GASTRO RETENTIVE DRUG DELIVERY SYSTEM: - A REVIEW

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ABSTRACT

The purpose of writing this review on floating drug delivery systems (fdds) was to compile the recent literature with special focus on the principal mechanism of floatation to achieve gastric retention. The recent developments of fdds including the physiological and formulation variables affecting gastric retention, approaches to design single-unit and multiple-unit floating systems and their classification and formulation aspects are covered in detail. This review also summarizes the in vitro techniques, in vivo studies to evaluate the performance and application of floating systems and applications of these systems. These systems are useful to several problems encountered during the development of a pharmaceutical dosage form.

KEYWORDS: Floating drug delivery system, approaches, application, mechanism, manufacturing techniques, characterization, evaluation in vitro and in vivo

INTRODUCTION

Current pharmaceutical scenario focuses on the development of sustained drug delivery systems to achieve required therapeutic concentration with less amount of dose. Oral drug delivery is the most useful form of drug delivery, having the highest degree of patient compliance. The pharmaceutical products are having their own merits and demerits and according to condition of patient and disease they are applied. Oral delivery continues to be the most popular route of administration due to its versatility, administered easily and most probably important patient compliance. Oral controlled release drug delivery has recently been of increasing interest in pharmaceutical field to achieve improved therapeutically benefits, such as easily administered dose, patient compliance and formulation flexibility. Drugs with short half-lives and drugs that easily absorbed from gastrointestinal tract (GIT) are eliminated quickly from the systemic circulation. For these types of drugs the
development of oral sustained-controlled release formulations is an attempt to release the drug slowly into the gastrointestinal tract (GIT) and maintain an effective drug concentration for a long time in the systemic circulation. After oral administration of this type of drug delivery they will retain in the stomach and release the drug in a controlled and systemic manner. Floating drug delivery system is an approach for prolongation gastric residence time, therefore targeting site-specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effects. Floating drug delivery system not only prolongs GI residence time but does so in an area of the GI tract that could maximize drug reaching its absorption site in solution and hence ready for absorption.\cite{1} Gastric emptying of dosage forms is an extremely variable process and ability to prolong and control emptying time is a valuable asset for dosage forms that retain in the stomach for a longer duration than conventional dosage forms. To control this type of physiological problem, different drug delivery systems with co-administration of gastric-emptying delaying drugs. Among these, the floating dosage forms have been most commonly used. Floating drug delivery systems (FDDS) have a bulk density.\cite{1,2,3}

CLASSIFICATION OF DRUG DELIVERY SYSTEM

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) Effervescent Systems (Gas-generating Systems)
These buoyant systems utilized matrices prepared with swellable polymers like HPMC, polysaccharides like chitosan, effervescent components like sodium bicarbonate, citric acid and tartaric acid or chambers containing a liquid that gasifies at body temperature. The optimal stoichiometric ratio of citric acid and sodium bicarbonate for gas generation is reported to be 0.76:1. The common approach for preparing these systems involves resin beads loaded with bicarbonate and coated with ethylcellulose. The coating, which is insoluble but permeable, allows permeation of water. Thus, carbon dioxide is released, causing the
beads to float in the stomach. Excipients used most commonly in these systems include HPMC, polyacrylate polymers, polyvinyl acetate, Carbopol®, agar, sodium alginate, calcium chloride, polyethylene oxide and polycarbonates.\textsuperscript{[4,5,6]}

