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Review Article

BILAYER TABLETS– A REVIEW

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ABSTRACT

Bilayer tablet is a new era for the successful development of controlled release formulation along with various features to provide a way of the successful drug delivery system. Bilayer tablets can be a primary option to avoid chemical incompatibilities between API by physical separation, and to enable the development of different drug release profiles like the immediate release with extended release. Bilayer tablet is a very different aspect of anti-inflammatory and analgesic. Bi-layer tablet is suitable for sequential release of two drugs in combination and also for sustained release tablet in which one layer is immediate release as initial dose and second layer is maintenance dose. Bilayer tablet is improved beneficial technology to overcome the short coming of the single layered tablet. There are various applications of the player tablet, it consists of monolithic partially coated or multilayered matrices.

Keywords: Bilayertablets, Preparation, Characterization, Various presses.

INTRODUCTION

Now a days various developed and developing countries move towards a combination therapy for treatment of various diseases and disorders requiring longterm therapy such as hypertension, Diabetes and Cardiovascular diseases[1]. Over 90% of the formulations manufactured today are ingested orally. It shows that this class of theformulation is the most popular world wide 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[2]. The design of modified release drug product is 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 newer a for the successful development of controlled release formulation and better than the traditionally used dosage forms. Bilayer tablet is suitable for sequential release of two drugs in combination it is also capable of separating the two types of incompatible substances and also for sustained release tablet in which one layer is immediate release as initial dose and the second player is maintenance dose. In certain cases bilayered tablets have 2 sustain release layers of different drugs[3].

Bilayer tablet is an improved technology to overcome the short coming of the single layered tablet. Player tablets contain immediate, sustained release layers, and the immediate release layer delivers the initial dose, it contains superdisintegrates, which promotes the drug release rate and attains the onset of action quickly (loading dose) where as sustained release(maintenance dose) layer releases the drug in a sustained manner for a prolonged time period[4-5]. The biphasic system isused mostly when maximum relief needs to be achieved quickly and it is followed by a sustained release phase. It also avoids repeated administration of a drug.

Coronary vasodilators, antihypertensive, antihistamines, analgesics, antipyretics and antiallergenic agents are mainly suitable for this type of drug delivery[6]. Some bilayer tablets have both the layers as the sustain release layers examples are a certain antidiabetic agents[7-8].

Needofbilayertablets[9-11]

- For the administration of fixed dose combinations of different APIs 13, prolong the drug product lifecycle, vocal mucoadhesive delivery systems, fabricates novel drug delivery systems such as chewing device and floating tablets for gastro-retentive drug delivery.
- Controlling the delivery rate of either single or two different active API'S.
- To modify the total surface area available for API layer either by sand wiching with one or two inactive layers inorder to achieve swellabl (or) erodible barriers for modified release.
- To separate in compatible Active pharmaceutical ingredient (APIs) from each other, to control the release of API from one layer by utilizing the functional property of the other layer.

Objectivesofbilayertablets[12-17]

- To control the delivery rate of either single or two different active pharmaceutical ingredients.
- To separate incompatible Active pharmaceutical ingredient from each other, to control the release of API from one layer by utilizing the functional property of the outer layer.
- To modify the total surface area available for API layer either by sand wiching with one or two inactive layers in order to achieve swellable or erodible barriers for modified release.
- To administer fixed dose combinations of different active pharmaceutical ingredients, prolong the drug product lifecycle, fabricaten ovel drug delivery systems such as chewing device buccal mucoadhesive delivery systems, and floating tablets for gastro-retentive drug delivery.

Advantges ofthebilayertablets

- Bi-Layer execution with optional single-layer conversion kit.
- The cost is lower compared to all other oral dosage forms.
- Greatest chemical and microbial stability over all oral dosage forms.
- Objection able odor and bitter taste can be masked by coating technique.
- Flexible Concept.
- They are a unit dosage form and offer the greatest capabilities of all oral dosage forms for the greatest dose precision and the least contentvariability.
- Easy to swallow with less tendency to hang-up.
- Suitable for large scale production.

Preparation

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 form. The bilayer tablets with two incompatible drugs can also be prepared by compressing separate layers of each drug so as to minimize the area of contact between two layers.

Compaction

To produce an adequate tablet formulation, certain requirements such as sufficient mechanical strength and desired drug release profile must be met. At times, this may be a difficult task for the for mulator to achieve these conditions, especially in the 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 layer1 was found to be a major factor influencing tablets delaminating.

