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FLOATING BILAYER TABLET: A REVIEW

***Saliya Parveen, R. B. Nawale, Sadhana Shahi, Nityanand S. Zadbuke and Shehla Khan**

Department of Pharmaceutics, Government College of Pharmacy, Osmanpura, Aurangabad 431005, Maharashtra.

***Corresponding Author: Saliya Parveen**

Department of Pharmaceutics, Government College of Pharmacy, Osmanpura, Aurangabad 431005, Maharashtra.

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ABSTRACT

Floating drug delivery system (FDDS) belongs to the group of gastroretentive drug delivery system (GRDDS). These dosage forms are designed to achieve prolong gastric residence time in sustained release manner. Incorporation of drug in GRDDS, shows improve bioavailability, enhance solubility of drug that are less soluble in high pH environment. By flotation mechanism controlled gastric retention of solid dosage form can be achieved. Bilayer floating drug delivery system shows the unique combination of bilayer with floating mechanism. It shows successful development of controlled release formulation. Bilayer floating tablet provide both immediate as well as sustained release layer formulation. An attempt has been made in the review to introduce FDDS, Floating bilayer, its mechanism, different technologies required for its preparation, summarize its characterization and in vivo success of GRDDS.

KEYWORDS: Floating drug delivery system, floating bilayer, technologies, release pattern, characterization and in vivo success of GRDDS.

INTRODUCTION

Oral route of administration is the predominant and most preferable route for drug delivery. Importantly, it allows unassisted administration by the patient without the need for trained personnel (as this is the case with most parenterally administered dosage forms).

Oral route of administration involve oral controlled drug delivery which aims to deliver drug for an extended period of time which provide good bioavailability and 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 GRDDS 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.

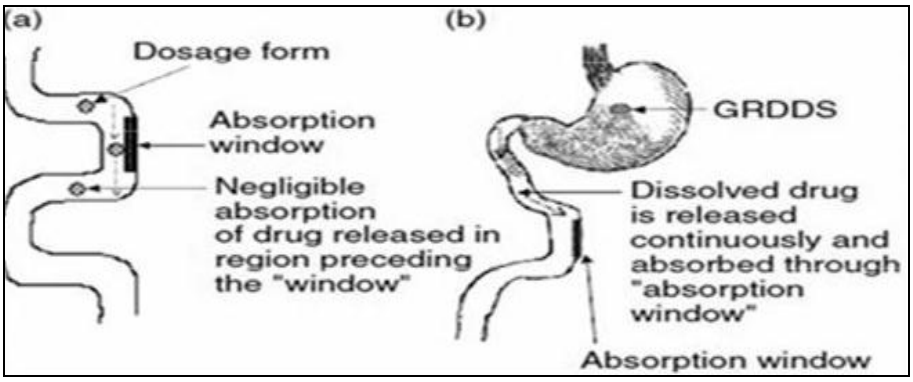

Fig. 1: Conventional Dosage Form shows negligible absorption whereas in GRDDS drug is continuously absorbed.

PHYSIOLOGY OF STOMACH

The stomach is a J shaped dilated portion of the alimentary tract situated in the epigastric, umbilical and left hypochondriac regions of the abdominal cavity. Its size varies with the amount of food it contains. The volume is 1.5 l or more in adult and after food has emptied a 'collapsed state' is obtained with a resting volume of only 25-30 ml. The stomach consists of

fundus, body and antrum; pylorus is a sphincter present in between the most terminal antrum and duodenum.

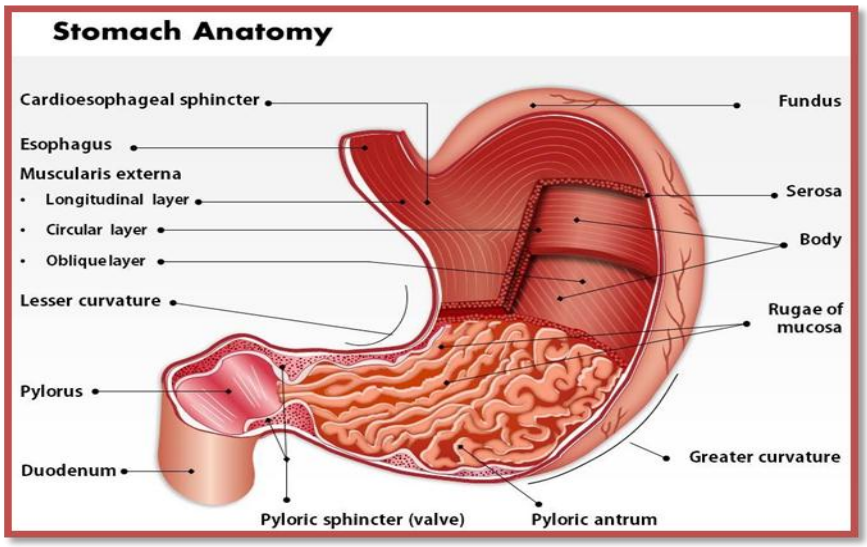

Fig. 2: Gross anatomy of stomach.

The fundus and body store food temporarily, secrete digestive juices and propels chymes, a milky mixture of food with gastric juices, to the antrum. The antrum grinds and triturates food particles and regulates the secretion of the hydrochloric acid as well as the emptying of food.

There are four consecutive phases of activity in the migrating myoelectric complex (MMC).

