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Bilayer Floating Tablet Technology: An Overview



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ABSTRACT

Novel drug delivery system overcomes the physiological problems of gastric retention by decreasing fluctuations in blood drug concentration with consequent reduction in undesirable toxicity and poor efficiency. Incorporation of drug in controlled release gastroretentive dosage forms 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. Several approaches are currently utilized in the prolongation of GRT, including floating drug delivery system, swelling and expanding systems, polymeric bioadhesive systems, high density systems, modified shape systems and other delayed gastric emptying devices. Bilayer floating drug delivery systems exhibit a unique combination of floatation and bilayer which prolongs residence in the stomach. Floatation due to bulk density less than gastric fluids and so, remain buoyant in the stomach for a prolonged period of time, releasing the drug slowly at the desired rate from the system and increase the bioavailability of narrow absorption window drugs. Bilayer tablet is better than the traditionally used dosage forms suitable for sequential release of two drugs in combination it is also capable of separating two incompatible substances and also for sustained release.

INTRODUCTION

The oral route is considered as the most promising route of drug delivery. Conventional drug delivery system achieves as well as maintains the drug concentration within the therapeutically effective range needed for treatment, only when taken several times a day¹. This results in a significant fluctuation in drug levels. Recently, several technical advancements have led to the development of several novel drug delivery systems (NDDS) that could revolutionize method of medication and provide a number of therapeutic benefits². The most important objectives of these new drug delivery systems are: First, it would be single dose, which releases the active ingredient over an extended period of time. Second, it should deliver the active entity directly to the site of action, thus, minimizing or eliminating side effects. To overcome the limitations of conventional drug delivery system, bilayer floating tablets have been developed. Drugs that have narrow absorption window in the gastrointestinal tract (GIT) will have poor absorption. For these drugs, gastroretentive drug delivery systems offer the advantages in prolonging the gastric emptying time.

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 dose³. 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 problem⁴. 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 tract⁵.

STOMACH OVERVIEW

The stomach is divided into 3 anatomic regions: fundus, body, and antrum (pylorus). The separation between stomach and duodenum is the pylorus. The 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 for the two states. During the fasting state an interdigestive series of electrical events take place, which cycle both through stomach and intestine every 2–3 h⁶. This is called the interdigestive myoelectric cycle or migrating myoelectric cycle (MMC), which is further divided into following 4 phases as

Phase I (basal phase) lasts from 40 to 60 minutes with rare contractions.

Phase II (pre-burst phase) lasts for 40 to 60 minutes with intermittent action potential and contractions. As the phase progresses the intensity and frequency also increases gradually.

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.

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. Scintigraphic studies determining gastric emptying rates revealed that orally administered controlled release dosage forms are subjected to basically 2 complications, that of short gastric residence time and unpredictable gastric emptying rate⁷.

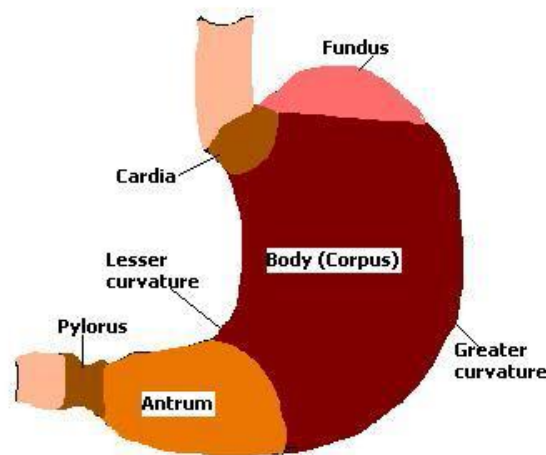


Figure 1: Stomach Overview

FLOATING DRUG DELIVERY SYSTEM

Floating drug delivery systems 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 reliably buoyant on the surface of the meal. Many buoyant systems have been developed based on granules, powders, capsules, tablets, laminated films and hollow microspheres. Floatation of drug delivery system in the drug can be achieved by incorporating floating chamber filled with vacuum, air or inert gas 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. However, besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force is also required to keep the dosage form^{8,9,10}.

Types of Floating Drug Delivery Systems

Based on the mechanism of buoyancy, two distinctly different technologies have been utilized in the development of FDDS.

