



FLOATING TABLET: GASTRORETENTIVE DRUG DELIVERY SYSTEM

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Article Received on 14/02/2022

Article Revised on 07/03/2022

Article Accepted on 28/03/2022

ABSTRACT

Floating tablets lengthen the gastric house time of drugs, enhance bioavailability, and facilitate neighborhood drug delivery to the stomach. Oral route has been the most handy and typical route of drug delivery. Owing to notable healing advantages of the oral managed launch dosage varieties are being desired as the interesting subject matter in pharmaceutical discipline to carried out increased therapeutics advantages. Gastroretentive drug transport gadget is novel drug shipping structures which has an higher hand owing to its potential of prolonged holding potential in the belly and thereby enlarge gastric residence time of capsules and additionally improves bioavailability of drugs. Attempt has been made to summarize essential elements controlling gastroretentive drug shipping systems. This evaluation covers the advantages, disadvantages, marketed coaching and some patents of gastroretentive drug shipping machine and represents the floating and non-floating gastroretentive device and additionally highlights some of the current gastroretentive approaches. Recent processes to enlarge the gastric house time of drug shipping structures consist of bioadhesive systems, floating structures (low density systems), non-floating structures (high density systems), magnetic systems, swelling systems, unfoldable and expandable systems, raft forming structures and superporous systems, biodegradable hydrogel systems.

KEYWORDS: Uoyancy time, floating tablets, FDSS.

INTRODUCTION

The center of attention of pharmaceutical lookup is step by step shifted from the improvement of new chemical entities to the improvement of novel drug delivery machine of current drug molecule to maximize their effectiveness in phrases of therapeutic action, lowering frequency of dosing and wastage of drugs, affected person compliance and decreased destructive effects.^[1] To minimize drug degradation and loss, to stop harmful side-effects and to expand drug bioavailability and the fraction of the drug accumulated in the required zone, a number of drug delivery and drug focused on structures are currently beneath development. Oral drug delivery is the most suited and favored method of drug shipping for reaching each systemic and neighborhood therapeutic effects. For many drugs, traditional oral formulations grant clinically fantastic remedy whilst retaining the required stability of pharmacokinetic and pharmacodynamic profiles with an applicable level of protection to the patient. The actual project in the improvement of a managed drug delivery device is no longer simply to preserve the drug release however additionally to lengthen the presence of the dosage structure in the belly or the top small intestine till all the drug is definitely released in the preferred duration of

time. The gastro intestinal tract (GIT) is the principal route of drug shipping to the systemic circulation.^[2,3] Oral controlled launch dosage varieties are now not appropriate for a range of essential drugs, characterized with the aid of a slim absorption window in the higher phase of the GIT. This is due to the relatively much less transit time of the dosage shape in these anatomical segments. Thus after only a short length of much less than 6 h, the managed release method has already left the top GIT and the drug is launched in short, non absorbing distal section of the GIT. This consequences in a short absorption phase, which is then accompanied by way of lesser bioavailability. These types of trouble can be overcome by means of floating drug shipping system.^[4-5]

Criteria Selection of Drug Candidate For Floating Drug Delivery System

- Readily absorption by using higher gastrointestinal tract.
- Drugs with low pKa, that does show off unionized characters.
- Drugs are possessing decrease solubility at greater pH.

- Effect of nearby motion of capsules e. g. treating *Helicobacter pylori* in treatment of ulcerative conditions.^[6-7]
- Drugs which get degraded in alkaline pH conditions; bioavailability of these can be more suitable with the aid of fabricating into gastro-retentive forms.
- Minimizing gastric infection as it may also end result in the amplify of drug attention stage in the stomach.^[8,9]

DEFINITION

Floating drug transport structures (FDDS) are systems that have a lower bulk density than gastric fluids and, as a result, remain buoyant in the stomach for longer periods of time (34 hours), altering the gastric emptying rate. The medicine is gently released from the device at the preferred price, and the residual machine is then evacuated from the stomach. As a result, GRT improves, and fluctuations in plasma drug concentration can be better managed.^[10]

Need of Floating Tablets :

