IJPSM

Chanchal Choudhary *et al*, International Journal of Pharmaceutical Sciences & Medicine (IJPSM), Vol.8 Issue. 4, April 2023, pg. 18-30

ISSN: 2519-9889
Impact Factor: 5.9

A REVIEW ON FLOATING TABLET

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DOI: 10.47760/ijpsm.2023.v08i04.002

ABSTRACT: Pharmaceutical industries have received much interest in pharmaceutical research in the area of oral drug delivery more over on Gastro retentive drug delivery system that is Floating Drug Delivery System (FDDS).The objective of this study to review on FDDS focusing on its current advancement and its future. Floating systems are low density systems that have sufficiently buoyancy to flow over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. Floating dosage forms can be prepared as tablets, capsule by adding suitable ingredients with excipients like hydrocolloids, inert fatty materials and buoyancy increasing agents. Various categories of drugs like antacids, antidiabetic, antifungal and anticancer drugs are formulated into FDDS. FDDS have bulk density less than gastric fluids that have sufficient buoyancy to float over the gastric contents and remain in the stomach for longer duration of time. This review article is in pursuit of giving detailed information on the pharmaceutical basis of their design, classification, advantages and disadvantages, factors affecting gastric residence time of FDDS, applications, and formulation of floating tablet.

1. Introduction: Floating systems or dynamically controlled systems are low density systems that have sufficiently buoyancy to flow over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. This result is an increased gastric retention time and a better control of the fluctuations in plasma drug

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Impact Factor: 5.9

concentration. Oral controlled release dosage forms have been developed over the past three decades due to their considerable therapeutic advantages such as:

1. Easily administrations.
2. Low cost of therapy.
3. Patient compliance and flexibility in formulation

The ultimate goal of any drug delivery is Effective disease disorder management, minimum side effects and greater patient compliance in the cost effective manner. More than 50% of the drug delivery systems available in the market are oral drug delivery systems. Controlled release drug delivery Systems (CRDDS) provide drug release at a predetermined, predictable and controlled rate. Controlled release drug delivery system is capable of achieving the benefits like maintenance of optimum Therapeutic drug concentration in blood with predictable and reproducible release rates for extended time period, enhancement of activity of duration for short half life drugs, elimination of side effects, reducing frequency of dosing and wastage of drugs, optimized therapy and better patient compliances. The controlled gastric retention of solid dosage forms may be achieved by mucoadhesive systems that causes bioadhesion to stomach mucosa, floating systems, swelling and expanding systems, modified-shape systems, high density systems and other delayed gastric emptying devices. Gastro retentive dosage form can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility of drugs that are less soluble in a high pH environment. Gastro retention helps to provide better availability of new products with suitable therapeutic activity and substantial benefits for patients[1].

1.1 Advantages of Floating Drug Delivery System[2]:

1. The floating drug delivery systems are advantageous for drugs absorbed through the stomach or proximal part of the small intestine. E.g. Ferrous salts, furosemide.

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2. The efficacy of the medicaments administered utilizing the sustained release principle of floating formulation has been found to be independent of the site of particular medicaments.

3. The floating drug delivery systems are advantageous for drugs meant for local action in the stomach. E.g. antacids

4. Acidic substances like aspirin cause irritation on the stomach wall when come in contact with it. Hence HBS formulation may be useful for the administration of aspirin and other similar drugs