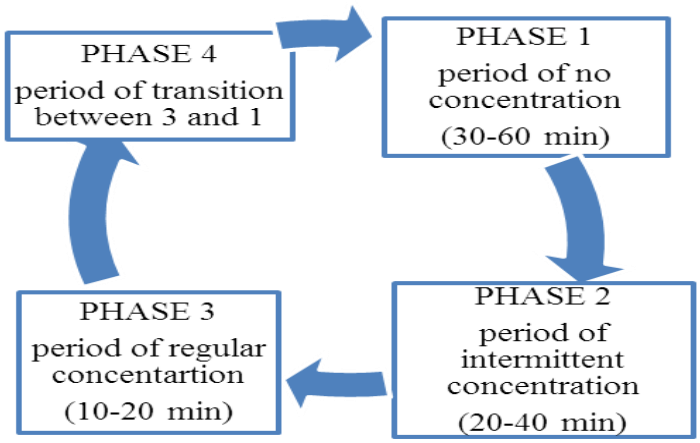

Fig. 3: Flow chart for four different phases.

Depending upon fasted and fed state of stomach two different patterns of GI motility and secretion has been observed.

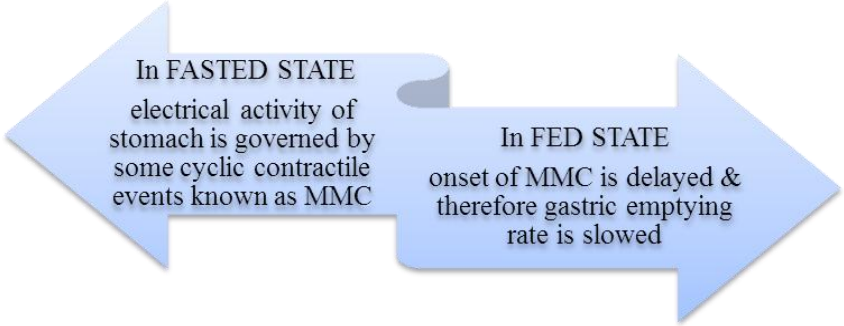

Fig. 4: Summary for fasted and fed state.

FLOATING DRUG DELIVERY SYSTEM

FDDS belong to the group of gastroretentive dosage forms initially described by Davis in 1968 (Davis, 1968). These dosage forms are able to achieve prolonged gastric residence time (GRT) with increased period for active pharmaceutical ingredients (API) to be released. 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.

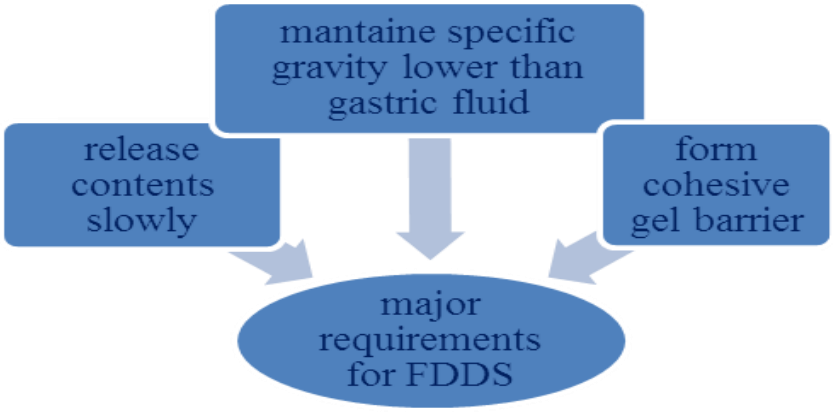

Fig. 5: Flow chart for FDDS requirements.

FACTOR AFFECTING ON FLOATING AND FLOATING TIME

1. Density: Density of a dosage form plays a vital role in determining its buoyancy and, its floating efficiency.

2. Shape of dosage form: Compared to other shapes, devices with tetrahedron and ring shape has better floating potential. They have 90-98% better retention for 24 h.

3. Single or multiple unit formulation: Multiple unit formulations permit a larger margin of safety against dosage form failure compared with single unit dosage form.

4. Fed or unfed state: Under fasting conditions, the GI motility is characterized by periods of strong motor activity or the MMC that occurs every 1.5 to 2 h.

5. 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.

6. Caloric content: A meal rich in protein and fat content can increase floating by 4-10 h.

7. Frequency of feed: - The floating can increase by over 400 minutes when successive meals are given compared with a single meal.

8. Age: Elderly people, above the age of 60, have a significantly longer floating.

9. Posture: Floating varies considerably between supine and upright ambulatory states of the patient.

10. Concomitant drug administration: Anticholinergics like atropine, opiates like codeine and prokinetic agents like metoclopramide and cisapride affect floating time.

11. Biological factors: floating may vary as per health conditions or physiological status of a person.eg. Diabetes and Crohn's disease alters floating time.

TYPES OF FLOATING DRUG DELIVERY SYSTEM

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

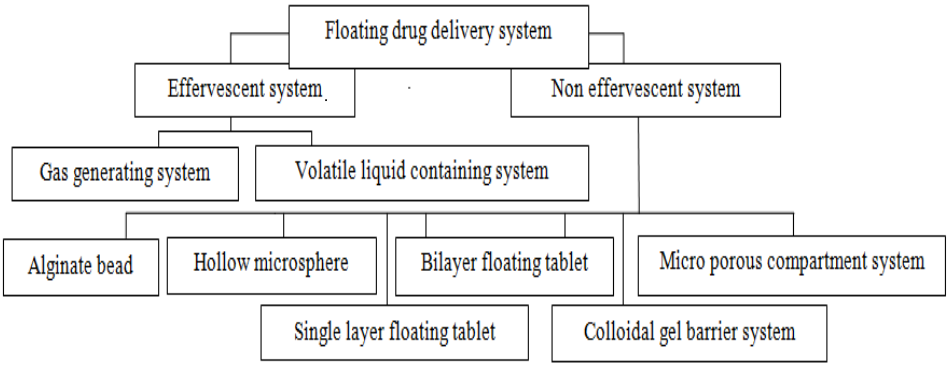

Fig 6: Classification of FDDS.

