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Review Article

A REVIEW ARTICLE ON DIFFERENT TYPES OF FLOATING DRUG DELIVERY SYSTEMS

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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 this review. This review also summarizes the advantages and limitations of FDDS. These systems are useful to several problems encountered during the development of a pharmaceutical dosage form.

Keywords: Floating drug delivery systems, Types of Floating drug delivery systems, Gastrointestinal tract, Gastric residence time

INTRODUCTION

GIT Physiology

The Human gastrointestinal tract refers to the stomach and intestine, and sometimes to all the structures from the mouth to the anus. (The "digestive system" is a broader term that includes other structures, including the accessory organs of digestion).

In an adult male human, the gastrointestinal (GI) are 5 metres (20 ft) long in a live subject, or up to 9 metres (30 ft) without the effect of muscle tone, and consists of the upper and lower GI tracts. The tract may also be divided into foregut, midgut, and hindgut, reflecting the embryological origin of each segment of the tract.

The GI tract releases hormones as to help regulate the digestion process. These hormones, including gastrin, secretin, cholecystokinin, and grehlin, are mediated through either intracrine or autocrine mechanisms, indicating that the cells releasing these hormones are conserved structures throughout evolution.

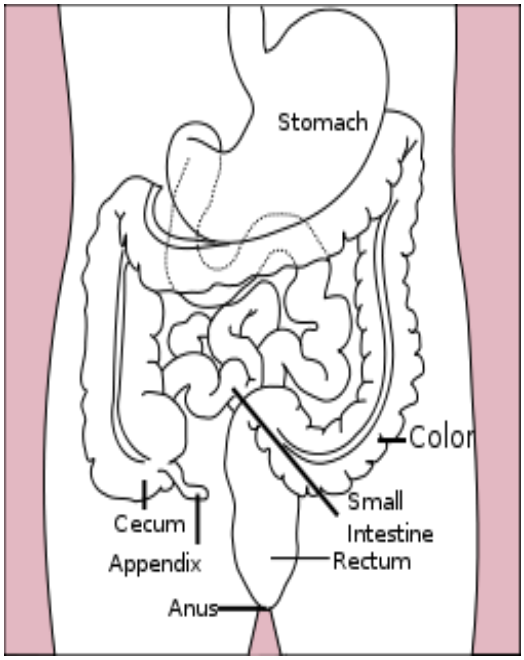

Fig. 1: Gastrointestinal Tract

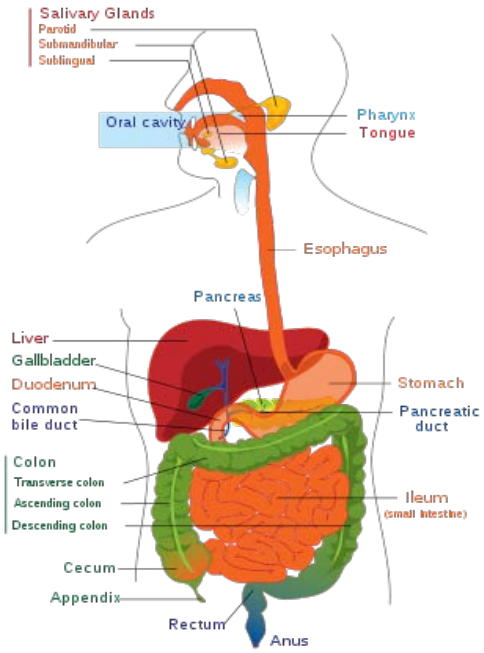

Fig. 2: Upper and Lower Gastrointestinal Tract

Upper Gastrointestinal Tract

The upper gastrointestinal tract consists of the esophagus, stomach, and duodenum. Some sources also include the mouth cavity and pharynx.

The exact demarcation between "upper" and "lower" can vary. Upon gross dissection, the duodenum may appear to be a unified organ, but it is often divided into two parts based upon function, arterial supply, or embryology.

Lower Gastrointestinal Tract

The lower gastrointestinal tract includes most of the small intestine and all of the large intestine. According to some sources, it also includes the anus.

