WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 13, Issue 11, 708-724. Review Article ISSN 2277–7105

AN OVERVIEW ON THE ANALYSIS OF THE FLOATING DRUG DELIVERY SYSTEM

Ravi Kumar Gupta*, Prabhudatta Panda and Dhiraj Kumar

Insituite of Technology and Management.

Article Received on
16 April 2024,

Revised on 06 May 2024,
Accepted on 26 May 2024

DOI: 10.20959/wjpr202411-32654

***Corresponding Author**
Ravi Kumar Gupta
Insituite of Technology and Management.

ABSTRACT

The idea behind the creation of a unique delivery method was to address some of the shortcomings of traditional dosage forms and to address issues with the physicochemical characteristics of drug molecules and formulation development. One potential delivery method is the controlled release floating medication delivery device, medicines that localize release in the stomach, have a restricted window of absorption, are sparingly soluble and insoluble, or have poor absorption in the colon. A gastroretentive drug delivery system, which offers continuously regulated administration of medications that are sparingly soluble at the absorption site, is what is referred to as a floating drug delivery system. The comprehensive situation pertaining to the floating drug delivery system is covered in this review, along with its benefits over the traditional drug delivery system and its drawbacks, which are useful for formulating dosage forms. Different kinds of methods used for creation of this dose format. Review of the effervescent floating medication delivery system's formulation and assessment methods was the main emphasis. Compiling the work being done on this delivery method is the aim of this thorough assessment. They cover the several aspects that impact stomach Retention and Offer useful knowledge on the formulation part of achieving it.

KEYWORDS: Gastroretentive drug delivery system, Absorption, Stomach retention, effervescent.

INTRODUCTION

For many medications, the most common and practical method is oral. The oral route is typically thought of as the best medication delivery method as it has two main characteristics:

a. For the longest-lasting effect, it should only be taken once.
b. Active medication should be administered straight to the intended location.

The creation of a regulated or continuous delivery system is the result of these factors. A medication delivery mechanism is described as sustained delivery having a prolonged or delayed pharmacological release.[1,2] The primary goal in creating these systems is to increase a product's safety and lengthen its duration of action. These methods have a number of drawbacks, including increased dosage dumping, increased variability in bioavailability, longer time to reach therapeutic blood levels, and heightened first pass impact. Generally speaking, these systems cost more than traditional systems.[3] Such goods may cause varying steady state drug levels in various persons because they are designed for the general population rather than for a specific person. If a drug's therapeutic range is sufficiently broad, there might not be any issues.[4]

There are several benefits of oral controlled release drug delivery systems over sustained release formulations, including the ability to stay in the stomach for extended periods of time. A controlled drug delivery system releases the medication over an extended period of time, allowing for a steady supply of the medication to reach the upper gastrointestinal tract, where it is absorbed.[4]

Floating drug delivery system is also known as hydrodynamically balanced system (HBS). While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of the drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration.[5]

Requirement for regulated discharge delivery of gastroretentive drugs

gastroretentive dosage form, which has a longer GRT, may open up significant new therapeutic possibilities, including.[6] This use works particularly well with medications that are insoluble and only sporadically soluble. It is well known that when a medication loses its solubility, there is less time for the drug to dissolve, which means that the transit time has a bigger impact on drug absorption. Erodible, gastroretentive dosage forms that offer

continuous, regulated delivery of sparingly soluble medications at the absorption site have been developed as a solution to this issue.

- Captopril
- Metformin
- Levodopa
- Baclofen
- Furosemide
- Ciprofloxacin

➢ Drugs with so-called absorption windows can be transported via GRDFs. Certain compounds, such as antibiotics, quinolones, penicillins, cephalosporins, aminoglycosides, tetracyclines, and antiviral, antifungal, and other drugs, are only absorbed from very particular locations within the GI mucosa.

➢ Through local drug release, GRDFs significantly enhance stomach pharmacotherapy by achieving high drug concentration at the gastric mucosa. Eliminating Helicobacter pylori from the stomach's submucosal tissue, for example, can cure gastritis, oesophagitis, stomach and duodenal ulcers, lower the risk of gastric cancer, and provide non-systemic controlled release antacid formulations (calcium carbonate).

➢ Generally speaking, molecules with low colonic absorption but superior absorption qualities at the upper regions of the GIT provide suitable candidates for controlled release gastroretentive dosage forms medications that alter the usual bacteria in the colon, such as amoxicillin trihydrat.

