment [24].

Non-Effervescent Systems

Non-effervescent floating dosage forms include matrix-forming polymers such as polycarbonate, polyacrylate, polymethacrylate, and polystyrene, as well as gel-forming or swellable cellulose type hydrocolloids. A simple approach of fully blending the drug and the hydrocolloid that forms gel is part of the formulation process. This dosage form swells upon oral administration and reaches a bulk density of less than one when it comes into contact with stomach juices. The dosage form gains buoyancy from the air trapped in the enlarged matrix. The resulting inflated, gel-like structure serves as a reservoir for the drug's continuous release through the gelatinous mass.

a) Microporous Compartment System: In this technology, a drug reservoir is encapsulated inside a microporous compartment with pores along its top and bottom walls. The peripheral walls of the drug reservoir compartment are completely sealed. This sealing prevents any direct contact of gastric surface with the undissolved drug. The flotation chamber containing the delivery system to float over the gastric content entrapped air allows, in the stomach. Gastric fluid enters through an aperture, dissolves the drug and carries the dissolved drug for continuous transport across the intestine for absorption.

b) Alginate Beads: The freeze-dried calcium alginate has been utilized to create floating dosage forms with multiple units. Calcium alginate can be precipitated by dropping sodium alginate solution into an aqueous solution of calcium chloride, resulting in spherical beads with a diameter of around 2.5 mm. After the beads are separated, freeze-dried at -40ºC for 24 hours, then snap-frozen in liquid nitrogen, a porous system that can sustain a floating force for more than 12 hours is formed. The residency period was extended by these floating beads by more than 5.5 hours [28].

c) Hollow Microspheres: A unique emulsion solvent diffusion approach was used to create hollow microspheres loaded with medication in their outer polymer shelf. An agitated solution of Poly Vinyl Alcohol (PVA) that was thermally regulated at 40^0C was filled with the drug's ethanol/dichloromethane solution as well as an enteric acrylic polymer. The distributed polymer droplet experiences the formation of an interior cavity in the polymer microsphere containing medication due to the evaporation of dichloromethane (Figure 4) [29]. Over the course of more than 12 hours, the microballoon floated constantly on top of an acidic dissolving medium containing surfactant.

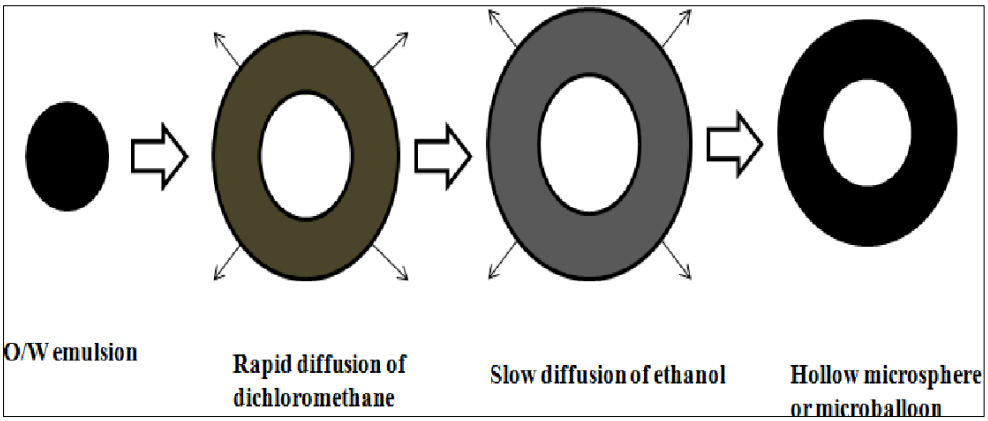

Figure 3: Formulation of Floating Microspheres

Advantages and Disadvantages of Floating Drug Delivery System [30, 31]

Floating Drug Delivery System is highly advantageous in the treatment of the disorders related to the stomach. As the prime objective of such systems is to produce a gastro retentive product or a product which has an enhanced retention time in the stomach.