2 Floating system: Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach[3]

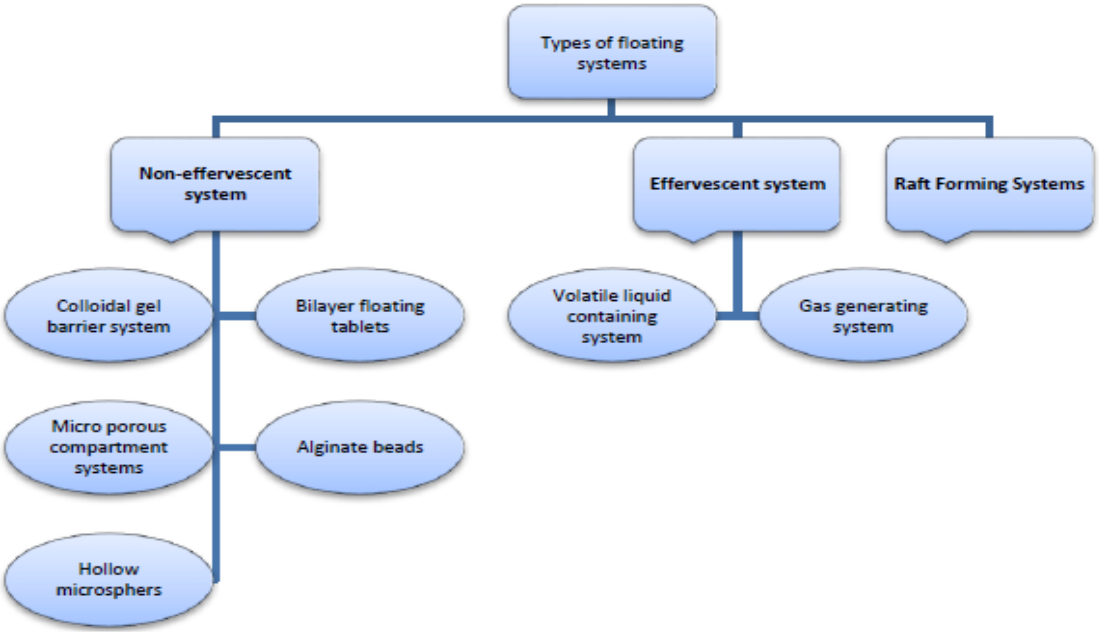

Figure 1 Classification of Floating System

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Non-effervescent system: The non effervescent FDDS based on mechanism of swelling of polymer or bioadhesion to mucosal layer in GI tract. The most commonly used excipients in non effervescent FDDS are gel forming or highly swellable cellulose type hydrocolloids, polysaccharides and matrix forming material such as polycarbonate, polyacrylate, polymethacrylate, polystyrene as well as bio-adhesive polymer such as chitosan and carbopol.[4]

Colloidal Gel Barrier System : Hydrodynamically balanced system first designed by Sheth and Tossounian. They remain buoyant in the stomach due to gel-forming hydrocolloids and this enhances GRT and increases the amount of drug at the absorption site. Various gel forming agents used in this system are highly soluble cellulose type hydrocolloids which are hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, polysaccharides and matrix forming polymers such as polycarbophil, polystyrene.

Bilayer floating tablet : A bilayer tablet contain two layer immediate release layer which release initial dose from system while the another sustained release layer absorbs gastric fluid, forming an impermeable colloidal gel barrier on its surface, and maintain a bulk density of less than unity and thereby it remains buoyant in the stomach

Micro porous Compartment System: In this inside the micro porous compartment which has pores in the top and bottom walls contains encapsulated drug reservoir. In drug reservoir peripheral walls are completely sealed due to this sealing direct contact of undissolved drug with gastric surface is prevented. Entrapped air in the floating chamber stimulates the system to float over gastric content. Through an aperture the gastric fluid enters which dissolves the drug for absorption across intestine.

Effervescent system: Effervescent systems include use of gas generating agents, carbonates (e.g. Sodium bicarbonate) and other organic acid (e.g. citric acid and tartaric acid) present in the formulation to produce carbon dioxide (CO2) gas, thus reducing the density of system and making it float on the gastric fluid. An alternative is the incorporation of matrix containing

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portion of liquid, which produce gas that evaporate at body temperature These effervescent systems further classified into two types[5,6]

Volatile liquid containing systems: Inflatable chamber with a liquid can be incorporated which provide sustained gastric retention of drug delivery system. Liquids in this system include cyclopentane, ether that gasifies at body temperature which causes inflatation of the chamber in the stomach. They contain hollow deformable unit which are osmotically controlled floating systems. System is divided into two compartments first compartment contains drug and there is volatile liquid in the second compartment

Gas generating systems : It basically contains polymers that gasify at body temperature effervescent compounds such as sodium bicarbonate, citric acid, tartaric acid, swellable polymers like methocel, and polysaccharides like chitosan. Resin beads loaded with bicarbonate and coated with ethylcellulose is the most common approach for preparation of these systems. The ethycellulose coating is insoluble but permeable to water which release carbon dioxide due to which it float.

Raft forming systems: Raft forming systems have received much attention for the delivery of antacids and drug delivery for gastrointestinal infections and disorders. The basic mechanism involved in the raft formation includes the formation of viscous cohesive gel in contact with gastric fluids, wherein each portion of the liquid swells forming a continuous layer called a raft. The raft floats. because of the buoyancy created by the formation of CO2 and act as a barrier to prevent the reflux of gastric Contents like HCl and enzymes into the esophagus. Usually, the system contains a gel forming agent and alkaline bicarbonates or carbonates responsible for the formation of to make the system less dense and float on the gastric fluid

3. Application of floating drug delivery system [7.8]:

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

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different processes, related to absorption and transit of the drug in the gastrointestinal tract, that act concomitantly to influence the magnitude of drug absorption

Sustained Drug Delivery: Oral CR formulations are encountered with problems such as gastric residence time in the GIT. These problems can be overcome with the HBS systems which can remain in the stomach for long periods and have a bulk density <1 as a result of which they can float on the gastric contents. These systems are relatively larger in size and passing from the pyloric opening is prohibited

