INTERNATIONAL RESEARCH JOURNAL OF PHARMACY
www.irjponline.com ISSN 2230 – 8407
Review Article

A REVIEW ON FLOATING TYPE GASTRORETENTIVE DRUG DELIVERY SYSTEM

Pallavi Pal*, Vijay Sharma, Lalit Singh
Department of Pharmacy Shri Ram Murti Smarak college of Engineering and Technology, (Pharmacy), Bareilly, India

Article Received on: 05/02/12 Revised on: 11/03/12 Approved for publication: 19/04/12

*Email: ppallavi676@gmail.com

ABSTRACT
Oral controlled release delivery systems are programmed to deliver the drug in predictable time frame that will increase the efficacy and minimize the adverse effects and increase the bioavailability of drugs. Oral route is considered mostnatural, uncomplicated, convenient and safe due to its ease of administration, patient acceptance, and cost-effective manufacturing process.Floating Drug delivery system are designed to prolong the gastric residence time after oral administration, at particular site and controlling the release of drug especially useful for achieving controlled plasma level a swell as improving bioavailability Several approaches are currently being used to prolong the GRT, including floating drug delivery systems (FDDS), also known as hydrodynamically balanced systems (HBS), swelling and expanding systems, high-density systems, and other delayed gastric emptying devices
Keywords: Floating Drug delivery system, Oral controlled release hydrodynamically balanced systems (HBS), gastric residence time.

INTRODUCTION

Oral controlled release drug delivery have recently been of increasing interest in pharmaceutical field to achieve improved therapeutic advantages, such as ease of dosing administration, patient compliance and flexibility in formulation. Drugs that are easily absorbed from gastrointestinal tract (GIT) and have short half-lives are eliminated quickly from the systemic circulation. Frequent dosing of these drugs is required to achieve suitable therapeutic activity. After oral administration, such a drug delivery would be retained in the stomach and release the drug in a controlled manner, so that the drug could be supplied continuously to its absorption sites in the gastrointestinaltract (GIT).[1]Prolonged gastric retention improves bioavailability, increases the duration of drug release, reduces drug waste, and improves the drug solubility that are less soluble in a high pH environment[2] Gastroretentive drug delivery is an approach to prolong gastric residence time, thereby targeting site-specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effects. Gastroretentive dosage forms can remain in the gastric region for long periods and hence significantly prolong the gastric retention time (GRT) of drugs. Over the last few decades, several gastroretentive drug delivery approaches being designed and developed, including: high density (sinking) systems that is retained in the bottom of the stomach[3], low density (floating) systems that causes buoyancy in gastric fluid[4,5,6], mucoadhesive systems that causes bioadhesion to stomach mucosa[7], unfoldable, extendible, or swellable systems which limits emptying of the dosage forms through the pyloric sphincter of stomach[8,9], superporous hydrogel systems[10] magnetic systems[11] etc. The current review deals with floating type gastroretentine drug delivery system.

BASIC GASTROINTESTINAL TRACT PHYSIOLOGY

The stomach is divided into 3 regions anatomically: fundus, body, and antrum pylorus. The proximal part is the fundus and the body acts as a reservoir for undigested material, where as the antrum is the main site for mixing motions and acts as a pump for gastric emptying by propelling actions. Gastric emptying occurs during fasting as well as fed states but the pattern of motility is distinct in the 2 states. During the fasting state an interdigestive series of electrical events take place, which cycle through both stomach and intestine every 2 to 3 hours. This is called the interdigestive myloelectric cycle or migrating myloelectric cycle (MMC), which is divided into following 4 phases.[12]

