



Floating Bilayer Tablet Technology: A Review

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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. Approaches have been introduced to prolong gastric residence time such as floating system, modified shape, swelling, expanding system and high density system. Bilayer floating drug delivery systems exhibits a unique combination of floatation and bilayer which prolongs residence in the stomach. Bilayer tablet is new era for the successful development of controlled release formulation. Drug incorporated in a controlled release gastroretentive dosage forms can remain in the gastric region for several hours and 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. Bilayer floating tablets provides both immediate as well as sustained released layer formulations. An attempt has been made in the review to introduce new technology of drug delivery system.

Keywords: Bilayer Floating Drug Delivery Systems, Controlled Release, Gastro retentive Dosage Forms, Immediate Release Layer.

INTRODUCTION

Drug delivery system aims to give prolonged non-toxic drug concentration in blood and various tissues which should be therapeutically active. Temporal and spatial drug delivery is the main target for any drug delivery system. In temporal drug delivery the rate of delivery of drug to specific organs and tissues is controlled whereas targeting to specific tissues and organs occurs in spatial drug delivery. This can only be achieved by controlled or sustained drug delivery.¹ For providing systemic action numbers of routes are available which are oral, rectal, parenteral, inhalational and sublingual.² Today various drug delivery system are available in market among which most common are the oral drug delivery. From immediate release to site specific development occurs in the oral drug delivery. Among oral route 90% of the drugs are administered today which provides good systemic effects. Solid oral dosage forms are more stable through which tablets are the most common solid oral dosage forms.³ But this immediate release dosage forms has many limitations as in this system effective plasma drug concentrations does not occurs because immediate release dosage form has to administered several times a day and it arises the problem of patient compliance. It also leads to toxicity due to fluctuation in plasma drug concentration. Due to this reason controlled drug delivery is gaining importance these days. Oral controlled drug delivery aims to deliver drug for an extended period of time which provide good bioavailability and which makes the dosage form reproducible. The system gets many difficulties due to physiological problems like absorption window is narrow for some drugs and alteration in emptying time of stomach and drugs has stability issues in intestine. To overcome these difficulties gastroretentive drug delivery system (GDDS) is designed which provide oral controlled

sustained dosage form as it delivers the drug at slow rate in systemic circulation and maintains effective plasma concentration because drug is retained in stomach for a prolonged period of time as compare to conventional oral dosage form.⁴