A. Effervescent system

These are matrix types of systems prepared using swellable polymer such as methylcellulose and effervescent compounds like sodium bicarbonate, tartaric acid. The matrices are fabricated so that upon coming in the stomach, CO_2 is liberated by the acidity of the gastric contents and is entrapped in the jellified hydrocolloid. This produces an upward motion of the dosage form and maintains its buoyancy. A decrease in specific gravity causes the dosage form to float on the chyme.

B. Non-effervescent system

The Non-effervescent FDDS is based on mechanism of swelling of polymer or bioadhesion to mucosal layer in GI tract. After swallowing the drug swells with the imbibition of gastric fluid in such a way that its 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. These systems may be referred to as the 'plug-type systems' since they have a tendency to remain stuck near the pyloric sphincter.

The most commonly used excipient in non effervescent floating drug delivery system are gel forming or highly swellable cellulose type hydrocolloids, polysaccharides and matrix forming polymers such as polyacrylate, polymethacrylate and polycarbonate.

MECHANISM OF FLOATING SYSTEM

FDDS has a bulk density less than gastric fluids so that they remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time.

F=F buoyancy-F gravity
= (Df-Ds) gv
Where,
F=total vertical force,
Df=fluid density,
Ds=object density,
V=volume,
g=acceleration due to gravity.

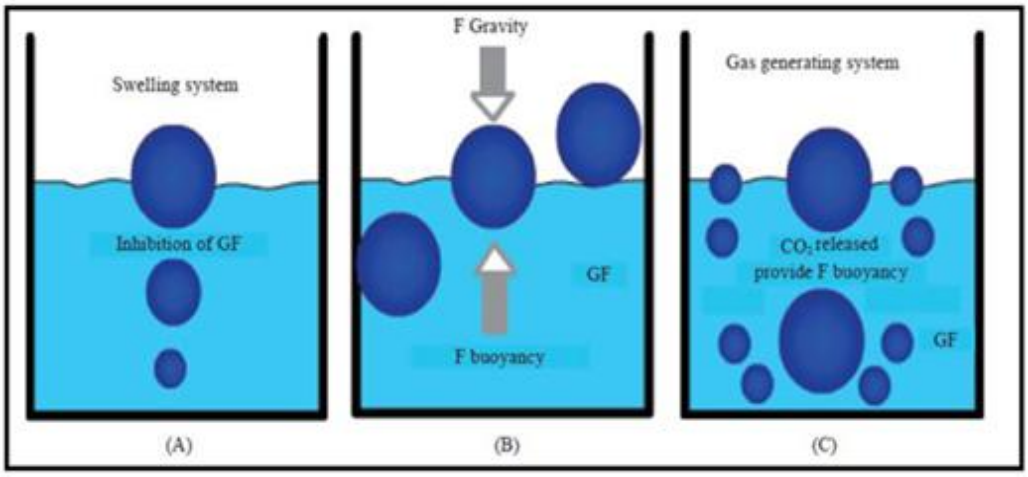

Fig. 7: Mechanism of floating.

Table 1: Different polymer used in FDDS.

Sustained Release Polymers	HPMC K100M, HPMC K15M, HPMC ELV, Polycarbonate, Polyethylene Glycol, Sodium Alginate, Carbopol, Eudragit.
Effervescent Generating System	Citric acid, 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.

Table 2: List of some common natural polymers used in floating drug delivery system and their sources.

Natural polymer	**Source**
Guar gum	Endosperm of the seed of *Cyamopsistetragonolobs*
Pectin	Citrus peel, apple pomace, sugar beet pulp etc.
Chitosan	Shell of marine invertebrate's
Xanthum gum	Fermentation of glucose by xanthomonascampestris
Psyllium husk starch	Seed coat of plant ago ovate storage polysaccharides in plants
Gellan gum	*Pseudomonas elodea*
Alginates	*Laminaeiahyperboria, Ascophyllumnodosum*

Table 3: List of Table Showing View of Different Scientist Based on Different Polymer Used and Their Effect in Floating.

Scientist	Polymer	Floating effect
Lee *et. Al*	Eudragit S100	The drug release rate and floating behaviour both were reported good
Jain *et. Al* Kale *et. al*	Eudragit	A good floating behaviour was observed, whereas dissolution rate was found to be slow, because of the low solubility of Eudragit at acidic pH
Sungthongjeen*et. Al*	Eudragit RL 30D, RS30D, and NE30D	The floating was reported for more than 24 h.
Nepal *et. Al*	Eudragit E100	The floating was reported for more than 24 h.
Tang *et. Al*	Eudragit E100	The drug release rate and floating behaviour both were reported good

Why Eudragit are prefferd mostly

A good floating behaviour was observed, whereas dissolution rate was found to be slow, because of the low solubility of eudragit at acidic pH.

FLOATING BILAYER TABLET

Bilayer tablets can be a primary option to avoid chemical incompatibilities between APIs by physical separation and to enable the development of different drug release profiles (immediate release with extended release).

Floating bilayer tablet is an innovative technique for the successful development of controlled release tablet formulation. This technique is suitable for the sequential release of two drugs in combination and it is capable of separating two incompatible substances.

This tablet contains two layers out of which one is immediate release layer and the other is sustained release layer. These tablets are specially designed to reduce the frequency of administration and to increase the duration of action. Immediate release layer deliver 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 agents and release the drug at sustained manner for prolonged period of time. The sustained release layer also called as the maintenance layer which maintains the therapeutic index.

