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BILAYER TABLET- A COMPREHENSIVE REVIEW

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ABSTRACT

From last decade, over 90% drugs are manufactured in the form of oral dosage form. This shows that oral dosage form gained attention now a day and become popular class of formulation worldwide. Conventional oral dosage form showing number of disadvantages i.e. mainly high frequency of dosing and dose. For overcome this problem there is increased interest in developing controlled drug delivery. Bilayer tablet is successful new era for development of controlled release formulation. Bilayer tablet technology, an excellent improved technique for providing combine release pattern of drug i.e. immediate release and sustained release. In this system two incompatible drugs combined together in single dosage form. There are different approaches available for bilayer tablet technique. Biphasic system formulated with drug having analgesics, antipyretics, antiallergenic, coronary vasodilators, antihypertensive and antihistaminic activity. Now a day several companies come in competition for development of bilayer tablet for number of reasons- patent extension, therapeutic, marketing to name a few.

KEYWORDS: Bilayer tablet, GMP requirement for bi-layer tablets, various tablet presses, Approaches.

INTRODUCTION

In the last decade, over 90% drugs are manufactured in the form of oral dosage form. This shows that oral dosage form gained attention now a day and become popular class of formulation worldwide. Now a day this class gained major attention from researcher too. Conventional oral dosage form showing number of disadvantages i.e. mainly high frequency of dosing and dose.

From the last decade there is increased interest in developing controlled drug delivery with major aim to reduce frequency of dosing. Now a day multilayer tablet dosage form shows great acceptability. Multilayer tablet are bilayer, trilayer and four layer tablets. Mainly bilayer tablet is the new era for the successful development of controlled release formulation. Bilayer tablet is single dosage form with combination of two or more Active Pharmaceutical Ingredients (API) which promoting patient convenience compliance.

Bilayer tablet are the great example of avoiding chemical incompatibilities between the APIS, and providing different drug release profile (immediate release with extended release).

In Bilayer tablet, amongst the two layers first layer act for loading dose purpose and second will for maintenance purpose.

Mainly the biphasic system used when there is need of fast action or relief and followed with continuous action Biphasic system formulated with drug having analgesics, antipyretics, antiallergenic, coronary vasodilators, antihypertensives and antihistaminics activity. There is also an example of bilayer tablet with both the layer as sustain release layers, example certain antidiabetic agents. In development of multilayer system with different release patterns, there is need of different rate controlling polymers which allows manipulation, resulted into different type of drug delivery of one or more drugs.

Bilayer tablet are of two types:
1) Homogeneous Type
2) Heterogeneous Type

1) Homogeneous Type

These are preferred when drug showing release profile different from each other. These are developed in such a manner that one layer acts as loading dose for immediate release and other layer for giving maintenance dose or extended release.[23]

2) Heterogeneous Type

These are formulated with two incompatible substances in single dosage form separated from each other. Two drugs providing sequential release in combination are the example of this type.[23]