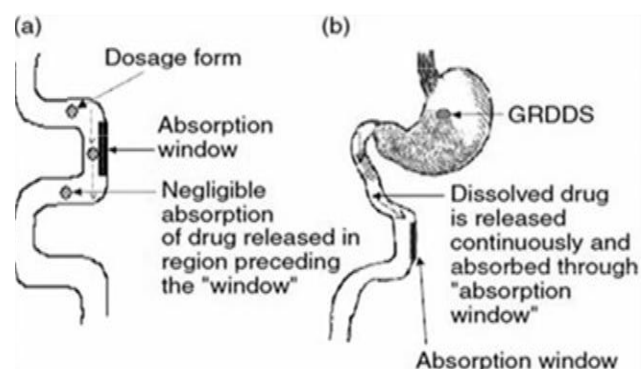
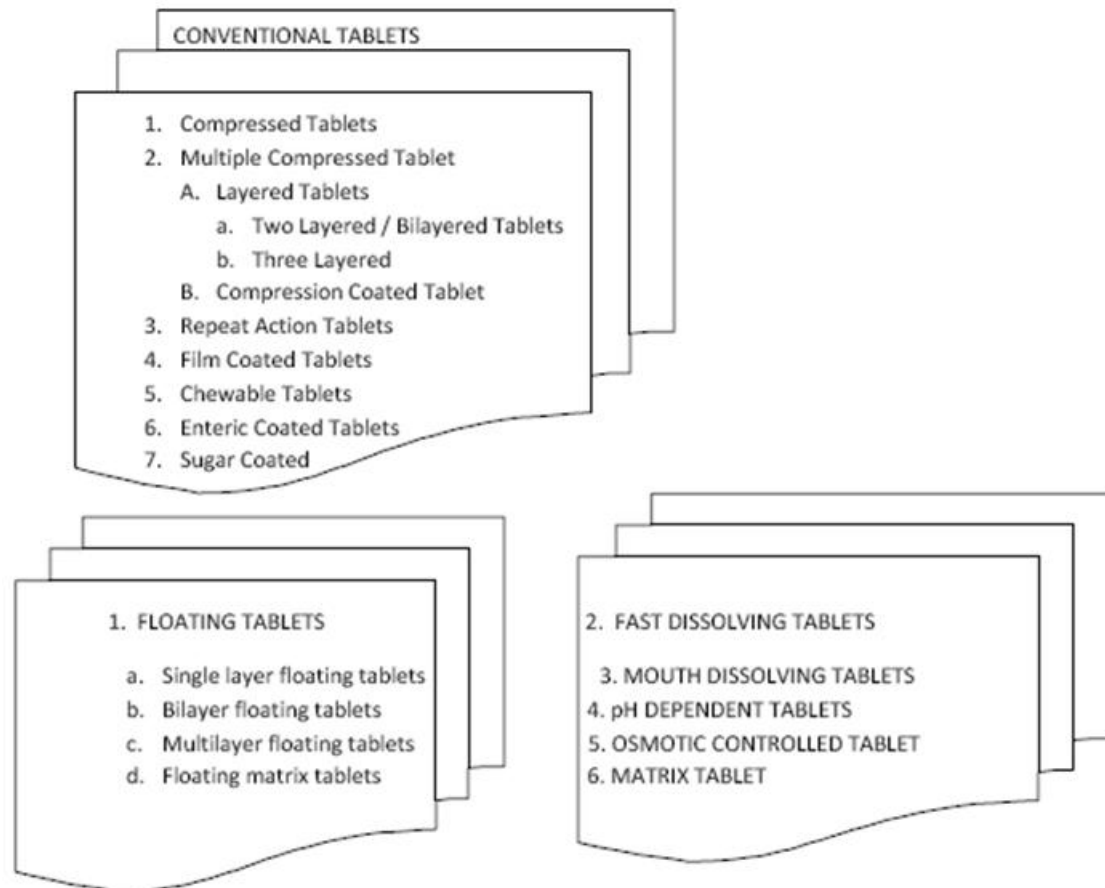


Figure 1: Conventional Dosage Form shows negligible absorption whereas in GRDDS drug is continuously absorbed.⁵

According to British Pharmacopoeia tablets are defined as convex or flat faces which are circular and are formed by compression of active pharmaceutical ingredient and other excipients.³ Tablets provide many advantages as they are the most stable dosage form since they are dry, easy to manufacture and cost effective, provide good patient compliance and extended shelf life⁶. According to their use they are of many types which are tablets for oral ingestion, tablets for oral cavity, and tablets for other routes. Tablets can be produced by two method granulation and direct compression. Granulation can be dry granulation and wet granulation. But now a day's direct compression method is commonly used due to increasing use of novel excipients.

TYPES OF TABLETS FOR ORAL INGESTION



FLOATING DRUG DELIVERY

Floating drug delivery is a technique to achieve gastric retention. Floating was first described in year 1968 by Davis. The system remains buoyant in stomach for a prolonged period of time because they have density lower than the gastric content. The drug in this system is released slowly at a particular rate as the system is floating on the gastric contents. Due to which better control over fluctuations occurs in plasma drug concentration and as a result increase in gastric retention occurs.³ Several approaches such single and multiple units have been used to design floating units.⁷ Floating system should have specific less than gastric content i.e. 1.004-1.01g/cc. And system should form cohesive gel barrier. It acts as a reservoir and releases the content slowly. To provide controlled and consistence drug delivery selection of excipients is very important. Improved floating property of drug delivery is achieved by high molecular weight and less hydrophilic polymers.⁸ Various approaches to increase gastric retention are designed and these are Hydrodynamically balanced intragastric delivery of drug, Intragastric floating gastrointestinal delivery of drugs, Intragastric osmotically controlled delivery of drugs, Inflatable gastrointestinal delivery of drugs, Bio(muco)adhesive delivery of drugs, Intrarumen controlled release delivery of drug through device and with coadministration of GI motility-reducing device.⁹

CLASSIFICATION OF FLOATING SYSTEM

- A. Non-effervescent system
 - a. Colloidal gel barrier system
 - b. Bilayer floating tablets
 - c. Microporous compartment system
 - d. Alginate beads
 - e. Hollow microspheres
- B. Effervescent system
 - a. Volatile liquid containing system
 - b. Gas generating system