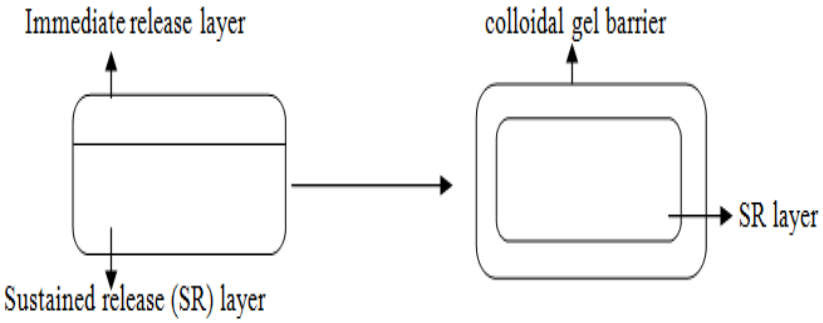

Fig 8: Sustained release layer forms colloidal gel barrier which floats.

NEED FOR THE BILAYER TABLET

1: For the administration of fixed dose combinations of different APIs, prolong the drug product life cycle.
2: Controlling the delivery rate of either single or two different APIs.
3: To modify the total surface area available for API layer in order to achieve swellable/erodible barriers for modified release.
4: To separate incompatible APIs from each other.

Release pattern in floating bilayer tablets

Floating dosage forms involves close mixing of drug with a gel-forming hydrocolloid, which swells in contact with gastric fluid after oral administration and maintain relative integrity of shape and a bulk density of less than unity within the outer gelatinous barrier.

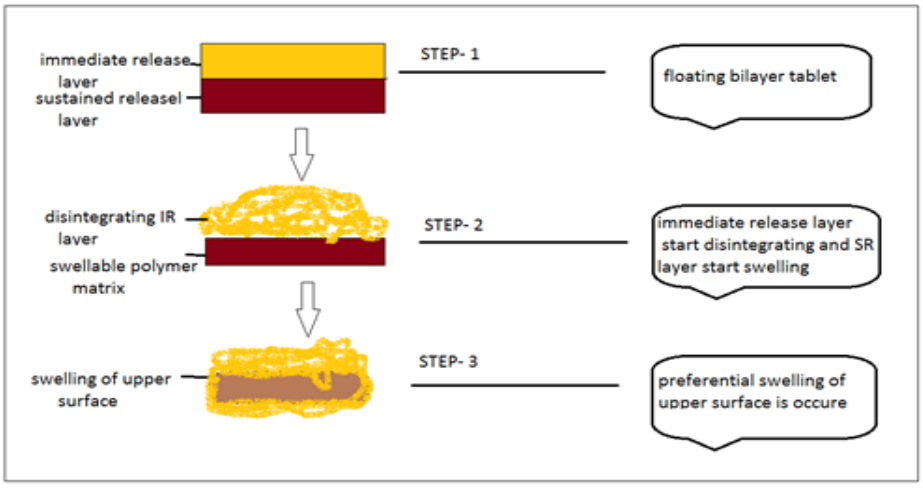

Fig. 9: Release pattern in floating bilayer tablet.

Ideal properties for bilayer tablet dosage form

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

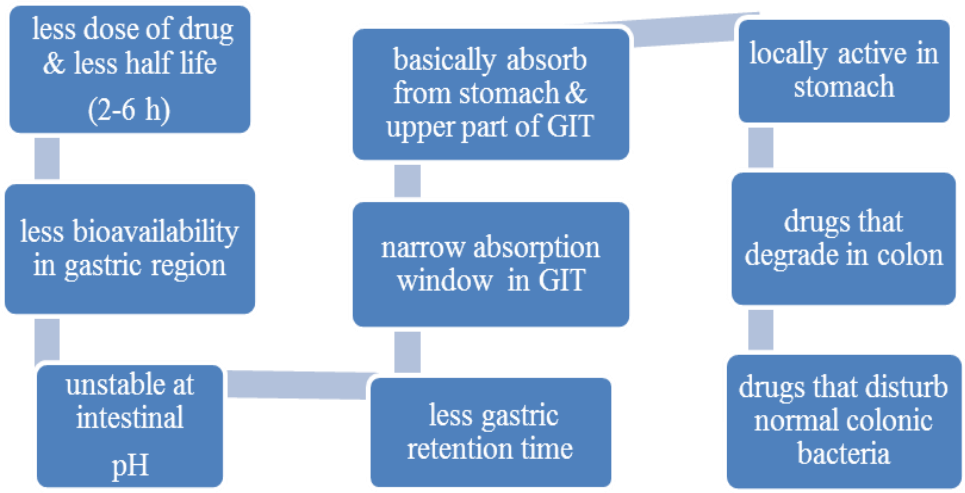

Fig. 10: Selection of Drugs for Bilayer Floating Tablet on its Suitability.