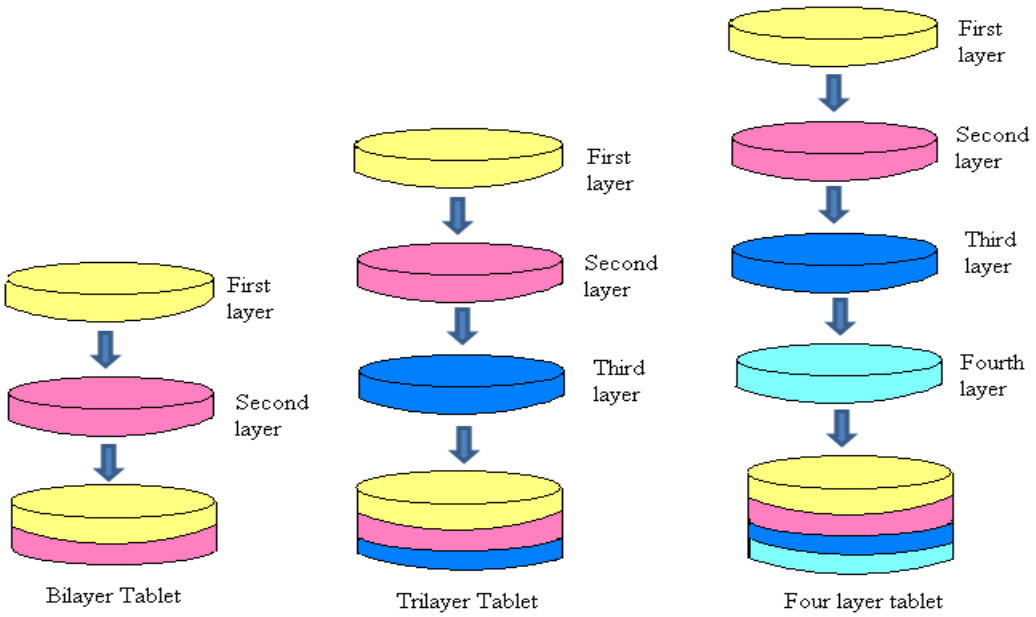

Fig. 1: Multilayer tablets.[5]

NEED OF BILAYER TABLET[4]

- For purpose of administration of dual release fixed dose combinations of different APIs.
- For the purpose of developing novel drug delivery system.such as buccal/mucoadhesive delivery system and floating tablets for gastroretentive drug delivery system.
- It helps in controlling drug delivery rate of single or two APIs.
- To modify bilayer tablet in such way that total surface area available for API layer by sandwiching with one or two in active layers for achieving swellable/erodible barrier for modified release.
- To incorporate two incompatible API in one dosage, this helps in control release of API from one layer by utilizing property of other layer (Such as, Osmotic Property).

ADVANTAGES[1,34,36]

- Low cost than other oral dosage form.
- It is suitable for large scale manufacturing.
- Increased patient compliance leading to improved drug regimen efficiency.
- Higher chemical and microbial stability than other oral dosage form.
- Unacceptable odour and bitter taste can be masked by coating technique.
- There is no any difficulty in swallowing bilayer tablet.
- Flexible concept.
- Bilayer tablet provide dual release pattern of drug. (Sustained release and immediate release)
- Two incompatible drugs can be incorporated in single dosage form.

DISADVANTAGES[1,34,36]

- Due to the amorphous nature, low density character some drugs resist compression into dense mass.
- There is need of coating for masking unacceptable odour of drugs, bitter tasting drugs or drugs sensitive to oxygen.
- There is problem of swallowing, for children and unconscious patients.
- There is difficulty in formulating bilayer tablet with drugs having poor wetting properties, slow dissolution rate, optimum absorption high in GIT.
- There is possibility of cross contamination between the layers.
- For manufacturing of bilayer tablet required different tablet presses are required which adds complexity.
- Insufficient hardness, layer separation, reduced yield.

TECHNIQUES OF BILAYER TABLET

1. Oros ® Push Pull Technology
2. L-Oros Tm Technology
3. DUROS Technology
4. Elan Drug Technologies' Dual Release Drug Delivery System (DUREDAS™ Technology)
5. EN SO TROL Technology
6. Rotab Bilayer
7. Geminex Technology
8. PRODAS or programmable oral drug absorption system
9. Erodible molded multilayer tablet

1. Oros ® Push Pull Technology

This technology composes of mainly two or three layers. From which the one or two layer are of active pharmaceutical ingredient and another is push layer. Drug layer is composed of drug along with two or more

excipients. Drug layer is of poorly soluble nature. Suspending agent and osmotic agent may be added further. A semipermeable layer separates tablet core from surrounding.[1]

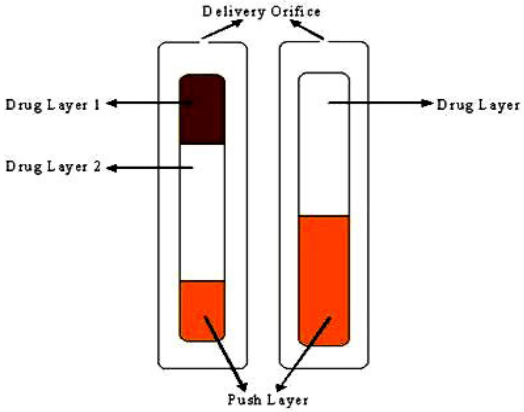

Fig. 2: Bilayer and trilayer OROS push pull technology.[1]

2. L-Oros Tm Technology

This technology comes into force to solve solubility issue; Firstly Alza developed L-OROS system. Drug in dissolved state initially developed in the form of lipid soft gel product. Then it coated with the help of barrier membrane, then osmotic push layer and finally drilled semipermeable membrane with an exit orifice.[3]

