Review Article

Bilayer: A Review

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ABSTRACT

Bilayered drug delivery system is well known modified release dosage form may offer one or more advantages over immediate release formulations of the same drug[1]. Also the formulation is much eaiser than the other controlled drug delivery systems . The major aim of controlled drug delivery is to reduce the frequency of dosing . The design of modified release drug product is usually intended to optimize a therapeutic regimen by providing slow and continuous delivery of drug over the entire dosing interval also providing greater patient compliance and convenience. Bilayer tablet is better than the traditionally used dosage forms suitable for sequential release of two drugs in combination it is also capable of separating two incompatible substances and also for sustained release. The present article provides a review on the oral drug delivery system, types of tablets, bilayer tablet manufacturing, various tablet presses used, quality and GMP requirements for their production and recent developments in the field of bilayer technology.

Keywords: Bilayer tablet, GMP requirement for bi-layer tablets, Various tablet presses.

INTRODUCTION [1]

Over 90% of the formulations manufactured today are ingested orally . This shows that this class of formulation is the most popular worldwide and the major attention of the researcher is towards this direction . The major aim of controlled drug delivery is to reduce the frequency of dosing . The design of modified release drug product are to optimize a therapeutic regimen by providing slow and continuous delivery of drug over the entire dosing interval providing greater patient compliance and convenience. Bilayer tablet is the new era for the successful development of controlled release formulation . Bilayer tablet is better than the traditionally used dosage forms . Bi-layer tablet is suitable for sequential release of two drugs in combination it is also capable of separating two incompatible substances and also for sustained release tablet in which one layer is immediate release as initial dose and second layer is maintenance dose. In certain cases bilayered tablets have 2 sustain release layers of different drugs . Bilayer tablet is an improved technology to overcome the shortcoming of the single layered tablet. Bilayer tablets contain immediate and sustained release layers. The immediate release layer delivers the initial dose, it contains superdisintegrants which promotes drug release rate and attains the onset of action quickly(loading dose) whereas sustained release(maintenance dose) layer releases drug in sustained manner for prolonged time period.The biphasic system is used mostly when maximum relief needs to be achieved quickly and it is followed by a sustained release phase . It also avoids repeated administration of drug. Coronary vasodilators, antihypertensives, antihistaminics, analgesics, antipyretics and antiallergenic agents are mainly suitable for thistype of drug delivery .Some bilayer tablets have both the layers as the sustain release layers examples are certain antidiabetic agents .

ADVANTAGES OF BILAYERED TABLETS [2 3]

These type of incompatabiliteis are commonly used to avoid chemical incompatabilities of formulation components by physical separation .

- Cost is lesser as compared to other dosage forms
- Greater chemical and microbiological stability
- Objectionable odor and bitter taste can be masked by coating technique
- Flexible concept
- Easy to swallow with least tendency for hang up
- Suitable for large scale production
- They are unit dosage form and often the greatest dose precision and least contact variability.

DISADVANTAGES OF BILAYERED TABLETS[4]

- Some drugs resist compression into dense compacts owing to amorphous nature

- Bitter testing drugs , drugs with an objectionable odor or drugs that are sensitive to oxygen may require encapsulation or coating
- Difficult to swallow in case of children and unconcisious patients
- Drugs with poor solubility , slow dissolution properties optimum absorption high in GIT may be difficult to formulate that will still provide adequate or full drug bioavailability.

