Review Article

A Brief Review on Floating Bilayer Tablet as a Convenient Gastroretentive Drug Delivery System

Sarvesh D Parsekar*, Shruti Prabhu, Amitha Shetty, Mohd Azharuddin and AR. Shabaraya

Department of Pharmaceutics, Srinivas College of Pharmacy, Valachil, Mangalore Karnataka, India.

ABSTRACT

Drug absorption in the gastrointestinal tract is a highly variable process and prolonging gastric retention of the dosage form extends the time for drug absorption. Incorporation of the drug in a controlled release gastroretentive dosage forms (CR-GRDF) which can remain in the gastric region for several hours would significantly prolong the gastric residence time of drugs and improve bioavailability, reduce drug waste, and enhance the solubility of drugs that are less soluble in high pH environment. Controlled gastric retention of solid dosage form may be achieved by the mechanisms of floatation.

Bilayer floating drug delivery system is combined principle of bilayer tablet as well as floating mechanism. Bilayer floating tablet is new era for the successful development of controlled release formulation along with various features to provide a way of successful drug delivery system. The purpose of this paper is to review the principle of floating drug delivery system, current technology used in the development of same as well as summarizes the applications, advantages and disadvantages, characterization, evaluation methods and future potential for bilayer floating tablets.

Keywords: Gastric retention, high pH, Bilayer Floating drug delivery system, characterization.

INTRODUCTION

Modified release dosage form is a general term used to describe the dosage forms having drug release features based on time, course and/or location and which are designed to accomplish therapeutic or convenience objectives not offered by conventional or immediate release forms.[1, 2, 3]

The main goal of any drug delivery system is to achieve desired concentration of the drug in blood or tissue, which is therapeutically effective and non-toxic for a prolonged period. Development of oral controlled-release systems has been a challenge to formulation scientists because of their inability to restrain and localize the system in the targeted area of the gastrointestinal tract. This approach is bedilled with several physiological difficulties such as inability to restrain and locate the controlled drug delivery system within the desired region of the GIT due to variable gastric emptying and motility. Furthermore, the relatively brief gastric emptying time (GET) in humans which normally averages 2-3 h through the major absorption zone, i.e., stomach and upper part of the intestine can result in incomplete drug release from the drug delivery system leading to reduced efficacy of the administered dose therefore, control of placement of a drug delivery system (DDS) in a specific region of the GI tract offers advantages for a variety of important drugs characterized by a narrow absorption window in the GIT or drugs with a stability problem**.** These considerations have led to the development of a unique oral controlled release dosage form with gastroretentive properties. After oral administration, such a drug formulation would be retained in the stomach and release the drug there in a controlled and prolonged manner, so that the drug could be supplied continuously to its absorption sites in the upper gastrointestinal tract.

The concept of floating drug delivery system (FDDS) was described in literature as early as 1968. Gastric floating drug delivery systems (GFDDS) offer numerous advantages over the gastric retentive systems. These systems have a density lower than the gastric fluids and thus 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 a desired rate from the stomach. Floating dosage forms are oral dosage forms of tablets, capsules, or micro beads and contain hydrocolloids that allow floating by swelling thereby prolong the residence time of dosage form GIT. Gastric emptying is a complex process and one of the most important obstacles in the better absorption and enhances bioavailability of oral drug delivery system.[4]

Stomach anatomy[4, 5, 6, 8, 9, 11, 12]

The main function of the stomach is to process and transport food. It serves as a short-term storage reservoir, allowing a rather large meal to be consumed quickly. Vigorous contractions of gastric smooth muscle mix and grind foodstuffs with gastric secretions, resulting in liquefaction of food. As food is liquefied in the stomach, it is slowly released into the small intestine for further processing. Anatomically the 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, whereas 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 inter digestive series of electrical events take place, which cycle both through stomach and intestine every 2 to 3 hours. This is called the inter digestive myloelectric cycle or migrating myloelectric cycle (MMC), which is further divided into 4 phases. Anatomy of stomach illustrated in figure1.