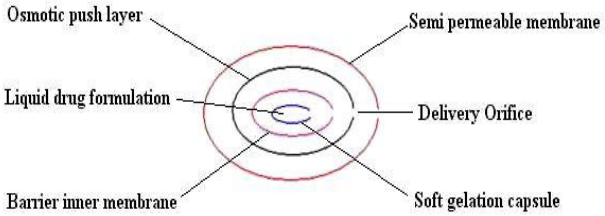

Fig. 3: L–OROS TM Technology.[1]

3. DUROS Technology

This system is also known as "Miniature drug dispensing technology", which works like miniature syringe which releases drug in, continues and consistent manner in small concentrated form over long time period. Drug molecules are protected from enzyme with help of outer cylindrical titanium alloy reservoir having high impact strength.[1,36]

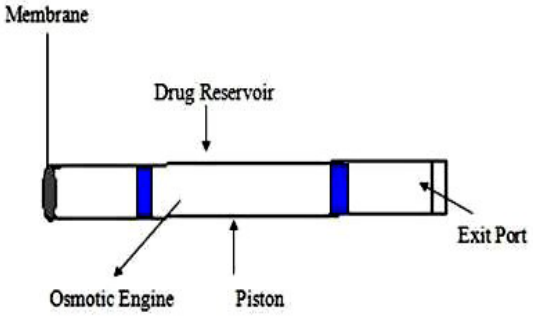

Fig. 4: DUROS Technologies.[1]

4. Elan Drug Technologies' Dual Release Drug Delivery System (DUREDAS™ Technology)

This technology provides combination release pattern of drug i.e. immediate or sustained release. In this system provides either one drug with different release pattern or two drugs of combination release pattern. In this system different release pattern achieved by using combination of hydrophilic polymer. This technology provides number of advantages i.e. combination release in one tablet or another advantage is two drugs incorporated in single dosage form. During process of manufacturing bilayer tablet by using DUREDAS™ Technology immediate release granulate compressed first followed by sustained release layer. DUREDAS™ Technology first used for development of OTC controlled release analgesics.[3]

5. EN SO TROL Technology

Shire laboratory uses an integrated approach for drug delivery system, with the help of identification and incorporation of enhancer for getting optimized dosage form in controlled release system. This approach useful in increasing solubility.[1,3]

Fig. 5: EN SO TROL Technology.[1]

6. Rotab Bilayer

1. Software

It's software of modular design, to which additional functions can be added. Fast graphical evaluations with accurate results can be achieved by one of the advanced system known, PC- system with 15" touch- screens''.

2. Working

RoTab bilayer is an automatically regulating system, when using for production mode switched towards it. With the help of it dose and compression force is automatically regulated by adjusting filling speed and die table. Hardness is also regulated when required.

3. R and D modified technique

R and D modified RoTab Bilayer are useful for graphical visualization and evaluation with measuring points on which there are. These playing important functions of controlling punch tightness. These have R and D plus with possibility of anytime upgration.

4. R and D Plus

R and D Plus showing great importance in tableting technology, provides improved standards. It is useful in controlling important functions such as control of punch tightness, force displacement display and scraper force of tablet.[2]

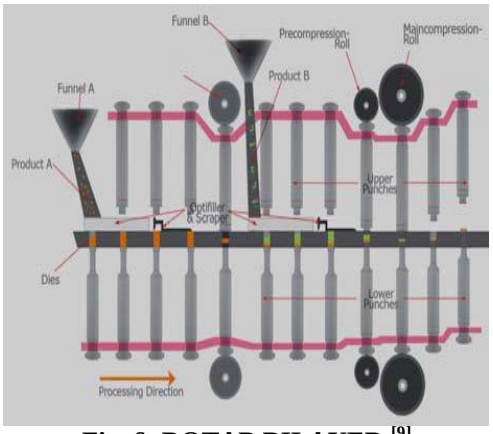

Fig. 6: ROTAB BILAYER.[9]

7. Geminex Technology

This technology is very useful one. With help of this the therapeutic efficacy of drugs can be increased greatly, also useful in minimizing side effects. This technology delivers one or more drug with different release rate in single dosage form. It is very useful both for industry as well patients. Geminex Technology actively applied by penwest in following areas – dibetes, cardiovascular diseases, cancer and CNS disorders.[2,3,7]

8. PRODAS or programmable oral drug absorption system-

PRODAS is also known as multi particulate drug technology (Elan Corporation). In this technology, controlled release mini tablets (size range 1.5 to 4 mm) are encapsulated. This technology having combination of multi particulate and hydrophilic matrix tablet technologies, used to provide usefulness of above technologies in single dosage form.