Floating drug delivery system applications

The limited absorption window in the upper gastrointestinal system of medications with low bioavailability can be addressed by floating drug delivery in a number of ways. By keeping the dose form where it is absorbed, it increases the bioavailability. Here is a summary of them:

1. Specific to the site dispensing of medicines

These systems are especially useful for medications like furosemide and riboflavin, which are selectively absorbed from the stomach or the proximal portion of the small intestine. The stomach is where furosemide is mainly absorbed, then the duodenum. There have been reports of the development of a monolithic floating dosage form with enhanced

bioavailability and an extended stomach residence duration. The floating pills' AUC was around 1.8 times higher than that of traditional furosemide tablets.[7] For the local delivery of misoprostol, a synthetic prostaglandin E1 analog used to prevent gastrointestinal ulcers brought on by NSAID use, a bilayer-floating capsule was created. Drug waste might be minimized and targeted therapeutic levels could be reached by slowing the transport of misoprostol to the stomach.[8]

2. Enhancement of absorption

Pharmaceuticals with site-specific absorption from the upper gastrointestinal tract that have low bioavailability might be designed as floating drug delivery devices to maximize absorption. Comparing floating dosage forms to currently available LASIX tablets (33.4%) and enteric coated LASIX-long product (29.5%), a notable improvement in bioavailability (42.9%) could be achieved.[7]

3. Sustained drug delivery

Because HBS systems may stay in the stomach for extended periods of time, they can release the medication gradually. These approaches can thereby solve the issue of the short stomach residence time that arises with an oral CR formulation. These are really extensive systems, and exiting the stomach through the pyloric aperture is forbidden. Recently, in vivo evaluations of nicardipine hydrochloride sustained release floating capsules were conducted. Using rabbits, the formulation was compared with MICARD pills that are sold commercially. When comparing sustained release floating capsules to traditional MICARD capsules, plasma concentration time curves revealed that the sustained release floating capsules required a longer administration period (16 hours) (8 hours).[9] In a similar vein, a comparison research comparing the Madopar standard formulation with the Madopar HBS formulation shown that while the medication was released in vitro for up to 8 hours in the former case, it was basically released in less than 30 minutes in the latter.[10]

Table 1: Floating formulations that are sold commercially.[11]

Brand name	Active ingredients	Classification
Valrelease Capsule	Diazepam (15 mg)	Anti-anxiety
Topalkan	Alginic acid, Aluminium and Magnesium salts	Antacid
Cytotec Bilayer capsule	Misoprostol (100 mcg/200 mcg)	-
Almagate flowcoat	Al-Mg antacid	Antacid

Categorization of floating drug delivery system

1) Multiple Unit Floating Dosage Systems

- Effervescent Systems (Gas-generating Systems)
- Raft Forming Systems
- Non-effervescent Systems
- Hollow Microspheres

2) Single Unit Floating Dosage Systems

- Non-effervescent Systems
- Effervescent Systems (Gas-generating Systems)

1. Multiple unit floating dosage systems

Due to their all-or-nothing gastric emptying nature, hydro dynamically balanced systems and other floating tablets have significant drawbacks despite extensive research and development. Specifically, these systems have a high variability of gastrointestinal transit time when administered orally. Multiple unit floating systems were created as a solution to this issue, which decreases the likelihood of dose-dumping and inter-subject variability in absorption (Fig. 1).[12]

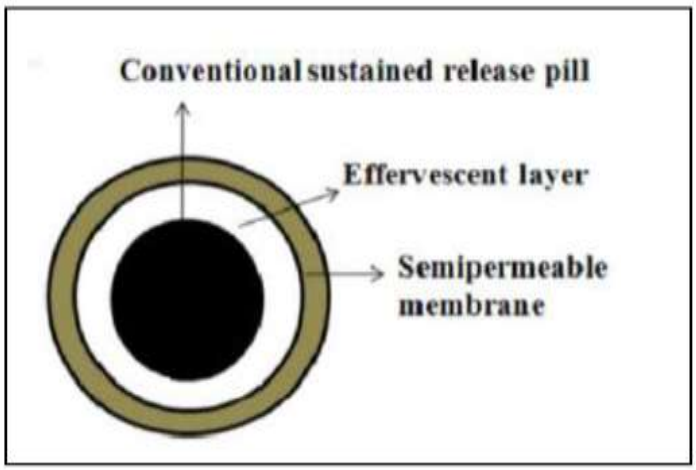

Fig. 1: Multiple unit floating system.