Needs for gastric retention

Drugs that are absorbed from the proximal part of the gastrointestinal tract (GIT).

Drugs that are less soluble or are degraded by the alkaline pH they encounters at the lower part of GIT.

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.[16]

Ideal drug characteristics for GRDDS[4, 5, 6, 8, 9, 11, 12]

1. Drugs acting locally in the stomach, e.g. Antacids and drugs for H. Pylori viz., Misoprostol
2. Drugs that are primarily absorbed in the stomach and upper part of GI, e.g. Amoxicillin, Calcium Supplements, Chlordiazepoxide and Cinnarazine
3. Drugs that is poorly soluble at alkaline pH, e.g. Furosemide, Diazepam, Verapamil HCL, Chlordiazepoxide etc.
4. Drugs with a narrow window of absorption in GIT, e.g. Riboflavin, Para Amino benzoic Acid, Cyclosporine, Methotrexate, Levodopa etc.
5. Drugs which are absorbed rapidly from the GI tract. e.g. Metonidazole, tetracycline.
6. Drugs that degrade or unstable in the colon. e.g. Captopril, Ranitidine HCL, Metronidazol, Metformin HCl.
7. Drugs that disturb normal colonic microbes, e.g. Amoxicillin Trihydrate, antibiotics against Helicobacter pylori.

Drugs unsuitable for GRDDS

Drugs which are unsuitable for GRDDS are as follows,

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.

Approaches for the gastric retention

A number of approaches have been used to increase the GRT of a dosage form in stomach by employing a variety of concepts explained in chart 1.

Advantages of floating drug delivery system[4, 5, 6, 8, 9, 11, 12]

1. The principle of HBS can be used for any particular medicament or class of medicament.
2. The HBS formulations are not restricted to medicaments, which are principally absorbed from the stomach. Since it has been found that these are equally efficacious with medicaments which are absorbed from the intestine e.g. Chlorpheniramine maleate.
3. 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.
4. The efficacy of the medicaments administered utilizing the sustained release principle of HBS has been found to be independent of the site of

absorption of the particular medicaments.

5. Administration of a prolonged release floating dosage form tablet or capsule will result in dissolution of the drug in gastric fluid.
6. When there is vigorous intestinal movement and a short transit time, poor absorption is expected under such circumstances it may be advantageous to keep the drug in floating condition in stomach to get a relatively better response.
7. The delivery of drugs with narrow absorption windows in the small intestinal region.
8. Many drugs categorized as once-a-day delivery have been demonstrated therefore, a system designed for longer gastric retention will extend the time within which drug absorption can occur in the small intestine.
9. Certain types of drugs can benefit from using gastro retentive devices. These include:

- Drugs acting locally in the stomach;
- Drugs those are primarily absorbed in the stomach;
- Drugs those are poorly soluble at an alkaline pH;
- Drugs with a narrow window of absorption;
- Drugs absorbed rapidly from the GI tract; and
- Drugs those degrade in the colon.

Disadvantages of floating drug delivery system

1. There are certain situations where gastric retention is not desirable. Aspirin and non-steroidal anti-inflammatory drugs are known to cause gastric lesions, and slow release of such drugs in the stomach is unwanted.
2. Thus, drugs that may irritate the stomach lining or are unstable in its acidic environment should not be formulated in gastro retentive systems.
3. Furthermore, other drugs, such as Isosorbide dinitrate, that are absorbed equally well throughout the GI tract will not benefit from incorporation into a gastric retention system.

Factors affecting floating drug delivery system

Various attempts have been made to retain the dosage form in the stomach as a way of increasing the retention time. These attempts include use of 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. Most of these approaches are influenced by a number of factors that affect their bioavailability and efficacy of the gastro retentive system:

• Density

gastric retention time (GRT) is a function of dosage form buoyancy that is dependent on the density.

• Size

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

• 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.

• 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.

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 patients.