ADVANTAGES OF FLOATING BILAYER TABLET

- This system provides sustained release principle of HBS that has been found to be independent of the site of absorption of the particular medicaments.
- It maintain optimum therapeutic window so that drug delivery with controlled release is achieved.
- Site specific drug delivery is achieved for the drug such as furosemide and riboflavin which are formulated as floating system.
- Certain types of drugs that can be beneficial for gastro retentive drug delivery ,these include
- drugs acting locally into stomach
- Drugs those primarily absorbed in stomach.
- Drugs those poorly absorbed in alkaline pH.
- Drugs having narrow absorption window.
- Drugs rapidly absorbed from GIT.
- Drugs those degrade in colon.
- Better patient compliance is achieved leading to improve drug regimen efficacy.
- It maintained constant blood level.
- Compare to other oral routes they are more stable.
- Offers greatest precision and least content uniformity.
- Flexible concept.
- Suitable for large scale production.
- Objectionable odour and bitter taste can be masked by coating technique.
- Swallowing of tablet is easy.
- lighter and compact
- low cost

DISADVANTAGES OF FLOATING BILAYER TABLET

- More fluid level is required in the stomach to float the system.
- Drugs having solubility and stability problem in stomach are not formulated.
- Drugs which show irritation to gastric mucosa are not formulated.
- Some drugs such as isosorbidedinirate that are equally absorbed through GIT will not beneficial for incorporation into gastric retention system.
- Separation of the layer may occur due to insufficient bonding.
- Capping is the major problem in bilayer tablet.
- Hardness is another problem.
- There may be chances of layer mixing to each other.
- Swallowing problem in case of children and unconscious patient.
- Bioavailability problem may arise in case of poor wetting and less dissolution properties.
- Those drugs that are oxygen sensitive, bitter in taste, bad odour they required encapsulation.

PREPARATION OF BILAYER TABLET

For preparation of bilayer tablet, double compression technique is involved, because of poor flow and compatibility characteristic of the drug which will result in capping and/or lamination. The compaction of a material involves both the compressibility and consolidation.

Compression: It is defined as reduction in bulk volume by eliminating voids and bringing particles into closer contacts.

Consolidation: It is the property of the material in which there is increased mechanical strength due to interparticulate interaction (bonding).

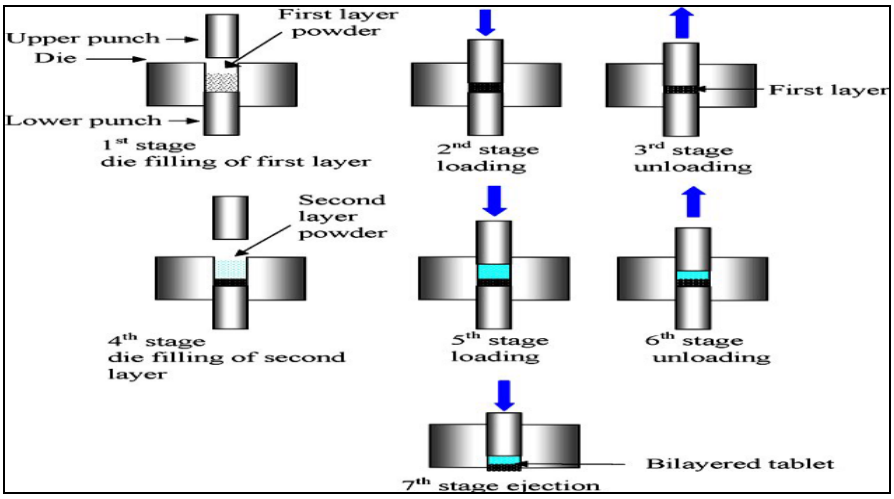

Fig. 11: Preparation of bilayer tablet.

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

In this technology the system consist of one or more layer out of which one is drug containing layer and other is push layer. The drug layer mainly consists of drug along with 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 core.

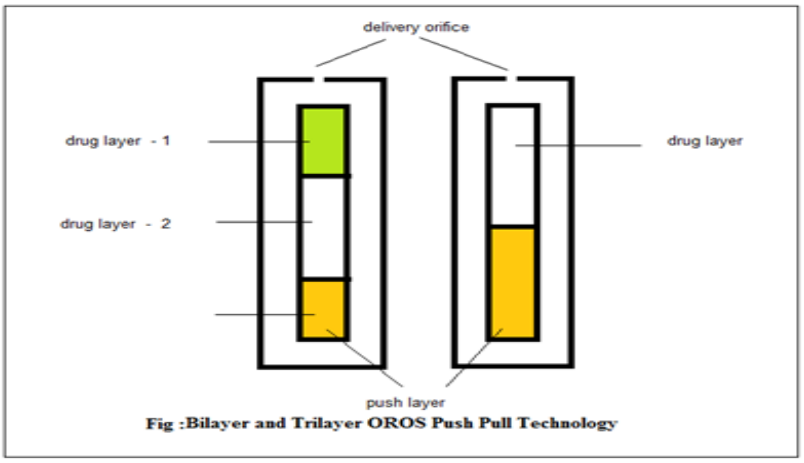

Fig. 12: OROS® Push Pulls Technology.

2. L-OROS TM Technology

This system mainly 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 orifice.

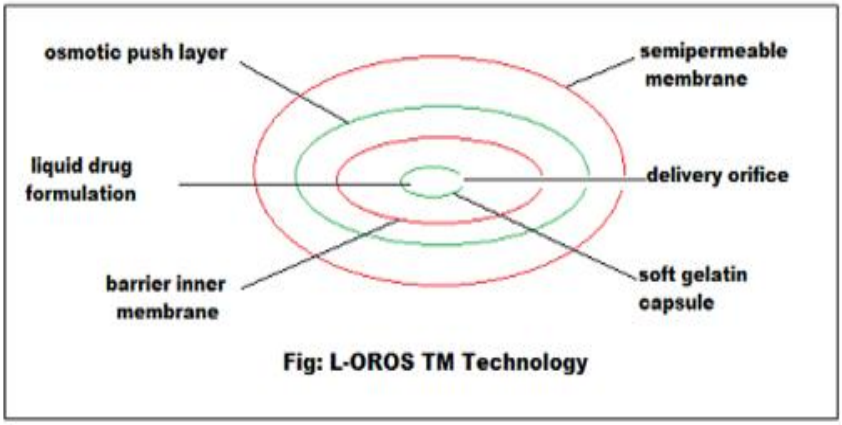

Fig. 13: L-OROS TM Technology.