A. Effervescent system

- a. Volatile liquid containing system
- b. Gas generating system

B. Non-effervescent system

- a) Alginate beads
- b) Hollow microspheres
- c) Single layer floating tablets
- d) Bilayer floating tablets
- e) Colloidal gel barrier system
- f) Microporous compartment system

A. Effervescent FDDS

- a) **Volatile liquid containing system:** The GRT of a drug delivery system can be sustained by incorporating an inflatable chamber, which contains a liquid e.g. ether, cyclopentane, that gasifies at body temperature to cause the inflation of the chamber in the stomach. The

device may also consist of a bioerodible plug made up of Polyvinyl alcohol, Polyethylene etc. that gradually dissolves causing the inflatable chamber to release gas and collapse after a predetermined time to permit the spontaneous ejection of the inflatable systems from the stomach¹¹.

b) Gas-generating Systems: These buoyant delivery systems utilize effervescent reactions between carbonate/bicarbonate salts and citric/tartaric acid to liberate CO₂, which gets entrapped in the jellified hydrocolloid layer of the systems thus decreasing its specific gravity and making it to float over gastric content⁴.

B. Non-Effervescent FDDS: The Non-effervescent FDDS is based on mechanism of swelling of polymer or bioadhesion to mucosal layer in GI tract. The most commonly used excipients in non-effervescent FDDS are gel forming or highly swellable cellulose type hydrocolloids, hydrophilic gums, polysaccharides and matrix forming materials such as polycarbonate, polyacrylate, polymethacrylate, polystyrene as well as bioadhesive polymers such as Chitosan and carbopol.

The various types of this system are as:

a) Alginate Beads: Multi-unit floating dosage forms were developed from freeze dried calcium alginate. Spherical beads of approximately 2.5 mm diameter can be prepared by dropping sodium alginate solution into aqueous solution of calcium chloride, causing precipitation of calcium alginate leading to formation of porous system, which can maintain a floating force for over 12 hours. When compared with solid beads, which gave a short residence time of 1 hour, and these floating beads gave a prolonged residence time of more than 5.5 hours.

b) Hollow Microspheres: Hollow microspheres (micro balloons), loaded with drug in their outer polymer shells are prepared by a novel emulsion solvent diffusion method. The ethanol: dichloromethane solution of the drug and an enteric acrylic polymer is poured into an agitated aqueous solution of PVA that is thermally controlled at 40°C. The gas phase generated in dispersed polymer droplet by evaporation of dichloromethane forms an internal cavity in microsphere of polymer with drug. The microballoons float continuously over the surface of acidic dissolution media containing surfactant for more than 12 hours^{12,13}.

- c) **Single Layer Floating Tablets:** They are formulated by intimate mixing of drug with a gelforming hydrocolloid, which swells in contact with gastric fluid and maintains bulk density of less than unity. They are formulated by intimate mixing of drug with low density enteric materials such as HPMC.
- d) **Bilayer Floating Tablets:** A bilayer tablet contains two layer one immediate release layer which releases 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 stomach¹³.
- e) **Colloidal gel barrier system:** Sheth and Tossounian first designated this ‘ hydrodynamically balanced system. These type of systems contain drug with gel forming hydrocolloids which allow them to remain buoyant on the stomach content. This prolongs GRT and maximizes the amount of drug at its absorption site in the solution form for ready absorption. This system incorporates a high level of one or more gel forming highly soluble cellulose type hydrocolloid as hydroxypropyl cellulose, hydroxy ethyl cellulose, hydroxyl propylmethylcellulose (HPMC), polysaccharides and matrix forming polymer such as polycarbophil, polyacrylate and polystyrene. This hydrocolloid hydrates and forms a colloidal gel barrier around its surface after coming in contact with gastric fluid and also helps in sustain releasing of drugs¹⁴.
- f) **Microporous compartment system:** In this technology a drug reservoir is encapsulated inside a microporous compartment with pores along its top and bottom walls. The peripheral walls of the drug reservoir compartment are completely sealed. This sealing prevents any direct contact of gastric surface with the undissolved drug. The floatation chamber containing entrapped air allows the delivery system to aperture dissolves the drug and carries the drug for dissolved drug for continuous transport across the intestine for absorption¹⁵.