1) BILAYER TABLET BASIC APPROACH

a) GEOMATIRX[5]

One of the examples of bilayered tablets is geomatrix tablet. Geomatrix tablet, which is composed of different layers. The system allows the incorporation of more than one drug into the dosage form. Formulation of layers from different polymers allows manipulation over more than one rate-controlling polymer, thus enabling different types of drug delivery of one or more drugs, i.e. where the drug may be released with a bolus and then at a controlled rate or by targeted drug delivery in the GI tract using pH dependant polymers system. The biphasic system some time may contain two drugs in separate release layers. There are clearly a number of issues of concern to the production of bilayered tablets. While the mechanical strength of layered tablets has been observed not to be a controlling factor in drug release the determination of this property could be beneficial in understanding the adhesion between various layers and provide an improved characterization of the systems. Bi-layer tablets are prepared with one layer of drug for immediate release while second layer designed to release drug, later, either as second dose or in an extended release manner. Bilayer tablet is suitable for sequential release of two drugs in combination, separate two incompatible substances and also for sustained release tablet in which one Layer is immediate release as initial dose and secondlayer is maintenance dose. The preparation of tablets in the form of multi layers is used to provide systems for the administration of drugs, which are incompatible and to provide controlled release tablet preparations by providing surrounding or multiple swelling layers. Control release systems that have been proposed for providing controlled release formulations showing how the different designs can be used to control the drug release profile such as constant, delayed pulsatile and multi modal release profiles.Several different geometries are described and to prepare these by compression will require various strategies.

b) FLOATING

In bilayer tablets one is immediate release and other is sustained release layer. Two drugsare present in same tablet but in different layers. Tablets having sustained release layer and floating layer. Gastric emptying is a complex process, is highly variable and makes the drug delivery systems uncertain . In order to avoid this variability, efforts have been made to increase the retention time of the drug delivery systems for more than 12 hrs. The floating or hydrodynamically controlled drug delivery systems are useful in such applications.

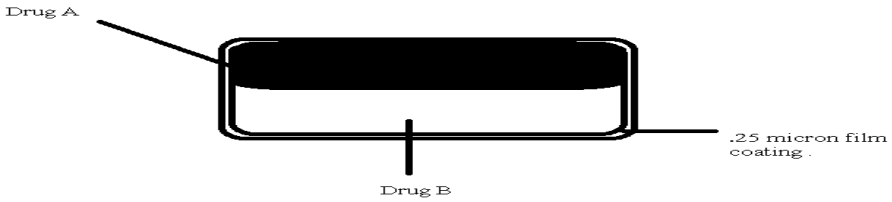
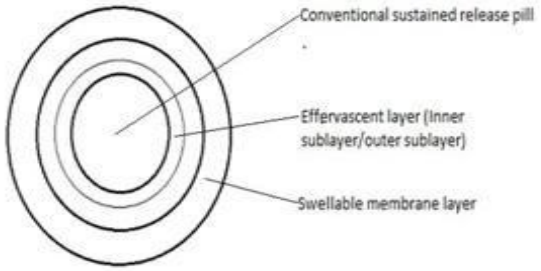


Fig. 1: Bilayer tablet

However, many floating systems reported are single-unit systems such as HBS, which are unreliable in prolonging the GRT owing to their ‘all-or-nothing’ emptying process . These systems thus, may result in high variability in bioavailability and local irritation due to a large amount of drug delivered at a particular site of GIT. The conventional dosage forms are retained in the stomach for 0.5-2 hrs which then passes to small intestine, where it gets absorbed within 3-6 hrs. Therefore it is difficult to adjust release retardation and stomach retention of drug for longer period of time. The concept of gastroretentive drug delivery system came from the need to localize the drug at a certain site in the body. In oral drug delivery, drug absorption is limited due to the gastrointestinal transit time of the dosage form. When the site of drug absorption is mainly stomach or upper part of GIT, then it is

necessary to retain the dosage form at the site of absorption for longer duration. The only limitation such dosage from is the gastrointestinal transit. Therefore gastroretentive dosage forms are formulated to increase the gastric residence time. The majority of drugs are preferentially absorbed from the upper part of GIT hence, drug release at site of absorption can improve.



The dosage forms are designed to have a low density and thus float on gastric contents after administration until the system either disintegrates or the device absorbs fluid to the point where its density is such that it loses bouyancy and can pass more easily from the stomach with a wave of motility responsible for gastric emptying .The bilayer tablet is designed in such a manner that , one layer gives immediate dosing if the drug which gives faster onset of action while other layer is designed as a floating layer which floats .