b) Non-Effervescent Systems

This type of system, after swallowing, swells unrestrained via imbibition of gastric fluid to an extent that it prevents their exit from the stomach. These systems may be referred to as the ‘plug-type systems’ since they have a tendency to remain lodged near the pyloric sphincter. One of the formulation methods of such dosage forms involves the mixing of 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 less than one within the outer gelatinous barrier. The air trapped by the swollen polymer confers buoyancy to these dosage forms. Examples of this type of FDDS include colloidal gelbarrier microporous compartment system, alginate beads, and hollow microspheres. Another type is a Fluid- filled floating chamber which includes incorporation of a gas-filled floatation chamber into a microporous component that houses a drug reservoir.\textsuperscript{[7]} Apertures or openings are present along the top and bottom walls through which the gastrointestinal tract fluid enters to dissolve the drug. The other two walls in contact with the fluid are sealed so that the undissolved drug remains therein. The fluid present could be air, under swallowable size, remains afloat within the stomach for a prolonged time and after the complete release the shell disintegrates, passes off to the intestine, and is eliminated. A newer self-correcting floatable asymmetric configuration drug delivery system has a 3-layermatrix to control the drug release. This 3-layer principle has been improved by development of an asymmetric configuration drug delivery system in order to modulate the release extent and achieve zero-order release kinetics by initially maintaining a constant area at the diffusing front with subsequent dissolution/erosion toward the completion of the release process. The system was designed in such a manner that it floated to prolong gastric residence time in vivo, resulting in longer total transit time within the gastrointestinal tract environment with maximum absorptive capacity and consequently greater bioavailability. This particular characteristic would be applicable to drugs that have pH-dependent solubility, a narrow window of absorption and are absorbed by active transport from either the proximal or distal portion of the small intestine.
B. Multiple Unit Floating$^{[8,9,10]}$

In spite of extensive research and development in the area of HBS and other floating tablets, these systems suffer from an important drawback of high variability of gastrointestinal transit time, when orally administered, because of their all-or-nothing gastric emptying nature. In order to overcome the above problem, multiple unit floating systems were developed, which reduce the inter-subject variability in absorption and lower the probability of dosedumping. Reports have been found on the development of both non-effervescent and effervescent multiple unit systems. Much research has been focused and the scientists are still exploring the field of hollow microspheres, capable of floating on the gastric fluid and having improved gastric retention properties.

a) Non-effervescent Systems$^{[11,12]}$

No much report was found in the literature on noneffervescent multiple unit systems, as compared to the effervescent systems. However, few workers have reported the possibility of developing such system containing indomethacin, using chitosan as the polymeric excipient. A multiple unit HBS containing indomethacin as a model drug prepared by extrusion process is reported. A mixture of drug, chitosan and acetic acid is extruded through a needle, and the extrudate is cut and dried. Chitosan hydrates and floats in the acidic media and the required drug release could be obtained by modifying the drug-polymer ratio.

b) Effervescent Systems (Gas-generating Systems)

There are reports of sustained release floating granules containing tetracycline hydrochloride. The granules are a mixture of drug granulates of two stages A and B, of which 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. 60 parts by weight of granules of stage A and 30 parts by weight of granules of stage B are mixed along with a lubricant and filled into capsule. In dissolution media, the capsule shell dissolves and liberates the granules, which showed a floating time of more than 8 h and sustained drug release of 80% in about 6.5 h. Floating minicapsules of pepstatin having a diameter of 0.1-0.2 mm has been reported by Umezawa. These minicapsules contain a central core and a coating. The central core consists of a granule composed of sodium bicarbonate, lactose and a binder, which is coated with HPMC. Pepstatin is coated on the top of the HPMC layer. The system floats because of the CO2 release in gastric fluid and the pepstatin resides in the stomach for prolonged period. Alginates have received much attention in the development of multiple unit systems.
Alginates are non-toxic, biodegradable linear copolymers composed of Lglucuronic and L-mannuronic acid residues. A multiple unit system was prepared comprising of calcium alginate core and calcium alginate/PVA membrane, both separated by an air compartment. In presence of water, the PVA leaches out and increases the membrane permeability, maintaining the integrity of the air compartment. Increase in molecular weight and concentration of PVA, resulted in enhancement of the floating properties of the system.