BILAYER FLOATING TABLET

Floating bilayer tablets contain two layers an immediaterelease layer and a sustained release layer. These tablets are mainly designed to reduce the frequency of administration and to increase duration of action. The immediate release layer releases the drug immediately and the

sustained release layer which is also called as maintenance layer release the drug over prolonged period of time and maintain therapeutic index. Two drugs can also be incorporated in two layers. Immediate release layer provides rapid absorption of drug and sustained release layer provides prolonged release of drug over a period of time in a productive and predictable way. After the release of immediate layer, the second layer i.e. sustained release layer forms colloidal gel barrier on the surface by absorbing gastric fluid and it forms a density less than gastric fluid due to this it remains by floating in the stomach for an extended time period¹⁶.

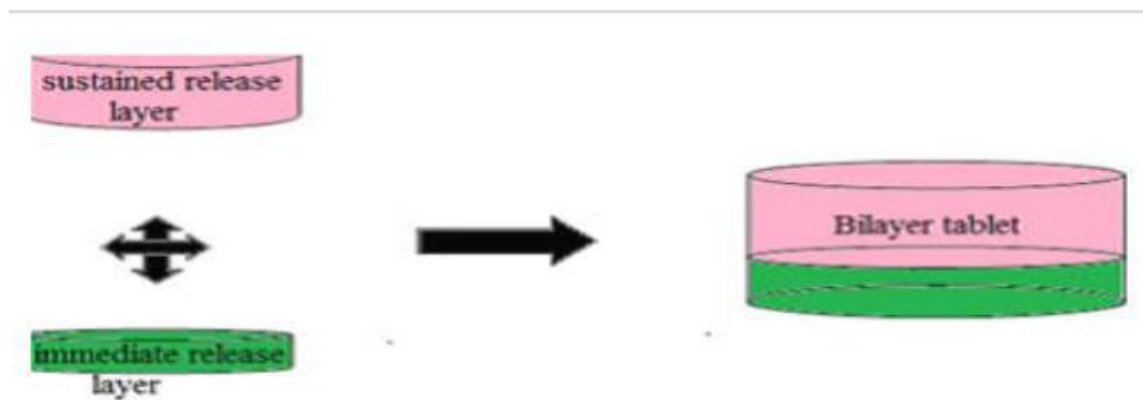


Figure 2: BiLayer Floating Tablet

Advantages of Floating Bilayer Tablet

- This system provides sustained drug delivery like HBS dosage form modify gastric residence time as this system remains in stomach for many hours.
- It maintains optimum therapeutic window as a result drug delivery with controlled released is achieved.
- Better patient compliance is achieved due to its ease of administration.
- It maintains constant blood level.
- Site specific drug delivery is achieved for the drugs such as furosemide and riboflavin which are formulated as floating system.
- Overall other oral routes these are microbiologically and chemically stable.
- Due to higher dose precision and lesser content variation they are the most compatible oral dosage form.
- They offer the most flexible dosage form.
- Better suited for large scale production.

- Masking of bitter taste and bad odor by coating.
- Swallowing of tablets is easy.
- Lesser cost compared to other oral dosage forms.
- These are the most lighter and compact¹⁷.

Disadvantages of Floating Bilayer Tablet

- Increased fluid levels are required in the stomach so that the system float properly.
- Drugs with solubility and stability problem in stomach cannot be formulated as floating dosage form.
- Irritation producing drugs on gastric mucosa can be formulated as floating dosage form.
- Capping is the major problem in bilayer tablets.
- Separation of layer occurs due to insufficient bonding and reduction in yield occurs.
- Hardness is other problem.
- There are chances of cross contamination between two layers.
- Due to low density and amorphous nature of some drugs, compacts do not form because they resist compression.
- There is less control over weight of individual layer.
- Swallowing problem in case of children and unconscious patients.
- Bioavailability problem occurs in case of poor wetting and less dissolution properties.
- Sometimes encapsulation or coating is required for the drugs that are oxygen sensitive, bitter tasting and with bad odour¹⁸.