PRODAS technology useful in targeted delivery of drug, for targeting to GIT. Different release rate Minitab, (immediate-release, delayed-release, and/or controlled release) lets combined together in single dosage form to provide desired release rate. Sometime Minitab let are combined with different API to form products of desired release pattern.[2,3,7,36]

9. Erodible molded multilayer tablet

Egalet delivery technology is erodible molded multilayered tablet technique. This technology developed based on standard plastic injection moulding, containing coat and matrix. Egalet erodible molded tablets, having mechanism for release pattern is erosion of matrix part. This technique useful in delivering zero order or delayed release pattern of drug without affecting GI conditions.

Release pattern controlled by designing and engineering of geometry of coat and matrix. For zero order release drug dispersed in matrix. The coat used is of poor water permeability and biodegradable. Erosion of matrix takes place when come in contact with available water or by GI fluids and promote by gut movements in the GI tract. This technique wholly desirable for drugs with stability issues while contacting with water i.e.chemical and physical stability issues. This technology assures accuracy, reproducibility and low production cost.[7,36]

Table 1: Technology used for different layer tablets.[5]

Company Name	Name of Technology	Approach
Skye Pharma	Geomatrix Technology	One or two impermeable polymeric coating applied on one Or both bases of the core tablet.
Accu-Break pharmaceutical s, Inc.	Accu-Break Technology: Accu-B &Accu-T bilayer or tri-layer tablet technology	Suitable for FDCs combination, easily divided, and ability to separate IR from CR and to take appropriate half tablets And the free layer drug does not affect drug release.
Alza Corporation	OROS push pull technology, Bilayer or trilayer core	Consists of one push layer and 1 or more drug layer, osmotic agent & water swellable polymer
Flamel Technologies	Flame Micro pump technology	Permits DR and ER drug delivery system
Elan Drug Technologies	DUREDAS Dual Release Drug Absorption System	Immediate and sustained release rates of drug

PREPARATION OF BILAYER TABLETS

Bilayer tablets are prepared with double compression technique. In which two incompatible drugs compressed individually as separate layers to avoid much contact between the drugs. Inert material which acting as an additional intermediate layer. Development of bilayer tablet is very challenging task for formulator because there is certain requirements regarding mechanical strength and release pattern of drug must be targeted.[1,3]

Challenges in development of bilayer tablet.[1]

- Cross contamination
- Production yield
- Cost
- Delamination[1]

The compaction of a material involves both the compressibility and consolidation.

1. Compression

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

2. Consolidation

It is the property of the material in which there is increased mechanical strength due to interparticulate interaction (bonding). The compression force on layer 1 was found to be major factor influencing tablet delamination.[1]