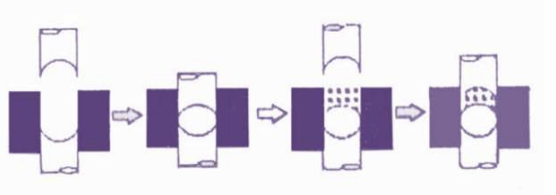

Fig. 1: PreparationofBilayerTablets

TYPES OF BILAYER TABLETS

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

1.Singlesidedpress

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 forcefed with a different powder,thus producing the 2 individual layers of the tablet. When the dye 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 two step. The two layers in the dye 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

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

2.Double sided tablet presses

Most of the double sided tablet press, which automates production control use the compression force to monitor and control the weight of the tablet weights. The effective compression force exerted on each individual tablet with the help of the compression system at the main compression of the layer. This system helps into reject out the tolerance tablets and correct the dies fill depth when required.

Advantages

- Low compression force exerted on the first layer to avoid chapping and separation of the individual layer.
- 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 two layers.
- A clear visual separation between the two layers.
- Displacement weight monitoring for accurate and independent weight control of the individual layer.
- Maximized yield.

- Separation of the two individual layers is due to insufficient bonding between the two layers during final compression of bi-layer tablet.
- **Limitations**
- 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 a final compression.
- Bonding is too restricted if the 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.

3. Bi Layer Tablets Presses with Displacement

The principle of bilayer tablet press is fundamentally 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 a tall fourcompression 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 chapping 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.
- Maximized yield.

4. Multilayer Compression Basics

Presses can be designed specifically for multi layer compression or a standard double press can be converted for multipliers. The multilayer tablet concept has been longutilized to develop sustained release formulations such tablets have fast releasing layer and may contain players or triple layers to sustain the drug release from the tablet.The pharmacokinetics 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.

VARIOUS APPROACHES OF BILAYER TABLETS[17-18]

A.Floating drug delivery system

These 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 buoyancy 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 the immediate dosing of the drug which gives faster onset of action while another layer is designed as a floating layer which floats in the stomach.

B.PolymericBioadhesiveSystem

These are designed to imbibe fluid following administration, such that the outer layer becomes a viscous, tacky material that adheres to the gastric mucosa/mucus layer. This should encourage gastric retention until the adhesive forces are weakened. These are prepared as one layer with immediate dosing and other layer with bioadhesive property.

C.Swelling System

These are designed to be sufficiently small on administration so as not to make ingestion of the dosage form difficult. On ingestion they rapidly swell or disintegrate or unfold to a size that precludes passage through the pylorus until after drug release has progressed to a required degree Gradual erosion of the system or its breakdown into smaller particles enables it to leave the stomach. The simple bilayer tablet may contain an immediate release layer with the other layer as extended release or conventional release.

TECHNIQUES OF BILAYER TABLETS[18]

1.OROS®push pull technology

This system consist of mainly two or three layers among which the one or more layer is essential of the drug and other layer are consist of push layer. The drug layer mainly consists of drug a long with two or more different agents. So this druglayer comprises of a drug which is poorly soluble form. There is a further addition to suspending agent and osmotic agent.

A semipermeable membrane surrounds the tablet core.

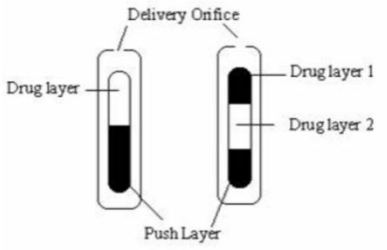

Fig. 2: OROS®PushPullsTechnology

2. L-ORO timetechnology

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

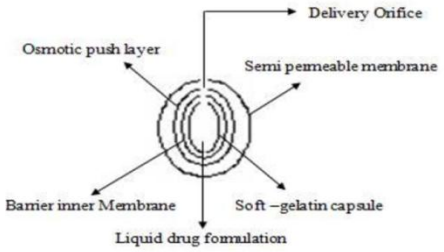

Fig. 3: L-ORO TimeTechnology

3. ENSOTROL technology

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

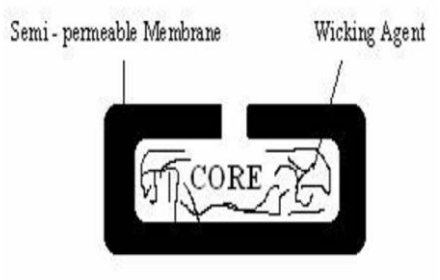

Fig.4:ENSOTROLTechnology

4.DUROS Technology

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

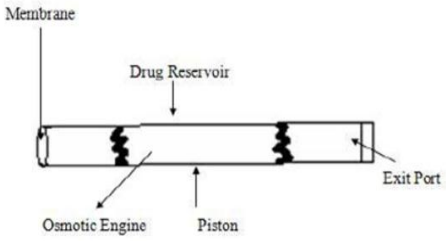

Fig.5: DUROTechnology

5E lan Drug Technologies Dual Release Drug Delivery System

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

Benefits

- Bilayer tableting technology.
- Tailored release rate of two drug Components.
- Capability for immediate release and modified release components in one tablet.
- Unit dose tablet.