Freeze-drying technique is also reported for the preparation of floating calcium alginate. Sodium alginate solution is added drop wise into the aqueous solution of calcium chloride, causing the instant gelation of the droplet surface, due to the formation of calcium alginate. The obtained beads are freeze-dried resulting in a porous structure, which aid in floating. The authors studied the behaviour of radio labeled floating beads and compared with non-floating beads in human volunteers using gamma scintigraphy. Prolonged gastric residence time of more than 5.5 h was observed for floating beads. The non-floating beads had a shorter residence time with a mean onset emptying time of 1h.\cite{13,14}

A new multiple type of floating dosage system had developed having a pill in the core, composed of effervescent layers and swellable membrane layers coated on sustained release pills (shown in figure 2). The inner layer of effervescent agents containing sodium bicarbonate and tartaric acid was divided into 2 sublayers to avoid direct contact between the 2 agents. These sublayers were surrounded by a swellable polymer membrane containing polyvinyl acetate and purified shellac. When this system was immersed in the buffer at 37°C, it settled down and the solution permeated into the effervescent layer through the outer swellable membrane. CO\textsubscript{2} was generated by the neutralization reaction between the 2 effervescent agents, producing swollen pills (like balloons) with a density less than 1.0 g/ml.

c) Hollow Microspheres\cite{15,16,17}
Hollow microspheres are considered as one of the most promising buoyant systems, as they possess the unique advantages of multiple unit systems as well as better floating properties, because of central hollow space inside the microsphere. The general techniques involved in their preparation include simple solvent evaporation and solvent diffusion and evaporation. The drug release and better floating properties mainly depend on the type of polymer, plasticizer and the solvents employed for the preparation. Polymers such as polycarbonate, Eudragit Sand cellulose acetate were used in the preparation of hollow microspheres and the drug release can be modulated by optimizing the polymer quantity and the polymer-
plasticizer ratio. Sustained release floating microspheres using polycarbonate were developed employing solvent evaporation technique. Aspirin, griseofulvin and p-nitroaniline were used as model drugs. Dispersed phase containing polycarbonate solution in dichloromethane and micronized drug, was added to the dispersion medium containing sodium chloride, polyvinyl alcohol and methanol

C. Raft Forming System
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.

CURRENT APPROACHES TO GASTRIC RETENSION
A Bio/Mucoadhesive systems Bio/Mucoadhesive systems are those which bind to the gastric epithelial cell surface or mucin and serve as a potential means of extending the GRT of drug delivery system (DDS) in the stomach, by increasing the intimacy and duration of contact of drug with the biological membrane. The surface epithelial adhesive properties of mucin have been well recognized and applied to the development of GRDDS based on bioadhesive/mucoadhesive polymers. The ability to provide adhesion of a drug (or a delivery system) to the GI walls provides a longer residence time in a particular organ site, thereby producing an improved effect in terms of local action or systemic effect. [18,19,20]

B Swelling and expanding system
There are the dosage forms, which after swallowing swell to an extent that prevents their exit from the pylorus. As a result, the dosage form is retained in the stomach for a long period of time. These systems may be named as “plug type systems,” since they exhibit the tendency to remain logged at the pyloric sphincter if that exceed a diameter of approximately 12-18mm in their expanded state. The formulation is designed for gastric retension ad controlled delivery of the drug into the gastric cavity for several hours even in the fed state. The balance between the extent and duration of swelling is maintained by the degree of cross-linking between the
polymeric chains. A high degree of cross-linking retards the swelling ability of the system maintaining its physical integrity for prolonged period.

C High density system These systems with a density of about 3g/cm³ are retained in the rugae of the stomach and are capable of withstanding its peristaltic movements. A density of 2.6-2.8g/cm³ acts as a threshold value after which such systems can be retained in the lower part of the stomach. High density formulations includes coated pellets. Coating is done by heavy inert materials such as barium sulphate, zinc oxide, titanium dioxide, iron powder etc.

