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Review Article

Floating Drug Delivery System: As A Novel Approach for Drug Delivery

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Abstract

The retention period of the drug and dosage form in the stomach is very challenging for the treatment of gastrointestinal disease. To solve this problem and improve the efficacy and bioavailability of the drug, most researchers develop a novel carrier system that is called a Floating drug delivery system (FDDS). The goal of this review on floating drug delivery systems (FDDS) is to synthesise contemporary material with a particular concentration on the main mechanism of flotation for stomach retention. The physiology of the stomach (including gastric pH and movement) has been shown a major effect on gastrointestinal holding period and drug delivery behaviour in both intra- and inter-subject variability. The most recent advancements in the Floating drug delivery system (FDDS) are thoroughly reviewed, including the physiological and formulation factors that influence stomach retention, design methods for single-unit and multiple-unit floating systems, and their categorization and formulation characteristics. A synopsis of the research that has been done to determine the effectiveness and utility of floating systems, as well as uses for such systems, is also included in this review. This study covers the most recent Floating drug delivery system (FDDS) technology advances, including patented delivery techniques and commercial devices, along with their benefits and potential applications for oral controlled drug administration in the future.

Keywords: Floating drug delivery system, Gastric-emptying time, Inter-digestive myoelectric cycle (IDMC), Polymers, Bioavailability, Membrane permeability.

Introduction-

One significant advantage of dosage forms that remain in the stomach for longer than usual dosage forms is the ability to delay and regulate the time until the stomach empties. The development of controlled-release devices for better absorption and bioavailability is fraught with difficulties. One of these difficulties is limiting the dose form in the desired region of the gastrointestinal tract. Drug absorption from the gastrointestinal system is a complicated process that is influenced by many factors. It is widely acknowledged that the length of time a medicine spends in contact with the small intestine mucosa influences how much of it is absorbed in the digestive system. Small intestinal transit time is, therefore, a crucial parameter for drugs that are only partially absorbed. It includes details on gastric emptying, motility patterns, physiological factors, and formulation factors that affect stomach emptying. Basic human physiology is also summarised. The time that pharmaceuticals spend in the stomach can be efficiently extended by gastroprotective systems, which can remain in the gastric region for several hours. Long-term retention in the stomach increases bioavailability, reduces medication waste, and increases solubility for drugs that are less soluble at high pH. Additionally, it can be utilised to deliver medications to the proximal small intestine and the stomach. Gastro retention contributes to the accessibility of cutting-edge medications with fresh treatment options and significant patient benefits. The classification of floating medication delivery devices is based on these principles of floating drug delivery systems (FDDS).[1,2] Classification of Gastro-retentive Drug Delivery System shown in figure-1.[3]

Physiology of the gastrointestinal tract at a basic level-

The fundus, body, and antrum are the three sections of the stomach (pylorus). While the antrum is the main location for mixing motions and acts as a pump for stomach emptying by pushing actions, the fundus and body of the proximal part function as a reservoir for undigested material. Gastric emptying happens both when you're fed and when you're fasting[3]. However, there are differences between the two states' movement patterns. Inter-digestive electrical events take place while fasting and cycle through the stomach and intestine every two to three hours. Wilson and Washington classified this into four phases and named it the inter-digestive myoelectric cycle (IDMC) or migratory myoelectric cycle (MMC). Detailed Structure of the Stomach is shown in figure-2.[3,4]