- **Effervescent systems**

There have been reports of Tetracycline Hcl sustained release floating granules. The granules are a combination of drug granulates of two stages, A and B, wherein A contains 60 parts of HPMC, 40 parts of polyacrylic acid, and 20 parts of drug, and B contains 70 parts of sodium bicarbonate and 30 parts of tartaric acid. Thirty parts by weight of stage B granules and sixty

parts by weight of stage A granules are combined with a lubricant and then filled into capsules. The granules exhibit a sustained drug release of 80% in about 6.5 hours and a floating period of more than 8 hours after the capsule shell dissolves in dissolving fluid. There have been reports of pepstatin floating minicapsules with a diameter of 0.1–0.2 mm. These minicapsules are composed of a covering and a core. Granules made of lactose, sodium bicarbonate, and a binder covered in HPMC polymer make up the center core. The top layer of the HPMC is covered with pepstatin. The gastric fluid's release of CO2 and the prolonged presence of pepstatin in the stomach are what keep the system afloat.[13]

- **Non-effervescent systems**

Compared to effervescent systems, there were very few reports in the literature on non-effervescent multiple unit systems. Few researchers have, however, discussed the potential for creating a system using indomethacin and chitosan as the polymeric excipient. A multiple unit HBS manufactured by the extrusion procedure that contains indomethacin as a model medication is presented. Through the use of a needle, a drug, chitosan, and acetic acid combination are extruded; the extrudate is then chopped and dried. In acidic environments, chitosan hydrates and floats, and by changing the drug-polymer ratio, the necessary drug release might be achieved.[14]

- **Hollow microspheres**

Since of the center hollow region inside the microsphere, they are thought to be among the most promising buoyant systems since they have the special benefits of numerous unit systems and enhanced floating qualities. Simple solvent evaporation method and solvent diffusion and evaporation method are two common procedures used in their preparation (Fig: 2). The kind of polymer, plasticizer, and solvents used in the formulation all have a major impact on the drug release and improved floating qualities. Hollow microspheres were made using polymers including Polycarbonate, Eudragit®, and Cellulose acetate. The polymer-plasticizer ratio and polymer amount may be modified to control the medication release. Using the solvent evaporation process, polycarbonate was used to create sustained release floating microspheres. Three medicines were employed as models: aspirin, griseofulvin, and p-nitroaniline.[15]

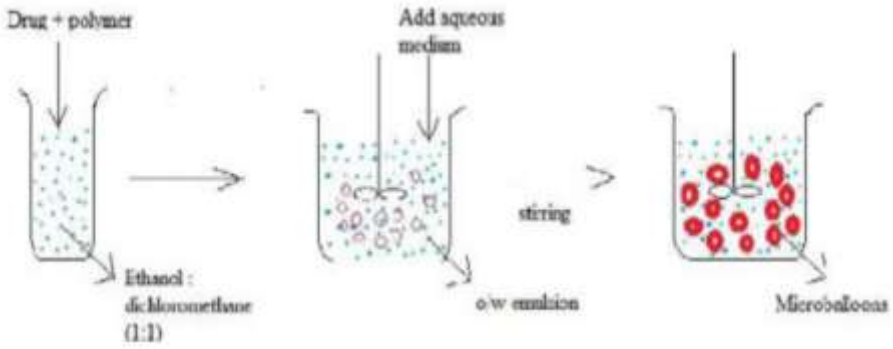

Fig. 2: Hollow microsphere.