- Bowel or intestine
  - Small intestine, which has three parts:
    - Duodenum - Here the digestive juices from pancreas and liver mix together
    - Jejunum - It is the midsection of the intestine, connecting duodenum to ileum.
    - Ileum - It has villi in where all soluble molecules are absorbed into the blood.
  - Large intestine, which has three parts:
    - Cecum (the vermiform appendix is attached to the cecum).
    - Colon (ascending colon, transverse colon, descending colon and sigmoid flexure)
    - Rectum
- Anus

The ligament of Treitz is sometimes used to divide the upper and lower GI tracts.

Embryology

The gut is an endoderm-derived structure. At approximately the sixteenth day of human development, the embryo begins to fold ventrally (with the embryo's ventral surface becoming concave) in two directions: the sides of the embryo fold in on each other and the head and tail fold toward one another. The result is that a piece of the yolk sac, an endoderm-lined structure in contact with the ventral aspect of the embryo, begins to be pinched off to become the primitive gut. The yolk sac remains connected to the gut tube via the vitelline duct. Usually this structure regresses during development; in cases where it does not, it is known as Meckel's diverticulum.

During fetal life, the primitive gut can be divided into three segments: foregut, midgut, and hindgut. Although these terms often are used in reference to segments of the primitive gut, they nevertheless are used regularly to describe components of the definitive gut as well.

Each segment of the gut gives rise to specific gut and gut-related structures in later development. Components derived from the gut proper, including the stomach and colon, develop as swellings or dilatations of the primitive gut. In contrast, gut-related derivatives—that is, those structures that derive from the primitive gut, but are not part of the gut proper—in general develop as outpouchings of the primitive gut. The blood vessels supplying these structures remain constant throughout development.

Table 1: Parts of gut and its Specifications

Part	Part in adult	Gives rise to	Arterial supply
Foregut	the pharynx, to the upper duodenum	pharynx, esophagus, stomach, upper duodenum, respiratory tract (including the lungs), liver, gallbladder, and pancreas	branches of the celiac artery
Midgut	lower duodenum, to the first two-thirds of the transverse colon	lower duodenum, jejunum, ileum, cecum, appendix, ascending colon, and first two-thirds of the transverse colon	branches of the superior mesenteric artery
Hindgut	last third of the transverse colon, to the upper part of the anal canal	last third of the transverse colon, descending colon, rectum, and upper part of the anal canal	branches of the inferior mesenteric artery

Transit Time

The time taken for food or other ingested objects to transit through the gastrointestinal tract varies depending on many factors, but roughly, it takes 2.5 to 3 hours after meal for 50% of stomach contents to empty into the intestines and total emptying of the stomach takes 4 to 5 hours. Subsequently, 50% emptying of the small intestine takes 2.5 to 3 hours. Finally, transit through the colon takes 30 to 40 hours[1].

APPROACHES TO DESIGN FLOATING DOSAGE FORMS

The following approaches have been used for the design of floating dosage forms of single- and multiple-unit systems.

Single-Unit Dosage Forms

In Low-density approach the globular shells apparently having lower density than that of gastric fluid can be used as a carrier for drug for its controlled release. A buoyant dosage form can also be obtained by using a fluid-filled system that floats in the stomach.In coated shells popcorn, poprice, and polystyrol have been exploited as drug carriers. Sugar polymeric materials such as methacrylic polymer and cellulose acetate phthalate have been used to undercoat these shells. These are further coated with a drug-polymer mixture. The polymer of choice can be either ethylcellulose or hydroxypropyl cellulose depending on the type of release desired. Finally, the product floats on the gastric fluid while releasing the drug gradually over a prolonged duration.