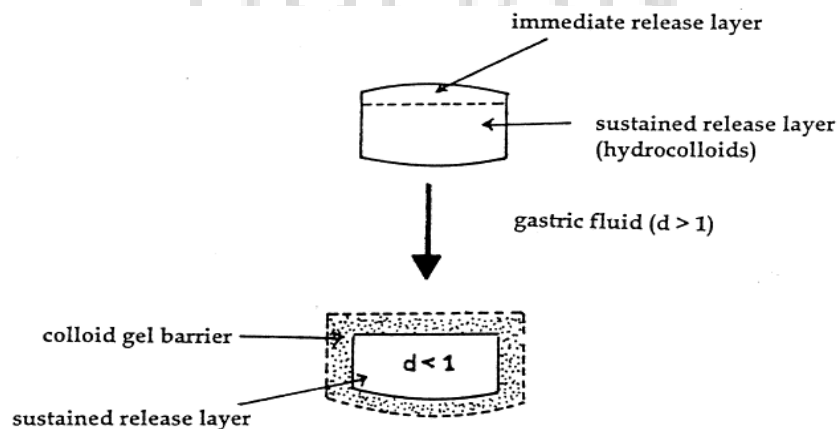


Figure 3: Schematic Diagram of BiLayer Floating Tablets

Need of Bilayer Floaying Tablets

- To control the delivery rate of either single or two different active pharmaceutical ingredients.
- For the administration of fixed dose combination of drug, prolong the product life cycle, buccal/mucoadhesive delivery systems, fabricate novel drug delivery system such as chewing device and floating tablets for gastroretentive drug delivery systems.
- To separate incompatible active pharmaceutical ingredients from each other, to control the release of API from one layer by utilizing the functional property of other layer (such as osmotic property).
- To modify the total surface area available for API layer either by sandwiching with one or two inactive layers in order to achieve swellable/erodible for modified release^{19,20,21}.

Selection of Drugs for Bilayer Floating Tablet on its Suitability

- Drugs should have less half- life (2-6 hour).
- Drugs have less bioavailability in gastric region.
- Unstable at intestinal pH
- Long term treatment of disease and drugs
- Less dose of drug
- Less gastric retention time
- Narrow absorption window in GI tract ex. Riboflavin and levodopa
- Basically absorbed from stomach and upper part of GIT
- Drugs that disturb normal colonic bacteria amoxicillin trihydrate
- Locally active in stomach ex. Antacid and misoprostol
- Drugs that degrade in colon ex. Ranitidine and metronidazole

Ideal Properties for Bilayer Floating Tablet

- Drug must be released in reproducible and expected manner in bilayer tablet.
- Chemical and physical stability is must.
- During product shelf life chemical stability is main concern.
- In product identification dosage form should be free from visual defects such as cracking.
- Discolouration²²

Dose calculation

For sustained drug release up to desired time, the total dose of drug required was calculated based on the conventional dose by using the following equation,

$$Dt = D_0 (1 + 0.693 t / t_{1/2})$$

Where, Dt = total dose, Dose = immediate release dose, t = total time period for which sustained release is required, $t_{1/2}$ = half life of the drug.

Methodology used for Bilayer Floating Tablet

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
8. PRODAS or Programmable Oral Drug Absorption System

1. OROS® Push Pulls Technology

This system consist of mainly two or three layer among which the one or more layer are essential of the drug and other layer are consist of push layer. The drug layer mainly consists of drug along with two or more different agents. So this drug layer comprises of drug which is in poorly soluble form. There is further addition of suspending agent and osmotic agent. A semi permeable membrane surrounds the tablet core²³.

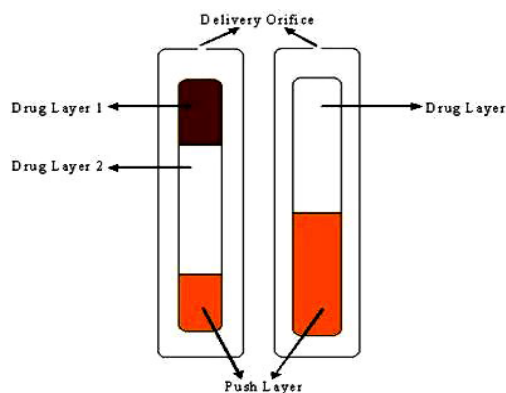


Figure 4: Bilayer and Trilayer OROS Push Pull Technology

2. L-OROS™ Technology

This system used for the solubility issue Alza developed the L-OROS system where a lipid soft gel product containing drug in a dissolved state is initially manufactured and then coated with a barrier membrane, than osmotic push layer and then a semi permeable membrane, drilled with an exit orifice²⁴.