Certain medications that have been absorbed through the gastrointestinal tract (and usually have short half-lives) are quickly removed from the circulatory system, necessitating daily dosing. To resolve this issue, novel gastroretentive drug delivery architectures have been devised. They have good plasma drug attention, therefore dosing frequency is reduced. Another feature of this technology is that it effectively eliminates variability in plasma drug awareness by delivering the drug in a controlled and repeatable manner.^[11]

CLASSIFICATION

A. Floating drug shipping structures

Floating drug transport structures (FDDS) have a bulk density much less than gastric fluids and so remain buoyant in the belly barring affecting gastric emptying price for an extended period of time. While the gadget is floating on the gastric contents, the drug is launched slowly at the preferred charge from the system. After launch of drug, the residual gadget is emptied from the stomach. This consequences in an increased GRT and a higher manipulate of the fluctuations in plasma drug concentration. FDDS can be divided into non-effervescent and gas generating machine.

(a) Non-effervescent structures

This kind of system, after swallowing, swells unrestrained through inhibition of gastric fluid to an extent that it prevents their exit from the stomach. One of the method strategies of such dosage varieties includes the mixing of the drug with a gel, which swells in contact with gastric fluid after oral administration and maintains a relative integrity of shape and a bulk density of much less than one inside the outer gelatinous barrier¹⁸. The air trapped via the swollen polymer confers buoyancy to these dosage forms. Excipients used most commonly in these structures encompass hydroxypropyl methyl cellulose (HPMC), polyacrylate polymers, polyvinyl

acetate, Carbopol, agar, sodium alginate, calcium chloride, polyethylene oxide and polycarbonates. This machine can be similarly divided into 4 sub-types:

(i) Colloidal gel barrier machine

Sheth and Tossounian first particular this 'hydrodynamically balanced system'¹⁹. Such a system carries drug with gel-forming hydrocolloids intended to continue to be buoyant on the stomach content. This prolongs GRT and maximizes the quantity of drug that reaches its absorption web sites in the answer structure for geared up absorption. This device contains an excessive level of one or greater gel-forming tremendously soluble cellulose kind hydrocolloid, e.g., hydroxypropyl cellulose, hydroxyethyl cellulose, hydroxypropyl methyl cellulose (HPMC), polysaccharides and matrix-forming polymer such as polycarbophil, polyacrylate and polystyrene. On coming in contact with gastric fluid, the hydrocolloid in the machine hydrates and varieties a colloid gel barrier around its surface.

(ii) Microporous compartment gadget

This technological know-how is primarily based on the encapsulation of a drug reservoir inner a microporous compartment with pores alongside its pinnacle and bottom walls. The peripheral partitions of the drug reservoir compartment are absolutely sealed to stop any direct contact of gastric surface with the undissolved drug. In the stomach, the floatation chamber containing entrapped air motives the transport device to float over the gastric content. Gastric fluid enters the aperture, dissolves the drug and incorporates the dissolved drug for continuous transport throughout the gut for absorption.

(iii) Alginate beads

Multi-unit floating dosage varieties have been developed from freeze-dried calcium alginate. Spherical beads of about 2.5 mm in diameter can be organized by using dropping sodium alginate answer into aqueous answer of calcium chloride, inflicting the precipitation of calcium alginate. The beads are then separated, snap-frozen in liquid nitrogen, and freeze-dried at -40°C for 24 hours, main to the formation of a porous system, which can hold a floating pressure for over 12 hours. These floating beads gave a prolonged dwelling time of extra than 5.5 hours.

(iv) Hollow microspheres

Hollow microspheres loaded with drug in their outer polymer shelf have been organized with the aid of a novel emulsion solvent diffusion method. The ethanol/dichloromethane answer of the drug and an enteric acrylic polymer was once poured into an agitated answer of Poly Vinyl Alcohol (PVA) that was once thermally managed at 40°C. The gasoline segment is generated in the dispersed polymer droplet by using the evaporation of dichloromethane shaped and inner cavity in the microsphere of the polymer with drug. The microballoon floated constantly over the surface of an

acidic dissolution media containing surfactant for extra than 12 h.