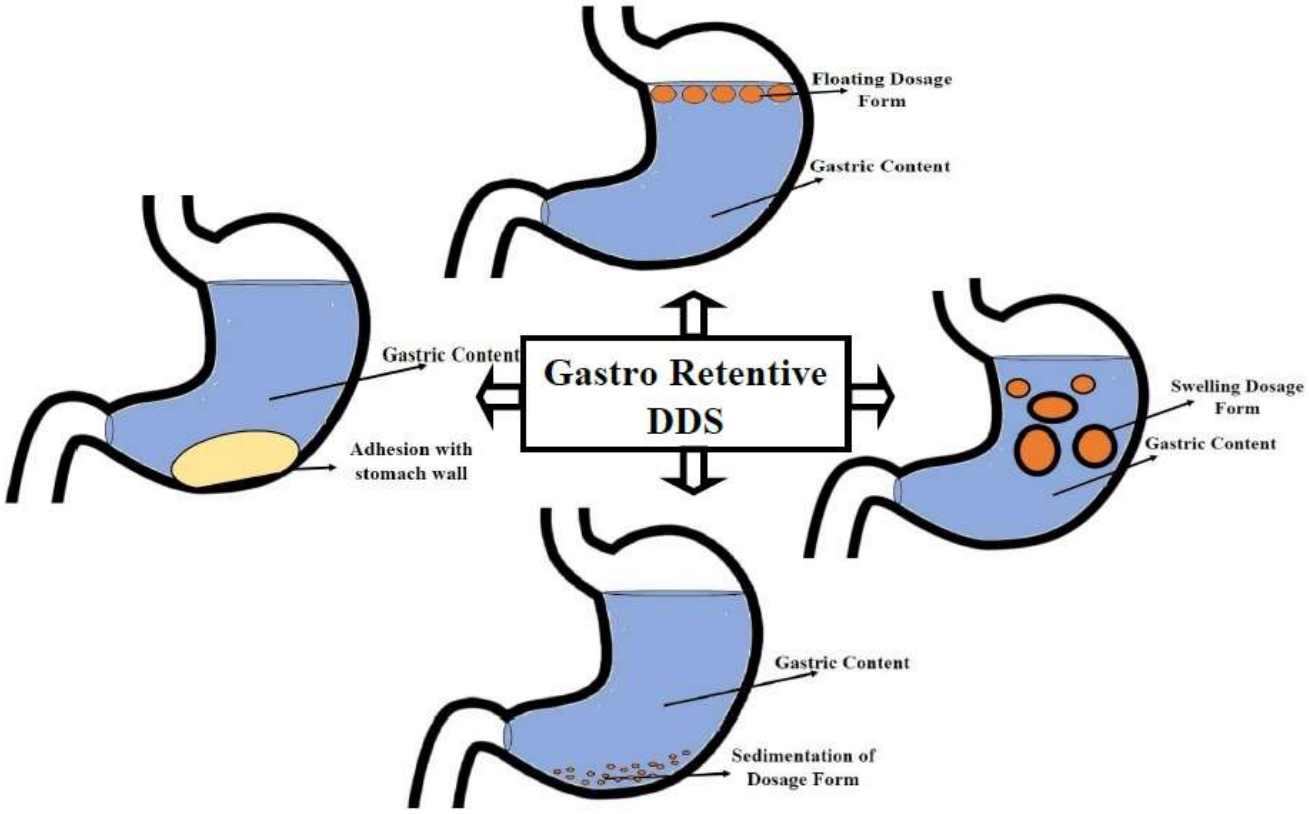

Figure 1: Classification of Gastro-retentive Drug Delivery System [3]

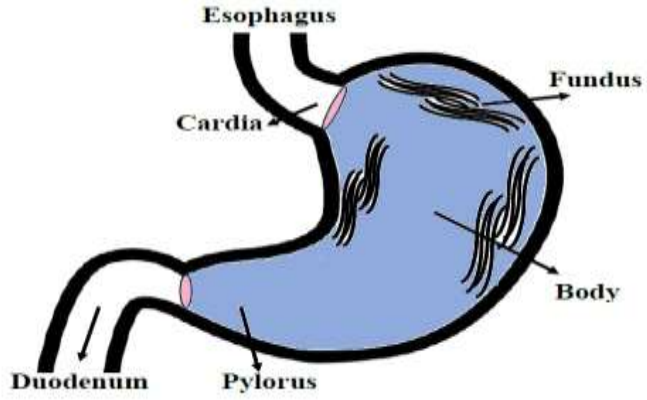

Figure 2: Detailed Structure of Stomach [3,4]

Phase I (Basal phase) lasts 40 to 60 minutes and includes only a few contractions.

Phase II (The pre-burst phase) lasts 40 to 60 minutes and is characterised by erratic action potential and contractions. As the period progresses, the attacks steadily get stronger and happen more frequently.

Phase III (The burst phase) lasts for 4 to 6 minutes. It has strong, frequent contractions that are short. This wave sweeps all undigested matter out of the stomach and into the small intestine.

Phase IV lasts 0 to 5 minutes and comes after phases III and I of two successive cycles.

After consuming a mixed meal, the pattern of contractions changes from a starved to a fed condition. This is also referred to as the digestive motility pattern and it entails ongoing contractions in phase II of the fasting state. These contractions cause food particles to condense in size (to less than 1 mm) and move in a suspension state in the direction of the pylorus. The fed state has a delayed onset of the migratory myoelectric cycle (MMC), which slows the pace at which the stomach empties. Orally administered controlled-release dosage forms are vulnerable to two main issues, short gastrointestinal residence time and unpredictable gastric emptying rate, according to scintigraphy analyses of gastric emptying rates. [5,6,7]

Classification of gastro-retentive drug delivery system (GDDS)-

A. Single Unit Floating Dosage Systems

a) Effervescent Systems (Gas-generating Systems)

b) Non-effervescent Systems

B. Multiple Unit Floating Dosage Systems

a) Non-effervescent Systems

b) Effervescent Systems (Gas-generating Systems)

c) Hollow Microspheres

C. Raft Forming Systems

A. Single unit floating dosage systems- A floating dosage form is generally used for drugs which act locally in the GI tract. [8] There are some systems that are- [7, 9,10,11,12]

a) Effervescent systems (Gas-generating systems)- These buoyant systems have utilised matrices made of swellable polymers like Hydroxy propyl methyl cellulose (HPMC), polysaccharides like chitosan, effervescent substances like sodium bicarbonate, citric acid, and tartaric acid, as well as chambers filled with a liquid that gasifiers at body temperature. According to studies, the stoichiometric ratio of citric acid and sodium bicarbonate for the formation of gas is 0.76:1. The most common way to create these systems is to employ resin beads that have been coated with ethyl cellulose

and loaded with bicarbonate. Water can pass through the covering, which is insoluble but permeable. The beads float in the stomach as a result of carbon dioxide being released. [10] Gas Filled Floatation Chamber shown in Figure-3. Among the excipients that are most frequently used in these systems are Hydroxy propyl methyl cellulose (HPMC), polyacrylate polymers, polyvinyl acetate, Carbopol®, agar, sodium alginate, calcium chloride, polyethene oxide, and poly carb. [13,14]