•**Concomitant drug administration**
anticholinergics like atropine and propantheline, opiates like codeine and prokinetic agents like metoclopramide and cisapride; can affect floating time.

• **Biological factors**
diabetes and Crohn's disease, etc.

Mechanism of floating system[5, 6, 8, 9]
While the system is floating on the gastric the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal. To measure the floating force kinetics, a novel apparatus for determination of resultant weight has been in the literature. The apparatus operates by measuring continuously the force equivalent to F (as a function of time) that is required to main submerged object. The object floats better if F is on the higher positive side. This apparatus helps in optimizing FDDS with respect to stability and durability of floating forces produced in order to prevent the drawbacks of unforeseeable intragastric buoyancy capability variations.

$$F = F_{buoyancy} - F_{gravity} = (Df - Ds)\, gv$$

Where, F= total vertical force, Df = fluid density,
Ds = object density, v = volume and g = acceleration due to gravity.

Introduction to floating bilayer tablet [4, 5, 7, 10, 13]

Bilayer tablets contain immediate and sustained release layer. Immediate release layer delivers the initial dose, it contains superdisintegrants which increase drug release rate and start onset of action whereas sustained release layer float due to gas generating agent and releases drug at sustained manner for prolonged period. Bilayer tablets are composed of two layers of granulation compressed together. They have appearance of a sandwich because the edges of each layer are exposed. They have the appearance of a sandwich because the edges of each layer are exposed.

Compression cycle for bilayer tablet
Bi-layer tablets are tablet, made by compressing two different granulations fed into a die succession, one on top of another, in layers. Each layer comes from a separate feed frame with individual weight control. Rotary tablet press can be set up for two or three layers. More are possible but the design becomes very special. Figure 6 represents compression cycle of bi-layer tablet.
Bilayer tablet press explained in figure No 2.
Release pattern of bilayer tablet explained in fig No. 3

Advantages of bilayer floating tablets [4, 5, 7, 20, 21]

1. This system provide sustained drug delivery like HBS dosage form modify gastric residence time as this system remains in stomach for many hours.
2. It maintains optimum therapeutic window as a result drug delivery with controlled released is achieved.
3. Better patient compliance is achieved due to its ease of administration.
4. It maintains constant blood level.
5. Site specific drug delivery is achieved for the drugs such as furosemide and riboflavin which are formulated as floating system.
6. Over all other oral routes these are microbiologically and chemically stable.

7. Due to higher dose precision and lesser content variation they are the most compatible oral dosage form.
8. They offer the most flexible dosage form.
9. Better suited for large scale production.
10. Masking of bitter taste and bad odour by coating.
11. Swallowing of tablets is easy.
12. Lesser cost compared to other oral dosage forms.
13. These are the most lighter and compact

Disadvantages of bilayer floating tablets

1. Increased fluid levels are required in the stomach so that the system float properly.
2. Drugs with solubility and stability problem in stomach cannot be formulated.
3. Irritation producing drugs on gastric mucosa can be formulated as floating dosage form.
4. Capping is the major problem in bilayer tablets.
5. Separation of layer occurs due to insufficient bonding and reduction in yield occurs.
6. Hardness is other problem.
7. There are chances of cross contamination between two layers.
8. Due to low density and amorphous nature of some drugs compacts do not form because they resist compression.
9. There is less control over weight of individual layer.
10. Swallowing problem in case of children and unconscious patients.
11. Bioavailability problem occurs in case of poor wetting and less dissolution properties.
12. Sometimes encapsulation or coating is required for the drugs that are oxygen sensitive, bitter tasting and with bad odour.

Ideal properties for bilayer tablet dosage form [22]

1) Drug must be released in reproducible and expected manner in bilayer tablet.
2) Chemical and physical stability is must.
3) During product shelf life chemical stability is main concern.
4) In product identification dosage form should be free from visual defects such as cracking, Discolouration.