DISADVANTAGES

Floating drug delivery is not applicable to dose levels of highly water soluble drugs as in such cases larger amounts of ploymers are required to retard the release of drug .Also the performance is posture dependent , like in case of supine position the tablet slips of the pyloric sphincter and the dosage form is eliminated from the body.

c) POLYMERIC BIOADHESIVE SYSTEM

In this type of drug delivery system fluid imbibes in the dosage it becomes viscous , tacky material that adheres to the gastric mucosa . The adherence to the mucosa ensure retention of the dosage form due adhesive forces . They majorly have one layer of immediate dosing and other layer with bioadhesive property.

DISADVANTAGES

The system adheres to mucous lining the mucosa and sometimes the mucous in which the drug dissolves sloughs off readily and in this manner the dissolved drug is eliminated from the body .

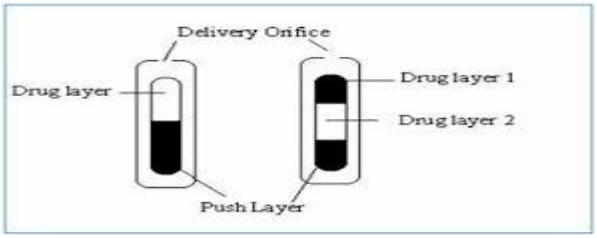
d) SWELLING SYSTEM / UNFOLDING SYSTEMS

They are designed sufficiently small on administration , once these systems are ingested they swell or unfold at the site of action and hence block the passage through the pyloric sphincter.On gradual erosion of the dosage form it becomes sufficiently small to leave the stomach.

2) DIFFERENT TECHNOLOGY FOR BILAYER TABLET

a) OROS® PUSH PULL TECHNOLOGY [3]

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



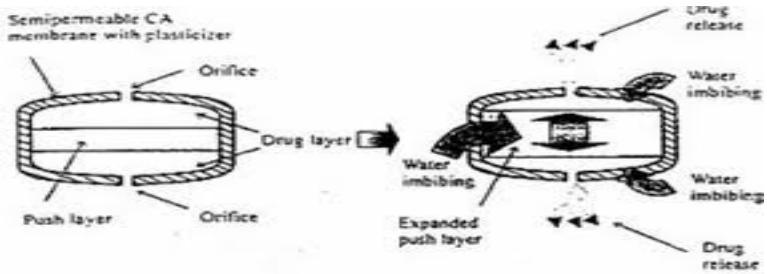


Fig. 3: Bilayer trilayer OROS Push pull technology

b) L-OROS tm TECHNOLOGY[3]

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

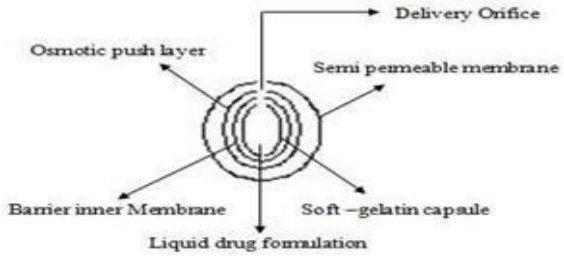


Fig. 4: L – OROS tm technology

c) EN SO TROL TECHNOLOGY [3 5]

Solubility enhancement of an order of magnitude or to create optimized dosage form Shire laboratory use an integrated approach to drug delivery focusing on identification and incorporation of the identified enhancer into controlled release technologies.