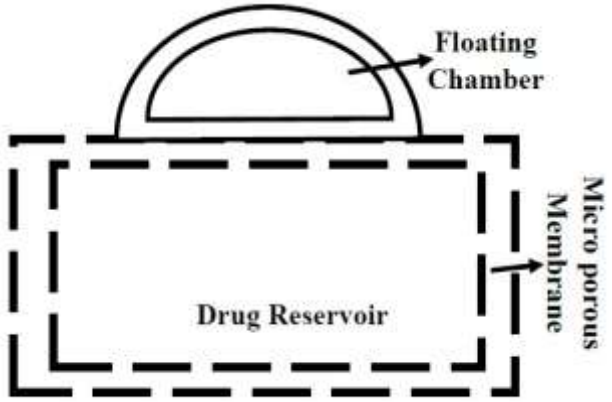

Figure 3: Gas-filled floatation chamber [13,14]

b) Non-effervescent systems- After swallowing, this sort of system swells unrestrainedly due to gastric fluid ingestion, preventing them from passing through the stomach. Because they tend to stay trapped around the pyloric sphincter, these systems are sometimes referred to as "plug-type systems." Combining the drug with a gel that expands when in contact with gastric fluid after oral administration while retaining relative shape integrity and a bulk density of less than one within the outer gelatinous barrier is one method for making such dosage forms. These dose forms have buoyancy due to the air trapped by the inflated polymer. Colloidal gel barriers are one example of this kind of floating drug delivery system (FDDS), hollow microspheres with alginate beads. Another design merges a gas-filled floatation chamber into a microporous component that holds a drug reservoir to create a floating chamber that is filled with fluid. To dissolve the drug, gastrointestinal tract fluid enters through apertures or openings along the top and bottom walls. The other two walls in contact with the fluid are sealed, preserving the position of the undissolved medication. Any appropriate gas, liquid, or solid with sufficient specific gravity and inert behaviour may be present, even air in a partial vacuum. [10,11] The system is made of a shell that disintegrates, goes through the colon and is expelled after it has been swallowed and remained floated for a long time within the stomach. In a contemporary self-correcting floatable asymmetric configuration drug delivery device, a 3-layer matrix regulates drug release. This three-layer principle has been improved by the creation of a drug delivery system with an asymmetric configuration. This system enables control of the release extent and zero-order release kinetics by maintaining a constant area at the diffusing front initially, followed by dissolution/erosion toward the end of the release process.[10,11]

The device was designed to float in living organisms to prolong stomach residence time, which led to a longer overall transit time with maximum absorptive capacity inside the gastrointestinal tract environment and, as a result, higher bioavailability. This property would be useful for medications with pH-dependent solubility, a narrow absorption window, and a long half-life and active transport from either the middle or distal section of the small intestine allow them to be absorbed.[10,11]

B. Multiple unit floating systems- Hydrodynamic Balance System (HBS) and other floating tablets have undergone extensive study and development, but because of their all-or-nothing gastric emptying character, these systems have the severe issue of having a wide range of gastrointestinal transit times when taken orally. The aforementioned issue was intended to be solved by multiple-unit floating systems, which restrict inter-subject variability in absorption and lower the danger of dose dumping. Multiple unit systems, both effervescent and non-effervescent, have been reported on in the past. There has been a lot of interest in the topic of hollow microspheres, which have better gastric retention capacities and can float on stomach fluid. Scientists are still researching this area. [15]

a) Non-effervescent systems- In comparison to effervescent systems, there was little information in the literature on non-effervescent multiple-unit systems. However, only a few researchers have suggested that employing chitosan as the polymeric excipient, such a system with indomethacin may be developed. Indomethacin was used as a model medication in the creation of a multi-unit Hydrodynamic Balance System (HBS).[16] A mixture of medicine, chitosan, and acetic acid is extruded through a needle before the extrudate is diced and dried. Chitosan hydrates and floats in acidic conditions and the required drug release can be accomplished by adjusting the drug-polymer ratio.

- **Micromeritic properties-** Proper equations are used to determine the angle of repose, density, Hausner's ratio, and compressibility index.
- **Particle size and shape-** Compared to light microscopy, scanning electron microscopy (SEM) has a greater resolution than light microscopy (LM). Traditional light microscopy (LM) and scanning electron microscopy (SEM) are the two most common methods for visualising tiny particles.