Polymers used in floating drug delivery[5, 6, 11, 12]

Sustained Release Polymers are HPMC K100M, HPMC K15M, HPMC ELV, Polycarbonate, Polyethylene glycol, Sodium alginate, Carbopol, Eudragit.
Effervescent Generating System: Citric and Tartaric Acid, Sodium Bicarbonate, Citroglycine.
Polymers which increase buoyancy: Ethyl cellulose
Polymers which decrease release: Talc, Magnesium Stearate, Dicalcium Phosphate.
Polymers which increase release: Mannitol, Lactose.
Inert Polymers: Long Chain Fatty Alcohol, Fatty Acid, Beeswax.
Polymers with low density: Foam powder of polypropylene.

Methodology used for bilayer floating tablets[5, 6, 11, 12.]

1. Oros ® Push Pull Technology
2. L-Oros Tm Technology
3. DUROS Technology
4. Elan Drug Technologies' Dual Release Drug Delivery System
5. EN SO TROL Technology
6. Rotab Bilayer
7. Geminex Technology.

1. Oros ® Push Pull Technology:
Two or three layer system a drug layer and push layer. Drug layer contain drug with other agents and due to this drug is less soluble. Sometimes suspending agent and osmotic agent are also added. The tablet core is surrounded by semi permeable membrane.

2. L-Oros Tm Technology
Alza developed L-OROS system due to solubility problem. The system contain a drug in dissolved state in a lipid soft gel product which is produced first and then barrier membrane, after which osmotic membrane and semi permeable membrane coat is applied and is then drilled out through external orifice.

3. DUROS Technology
This technology is also known as miniature drug dispensing system which works like a miniature syringe and release small quantity of drug consistently over a period of time .There is an outer cylindrical titanium alloy reservoir which has high impact strength due to which drug molecules inside it are protected from enzymes.

4. Elan Drug Technologies' Dual Release Drug Delivery System

The DUREDASTM Technology provides combination release of drugs together and different release pattern of single drug i.e. it provides sustained release as well as immediate release. This technology provides various advantages i.e. two drug components provide tailored release and its another benefit is that it consist of bilayered tablet technology in which it contain modified as well as immediate release pattern in one tablet. In these different controlled release formulations are combined together.

5. EN SO TROL Technology

An integrated approach is used by Shire laboratory for drug delivery system which focus on identification and incorporation of enhancer which is identified to form optimized dosage form in controlled release system. By this enhancement in solubility is achieved.

6. RoTab Bilayer

RoTab bilayer when using is switched to production mode. Dose and compression force is automatically regulated by adjusting filling speed and die table. Hardness is also regulated when required.

7. Geminex Technology

In this drug delivery system at different times more than one drug can be delivered. This technology basically increases the therapeutic efficacy of the drug by decreasing its side effects. It is useful both to industry as well as patient as in single tablet it provides delivery of drug at different rates.

Characterization of bilayer floating tablets[19]

In-vitro evaluation of floating tablets Evaluation was performed to assess the physicochemical properties and release characteristics of the developed formulations.

Pre-compression parameters

Angle of Repose

In powder frictional forces can be measured with the help of angle of repose. Angle of repose is the maximum angle which is possible between surface of pile of powder and horizontal plane i.e. height.

$$\tan\Theta = h/r$$

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

Where Θ = Angle of repose, h= height of pile, r = radius of pile.

Compressibility Index

The propensity of the powder to be compressed is measured by compressibility index and it also helps in measurement of settling property and interparticulate interaction.

Compressibility index (%) = ρt – ρo* 100 / ρt

Where ρt = Tapped density gram/ml, ρo = Bulk density gram/ml.

Bulk Density

It is denoted by ρb and is defined as mass of powder divided by bulk volume (The United States Pharmacopeial Convention Stage 6 Harmonization Official December 1, 2012, 616.).

Tapped Density

An increase in bulk density which is attained after mechanical tapping in measuring cylinder is called as tapped density.

Tapped density= Weight of powder taken/ Tapped Volume

Hausner Ratio

The propensity of the powder to be compressed is measured by Hausner ratio. Interparticulate interaction and settling property can be measured by Hausner ratio.