A. Non-Effervescent Systems:

After swallowing the drug swells with the imbibition of gastric fluid in such a way that it's exit from stomach is prevented. Mainly the drug is mixed with gel due to which it swells when comes in contact with gastric fluid and it also maintain its shape.⁸ They remain lodged near pyloric sphincter due to which they are also called as plug-type systems. The bulk density of this system is <1. The buoyancy to the dosage form is mainly due to the air entrapped within swollen matrix and this swollen matrix acts as a reservoir which imparts sustained release of drug.¹⁰ Gel forming and swellable cellulose type of hydrocolloids, polysaccharides and matrix forming

polymers like polyacrylate, polystyrene, polycarbonate, carbopol, sodium alginate and polymethacrylate are used in non-effervescent system.¹¹

a. Colloidal Gel Barrier System

Hydrodynamically balanced system first designed by Sheth and Tossounian. They remain buoyant in the stomach due to gel-forming hydrocolloids and this enhances GRT and increases the amount of drug at the absorption site. Various gel forming agents used in this system are highly soluble cellulose type hydrocolloids which are hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, polysaccharides and matrix forming polymers such as polycarbophil, polystyrene.¹²

b. Bilayer Floating Tablets

This system basically contained two layers an immediate release layer and sustained release layer. Immediate release layer release the initial dose immediately and sustained layer forms colloidal gel barrier by absorbing gastric fluid and thereby it maintain density of less than one and remain floating in stomach.¹³

c. Microporous Compartment System

In this inside the microporous compartment which has pores in the top and bottom walls contains encapsulated drug reservoir. In drug reservoir peripheral walls are completely sealed due to this sealing direct contact of undissolved drug with gastric surface is prevented. Entrapped air in the floating chamber stimulates the system to float over gastric content. Through an aperture the gastric fluid enters which dissolves the drug for absorption across intestine.¹⁴

d. Alginate Beads

By freeze-dried calcium alginate beads multi-unit floating dosage forms have been developed. By precipitation method spherical beads of approximately 2.5 mm have been prepared by dropping sodium alginate solution into aqueous solution of calcium chloride.

Separated beads form porous system when they are snap-frozen in liquid nitrogen and then freeze dried for 24 hours at -40 C. The prepared beads float for over 12 hours and increases the residence time for more than 5.5 hours.¹⁵

e. Hollow Microspheres

To prepare hollow microspheres loaded with drug a novel emulsion solvent diffusion method and solvent evaporation method was used which prolong the gastric retention time of dosage form. The drug release and buoyancy for dosage form depends mainly upon the quantity of polymer, solvent system and plasticizer to polymer ratio. Mainly polymers used are calcium alginate, cellulose acetate, eudragit S, polycarbonate and pectin.¹⁶

B. Effervescent Systems:

Various types of swellable polymers such as chitosan and methylcellulose and effervescent material such as sodium bicarbonate, citric acid, tartaric acid and calcium carbonate are used to formulate effervescent dosage form. The system when come in contact with acidic gastric content liberates carbon dioxide and in swollen hydrocolloid it gets entrapped and provides buoyancy to the dosage form.¹⁷

a. Volatile Liquid Containing System

Inflatable chamber with a liquid can be incorporated which provide sustained gastric retention of drug delivery system. Liquids in this system include cyclopentane, ether that gasifies at body temperature which causes inflation of the chamber in the stomach.¹⁸ They contain hollow deformable unit which are osmotically controlled floating systems. System is divided into two compartment first compartment contains drug and there is volatile liquid in the second compartment.¹⁹

b. Gas Generating System

It basically contains polymers that gasifies at body temperature effervescent compounds such as sodium bicarbonate, citric acid, tartaric acid, swellable polymers like methocel, polysaccharides like chitosan. Resin beads loaded with bicarbonate and coated with ethylcellulose is the most common approach for preparation of these systems. The ethylcellulose coating is insoluble but permeable to water which release carbon dioxide due to which it float.²⁰

Table 1: Polymers used in floating drug delivery²¹

Sustained Release Polymers	HPMC K100M, HPMC K15M, HPMC E LV, Polycarbonate, Polyethylene Glycol, Sodium Alginate, Carbopol, Eudragit.
Effervescent Generating System	Citric acid, Tartaric Acid, Sodium Bicarbonate, Citroglycine.
Polymers which increase buoyancy	Ethylcellulose
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.