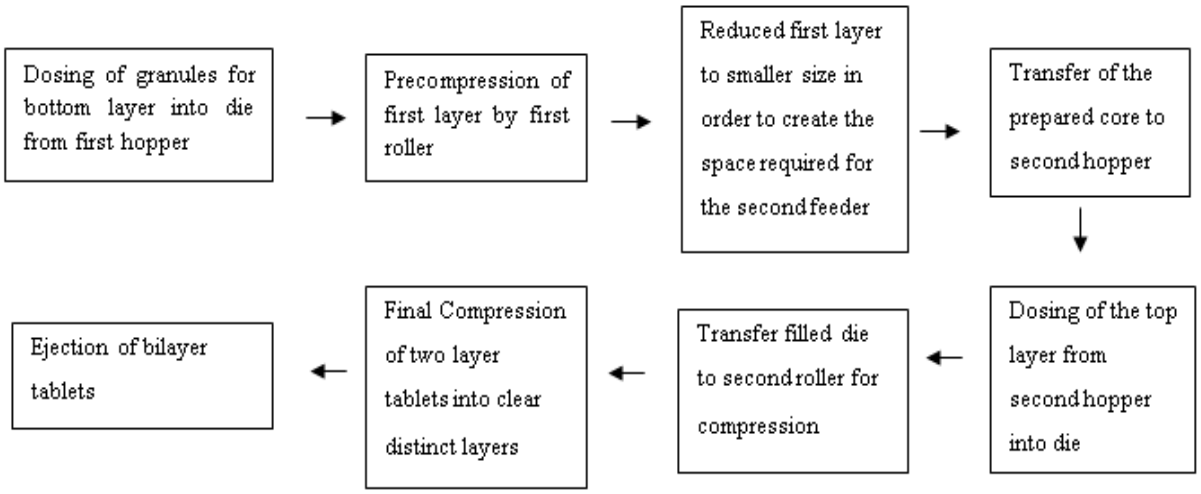

Fig. 7: Steps involved in preparation of bilayer tablets.[5]

QUALITY AND GMP-REQUIREMENTS[7]

These requirements are important for producing quality bilayer tablet. These are helpful in selection of press capable of,

- These should provide bilayer tablet with no capping and separation problem between the layers.
- Press should capable of providing sufficient strength to tablet i.e. Hardness.
- Providing bilayer tablet with no cross-contamination between two layers.
- Produces two layers with clear visual separation.
- Producing bilayer tablet with individual weight control of two layers and with high yield accuracy.

TYPES OF BILAYER TABLET PRESS

1. Single sided tablet press.
2. Double sided tablet press
3. Bilayer tablet press with displacement monitoring.
4. Multilayer compression basics

1. Single sided tablet press[1,3]

There are number of presses available for bilayer tablet manufacturing, but single sided tablet press is simplest design available for bilayer tablet development. In these tablet presses double feeder chambers separated from each other. Each chamber run as per gravitational force, or force fed with different powders thus producing bilayer tablet. As the die comes under the feeder firstly get loaded with first layer of powder followed by pre compression and then second layer powder with following second pre compression and then final main compression, hence entire tablet manufactured in one or two steps (two pre and main compression). While developing bilayer tablet there should be sufficient bond between two layers so that no layer separation occurs when the tablet is produced.

LIMITATIONS OF SINGLE SIDED PRESS

- There is no proper weight monitoring or control of the individual layers.
- No distinct visual separation between the 2 layers.
- Dwell time
- Compression force.
- Poor deration capping and hardness problems

DWELL TIME

It is defined as the time during which compression force is above 90% of its peak value. Major factor in the production of quality tablets is longer dwell time.

COMPRESSION FORCE

Compression force of 100 daN require for many bilayer tablets for first layer compression for the retaining ability to form bond with the second layer. 100 daN compression force. Sufficient for proper bonding between two layers but above this force, ability of bonding may be lost. This results in separation of the 2 layers due to low hardness of bilayer tablet.

Fig. 8: Single Sided Tablet Press.[7]

2. Double sided tablet press[3]

Automated production control used by most of double sided tablet presses, which with compression force is useful in monitor and control of tablet weight. Control system is used for measuring peak compression force exerted on each individual tablet or layer at the stage of final main compression of bilayer tablet.it proved useful for rejection out of tolerance and correction of the die fill depth with help of the signal produced by control system.

ADVANTAGES

- To avoid capping and separation of the individual layer by applying low compression force on first layer.
- Sufficient hardness is built in tablet by increasing dwell time at pre compression of both first and second layer.
- There is maximum avoidance of cross contamination in bilayer tablet.
- In bilayer tablet clear visual separation between the layers.
- High production yield.
- Control system is very useful in accurate and independent weight control of the individual layer.

LIMITATIONS

As for proper bonding between two layers in bilayer pre compression force required for first layer should be less than second one. Bonding is not possible if pre compression done at high compression force. Accuracy of the weight monitoring/control of the first layer in the case of tablet presses with "compression force measurement" reduces unfortunately by low compression force used for the first layer pre compression. Most of automatically controlled tablet presses have principle of compression force.

Fig. 9: Double Sided Tablet Press.[37]

3. Bilayer tablet press with displacement monitoring[3]

This tablet press worked on principle displacement tablet weight control, which is different from the principle of compression force. As based on principle sensitivity of control system does not depend on the tablet weight but depends on applied pre compression force. In this case the risk of capping and separation increases at higher production speed increases but can be reduced by sufficient dwell time at all four compressions.