Hausner ratio= Tapped density/ Bulk density

Hausner ratio= Vo/Vf

Where, Vo= Unsettled apparent volume, Vf= Final tapped volume.

Particle Size Distribution

Particle size distribution was done by sieving method.

Post-compression parameters[19]

Tablet Thickness

In this three tablets are randomly taken and then their thickness and diameter are measured by Vernier calliper or by using calibrated screw gauze.

Weight Variation Test

Twenty tablets are selected and weighed individually. Then the average weight and standard deviation is calculated. Test passes when not more than two tablets deviate from average weight.

Hardness

Expressed in kg/cm^2 and it is checked using Monsanto hardness tester by randomly picking three tablets. Hardness helps in knowing

ability of the tablet to withstand mechanical shock during handling of tablets.

Friability
Ten tablets are selected and weighed and then placed in friabilator apparatus which rotate at 25 rpm speed for 4 minutes. After 4 minutes tablets are weighed again.
%F= [1-(Wt/W)]*100 where W– Initial weight of tablet, Wt - Weight of tablet after revolution.
If % Friability of tablets is less than 1% is considered acceptable.

Tablet Density
t is an important parameter in case of floating tablets. If density is less than (1.004) gastric fluid, than only the tablets will float. It is calculated using formula:
V=πr2h, d = m/v, r = Radius of tablet, h = crown thickness (g/cc), m = Mass of tablet.

Disintegration Time
In this one tablet is placed in disintegration apparatus containing buffer 0.1N Hcl or PBS pH 6.8 and test is carried out at 37oC. The time taken by tablet to
Disintegrate is noted as disintegration time.

***In Vitro* Dissolution Studies**
Dissolution study is performed using USP paddle apparatus by maintaining optimum temperature i.e., 370C at 50 rpm rotational speed. At various time interval 5 ml sample is withdrawn and is replaced with same amount of buffer.

Floating Lag Time
It is the time interval taken by the tablets to start floating. It should be less than one minute. It is measured by dissolution test apparatus containing 0.1 N Hcl (900ml).

Floating Time
It is the total time taken by which the tablets remain floating in the media.

Drug Content Uniformity
Ten tablets are taken and powdered equivalent weight of drug dose is taken and is transferred to volumetric flask and then buffer is added and absorbance is determined using U.V spectrophotometer.

Swelling Study
Initially tablet is weighed (W1) and placed in a glass beaker, containing 200 mL of 0.1 N HCl, maintained in a water bath at 37 ± 0.5 _C. At different time intervals, the tablet is removed and the excess of liquid is carefully removed by a filter paper. The swollen tablet is reweighed (W2). The swelling index (SI) is calculated using the formula

$$SI= W_t -W0/W0*100$$

W_t= (Weight of swollen tablet), W0= (Initial weight of tablet).

***In-vivo* evaluation**

a) **Radiology**
X-ray is widely used for examination of internal body systems. Barium Sulphate is widely used Radio Opaque Marker. So, BaSO4 is incorporated inside dosage form and X-ray images are taken at various intervals to view gastric retention.

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 99Tc.

c) **Gastroscopy**
Gastroscopy is peroral endoscopy used with fiber optics or video systems. Gastroscopy is used o 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 of this method 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) **13C Octanoic Acid Breath Test**
13C Octanoic acid is incorporated into GRDDS. In stomach due to chemical reaction, octanoic acid liberates CO2 gas which comes out in breath. The important Carbon atom which will come in CO2 is replaced with 13C isotope. So time up to which 13CO2 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 CO2 release. So this method is cheaper than other.

Recent advances[14, 15]

Strübing et al investigated the mechanism of floating and drug release behaviour of poly(vinyl acetate)- based floating tablets with membrane controlled drug delivery. Tablets containing propranolol HCl with Kollidon® SR as an excipient for direct compression and different Kollicoat® SR 30 D/Kollicoat® IR coats, varying from 10 to 20 mg polymer/cm2, were investigated with regard to drug release in 0.1 mol/l HCl. Furthermore, the onset of floating, the floating duration and the floating strength of the device were determined.