D Low density systems
To avoid premature evacuation of drug through the pyloric sphincter low density systems (≤1g/cm³) with immediate buoyancy have been developed. They are made of low density materials, entrapping oil or air. Most are multiple unit systems and are also called microballoons because of low density core.[21,22,23,24]

F Magnetic systems
This approach to enhance the GRT is based on the simple principle that the dosage form contains a small internal magnet and a magnet is placed on the abdomen over the position of the stomach. Although magnetic system seems to work, the external magnet must be positioned with a degree of precision that might compromise patient compliance. The technological approach in rabbits with bioadhesive granules containing ultra- fine ferrite. They guided them to oesophagus with an external magnet for the initial 2 minutes and almost all the granules were retained in the region after 2 hours.

g) Incorporating delaying excipient
Delayed gastric emptying approach of interest include feeding of digestible polymers or fatty acid salts that charges the motility pattern, of the stomach to a fed stage thereby decreasing the gastric emptying rate and prolongation of the drug release with the help of delivery system incorporating delaying excipient like trietanolamine myristate in a delivery system.

h) Modified systems
The non disintegrating geometric shape molded from silastic elastomers or extruded from polyethylene blends, which extend the GRT depending on size, shape and flexural modules of drug delivery device.
i) Mucoadhesive & Bioadhesive systems
The Bioadhesive delivery systems are used to localize a delivery device within the lumen to increase the drug absorption in a site specific manner. Some of the most promising excipient that have been used commonly in these systems include polycarbophil, carbopol, lectins, chitosan, CMC and gliadin28, etc.

j) Floating systems\[26,27\]
Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids though the system is floating on the gastric contents. After release of drug, the residual system is emptied from the stomach. Floatation of a drug delivery system in the stomach can be achieved by incorporating floating chamber filled with vacuum, air, or inert gas.

Evaluation
Factors affecting gastric retention\[28,29\]
Several factors include like density, size and shape of dosage form, concomitant intake of food and drugs such as anticholinergic agents (eg. atropine, propantheline), opiates (eg. codeine) and prokinetic agents (eg. metoclopramide) and biological factors such as gender, posture, age, body mass index and disease state (eg. diabetes). The floating force kinetics of such dosage forms has shown that the bulk density of a dosage form is not the most appropriate parameter for describing its buoyancy. This is because the magnitude of floating strength may vary as a function of time and usually decreases after immersion and its hydrodynamical equilibrium. The prolongation of gastric residence time by food is expected to maximize drug absorption from floating drug delivery system due to increased dissolution of drug and longer residence at the most favorable sites of absorption.

Drugs Used In the Formulations of Stomach Specific Floating Dosage Forms
Floating microspheres – Aspirin, Griseofulvin, pnitroaniline, Ibuprofen, Ketoprofen24, Piroxicam, Verapamil, Theophylline, Nifedipine, Nicardipine, Tranilast25 and Terfinadine26
Floating granules - Diclofenac sodium, Indomethacin and Prednisolone.

Films – Cinnarizine24, Albendazole.

Floating tablets and Pills - Acetaminophen, Acetylsalicylic acid, Ampicillin, Atenolol, Fluorouracil, Isosorbide mononitrate28, Piretanide, Theophylline23, Chlorpheniramine maleate, Aspirin, Calcium Carbonate, Fluorouracil, Prednisolone, Sotalol,
**Floating Capsules** - Chlordiazepoxide hydrogen chloride, Diazepam24, Furosemide, Misoprostol, LDopa, Ursodeoxycholic acid, Pepstatin and Propranolol.

**MECHANISM OF FLOATING SYSTEMS 30**

There are various attempts have been made to retain the dosage form in the stomach as a way of increasing the retention time. These attempts include introducing floating dosage forms (gas-generating systems and swelling or expanding systems, mucoadhesive systems, high-density systems, modified shape systems, gastric-emptying delaying devices and 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 (a), the drug is released slowly at the desired rate from the system. After release of 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. However, besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal. To measure the floating force kinetics, a novel apparatus for determination of resultant weight has been reported in the literature. The apparatus operates by measuring continuously the force equivalent to F (as a function of time) that is required to maintain the submerged object. The object floats better if F is on the higher positive side. This apparatus helps in optimizing FDDS with respect to stability and durability of floating forces produced in order to prevent the drawbacks of unforeseeable intragastric buoyancy capability variations  

\[ F = F_{buoyancy} - F_{gravity} = (D_f - D_s) \cdot g \cdot v \]