Fluid- filled floating chamber type of dosage forms includes incorporation of a gas-filled floatation chamber into a microporous component that houses a drug reservoir. 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 partial vacuum or any other suitable gas, liquid, or solid having an appropriate specific gravity and an inert behavior. The device is of 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. Hydrodynamically balanced systems (HBS) are designed to prolong the stay of the dosage form in the gastro intestinal tract and aid in enhancing the absorption. Such systems are best suited for drugs having a better solubility in acidic environment and also for the drugs having specific site of absorption in the upper part of the small intestine. To remain in the stomach for a prolonged period of time the dosage form must have a bulk density of less than 1. It should stay in the stomach, maintain its structural integrity, and release drug constantly from the dosage form. The success of HBS capsule as a better system is best exemplified with chlordiazeopoxide hydrochloride. The drug is a classical example of a solubility problem wherein it exhibits a 4000-fold difference in solubility going from pH 3 to 6 (the solubility of chlordiazepoxide hydrochloride is 150 mg/mL and is ~0.1 mg/mL at neutral pH).

HBS of chlordiazeopoxide hydrochloride had comparable blood level time profile as of three 10-mg commercial capsules. HBS can either be formulated as a floating tablet or capsule. Many polymers and polymer combinations with wet granulation as a manufacturing technique have been explored to yield floatable tablets.

Various types of tablets (bilayered and matrix) have been shown to have floatable characteristics. Some of the polymers used are hydroxypropyl cellulose, hydroxypropyl methylcellulose, crosspovidone, sodium carboxymethyl cellulose, and ethyl cellulose.Self-correcting floatable asymmetric configuration drug delivery system employs a disproportionate 3-layer matrix technology to control drug release.

The 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.

Single-unit formulations are associated with problems such as sticking together or being obstructed in the gastrointestinal tract, which may have a potential danger of producing irritation.

MULTIPLE-UNIT DOSAGE FORMS

The purpose of designing multiple-unit dosage form is to develop a reliable formulation that has all the advantages of a single-unit form and also is devoid of any of the above mentioned disadvantages of single-unit formulations. In pursuit of this endeavor many multiple-unit floatable dosage forms have been designed. Microspheres have high loading capacity and many polymers have been used such as albumin, gelatin, starch, polymethacrylate, polyacrylamine, and polyalkylcyanoacrylate. Spherical polymeric microsponges, also referred to as "microballoons," have been prepared. Microspheres have a characteristic internal hollow structure and show an excellent in vitro floatability. In Carbon dioxide–generating multiple-unit oral formulations several devices with features that extend, unfold, or are inflated by carbon dioxide generated in the devices after administration have been described in the recent patent literature. These dosage forms are excluded from the passage of the pyloric sphincter if a diameter of ~12 to 18 mm in their expanded state is exceeded[2].

TYPES OF FLOATING DOSAGE FORMS

Noneffervescent Fdds

The most commonly used excipients in noneffervescent FDDS are gel forming or highly swellable cellulose type hydrocolloids, polysaccharides, and matrix forming polymers such as polycarbonate, polyacrylate, polymethacrylate and polystyrene. One of the floating formulations is a gel-forming hydrocolloid in a capsule, which swells in contact with gastric fluid after oral administration and maintains a relative integrity of shape and a bulk density of less than unity within the outer gelatinous barrier. The air trapped by the swollen polymer confers buoyancy to these dosage forms. When such DF comes in contact with an aqueous medium, the hydrocolloid starts to hydrate by forming a gel, which controls the rate of diffusion of solvent-in and drug-out of the DF.

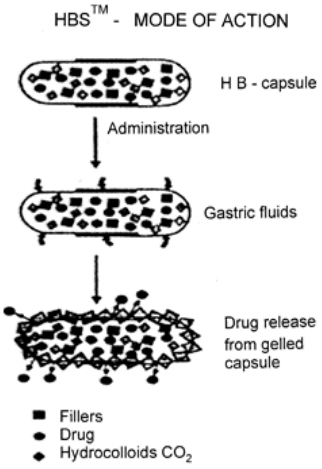

Fig. 3: Working principle of hydro dynamically balanced system within gel structure

As the exterior surface of the DF goes into solution, the immediate adjacent hydrocolloid layer becoming hydrated maintains the gel layer. As a result, the drug dissolves in and diffuses out with the diffusing solvent, creating a receding boundary within a gel structure. When capsule containing a mixture of a drug and hydrocolloids come in contact with gastric fluid, the capsule shell dissolves; the mixture swells and forms a gelatinous barrier thereby remaining buoyant in the gastric juice for an extended period of time.