- **Raft forming systems**

The distribution of antacids and medications for GI infections and illnesses has drawn a lot of interest in raft-forming systems. The fundamental process of raft formation involves the development of a cohesive gel that is viscous when it comes into touch with the stomach contents. As a result, every part of the liquid swells and forms a continuous layer known as a raft (Fig. 3). Because of the buoyancy that CO2 production creates, the raft floats and acts as a barrier to stop stomach contents like HCl and enzymes from refluxing into the oesophagus. In order for the system to become less thick and float on the stomach juices, it often contains a gel forming agent along with alkaline bicarbonates or carbonates that cause the formation.[16]

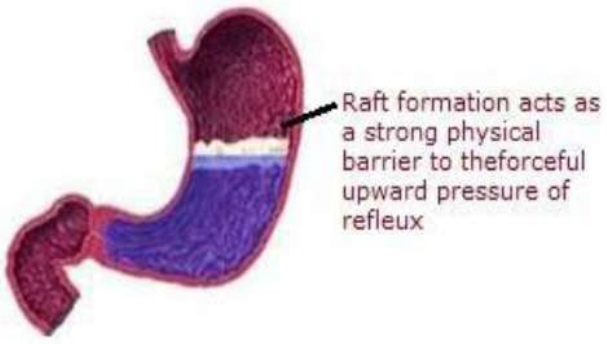

Fig. 3: Raft delivery system.

2. **Single unit floating dosage systems**

- **Non-Effervescent systems**

This kind of system expands uncontrollably after swallowing by consuming so much gastric juice that it stops the food from leaving the stomach. Because these systems tend to stay stuck close to the pyloric sphincter, they may be referred to as "plug-type systems." One way to

formulate these dose forms is to combine the medication with a gel that expands when it comes into contact with stomach fluid. These dose forms are buoyant due to the trapped air created by the inflated polymer. Alginate beads, hollow microspheres, micro porous compartment systems, and colloidal gel barrier are a few examples of this kind of FDDS.

A different kind is called a fluid-filled floating chamber, which consists of a microporous component that contains a drug reservoir integrated with a gas-filled flotation chamber. The gastrointestinal tract fluid enters through apertures or holes at the top and bottom walls, dissolving the medication. The medicine that hasn't dissolved is kept within by sealing the other two walls that are in touch with the liquid. Air, a partially vacuum, or any other acceptable gas, liquid, or solid with a sufficient specific gravity and inert behavior might be the fluid that is present. The gadget may expand to a large size and floats in the stomach for a long time. Once it is fully released, the shell breaks down, moves to the intestine, and is expelled. A three-layer matrix regulates the release of the medicine in a more recent self-correcting floatable asymmetric configuration drug delivery device. In order to achieve zero-order release kinetics and modulate the release extent, the 3-layer principle has been improved through the development of an asymmetric configuration drug delivery system. This system maintains a constant area at the diffusing front initially, then dissolves or erodes as the release process progresses. Because the system floated to extend the gastric residence time in vivo, it had a longer total transit time in the environment of the gastrointestinal tract, which allowed it to absorb more material and increase its bioavailability. Medications with a restricted window of absorption, pH-dependent solubility, and active transport absorption from either the proximal or distal region of the small intestine would be covered by this specific feature.[17,18]

- **Effervescent systems**

The matrices used in these buoyant systems were made with swellable polymers (HPMC), polysaccharides (Chitosan), effervescent substances (Sodium bicarbonate, citric acid, and tartaric acid), or chambers that held a liquid that gasified at room temperature. It is stated that a stoichiometric ratio of 0.76:1 between sodium bicarbonate and citric acid is ideal for gas production. Preparing these systems usually entails using resin beads coated with ethylcellulose and filled with bicarbonate. Water can pass through the covering since it is permeable but insoluble. As a result, the stomach releases carbon dioxide, which makes the beads float. Most often, agar, sodium alginate, calcium chloride, polyethylene oxide,

polycarbonates, polyvinyl acetate, polyacrylate polymers, HPMC, and Carbopol® are utilized as excipients in these systems.[17]

Advantages of FDDS[19]

- With their stomach retentive characteristic, floating dosage devices constitute significant technical drug delivery methods and provide several benefits for the delivery of drugs.

Among these benefits are

- Better medication absorption, resulting from higher GRT and longer dosage form residence times at the absorption site.
- Medication delivery under control.
- The administration of medication for localized stomach action.
- Reducing the amount of medication-induced mucosal irritation by releasing the medicine gradually and at a regulated pace.
- Management of digestive issues, including reflux disease of the stomach.
- Basic and traditional manufacturing equipment.
- Simpler administration and more patient cooperation.
- Delivery of drugs to specified sites.