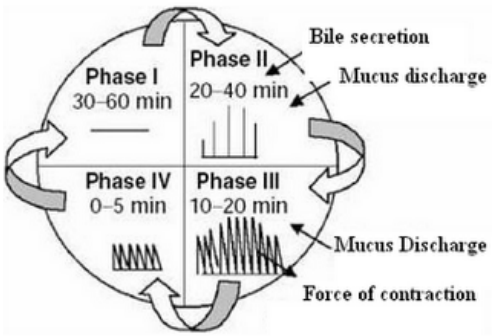

Figure1: Schematic Representation of Interdigestive Motility

Phase I: This period lasts about 30 to 60 minutes with no contractions.
Phase II: This period consists of intermittent contractions that increase gradually in intensity as the phase progresses, and it lasts about 20 to 40 minutes. Gastric discharge of fluid and very small particles begins later in this phase.
Phase III: This is a short period of intense distal and proximal gastric contractions (4-5 contractions per minute) lasting about 10 to 20 minutes these contractions, also known as ‘‘house-keeper wave,’’ sweep gastric contents down the small Intestine.
Phase IV: This is a short transitory period of about 0 to 5 minutes, and the contractions dissipate between the last part of phase III and quiescence of phase I.

NEED FOR GASTRORETENTION

- Drugs that are absorbed from the proximal part of the gastrointestinal tract (GIT).
- Drugs that are less soluble or that degrade at the alkaline pH.
- Drugs that are absorbed due to variable gastric emptying time.

- Local or sustained drug delivery to the stomach and proximal small intestine to treat certain conditions.
- Particularly useful for the treatment of peptic ulcers caused by H.Pylori infections.[12]

FACTORS CONTROLLING GASTRIC RETENTION OF DOSAGE FORMS

There are several factors that can affect gastric emptying of an oral dosage form which include density, size and shape of dosage form, feeding state, biological factors such as age, gender, posture, body mass index, disease state etc.

1.Effect Of Dosage Form Size & Shape

Small size tablets are emptied from the stomach during the digestive phase while large size units are expelled during the house keeping waves found that floating unit with a diameter equal or less than 7.5 mm had larger gastric residence time (GRT) compared to nonfloating units but the GRT was similar for floating and non-floating units having a large diameter of 9.9 mm. They found that GRT of nonfloating units were much more variable and highly dependent on their size which are in the order of small < medium < large units. Moreover, in supine subjects, size influences GRT of floating and non- floating form. Tetrahedron and ring shaped devices have a better GRT as compared with other shapes.[13,14]

2. Density

The density of a dosage form also affects the gastric emptying rate and determines the location of the system in the stomach. Dosage forms having a density lower than the gastric contents can float to the surface, while high density systems sink to bottom of the stomach [16]. Both positions may isolate the dosage system from the pylorus. A density of < 1.0 gm/ cm3 is required to exhibit floating property.[15]

3. Gender, Posture & Age

Generally females have slower gastric emptying rates than male. The effect of posture does not have any significant difference in the mean gastric retention time (GRT) for individuals in upright, ambulatory and supine state. In case of elderly persons, gastric emptying is slowed down.[16]

4. Effect of Food & Specific Gravity

To float FDDS in the stomach, the density of dosage form should be less than gastric content i.e.1.0 g/cm3. Since, the bulk density of a dosage form is not a sole measure to describe its buoyant capabilities because the magnitude of floating strength may vary as a function of time and gradually decrease after immersing dosage form into fluid as a result of development of its hydrodynamic equilibrium. Various studies have shown the intake of food as main determinant of gastric emptying rather than food. Presence of food is the most important factor effecting GRT than buoyancy. GRT is significantly increased under fed condition since onset of MMC is delayed. Studies show that GRT for both floating and non-floating single unit are shorter in fasted subjects (less than 2 hour), but significantly prolonged after meal (around 4 hour).[12]

5. Nature of Meal & Frequency of Food

Feeding of indigestible polymers or fatty acid salts can change the motility pattern of the stomach to fed state, to increase gastric emptying rate and prolonging the drug release. Diet rich in protein and fat can increase GRT by 4-10 hours.[12]

6. Type of Formulation

Multiple unit formulation show a more predictable release profile and insignificant impairing of performance due to failure of units, allow co-administration of units with different release profile or containing incompatible substances and permit a large margin of safety against dosage form failure compared with single unit dosage form.[13]

FUTURE POTENTIAL

- Floating dosage form offers various future potential as evident from several recent publications. The reduced fluctuations in the plasma level of drug results from delayed gastric emptying. Drugs that have poor bioavailibility because of their limited absorption to the upper gastrointestinal tract can be delivered efficiently thereby maximizing their absorption and improving their absolute bioavalability.
- Buoyant delivery system considered as a beneficial strategy for the treatment of gastric and duodenal cancers.
- The floating concept can also be utilized in the development of various anti-reflux formulations.
- Developing a controlled release system for the drugs, which are potential to treat the Parkinson's disease.
- To explore the eradication of Halico-bector pylori by using the narrow spectrum antibodies. [14]

