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Review Article

Floating Drug Delivery System: A Novel Approach

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ABSTRACT

Floating drug delivery system are designed to prolong the gastric residence time after oral administration at particular site and controlling the release of drug for achieving the controlled plasma level as well as improving bioavailability. They provide local delivery to specific regions like stomach and proximal small intestine and shows better bioavailability and improved therapeutic activity and substantial benefit to patients. They offer several advantages over conventional dosage forms. Effervescent and Non-effervescent are two classes of floating drug delivery system and can formulate either in single unit dosage form or in multiple unit dosage form.

INTRODUCTION

Oral delivery of drugs is by far the most preferable route of drug delivery due to the ease of administration, low cost of therapy, patient compliance and flexibility in formulation etc. Oral sustained drug delivery formulations show some limitations connected with the gastric emptying time. Variable and too rapid gastrointestinal transit could result in incomplete drug release from the device into the absorption window leading to diminished efficacy of the administered dose [1]. Gastro retentive drug delivery systems are the systems which are retained in the stomach for a longer period of time and thereby improve the bioavailability of drugs that are preferentially absorbed from upper GIT [2]. The drug bioavailability of pharmaceutical dosage forms is influenced by various factors. One of the important factors is the gastric residence time (GRT) of these dosage forms. The gastric emptying process from the stomach to small intestine generally lasts from a few minutes to 12 h. This variability leads to an unpredictable bioavailability of an orally administered dosage form [3]. The relatively brief gastric emptying time in humans, which normally averages 2–3 h through the major absorption zone (stomach or upper part of the intestine), can result in incomplete drug release from the drug delivery system leading to diminished efficacy of the administered dose [4].

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Gastroretensive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste and improves solubility for drugs that are less soluble in a high pH environment. It has applications also for local drug delivery to the stomach and proximal small intestines. Gastro retention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patients [5]. The identification of new diseases and the resistance shown towards the existing drugs called for the introduction of new therapeutic molecules. In response, a large number of chemical entities have been introduced, of which some have absorption all over the gastrointestinal tract (GIT), some have absorption windows (i.e. absorption sites, especially the upper part of the small intestine) and some drugs have poor solubility in intestinal media. The drugs belonging to the second and third categories and the drugs which are required for local action in the stomach, require a specialized delivery system. All the above requirements can be met and effective delivery of the drugs to the absorption window, for local action and for the treatment of gastric disorders such as gastro-oesophageal reflux, can be achieved by floating drug delivery systems (FDDS) [6].

Basic Gastrointestinal Tract Physiology [7-8]

Basically stomach is divided into 3 regions: fundus, body, and antrum (pylorus). The

proximal part made of fundus and body acts as a reservoir for undigested material, the antrum is the main site for mixing motions and act as a pump for gastric emptying by propelling actions. Gastric emptying occurs during fasting as well as fed states. The pattern of motility is however distinct in the 2 states. During the fasting state an interdigestive series of electrical events take place, which cycle both through stomach and intestine every 2 to 3 hours. This is called the interdigestive myloelectric cycle or migrating myloelectric cycle (MMC) which is further divided into following 4 phases.

1. Phase I (basal phase) lasts from 40 to 60 minutes with rare contractions.
2. Phase II (preburst phase) lasts for 40 to 60 minutes with intermittent action potential and contractions. As the phase progresses the intensity and frequency also increases gradually.
3. Phase III (burst phase) lasts for 4 to 6 minutes. It includes intense and regular contractions for short period. It is due to this wave that all the undigested material is swept out of the stomach down to the small intestine. It is also known as the housekeeper wave.
4. Phase IV lasts for 0 to 5 minutes and occurs between phases III and I of 2 consecutive cycles.

After the ingestion of a mixed meal, the pattern of contractions changes from fasted to that of fed state. This is also known as digestive motility pattern and comprises continuous contractions as in phase II of fasted state. These contractions result in reducing the size of food particles (to less than 1 mm) which are propelled toward the pylorus in a suspension form. During the fed state onset of MMC is delayed resulting in slowdown of gastric emptying rate.