3. DUROS Technology

The system comprises 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 year.

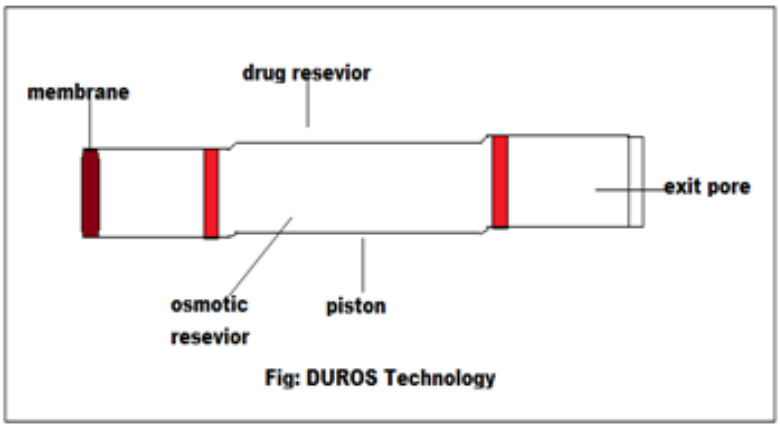

Fig. 14: DUROS Technology.

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. In this different controlled release formulations are combined together.

5. EN SO TROL Technology

This technology focuses on identification and incorporation of enhancer which is identified to form optimized dosage form in controlled release system. By this enhancement the solubility is achieved.

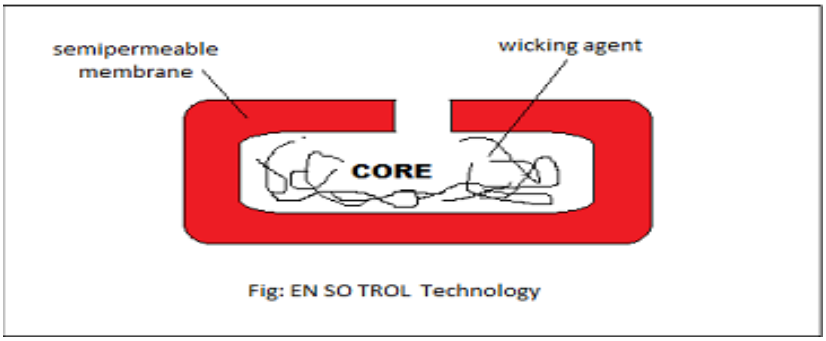

Fig. 16: EN SO TROL Technology.

6. RoTab Bilayer

RoTab bilayer when using is switched to production mode. By this technique dose and compression force is automatically regulated by adjusting filling speed and die table. Hardness is also adjusted.

7. Geminex Technology

In this system at different time's 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 rates.

8. PRODAS or Programmable Oral Drug Absorption System

This technology represents a grouping of multiparticulate and hydrophilic matrix tablet technologies. Mini tablets 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 mini tablets.

Characterisation of floating bilayer tablet

Table 4: Pre compression test.

<table>
<tr><th>Test</th><th>method</th></tr>
<tr><td>Angle of repose</td><td>To measure powder frictional forces.
Formula :
tanθ=h/r
θ=tan-1h/r
Where,
θ=angle of repose
h=height of pile
r=radius of pile
<table>
<tr><th>Angle of repose</th><th>Powder flow</th></tr>
<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>
</table></td></tr>
<tr><td>Compressibility index</td><td>Formula :
Compressibility index(%)=t-b*100/t
Where,
t=tapped density g/ml
b=bulk density g/ml</td></tr>
<tr><td>Bulk density</td><td>Formula :
b=mass of powder/bulk volume
where, b=bulk density</td></tr>
<tr><td>Tapped density</td><td>Formula:
t=mass of powder/tapped volume
where, t=tapped density</td></tr>
<tr><td>Particle size distribution</td><td>By sieving method</td></tr>
</table>

Table 5: Post compression test.

Test	Method
Shape of tablet	By magnifying lens after compression.
Tablet dimension	Randomly tablets are selected and their thickness and diameter are measured by verniercalliper or using screw gauze.
Hardness	Twenty tablets are selected randomly, than average weight and standard deviation are calculated. Test passes when not>20 tablets deviate from average weight. **Limits of weight variation** weight: < 80 mg — % variation: 10% weight: 80-250 mg — % variation: 7.5% weight: > 250 mg — % variation: 5%
Friability	Randomly select 10 tablets, weighed and placed in friability apparatus which rotate at 25 rpm for 4 min.After 4 min tablets are weighed again. Formula : % F=[1-(Wt/W)*100 Where,W-initial weight of tablets Wt-weight of tablets after revolution **Limit**: if friability is < 10% is considered acceptable.
Disintegration test	Buffer 0.1N HCl or PBS PH6.8 is used as disintegration media, at 37^0C.The time taken for tablets to disintegrate is noted as disintegration time.
In vitro dissolution	Using USP paddle apparatus by maintain temperature 370^0 C at 50 rpm speed. Withdrawn 5ml of sample at various time intervals and replaced it with same amount of buffer.
Drug content uniformity	Using UV spectrophotometer
Specific gravity	Displacement method is used, by using benzene as displacing medium to find specific gravity of floating system.
Floating Lag Time	It is the time interval required for tablets to start floating. It should be <1 min.it should be measured by dissolution test apparatus containing 0.1N HCl(900ml)
Floating time	The total time required for tablets to remain float in media.
Swelling index	Initially tablet is weighed (W1) and placed in a glass beaker, containing 200 ml of 0.1 N HCl, maintained temperature in a water bath at 37 ± 0.5 ^{0}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=Wt -W0/W0*100 Where: Wt - Weight of swollen tablet W0 - Initial weight of tablet

Table 6: In vivo evaluation.