Both techniques can be used to use Sharma et al. to determine the shape and external structure of multiparticulate. In the case of double-walled microspheres, Traditional light microscopy (LM) allows you to modify the coating parameters. Before and after coating, the multiparticulate formations can be seen and the difference is evaluated microscopically. scanning electron microscopy (SEM) can be used to investigate multiparticular surfaces and cross-sectioned particles. [16]

- **Entrapment efficiency-** The drug is extracted using a suitable method, examined, and the following equation is used to compute it:

$$\% \text{ Entrapment} = \frac{Actual\ content}{Theoritical\ content} X100$$

b) Effervescent systems (Gas-generating systems)- There have been instances of tetracycline hydrochloride-containing floating granules with a sustained release.[17] The drug granulates from stages A and B are combined to make the granules; stage A has 60 parts Hydroxy propyl methyl cellulose (HPMC), 40 parts polyacrylic acid, and 20 parts drugs; while stage B contains 70 parts sodium bicarbonate and 30 parts tartaric acid. Stage A and stage B granules are blended with a lubricant and put in a capsule at a ratio of 60 to 30 parts by weight each. With a floating time of more than 8 hours and sustained drug release of 80% in around 6.5 hours, the capsule shell dissolves and liberates the granules in dissolution fluid. 0.1-0.2 mm-diameter floating pepstatinmini capsules were found by Umezawa (Umezawa and Hamao, 1978).[18] These mini capsules have a covering and a central

core. The centre core is a Hydroxy propyl methyl cellulose (HPMC)-coated granule comprised of lactose, sodium bicarbonate, and a binder. Pepstatin is layered over the Hydroxy propyl methyl cellulose (HPMC) layer. The system floats as a result of CO_2 release in gastric fluid, which prolongs the time that pepstatin spends in the stomach. In the development of multiple-unit systems, alginates have received much interest. Alginates are linear copolymers made up of L-glucuronic and L-mannuronic acid residues that are non-toxic and biodegradable. A multi-unit system was developed, which consists of a calcium alginate core [15] and a gas-filled flotation chamber and an air compartment that separates the calcium alginate/ Polyvinyl alcohol (PVA) membrane. In the presence of water, Polyvinyl alcohol (PVA) leaches out and improves membrane permeability, maintaining the integrity of the air compartment. As the molecular weight and Polyvinyl alcohol (PVA) concentration rose, the system's floating characteristics got better. It has also been documented utilising the freeze-drying technique to create floating calcium alginate beads.[19] The surface of the droplets immediately gels as calcium alginate is produced when sodium alginate solution is added drop by drop to an aqueous calcium chloride solution. The beads are then freeze-dried, resulting in a porous structure that helps them float. The authors used gamma scintigraphy to compare the behaviour of radio-tagged floating beads to that of non-radio-labelled floating beads in human volunteers. A stomach residence time of more than 5.5 hours has been recorded for floating beads. The non-floating beads showed a shorter residence time with a mean onset emptying time of 1h. Sustained-release tablets were coated with a novel floating dose system that features a pill in the centre, effervescent layers, and swellable membrane layers. Different Layers of the floating system are shown in Figure-4 (a)[22,23]. The inner layer of effervescent substances, which included tartaric acid and sodium bicarbonate, was divided into two sublayers to prevent direct contact between the two substances. These sublayers are encircled by a swellable polymer barrier made of pure shellac and polyvinyl acetate. This system calmed down and the solution went through the outer swellable membrane into the effervescent layer when it was placed in the buffer at 37°C. CO_2 was created as a result of the neutralising interaction between the two effervescent agents, resulting in expanded tablets (similar to balloons) with a less density than 1.0 g/ml.[20] Mechanism of Floatation Via CO_2 Generation shown in Figure 4 (b). [17,19, 21,22,23]

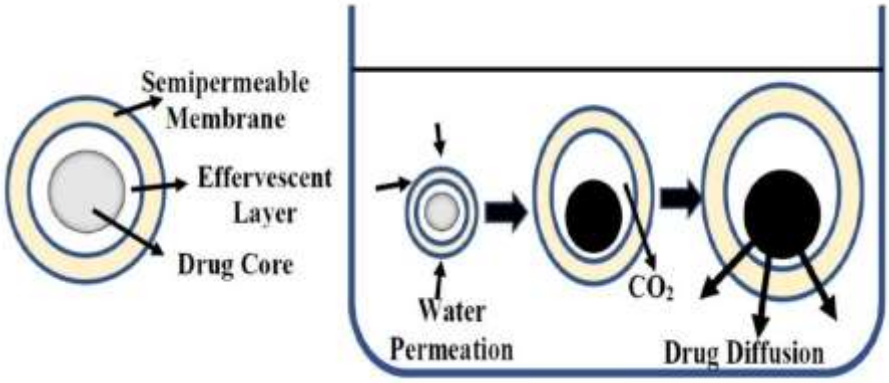

Figure 4: (a) Different Layer-Semi Permeable Member, Effervescent Layer, Core Pill Layer,[22]