CLASSIFICATION OF GASTRORETENTIVE DRUG DELIVERY SYSTEM

The main approaches that have been examined for gastroretentive dosage forms (GRDFs) are: low density of GRDF that cause buoyancy above gastric fluid (Floating system), high density which retain the dosage form in the body of stomach, concomitant administration of drugs or excipients which slow the motility of the GIT, bioadhesion to gastric mucosa, swelling to a large size which prevents emptying of dosage form through the pyloric sphincter.[17,18]

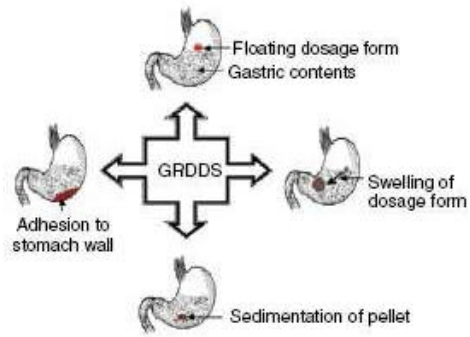

Figure 2: Types of Gastroretentive Drug Delivery System

FLOATING DRUG DELIVERY SYSTEMS

A floating dosage form is useful for drugs acting locally in the proximal gastrointestinal tract. These systems are also useful for drugs that are poorly soluble (or) unstable in intestinal fluids. The floating properties of these systems help to retain in the stomach for a long time. Various attempts have been made to develop floating systems, which float on the gastric contents and release drug molecules for the desired time period. After the release of a drug, the remnants of the system are emptied from the stomach.

Based on the mechanism of buoyancy, two different technologies have been used in development of floating drug delivery systems. These include:

a) Effervescent system.

b) Non- Effervescent system.

A) EFFERVESCENT SYSTEMS

Effervescent systems[10] include use of gas generating agents, carbonates (e.g. Sodium bicarbonate) and other organic acid

(e.g. citric acid and tartaric acid) present in the formulation to produce carbon dioxide (CO_2) gas, thus reducing the density of the system and making it float on the gastric fluid. An alternative is the incorporation of matrix containing portion of liquid, which produce gas that evaporate at body temperature.

These effervescent systems further classified into two types:

1) Gas generating systems.
2) Volatile liquid or Vacuum containing systems.

1) Gas Generating Systems

a) Tablets

Intragastric Single layer Floating Tablets or Hydrodynamically Balanced System (HBS)

These formulations have bulk density lower than gastric fluids and thus float in the stomach that increases the gastric emptying rate for a prolonged period,[19] (Fig.3). These are formulated by intimately mixing the gas (CO_2) generating agents and the drug within the matrix tablet. The drug is released slowly at a desired rate from the floating system and the residual system is emptied from the stomach after the complete release of the drug. This leads to an increase in the gastric residence time (GRT) and a better control over fluctuations in plasma drug concentration.

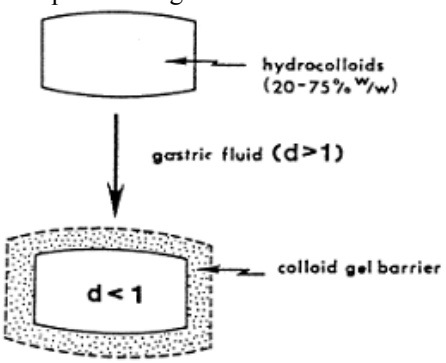

Figure 3: Intragastric Single Layer Floating Tablet

Intragastric Bilayer Floating Tablets

These are also compressed tablets[19] containing two layers :