Test	Method
Radiology	Barium sulphate ($BaSO_4$) is incorporated inside dosage form and X-ray images are taken at various intervals to view gastric retention.
Scintigraphy	Emitting materials (^{99}Tc) are incorporated in dosage form and images are taken by scintigraphy.
Gastroscopy	Used to inspect visually the effect of prolongation in stomach. it can also give the detailed evaluation of GRDDS.
Magnetic marker monitoring	Dosage form is magnetically marked with incorporating iron powder in it, and image can be taken by very sensitive bio-magnetic measurement equipment.
Ultrasonography	Not used generally because it is not traceable at intestine.
^{13}C Octanoic acid breath test	^{13}C Octanoic acid is incorporated into GRDDS.In stomach octanoic acid liberates CO_2 gas which comes out in breath. The C-atom in CO_2 is replaced with ^{13}C isotope. Time up to which $^{13}CO_2$ gas is observed in breath can be considered as GRT of dosage form.

IN VIVO SUCCESS OF GRDDS

Table 7: Animal study.

Scientist	Developed	Animal	Observation
Klausner et al.	GRDDS of Levodopa by using unfolding polymeric membranes with extended dimensions and high rigidity.	beagle dogs	the optimized controlled release GRDDS of Levodopa was able to maintain the therapeutic concentrations of Levodopa (>500 ng/ml) over 9 h.
Jain et al	Floating microsphere of repaglinide (hypoglycemic agent) where calcium silicate was used as porous carrier and Eudragit as polymer.	male rats	Organ distribution of the test compound was found to be uniform and the relative bioavailability was 3.17 times compared to marketed tablets.
Shishu and Aggarwal	therapeutic efficacy of floating calcium alginate beads of 5-flurouracil	mice	The multiple unit floating system was able to reduce gastric tumor incidence by 74%
Pande et al.	cefpodoxime proxetil microspheres as GRDDS	male albino rats	increase of the relative bioavailability of the drug formulated into the microspheres which was 1.5 times more compared to the suspension
Khan and Dehghan	Cephalexin loaded gastro-floating tablets were prepared by hydroxypropyl methylcellulose (HPMC K100M) as a matrix	albino rabbits	Floating lag time below 15 s and floating duration of more than 12 h with a satisfactory *in vitro* sustained-release profile for 12 h.
Thakar et al.	Floating tablets containing baclofen Composed of Polyox WSR 303 and HPMC K4M as swelling polymers and sodium bicarbonate as gas generating agent	rabbits	Favorable gastro-retentive properties like a floating lag time of 4 to 5 s and floating duration of more than 12 h.

Table 8: Human study.

Scientist	Drug	Formulation	Observation
Chen et al.	Losartan	gastro-retentive tablets based on swelling/effervescence mechanism	the optimized tablets achieved an enhanced bioavailability of approximately 164% relative to the immediate release market formulation named Cozaar®
Bomma and Veerabrahma	cefuroxime axetil	gastro-retentive tablets based on swelling/effervescence mechanism	an increase of 1.61-fold relative bioavailability.
Meijerink et al.	nicotinamide	Hypromellose was used as a swelling agent in that formulation	An increase nicotinamide plasma levels for a period of at least 8 h after ingestion
Ranade et al.	ellagic acid and aloevera gel	bilayer floating tablet	75% ulcer inhibition in comparison to 57% ulcer inhibition with ellagic acid alone.

Table 9: Patent on floating bilayer tablet.

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

Table 10: Commercially Available Bilayer Tablet.

Sr.no	Brand name	Chemical name	Manufacturer
1	ALPRAXPLUS	Sertraline, Alprazolam	Torrent Pharmaceutcals Ltd.
2	Glycomet®-GP2Forte	Metformin hydrochloride, Glimepiride	USV Limited
3	Newcold Plus	Levocetrizine hydrochloride, Phenylpropanolamine, Paracetamol	Piramal Healthcare Ltd.
4	DIAMICRON®XRNEX500	Gliclazide, Metformin hydrochloride	Serdia® Pharmaceuticals (India) Pvt. Ltd.
5	DIUCONTIN-K®20/250	Furosemide, Potassium chloride	T.C. Health Care Pvt. Ltd.
6	TRIOMUNE 30	Nevirapine, Lamivudine, Stavudine	Cipla Ltd.
7	PIOKIND®-M15	Pioglitazone, metformine hydrochloride	Psychotropic India Ltd
8	Revelol®-Am 25/5	Metoprolol succinate, Amlodipine besilate	Ipca Laboratories Ltd.

Table 11: Summary of Recent Research on FDDS for tablets.