ADVANTAGES

- Principle useful for accurate independent weight control of the individual layers.
- Proper bonding possible as there is use of low compression force applied on the first layer avoids capping and separation of the two individual layers.
- Maximum production yield and clear visual separation between layers in tablet.
- Avoid cross contamination between the layers.
- Ability to build sufficient hardness to tablet at maximum turret speed by increased dwell time at pre-compression of both first and second layer.
- There is no any effect of stiffness on bilayer tablet.

Fig. 10: Bilayer tablet press with displacement.[7]

4. Multilayer compression basics[3]

Multilayer tablet means two or more layers in tablets and are able to provide multiple release pattern of drugs. Multilayer tablets are developed on presses designed specifically for multilayer compression or standard double press can be converted for multilayers. Multilayer tablet technology used for sustained release purpose. Release pattern of drug depends on granules, fast releasing granules leads to sudden rise in blood concentration work as loading dose whereas plasma drug level maintained at a steady state by sustained releasing granules.

BILAYER TABLET BASIC APPROACH

1. GEOMATIRX
2. FLOATING
3. POLYMERIC BIOADHESIVE SYSTEM
4. SWELLING SYSTEM / UNFOLDING SYSTEMS

1. GEOMATIRX[3]

Geomatrix tablet is one of the examples of bilayer tablet. In this system more than one drug is tableting in single tablet. In this different types of polymers used for combine release pattern of one or more drugs. There are number of problems faced in development of bilayer tablet with combine release pattern. There is problem in controlling mechanical strength of bilayer tablet. Mechanical strength of tablet is very important to understand the bonding between various layers and provide an improved characterization of the systems. Bilayer tablet characterized by having combine release

pattern with one layer of drug for immediate release while second layer either as second dose or for extended release.

Multilayer tablet technology is very helpful for supplying incompatible drugs in single dosage form, for controlled release system. In which initial dose is for loading purpose whereas second one for maintenance of plasma drug level of drug. There are different release pattern that are constant, delayed, pulsatile and multi modal release profiles in control release systems. Geometries are prepared by compression which requires various strategies which are described.

2. POLYMERIC BIOADHESIVE SYSTEM[1]

In this system, adherence to the gastric mucosa is very important factor which is achieved by imbibing dosage form in fluid and it becomes viscous, tacky material. Polymeric bioadhesive system, bilayer tablet prepared with one layer with immediate release property and other layer with bioadhesive property. Gastric retention of bioadhesive layer only possible when adhesive force is strong.

DISADVANTAGES

- As mucous layer in human body slough off readily from body after some time. As in these, system adheres on mucous linings it sloughs off readily with mucous. Hence drug gets eliminated from body in short period of time. Hence bioadhesive dosage form should not be solution for extended delivery of drug.
- This system shows success only on animal model which is not comparable with humans due to differences in mucous amounts, consistency between animals and humans. The system adheres to mucous not mucosa.

3. SWELLING SYSTEM/UNFOLDING SYSTEMS[1]

These system formulated in sufficiently small design easy to administer. After administration reaches to site of action where it get swelled or unfolded. On swelling not able to leave the pyloric sphincter. As time passes there is release of drug by erosion mechanism. As it converted into smaller particles on gradual erosion it able to leave the stomach.

4. FLOATING DRUG DELIVERY SYSTEM[1]

This system developed first by Davis in the year of 1968. As we know the conventional dosage form are retained in stomach for short period of time i.e. 0.5-2 hours, then get passed to the small intestine from which it get absorbed within 3-6 hours. It shows difficulty for those dosage forms mainly absorbed from upper part of GIT or stomach.

Oral route of administration have disadvantage of gastrointestinal transit time of the dosage form. Hence there is difficulty in developing such dosage form with increased gastric retention and controlled release retardation. For overcoming all these problems, this system comes into force. This is considerably easy and logical approach in the development of such dosage form with increased gastric retention. For development of Gastro retentive dosage forms (GRDFs).

In floating system there are two layers, first immediate release layer for loading purpose and second sustained release layer of maintenance purpose. This system developed with the aim of reducing dosing frequency and for increasing duration of action. As there is release of first layer i.e. loading dose, second layer get swelled by absorbing gastric fluid, it forms colloidal gel barrier which have less density than gastric fluid due to that the dosage form remains floated in stomach.