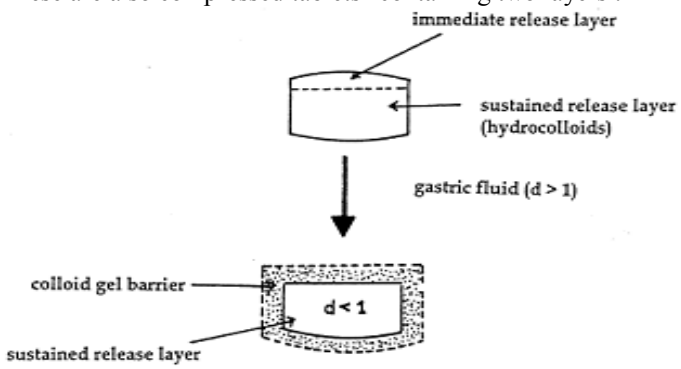

Figure 4: Intragastric bilayer floating tablet

- Immediate release layer and
- Sustained release layer.

b) Floating Capsules

These floating capsules[20] are formulated by filling with a mixture of sodium alginate and sodium bicarbonate. The systems float as a result of the generation of CO_2 that was trapped in the hydrating gel network on exposure to an acidic environment.

c) Multiple Unit Type Floating Pills

These multiple unit type floating pills[20] are sustained release pills, known as seeds, which are surrounded by two layers (Fig.5). The outer layer is of swellable membrane layer while the inner layer consists of effervescent agents. This system sinks at once and then it forms swollen pills like balloons which float as they have lower density, when it is immersed in the dissolution medium at body temperature. The lower density is due to generation and entrapment of CO_2 within the system.

Key: (a) conventional SR pills; (b) effervescent layer; (c) swellable layer; (d) expanded swellable membrane layer; (e) surface of water in the beaker (37^0C).

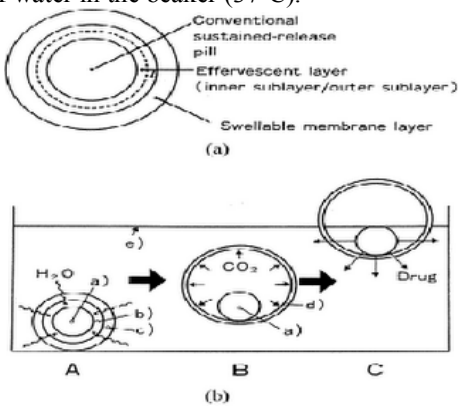

Figure 5: (a) A multiple-unit oral floating dosage system. (b) Stages of floating mechanism: (A) penetration of water; (B) generation of CO_2 and floating; (C) dissolution of drug.

d) Floating System with Ion-Exchange Resins

Floating system using bicarbonate loaded ion exchange resin was made by mixing the beads with 1M sodium bicarbonate solution, and then the semi-permeable membrane is used to surround the loaded beads to avoid sudden loss of CO_2. On contact with gastric contents an exchange of bicarbonate and chloride ions takes place that results in generation of CO_2 that carries beads towards the top of gastric contents and producing a floating layer of resin beads.[20]

2) **Volatile liquid or Vacuum Containing Systems**

a) **Intragastric Floating Gastrointestinal Drug Delivery System**

This system floats in the stomach because of floatation chamber, which is vacuum or filled with a harmless gas or air, while the drug reservoir is encapsulated by a microporous compartment,[19] (Fig.6).

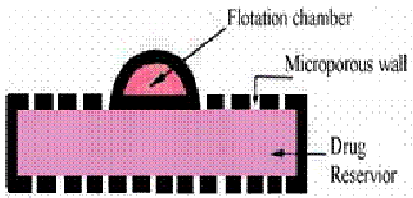

Figure 6: Intragastric Floating Gastrointestinal Drug Delivery Device

b) **Inflatable gastrointestinal delivery systems**

Inflatable chamber are incorporated, which contains liquid ether that gasifies at body temperature to inflate the chamber in the stomach. These systems are fabricated by loading the inflatable chamber with a drug reservoir, which can be a drug, impregnated polymeric matrix, then encapsulated in a gelatin capsule, [19](Fig.7). After oral administration, the capsule dissolves to release the drug reservoir together with

the inflatable chamber. The inflatable chamber automatically inflates and retains the drug reservoir compartment in the stomach. The drug is released continuously from the reservoir into gastric fluid.