(b) Gas-generating (Effervescent) structures

Matrixes made with swellable polymers such as methocel, polysaccharides (e.g., chitosan), and effervescent components are used to create these buoyant structures (e.g., sodium bicarbonate, citric acid or tartaric acid). The system is so well designed that when it reaches the stomach, carbon dioxide is released, causing the components to flow. Other approaches and substances that have been reported include a combination of sodium alginate and sodium bicarbonate, multiple unit floating pills that produce carbon dioxide when swallowed, floating minicapsules with a core of sodium bicarbonate, lactose, and polyvinylpyrrolidone lined with hydroxypropyl methylcellulose (HPMC), and floating structures entirely based on ion alternate resin technology, among others. The use of gas bubble technology aids in achieving floatability. Several effervescent chemicals and swellable polymers, such as methylcellulose and chitosan. They are created in a manner that upon contact with gastric contents CO₂ is launched sooner or later entrapping in swollen hydrocolloids, that makes dosage varieties buoyant.

These structures are in addition categorized as below:

1. Volatile Liquid Containing System

This system involves of twin chambers having an impermeable, stress responsive, movable bladder separation. The former chamber has tablets and the latter has volatile liquid. To preserve the GRT of a drug transport gadget an inflatable chamber has to be incorporated, that includes a liquid e.g. ether, cyclopentane. It turns to gaseous form at physique temperature inflicting inflation of the chamber in the stomach. It may include a biodegradable plug, made of polyvinyl alcohol, polyethylene, etc. This plug step by step dissolves making the chamber launch gasoline and to fall down after a specific period to permit spontaneous release of the inflatable structures from the stomach. The drug continues to launch as the gadget inflates.

These structures are similarly categorised as below:

- Intragastric floating gastrointestinal drug system.
- Inflatable gastrointestinal transport system
- Intragastric-osmotically managed drug delivery system^[12]

2. Matrix Tablets

It can be formulised in a single layer matrix desk with the aid of enforcing bicarbonates in the matrix forming hydrocolloid gel agent or in a twin layer matrix alongside with gasoline producing matrix together as an character layer. The drug acts as the 2nd layer. There is a possibility of triple layer matrix tablet. However now the fuel producing matrix is one layer and relaxation two are drug layers.^[13]

3. Gas Generating Systems

- Floating capsules
- Floating pills
- Floating machine with ion trade resins

B. Expandable structures

Expandable gastroretentive dosage varieties (GRDFs) have been designed over the previous three decades. They have been at first created for possible veterinary use however later the plan was modified for more desirable drug remedy in humans. These GRDFs are without difficulty swallowed and attain a considerably large measurement in the stomach due to swelling or unfolding processes that lengthen their GRT. After drug release, their dimensions are minimized with subsequent evacuation from the stomach. Gastroretentivity is more suitable by way of the combination of extensive dimensions with high pressure of the dosage shape to face up to the peristalsis and mechanical contractility of the stomach. Positive outcomes have been received in preclinical and medical research evaluating the GRT of expandable GRDFs. Narrow absorption window tablets compounded in such systems have elevated in vivo absorption properties.

C. Bio/Muco-adhesive structures

Bioadhesive drug transport structures (BDDS) are used as a shipping system inside the lumen to beautify drug absorption in a site specific manner. This method includes the use of bioadhesive polymers, which can adhere to the epithelial floor in the stomach. Gastric mucoadhesion does now not tend to be sturdy ample to impart to dosage varieties the capability to face up to the sturdy propulsion forces of the belly wall. The continuous manufacturing of mucous by way of the gastric mucosa to substitute the mucous that is misplaced thru peristaltic contractions and the dilution of the belly content material additionally seem to restrict the manageable of mucoadhesion as a gastroretentive force. Some of the most promising excipients that have been used oftentimes in these structures encompass polycarbophil, carbopol, lectins, chitosan and gliadin, etc.

D. High-density structures

Pellets that are small enough to be kept in the rugae or folds of the belly tissue near to the pyloric area, which is the phase of the organ with the lowest involvement in an upright posture, have been subjected to sedimentation as a retention mechanism. Dense pellets caught in rugae (about 3g/cm³) also have a tendency to face up to the peristaltic movements of the belly wall. The GI transit time with pellets can be extended from an average of 5.825 hours, depending more on density than pellet diameter. Excipients such as barium sulphate, zinc oxide, titanium dioxide, and iron powder are commonly employed.