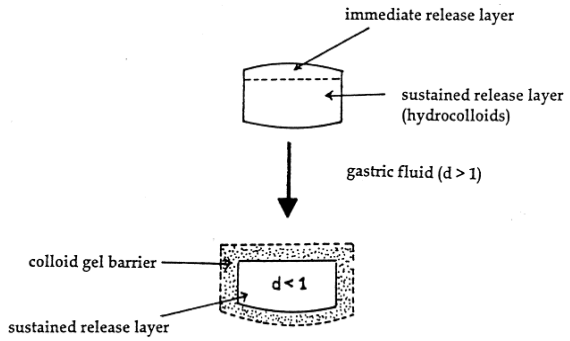

Fig. 11: Schematic diagram of Bi-layer floating tablet.[2]

Approaches to design Floating Drug Delivery System

For development of Floating dosage form of single or multiple units systems following approaches are used-

1. Intragastric bilayered floating tablets

These tablets having two layer i.e. Immediate and sustained release and these are prepared by compression hence known to be compressed tablet.

2. Multiple unit type floating pills

This system having double layers which covers 'seeds' of sustained release pills. Where inner layer with effervescent agents while outer layer with swellable membrane. This system sinks when immersed in dissolution medium at body temperature, then forms swollen pills like balloons, which have lower density and it 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.

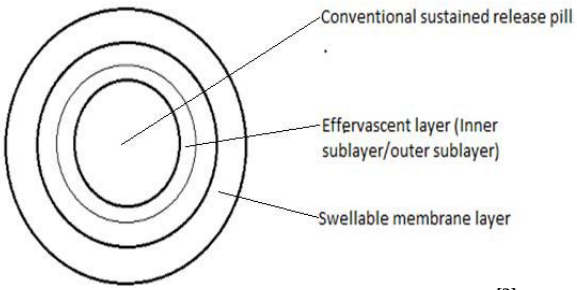

Fig. 12: Multiple Units of Oral FDDS.[3]

DISADVANTAGES

- There should be increased fluid levels in stomach so that the system can float properly.
- Floating system cannot formulate with drugs having solubility and stability problem in stomach.
- Drug with property of producing irritation cannot formulate as floating system.
- There is less control over weight of individual layer.

CHARACTERIZATION OF BILAYER TABLET

1. PARTICLE SIZE DISTRIBUTION

There are number of methods for measuring particle size. Mostly sieving method used for measuring particle size distribution.[3]

2. PHOTON MICROSCOPE STUDY

Photomicroscope (X450 magnifications) used for taking Photo-microscope image of TGG and GG.[3]

3. ANGLE OF REPOSE

Angle made by the pile of the powder from horizontal surface. The diameter of the powder cone measured and the angle of repose was calculated. By using following equation,[3]

Tan Ø=h/r

OR

Ø= Tan¯ h/r

Where,
Ø =Angle of repose,
h = height of the pile,
r = radius of the powder cone.

Table2. Angle of Repose I.P limits.[32]

Angle of Repose	Powder flow
< 25	Excellent
25 – 30	Good
30 – 40	Passable
> 40	Very Poor

4. MOISTURE SORPTION CAPACITY

There are different patterns of moisture absorption, by all disintegrate from atmosphere which affects moisture sensitive drugs. This property checked with help of taking 1 g disintegrant in Petri-dish. Which at 37± 1°C kept in stability chamber and at 100% RH for 2 days. Amount of moisture uptake was calculated by weight difference.[3]

5. DENSITY

This is important parameter of characterization bilayer tablet. Density i.e. LBD (loose bulk density) and TBD (tapped bulk density) determined by using following formulas.

LBD ¼ weight of the powder=volume of the packing ð2Þ
TBD ¼ weight of the powder=tapped volume of the packing ð3Þ.[3]

6. COMPRESSIBILTY

Compressibility measured with help of Carr's Index. For measurement of Carr's Index, values of bulk density and tapped density have to be known.
CI = (TD-BD) /TD × 100
Where,
TD = Tapped density,
BD = Bulk density.