FLOATING BILAYER TABLETS

Floating bilayer tablets contain two layers an immediate release layer and a sustained release layer. These tablets are mainly designed to reduce the frequency of administration and to increase duration of action. In this immediate release layer release the drug immediately and the sustained release layer which is also called as maintenance layer release the drug over prolong period

of time and maintain therapeutic index. Two drugs can also be incorporated in two layers.

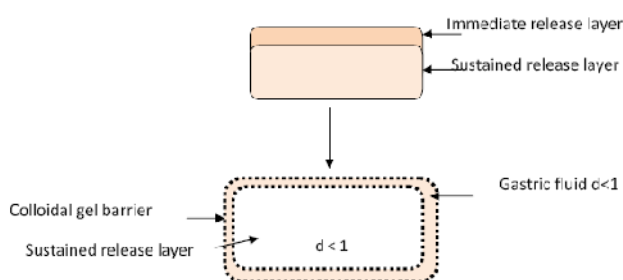


Figure 2: Sustained release layer forms colloidal gel barrier which floats.

Immediate release layer provide 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 remain by floating in the stomach for an extended time period.⁹

ADVANTAGES OF FLOATING BILAYER TABLETS

1. This system provide sustained drug delivery like HBS dosage form modify gastric residence time as this system remain 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.²²
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.²³

DISADVANTAGES OF FLOATING BILAYER 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 as floating dosage form.

3. Irritation producing drugs on gastric mucosa can be formulated as floating dosage form.²²
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 donot 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.²⁴
12. Sometimes encapsulation or coating is required for the drugs that are oxygen sensitive, bitter tasting and with bad odour²⁵

Table 2: Patent on Floating Bilayer Tablet

Drug	Patent number	application	Ref
Ciprofloxacin, Acyclovir, Ofloxacin	US Patent 2006013876	Appln	26
Heparin and Insulin	US Patent 2008153779	Appln	27
Acyclovir, Ganciclovir, Ritonavir, Minocycline, Cimetidine, Ranitidine, Captopril, Methyldopa, Selegiline, Fexofenadine, Bupropion, Orlistat & Metformin.	US Patent 6120803		28
Ciprofloxacin	US Patent 2003232081.	Appl	29
Calcitriol, combined with delayed release of a bis-phosphonate calcium resorption inhibitor such as alendronic acid and its salts and hydrates.	US Patent 2007104786.	Appl	30

BILAYER TABLET

Bilayer tablets contain two layers one with immediate release layer and other with extended release layer or sustained or both layers with immediate release³¹. Two drugs can be combined in different layers of tablets and these tablets incompatible substances are also separated which helps in reducing chemical incompatibilities. Due to this reason bilayer tablets offer advantage over conventional single layered tablets. In bilayer tablets delivery rate of either single or two active pharmaceutical ingredients can be controlled. It is also beneficial to active gastric retention by forming floating bilayer tablets with different active pharmaceutical ingredient in a fixed dose combination and also to increase the life cycle of drug

product. Various forms of bilayer tablets are bilayer modified release tablets, bilayer floating tablets, bilayer bucoadhesive tablets, bilayer mucoadhesive tablet.

DIFFERENT TECHNIQUES FOR BILAYER TABLETS³²

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.³³

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.³⁴

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.³⁵

4. Elan Drug Technologies' Dual Release Drug Delivery System :

The DUREDAS[™] Technology provide 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. Various manipulations can be done in this system as it provides enhancement in duration of sustained release formulation. Immediate release layer is first compressed followed by compression of sustained release layer. OTC controlled release analgesics were first developed using DUREDAS[™] technology.³⁶

5. EN SO TROL Technology:

An integrated approach is used by Shire laboratory for drug delivery system which focus on identificator. incorporation of enhancer which is identified to form optimized dosage form in controlled release system. By this enhancement in solubility is achieved³⁷.