These substances enlarge density by means of upto 1.5–2.4g/cm⁻³.^[14-23]

MECHANISM OF FLOATING SYSTEM

While the gadget is floating on the gastric content the drug is launched slowly at the desired price from the system. After launch of drug, the residual gadget is emptied from the stomach. However, barring a minimal gastric content wished to permit the perfect achievement of the buoyancy retention principle, a minimal degree of floating pressure is additionally required to maintain the dosage structure reliably buoyant on the floor of the meal. To measure the floating pressure kinetics, a novel equipment for determination of resultant weight has been reported in the literature. The equipment operates through measuring consistently the pressure equivalent to F as a characteristic of time that is required to keep the submerged objects. The equipment helps in optimizing FDDS with respect to balance to steadiness and sturdiness of floating forces produced in order to stop the drawbacks of unforeseeable intragastric buoyancy functionality variations.^[24]

$$F = F_{\text{buoyancy}} - F_{\text{gravity}} \\ = (D_f - D_s) g v$$

Where, F = Total vertical force, D_f = fluid

Density, D_s = object density, v = volume

Major Advantages of FDDS

1. Increase in bioavailability and healing efficiency of pills and financial utilization of dosage.^[25]
2. FDDS can stay in the belly for a number of hours and therefore lengthen the gastric retention time of a range of drugs.^[26]
3. FDDS are high-quality for capsules intended for neighborhood action in the belly eg: Antacids.
4. FDDS dosage types are positive in case of vigorous intestinal motion and in diarrhea to maintain the drug in floating situation in belly to get a exceedingly better response.
5. FDDS improves affected person compliance via reducing dosing frequency.^[27]
6. Bioavailability enhances notwithstanding first pass by impact because fluctuations in plasma drug awareness are avoided; a applicable plasma drug awareness is maintained via non-stop drug release.^[28]
7. Acidic substance like aspirin motives inflammation on the stomach wall when come in contact with it hence; HBS/FDDS formulations may also be useful for the administration of aspirin and different comparable drugs.
8. The FDDS are high quality for pills absorbed through the belly eg: Ferrous salts, Antacids. Improved drug absorption, due to the fact of extended GRT and extra time spent with the aid of the dosage shape at its absorption site.
9. Site-specific drug delivery.^[29]

Disadvantages

1. Need for expanded stage of fluids in the stomach.
2. Unsuitable for such tablets as:
 - Problematic with solubility in gastric fluid
 - Causing G.I irritation

- Inefficient in acidic environment
3. Drugs supposed for selective launch in the colon.
 4. Unpredictable adherence owing to country of constant renewal of mucus wall of stomach.
 5. GRDDS is fed into the device after the meal as time of continue to be in belly relies upon on digestive state.
 6. The capability of the drug to stay in the stomach relies upon upon the concern being positioned upright.
 7. Hydrogel based totally swelling gadget takes longer time to swell.
 8. Upon more than one administrations, dimension increasing drug shipping structures pose the threat to existence owing to feasible hazard of permanent retention in stomach.
 9. Superporous structures having downside like problematical storage of a good deal without difficulty hydrolysable, biodegradable polymers.^[30-32]