Advantages of Floating Drug Delivery System
Drugs with considerably short half-life can be administered in this manner to get an appreciable therapeutic activity
Enhancement of the bioavailability for drugs which can metabolized in the upper GIT.
They have an advantage over the conventional system as it can be used to overcome the adversities of gastric retention time as well as the gastric emptying time.
The active entity is delivered specifically to the site of action, thus minimizing or eliminating the side effects.
For diarrhea and difficult gastrointestinal movements, FDDS dose forms are effective because they keep the medication floating in the stomach and significantly improve the response.
Aspirin and other like drugs ought to be used with HBS/FDDS formulations since they irritate the stomach wall when they come into contact with acidic materials like aspirin.
Disadvantages of Floating Drug Delivery System
The main drawback of the floating system is that it requires a high enough level of stomach fluids in order for the drug delivery to float. This restriction can be addressed, though, by covering the dosage form with bioadhesive polymers, which stick to the stomach's mucosal lining with ease.
Gastric retention is influenced by many factors such as gastric motility, pH and presence of food. These factors are never constant and hence the buoyancy cannot be predicted.
It is not appropriate to manufacture substances for use in floating drug delivery systems that irritate or damage the stomach mucosa.
High variability in gastric emptying time due to its all (or) non-emptying process.
Patients should not be dosed with floating forms just before going to bed.
For medications that have issues with solubility or stability in gastric fluids, a floating device is not practical. The medications (propranolol, nifedipine, etc.) that undergo first-pass metabolism and are absorbed throughout the GIT are not good candidates.

List of Drugs Explored for Various Floating Dosage Forms [32]

Microspheres Tablets /Pills	Chlorpheniramine Maleate, Aspirin, Griseofulvin, Acetaminophen, P-Nitroaniline, Acetylsalicylic Acid, Ibuprofen, Amoxycillin Trihydrate, Terfenadine, Ampicillin, Tranilast, Atenolol, Theophylline, Captopril, Isosorbide Di Nitrate, Sotalol, Isosorbide Mononitrate.
Films	P-Aminobenzoic Acid, Cinnarizine, Piretanide, Prednisolone, Quinidine Gluconate.
Granules	Cinnarizine, Diclofenac Sodium, Diltiazem, Indomethacin, Fluorouracil, Prednisolone, Isosorbide Mononitrate, Isosorbide Dinitrate.
Powders	Riboflavin Phosphate, Sotalol, Theophylline.
Capsules	Verapamil Hcl, Chlordiazepoxide Hcl, Diazepam, Furosemide, Benserazide Misoprostol, Propranolol Hcl, Nicardipine

Polymers and other ingredients used to preparations of Floating Drugs [32]

Polymers:	HPMC K4 M, Calcium alginate, Eudragit S100 Eudragit RL, Propylene foam, Eudragit RS, ethyl cellulose, poly methyl methacrylate, Methocel K4M, Polyethylene oxide, _ Cyclodextrin, HPMC 4000, HPMC 100, CMC, Polyethylene glycol, polycarbonate, PVA, Polycarbonate, Sodium alginate, HPC-L, CP 934P, HPC, Eudragit S, HPMC, Metolose S.M. 100, PVP, HPC-H, HPC-M, HPMC K15, Polyox, HPMC K4, Acrylic polymer, E4 M and Carbopol.
Inert fatty materials (5%-75%):	Edible, inert fatty materials having a specific gravity of less than one can be used to decrease the hydrophilic property of formulation and hence increase buoyancy. E.g. Beeswax, fatty acids, long chain fatty alcohols.
Effervescent agents:	Sodium bicarbonate, citric acid, tartaric acid, Di-SGC (Di-Sodium Glycine Carbonate, CG (Citroglycine).
Release rate accelerants (5%-60%):	Lactose, mannitol.
Release rate retardants (5%-60%):	Dicalcium phosphate, talc, magnesium stearate.
Buoyancy increasing agents (upto80%):	Ethyl cellulose.