Recent approach in FDDS is based on low-density foam powder based micro particles. This system is advantageous because of its zero to negligible lag time before starting of floatation. These floating microcapsules, prepared by emulsion solvent evaporation technique, contain polypropylene foam powder, polymers (Eudragit RS /ethyl cellulose / Methacrylate polymer) and model drug (verapamil HCL). Drug release rate increases significantly with different type of polymers in following order: PMMA> EC > Eudragit RS.20. Another study on foam powder based microcapsules includes the effect of formulation and processing parameters on drug release using different matrix forming polymers e.g. HPMC; polyacrylates, Na-alginate, corn starch, carageenan, gum guar and gum Arabic. The study indicated that the release rate can be modified by varying the matrix forming polymer/foam powder ratio, initial drug loading, tablet geometry (radius and height), type of matrix forming polymer, use of polymer blends, water soluble /insoluble fillers (lactose/MCC).

The floating flap of albendazole, prepared with concentrations of 8.8, 10.0 and 8.5 % w/v of Eudragit RL 100, Eudragit RS 100 and Poly lactide co-glycolide respectively by mercury casting technique, was found to be of good floating behavior and was selected for release rate studies. Chitosan granules having internal cavity were prepared by de-acidification. When added to acidic (pH 1.2) and neutral (deionized distilled water) media, these granules were immediately buoyant and provided a controlled release of the candidate drug prednisolone. Laminated preparations prepared by coating with chitosan granules layer with chitosan membranes were also buoyant and provided controlled release of the drug. Floating chitosan microcapsules can be prepared by ionic interaction of chitosan and negatively charged surfactant sodium dioctyl sulfosuccinate.

Many lipid-based sustained release matrix systems are reported. Kiran Kumar et al reported floating glycerol monooleate (GMO) single-unit lipid matrix containing high drug: excipient ratio (1:30) to achieve sustained drug release. Hydrophobic lipid, Gelucire 43/01, can be considered as an effective carrier for design of a multi-unit FDDS of highly water-soluble drugs such as diltiazem HCl. Tablet with Spray dried PVA -PVP shows immediate floating with almost no lag time, floating for 24 h and do not sink. No swelling and erosion takes place in the GIT, so the release does not depend upon osmolarity of the medium. Buoyancy in such system is due to high porosity in the tablet. The exceptionally good compressibility of spray dried PVA-PVP combination makes it possible to produce mechanically stable oral DF, even with extremely low pressures.

In addition to the approaches outlined above, gastroretentive drug delivery systems have been made from a new category of synthetic acrylamide/ sulfopropyl acrylates, acrylic acid polymers containing crosscarmelose sodium, also known as "superporous hydrogel composites".

Effervescent FDDS

These buoyant delivery systems utilize matrices prepared with swellable polymers such as Methocel or polysaccharides, e.g., chitosan and effervescent components, e.g., sodium bicarbonate and citric or tartaric acid. Another system consists of a liquid that gasify at body temperature. The matrices are so fabricated that on arrival in the stomach, CO_2 is liberated by the acidity of the gastric contents and is entrapped in the gellified hydrocolloid. This produces an upward motion of the dosage form and maintains its buoyancy. The CO_2 generating components may be intimately mixed within the tablet matrix, to produce a single-layered tablet or a bilayered tablet may be compressed which contains the gas generating mechanism in one hydrocolloid containing layer and the drug in the other layer formulated for a SR (sustained release) effect.

A multiple-unit type of floating pill, which generates CO_2 gas, has been developed. The system consists of SR pills as seeds surrounded by double layers. The inner layer was an effervescent layer containing both sodium bicarbonate and tartaric acid. The outer layer was a swellable membrane layer. Moreover, the effervescent layer was divided into two sub layers to avoid direct contact between sodium bicarbonate and tartaric acid. Sodium bicarbonate was contained in the inner sub layer and tartaric acid was in the outer layer. When the system was immersed in a buffer solution at 37°C, it sank at once in the solution and formed swollen pills, like balloons (density <1 g/ml). Attempts have also been made to develop SR floating tablets using a mixture of sodium bicarbonate, citric acid and chitosan.