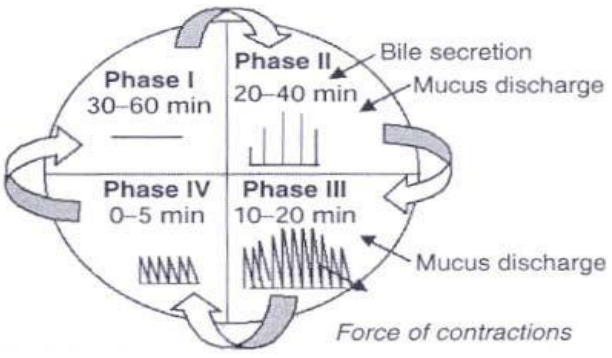

Figure 1: Motility pattern in GIT

Floating drug delivery system (FDDS) [9]

FDDS have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of fluctuations in plasma drug concentration. The floating sustained release dosage forms present most of the characteristics of hydrophilic matrices and are known as hydrodynamically balanced systems (HBS) since they are able to maintain their low apparent density while the polymer hydrates and builds a gelled barrier at the outer surface. The drug is released progressively from the swollen matrix, as in the case of conventional hydrophilic matrices. These forms are expected to remain buoyant on the gastric contents without affecting the intrinsic rate of emptying because their bulkdensity is lower than that of the gastric contents. Among the different hydrocolloids recommended for floating formulations, cellulose ether polymers are most popular, especially hydroxypropyl methylcellulose (HPMC). Fatty material with a bulk density lower than one may be added to the formulation to decrease the water intake rate and increase buoyancy.

Mechanism of floating systems [10]

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 co-administration of gastric emptying delaying drugs. Among these the floating dosage forms are the most commonly used. Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents (Fig. 2A), the drug is released slowly at the desired rate from the system. After release of drug, the residual system is eliminated from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration.

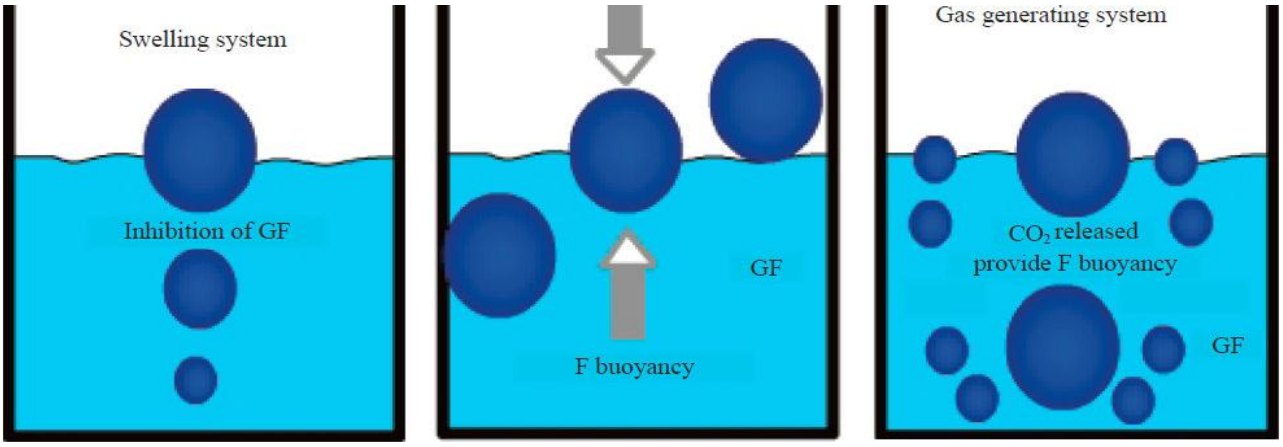

Figure 2: Mechanism of floating systems

Table 1: Marketed products of FDDS [29]

Brand Name	Delivery System	Drug Dose	Company Name
Val release®	Floating Capsule	Diazepam (15mg)	Hoffmann-LaRoche
Topalkan®	Floating liquid alginate preparation	Al-Mg Antacid	Pierre Fabre Drug, France
Conviron®	Colloidal gel forming FDDS	Ferrous sulphate	Ranbaxy, India
Cytotech®	Bilayer floating capsule	Misoprostol (100µg/200µg)	Pharmacia, USA
Cifran OD®	Gas generating floating form	Ciprofloxacin(1gm)	Ranbaxy, India
Liquid Gaviscon®	Effervescent floating liquid alginate preparation	Al hydroxide (95mg), Mg Carbonate (358mg)	GlaxoSmithKline, India
Madopar HBS	Floating CR capsule	Levodopa & Benserazide	Roche product, USA

However, besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention effect, a minimal level of floating force (F) is also required to maintain the buoyancy of the dosage form 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 a submerged object. The object floats better if F is on the higher positive side (Fig. 2B). This apparatus helps in optimizing FDDS with respect to stability and sustainability of floating forces produced in order to prevent any unforeseeable variations in intragastric buoyancy.