(b) Mechanism of floatation via CO_2 generation [22]

c) Hollow microspheres- Hollow microspheres are one of the most promising buoyant systems because of the central hollow region within the microsphere, which offers the special benefits of various unit systems as well as improved floating abilities. Simple solvent evaporation, as well as solvent diffusion and evaporation, are two common procedures used in their preparation. The type of polymer, plasticizer, and solvents used for the preparation has a significant impact on drug release and floating qualities. Polymers like polycarbonate and Eudragit® Sand cellulose acetate were used to create hollow microspheres, and medicine release was controlled by varying the polymer's concentration and plasticizer-to-polymer ratio. The solvent evaporation approach was used to create sustained-release floating microspheres made of polycarbonate. The medications utilised as models were aspirin, griseofulvin, and p-nitroaniline. A dispersed phase containing a polycarbonate solution in dichloromethane and micronized medicine was introduced to a dispersion medium consisting of sodium chloride, polyvinyl alcohol, and methanol. The dispersion was stirred for three to four hours to achieve complete solvent evaporation, and then the microspheres were filtered, washed with cold water, and dried. [24,25,26,27]

Scanning electron microscopy investigations confirmed the microspheres' spherical and hollow structure. More than 50% of the microspheres contained drugs, and it was shown that the quantity added affected both the distribution of drug release and particle size. At high drug loading, a higher proportion of larger particles was observed, which can be attributable to the dispersed phase's increased viscosity. [24,27,28]

C. Raft forming systems- Raft forming systems have gotten a lot of press for their use in delivering antacids and drugs to treat gastrointestinal infections and illnesses. The primary mechanism involved in raft formation is the formation of a viscous cohesive gel in contact with stomach contents, where each part of the liquid expands to form a continuous layer known as a raft. Due to the buoyancy brought on by the creation of CO_2, the raft floats and serves as a barrier to stop gastric contents like HCL and enzymes from refluxing into the oesophagus. Alkaline bicarbonates or carbonates, which are responsible for the development of to make the system less thick and float on the stomach secretions, are typically present in the system along with a gel-forming element. [29]

Mechanism of the floating system- Many attempts have been made to extend the retention time by keeping the dosage form in the stomach for a longer amount of time. These efforts include the development of floating dosage forms, including gas-generating and swelling or expanding systems, mucoadhesive systems, high-density systems, modified shape systems, gastric-emptying delaying devices, and co-

administration of gastric-emptying delaying pharmaceuticals. The floating dose formulations have been the ones that have been used the most frequently. Floating drug delivery systems (FDDS) float in the stomach for longer periods without slowing down the gastric emptying rate because they have a lower bulk density than gastric fluids. The medication is progressively expelled from the system at the proper pace while it is floating on the stomach's contents. Once the medication has been released, the stomach's residual system is emptied. Gastric residence time (GRT) is increased as a result, and variations in plasma medication concentration are better managed. In addition to a minimum stomach content needed to properly implement the buoyancy retention principle, the dosage form also needs to have a certain amount of floating force (F) to stay buoyant on the surface of the meal. To evaluate the dynamics of the floating force, a novel method for calculating resultant weight has been disclosed in the literature. The apparatus operates by continuously measuring the force F (measured as a function of time) needed to maintain the submerged object's submerged state. The object floats more effectively if F is higher on the positive side. Different Mechanisms of Floating Systems are shown in Figure 5. [30] To prevent the drawbacks of unanticipated intragastric buoyancy capability variations, this device helps to optimise floating drug delivery systems (FDDS) in terms of the stability and duration of the floating forces produced. [30]

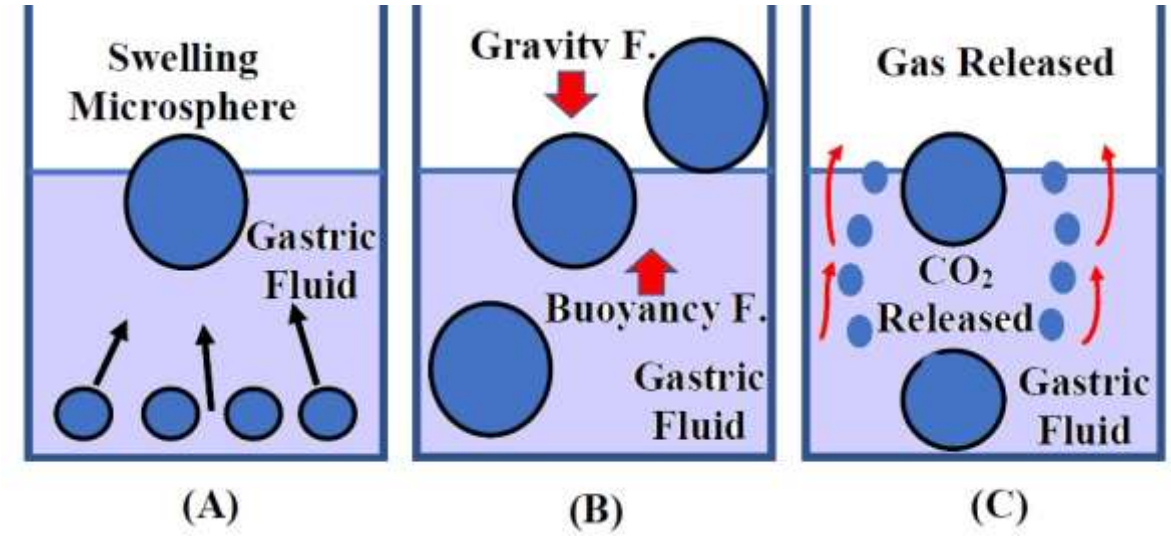

Figure 5: Different mechanisms of floating systems [30]