Evaluation of BilayerTablets[19-20]

1General Appearance

The general appearance of a tablet, its visual identity and over all elegance is essential for consumer acceptance. Includes in are tablets size, shape, color, presence or absence of an odor, taste, surfacetexture, physical flaws and consistency and legibility of any identifying marking.

2Size and Shape

The size and shape of the tablet can be dimensionally described monitored and controlled.

3Tablet thickness

Tablet thickness is an important characteristic in reproducing appearance and also in counting by using filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Ten tablets were taken and their thickness was recorded using micrometer.

4Weight variation[21]

Standard procedures are followed as described in the official books.

5Friability

Friction and shock are the forces that most often cause the tablets to chip, chop or break. The friability testis closely related to tablet hardness and is designed to evaluate the ability of the tablet to with stand abrasion in packaging, handling and

shipping. It is usually measured by the use of the Roche friabilator. A number of tablets are weighed and placed in the apparatus where they are exposed to rolling and repeated shocks as they fall 6inches in each turn within the apparatus. After four minutes of this treatment or 100 revolutions, the tablets are weighed and the weight compared with the initial weight. The loss due to abrasion is a measure of the tablet friability. The value is expressed as a percentage. A maximum weight loss of not more than 1% of the weight of the tablets being tested during the friability test is considered generally acceptable and any broken or smashed tablets are not picked up. Normally, when capping occurs, friability values are not calculated. A thick tablet may have fewer tendencies to cap where as thin tablets of large diameter, often show extensive cupping, thus indicating that tablets with greater thickness have reduced internal stress the loss in the weight of the tablet is the measure of variability and is expressed in percentageas.

%Friability=1-(lossinweight/Initialweight)X100

6 Hardness[22]

The resistance of tablets to capping, abrasion or breakage under conditions of storage, transportation and handling before usage depends on its hardness**.**The small and portable hardness tester was manufactured and introduced by Monsanto in the Mid 1930s. It is now designated as either the Monsanto or Stokes hardness tester. The instrument measures the force required to break the tablet when the force generated by a coil spring is applied diametrally to the tablet. The strong-Cobb Pfizer and Schleuniger apparatus which were later introduced measures the diametrically applied force required to break the tablet. Hardness, which is now more appropriately called crushing strength determinations are made during tablet production and are used to determine the need for pressure adjustment on tablet machine. If the tablet is too hard, it may not disintegrate in the required period of time to meet the dissolution specifications, if it is too soft, it may not be able to withstand the handling during subsequent processing such as coating or packaging and shipping operations. The force required to break the tablet is measured in kilograms and a crushing strength of 4Kg is usually considered to be the minimum for satisfactory tablets. Oral tablets normally have a hardness of 4to10 kg however, hypodermic and chewable tablets are usually much softer (3kg) and some sustained release tablets are much harder(10-20kg). Tablet hardness has been associated with other tablet properties such as density and porosity. Hardness generally increases with normals to rage of tablets and depends on the shape, chemical properties, binding agent and pressure applied during compression.

7StabilityStudy

The bilayer tablets are packed in suitable packaging and stored under the following conditions for a period as prescribed by ICH guideline for accelerated studies.The tablets were withdrawn after a period of 15days and analyzed for physical characterizations Visualdefects, Hardness, Friability and Dissolution and drug content. The data obtained is fitted into first or derequations to determine the kinetics of degradation. Accelerated stability data are plotted according Arrhenius equation to determine the shelf life at 25°C.

CONCLUSION

Bilayer tablet is improved beneficial technology to over come the short coming of the single layered tablet. There are various application of the bilayer tablet, it consist of monolithic partially coated or multilayered matrices. 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. The preparation of tablets in the form of multilayer isused to provide systems for the administration of drugs, which are incompatible and to provide control release tablet preparations by providing surrounding or multiple swelling layers. Bilayer tablet quality and GMP-requirements can vary widely. This explains why many different types of presses are being used to produce bilayer tablet, ranging from simple single-sided presses to highly sophisticated machines.

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