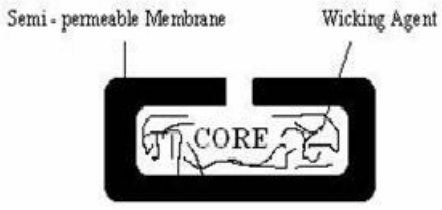


Fig. 5: EN SO TROL Technology

d) DUROS TECHNOLOGY [4 6]

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

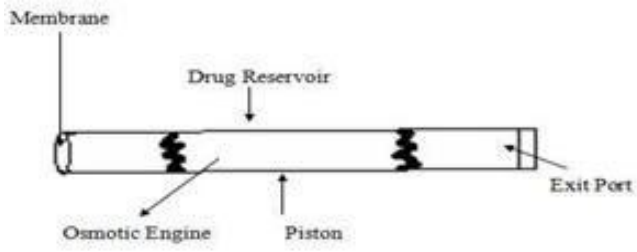


Fig. 6: The DUROS technology

e) ELAN DRUG TECHNOLOGY[6]

(DUREDAS™ Technology) is a bilayer tablet which can provide immediate or sustained release of two drugs or different release rates of the same drug in one dosage form. The tabletting process can provide an immediate release granulate and a modified-release hydrophilic matrix complex as separate layers within the one tablet. The modified-release properties of the dosage form are provided by a combination of hydrophilic polymers.

DUREAS TECHNOLOGY ITS BENEFITS

The DUREDAS™ system can easily be manipulated to allow incorporation of two controlled release formulations in the bilayer. Two different release rates can be achieved from each side. In this way greater prolongation of sustained release can be achieved. Typically an immediate release granulate is first compressed followed by the addition of a controlled release element which is compressed onto the initial tablet. This gives the characteristic bilayer effect to the final dosage form. A further extension of the DUREDAS™ technology is the production of controlled release combination dosage forms whereby two different drugs are incorporated into the different layers and drug release of each is controlled to maximize the therapeutic effect of the combination. Again both immediate release and controlled release combinations of the two drugs are possible. number of combination products utilizing this

technology approach have been evaluated. The DUREDAS™ technology was initially employed in the development of a number of OTC controlled release analgesics. In this case a rapid release of analgesic is necessary for a fast onset of therapeutic effect. Hence one layer of the tablets is formulated as immediate releases granulate. By contrast, the second layer of the tablet, through use of hydrophilic diffusion and erosion through the hydrophilic polymer matrix.

f) PRODAS or programmable oral drug absorption system [8,7]

PRODAS is a mutliparticulate drug delivery technology that is based on the encapsulation of controlled release minitablets in the size range of 1.5 to 4 mm in diameter .This tecnology reprsents a combination of multiparticulate and hydrophilic matrix tablet technologies and thus provide the desired release rates .These considerations may include immediate release , delayed release and / or controlled release minitablets . In addition to controlled release absorption over a specified period .PRODAS tecnology also enables targeted delivery of drug to specified sites of absorption throughout the GI tract .C ombination products also are possible by using minitablets formulated with different ingredients.

g) GEMINEX TECHNOLOGY[9]

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.

h) ERODIBLE MOLDED MULTILAYER TABLET [9 10]

Egalet erodible molded tablets in an erosion based platform. It has the advantage of delivering zero order or delayed release with minimal impact from the gastrointestinal conditions . Egalet erodible molded multilayered tablets are prepared by injection moulding egalet technology contains a coat and a matrix . Drug release is controlled through the gradual erosion of the matrix part . the mode and rate of release are designed and engineered by altering the matrix the coat and the geometry to achieve by altering the matrix ,the coat, the geometry to achieve either a zero order release or a delayed. For a zero order , a drug is dispersed through the matrix . The coat is biodegradable but has poor water permeability to prevent its penetration . The matrix tends to erode when in contact with available water .The erosion of the mat rix is caused by GI fluids and promote by gut movements in the GI tract .The drug release is mediated almost wholly by erosion because the dosage form is designed to slow down the water diffusion into the matrix .It is definitely more desirable for drugs with chemical and physical stability issues after contacting with water .Egalet delivery technology is developed based on standard plastic injection molulding to ensure accuracy , reproducibility and low production cost .