Disadvantages of FDDS[20]

1. Numerous variables, including pH, the presence of food, and stomach motility, affect gastric retention. These elements are never constant, making it impossible to forecast the buoyancy.
2. Medications that irritate or damage the stomach mucosa should not be designed for use in floating drug delivery systems.
3. A high degree of variability in the time it takes for the stomach to empty entirely or partially.
4. In supine patients, the gastric emptying of floating forms is largely dependent on the size and diameter and might happen randomly. Consequently, it is not advisable to provide floating forms to patients right before bed.

Aspects of formulation

Three key factors—drug, delivery, and destination—should be considered when designing new controlled release dosage forms. Drugs' physiochemical characteristics can be studied with the use of preformulation experiments. These characteristics include compatibility,

solubility, pH, and pKa. The chemical is naturally maintained if its solubility is very low—less than 0.01 mg/ml. When given to the gastrointestinal tract, a medication must overcome a number of biological memories in order to have a therapeutic impact. Therefore, a drug's partition coefficient plays a crucial role in determining how well it penetrates these membrane barriers. Poor bioavailability is the result of compounds with extremely low partition coefficients being unable to pass across these membranes with ease. Orally given medications are attacked by enzyme breakdown and acid-base hydrolysis. Propantheline is one of the unstable compounds in the small intestine. This leads to a reduction in bioavailability when given in a controlled release delivery format. The gastrointestinal tract is the initial target for oral medication delivery systems. The medication is then transported to the site of action after being absorbed. Therefore, the design of controlled release delivery devices is directly influenced by the physiology of the gastrointestinal tract. Additionally, the design is impacted by the effects of co-administered medications and illness conditions.[20]

- **Absorption window:** The creation of this formulation is also facilitated by the absorption window, or location of absorption. Reduced biological half-life: The formulations benefit from ranitidine hydrochloride's reduced biological half-life.

- **Drug solubility:** It is more soluble in acidic environments and has a particular absorption location in the upper section of the small intestine. medication stable at the pH of the stomach.

- **Dose:** medications administered topically in the stomach, such as famotidine (H2-receptor antagonist) and ranitidine hydrochloride. It is frequently given or used to treat erosive esophagitis, gastric ulcers, duodenal ulcers, zollinger-ellisons syndrome, and gastrooesophageal reflex illness.

- **Others:** owing to a few other factors, such as: traditional dosage forms' poor patient compliance; medications' shorter half lives, which necessitate frequent administration; and an increased risk of drug skipping doses. Due to dose missing, it is exceedingly difficult to maintain the plasma concentration time profile in a steady state when using traditional dosage forms.

Evaluation techniques

Assessment of floating tablets in vitro generated formulations' physicochemical parameters and release characteristics were evaluated.

1. Pre-compression parameters

➢ **Angle of repose**

The angle of repose is a useful tool for measuring the frictional forces in loose powder or grains. This is greatest angle that can exist between a granule or powder pile's surface and the horizontal plane. displayed in fig. 4.[21]

Fig. 4: Angle of repose.

Granules were permitted to pass through a funnel that was attached to a stand at a specific height (h). Next, the height and radius of the granule heap that had developed were measured in order to determine the angle of repose.

$\tan \theta = h/r$

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

Where, **θ** = angle of repose

h = height of the heap

r = radius of the heap

Table 2 shows the link between powder flow and angle of repose.

Table 2: Powder Flow and Angle of repose relationship.

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

➢ **Compressibility index**

By comparing the powder's bulk density (ρo), tapped density (ρt), and packing rate, one may assess the flowability of the material. The Compressibility Index was determined using:

$$\textbf{Compressibility index (\%)} = \frac{\rho t - \rho o}{\rho t} \times 100$$

Where **ρo** = Bulk density g/ml002E

ρt = Tapped density g/ml.

2. Post-compression parameters

➢ **Shape of tablets**

The form of compressed tablets was investigated using a magnifying lens.