F- F buoyancy, F gravity = (Df - Ds) gv

Where, F- total vertical force Df - fluid density Ds- Object density v- Volume and g- Acceleration due to gravity

Advantages of floating drug delivery system-

Some advantages are [2,30,31]

- Gastroretentive systems are advantageous for medications that are absorbed through the stomach, such as antacids and ferrous salts.
- Acidic substances, like aspirin, irritate the stomach wall when they come into contact with it. Therefore, the Hydrodynamic Balance System (HBS) formulation may help give aspirin and other medicines of a similar nature.
- The medication will dissolve in the stomach juice when prolonged-release floating dosage forms, such as tablets or capsules, are used. The contents of the stomach dissolve in the gastric fluid after it has been emptied, making them available for absorption in the small intestine. Therefore, it is projected that a medication will be completely absorbed from floating dosage forms if it stays in the solution state, even at the alkaline pH of the colon.
- The use of gastro retentive systems is advantageous for medications that act locally in the stomach. For instance, antacids.
- When there is a lot of digestive movement and a short transit period, as in some types of diarrhoea, poor absorption is expected. In certain circumstances, it may be beneficial to keep the medication in the stomach in a floating form to produce a better reaction.
- By reducing dose frequency, floating drug delivery systems (FDDS) increases patient compliance.
- Despite the first pass effect, the bioavailability increases because continuous drug release maintains a constant plasma drug concentration and prevents oscillations in drug concentration.
- Short half-life medications can have a better therapeutic effect.
- Buoyancy causes an increase in gastric retention time.
- Increased absorption of medications that are only soluble in the stomach.
- Microspheres are superior to single-unit floating dosage forms in that they distribute medicine uniformly and without the possibility of dose dumping.
- The drug's sustained release action, floatability, and uniform release from a multi-particulate system prevent gastric discomfort.

Limitations of FDDS-

Some limitations like- [31,32]

- For the floating system to work, the stomach must contain an adequate volume of fluid. Giving the dosage form in a glass of water or coating it with a bioadhesive polymer that sticks to the gastric mucosa can also help with this issue (200-250 ml).

- Floating systems are ineffective for drugs that cause stomach mucosal irritation or have issues with gastrointestinal fluid stability or solubility.
- For floating drug delivery systems (FDDS), medications having different sites of absorption or those that undergo first-pass metabolism were disqualified.
- Since stomach emptying occurs quickly while a person is lying down, floating dosage forms shouldn't be administered to patients shortly before bed.
- The "all to no" idea is connected with the single-unit floating dose form. Multiple unit systems, such as floating microspheres or micro balloons, can be used to solve this challenge.

Stomach-specific floating drug delivery system parameter and evaluation-

Pharmaceutical dosage forms with floating behaviour during gastric residence in vitro had longer stomach residences during in vivo testing, according to several studies in the literature. It should be highlighted, though, that excellent in vivo stomach retention does not necessarily follow from good in vitro floating behaviour. It's tough to predict the effects of having food and having complex stomach motility at the same time. Only in vivo investigations can give conclusive evidence of prolonged gastric retention. [33-41]