F = *F*buoyancy – *F*gravity = (Df – Ds) g v

Where, F = total vertical force

Df = fluid density

Ds = object density

v = volume and

g = acceleration due to gravity

Advantages of floating drug delivery system [28]

1. The Floating systems are advantageous for drugs meant for local action in the Stomach e.g. Antacids.
2. Acidic substances like aspirin cause irritation on the stomach wall when come in contact with it. Hence FDDS may be useful for the administration of aspirin and other similar drugs.
3. The Floating systems are advantageous for drugs absorbed through the stomach. E.g. Ferrous salts, antacids.
4. Administration of prolongs release floating dosage forms, tablet or capsules, will result in dissolution of the drug in the gastric fluid. They dissolve in the gastric fluid and then will be available for absorption in the small intestine after emptying of the stomach contents.
5. It is therefore expected that a drug will be fully absorbed from floating dosage forms if it remains in the solution form even at the alkaline pH of the intestine.
6. FDDS provides advantages such as the delivery of drugs with narrow absorption windows in the small intestinal region.

7. Certain types of drugs can benefit from using FDDS. These include:
   a) Drugs acting locally in the stomach.
   b) Drugs those are primarily absorbed in the stomach.
   c) Drugs those are poorly soluble at an alkaline pH
   d) Drugs with a narrow window of absorption.
   e) Drugs absorbed rapidly from the GI tract.
   f) Drugs those degrade in the colon

Disadvantages of floating drug delivery systems [6, 27]

1. Floating system is not feasible for those drugs that have solubility or stability problem in GIT.
2. These systems require a high level of fluid in the stomach for drug delivery to float and work efficiently.
3. Drugs such as Nifedipine which is well absorbed along the entire GIT and which undergoes first pass metabolism may not be desirable.
4. Drugs which are irritants to gastric mucosa are not suitable.
5. Drug substances that are unstable in the acidic environment of the stomach are not suitable candidates to be incorporated in the system.
6. The dosage form should be administered with a full glass of water (200-250ml).
7. These systems do not offer significant advantages over the conventional dosage forms for drugs which get absorbed throughout gastrointestinal tract.

Suitable drug candidates for gastroretention [8]

In general, appropriate candidates for GRDDS are molecules that have poor colonic absorption but are characterized by better absorption properties at the upper parts of the GIT:

1. Narrow absorption window in GI tract e.g., riboflavin and levodopa.
2. Primarily absorbed from stomach and upper part of GI tract, e.g., calcium supplements, chlordiazepoxide and cinnarazine.
3. Drugs that act locally in the stomach, e.g., antacids and misoprostol.
4. Drugs that degrade in the colon, e.g., ranitidine HCl and metronidazole.
5. Drugs that disturb normal colonic bacteria e.g., amoxicillin trihydrate.

Drugs unsuitable for gastro retentive drug delivery [8]

1) Drugs that have very limited acid solubility e.g. phenytoin etc.
2) Drugs that suffer instability in the gastric environment e.g. erythromycin etc.
3) Drugs intended for selective release in the colon e.g. 5- amino salicylic acid and corticosteroids etc.

Factors affecting gastric retention [8][24]

The gastric retention time (GRT) of dosage form is controlled by several factors that affect their efficacy as a gastroretentive system.

- **Density** – GRT is a function of dosage form buoyancy that is dependent on the density.
- **Size** – Dosage form units with a diameter of more than 9.5mm are reported to have an increased GRT.
- **Shape of dosage form** – Tetrahedron and ring-shaped devices with a flexural modulus of 48 and 22.5 kilopounds per square inch (KSI) are reported to have better GRT. 90% to 100% retention at 24 hours compared with other shapes.
- **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 coadministration 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.
- **Fed or unfed state** – Under fasting conditions, the 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.
- **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.
- **Caloric content** – GRT can be increased by four to 10 hours with a meal that is high in proteins and fats.
- **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.