3) QUALITY AND GMP REQUIREMENTS [11 12]

- Preventing capping and separation of the 2 individual layers that constitute the bilayer tablet .
- Providing sufficient tablet hardness
- Preventing crosss contamination between the 2 layers .
- High yeild
- Accurate and individual control of the 2 layers .

4) SIZE AND SHAPES

Size is limited by the capacity of the machine with the total thickness being the same as for a single layer tablet .Many shapes other than round are possible and are limited only by the ingeniuity of the die maker .However , deep concavities cause distortion of the layers .Therefore standard concave and flatface beveled edge tooling mak for the best appearance , espicially when layers are of different colour .

The shape of the punches

Punches with beveled edges or concaves face will make the top and bottom layers of a 3 layer tablets and appear thinner than the middle one flat faced tooling will produce equal thickness of the layers but unfortunately the edges of the tablets tend to dip readily .

Cross section of the layer tablet

1) Upper layer
2) Lower layer

If the upper punch faces have a monogram or any other marking , the bonding between the layers will be strengthen because the device will act as key between the layers

5) IDEAL PROPERTIES FOR A BILAYER TABLET PRESS

- Prevent capping and separation of the 2 individual layers that constitute the bilayer tablet
- Preventing cross contamination between the 2 layers

- Producing a clear visual separation between the 2 layers
- Accurate weight control of the 2 layers.

6) TYPES OF BILAYER TABLET PRESS [14]

A) Single sided tablet press.
B) Double sided tablet press
C) Bilayer tablet press with displacement monitoring .
D) Multilayer compression basics .

1) SINGLE SIDED PRESS

Various types of bilayer presses have been designed over the years .The simplest design is a single sided press with both chambers of the double feeder separated from each other .Each chamber in gravity fed , or force fed with a different powder , thus producing the 2 individual layers of the tablet .When the die passes under the feeder, it is at first loaded with the first layer of powder followed by the second-layer powder then the entire tablet is compressed in one or 2 steps (two pre and main compression) . The 2 layers in the die mix slightly at their interface and in most cases bond sufficiently so that no layer separation occurs when the tablet is produced this is the simplest way of producing a bilayer tablet .

LIMITATIONS OF SINGLE SIDED PRESS

- No weight monitoring or control of the individual layers
- No distinct visual separation between the 2 layers
- Dwell time due to the small compression roller possible resulting in poor deareation capping and hardness problems.

DWELL TIME

Dwell time is defined as the time during which compression force is above 90% of its peak value. Longer dwell time is the major factor in the production of quality tablets .

COMPRESSION FORCE

Many bilayer tablets require a first layer compression force of 100 daN in order to retain the ability to bond with the second layer . above 100daN this ability may be lost and bonding between both layers may not be sufficient . this results in low hardness bilayer tablets and might cause separation of the 2 layers .

2) DOUBLE SIDED TABLET PRESSES

Most of the double sided tablet presses which are automated production control, use the compression force to monitor and control te weight of the tablet weights . The effective compression force exerted on each individual tablet with the help of the compression sytem at the main compression of the layer . This system helps in to reject out the toleranvce tablets and correct the dies fill depth when required .

ADVANTAGES

1. Low compression force exerted on the first layer to avoid capping and separation of the individual layer.
2. Increased dwell time at pre compression of both first and second layer to provide sufficient hardness at maximum turret speed.
3. Maximum prevention of cross contamination between two layers.
4. A clear visual separation between the two layers
5. Displacement weight monitoring for accurate and independent weight control of the individual layer.
6. Maximized yield.