Where, \( F \) = total vertical force  
\( D_f \) = fluid density  
\( D_s \) = object density  
\( v \) = volume and  
\( g \) = acceleration due to gravity

**Advantages**

Floating dosage systems form important technological drug delivery systems with gastric retentive behavior and offer several advantages in drug delivery. These advantages include:

1. Floating dosage forms such as tablets or capsules will remain in the solution for prolonged time even at the alkaline pH of the intestine.
2. FDDS dosage forms are advantageous in case of vigorous intestinal movement and in diarrhoea to keep the drug in floating condition in stomach to get a relatively better response.
3. Acidic substance like aspirin causes irritation on the stomach wall when come in contact with it hence; HBS/FDDS formulations may be useful for the administration of aspirin and other similar drugs.
4. The FDDS are advantageous for drugs absorbed through the stomach eg: Ferrous salts, Antacids. Improved drug absorption, because of increased GRT and more time spent by the dosage form at its absorption site.
5. Controlled delivery of drugs. It minimizes the mucosal irritation by releasing drug slowly.
6. Treatment of gastrointestinal disorders such as gastro esophageal reflux.

**Disadvantages of floating drug delivery system:** system is not feasible for those drugs that have solubility or stability problem in GI tract.
2. These systems require a high level of fluid in the stomach for drug delivery to float and work efficiently coat, water
3. The drugs that are significantly absorbed throughout gastrointestinal tract, which undergo significant first pass metabolism, may not be desirable candidate. E.g. Nifedipine.
4. The ability of drug to remain in the stomach depends upon the subject being positioned upright.
5. The residence time in the stomach depends upon the digestive state. Hence, FDDS should be administered after the meal.
6. Not suitable for drugs that cause gastric lesions e.g. Non steroidal anti inflammatory drugs. Drugs that are unstable in the strong acidic environment, these systems do not offer, significant advantages over the conventional dosage form for drugs, which are absorbed throughout the gastro intestinal tract.
7. The mucus on the walls of the stomach is in the state of constant renewal, resulting in the unpredictable adherence.
8. Faster swelling properties are required and complete swelling of the system should be achieved well before the gastric emptying time.
9. The ability to float relies in the hydration state of dosage form.
10. In all the above, the most important and primary requirement for the success is the physical integrity of the system

**APPLICATIONS OF FLOATING DRUG DELIVERY SYSTEMS:**

- **Bioavailability**

The bioavailability of CR-GRDF is significantly enhanced in comparison to the administration of non-GRDF CR polymeric formulations. There are several different processes, related to absorption and transit of the drug in the gastrointestinal tract, that act concomitantly to influence the magnitude of drug absorption.
• **Sustained drug delivery**
  In this systems dose large in size and passing from the pyloric opening is prohibited. New sustained release floating capsules of nicardipine hydrochloride were developed and were evaluated in vivo. Plasma concentration time curves a longer duration for administration (16 hours) in the sustained release floating capsules as compared with conventional MICARD capsules (8 hours). Similarly a comparative study between the Madopar HBS and Madopar standard formulation was done it shown the drug was released up to 8 hours in vitro in the former case and the release completed in less than 30 minutes in the latter case.

• **Site–specific drug delivery systems**
  These systems are particularly advantageous for drugs those are specifically intestine. The controlled, slow delivery of drug to the stomach provides sufficient local therapeutic levels and limits the systemic exposure to the drug. It reduces the side effects which are caused by the drug in the blood circulation. In addition, the prolonged gastric availability from a site directed delivery system may also reduce the dosing frequency.

• **Absorption enhancement**
  Drugs which are having poor bioavailability because of site specific absorption from the upper part of the GIT are potential candidates to be formulated as floating drug delivery systems, thereby maximizing their absorption.