- **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.
- **Age** – Elderly people, especially those over 70, have a significantly longer GRT.
- **Posture** – GRT can vary between supine and upright ambulatory states of the patient.
- **Concomitant drug administration**– Anticholinergics like Atropine and Propantheline, Opiates like Codeine and Prokinetic agents like Metoclopramide and Cisapride.
- **Biological factors** – Diabetes and Crohn's disease.

Approaches to design floating dosage [26]

1. 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 24 popcorn, poprice, and polystyrol have been used as drug carriers. Sugarpolymeric 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.

2. 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 disadvantages of single-unit formulations. Single unit formulations are associated with problems such as sticking together or being obstructed in gastrointestinal tract, which may have a potential danger of producing irritation. Multiple unit systems avoid the all-or-none gastric emptying nature of single unit systems. It reduces the intersubject variability in absorption and the probability for dose dumping is lower. 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.

Classification of Floating Drug Delivery System [11]

A. Effervescent system
  a. Gas generating system
  b. Volatile liquid containing system

B. Non-effervescent System
  a. Colloidal gel barrier system.

b. Alginate beds.
c. Hollow microspheres / Microballons.
d. Intragastric Floating Drug Delivery Device / Microporous compartment system

A. Effervescent Floating Dosage Forms:

These are matrix types of systems prepared with the help of swellable polymers (methylcellulose and chitosan) and various effervescent compounds (sodium bicarbonate, tartaric acid, and citric acid). They are formulated in such a way that when come in contact with acidic gastric contents, CO2 liberate and gas entrapped in swollen hydrocolloids which provides buoyancy to the dosage forms [12, 13] .

a. Gas-generating Systems:

These buoyant delivery systems utilize effervescent reactions between carbonate/bicarbonate salts and citric/tartaric acid to liberate CO_2 which gets entrapped in the gellified hydrocolloid layer of the systems thus decreasing its specific gravity and making it to float over chime [14, 15].

b. Volatile liquid containing systems:

The GRT of a drug delivery system can be sustained by incorporating an inflatable chamber, which contains a liquid (like ether, cyclopentane), that gasifies at body temperature to cause the inflatation of the chamber in the stomach. The device may also consist of a bio-erodible plug made up of PVA, Polyethylene, etc. that gradually dissolves and causing the inflatable chamber to release gas and collapse after a predetermined time to permit the spontaneous ejection of the inflatable systems from the stomach [16, 17].

B. Non-effervescent Floating Dosage Forms:

The non-effervescent FDDS works on the mechanism of polymer swelling, bioadhesion of the polymer to mucosal layer of GI tract. The most commonly used excipients for the preparations of non-effervescent FDDS are gel forming or swellable cellulose type hydrocolloids, polysaccharides and matrix-forming polymers like polycarbonate, polyacrylate, polymethacrylate, and polystyrene. The formulation method includes simple approach of thoroughly mixing of the drug and the gel-forming hydrocolloid. After oral administration this dosage form swells in contact with gastric fluids and attains bulk density of less than 1. The air entrapped within the swollen matrix imparts buoyancy to the dosage form, so formed swollen gel-like structure acts as a reservoir and allows sustained release of drug through the gelatinous mass [12, 16, 18].

a. Colloidal gel barrier system:

A system that contains drug with gel-forming hydrocolloids meant to remain buoyant on the stomach content. This prolongs GRT and maximizes the amount of drug that reaches its absorption sites in the solution form for ready absorption. This system incorporates a high level of one or more gel forming highly swellable cellulose type hydrocolloids.e.g. HEC, HPMC, NaCMC, Polysacchacarides and matrix forming polymer such as polycarbophil, polyacrylates and polystyrene, incorporated either in tablets or in capsule. On coming in contact with gastric fluid, the hydrocolloid in the system hydrates and forms a colloidal gel barrier around the gel surface. The air trapped by the swollen polymer maintains a density less than unity and confers buoyancy to these dosage forms [17, 18].