In addition, benchtop MRI studies of selected samples were performed. Coated tablets with a 10 mg polymer/cm2 SR/IR, and an 8.5: 1.5 coating exhibited the shortest lag-times prior to drug release and the onset of floating, and also the fastest increase in and the highest maximum values of the floating strength.

Jang et al prepared a gastro-retentive drug delivery system of DA-6034, a new synthetic flavonoid derivative, for the treatment of gastritis using an effervescent floating matrix system (EFMS). The therapeutic limitations of DA-6034 caused by its low solubility in acidic conditions were overcome by using the EFMS, which was designed to allow the tablets to float in gastric fluid and release the drug continuously. The release of DA-6034 from the tablets in acidic media was significantly improved by using EFMS, and this was attributed to the effect of the solubilizers and the alkalizing agent such as, sodium bicarbonate, used as gas generating agent. DA-6034 EFMS tablets showed enhanced gastro-protective effects in gastric ulcer-induced beagle dogs, indicating the therapeutic potential of EFMS tablets for the treatment of gastritis.

Marketed preparations

List of various floating gastroretentive marketed formulations is given in table no 1 below.

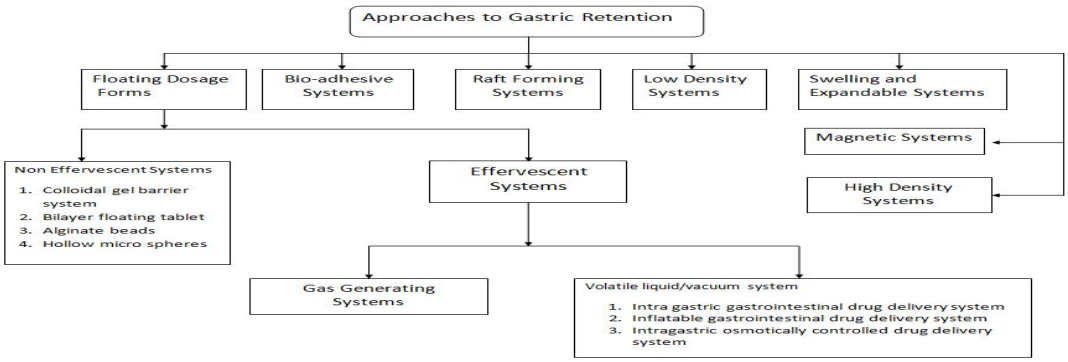
Future potential for bilayer floating tablets[17, 18]

Future prospects with respect to herbal drugs Herbal drug delivery is the emerging field in the pharmacy. The use of FBDDS for herbal medicament is the novel approach for the better delivery. The drug release profile has been a major focusing area for the pharmaceutical research scientists for the past two decades. The scientists are finding it a great opportunity to work on GI transit profiles. This has given rise to new products with substantial benefits to the patients. Now with the advent of FBDDS the products have been designed which could release drug for up to 12 or 24 hrs. Using bilayer floating approach combination of two herbal drugs can be also given for more therapeutic effect. Bilayer floating also provide the IR and SR concept for herbal drug as well. Bilayer floating tablets can be beneficial in hypertension and diabetes as immediate response can be achieved by using loading dose as one layer along with sustained release layer which will maintain the concentration of the drug in plasma for prolonged period of time.