S.no	Drug	Category	Polymer/excipient	Method	Result
1	Captopril	Anti Hypertensive-ACE inhibitor	HPMCK100, Ethylcellulose7cps,MCC	Direct compression	Prolonged gastric GRT and Increased bioavailability.
2	Acyclovir	antiviral drug	Psyllium husk, HPMC K4M, sodium bicarbonate	Wet granulation	Increased GRT, bioavailability
3	Ciprofloxacin	First generation Fluroquinolone	HPMC 4M, K15M, K100M, Citric acid, anhydrous, sodium bicarbonate	Direct compression	Improved GI absorption and Controlled release of drug.
4	Clarithromycin	Macrolide Antibiotic	HPMC K4M, sodium bicarbonate	Wet granulation	Improved bioavailability.
5	Propranolol HCL	Anti Hypertensive	HPMC, HPC, Xanthan gum sodium alginate	Direct compression	Increase bioavailability and GRT
6	Ranitidine	Histamine H2 receptor Antagonist	HPMC K4M Guar gum, Xanthan gum	Direct compression	Increased GRT and better sustained effect.
7	Silymarin	Anti-Oxidant	Psyllium husk, HPMC K4M, k15M, sodium bicarbonate, crosprovidone, MCC.	Direct compression	Prolonged drug release and improved the bioavailability and patient compliance
8	Tizanidine HCL	central acting muscle relaxant	HPMC, MCC PH 102, Dicalcium phosphate, Lactose	Wet granulation	Sustained release over 24h
9	Zidovudine	antiviral drug	HPMC K4M, Xanthan gum, carbapol 934P	Direct compression technique	Improved the bioavailability and control release
10	Itopride	peptic ulcer	HPMC K100M, K4M, K15M, NaHCo3	Direct compression	Improved bioavailability
11	Verapamil HCL	Anti Hypertensive Calcium channel blocker	MCC 102, HPMC K4M, HPMC 15M.	Direct compression	pH dependent and controlled release was obtained
12	Atenolol	Beta adrenergic Blocker	HPMC K4m, K100m, Directly compressible lactose, xanthan gum	Direct compression	Prolonged GRT.
13	Gabapentin	Anti-convulsant	HPMC K100M, K15M, PVPK30, MCC.	Direct compression	Increased bioavailability and Prolonged drug release
14	Metoprolol Tartrate	cardio selective β blocker	HPMC K15M, PVPK30, HCl, MCC.	Wet granulation	Increased GRT
15	Cefpodoxime Proxetil	cephalosporin prodrug	HPMC K4M, sodium CMC, carbopol 934P.	Direct compression	Prolonged GRT and increased drug absorption and bioavailability
16	Cefuroxime HCl	Cephalosporin	HPMC K4M, sodium Bicarbonate.	Direct compression	Buoyancy over 8-24h.
17	Atorvastatin Calcium	HMG-CoA Reductase inhibitor	HPMC K4M, Ethyl Cellulose Bees wax	Melt granulation	Drug release in a controlled manner for extended Period of time.
18	Carbamazepine	Anti-convulsant	HPMC, sodium bicarbonate, and EC	Melt granulation	Improved drug absorption and Bioavailability
19	Labetalol Hydrochloride	non-selective α, β-adreno receptor antagonist	HPMCK4M Carbopol 934P, Sod CMC, citric acid, sodium bicarbonate	Simplex Centroid Design	Improved bioavailability and controlled over 12h.
20	Levofloxacin	Antibiotic	Citric Acid and Sodium Bicarbonate. HPMC, EC	Direct compression	Drug release with prolonged Period
21	Lornoxicam	NSAID	HPMC K15M, calcium Carbonate (13%).	Direct compression	Prolonged GRT and improved Bioavailability.
22	Montelukast	Selective leukotriene Receptor antagonist.	HPM(K4M, K15M), xanthan gum sodium bicarbonate	Direct compression	Prolonged drug release over 24h.
23	Nifedipine	calcium channel blocking agent	HPMC K100M	Fabrication	Prolonged GRT, controlled release over 24h and improved bioavailability.
24	Nizatidine	Antiulcer	HPMC (K100, K4M, K15M & K100M), sodiumbicarbonate	Direct compression	Controlled release and enhanced bioavailability
25	Norfloxacin	Antibiotic	HPMC K4M, HPMC K100M, xanthan gum, Citric acid	Direct compression	Increased bioavailability
26	Ofloxacin	Antibacterial	guar gum, locust bean gum, HPMC K100M, sodium bicarbonate	Wet granulation	Prolonged GRT and controlled and uniform release
27	Ondansetron HCL	selective serotonin 5HT3 receptor antagonist	HPMC-E6; Eudragit RL- 100 (ERL) RS-100 (ERS) cetyl alcohol. NaHCO3, PEG6000	Direct compression	Prolonged GRT and increased Bioavailability
28	Cephalexin	β-lactum antibiotic	Citric Acid, Sodium Bicarbonate. HPMC K100M.	Wet granulation	Drug release over 12h
29	Pregabalin	Anti convulsent	HPMC K4M ethyl cellulose, crospovidone	Wet granulation	Improved bioavailability
30	Tinidazole	Antibacterial and anti protozaol	HPMC, Sodium Bicarbonate, citric acid.	Direct compression	Good Controlled release improved bioavailability
31	Tramadol	Opoid analgesic	15M, HPMC 100 LV, Sodium bicarbonate, gum tragacanth.	Direct compression	Prolonged GRT and enhanced Bioavailability
32	Amoxycillin Trihydrate	Anti-bacterial	HPMC K4M, xanthan gum, ethocel	Direct Compression	Sustained release over 12h
33	Glipizide	Antidiabetic	HPMC K100M, sodium alginate, Carbopol 940, and PVP K30	Direct Compression	Prolonged GRT and improved Bioavailability

CONCLUSION

GRDDS facilitate prolonged and continuous input of the drug to the upper part of the GIT and improve bioavailability of medication that are characterised by narrow absorption window. 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 h. Pharmaceutical industries are trying to prepare one of the

most economic and conventional 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 permit for more effective oral use of peptide and protein drugs such as calcitonin, erythropoietin, vasopressin, insulin, low molecular weight heparin and LHRH.

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