b. Alginate beads:

Multi-unit floating dosage forms have been developed from freeze-dried calcium alginate. Spherical beads of approximately 2.5 mm in diameter can be prepared by dropping sodium alginate solution into aqueous solution of calcium chloride, causing the precipitation of calcium alginate. The beads are then separated, snap-frozen in liquid nitrogen, and freeze-dried at -40ºC for 24 hours, leading to the formation of a porous system, which can maintain a floating force for over 12 hours [16, 18].

c. Hollow microspheres / Microballons:

It is prepared by a novel emulsion solvent diffusion method. The ethanol/dichloromethane solution of the drug and an enteric acrylic polymer was poured into an agitated solution of Poly Vinyl Alcohol (PVA) that was thermally controlled at 40ºC. The gas phase is generated in the dispersed polymer droplet by the evaporation of dichloromethane formed and internal cavity in the microsphere of the polymer with drug [18, 19].

d. Intragastric / Microporous compartment system:

The system composed of a drug reservoir encapsulated in a microporous compartment having pores on top and bottom surfaces. The peripheral walls of the reservoir compartment were completely sealed to prevent any physical contact of the undissolved drug with walls of the stomach [19, 20]. Novel levodopa gastro retentive dosage form based on unfolding polymeric membranes which combines extended

dimensions with high rigidity. It was folded into a large size gelatin capsules. *In vitro* studies showed that unfolded form reached within 15 minutes after administration and it was confirmed *in vivo* in beagle dogs. The unfolded form was maintained for at least 2 hours. It was concluded that this dosage form could improve therapy of different narrow absorption window drugs. However, there are possibilities of the polymeric films to get stuck in the oesophagus causing extreme discomfort to the patient or drug related injuries and repeated administration of rigid dosage form may result in gastric obstruction [20][21].

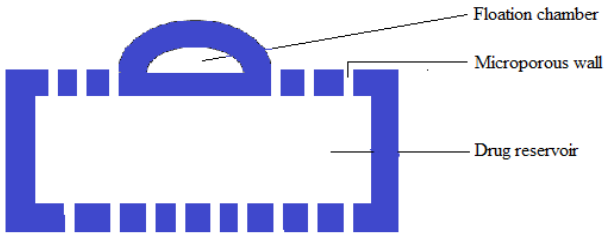

Figure 3: It shows intra-gastric floating drug delivery device

Applications of floating drug delivery systems [22]

- ***Enhance 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:*** Oral CR formulations are encountered with problems such as gastric residence time in the GIT. These problems can be overcome with the HBS systems which can remain in the stomach for long periods and have a bulk density <1 as a result of which they can float on the gastric contents. These systems are relatively larger in size and passing from the pyloric opening is prohibited.
- ***Site–specific drug delivery systems:*** These systems are particularly advantageous for drugs those are specifically absorbed from the stomach or the proximal part of the small 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, there by 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.
- ***Reduce fluctuations of drug concentration:*** Continuous input of the drug following controlled release gastro-retentive dosage form administration produces blood drug concentrations within a narrower range compared to the immediate release dosage forms. Thus, fluctuations in drug effects are minimized and concentration dependent adverse effects that are associated with peak concentrations can be prevented. This feature is of special importance for drugs with a narrow therapeutic index.

Evaluation Techniques [23]

In vitro evaluation of floating tablets

Evaluation was performed to assess the physicochemical properties and release characteristics of the developed formulations.

I. Pre-compression parameters

a) Angle of Repose (Θ)

The frictional forces in a loose powder or granules can be measured by angle of repose. This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane. The granules were allowed to flow through the funnel fixed to a stand at definite height (h). The angle of repose was then calculated by measuring the height and radius of the heap of granules formed.

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

Where Θ = angle of repose
h = height of the heap
r = radius of the heap

Table 2: It shows relationship between angle of repose and powder flow

Angle of Repose	Powder Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very Poor

b) Compressibility Index

The flowability of powder can be evaluated by comparing the bulk density (ρo) and tapped density (ρt) of powder and the rate at which it packed down. Compressibility index was calculated by;

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

Where **ρo** = Bulk density g/ml
ρt = Tapped density g/ml.