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. E.g. Furosemide is primarily absorbed from the stomach followed by the duodenum. It has been reported that a monolithic floating dosage form with prolonged gastric residence time was developed and the bioavailability was increased. AUC obtained with the floating tablets was approximately 1.8 times those of conventional furosemide tablets

Absorption or Bioavailability Enhancement: Drugs that have poor Bioavailability because of site-specific absorption from the upper part of the gastrointestinal tract are potential candidates to be formulated as floating drug delivery systems, thereby maximizing their absorption. A significant 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. 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 compared to the immediate release dosage forms. Thus, fluctuations in drug effects are minimized and concentration dependent adverse effects that are associated with peak

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concentrations can be prevented. This feature is of special importance for drugs with a narrow therapeutic index Formulation of floating tablets

- Polymers
- Sustained release polymer
- Effervescent generating system
- Hydrocolloids
- Inert fatty materials
- Release rate accelerants
- Release rate retardant
- Buoyancy increasing agents
- Low density material
- Miscellaneous

Polymers: The following polymers used in preparations of floating drugs - HPMC K4, HPMC K4 M, HPMC K15, Calcium alginate, Eudragit S100, Eudragit RL, Methocel K4M, Polyethylene oxide, a Cyclodextrin, HPMC 4000, HPMC 100, CMC, Polyethylene glycol, polycarbonate, PVA, Polycarbo-nate, Sodium alginate, HPC-L, CP 934P, HPC, Eudragit S, HPMC, Metolose S.M. 100, Propylene foam, Eudragit RS, ethyl cellulose, poly methyl methacrylate, PVP, HPC-H, HPC-M, Polyox, Acrylic polymer, E4 M and Carbopol [9].

Sustained release polymer: These are the polymers which are used for sustained release action. E.g. HPMC K100M, HPMC K15M, HPMC ELV, Polycarbonate, Polyethylene glycol, Sodium alginate, Carbopol, Eudragit

Effervescent generating system: E.g. Citric acid, Tartaric Acid, Sodium Bicarbonate, Citroglycine etc

Hydrocolloids: Suitable hydrocolloids are synthethics, anionic or non ionic like hydrophilic gumes, modified cellulose derivatives. E.g. Accasia, pectin, agar, alginates, gelatin, casein,

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bentonite, veegum, MC, HPC, HEC, and Na CMC can be used. The hydrocolloids must hydrate in acidic medium i.e. gastric fluid is having pH 1.2.Although the bulk density of the formulation may initially be more than one, but when gastric fluid is enter in the system, it should be hydrodynamically balanced to have a bulk density of less than one to assure buoyancy[10]

Inert fatty materials: Edible, pharmaceutical inert fatty material, having a specific gravity less than one can be added to the formulation to decrease the hydrophilic property of formulation and hence increases the buoyancy. Example: Purified grades of beeswax, fatty acids, long chain alcohols, glycerides, and mineral oils can be used

Release rate accelerants: The release rate of the medicament from the formulation can be modified by including excipient like lactose and/or mannitol. These may be present from about 5-60% by weight

Release rate retardant: Insoluble substances such as dicalcium phosphate, talc, magnesium stearate decreased the solubility and hence retard the release of medicaments

Buoyancy increasing agents: Materials like ethyl cellulose, which has bulk density less than one, can be used for enhancing the buoyancy of the formulation. It may be adapted up to 80 % by weight

Low density material: Polypropylene foam powder

Miscellaneous: Pharmaceutically acceptable adjuvant like preservatives, stabilizers, and lubricants can be incorporates in the dosage forms as per the requirements. They do not adversely affect the hydrodynamic balance of the systems.

5. Methods of preparation

Methodology for single layer floating tablets: Basically single layer floating tablets are prepared by compression methods. For this normally three basic compression methods are used. They are as follows:-

- Direct compression,
- Dry granulation,

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- Wet granulation.

Direct compression method: Direct compression is the process of compressing tablets directly from powdered materials without modifying physical nature of materials into the tablets. This method is used for crystalline chemicals having good compressible characteristic and flow properties such as: Potassium salt (chloride, chlorate, bromide), Ammonium chloride, Sodium chloride, Methenamine etc. Compressed tablets are prepared by single compression using tablet machines. After a quantity of powdered or granulated tabletting material flow into a die, the upper and lower punches of the tablet machine compress the material under a high pressure (~tons/in2)[11,12]

Dry granulation method: It is defined as the formation of granules by slugging, if the tablet ingredients are sensitive to moisture and/or unable to withstand elevated temperature during drying[13]