➢ **Tablet dimensions**

Using a calibrated vannier caliper, the thickness and diameter were measured. Three tablets of each formulation were chosen at random, and each tablet's thickness was measured separately.[21]

➢ **Hardness**

A tablet's hardness level reveals how well it can tolerate handling-related mechanical shocks. A Monsanto hardness tester was used to measure the tablets' hardness. The unit of expression was kg/cm2. The pills' hardness was assessed after three were chosen at random.[22]

➢ **Friability test**

The Roche Friabilator was used to assess the friability of tablets. The indicated value was in percentage (%). After weighing ten pills (W initial), they were put into a friabilator. The friabilator was run for four minutes at 25 rpm or up to 100 rotations. Once more, the pills were weighed (Wfinal). Next, the percentage friability was determined by:

%F = 100 (1-W0/W)

Less than 1% of pills had friability, which was deemed acceptable.[21]

➢ **Tablet density**

One crucial factor in floating tablets was tablet density. Only when the tablet's density was lower than that of stomach fluid (1.004) would it float. The relationship shown below was used to calculate the density.[23]

V = πr2h

d = m/v

v = volume of tablet (cc)

r = radius of tablet (cm)

h = crown thickness of tablet (g/cc)

m = mass of tablet

- **Floating test**

Measured were the intervals between the dosage form's introduction and buoyancy on the simulated stomach fluid, as well as the duration of the dosage form's buoyancy. The period of time that the dose form remains buoyant is known as Total Floating Time (TFT), and the time it takes for it to emerge on the medium's surface is known as Floating Lag Time (FLT) or Buoyancy Lag Time (BLT).[22-24]

- **Swelling study**

A dosage form's swelling behavior was assessed by observing how much water it absorbed or gained in weight. The growth in tablet thickness or diameter over time might be used to quantify the dimensional changes. The calculation provided the weight gain percentage as a measure of water uptake.

$$WU = \frac{(W1 - W0)}{W0} \times 100$$

Wt = Weight of dosage form at time t.

W0 = Initial weight of dosage form.

- ***In vitro* drug release studies**

In vitro drug release investigations and buoyancy tests are often conducted in simulated stomach and intestinal fluids that are kept at 37 °C. In actual use, the USP dissolving equipment with 900ml of 0.1 HCl as a testing medium kept at 37 °C is used to calculate floating time. Floating (Also known as flotation) time is the amount of time needed to make the HBS dosage form float. The USP dissolving device is used for dissolution testing. After a suitable dilution, samples are taken out of the dissolving medium on a regular basis, refilled with the equal amount of new medium, and their drug content is examined. Current practice, as outlined in USP XXIII, stipulates that before beginning the blade's rotation, the dosage unit must sink to the bottom of the vessel. The dose units that would ordinarily float can have a tiny, loose piece of non-reactive material connected to them, such as a wire helix with a few twists. Furthermore, the suggested approach was discovered to offer uniform release profiles

and repeatable hydrodynamic circumstances. In the instance of swellable floating systems containing the highly water soluble medication diltiazem, the authors did not discover any variation in the drug's release between the USP approach and the suggested method. These results led to the conclusion that full surface exposure, unrestricted swelling, and the drug's solubility in water are necessary for drug release from swellable floating devices. Burns et al. modified official dissolution procedures in another way.[25] In follow-up research, the scientists altered a typical dissolving vessel to enable more accurate evaluation of the floating dosage forms' performance—especially for those that depend on an erosion mechanism for medication release. The outcome demonstrated a more consistent dissolving profile and did away with the requirement to place the paddle blades at the dissolution medium's surface, which made sample processes easier and prevented dosage forms from sticking to the paddle blades. However, the approach was still able to distinguish between acceptable and unsatisfactory disintegration performance.[26] Additionally, it is important to optimize floating formulations with regard to the longevity and stability of the floating capability that may be seen in in vivo research. The scientists have also delineated a methodology for ascertaining the buoyant properties of floating forms and the sinking properties of non-floating forms.[28,29] Using a specifically made device, the approach measures the total force exerted vertically on an item submerged in a liquid. The equipment used to measure the total force acting vertically on an item submerged in a liquid and its technical specifications have been previously discussed.[27,28] The determination of floating dosage forms' in vivo gastric receptivity is often accomplished by γ-scintigraphy54. Studies utilizing floating and non-floating dose forms are conducted under both fed and fasting settings. The fact that both dose forms are non-disintegrating units is also crucial.[29-31]

Mechanism of floating drug delivery system

Because floating drug delivery systems (FDDS) have a lower bulk density than gastric fluids, they float in the stomach for extended periods of time without slowing down the rate at which the stomach empties. The medicine is released from the system gradually and at the correct rate while it is floating on the stomach contents (Fig. 5). The stomach is cleared of any leftover medication once the substance has been released. As a result, the variations in plasma drug concentration are better controlled and the GRT is raised. Nevertheless, in addition to the minimal gastric content necessary for the appropriate realization of the buoyancy retention principle, a minimal degree of floating force (F) is also necessary to maintain the dosage form consistently buoyant on the meal's surface. To quantify the floating force

kinetics, a novel apparatus for determining the resultant weight has been documented in the literature; it measures the force equivalent to F (as a function of time) continuously in order to sustain the submerged object.[32]

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.