Floating rafts are used in the treatment of gastric oesophageal reflux. Gaviscon liquid (Reckitt andColman) is an established floating raft formulation based on an alginate biopolymer. On ingestion, this formulation reacts with gastric acid to form a floating raft structure, which impedes the reflux of acid and food by acting as a physical barrier. The raft has a pH value higher than that of the stomach contents so thatin the event of gastric reflux, the wall of the esophagus is not subjected to irritation by HCl. Such formulation on entering the stomach forms a colloidal gel. Sodium alginate solution reacting with gastric acid and this gel floats on the surface of the gastric contents due to CO2 generation by gas generating
excipients impeding reflux of acid into the oesophagus[3].

Bioadhesive Systems

Bioadhesive drug delivery systems (BDDS) are used to localise a delivery device within the lumen to enhance the drug absorption in a site-specific manner. This approach involves the use of bioadhesive polymers, which can adhere to the epithelial surface in the stomach. A microbalance-based system is reported for measuring the forces of interaction between the GI mucosa and the individual polymers, and the Cahn Dynamic Contact Angle Analyzer has been used to study the adherence.5 Gastric mucoadhesion does not tend to be strong enough to impart to dosage forms the ability to resist the strong propulsion forces of the stomach wall. The continuous production of mucous by the gastric mucosa to replace the mucous that is lost through peristaltic contractions and the dilution of the stomach content also seems to limit the potential of mucoadhesion as a gastroretentive force. Some of the most promising excipients that have been used commonly in these systems include polycarbophil, carbopol, lectins, chitosan, CMC and gliadin, etc. Some investigators have tried out a synergistic approach between floating and bioadhesion systems. Other approaches reported include use of a novel adhesive material derived from the fimbriae (especially Type 1) of bacteria or synthetic analogues combined with a drug to provide for attachment to the gut, thereby prolonging the transit time, a composition comprising an active ingredient and a material that acts as a viscogenic agent (for example curdlan and/or a low-substituted hydroxypropylcellulose), etc.

High – Density Systems

Sedimentation has been employed as a retention mechanism for pellets that are small enough to be retained in the rugae or folds of the stomach body near the pyloric region, which is the part of the organ with the lowest position in an upright posture. Dense pellets (approximately 3g/cm3) trapped in rugae also tend to withstand the peristaltic movements of the stomach wall. With pellets, the GI transit time can be extended from an average of 5.8–25 hours, depending more on density than on diameter of the pellets, although many conflicting reports stating otherwise also abound in literature. Commonly used excipients are barium sulphate, zinc oxide, titanium dioxide and iron powder, etc. These materials increase density by up to 1.5–2.4g/cm-3. However, no successful high-density system has made it to the market.

Large Single Unit Dosage Forms

These dosage forms are larger than the pyloric opening and so are retained in the stomach. There are some drawbacks associated with this approach. Permanent retention of rigid large-sized single-unit forms can cause bowel obstruction, intestinal adhesion and gastroplasty.

Co-Administration of Gastric Emptying Delaying Drugs

This concept of simultaneous administration of a drug to delay gastric emptying together with a therapeutic drug has not received the favour of clinicians and regulatory agencies because of the questionable benefit-to-risk ratio associated with these devices[4].

APPLICATIONS OF FLOATING DRUG DELIVERY SYSTEMS

Floating drug delivery offers several applications for drugs having poor bioavailability 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. These are summarized as follows.

Sustained Drug Delivery

HBS systems can remain in the stomach for long periods and hence can release the drug over a prolonged period of time. The problem of short gastric residence time encountered with an oral CR formulation hence can be overcome with these systems. These systems have a bulk density of <1 as a result of which they can float on the gastric contents. These systems are relatively large in size and passing from the pyloric opening is prohibited.

Recently sustained release floating capsules of nicardipine hydrochloride were developed and were evaluated in vivo. The formulation compared with commercially available MICARD capsules using rabbits. 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 study between the Madopar HBS and Madopar standard formulation was done and it was shown that the drug was released up to 8 hours in vitro in the former case and the release was essentially complete 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 and furosemide.