6. RoTab Bilayer³⁷ :

a. Software:

It is modular designed software to which additional functions can be added. PC- system with 15" touch-screens is an advanced system which provides fast graphical evaluations with accurate results.

b. Working:

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.

c. R and D modified technique :

R and D modified RoTab Bilayer is featured with measuring points on which there are graphical visualization and evaluation are possible. There is an additional alarm function on which punch tightness is controlled. Anytime upgration is possible which is R and D Plus.

d. R and D Plus:

R and D Plus provides improved standards in tableting technology with all important functions such as punch tightness control, display of force displacement and tablet scraper force.

7. Geminex Technology:

In this drug delivery system at different times more than one drugs 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.³⁸

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 minitabets.³⁹

Ideal properties for bilayer tablet dosage form⁴⁰

- 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, discolouration.

FLOATING BILAYER TABLET DEVELOPMENT

Various gastrointestinal dynamics are considered important such as small intestinal transit, gastrointestinal transit and colonic transit for the optimum working of

controlled release dosage form. Rate and extent of absorption of drug at different sites helps in designing dosage form. Drugs with low oral bioavailability such furosemide, theophylline, sulphuride and albuterol offers potential for designing gastroretentive dosage form. Invention of g-scintigraphy helps in knowing various pharmaceutical and physiological factors helps in designing dosage form. Excipients play a very critical role in designing gastroretentive controlled release dosage form for example excipients which increase the sustained delivery character of drug and have bulk density of less than unity. Water soluble derivatives excipients are commonly used which shows property of swelling. Slower hydration rate polymers and polymers with increased weight usually shows good floating behaviour.⁴¹

Table 3: Floating Bilayer Tablet

Drug	Polymers	Method of preparation	Ref
Cefuroxime Axetil	HPMC K4M, Sodium Bicarbonate, Sodium Citrate, Tulsion T-339	Direct Compression Technique	42
Metformin Hcl	HPMC K 100M, HPMC K 4M, SSG, PVP K, MCC, Sodium Bicarbonate, Iron Oxide-Red.	Direct Compression Technique	43
Trifluoperazine Hcl	HPMC K100M, Carbopol 934P, Eudragit RS100, MCC, Maize Starch, Magnesium Stearate, SSG, Aerosil, Ferric Oxide Yellow.	Direct Compression Technique	44
Metoprolol Tartrate	HPMC K4M, HPMC K10M, SCMC PVP, MCC, Starch Soluble, Aerosil, Methocel K4000, Methocel K 10000 Cp, DCP.	Direct Compression Method.	45
Rosiglitazone Maleate	HPMC K 100M, SSG, CCS, Carbopol 934P, Sodium Bicarbonate.	Direct Compression Method.	46
Rantidine	HPMCK-4M, HPMC-E-15, Carbopol-934, Sodium Bicarbonate, Citric Acid.	Direct Compression Method.	47
Domperidone	HPMC K100M, CCS, MCC, PVPK30, Starch, Magnesium Stearate, Talc	Wet Granulation Method Direct Compression Method.	48
Amoxicillin Trihydrate	HPMC K4M, HPMC K15M, SCMC, SSG, Starch, Magnesium Stearate, Lactose, Sodium Bicarbonate.	Direct Compression Technique.	49
Ciprofloxacin Hcl	HPMC K15 M, HPMC K100 M, Carbopol 934P, CP, DCP, Na Bicarbonate, Magnesium Stearate, Talc.	Direct Compression Method.	50
Atenolol And Lovastatin	HPMC K100M, XG, Sodium Starch Glycolate, Spray Dried Lactose (Tablettose 80), Magnesium Stearate, DCP, Sodium Bicarbonate.	Direct Compression Technique.	51
Furosemide	Hpmc 4000, Hpmc 100, CMC, PEG 400, Di-Pac	Direct Compression Method.	52
Trimetazidine Dihydrochloride	Hypermellose(K-4M), Povidone K-30, Magnesium Stearate, Dicalcium Phosphate, Carbopol 971 P, SSG, Sodium Bicarbonate, Citric Acid.	Compression Method.	53
Rosiglitazone Maleate	Methocel K100M, Starch 1500, Maize Starch, DCP And Sodium Bicarbonate.	Granulation and Direct Compression Method.	54
Diltiazem Hcl	HPMC K4M, HPMC K100M, MCC, Sodium Bicarbonate, Citric Acid, HPMC E50 LV.	Direct Compression	55
Metformin And Pioglitazone	HPMC E15, HPMC K4M, Carbopol 934 P, PVP, Sodium Bicarbonate, Citric Acid.	Modified Direct Compression Technique.	56
Cefodoxime Proxetil	HPMC K100M, Carbopol 934, Sodium Bicarbonate, Lactose, HPC-HF, Tulsion T-339.	Direct Compression Technique.	57
Rifampicin And Isoniazid	HPMC K100, Sodium Bicarbonate, CP, PVP K30, β -Cyclodextrin.	Direct Compression Method.	58
Baclofen	HPMC K4M, SSG, Sodium Bicarbonate, Citric Acid	Direct Compression	59
Repaglinide And Glipizide	HPMC K4M, SCMC, SSG, MCC, SLS, PVP.	Direct Compression Method.	60
Ziprasidone Hcl And Trihexyphenidyl Hcl	HPMC K4M, HPMC K15M, Sodium Bicarbonate, Colloidal Silicone Dioxide.	Direct Compression Method.	61
Atrovastatin Calcium And Nicotinic Acid	Sodium Bicarbonate, Calcium Carbonate, SLS, Polysorbate 80.	Direct Compression Method.	62
Verapamil Hcl	HPMC K 100M, HPMC K15M, Carbopol 971 P, CP, DCP, Sodium Bicarbonate, Citric Acid, SSG.	Direct Compression Method.	63
Atenolol	Psyllium Husk, HPMC K4M, Sodium Bicarbonate, PVP K30.	Wet Granulation. Direct Compression Method.	64