• **Minimize adverse activity at the colon**
  Retention of the drug in the HBS systems at the stomach minimizes the amount of drug that reaches the colon. Thus, undesirable activities of the drug in colon may be prevented. This pharmacodynamic aspect provides the rationale for GRDF formulation for beta-lactam antibiotics that are absorbed only from the small intestine and whose presence in the colon leads to the development of microorganism’s resistance.

**Evaluation parameters of Gastroretentive system**
There are different studies reported in the literature indicate that pharmaceutical dosage forms exhibiting gastric residence in vitro floating behaviour show prolonged gastric residence in vivo. However, it has to be pointed out that good in vitro floating behaviour alone is not sufficient of the complex motility of the stomach are difficult to estimate. Obviously, only in vivo studies can provide definite proof that prolonged gastric residence is obtained.
1. Floating time and dissolution
The test for floating time measurement is usually performed in stimulated gastric fluid or 0.1 mole/lit HCl maintained at 37°C. It is determined by using USP dissolution apparatus containing 900 ml of 0.1 mole/lit HCl as the dissolution medium at 37°C. The time taken by the dosage form to float is termed as floating lag time and the time for which the dosage form floats is termed as the floating or flotation time. A more relevant in-vitro dissolution method proposed to evaluate a floating drug delivery system (for tablet dosage form). A 100 ml glass beaker was modified by adding a side arm at the bottom of the beaker so that the beaker can hold 70 ml of 0.1 mol/lit HCl dissolution medium and allow collection of samples. A burette was mounted above the beaker to deliver the dissolution medium at a flow rate of 2 ml/min to mimic gastric acid secretion rate. The performance of the modified dissolution apparatus was compared with USP dissolution. Apparatus 2 (Paddle): The problem of adherence of the tablet to the shaft of the paddle was observed with the USP dissolution apparatus. The tablet did not stick to the agitating device in the proposed dissolution method. The drug release followed zero-order kinetics in the proposed method. Similarity of dissolution curves was observed between the USP method and the proposed method at 10% difference level. The proposed test may show good in vitro-in vivo correlation since an attempt is made to mimic the in vivo conditions such as gastric volume, gastric emptying, and gastric acid secretion.

2. Drug release
Dissolution tests are performed using the dissolution apparatus. Samples are withdrawn periodically from the dissolution medium with replacement and then analyzed for their drug content after an appropriate dilution.

3. Drug loading, drug entrapment efficiency, particle size analysis, surface characterization (for floating microspheres and beads)
Drug loading is assessed by crushing accurately weighed sample of beads or microspheres in a mortar and added to the appropriate dissolution medium which is then centrifuged, filtered and analyzed by various analytical methods like spectrophotometry. The percentage drug loading is calculated by dividing the amount of drug in the sample by the weight and simulated meal, total beads or microspheres. The particle size and the size distribution of beads or microspheres are determined in the dry state using the optical microscopy method. The external and cross-sectional morphology (surface characterization) is done by scanning electron microscope (SEM).
4) Hardness, friability, assay, content uniformity (Tablets)
These tests are performed as per described in specified monographs.

4) Drug loading, drug entrapment efficiency, particle size analysis, surface characterization, micromeritics studies and percentage yield (for floating microspheres and beads)
Drug loading by crushing accurately weighed sample of beads or microspheres in a mortar and added to the appropriate dissolution medium and centrifuged, filtered and analyzed by various analytical methods like spectrophotometry. The percentage drug loading is calculated in beads or microspheres and the size and shape calculate by optical microscopy method. The external and cross-sectional morphology which is surface characterization is done by scanning electron microscope (SEM). The measured weight of prepared microspheres was divided by total amount of all non-volatile components used for the preparation of microspheres, which will give the total percentage yield of floating microspheres.