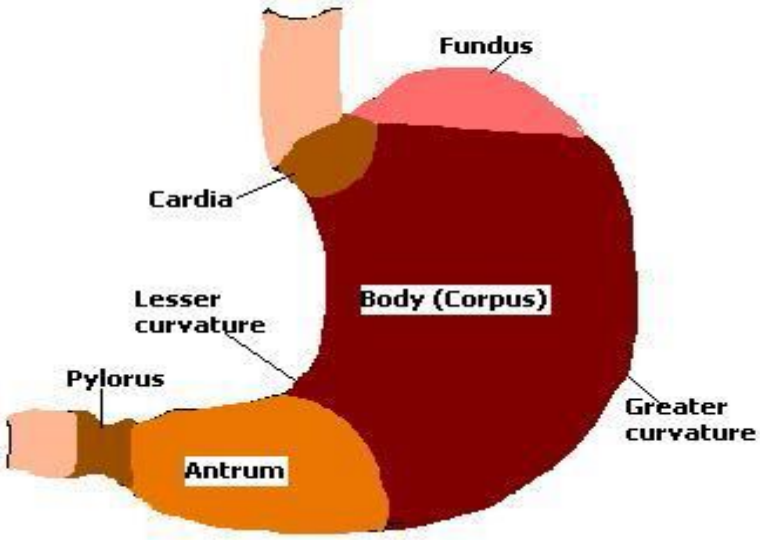
CONCLUSION

FBDDS approach may be used for various potential active agents with narrow absorption window, e.g. antiviral, antifungal and antibiotic agents (sulphonamides, quinolones, penicillins, cephalosporins, aminoglycosides and tetracyclines) which are absorbed from very specific regions of GI tract and whose development has been halted due to the lack of appropriate pharmaceutical technologies. So Pharmaceutical industries are trying to prepare one of the most economic and convetional dosage form, and Floating bilayer tablet is best then any other approaches. In addition, by continual supplying the drug to its most efficient site of absorption, the dosage form may allow for more effective oral use of peptide and protein drugs such as calcitonin, erythropoetin, vasopressin, insulin, low molecular weight heparin, and LHRH. Some of the unresolved critical issues related to the rational development of FBDDS include, the quantitative efficiency of floating delivery systems in the fasted and fed states and the correlation between prolonged GRT and SR/PK characteristics. However, we are as close as we have ever been to see a greater transition of gastric retention devices from developmental level to the manufacturing and commercial level.