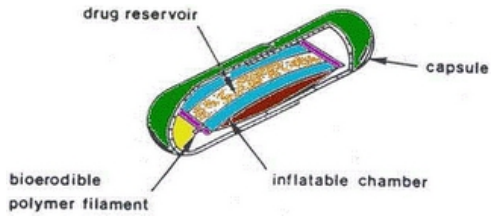

Figure 7: Inflatable Gastrointestinal Delivery System

c) **Intragastric Osmotically Controlled Drug Delivery System**

It is comprised of an osmotic pressure controlled drug delivery device and an inflatable floating support in a biodegradable capsule. In the stomach, the capsule quickly disintegrates to release the intragastirc osmotically controlled drug delivery device. The inflatable support inside forms a deformable hollow polymeric bag that contains a liquid that gasifies at body temperature to inflate the bag. The osmotic pressure controlled drug delivery device consists of two components; drug reservoir compartment and an osmotically active compartment. The floating support is also made to contain a bioerodible plug that erodes after a predetermined time to deflate the support. The deflated drug delivery system is then emptied from the stomach.

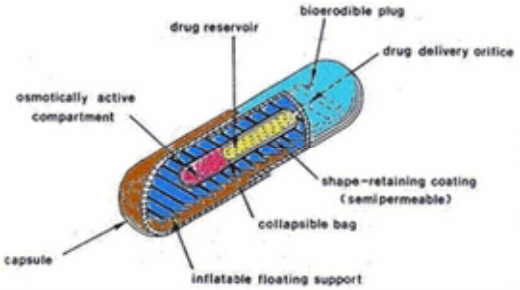

Figure 8: Intragastric Osmotically Controlled Drug Delivery System

B) NON-EFFERVESCENT SYSTEMS

Non-effervescent floating drug delivery systems are normally prepared from gel-forming or highly swellable cellulose type hydrocolloids, polysaccharides or matrix forming polymers like polyacrylate, polycarbonate, polystyrene and polymethacrylate. In one approach, intimate mixing of drug with a gel forming hydrocolloid which results in contact with gastric fluid after oral administration and maintain a relative integrity of shape and a bulk density less than unity within the gastric environment [21]The air trapped by the swollen polymer confers buoyancy to these dosage forms. Excipients used most commonly in these systems include hydroxypropyl methylcellulose (HPMC) polyacrylates, polyvinyl acetate, carbopol, agar, sodium alginate, calcium chloride, polyethylene oxide and polycarbonates [22]. This system can be further divided into the sub-types:

Single Layer Floating Tablets

These are formulated by intimate mixing of drug with a gel forming hydrocolloid, that swells on contact with gastric fluid and maintain bulk density of less than unity. The air trapped by the swollen polymer confers buoyancy to these dosage forms.[19]

Bilayer Floating Tablets

A bilayer tablet contain two layer one immediate release layer which release initial dose from system while the another sustained release layer absorbs gastric fluid, forming an impermeable colloidal gel barrier on its surface, and maintain a bulk density of less than unity and thereby it remains buoyant in the stomach.[19]

Alginate Beads

Talukdar and Fassihi[32] recently developed a multiple-unit floating system based on cross-linked beads. They were made by using Ca^{++} and low methoxylated pectin (anionic polysaccharide) or Ca2+ low methoxylated pectin and sodium alginate. In this approach, generally sodium alginate solution is dropped into aqueous solution of calcium chloride and causes the precipitation of calcium alginate. These beads are then separated and dried by air convection and freeze drying, leading to the formulation of a porous system, which can maintain a floating force for over 12 hrs. These beads improve gastric retention time (GRT) more than 5.5 hrs [22, 23]

Hollow Microspheres

Hollow microspheres (microballons), loaded with drug in their outer polymer shells were prepared by a novel emulsion-solvent diffusion method (Fig.9). The ethanol: dichloromethane solution of the drug and an enteric acrylic polymer was poured into an agitated aqueous solution of PVA that was thermally controlled at 40^0C. The gas phase generated in dispersed polymer droplet by evaporation of dichloromethane formed an internal cavity in microsphere of polymer with drug. The microballons floated continuously over the surface of acidic dissolution media containing surfactant for more than 12 hours in vitro.[19]