Mechanism of Floating Drug Delivery Systems

There have been multiple attempts to retain the dosage form in the stomach in order to extend the retention period. A number of innovative approaches have been proposed, such as the co-administration of gastric-emptying delaying drugs and the use of floating, mucoadhesive, high-density, and modified dose forms [33]. The floating dose forms are the ones that are utilized the most frequently. Gastric fluids float in the stomach without slowing down the rate of stomach emptying because they have a lower bulk density than Floating Drug Delivery Systems (FDDS). The medication floats on the contents of the stomach and is gradually removed from the system at the desired rate. After release, the drug's residual system is eliminated from the stomach. Consequently, there is an improvement in the management of plasma drug concentration oscillations and an increase in stomach residence time. However, in addition to the minimal stomach content required to allow the successful accomplishment of the buoyancy retention effect, a minimal level of floating Force (F) is also required to maintain the buoyancy of the dosage form on the surface of the meal. The device works by continually measuring the force F (as a function of time) that is needed to keep an object submerged [34].

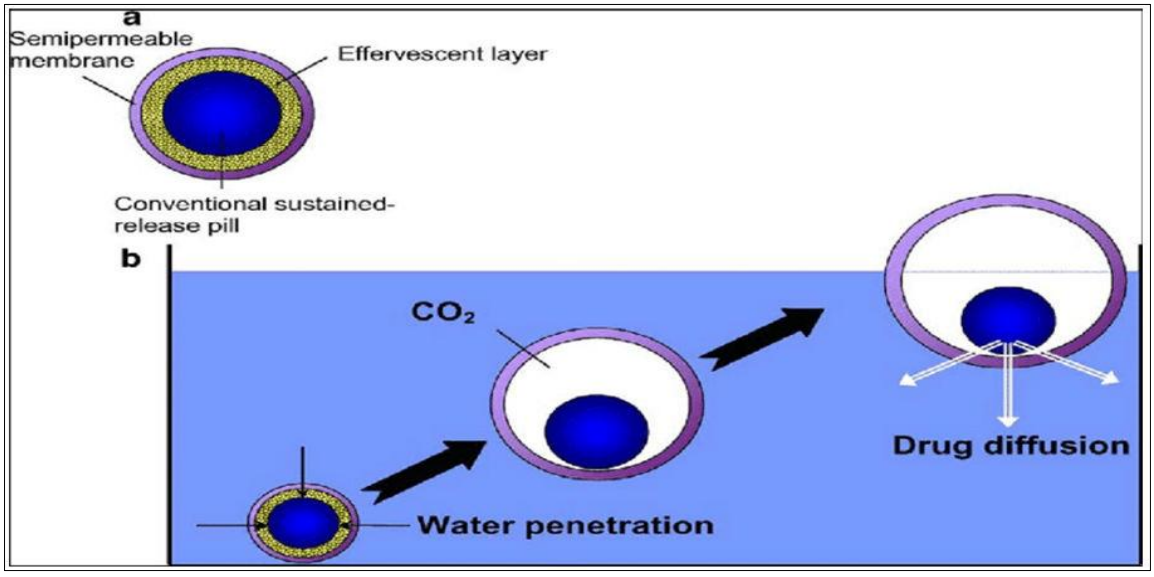

Figure 4: Mechanism of floating drug delivery system

Factors Affecting Gastric Residence Time of the Floating Drug Delivery System

Formulation Factors

Size of Tablets

Floating retention phenomenon of dosage forms in the stomach basically depends on the size of tablets. Small tablets are expelled rapidly from the stomach compared to large ones are emptied during the digestive phase. i.e., Dosage form having diameter of more than 7.5 mm have more gastric residence time than that of 9.9 mm diameter dosage form [35].