Factors Controlling FDDS

1. **Density:** Dosage structure with decrease density in the gastric content material can flow to the floor while excessive density sink to the backside of the stomach. Suitable density required for floating property is much less than 1.0 gm/ cm³
2. **Size:** Size need to be greater than 7.5 mm in diameter.
3. **Shape:** Either spherical or spherical fashioned dosage shape show off higher property associated to different shapes.
4. **Single or a couple of unit formulation:** Multiple gadgets are appropriate due to foretell release profile.
5. **Fed or Unfed State:** Gastric retention time is much less all through fasting circumstance due to upward push in gastric motility.
6. **Nature of Meal:** High quantity of fatty acid and different indigestible polymers gradual down the gastric retention time due to version in gastric motility.
7. **Frequency of Feed:** Low frequency of migrating myoelectric complicated (MMC) contributes to GRT upto four hundred instances which inturn relies upon on the frequency of meals intake.
8. **Caloric Content:** A excessive protein and fats rich weight-reduction plan can expand GRT by using four to 10h.
10. **Gender:** Males have higher GRT than females.
11. **Age:** GRT is greater in geriatric sufferers and less in neonates and children. Age above 70 (>70) showcase longer GRT.
12. **Posture:** GRT can differ between supine and upright ambulatory states of the patient.
13. **Disease State:** Gastric disorder such as diabetes, chrone disease, hypothyroidism, hyperthyroidism, duodenal ulcers and so forth fluctuates the GRT.
14. **Concomitant Intake of Drug:** Combination of some capsules alongside with gastric motility enhancers or depressants, affect GRT.^[33-35]

Preparation Methods of Floating Tablets

- 1. Direct Compression Technique:** Involves compressing drugs without delay from powdered cloth except editing the physical nature of the fabric itself. Direct compression cars or carriers need to have good glide and compressible characters these properties are imparted by using predisposing these vehicles to slugging, spray drying or crystallization. Most frequently used carriers are di calcium phosphate trihydrate, tri calcium phosphate and so on.
- 2. Melt Granulation Technique:** It is a method via which the pharmaceutical powders are agglomerated through the use of a soften capable binder and no water or natural solvents are required for granulation. Because there is no drying step, the system is much less time ingesting and makes use of less energy. Granules have been organized in a lab scale excessive shear mixer, the use of a jacket temperature of 60 °c and an impeller pace of 20000 rpm.
- 3. Melt Solidification Technique:** This technique includes emulsification of the molten mass in the aqueous section observed by using its solidification via chilling. The carriers used for this method are lipids, waxes, polyethylene glycols. Drug is included into These carriers to gain managed release.
- 4. Wet Granulation Technique:** Wet granulation technique entails the moist massing of powders, moist sizing or milling and drying. Wet granulation types the granules through binding the powders collectively with an adhesive instead of compaction. The moist granulation approach employs a answer suspension or slurry containing a binder which is normally added to the powder combination alternatively the binder may additionally be integrated into the dry powder combine and the liquid can also be introduced by means of itself. The approach of introducing the binder depends on its solubility and on the components of the combination since, in general, The mass have to only be moist instead than wet or pasty, and there is a restrict to the quantity of solvent that may additionally be employed. Once the granulating liquid has been delivered mixing continues till a uniform dispersion is attained and all the binder has been activated. Then the wet mass is made to endure moist screening by using passing thru a hammer mill or multi mill equipped with displays having massive perforations. The milled moist mass is dried via either the usage of tray drier or fluidized mattress drier, after whole the drying lubrication substances is blended with dried granules. This lubricated granules is made to bear compression.
- 5. Effervescent Technique:** The floating chamber of the drug shipping system can be crammed with inert gasoline [CO₂] through the effervescent response between natural acid [citric acid] and bicarbonate salts.

- 6. Spray Drying Technique:** It entails dispersing the core fabric in a liquefied coating fabric and spraying the core-coating combination in to the surroundings to effect solidification of coating. Solidification is accomplished by using fast evaporation of the solvent in which coating cloth is solubilized^[36]

APPLICATION OF FDDS

1. FDDS are claimed for the extended efficacy of capsules as current.
2. studies exhibit that the administration of diltiazem floating drugs twice a day would be extra fantastic in contrast to regular pills in hypertensive patients.
3. In case of Parkinson patient, FDDS is high quality in absorption of the drug over a length of 6-8 h and maintained good sized plasma concentration.
4. FDDS is site-specific drug delivery: These structures are particularly superb for capsules that are particularly absorbed from the belly or the proximal phase of the small intestine, e. g. Riboflavin and Furosemide.
5. FDDS served as an amazing drug transport machine in the eradication of Helicobacter pylori, blamed for continual gastritis and peptic ulcers.
6. FDDS are best HBS dosage structure to grant higher shipping of drugs and decreased its GI facet results.^[37-39]