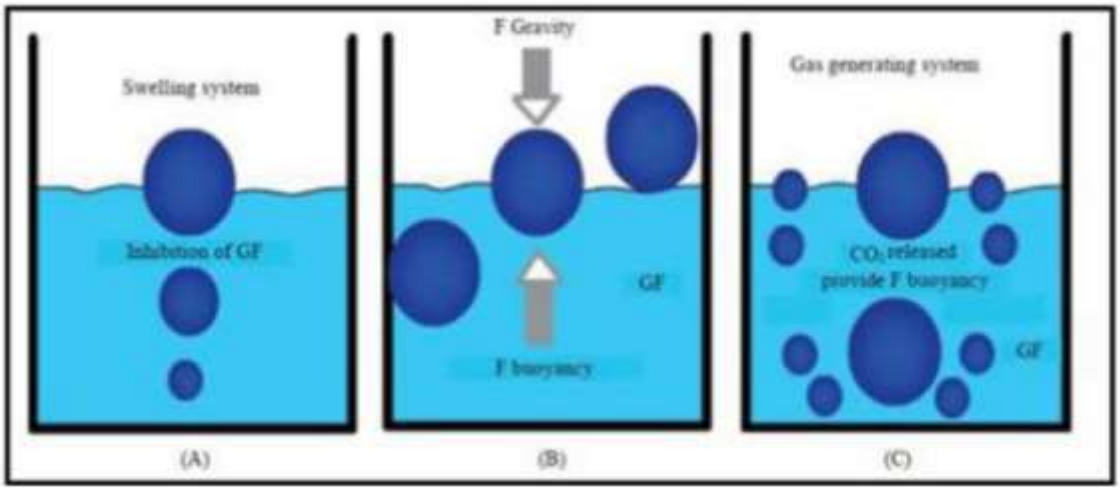

Fig. 5: Mechanism of FDDS.

CONCLUSION

For drugs that are absorbed primarily in the upper segments of the GI tract—the stomach, duodenum, and jejunum—the FDDS becomes an added benefit. Polymers are substances that are used in formulations for a variety of purposes, such as gelling agents, emulsifying agents, viscosity increasing agents, rate retarding agents, etc., so knowledge of polymers in the field of drug delivery plays an important role. Nevertheless, much work remains to be done to overcome the various physiological and pharmaceutical barriers in order to develop more effective dosage forms. Future research in the FDDSs is advised to focus on figuring out how to precisely regulate the drug input rate into the GI tract in order to optimize the pharmacokinetic and toxicological profiles of pharmaceuticals.