Density of Tablets

Density also considered as contributing factor affecting the gastric residence time of dosage form. A buoyant dosage with a density less than that of the gastric fluids would float as it is long enough from the pyloric sphincter, thus having more retention in the stomach for a longer period. Density tablets about 1.0 g/ml (usually considered as less dense than that of gastric contents) have been reported more effective. However, the floating force kinetics has shown that the bulk density of a dosage form would not be the crucial parameter affecting its buoyancy capabilities [35].

Shape of Tablets

The shape of the dosage form is also considered as one of the affecting factors as it interferes with gastric residence time. Six different types of shapes *viz.* ring tetrahedron, cloverleaf, string, pellet, and disk) are screened *in vivo* for their gastric retention potential; during this study, the tetrahedron shape (each leg 2 cm long) rings (3.6 cm in diameter) passed nearly 100% retention at 24 [35, 36].

Viscosity of Polymers

The viscosity of various polymer grades and their interactions have a considerable impact on drug release and the floating features of FDDS. It has been discovered that low viscosity polymers—like HPMC K100 LV—are more effective than high viscosity polymers—like HPMC K4M—when it comes with enhancing the dosage form's floating characteristics. Additionally, it was shown that a reduction in the release rate was also associated with an increase in the viscosity of the polymer [37, 38].

Single or Multiple Unit Formulation

When compared to single unit dosage forms, multiple unit formulation presents a more predictable release profile, allows for co-administration of units with different release profiles or containing incompatible substances, and permits a larger margin of safety against dosage form failure. Additionally, the performance impairment resulting from unit failure is small [36].

Idiosyncratic Factors

Gender: A study shows women have slower gastric emptying time in comparison with men. Mean ambulatory gastric retention time in men (3.4±0.4 h) is lower in comparison with their age and race with female counterparts (4.6±1.2 h), regardless of the weight, height and body surface [34].

Age: Lower gastric emptying time is also observed with high frequent in elderly than do in younger. Intra and inter-person variations are also existing in gastric and intestinal transit time. Elderly people, especially those over 70 y have a significantly longer gastric retention time [36].

Posture

Upright Position: An upright position prolongs floating forms against postprandial emptying since the floating form remains above the gastric contents irrespective of its size. Floating dosage forms show longer and reproducible gastric retention time while the conventional dosage forms tend to sink at the lower part of the distal stomach from where they are expelled through the pylorus by peristaltic movements.

Supine Position: There is no consistent defense against early and irregular emptying at this position. Large dosage forms (conventional and floating) may have longer retention times in supine patients. The gastric retention of floating forms appears to remain buoyant anywhere between the lesser and greater curvature of the stomach. In comparison to upright participants, there may be a significant reduction in gastric retention time as a result of these units being swept away by the peristaltic movements that push the stomach contents towards the pylorus when moving distally [40].

Concomitant Intake of Drugs

Different drugs with a concomitant intake like prokinetic agents (e. g., metoclopramide and cisapride), anticholinergic (e. g., atropine or propantheline), opiates (e. g., codeine) may affect the performance of the floating drug delivery system. The co-administration of GI motility decreasing drugs can increase gastric emptying time and *vice versa* [31].

Feeding Regimen

Gastric residence time shows enhancement in the presence of food, leading to increased drug dissolution rate of the dosage form at the favorable site of absorption. A gastric retention time of about 4 to 10 h has been reported after a diet of fats and proteins [31].

Evaluation of Floating Drug Delivery Systems

1. **Determination of Hardness of Tablet:** Randomly sampled twenty tablets in each batch of formulations should be used for the determination of hardness with the help of Monsanto type hardness tester [41].
2. **Determination of Weight Variation:** Twenty tablets selected at the random are weighed accurately and the average weight of the tablet is calculated. Then the deviation of individual weight from the average weight is calculated.
3. **Determination of Thickness of the Tablet:** The individual crown to crown thickness of ten tablets is determined using slide calipers for each batch [42].