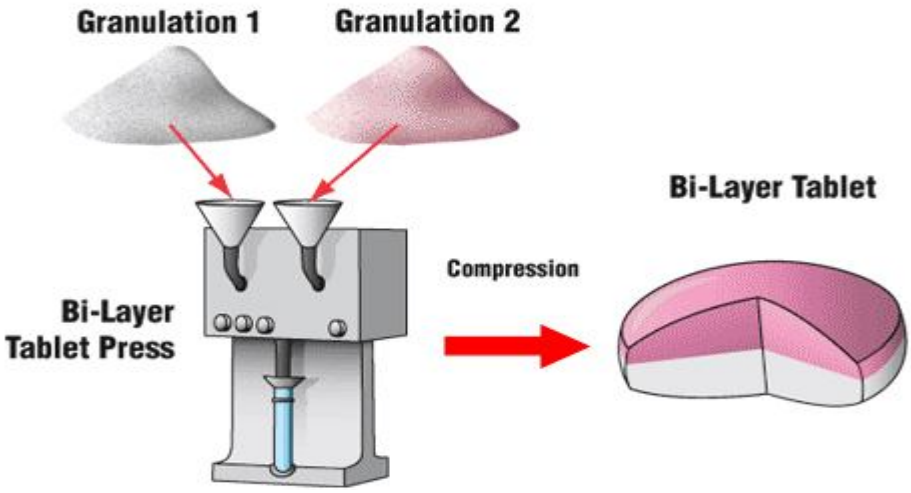
Chart 1

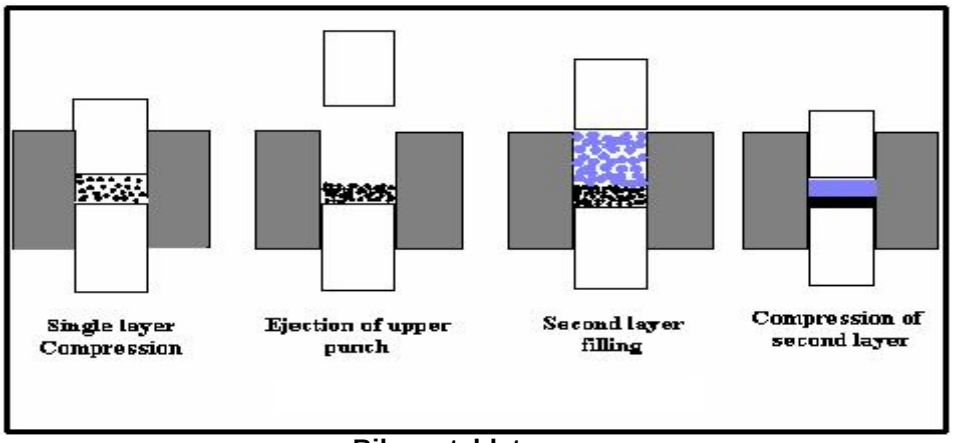


Approaches to gastric retention

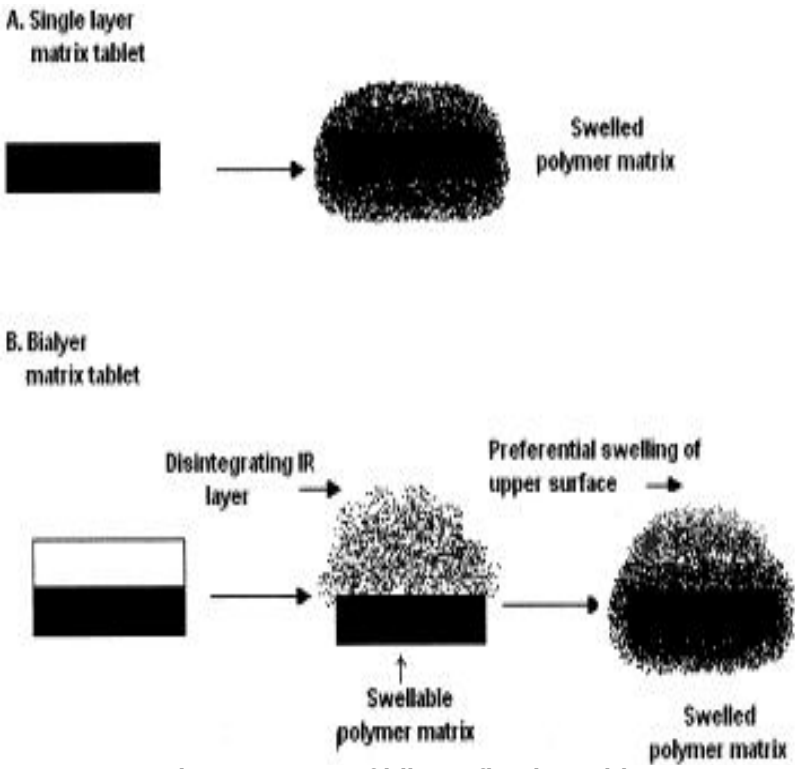


Anatomy of stomach





Bilayer tablet press



Release pattern of bilayer floating tablet

Table 1: List of various floating gastroretentive marketed formulations

S. No.	Drug	Brand name	Manufacturer
1.	Diazepam floating capsule	Valrelease®	Roche, USA
2.	Antacid preparation	Almagate Flot- Coat®	----------
3.	Aluminium- magnesium Antacid	Topalkan®	Pierre Fabre Drug, France
4.	Benserazide and L- Dopa	Madopar®	Roche products, USA
5.	Ciprofloxacin floating tablets	Cifran OD	Ranbaxy, India
6.	Effervescent floating liquid alginate preparation	Liquid Gaviscon®	Glaxo SmithKline, India
7.	Ferrous Sulphate colloidal gel forming FDDS	Conviron®	Ranbaxy, India
8.	Misoprostol bilayer floating capsule	Cytotec®	Pharmacia, USA

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