Wet granulation method: In wet granulation the active ingredient, diluents and disintegrants are mixed or blended well in a rapid mixer granulator (RMG). The RMG is a multi-purpose chopper which consists of an impeller and a chopper and is used for high speed dispersion of dry powders and aqueous or solvent granulations. Moist materials from wet milling steps are placed on large trays and placed in drying chambers with a circulating air current and thermo stable heat controller. Commonly used dryers are tray dryer, fluidized bed dryer. After drying, the granules are reduced in particle size by passing through smaller mesh screen. After this, the lubricant or glidant is added as fine powder to promote flow of granules. These granules are then compressed to get a tablet. Dry granulation when compared with wet granulation has a shorter, more cost-effective manufacturing process. Because it does not entail heat or moisture, dry granulation is especially suitable for active ingredients that are sensitive to solvents, or labile to moisture and elevated temperatures[14]

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6. METHOD OF EVALUATION

Bulk density: It is a ratio of mass of powder to bulk volume. The bulk density depends on particle size distribution, shape and cohesiveness of particles. Accurately weighed quantity of powder was carefully poured in to graduated measuring cylinder through large funnel and volume was measured, which is called initial bulk volume. It is expressed in gm/ml and is given by the formula:[15]

Bulk density=M/Vo

Where,

M = mass of the powder

Vo = bulk volume of the powder.

Tapped density: 10 gm of powder was introduced into a clean, dry 100 ml measuring cylinder. The cylinder was then tapped 100 times from a constant height and the tapped volume was read. It is expressed in gm/ml and is given by: [16]

Tapped density=M/Vt

Where, M = mass of the powder

Vt = final tapping volume of the powder.

Angle of repose (θ) : is defined as the maximum angle possible between the surface of the pile of the powder and the horizontal plane. Fixed funnel method was used. A funnel was fixed with its tip at a given height 'h, above a flat horizontal surface to which a graph paper was placed. Powder was carefully poured through a funnel till the apex of the conical pile just touches the tip of the funnel. The angle of repose was then calculated using following equation:[17]

Angle of repose Ø = tan1(h/r)

Hausner's ratio : Hausner's ratio is used to predict the flowability of the powders. This method is similar to compressibility index. Hausner's ratio can be represented by equation:

Hausner's ratio = Tapped density / bulk density

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Weight Variation test (U.S.P.): Take 20 tablet and weighed individually. Calculate average weight and compare the individual tablet weight to the average. The tablet pass the U.S.P. test if no more that 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit[18]

Hardness : Tablet hardness and strength are the essential to see that the tablet can with the shock and stress during manufacturing packing and transportation, and while handled by the patient To test the hardness of the tablet Monsanto tester, Strong-cobb tester, the Pfizer tester, the Erweka tester, the Schleuniger tester are used.[19]

Dimensionl Analysis : The thickness and diameter of tablets was determined using vernier caliper. Twenty tablets from each batch were used and average values were calculated.

Size and Shape It can be dimensionally described & controlled. The thickness of a tablet is only variables. Tablet thickness can be measured by micrometer or by other device. Tablet thickness should be controlled within a ± 5% variation of standard value[20]

Floating lag time and total floating time : Floating lag time (FLT) and total floating time (TFT) of floating tablets were measured visually in dissolution apparatus type II containing100 mL 0.1 N HCl with a paddle rotated at50 rpm (pH 1.2) at 37 ± 0.5 °C.[21]

Dissolution Study : In vitro drug release of the formulation was carried out using USP dissolution apparatus type II paddle type under sink condition with rotating speed of 50 rpm and at temperature of37 ± 0.5 °C. The dissolution medium used was 900ml 0.1NHCl. The samples were withdrawn at predetermined time intervals for period of 6hours and replaced with the fresh medium, suitably diluted and were analyzed using UV/Visible spectrophotometer.[22]

Disintegration Test (U.S.P.) The U.S.P. device to test disintegration uses 6 glass tubes that are 3" long; open at the top and 10 mesh screens at the bottom end. To test for disintegration time, one tablet is placed in each tube and the basket rack is positioned in a 1-L beaker of water, simulated gastric fluid or simulated intestinal fluid at 37 ± 2 0 C such that the tablet remain 2.5 cm below the surface of liquid on their upward movement and not closer than 2.5 cm from the

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bottom of the beaker in their downward movement Move the basket containing the tablets up and down through a distance of 5-6 cm at a frequency of 28 to 32 cycles per minute. Floating of the tablets can be prevented by placing perforated plastic discs on each tablet. According to the test the tablet must disintegrate and all particles must pass through the 10 mesh screen in the time specified. If any residue remains, it must have a soft mass. Disintegration time: Uncoated tablet: 5-30 minutes coated tablet: 1-2 hours.[23]

7. Conclusion: Floating tablets have emerged as the power full means of improving the bioavailability and providing sustained release and avoiding the adverse effects of many drugs. Floating tablets have proved to be potential approach for gastric retention. These systems have special advantage for the drug that are primarily absorbed from the upper part of GIT. So with an improved knowledge of formulation development aspect, physiochemical and pharmacological prospects of drug there is lot of future scope for designing of optimum floating drug delivery system.

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