4. **Floating Lag Time:** It is the time taken by the tablet to emerge on to the surface of dissolution medium and is expressed in seconds or minutes [43].
5. **Measurement of Floating Capacity:** Three individual tablets are put in individual flask containing 400ml of 0.1(N) HCL solutions. Then the time in minutes for each tablets to go from the bottom to the top of the flask (floating lag time) and the time for which tablets constantly float on the water surface (duration of floating) are measured. The sample mean and standard deviation are then calculated [44].
6. **Angle of Repose: -** The frictional forces in a loose powder or granules can be measured by 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 were allowed to flow through the funnel fixed to a stand at definite height (h). The angle of repose was then calculated by measuring the height and radius of the heap of granules formed [45].

tan θ = h/r θ = tan-1 (h/r) θ = angle of repose **h** = height of the heap **r** = radius of the heap

7. **Determination of *In Vitro* Dissolution Study:** The test for buoyancy and *in vitro* drug release studies are usually carried out in simulated gastric and intestinal fluids maintained at 37ºC. In practice, floating time is determined by using the USP dissolution apparatus containing 900ml of 0.1 HCl as a testing medium maintained at 37ºC. The time required to float the HBS dosage form is noted as floating (or floatation) time [46].

Pharmacokinetic and Pharmacodynamic Aspects of Floating Drug Delivery Systems

The aim of this section is to delineate these aspects in order to suggest rational selection of drugs for which FDDS would be a beneficial strategy [47-49].

1. Pharmacokinetic aspects of Floating Drug Delivery Systems

Absorption Window

Validation that the medication falls within the class of narrow absorption window agents currently, a number of experimental methods are available that allows to confirm the tested molecule's absorption characteristics, identify the intestinal absorption mechanism, and clarify the permeability at various GI tract locations. When the drug is presented to the transporting enzymes over an extended period of time in the case of capacity-limited active transporters, the transport activity's effectiveness may rise compared to non-control release modes of administration.

Enhanced Bioavailability

The prospect of increasing bioavailability by continuously delivering the chemical to the designated site should be investigated once it has been determined that the drug in question is classified as having a narrow absorption window. For example, we have found that certain bisphosphonates, including alendronate, are absorbed directly from the stomach. However, the magnitude of this pathway remains modest even in the case where the prolonged gastric retention of the bisphosphonate in rats is produced by experimental/surgical means. On the other hand, the bioavailability of control release (CR) floating systems of Riboflavin and Levodopa are significantly enhanced in comparison to administration of simple CR polymeric formulations. It may be that several different processes, related to absorption and transit of the drug in the gastrointestinal tract, act concomitantly and influence the magnitude of drug absorption. Therefore, in vivo studies are necessary to determine the release profile of the drug from the dosage form that will provide enhanced bioavailability [50].

Enhanced First Pass Biotransformation

In a similar fashion to increased efficacy of active transporters exhibiting capacity limited activity, the pre-systemic metabolism of the tested compound may be considerably increased when the drug is presented to the metabolic enzymes (cytochrome P450, in particular CYP3A4) in a sustained manner, rather than by a bolus input.

Improved Bioavailability Due to Reduced P-Glycoprotein (P-gp) Activity in the Duodenum

In apparent contrast to the higher density of CYP3A4 at the upper part of the intestine, P-gp mRNA levels increase longitudinally along the intestine such that the highest levels are located in the colon. Therefore, for drugs that are P-gp substrate and do not undergo oxidative metabolism, such as Digoxin, floating systems may elevate absorption compared to the immediate and CR dosage forms.

Reduced Frequency of Dosing

For drugs with relatively short biological half-life, sustained and slow input from control release floating system may result in a flip-flop pharmacokinetics and enable reduced dosing frequency. This feature is associated with improved patient compliance, and thereby improves therapy.

Targeted Therapy for Local Ailments in the Upper GIT

The prolonged and sustained administration of the drug from the floating systems to the stomach may be advantageous for local therapy in the stomach and the small intestine.