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 NSAIDs. By targeting slow delivery of misoprostol to the stomach, desired therapeutic levels could be achieved and drug waste could be reduced.

Absorption 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%).

The absorption of bromocriptine is limited to 30% from the gastrointestinal tract, however an HBS of the same can enhance the absorption. It was also studied that if metoclopramide is co delivered with bromocriptine, the side effects associated with high doses of bromocriptine can be prevented and the dosage from becomes therapeutically more potential.

In few cases the bioavailability of floating dosage form is reduced in comparison to the conventional dosage form. In a recent study 3 formulations containing 25 mg atenolol, a floating multiple-unit capsule, a high-density multiple-unit capsule, and an immediate-release tablet were compared with respect to estimated pharmacokinetic parameters. The bioavailability of the 2 gastroretentive preparations with sustained release characteristics was significantly decreased when compared with the immediate-release tablet. This study showed that it was not possible to increase the bioavailability of a poorly absorbed drug such as atenolol using gastroretentive formulations.

In some cases the reduction in bioavailability is compensated by advantages offered by FDDS, for example a hydrodynamically balanced system of L-dopa provided better control over motor fluctuations in spite of reduced bioavailability of up to 50% to 60% in comparison with standard L-dopa treatment. This could be attributed to reduced fluctuations in plasma drug levels in case of FDDS.

FDDS also serves as an excellent drug delivery system for the eradication of *Helicobacter pylori*, which causes chronic gastritis and peptic ulcers. The treatment requires high drug concentrations to be maintained at the site of infection that is within the gastric mucosa. By virtue of its floating ability these dosage forms can be retained in the gastric region for a prolonged period so that the drug can be targeted.

Floating drug delivery is associated with certain limitations. Drugs that irritate the mucosa, those that have multiple absorption sites in the gastrointestinal tract, and those that are not stable at gastric pH are not suitable candidates to be formulated as floating dosage forms.

Floatation as a retention mechanism requires the presence of liquid on which the dosage form can float on the gastric contents. To overcome this limitation, a bioadhesive polymer can be used to coat the dosage so that it adheres to gastric mucosa, or the dosage form can be administered with a full glass of water to provide the initial fluid for buoyancy. Also single unit floating capsules or tablets are associated with an "all or none concept," but this can be overcome by formulating multiple unit systems like floating microspheres or microballoons.

The use of large single-unit dosage forms sometimes poses a problem of permanent retention of rigid large-sized single-unit forms especially in patients with bowel obstruction, intestinal adhesion, gastropathy, or a narrow pyloric opening (mean resting pyloric diameter 12.8 ± 7.0 mm). Floating dosage form should not be given to a patient just before going to bed as the gastric emptying of such a dosage form occurs randomly when the subject is in supine posture. One drawback of hydrodynamically balanced systems is that this system, being a matrix formulation, consists of a blend of drug and low-density polymers. The release kinetics of drug cannot be changed without changing the floating properties of the dosage form and vice versa[5].

FACTORS AFFECTING GASTRIC RETENTION

1. Density: GRT is a function of dosage form buoyancy that is dependent on the density.

2. Size: Dosage form units with a diameter of more than 7.5mm are reported to have an increased GRT compared with those with a diameter of 9.9mm.

3. Shape of dosage form: Tetrahedron and ring shaped devices with a flexural modulus of 48 and 22.5 kilo pounds per square inch (KSI) are reported to have better GRT 90% to 100% retention at 24 hours compared with other shapes.

4. Single or multiple unit formulation: Multiple unit formulations show a more predictable release profile and insignificant impairing of performance due to failure of units, allow co- administration of units with different release profiles or containing incompatible substances and permit a larger margin of safety against dosage form failure compared with single unit dosage forms.

5. Fed or unfed state under fasting conditions: GI motility is characterized by periods of strong motor activity or the migrating myoelectric complex (MMC) that occurs every 1.5 to 2 hours. The MMC sweeps undigested material from the stomach and, if the timing of administration of the formulation coincides with that of the MMC, the GRT of the unit can be expected to be very short. However, in the fed state, MMC is delayed and GRT is considerably longer.