1. **Evaluation of the floating drug delivery systems (FDDS) buoyancy capabilities-** Weight measurements were used to assess the floating behaviour of the floating drug delivery systems (FDDS). The experiment was done in two different mediums, deionized water and distilled water, to see whether there were any differences. Earlier in this essay, the apparatus and its mechanism were discussed. According to the study, higher molecular weight polymers with slower hydration rates exhibited superior floating action, which was seen more in simulated meal medium than in deionized water. [32]
2. **Floating time and dissolution-** Using a USP dissolving apparatus and 900 ml of 0.1mole/lit HCl as the dissolution medium, it is determined at 37°C. The time it takes for a dose form to float is known as the floating lag time, and the time it stays afloat is known as the floating or flotation time. To evaluate a floating drug delivery system (for tablet dosage form), a more relevant in-vitro dissolution approach was proposed. A side arm was added to the bottom of a 100 ml glass beaker to allow it to hold 70 ml of 0.1 mol/lit HCl dissolution medium and collect samples. A burette was positioned above the beaker and administered the dissolving solution at a rate of 2 ml/min to simulate the release of gastric acid. The performance of the newly constructed dissolve device was compared to USP dissolution. Apparatus 2 (Paddle): The USP dissolution apparatus had difficulty with the tablet sticking to the shaft of the paddle. The tablet did not stick to the agitation device during the suggested dissolve procedure. The proposed method has zero-order kinetics for drug release. At a 10% difference value (f2=57), dissolution curves for the USP approach and the suggested method were found to be comparable. The recommended test may demonstrate good in vitro correlation since an effort is made to imitate in vivo settings including gastric volume, gastric emptying, and gastric acid secretion rate. [33]
3. **Drug release –** After a suitable dilution, samples are taken from the dissolution medium and replaced, and their drug concentration is determined.
4. **Drug loading, encapsulation efficiency, particle size analysis, and surface characterization (for microspheres and beads that float**)- A precisely weighed sample of granules or microspheres is crushed in a mortar and added to the proper dissolving media. The mixture is then autoclaved at 121°C, filtered, and assessed using spectrophotometry and other analytical techniques to determine the drug loading. The percentage of drug loading can be calculated by dividing the amount of drug in the sample by the weight and simulated meal, total beads, or microspheres. The particle size and size distribution of beads or microspheres in the dry condition are assessed using optical microscopy. A scanning electron microscope (SEM) is used to examine the exterior and cross-sectional morphology (surface characterization) [34].
5. **X-Ray/Gamma scintigraphy**- Nowadays, X-Ray/Gamma scintigraphy is a highly prominent evaluation parameter for floating dose forms. It facilitates dosage form passage, predicts stomach emptying time, and correlates dosage form passage with a location in the gastrointestinal system (GIT). An X-ray image can be seen when a solid dose form is combined with a radio-opaque material. Similar to this, it is possible to view a formulation containing a radionuclide indirectly from the outside by using a camera or scinti-scanner. In -scintigraphy, the radionuclide's -rays are concentrated on a camera to track the position of the dosage form inside the gastrointestinal system.[34]
6. **Pharmacokinetic studies**- There have been several studies on the topic of pharmacokinetic studies, which are a crucial component of in vivo investigations. Verapamil's pharmacokinetics were investigated using loading pellets that contained the medication, which was subsequently put into capsules and contrasted with conventional verapamil tablets of comparable doses (40 mg). The tmax and Area under the curve (AUC) (0-infinity) values for floating pellets were higher than those for traditional verapamil tablets (tmax value 1.21h and Area under curve (AUC) value 224.22ng/mlh), which were 3.75h and 364.65 ng/mlh, respectively. The Cmax values of both formulations were found to be almost identical, indicating that the floating pellets have better bioavailability than regular tablets. In rabbits, piroxicam in hollow polycarbonate microspheres was found to enhance bioavailability. The bioavailability of the microspheres was 1.4 times higher, and the elimination half-life was three times longer than the free medication. [35]

Gastro retention of dosage controlling factors- The density and size of the dosage form, food intake, food type, posture, age, sex, sleep, and the patient's disease state (such as gastrointestinal disorders and diabetes), as well as the administration of medications like antispasmodic agents, all have an impact on the gastric retention time (GRT) of dosage forms (cisapride and metoclopramide). [39-41,42,43]

- **Dosage form density**- Dosage forms with a lower density than stomach fluid float, causing gastric retention. To have floating property, the density must be less than 1.0 gm/cm3. As the dosage form is immersed in the fluid, however, the floating ability of the dosage form normally reduces as a function of time as the fluid develops hydrodynamic equilibrium. [41]
- **Dosage form size**- Another element that influences gastric retention is the size of the dose form. The mean stomach residence times of non-floating dose forms are very variable and mostly dependent on their size, which can range from small to enormous units. In fed settings, smaller units are expelled from the stomach during the digesting phase, whereas larger units are expelled during the housekeeping waves. In most cases, a bigger dose form will result in a longer gastric retention time since its bulk prevents it from quickly passing through the pyloric antrum and entering the

intestine. As a result, it appears that a key variable affecting stomach absorption is the size of the dose form. [41]

- **The size of the dosage form**- Another aspect that affects stomach retention is the size of the dosage form. Non-floating dosage forms' average stomach residency times vary widely and are mostly influenced by their size, which can range from small to large units. Larger units are emptied during the housekeeping waves whereas smaller units are removed during the digesting phase in fed settings. Since bigger dosage forms have a harder time swiftly passing through the pyloric antrum and into the intestine, they have longer gastric retention times. As a result, the dose form's size appears to have a major impact on stomach absorption. [44]

- **Gender, posture, and age effects**- The researchers also examined how posture affected gastric retention time (GRT) and discovered no appreciable variations in mean gastric retention time (GRT) between individuals who were standing, walking, or lying down. The floating and non-floating systems, however, responded differently in research comparing them to humans. The floating systems floated to the top of the gastric contents in the upright posture and stayed there for a longer duration, indicating prolonged gastric retention time (GRT). However, due to peristaltic contractions, the non-floating units descended to the lower section of the stomach and experienced rapid emptying, while the floating units remained away from the stomach. Floating units, on the other hand, are emptied faster in the supine position than non-floating units of equivalent size [44].