REFRENCES

1. Friend DR. Oral delivery: A new approach to dosage forms. Pharmaceutical News, 2006; 9: 375-80.

2. Robinson JR, Lee VHL. Controlled drug delivery: fundamentals and applications, Marcel Dekker: New York, 1978; 2: 335-410.
3. Brahmankar DM, Jaiswal SB. Biopharmaceutics and pharmacokinetics a treatise. New Delhi; Vallabh Prakashan: New Delhi, 1995; 1: 10-48.
4. Chein YW. Novel drug delivery systems, Marcel Dekker, New York, 1992; 2: 185-210.
5. Nayak AK, Maji R, Das B. Gastroretentive Drug Delivery Systems: A Review. Asian Journal of Pharmaceutical and Clinical Research, 2010; 3(1): 2- 9.
6. Gennaro RA. Remington: The Science and Practice of Pharmacy. Lippincott Williams, New York, 2000; 20: 153-225.
7. Menon A, Ritschel WA, Sakr A. Development and evaluation of a monolithic floating dosage form for furosemide. J Pharm Sci, 1994; 83: 239Y245.
8. Oth M, Franz M, Timmermans J, Moes A. The bilayer floating capsule: a stomach directed drug delivery system for misoprostal. Pharm Res, 1992; 9: 298Y302.
9. Moursy NM, Afifi NN, Ghorab DM, El-Saharty Y. Formulation and evaluation of sustained release floating capsules of Nicardipine hydrochloride. Pharmazie, 2003; 58: 38Y43.
10. Erni W, Held K. The hydrodynamically balanced system: a novel principle of controlled drug release. Eur Neurol, 1987; 27: 215Y275.
11. Jain SK, Jain NK, Agrawal GP. Gastroretentive floating drug delivery: An overview. Drug Deliv Technol, 2005; 5: 7-15.
12. Iannuccelli V, Copp G, Sansone R, Ferolla G, Air compartment multiple-unit system for prolonged gastric residence part II in-vivo evaluation, International Journal of Pharmaceutics, 1998; 174: 55-62.
13. Gholap SB, Banarjee SK, Gaikwad DD, Jadhav SL, Thorat R M, Hollow microspheres: A Review, International Journal of pharma science research, 2010; 1(1): 74-79.
14. Tardi P, Troy H, European patent no, 2002; EP1432402.
15. Paterson RS, Omahony B, Eccleston GM, Stevens HNE, Fost er J, Murray JG, An assessment of floating raft formation in a man using magnetic resonance imaging, Journal of Pharm Pharmacol, 2008; 8(1).
16. Mayavanshi AV and Gajjar SS: Floating drug delivery system to increase gastric retention of drugs: A review. Research Journal of Pharmaceutical Technology, 2008; 1(4): 345-48.
17. Rubinstein A, Friend D.R, Specific delivery to the gastrointestinal tract, in: Domb A. J (Ed.), Polymeric Site Specific Pharmacotherapy, Wiley, Chichester, 1994; 282-283.

18. Desai S. A Novel Floating Controlled Release Drug Delivery System Based on a Dried Gel Matrix Network [master's thesis]. NY, St John's University, 1984.
19. KRW, Waugh A. Anatomy and Physiology in Health and Illness. London: Churchill Livingstone, 1996; 9.
20. Davis, S. S; Stockwell, A. F; Taylor, M. J. Hardy, J. G; Whalley, D. R; Wilson, C. G; Bechrgaard, H; Cristen, F. N; The effect of density on the gastric emptying of single and multiple-unit dosage forms. Pharm. Res, 1986; 3: 208.
21. Waldwell, L. J; Gardner. C. R; Cargil, R. C; US Patent, 1988; 4: 735-804.
22. Timmermans J, Moes AJ. Factors controlling the buoyancy and gastric retentioncapabilities of floating matrix capsules: New data for reconsidering the controversy. J. Pharm. Sci, 1994; 83: 18-24.
23. Clarke GM, Newton JM, Short MD. Comparative gastrointestinal transit of pellet systems of varying density. Int. J.Pharm, 1995; 114: 1-11.
24. Timmermans J, Moes AJ. The cut off size for gastric emptying of dosage forms. J.Pharm. Sci, 1993; 82: 854.
25. Marvola M, Kannikoski A, Aito H. The effect of food on gastrointestinal transit and drug absorption of a multiparticular sustained-release Verapamil formulation. Int. J. Pharm, 1989; 53: 145-55.
26. Mojaverian P, Vlasses PH, Kellner PE, Rocci Jr. ML. Effects of gender, posture and age on gastric residence time of an indigestible solid: Pharmaceutical Considerations. Pharma. Res, 1980; 10: 639-44.
27. Bhavana V, Khopade AJ, Jain WD, Shelly and Jain NK. Targeted oral drug delivery. Indian Drugs, 1996; 33: 365-73.
28. Deshpande AA, Shah NH, Rhodes CT, Malick W. Development of a novel controlled release system for gastric retention. Pharm. Res, 1997; 14(6): 815-819.
29. Castellanos RM, Zia H, Rhodes TC. Design and testing in-vitro of a bioadhesive and floating drug delivery system for oral application. Int J Pharm, 1994; 105: 650.
30. Edith Madithowitz. Encyclopedia of Controlled Drug Delivery. New York: Jhon Wiley and Sons, 1999; 1.
31. David SS. The effect of density on the gastric emptying on single and multiple unit dosage forms. Pharm Res, 1986; 3: 208-13.
32. Paterson RS, Omahony B, Eccleston GM, Stevens HNE, Fost er J, Murray JG, An assessment of floating raft formation in a man using magnetic resonance imaging, Journal of Pharm Pharmacol, 2008; 8(1).