Pharmacodynamic Aspects of Floating Drug Delivery Systems

- **Reduced Fluctuations of Drug Concentration:** Compared to immediate release dose forms, blood drug concentrations produced by continuous drug input after floating system administration fall within a narrower range. As a result, concentration-

dependent side effects linked to peak concentrations can be avoided and variations in the drug's effects are reduced. This particular feature is especially significant for medications with a limited therapeutic index.

- **Improved Selectivity in Receptor Activation:** Minimization of fluctuations in drug concentration also makes it possible to obtain certain selectivity in the elicited pharmacological effect of drugs that activate different types of receptors at different concentrations.
- **Reduced Counter-Activity of the Body:** The pharmacological response frequently causes the body to go into rebound mode, which reduces the amount of drug activity by interfering with normal physiological processes. It has been demonstrated that introducing the medication gradually into the body reduces counteractivity and increases pharmacological effectiveness.
- **Minimized Adverse Activity at the Colon:** Retention of the drug in the GRDF at the stomach minimizes the amount of drug that reaches the colon. Thus, undesirable activities of the drug in colon may be prevented. This pharmacodynamic aspect provides the rationale for floating formulation for beta-lactam antibiotics that are absorbed only from the small intestine and presence in the colon leads to development of microorganisms [51].

Application of Floating Drug Delivery Systems

Floating drug delivery offers several applications for drugs having poor bioavailability because of the narrow absorption window in the upper part of the gastrointestinal tract. It retains the dosage form at the site of absorption and thus enhances the bioavailability. These are summarized as follows [52].

1. Sustained Drug Delivery

FDDS can remain in the stomach for long periods and hence can release the drug over a prolonged period of time. The problem of short gastric residence time encountered with an oral CR formulation hence can be overcome with these systems. These systems have a bulk density of <1 as a result of which they can float on the gastric contents. These systems are relatively large in size and passing from the pyloric opening is prohibited.
E.g. Sustained release floating capsules of Nicardipine Hydrochloride.

2. Site-Specific Drug Delivery:

These systems are particularly advantageous for drugs that are specifically absorbed from stomach or the proximal part of the small intestine.
E.g. Riboflavin and Furosemide.

3. Absorption Enhancement

It may be possible to construct medications as floating drug delivery systems to maximize absorption of those with poor bioavailability due to site-specific absorption from the upper gastrointestinal tract.
E.g. A significantly increase in the bioavailability of floating dosage forms (42.9%) could be achieved as compared with commercially available LASIX tablets (33.4%) and enteric coated LASIX-long product (29.5%).

4. Enhanced Bioavailability

The bioavailability of riboflavin CR-GRDF is significantly enhanced in comparison to the administration of non-GRDF CR polymeric formulations. There are several different processes, related to absorption and transit of the drug in the gastrointestinal tract, that act concomitantly to influence the magnitude of drug absorption [53].

4. Reduced Fluctuations of Drug Concentration

Continuous input of the drug following CRGRDF administration produces blood drug concentrations within a narrower range compared to the immediate release dosage forms. Thus, fluctuations in drug effects are minimized and concentration dependent adverse effects that are associated with peak concentrations can be prevented. This feature is of special importance for drugs with a narrow therapeutic index.

CONCLUSION

As floating drug delivery systems, numerous medications have been developed recently with the goal of limiting the area of drug release to the stomach and achieving sustained release. This drug delivery strategy has been increasingly popular recently due to patient acceptance and compliance. Increased gastrointestinal residence time for the dosage form and sustained drug release can be achieved with simplicity using the buoyant preparation technique. The polymer-mediated effervescent and non-effervescent FDDS that are now on the market seem to be a very successful method of modulating controlled oral drug delivery because they are based on delayed stomach emptying and buoyancy principles. The flotation mechanism makes this dosage form the most suitable choice when the drug is needed to be absorbed primarily in the upper part of GI tract, i.e., the stomach, duodenum, and jejunum.

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