LIMITATIONS

Separation of the two individual layers is due to insufficient bonding between the two layers during final compression of bi-layer tablet. Correct bonding is only obtained when the first layer is compressed at a low compression force so that this layer can still interact with the second layer during final compression. Bonding is too restricted if first layer is compressed at a high compression force. The low compression force required when compressing the first layer unfortunately reduces the accuracy of the weight monitoring/control of the first layer in the case of tablet presses with “compression force measurement”. Most of the double sided tablet presses with automated production control use compression force

3) BILAYER TABLET PRESSES WITH DISPLACEMENT[15]

The principle of bilayer tablet press is fundametnally different from the principle of compression force . In this case the accuracy increases with reduced compression force .At higher production speed the risk of capping and separation increases but can be reduced by sufficient dwell time at all four compression stages .

ADVANTAGES

- Displacement weight monitoring /control for accurate independent weight control of the individual layers .

- Low compression force exerted on the first layer to avoid capping and separation of the 2 individual layers .
- Increased dwell time at precompression of both first and second layer to provide sufficient hardness at maximum turret speed
- Maximum prevention of cross contamination between the layers .
- A clear visual separation of the layers
- Maximised yeild .

4) MULTILAYER COMPRESSION BASICS [15]

Presses can be designed specifically for multilayer compression or a standard double press can be converted for multilayers . The multilayer tablets concept has been long utilized to develop sustained release formulatins such tablets have fast releasing layer and may contain bilayers or triple layers to sustain drug release from the tablet. The pharmacokinetic advantage relies on the fact that drug release from fast releasing granules leads to sudden rise in blood concentration however the blood level is maintained at a steady state as the drug is released from the sustained granules .

PREPARATION OF BILAYER TABLET[14,15]

Bilayer tablets are prepared with one layer of drug for immediate release with the second layer designed to release drug later, either as a second dose or in an extended release form8. The bilayer tablets with two incompatible drugs can also be prepared by compressing separate layers of each drug so as to minimize area of contact between two layers. An additional intermediate layer of inert material may also be included.

COMPACTION

To produce adequate tablet formulation, certain requirements such as sufficient mechanical strength and desired drug release profile must be met. At times, this may be difficult task for formulator to achieve these conditions especially in bilayer tablet formulation where 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). The compression force on layer 1 was found to be major factor influencing tablet delamination.

5) DIFFERENT TYPES OF BILAYER TABLET PRESSES

A) PICCOLA BILAYER

This rotary press was designed to represent two-layer tablet production conditions at a small scale, according to the needs of new product development.Piccola Bi-layer press meets cGMP standards and can use type D or B tooling complying with TSM or EU standards, which allows the employment of the same punches used in production.For an appropriate adjustment in tablet production, there are totally independent systems for weight, height and hardness adjustment, both for the first and second layers. A PLC system having a touch screen and a software designed for Galenic Development and Production Control allows the integrated control of all parameters, including production rate and, separately, the rate of each of the star forced feeder. There are varied accessories and options for the software used; such as the possibility of weight control during production and the use of data obtained for calculation and statistics.

B) ROTAB BILAYER[14]

a) Software
   It is modular designed software to which additional functions can be added. PC-systemwith 15” touchscreens 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 tabletting technology with all important functions such as punch tightness control, display of force displacement and tablet scraper force.

C) BILAYER TABLET PRESS [16 17]

The Xm bilayer tablet press features a rectangle second layer feeder that permits automated first layer sampling at production speeds . The first layer sampling capability also offers a hardening feature , which the main compression station will automatically compress , the first layer tablet for in-process measurement .The two feeders are zero clearance and are configured with an integrated dust extraction manifold which cleans the dis table and completely eliminates any potential of cross contamination .wip con ® solution available for potent for layer tablet press is a small scale press which is ideal for product development, scale up, clinical trials and midrange production . The bilayer execution, single layer conversion kit and exchangeable turret offers, a new standard in GMP with extreme accessibility to the compression zone and a combination of quick disconnects and smooth surfaces that permit fast cleaning and changeover .

The machine concept:-

ADVANTAGES

Flexible concept.

Bilayer execution with optional single layer.