(Indian Pharmacopoeia, 1996; United States Pharmacopoeia, 2000:1944).[3]

Table3. Carr's Index I.P limits.[32]

Carr's Index	I.P Limits value
<10	Excellent
11 – 15	Good
16 – 20	Fair
21 – 25	Possible
26 – 31	Poor
32 – 37	Very poor
>38	Very very poor

7. HAUSNERS RATIO

It is important to indicate flow properties of powder or granules. It calculated with help of following formula.
Hausner's Ratio = Tapped density/Bulk density[32]

Table 4: Hausner's Ratio I.P Limits.[32]

Hausner's Ratio	I.P Limits value
Excellent	1.00 – 1.11
Good	1.1 – 1.18
Fair	1.19 – 1.25
Possible	1.26 -1.34
Very poor	1.35 -1.45

EVALUATION OF SUSTAIN RELEASE BILAYER TABLET

1. TABLET THICKNESS AND SIZE

Vernier caliper was used for measurement of thickness and diameter. These parameters are important for uniformity of tablet size.[4]

2. TABLET HARDNESS

Hardness, an important indication for tablet strength for shipping or breakage under conditions of storage, transportation and handling before usage.

The resistance of tablets hardness measured with hardness tester i.e. mainly by Monsanto Hardness tester. The unit for hardness is kg/cm^2.[4]

3. FRIABILITY

Friability is an indicator for tablet strength. Electrolab EF- 2 friabilator (USP) used for testing of friability with following procedure. Twenty tablets were weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution. After 4 min, the tablets were weighed and the percentage loss in tablet weight was determined.

% loss = [(Initial wt. of tablets – Final wt. of tablets)/ Initial wt. of tablets] ×100.[3]

4. UNIFORMITY OF WEIGHT

It checked by selecting twenty random tablets and average weight was calculated.[4]

5. DISSOLUTION

In- vitro drug release studies was performed by using dissolution apparatus. These studies are carried out using USP dissolution test apparatus I at 100 rpm, 37±0.5°C, and pH 1.2 buffer (900 ml) (i.e. 0.1 N HCl) for 2 hour (average gastric emptying time is about 2 hours) in simulated gastric or intestinal fluids are used. Experiment continued for another 10 hours with pH 6.8 phosphate buffer (900ml) as the dissolution medium. 5ml of the samples were withdrawn and replaced with 5ml of drug-free dissolution medium at different time intervals. The samples withdrawn were analyzed by using UV spectrophotometer.[3]

Applications

- Bi-layer tablets are the example of combination release of two drugs from single dosage.
- Shortcomings of single layered tablets are avoided with use bilayer tablets.
- It is improved technology having ability of providing combination of loading and maintenance dose of the same or different drugs.
- These are developed with the purpose of delivering different release profile of two different drugs.[14]

Table 6. Different two drugs in individual layer of bilayer tablet.[5]

Drug 1	Drug 2	Objective	Purpose	Ref.
Paracetamol	Diclofenac sodium	Immediate release of Paracetamol and tailored release of diclofenac sodium	Reduce dose frequency and decrease incidence of GI side effects	35
Metformin HCl	Pioglitazone HCl	Metformin HCl in extended release matrix form and Pioglitazone HCl in immediate release form for the treatment of diabetes mellitus	Decrease frequency of administration and improve patient compliance	15
Metoclopramide HCl	Ibuprofen	Immediate release of metoclopramide hydrochloride and sustained release ibuprofen for the effective treatment of migraine	Effective treatment of migraine and avoid chemical incompatibility between drugs	19
Salbutamol	Theophylline	Bilayer sustained release tablet of salbutamol and theophylline	Increase patient compliance and prolong bronchodilation	6
Metoclopramide HCl	Aceclofenac	both drugs in combination for the effective treatment of migraine	To avoid the degradation of the drug, with the desired release pattern and thus to maximize the efficacy in migraine	10
Metoclopramide HCl	Diclofenac Sodium	Immediate release of metoclopramide hydrochloride and sustained release ibuprofen for the effective treatment of migraine headache	For treatment of migraine	11

Table 5: Commercially available bilayer tablets.[5]

Product Name	Chemical Name	Developer	Therapeutic
Alprax Plus	Sertraline, Alprazolam	Torrent Pharmaceutcals Ltd	Anti-depressant
Glycomet ®-GP2Forte	Metformin hydrochloride, Glimepiride	USV Limited	Anti-dibetic

CONCLUSION

Bilayer tablet technology is an excellent improved technique for providing combine release pattern of drug i.e. immediate release and sustained release. This technology is very efficient for incorporating incompatible drugs together in single dosage form.it is very efficient way of overcoming shortcomings of single layer tablet. There are different approaches available for bilayer tablet technique.

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