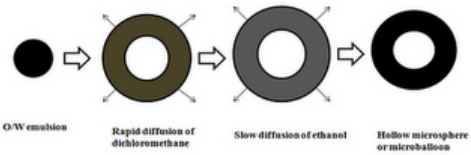

Figure 9: Formulation Of Floating Hollow Microsphere Or Microballoon

TABLE: DRUGS AVAILABLE AS FLOATING DRUG DELIVERY SYSTEM [19,24,25,26,27,28]

S.NO:	Dosage Form	Drugs Used
1.	Floating Tablets/Pills	Acetaminophen, Acetylsalisylic acid, Amoxicillin trihydrate, Ampicillin, Atenolol, Cinnazirine, captopril, Cinnarazine, carbamazepine, Chlorpheniramine maleate, Ciprofolxacin, Dia
2.	Floating Capsules	Benserazide, Chlordiazepoxide HCl, Diazepam, Furosemide, Nicardipine, Misoprostal, L-Dopa, Propranolol HCl, Pepstatin,
3.	Floating Microspheres/ Floating beads	Amoxicillin, Aspirin, Cholestyramine, Dipyridamol, Griseofulvin, Ibuprofen, Ketoprofen, p-nitroaniline, Piroxicam
4.	Floating Granules	Diclofenac sodium, Indomethacin, Meloxicam, Nicardepine, Prednisolone, Riboflavin.
5.	Powders	Several basic drugs.
6.	Films	Albendazole, Cinnarizine.

ADVANTAGES OF FLOATING DRUG DELIVERY SYSTEM

For any particular medicament or class of medicament hydrodynamically balanced system can be used. It is not restricted to medicaments, which are principally absorbed from the stomach.The HBS are advantageous for drugs absorbed through the stomach e.g. ferrous salts and for drugs meant for local action in the stomach and treatment of peptic ulcer disease e.g. antacids.

Medicaments administered utilizing the sustained release principle of HBS has independent efficacy of the site of absorption of the particular medicaments.

Dissolution of the drug in gastric fluid will occur by administration of a prolonged release floating dosage form tablet or capsule. The dissolved drug is available for absorption in the small intestine, after emptying of the stomach contents, therefore it is expected that a drug will be fully absorbed from the floating dosage form if it remains in solution form even at alkaline p^H of the intestine.

Many drugs categorized as once-a-day delivery have been demonstrated to have suboptimal absorption due to dependence on the transit time of the dosage form, making traditional extended release development challenging. Therefore, a system designed for longer gastric retention will extend the time within which drug absorption can occur in the small intestine.

Certain type of diarrhoea, poor absorption is expected when there is vigorous intestinal movement and a short transit time under such circumstances it may be advantageous to keep the drug in floating condition in stomach to get a relatively better response.

Gastric retention will provide advantages such as the delivery of drugs with narrow absorption windows in the small intestinal region. [19]

LIMITATIONS

Require a higher level of fluids in the stomach.

Not suitable for Drugs that Have solubility problems in gastric fluid.

e.g. phenytoin Cause G.I irritation.

e.g. NSAIDS are unstable in acidic environment.

Drugs intended for selective release in the colon E.g. 5-amino salicylic acid and corticosteroids etc

The floating systems in patients with achlorhydria can be questionable in case of swellable system.

Retention of high density systems in the antrum part under the migrating waves of the stomach is questionable.

The mucus on the walls of the stomach is in a state of constant renewal, resulting in unpredictable adherence.

The mucus on the walls of the stomach is in a state of constant renewal, resulting in unpredictable adherence.

EVALUATION OF GASTRORETENTIVE DOSAGE FORM

Different studies indicate that pharmaceutical dosage forms exhibiting gastric residence in vitro floating behaviour exhibit prolonged gastric residence in vivo. However, it should be noted that good in vitro floating behaviour alone is not sufficient proof of efficient gastric retention in vivo. The effects of the simultaneous presence of food and the complex motility of the stomach are difficult to assess. Obviously, only *in vivo* studies can provide definite proof that prolonged gastric residence is obtained:

