



A BRIEF REVIEW ON BILAYER TABLETS

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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. Bilayer 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: Bilayer tablets, Preparation, Characterization, Various presses

INTRODUCTION :

Over the past 30 years greater attention has been focused on development of sustained or controlled release drug delivery systems. The development of combination of two or more active pharmaceutical ingredients (API) in a single dosage form has increased in the pharmaceutical industry, promoting patient convenience and compliance [1] Bilayer tablet is new era for the successful development of controlled release formulation along with various features to provide a way of successful drug delivery system. 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 [2] The goal in designing sustained or controlled delivery systems is to reduce the frequency of the dosing or to increase effectiveness of the drug by localization at the site of action, reducing the dose required or providing uniform drug delivery. The primary objective of sustained release drug delivery is to ensure safety and to improve efficacy of drugs as well as patient compliance [3]

(Kumar et al., 2010). Bi-layer 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 (Shiyani et al., 2008). There is various application of the bi-layer tablet it consist of monolithic partially coated or multilayered matrices. In the case of bi-layered tablets drug release can be rendered almost unidirectional if the drug can be incorporated in the upper non-adhesive layer its delivery occurs into the whole oral cavity

Objectives of bilayer tablets12-17 :

- 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 witching 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, fabricate ovel drug delivery systems such as chewing device buccal mucoadhesive delivery systems, and floating tablets for gastro-retentive drug delivery.

Advantages of the bilayer tablets

- 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

- Objectionable 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 content variability.
- Easy to swallow with less tendency to hang-up.
- Suitable for large scale production.

Need of bilayer tablets9-11

- 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 APIs.
- To modify the total surface area available for API layer either by sandwiching with one or two inactive layers in order to achieve swellable (or) erodible barriers for modified release.
- To separate incompatible 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.

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.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 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.

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.

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 four compression stages

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 long utilized to develop sustained release formulations such tablets have fast releasing layer and may contain layers 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 granule

VARIOUS APPROACHES OF BILAYER TABLETS16,17

1.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.

2.Polymeric Bio adhesive System

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 bio adhesive property.

3.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.

ADVANCED TECHNIQUES USED IN PREPARATION OF BILAYER TABLET:

- **Elan Drug Technology' Dual release Drug Delivery System OROS Push Pull Technology:** This approach comprises mainly two or three layers, one or more of which must contain the drug, and the other is a push layer. Generally, it consists of a drug and two or more agents utilized in the drug layer such as suspending and osmotic agents. A semipermeable membrane surrounds the core of the tablet [12]
- **L-OROS Technology:** This system is used to resolve the solubility problem associated with the drug. L-OROS system contains a lipid soft gel product holding drug in a dissolved state and an osmotic push layer with semi permeable membrane and a drilled for exit orifice [12]
- **ENSOTROL Technology:** Increased solubility by an order of magnitude or creation of an optimal dose form. Shire's drug delivery laboratory takes an integrated strategy, concentrating on the identification and implementation of discovered enhancers into controlled release technologies [13]
- **DUROS Technology:** The system is comprised of an outer cylindrical titanium alloy reservoir and an inner cylindrical titanium alloy reservoir. This reservoir is extremely robust and effectively protects the drug molecules from enzymes. The DUROS technology is a small medicine delivery system that resembles a miniature syringe and continuously and consistently releases minute amounts of concentrated medication over months or years.

EVALUATION OF BILAYER TABLETS

1. **General Appearance** The general appearance of a tablet, its visual identity and overall "elegance" is essential for consumer acceptance. Includes in are tablet's size, shape, colour, presence or absence of an odour, taste, surface texture, physical flaws and consistency and legibility of any identifying marking.
2. **Size and Shape** The size and shape of the tablet can be dimensionally described, monitored and controlled.
2. **Tablet 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 micrometre.
3. **Weight variation** Standard procedures are followed as described in the official books.
4. **Friability** Friction and shock are the forces that most often cause tablets to chip, cap or break. The friability test is closely related to tablet hardness and is designed to evaluate the ability of the tablet to withstand 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 6 inches 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 less tendency to cap where as thin tablets of large diameter often show extensive capping, thus indicating that tablets with greater thickness have reduced internal stress the loss in the weight of tablet is the measure of friability and is expressed in percentage as:
 - a. $\% \text{ Friability} = 1 - (\text{loss in weight} / \text{Initial weight}) \times 100$
5. **Hardness (Crushing strength)** 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 diametral 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 4 Kg is usually considered to be the minimum for satisfactory tablets. Oral tablets normally have a hardness of 4 to 10 kg; however, hypodermic and chewable tablets are usually much softer (3 kg) and some sustained release tablets are much harder (10 -20 kg). Tablet hardness have been associated with other tablet properties such as density and porosity. Hardness generally increases with normal storage of tablets and depends on the shape, chemical properties, binding agent and pressure applied during compression.
6. **Stability Study (Temperature dependent)** The bilayer tablets are packed in suitable packaging and stored under the following conditions for a period as prescribed by ICH guidelines for accelerated studies.

CHARACTERIZATION OF BILAYER TABLET [23-24]

- **Particle size distribution:** The particle size distribution was measured using sieving method
- **Photo-microscope study:** Photo-microscope image of TGG and GG was taken (X450 magnifications) by Photomicroscope.
- **Angle of repose:** The diameter of the powder cone was measured and the angle of repose was calculated using the following equation.
 $\tan \phi = h/r$ Where, h = Height, r = Radius of the powder cone.
- **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 $37 \pm 1^\circ\text{C}$ and 100% relative Humidity for 2 days and investigated for the amount of moisture uptake by difference Between weights.
- **Density:** The loose bulk density (lbd) and tapped bulk density (tbd) were determined and Calculated using the following formulas.
 $\text{LBD} = \frac{\text{weight of the powder}}{\text{volume of the packing}}$
 $\text{TBD} = \frac{\text{weight of the powder}}{\text{tapped volume of the packing}}$
- **Compressibility:** The compressibility index of the disintegrate was determined by Carr's compressibility index.
 $C = 100 \times (1 - \frac{\text{tbd}}{\text{lbd}})$

QUALITY AND GMP-REQUIREMENTS^{19,20}

- To produce a quality bi-layer tablet, in a validated and GMP-way, it is important that the selected press is capable of • Preventing capping, separation of the two individual layers that constitute the bi-layer tablet. • Providing sufficient tablet hardness.
- Preventing cross-contamination between the two layers.
- Producing a clear visual separation between the two layers.
- High yield.
- Accurate and individual weight control of the two layers these requirements seem obvious but are not as easily accomplished.

CONCLUSION :

Bilayer tablet is improved beneficial technology to overcome the shortcoming of the single layered tablet. There is 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 substance and also for sustain 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 multilayers is used 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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