Application of Floating Drug Delivery Systems (FDDS)-

Due to a small absorption window in the upper GI tract, drugs with low bioavailability can be administered using floating drug delivery systems (FDDS). The dosage form is kept at the site of absorption, which increases bioavailability. [4,45] Commercial Gastro-retentive Floating Formulations are shown in Table 1. [46, 47]

TABLE 1: Commercial gastro-retentive floating formulations

Name	Type and Drug	Company, Country	Remarks	Ref
Valrelease	Floating capsule, diazepam	Hoffmann-LaRoche, USA	Floating Capsules	46, 47
Madopar HBS (Propal HBS)	Floating capsules, levodopa and benserazide.	Roche Products, USA	Floating CR Capsules	
Cytotech	Misoprostol (100 mg/200 mcg)	Pharmacia, USA	Bilayer Floating Capsule	
Topalkan	Floating antacid, Aluminium and Magnesium mixture	Pierre Fabre Drug, France	Effervescent floating liquid alginate preparation	
Conviron	Ferrous Sulphate	Ranbaxy, India	The colloidal gel forming FDDS	
Liquid Gaviscone	Mixture of alginate	Glaxo Smith Kline, India	Suppress gastro-oesophagal reflux and alleviate the heartburn	
Amalgate Float Coat	Floating antacid, Floating gel	-	Floating dosage form	
Cifran OD	Ciprofloxacin (1g)	Ranbaxy, India	A gas-generating floating form	

- **Prolonged drug release**- Hydrodynamically balanced system (HBS) dosage forms persist in the stomach for several hours, lengthening the time the medicine is present in the stomach and enabling a more gradual release of the drug. These large dosage forms did not easily pass through the pylorus, had a bulk density of less than one, and had a low bulk density. Levodopa was released from the Madopar Hydrodynamically balanced system (HBS) formulation in vitro for up to 8 hours, but it was released from the standard formulation in less than 30 minutes. [45]

- **Drug delivery at a specific area**- Floating drug delivery systems (FDDS) are particularly helpful for medications like riboflavin and furosemide that can only be absorbed from the stomach or the proximal part of the small intestine. It has been discovered that the stomach and duodenum are the two most frequent sites for captopril absorption. Due to this property, a monolithic floating dosage form of captopril was developed. By increasing the stomach residence time, this form may increase bioavailability. The Area under the curve (AUC) of the floating tablet was nearly 1.8 times greater than that of conventional tablets. Misoprostol, a synthetic prostaglandin E1 blocker, is now available in a bilayer floating capsule that is used to prevent stomach ulcers brought on by the use of Nonsteroidal anti-inflammatory drugs (NSAIDs). By aiming for gradual delivery of the medicine to the stomach, the desired therapeutic amounts of misoprostol could be attained and drug waste could be reduced. [45]

- **Absorption enhancement**- To increase absolute bioavailability, drugs with low bioavailability due to upper gastrointestinal tract (GIT) absorption might be administered selectively. For instance, the captopril floating dosage form has a much greater bioavailability when compared to commercially available tablets. [45]

- In some situations, the relative bioavailability of floating dosage forms is reduced when compared to traditional dosage forms, for example, when compared to normal capsules, the bioavailability of floating tablets of amoxicillin trihydrate is lowered to 80.5 per cent. In many cases, the benefits of Floating drug delivery systems (FDDS) outweigh the lower bioavailability, as is the case for patients with severe Parkinson's disease who had dramatic symptom swings while receiving standard L-

dopa therapy. A Hydrodynamically balanced system (HBS) dosage form offered better motor control while having a bioavailability that was 50–60% lower than the standard formulation. [45]

- For the removal of Helicobacter pylori, which is regarded to be the cause of chronic gastritis and peptic ulcers, Floating drug delivery systems (FDDS) are a successful medication delivery approach. At the infection site, which is within the gastric mucosa, the patients need to be very focused. Due to its floating characteristic, the floating dose form was kept in the stomach, where it was kept at a high concentration. A prolonged liquid ampicillin preparation that spreads out and binds to the gastric mucosal surfaces releases the medication continuously was made using sodium alginate. [45]
- Floating systems are particularly useful for medications that are acid-stable, for drugs that are weakly soluble in intestinal fluids or unstable there, and for medications that exhibit abrupt changes in pH-dependent solubility due to diet, ageing, or gastrointestinal tract (GIT) pathology. For instance, Parkinson's disease could be treated with a floating furosemide system. About 30% of the drug was absorbed after oral administration. [45]

Future aspect-

- As evidenced by several recent studies, floating dosage forms have a wide range of future potential. Due to delayed stomach emptying, there are fewer changes in the drug's plasma level.
- Effective administration of drugs can improve absorption and increase absolute bioavailability in cases where the drug's absorption is limited in the upper gastrointestinal tract.
- A buoyant delivery system is being explored as a promising therapy option for gastric and duodenal cancer.
- The formulation of anti-reflux medications can also be done using the floating principle.
- Developing a controlled release technique for drugs that might be utilised to treat Parkinson's disease.
- To investigate the use of narrow-spectrum antibodies to eliminate Helicobacter pylori.

Conclusion-

The Floating drug delivery system (FDDS) turns into an extra benefit for drugs that are absorbed mostly in the upper gastrointestinal tract (GIT), such as the stomach, duodenum, and jejunum. The time it takes for a medication to be absorbed in the gastrointestinal tract is a highly variable process, and increasing the dosage from gastric retention increases that time. A method that shows promise for gastric retention is Floating drug delivery systems (FDDS). Formulating an efficient Floating drug delivery system (FDDS) appears to be difficult, and effort will continue until an optimum method with industrial applicability and viability is found.

Conflict of interest-

The author declared that there is no conflict of interest regarding the publication of this paper.

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