6) CHARACTERIZATION OF BILAYER TABLET[18-21]

A) PARTICLE SIZE DISTRIBUTION

The particle size distribution was measured using sieving method.

B) PHOTON MICROSCOPE STUDY

Photo-microscope image of TGG and GG was taken (X450 magnifications) by photomicroscope.

C) ANGLE OF REPOSE

The diameter of the powder cone was measured and the angle of repose was calculated using the following equation.

Tan Ø=h/r

where h and r are the height and radius of the powder cone.

D) MOISTURE SORPTION CAPACITY

All disintegrates have capacity to absorb moisture from atmosphere which affects moisture sensitive drugs. Moisture sorption capacity was performed by taking 1 g of disintegrate uniformly distributed in Petri-dish and kept in stability chamber at 37±1°C and 100% relative humidity for 2 days and investigated for the amount of moisture uptake by difference between weights.

E) DENSITY

The loose bulk density (LBD) and tapped bulk density (TBD) were determined and calculated using the 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

F) COMPRESSIBILTY

The compressibility index of the disintegrate was determined by Carr's compressibility index.

C = 100 x (1-ÞB/ÞT)

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

G) HAUSNERS RATIO

It is calculated by the formula,

freely settled bulk density of the powder
tapped density of the powder

7) EVALUATION OF SUSTAIN RELEASE BILAYER TABLET [20]

A) TABLET THICKNESS AND SIZE

Thickness and diameter of tablets were important for uniformity of tablet size. Thickness and diameter was measured using venire calliper.

B) TABLET HARDNESS

The resistance of tablets to shipping or breakage under conditions of storage, transportation and handling before usage depends on its hardness. The hardness of tablet of each formulation was measured by Monsanto hardness tester. The hardness was measured in kg/cm^2.

C) FRIABILITY

Friability is the measure of tablet strength . Electrolab EF- 2 friabilator (USP) was used for testing the friability using the 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.

D) UNIFORMITY OF WEIGHT

Twenty tablets were selected at random and the average weight was calculated. Weight

Variation was calculated and was compared with I. P. standards.

E) DISSOLUTION STUDIES

Bilayer tablets were subjected to in vitro drug release studies in simulated gastric and intestinal fluids to assess their ability in providing the desired controlled drug delivery . Drug release studies were 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 hours, since the average gastric emptying time is about 2 hours. The dissolution medium was replaced with pH 6.8 phosphate buffer (900ml) and experiment continued for another 10 hours. At different time intervals, 5ml of the samples were withdrawn and replaced with 5ml of drug-free dissolution medium. The samples withdrawn were analyzed by UV spectrophotometer using multi component mode of analysis.

8) SOME EXAMPLES OF BILAYER TABLETS RESEARCHED

Amlodipine Besilate Metoprolol Succinate	Synergistic effect in hypertension	Atram S etal[22]
Metformin HCl and Glimipride	Synergistic effect in diabetes	Pattanaya K etal [23]
Losartan	Biphasic release profile	Hiremath etal[24]
Metformin HCl Pioglitazone	Synergistic effect in diabetes mellitus	Kumar etal [25]
Diclofenac Sodium Paracetamol	Synergistic effect in pain	Mules etal [26]
Ibuprofen Methacarbamol	Synergistic effect of drugs in back pain	Remya etal[27]
Telmisartan-Simvastatin	To minimize contact b/w simvastatin and telmisartan .	Kohlrausch etal[28]

CONCLUSION

Bilayer tablet is suitable for sequential release of two drugs in combination, separate two incompatible substances and also for sustained release tablet in which one layer is immediate release as initial dose and second layer is maintenance dose. Bi-layer tablet quality and GMP-requirements can vary widely. This explains why many different types of presses are being used to produce bi-layer tablets, ranging from simple single-sided presses to highly sophisticated machines are used . Whenever highquality bi-layer tablets are needed to be produced , high speed and use of an ‘air compensator’ in combination with displacement control appears to be the best solution.

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