A) IN VITRO AND IN VIVO EVALUATION PARAMETERS OF STOMACH SPECIFIC FDDS [13,29]

a) Buoyancy Lag Time

The floating behaviour was evaluated with resultant weight measurements. The experiment was carried out in two different media like deionised water and simulated meal, in order to monitor possible difference. The results showed that higher molecular weight polymers with slower rate of hydration had enhanced floating behaviour and which was more in simulated meal medium compared to deionised water [39,30]

b) Floating Time

The test for floating time is usually performed in simulated gastric fluid or 0.1 mole.lit-1 HCl maintained at 37^0 C, by using USP dissolution apparatus containing 900 ml of 0.1 molar HCl as the dissolution medium. 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.[32,31]

c) Specific Gravity / Density

Density can be determined by the displacement method using Benzene as displacement medium.[33]

d) Resultant Weight

Now we know that bulk density and floating time are the main parameters for describing buoyancy. But only single determination of density is not sufficient to describe the buoyancy because density changes with change in resultant weight as a function of time. For example a matrix tablet with bicarbonate and matrixing polymer floats initially by gas generation and entrapment but after some time, some drug is released and simultaneously some outer part of matrixing polymer may erode out leading to change in resultant weight of dosage form. The magnitude and direction of force/resultant weight (up or down) is corresponding to its buoyancy force (Fbuoy) and gravity force (Fgrav) acting on dosage form.[33]

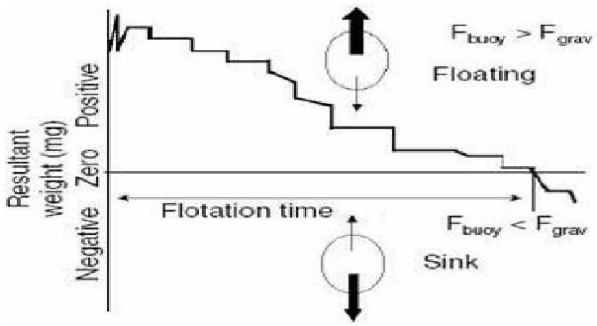

Figure 10: Resultant Weight Versus Flotation Time

F = Fbuoy - FgravF = Df g V – Ds g V F = (Df – Ds) g V
F = (Df – M/V) g V

Where,

F = resultant weight of object
Df = Density of Fluid
DS = Density of Solid object
g = Gravitational force
M = Mass of dosage form
V = Volume of dosage form

So when Ds, density of dosage form is lower, F force is positive gives buoyancy and when it is Ds is higher, F will negative shows sinking

e) Drug loading, Drug Entrapment Efficiency, Particle Size Analysis, Surface Characterization (for floating microspheres and beads)

Drug loading is assessed by crushing an accurately weighed sample of beads or microspheres in a mortar and adding it to the appropriate dissolution medium which is then centrifuged, filtered and analyzed by a variety of analytical methods like spectrophotometry. The percentage drug loading is calculated by dividing the amount of drug in the sample by the weight of total beads or microspheres. The particle size and the size distribution of the beads or microspheres are determined in the dry state by optical microscopy. The external an cross-sectional morphology (surface characterization) is carried out by scanning electron microscopy (SEM).

ii) Swelling systems

a) Swelling Index

After immersion of swelling dosage form into SGF at 370C, dosage form is removed out at regular interval and dimensional changes are measured in terms of increase in tablet thickness / diameter with time.

b) Water Uptake

It is an indirect measurement of swelling property of swellable matrix. Here dosage form is removed out at regular interval and weight changes are determined with respect to time. So it is also termed asWeight Gain.

Water uptake = WU = (Wt – Wo) * 100 / Wo

Where, Wt = weight of dosage form at time t

Wo = initial weight of dosage form

B) IN-VITRO DISSOLUTION TESTS

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.