EVALUATION STUDY

1. Determination Of Hardness Of Tablet

Randomly sampled twenty drugs in every batch of formulations need to be used for the willpower of hardness with the assist of Monsanto kind hardness tester.^[40]

2. Determination Of Weight Variation

Twenty capsules chosen at the random are weighed accurately and the common weight of the pill is calculated. Then the deviation of character weight from the average weight is calculated.^[41,42]

3. Determination Of Thickness Of Tablet

The person crown to crown thickness of ten capsules is determined the use of slide calipers for every batch.^[43]

4. Measurement Of Floating Capacity

Three character capsules are put in man or woman flask containing 400ml of 0.1(N) HCl solutions. Then the time in minutes for every drugs to go from the backside to the pinnacle of the flask (floating lag time) and the time for which tablets constantly go with the flow on the water floor (duration of floating) are measured. The pattern suggest and preferred deviation are then calculated.^[44]

5. Angle of Repose

Angle of repose is decided by means of the use of funnel method; the accurately weighed spheres are taken in funnel. The height of funnel is adjusted in such a way that the tip of funnel just touches the apex of heap of

blends. The blends are then allowed to waft thru funnel freely on to surface. The diameter of powder cone was once measured; perspective of repose is calculated by using the use of following equation^[45]

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

6. Floating Lag Time

It is the time taken with the aid of the pill to emerge on to the surface of dissolution medium and is expressed in seconds or minutes.^[46]

In Vitro Dissolution Study

The pill used to be positioned inner the dissolution vessel. 5 ml of pattern is withdrawn at time intervals of 1h, 2h, 3h, 4h, 5h, 6h, 8h, 10 h, and 12h or any different time intervals as needed. The quantity of dissolution fluid adjusted to 900 ml via changing sparkling 5 ml of dissolution medium after each

sampling. The launch research had been performed with “n” tablets, and the suggest values are plotted versus time. Each pattern is analyzed at most wavelength the usage of UV seen spectrophotometer in opposition to a reagent clean and the corresponding attention is decided from the respective calibration curve.^[47,48]

Buoyancy/Floating Test

The time between introduction of the dosage structure and its buoyancy on the simulated gastric fluid and the time at some stage in which the dosage form stay buoyant are measured. The time taken for the dosage form to emerge on the floor of a medium referred to as floating lag time (FLT) or buoyancy lag time (BLT) and complete length of time with the aid of which dosage shape continue to be buoyant is known as complete floating time (TFT).^[49,50]

MARKETED PREPARATION

Brand Name	Drug	Dosage Forms	Dose	Indications	Company
Cifran O.D	Ciprofloxacin	Tablet	500mg, 1g	Systematic treatment of infections	Ranbaxy, India
Liquid Gavison	Al hydroxide and Mg carbonate	Liquid	95mg and 358mg respectively	Antacid	Glaxo Smith Kline, India
Madopar	Levodopa and Benserazide	Capsule	100mg and 25mg respectively	Parkinson's disease	Roche Products, USA
Glumetza	Metmorfin Hydrochloride	Tablet	500mg and 1000mg	Type 2 diabetes	Depomed, Canada
Valrelease	Diazepam	Capsule	15mg	Anxiety disorders, alcohol withdrawa symptoms, muscle spams	Hoffmann-LaRoche, USA
Topalkan	Aluminium-Magnesium antacid	Liquid Alignate	–	Antacid	Pierre Fabre Drug, France
Cyotec	Misoprostal	Bilayer Capsule	100mcg/200mcg	Used with non-steroidal anti-inflammatory drug to prevent gastric ulcers	Pharmacia, USA
Conviron	Ferrous Sulphate	Colliodal Gel	–	Antianaemic	Ranbaxy, India
Oflin OD	Ofloxacin	Tablet	400mg	Genito urinary, respiratory, gastro intestinal, skin and soft tissue infections	Ranbaxy, India

ACKNOWLEDGEMENT

Authors are thankful to the management and principal of MGVS Samajshri Prashantdada Hiray, College Of Pharmacy, Malegaon, (Nashik) and Savitribai Phule Pune University, Pune.

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