II. Post-compression parameters

a) Shape of Tablets

Compressed tablets were examined under the magnifying lens for the shape of the tablet.

b) Tablet Dimensions

Thickness and diameter were measured using a calibrated varnier caliper. Three tablets of each formulation were picked randomly and thickness was measured individually.

c) Hardness

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It was expressed in kg/cm2. Three tablets were randomly picked and hardness of the tablets was determined.

d) Friability test

The friability of tablets was determined by using Roche Friabilator. It was expressed in percentage (%). Ten tablets were initially weighed (W initial) and transferred into friabilator. The friabilator was operated at 25rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again (W_{final}). The % friability was then calculated by;

$$\%F = 100\ (1\text{-}W0/W)$$

% Friability of tablets less than 1% was considered acceptable.

e) Tablet Density

Tablet density was an important parameter for floating tablets. The tablet would floats only when its density was less than that of gastric fluid (1.004). The density was determined using following relationship.

$$V = \pi r^2 h$$

d = m/v
v = volume of tablet (cc)
r = radius of tablet (cm)
h = crown thickness of tablet (g/cc)
m = mass of tablet

f) Weight Variation Test

Ten tablets were selected randomly from each batch and weighed individually to check for weight variation. A little variation was allowed in the weight of a tablet by U.S Pharmacopoeia. The following percentage deviation in weight variation was shown in Table 3.

Table 3: It shows percentage deviation in weight variation

Average weight of a tablet	Percentage deviation
130 mg or less	10
>130 mg and <324 mg	7.5
324 mg or more	5

g) Buoyancy / Floating Test

The time between introduction of dosage form and its buoyancy on the simulated gastric fluid and the time during which the dosage form remain buoyant were measured. The time taken for dosage form to emerge on surface of medium called Floating Lag Time (FLT) or Buoyancy Lag Time (BLT) and total duration of time by which dosage form remain buoyant is called Total Floating Time (TFT).

h) Swelling Study

The swelling behavior of a dosage form was measured by studying its weight gain or water uptake. The dimensional changes could be measured in terms of the increase in tablet diameter and/or thickness over time. Water uptake was measured in terms of percent weight gain, as given by the equation.

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

Wt = Weight of dosage form at time t.
W0 = Initial weight of dosage form.

i) *In-vitro* Dissolution Test [25]

A. *In-vitro* dissolution test is generally done by using USP apparatus with paddle and GRDDS is placed normally as for other conventional tablets. But sometimes as the vessel is large and paddles are at bottom, there is much lesser paddle force acts on floating dosage form which generally floats on surface. As floating dosage form not rotates may not give proper result and also not reproducible results. Similar problem occur with swellable dosage form, as they are hydrogel may stick to surface of vessel or paddle and gives irreproducible results. In order to prevent such problems, various types of modification in dissolution assembly made are as follows.

B. To prevent sticking at vessel or paddle and to improve movement of dosage form, method suggested is to keep paddle at surface and not too deep inside dissolution medium.

C. Floating unit can be made fully submerged, by attaching some small, loose, non- reacting material, such as few turns of wire helix, around dosage form. However this method can inhibit three dimensional swelling of some dosage form and also affects drug release.

D. Other modification is to make floating unit fully submerged under ring or mesh assembly and paddle is just over ring that gives better force for movement of unit.

E. Other method suggests placing dosage form between 2 ring/meshes.

F. In previous methods unit have very small area, which can inhibit 3D swelling of swellable units, another method suggest the change in dissolution vessel that is indented at some above place from bottom and mesh is place on indented protrusions, this gives more area for dosage form.

G. Inspite of the various modifications done to get the reproducible results, none of them showed co-relation with the in-vivo conditions. So a novel dissolution test apparatus with modification of Rossett-Rice test apparatus was proposed.

CONCLUSION

Drug absorption in the gastrointestinal tract is a highly variable procedure and prolonging gastric retention of the dosage form extend the time for drug absorption. They can be delivered efficiently thereby capitalizing on their absorption and enhancing absolute bioavailability. FDDS promises to be a potential approach for gastric retention. FDDS is advantageous for drugs that are absorbed primarily in the upper segment of GI tract i.e. stomach, duodenum and jejunum when compared to the conventional dosage forms. The increasing sophistication of 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.

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