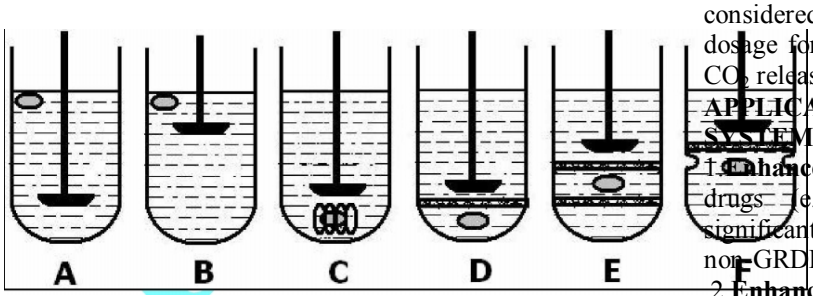

Figure 11: dissolution of floating dosageform

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.[31,34]

C) IN-VIVO EVALUATION

a) Radiology

X-ray is widely used for examination of internal body systems. Barium Sulphate is widely used. So, $BaSO_4$ is incorporated inside dosage form and X-ray images are taken at various intervals to view GR.

b) Scintigraphy

Similar to X-ray, emitting materials are incorporated into dosage form and then images are taken by scintigraphy. Widely used emitting material is ^{99}Tc.

c) Gastroscopy

Gastroscopy is peroral endoscopy used with fiber optics or video systems. Gastroscopy is used to inspect visually the effect of prolongation in stomach. It can also give the detailed evaluation of GRDDS.

d) Magnetic Marker Monitoring

In this technique, dosage form is magnetically marked with incorporating iron powder inside, and images can be taken by very sensitive bio-magnetic measurement equipment. Advantage is that it is radiation less and so not hazardous.

e) Ultrasonography

Used sometimes, not used generally because it is not traceable at intestine.

f) ^{13}C Octanoic Acid Breath Test

^{13}C Octanoic acid is incorporated into GRDDS. In stomach due to chemical reaction, octanoic acid liberates CO_2 gas which comes out in breath. The important Carbon atom which will come in CO_2 is replaced with ^{13}C isotope. So time up to which $^{13}CO_2$ gas is observed in breath can be considered as gastric retention time of dosage form. As the dosage form moves to intestine, there is no reaction and no CO_2 release. So this method is cheap.[31]

APPLICATIONS OF FLOATING DRUG DELIVERY SYSTEM

1.**Enhanced Bioavailability** The bioavailability of some drugs (e.g. riboflavin and Levodopa) CR-GRDF is significantly enhanced in comparison to administration of non-GRDF CR polymeric formulations.[35]

2.**Enhanced First-Pass Biotransformation** When the drug is presented to the metabolic enzymes (cytochrome P-450, in particular CYP-3A4) in a sustained manner, the presystemic metabolism of the tested compound may be considerably increased rather than

by a bolus input.[22]

3.**Sustained Drug Delivery/Reduced Frequency of Dosing** The drugs having short biological half life, a sustained and slow input from FDDS may result in a flip-flop

pharmacokinetics and it reduces the dose frequency. This feature is associated with improved patient compliance and thus improves the therapy.[22]

4.**Targeted Therapy for Local Ailments in the Upper GIT** The prolonged and sustained administration of the drug from FDDS to the stomach may be useful for local therapy in the stomach.

5.**Reduced Fluctuations of Drug Concentration** The fluctuations in plasma drug concentration 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.[35]

6.**Improved Receptor Activation Selectivity** FDDS reduces the drug concentration fluctuation that makes it possible to obtain certain selectivity in the elicited pharmacological effect of drugs that activate different types of receptors at different concentrations.[22]

7.**Reduced Counter-activity of the Body** Slow release of the drug into the body minimizes the counter activity leading to higher drug efficiency.

8.**Extended Time Over Critical (Effective) Concentration** The sustained mode of administration enables extension of the time over a critical concentration and thus enhances the pharmacological effects and improves the clinical outcomes.

9. **Minimized Adverse Activity at the Colon** Retention of the drug in GRDF at stomach minimizes the amount of drugs that reaches the colon and hence prevents the degradation of drug that degraded in the colon.

10. **Site Specific Drug Delivery** A floating dosage form is a widely accepted approach especially for drugs which have limited absorption sites in upper small intestine.

CONCLUSION

This review summarizes the in vitro techniques, in vivo studies to evaluate the performance and application of floating systems, and applications of these systems. A novel floating controlled-release drug delivery system was formulated in an effort increase the gastric retention time of the dosage form and to control drug release. One of the most feasible approaches for achieving a prolonged and predictable dug delivery profiles in the gastrointestinal tract is to control the gastric residence time, using gastro retentive dosage forms that will provide us with new and important therapeutic options.

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