6. **Nature of meal:** feeding of indigestible polymers or fatty acid salts can change the motility pattern of the stomach to a fed state, thus decreasing the gastric emptying rate and prolonging drug release.

7. Caloric content: GRT can be increased by 4 to 10 hours with a meal that is high in proteins and fats.

8. Frequency of feed: the GRT can increase by over 400 minutes, when successive meals are given compared with a single meal due to the low frequency of MMC.

9. Gender: Mean ambulatory GRT in males (3.4±0.6 hours) is less compared with their age and race matched female counterparts (4.6±1.2 hours), regardless of the weight, height and body surface.

10. Age: Elderly people, especially those over 70, have a significantly longer GRT.

11. Posture: GRT can vary between supine and upright ambulatory states of the patient.

12. Concomitant drug administration: Anticholinergics like atropine and propantheline, opiates like codeine and prokinetic agents like metoclopramide and cisapride.

13. Biological factors: Diabetes and Crohn's disease[6].

Some of the Marketed Formulations

Table 2: Marketed Floating Dosage Forms

S no.	Marketed formulation	Active ingredient
1	Valrelease[7]	Diazepam
2	Madopar[8]	Benserazide and L-Dopa
3	Topalkan[9]	Aluminium – Magnesium antacid
4	Cifran OD[10]	Ciprofloxacin

EVALUATION OF GASTRORETENTIVE DOSAGE FORMS

1. For Single Unit Dosage Forms (Eg: tablets)

i. Floating lag time: It is the time taken by the tablet to emerge onto the surface of dissolution medium and is expressed in seconds or minutes.

ii. In vitro drug release and duration of floating: This is determined by using USP II apparatus (paddle) stirring at a speed of 50 or 100 rpm at 37 ± 0.2 °c in simulated gastric fluid (pH 1.2 without pepsin). Aliquots of the samples are collected and analyzed for the drug content. The time (hrs) for which the tablets remain buoyant on the surface of the dissolution medium is the duration of floating and is visually observed.

iii. In vivo evaluation for gastro-retention: This is carried out by means of X-ray or Gamma scintigraphic monitoring of the dosage form transition in the GIT. The tablets are also evaluated for hardness, weight variation, etc.

For Multiple Unit Dosage Forms (Eg: microspheres)

Apart from the In vitro release, duration of floating and in vivo gastro-retention tests, the multiple unit dosage forms are also evaluated for:

i. Morphological and dimensional analysis with the aid of scanning electron microscopy (SEM). The size can also be measured using an optical microscope.

ii. % yield of microspheres: This is calculated from

$$\frac{\text{Weight of microspheres obtained} \times 100}{\text{Total weight of drug and polymer}}$$

iii. Entrapment efficiency: The drug is extracted by a suitable method, analysed and is calculated from

$$\frac{\text{Practical amount of drug present} \times 100}{\text{Theoretical drug content}}$$

iv. In vitro floating ability (Buoyancy %):

A known quantity of microspheres are spread over the surface of a USP (Type II) dissolution apparatus filled with 900 ml of 0.1 N HCl containing 0.002% v/v Tween 80 and agitated at 100 rpm for 12 hours. After 12 hours, the floating and settled layers are seperated, dried in a dessicator and weighed. The buoyancy is calculated from the following formula.

$$\text{Buoyancy (\%)} = Wf / (Wf + Ws) \times 100$$

Where Wf and Ws are the weights of floating and settled microspheres respectively

v. Drug-excipient (DE) interactions: This is done using FTIR. Appearance of a new peak, and/or disappearance of original drug or excipient peak indicate the DE interaction. Apart from the above mentioned evaluation parameters, granules are also evaluated for the effect of ageing with the help of Differential Scanning Calorimeter or Hot stage polarizing microscopy[11].

CONCLUSION

FDDS is a potential approach for gastric retention. Also FDDS through the local drug release increases the pharmacotherapy of stomach leading to high concentrations of gastric mucosa which are sustained over a large period. Although there are number of difficulties to be worked out to achieve prolonged gastric retention, a large number of companies are focusing toward commercializing this technique.

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