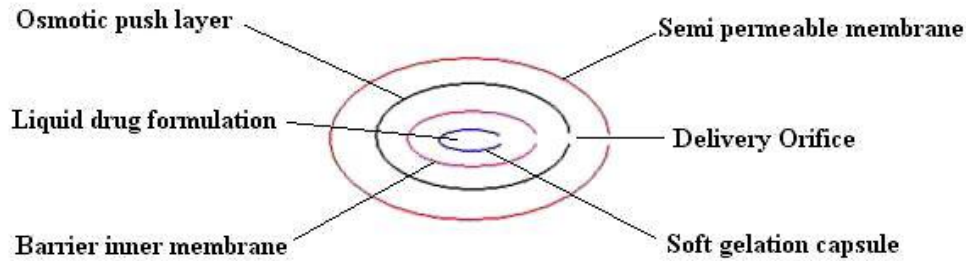


Figure 5: L-OROS™ Technology

3. DUROS Technology

The system consists from an outer cylindrical titanium alloy reservoir. This reservoir has high impact strength and protects the drug molecules from enzymes. The DUROS technology is the miniature drug dispensing system that opposes like a miniature syringe and release minute quantity of concentrated form in continues and consistent from over months or year²⁵.

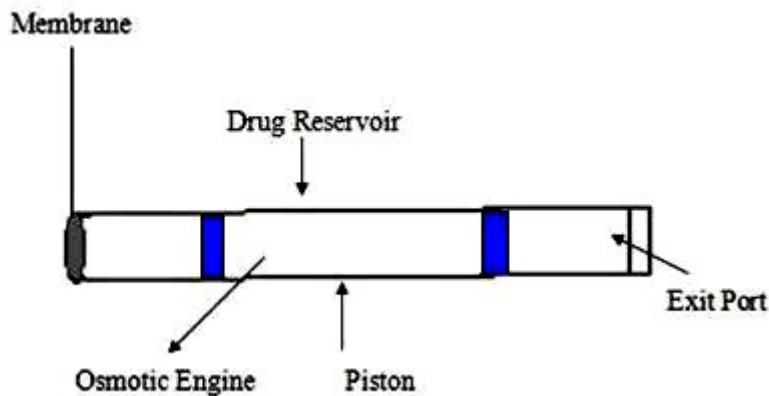


Figure 6: DUROS Technology

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 consists of bilayered tablet technology in which it contains 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 focuses on identification and incorporation of enhancer which is identified to form optimized dosage form in controlled release system. By this enhancement in solubility is achieved²⁶.

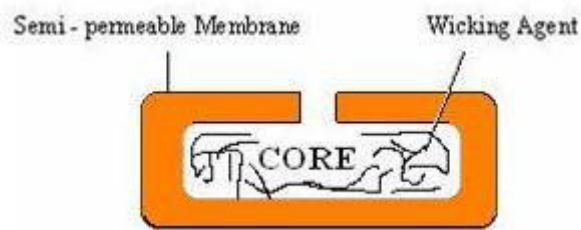


Figure 7: EN SO TROL Technology

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 required²⁷.

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 to both industry as well as patient as in single tablet it provides delivery of drug at different rates²⁷.

8. PRODAS or Programmable Oral Drug Absorption System

(Elan Corporation) is a multiparticulate drug delivery technology that is based on the encapsulation of controlled release minitabets in the size range of 1.5 to 4 mm in diameter. This technology represents a combination of multiparticulate and hydrophilic matrix tablet technologies and thus provides the benefits of both these drug delivery systems in one dosage form. Minitabets with different release rates can be combined and incorporated into a single dosage form to provide the desired release rates. These combinations may include immediate release, delayed release, and/or controlled release minitabets²⁸.

EVALUATION TECHNIQUES OF BILAYER FLOATING TABLET

A. In Vitro Evaluation of Bilayer Floating Tablet: 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 pile²⁹.

The relationship between angle of repose and powder flow is as follows in table:

Table 1: Relationship between angle of repose and powder flow

Angle of repose	Powder flow
< 25	Excellent
25-30	Good
30-40	Passable
> 40	Very poor

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.

$$\text{Compressibility index (\%)} = \rho_t - \rho_0^* 100 / \rho_t$$

Where ρ_t = Tapped density gram/ml

ρ_0 = Bulk density gram/ml

Bulk Density:

It is denoted by ρ_b and is defined as mass of powder divided by bulk volume. Method: 50 cm³ of powder has been taken is passed through sieve no. 20 which is introduced in 100 ml graduated cylinder. The cylinder is allowed to tapped on hard wood surface for about 500 times³⁰.

Tapped Density:

An increase in bulk density which is attained after mechanical tapping in measuring cylinder is called as tapped density³¹.

$$\text{Tapped density} = \text{Weight of powder taken} / \text{Tapped Volume}$$

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.

$$\text{Hausner ratio} = \text{Tapped density} / \text{Bulk density}$$

$$\text{Hausner ratio} = V_0 / V_f$$

Where, V_0 = Unsettled apparent volume

V_f = Final tapped volume

Particle Size Distribution:

Particle size distribution was done by sieving method.