Drug	Polymers	Method of preparation	Ref
Trimetazidine Hydrochloride and Metoprolol Succinate	EC, HPMC K4M, HPMC K100 M, SSG, XG, PVP K30, MCC.	Wet Granulation Direct Compression Method.	65
Nizatidine	HPMC K4M, HPMC K15M, HPMC K100M, Carbopol 934, CP.	Direct Compression Method.	66
Famotidine	HPMC K100LV, HPMC K4M, Crosscarmellose, CP, SSG.	Direct Compression Method.	67
Tramadol Hydrochloride	HPMC K4M, HPMC K100M, PVP K30, Sodium Alginate, Sodium Bicarbonate, Citric Acid, MCC.	Wet Granulation Direct Compression Method.	68
Carvedilol Phosphate	HPMC K100M, Ocimum Basilicum Mucilage, Sodium Bicarbonate, MCC.	Direct Compression Method.	69
Metoprolol Tartarate	Methocel K 4000, Methocel K 15000 Cp, SCMC, PVP K30, Sodium Bicarbonate.	Direct Compression Method.	70
Metformin Hydrochloride And Sitagliptin Phosphate.	HPMC K100M, SCMC, PVP K30, Sodium Bicarbonate, CP, MCC, CCS, SSG, Pre Gelatinised Starch.	Direct Compression Method.	71
Amoxicillin And Aloe Vera Gel Powder	HPMC K4M, HPMC K100M, Avicel Ph 102, Citric Acid, Sodium Bicarbonate.	Direct Compression Method	72
Propranolol Hydrochloride	Methocel K100M, Starch 1500, Maize Starch.	Direct Compression Method.	73
Nizatidine	HPMC K4M, HPMC K15M, HPMC K 100M, Carbopol 934, Sodium Bicarbonate, Citric Acid.	Direct Compression Method	74