5) Resultant weight determination
Bulk density and floating duration have been the main parameters of a dosage form’s buoyancy. Although single density determination does not predict the floating force evolution the dosage forms. It operates by force equivalent to the force F required to keep the object totally submerged in the fluid. The magnitude, direction of the force and the resultant weight corresponds to the Victoria sum of buoyancy (Fbuoy) and gravity (Fgrav) forces acting on the objects as shown in the equal
\[ F = F_{buoy} - F_{grav} \]
\[ F = d_f g V - d_s g V = (d_f - d_s) g V \]
\[ F = (d_f - M/V) g V \]
In which the F is total vertical force (resultant weight of the object), g is the acceleration due to gravity, df if the fluid density, ds is the object density is the object mass and V is the volume of the object.

7) X Ray/Gamma scintigraphy
For in vivo studies, X-Ray/Gamma Scintigraphy is the main evaluation parameter for floating system. In each experiment, the animals are allowed to fast overnight with free access to water, in a formulation allows indirect external observation using a γ-camera or scintiscanner. But the main drawback of γ- scintigraphy are the associated ionizing radiation for the patient,
the limited topographic information, low resolution inherent to the technique and the complicated and expensive preparation of radiopharmaceutical26.

6) Pharmacokinetic studies
Pharmacokinetic studies include AUC (Area under Curve), C max, and time to reach maximum and a radiograph is made just before the administration of the floating tablet to ensure the absence of radio-opaque material. Visualization of dosage form by X-ray is due to the inclusion of a radio-opaque material. The formulation is administered by natural swallowing followed by 50 mL of water. Gastric radiography was done at 30-min time intervals for a period of 5 h using an X-ray machine. The inclusion of a γ-emitting radionucleide plasma concentration (T max) were estimated using a computer. Statistical analyses were performed using a Student t test with p, 0.05 as the minimal level of significance.

7) Specific Gravity
The displacement method is used to determine the specific gravity of floating system using compound benzene as a displacing medium.

Applications of Floating Drug Delivery Systems
Floating drug delivery offers several applications on poor bioavailability drugs because of the narrow absorption window in the upper part of the gastrointestinal tract. It retains the dosage form at the site of absorption and thus enhances the bioavailability. Some of these are;

Sustained Drug Delivery
In this systems dose large in size and passing from the pyloric opening is prohibited. New sustained release floating capsules of nicardipine.

In this systems dose large in size and passing from the pyloric opening is prohibited. New sustained release floating capsules of nicardipine hydrochloride were developed and were evaluated in vivo. Plasma concentration time curves showed a longer duration for administration (16 hours) in the sustained release floating capsules as compared with conventional MICARD capsules (8 hours). Similarly a comparative study28 between the Madopar HBS and Madopar standard formulation was done it shown the drug was released up to 8 hours in vitro in the former case and the release completed in less than 30 minutes in the latter case.
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, eg, riboflavin. 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. A bilayer floating capsule was developed for local delivery of misoprostol, which is a synthetic analog of prostaglandin E1 used as a protectant of gastric ulcers caused by administration of NSAIDs28.

Absorption Enhancement

Drugs which have poor bioavailability at the site specific absorption from the upper part of the gastrointestinal tract are potential candidates to be formulated as floating drug delivery systems. In some cases increase in the bioavailability of floating dosage forms (42.9%) could be achieved as compared with commercially available LASIX tablets (33.4%). 29.

CONCLUSION

Drug absorption in the gastrointestinal tract is a highly variable procedure. The prolong gastric retention of the dosage form extends the time for drug absorption is now available in floating drug delivery system. Floating controlled drug delivery systems are employed to solve this problem. It also provide intimate contact between a dosage form and the absorbing tissue which may result in high drug concentration in a local area and hence, high drug flux through the absorbing tissue, producing the pharmacological effect for extended period of time with maximum bioavailability and less side effects for drugs that are absorbed primarily in the upper part of GI tract, i.e., the stomach, duodenum and jejunum. The increasing delivery technology will ensure the development of increase number of gastroretentive drug delivery to optimize the delivery of molecules that exhibit absorption window, low bioavailability and extensive first pass metabolism.

REFERENCE