POST-COMPRESSION PARAMETERS

Tablet Thickness:

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 weight³².

Table 2:Limit of Weight Variation

Weight	% Variation
Less than 80 mg	10%
80-250 mg	7.5%
Above 250 mg	5%

Hardness:

Expressed in kg/cm² 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 tablets³³.

Friability:

Ten tablets are selected and weighed and then placed in friabilator apparatus which rotates at 25 rpm speed for 4 minutes. After 4 minutes tablets are weighed again.

$$\%F = [1 - (Wt/W)] * 100$$

W – Initial weight of tablet

Wt - Weight of tablet after revolution.

If % Friability of tablets is less than 1% is considered acceptable³⁴.

Tablet Density:

It is an important parameter in case of floating tablets. If density is less than (1.004) gastric fluid, the tablets will float. It is calculated by using formula:

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

$$d = m/v$$

r = Radius of tablet

h = crown thickness (g/cc)

m = Mass of tablet³⁵

Disintegration Time:

One tablet is placed in disintegration apparatus containing buffer 0.1N HCl or PBS pH 6.8 and test is carried out at 37°C. The time taken by tablet to disintegrate is noted as disintegration time³⁶.

Dissolution Studies:

Dissolution study is performed using USP paddle apparatus by maintaining optimum temperature i.e., 37°C at 50 rpm rotational speed. At various time interval 5 ml sample is withdrawn and is replaced with same amount of buffer³⁷.

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 media³⁸.

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. spectrophotometer³⁹.

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

$$SI = \frac{W_t - W_0}{W_0} * 100$$

W_t (Weight of swollen tablet)

W₀ (Initial weight of tablet)

B. In Vivo Evaluation of Bilayer Floating Tablet:

Radiology:

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

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 .

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.

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 so not hazardous.

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

C^{13} Octanoic Acid Breath Test: C^{13} 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 C^{13} isotope. So time up to which C^{13}O_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 cheaper than other⁴⁰.

PATENT ON FLOATING BILAYER TABLET⁴¹⁻⁴⁵

Drug	Patent application number
Ciprofloxacin, Acyclovir, Ofloxacin	US Patent Appln 2006013876
Heparin and Insulin	US Patent Appln 2008153779
Acyclovir, Ganciclovir, Ritonavir, Minocycline, Cimetidine, Ranitidine, Captopril, Methyldopa, Selegiline, Fexofenadine, Bupropion, Orlistat & Metformin	US Patent 6120803
Ciprofloxacin	US Patent Appl 2003232081
Calcitriol, combined with delayed release of a bisphosphonate calcium resorption inhibitor such as alendronic acid and its salts and hydrates	US Patent Appl 2007104786

COMMERCIALY MARKETED BILAYER TABLETS

Product Name	Chemical Name	Developer
ALPRAXPLUS	Sertraline, Alprazolam	Torrent Pharmaceuticals Ltd.
Glycomet®-GP2Forte	Metformin hydrochloride, Glimepiride	USV Limited
Newcold Plus	Levocetirizine hydrochloride, Phenylpropanolamine, Paracetamol	Piramal Healthcare Ltd.
DIAMICRON®XRNEX500	Gliclazide, Metformin hydrochloride	Serdia® Pharmaceuticals (India) Pvt. Ltd.
DIUCONTIN-K®20/250	Furosemide, Potassium chloride	T.C. Health Care Pvt. Ltd.
TRIOMUNE 30	Nevirapine, Lamivudine, Stavudine	Cipla Ltd.
PIOKIND®-M15	Pioglitazone, metformine hydrochloride	Psychotropics India Ltd.
Revelol®-Am 25/5	Metoprolol succinate, Amlodipine besilate	Ipca Laboratories Ltd.

CONCLUSION

Drug release is the major area in the pharmaceutical research work. Through floating bilayer tablets both type of release i.e. sustained as well as immediate release can be obtained and sustained release can be increased up to 24 hours. It is also beneficial in providing gastric retention thereby increasing gastric emptying time as well as increasing bioavailability. Another advantage is that two drugs can be administered concurrently at the same time which provides better patient compliance. Drugs which has narrow absorption window such as antiviral, antibiotic and antifungal can be given in floating bilayer dosage form.

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