CHARACTERIZATION OF FLOATING BILAYER TABLETS

PRE-COMPRESSION PARAMETERS

Test	Method	Ref										
1. Angle of Repose	<p>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.</p> $\tan\theta = h/r$ $\theta = \tan^{-1}h/r$ <p>Where θ = Angle of repose h = height of pile r = radius of pile</p> <p>Flow property according to angle of repose is</p> <table border="1"> <thead> <tr> <th>Angle of repose</th> <th>Powder flow</th> </tr> </thead> <tbody> <tr> <td><25</td> <td>Excellent</td> </tr> <tr> <td>25-30</td> <td>Good</td> </tr> <tr> <td>30-40</td> <td>Passable</td> </tr> <tr> <td>>40</td> <td>Very poor</td> </tr> </tbody> </table>	Angle of repose	Powder flow	<25	Excellent	25-30	Good	30-40	Passable	>40	Very poor	75
Angle of repose	Powder flow											
<25	Excellent											
25-30	Good											
30-40	Passable											
>40	Very poor											
2. Compressibility Index	<p>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.</p> $\text{Compressibility index (\%)} = \frac{p_t - p_o}{p_t} \times 100$ <p>Where p_t = Tapped density gram/ml p_o = Bulk density gram/ml</p>	76										
3. Bulk Density	<p>It is denoted by p_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 the introduced in 100 ml graduated cylinder. The cylinder is allowed to tapped on hard wood surface for about 500 times.</p>	77										
4. Tapped Density	<p>An increase in bulk density which is attained after mechanical tapping in measuring cylinder is called as tapped density.</p> $\text{Tapped density} = \frac{\text{Weight of powder taken}}{\text{Tapped Vol}}$	77										
5. Hausner Ratio	<p>The propensity of the powder to be compressed is measured by hausner ratio. Interparticulate interaction and settling property can be measured by hausner ratio.</p> $\text{Hausner ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$ $\text{Hausner ratio} = \frac{V_o}{V_f}$ <p>Where, V_o = Unsettled apparent volume V_f = Final tapped volume</p>	76										
6. Particle Size Distribution	By sieving method	32										



POST-COMPRESSION PARAMETERS

Test	Method	Ref								
Shape of Tablet	Tablet shape is checked by magnifying lens after compression.	23								
Tablet Dimensions	In this three tablets are randomly taken and then their thickness and diameter are measured by vernier calliper or by using calibrated screw gauge.	79, 48, 78								
Weight Variation Test	<p>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.</p> <p>LIMIT OF WEIGHT VARIATION</p> <table border="1"> <thead> <tr> <th>WEIGHT</th> <th>% VARIATION</th> </tr> </thead> <tbody> <tr> <td>Less than 80 mg</td> <td>10%</td> </tr> <tr> <td>80-250 mg</td> <td>7.5%</td> </tr> <tr> <td>Above 250 mg</td> <td>5%</td> </tr> </tbody> </table>	WEIGHT	% VARIATION	Less than 80 mg	10%	80-250 mg	7.5%	Above 250 mg	5%	80
WEIGHT	% VARIATION									
Less than 80 mg	10%									
80-250 mg	7.5%									
Above 250 mg	5%									
Hardness	Expressed in kg/cm ² and it is checked using Monsanto hardness tester by randomly picking three tablets. Hardness help in knowing ability of the tablet to withstand mechanical shock during handling of tablets.	44								
Friability	<p>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.</p> <p>$\%F = [1 - (Wt/W)] * 100$</p> <p>W – Initial weight of tablet</p> <p>Wt- Weight of tablet after revolution.</p> <p>If % Friability of tablets is less than 1% is considered acceptable.</p>	81, 79								
Tablet Density	<p>It is an important parameter in case of floating tablets. If density is less than gastric fluid (1.004) than only the tablets will float. It is calculated using formula :</p> <p>$V = \pi r^2 h$</p> <p>$d = m/v$</p> <p>r = Radius of tablet</p> <p>h = crown thickness (g/cc)</p> <p>m = Mass of tablet</p>	69								
Disintegration Time	In this one tablet is placed in disintegration apparatus containing buffer 0.1 N 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 time.	43								
<i>In Vitro</i> 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 buffer.	45								
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).	82								
Floating Time	It is the total time taken by which the tablets remain floating in the media.	82								
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.	61								
Swelling Study	<p>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</p> <p>$SI = W_t - W_0 / W_0 * 100$</p> <p>W_t (Weight of swollen tablet)</p> <p>W₀ (Initial weight of tablet)</p>	43								
Gamma Scintigraphy/ X – Ray	In this technique radio opaque material is added to the dosage form which is visualised by X- rays and this technique helps in locating drug in gastrointestinal tract and also helps to know drug passage through GIT and its gastric emptying time.	83								
Specific Gravity	The displacement method is used in which benzene is used as displacing medium to determine the specific gravity of floating system	17								

FUTURE PROSPECTIVE

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. Bilayer floating can be beneficial in diabetes as two drugs can be administered concurrently at the same time which provides better patient compliance. It provides a great opportunity in case of herbal drugs as these drugs can also be given in bilayer dosage form which provide both immediate as well as sustained effects. Drugs which has narrow absorption window such as anti- viral, antibiotic and antifungal can be given in floating bilayer dosage form.

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