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Review Article

A REVIEW ON BI-LAYERED TABLETS**Palivela Durga Chandra Vamshi^{1*}, V.Suresh, Brahmaiah Bonthagarala²,
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(Autonomous), Bhimavaram-534202, Andhra Pradesh, India.**Article Received:** January 2023**Accepted:** February 2023**Published:** March 2023**Abstract:**

Bilayer (and multilayer) tablet-based therapeutic strategies are becoming more popular among both brand-name and generic medications as a result of a number of interrelated aspects, such as sophisticated delivery methods, patient compliance, and combination therapy. In order to successfully manufacture these increasingly sophisticated systems, a number of obstacles must be overcome, ranging from formulation design through tablet press monitoring and control. The key advantages of this class of oral dosage forms are highlighted in this article, which also gives a summary of the most recent developments in bilayer tablet technology. It also describes the present obstacles to improving production procedures and product quality.

Keywords: *Bilayer tablet technology, generic medication, oral dosage forms***Corresponding author:****Palivela durga chandra vamshi,***II/II M.Pharmacy.**Department of Pharmaceutical Quality Assurance,**Shri Vishnu College of Pharmacy,**(Autonomous), Bhimavaram-534202, Andhra Pradesh, India*

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INTRODUCTION [1-5]:

The pharmaceutical industry has grown more interested in recent years in creating bi-layer tablets, which combine two or more active pharmaceutical ingredients (API) in a single dosage form to promote patient convenience and compliance. To prevent chemical incompatibilities between API's by physical separation and to enable the development of various drug release profiles (immediate release with longer release), bi-layer tablets can be a major choice. Due to the intense focus on the marketing of new drug molecules and the increasing use of these new drug molecules in combination to treat multiple diseases that require various dosage regimens, the development of sustained or controlled drug delivery systems has gained momentum over the past ten years. Bilayer tablets are excellent for continuous and immediate release of the same medicine, one as an initial dose and the other as a maintenance dose, and have patient compliance. Therefore, the purpose of this paper is to clarify the role that bilayer tablets play in the drug delivery system and address issues that arise during their production. The material properties, lubrication, layer ordering, layer thickness, layer weight control, as well as the first and final compression pressures are all topics that are relevant to the manufacturing of bilayer tablets. Bilayer tablet characterisation, which presents additional complexity related to interactions between layers, is also covered in a section. The features of the manufacturing equipment for the production of bilayer tablets are also explained, along with the many sensing and control options provided by the producers of bilayer tablet presses. The development of a production road map for bilayer tablets serves as a final directive for formulation design and the choice of process variables and machinery.

Requirement of bilayer tablets:

1. To create novel drug delivery methods, such as chewing devices and floating tablets for gastro-retentive drug delivery, to extend the life cycle of drug products that are administered in fixed dose combinations of various APIs using buccal/mucoadhesive delivery systems.
2. Regulating the rate of administration of either one or two active ingredients
3. To create swellable/erodible barriers for modified release by either sandwiching one or two active layers between the whole surface area available for the API layer.
4. To separate Active Pharmaceutical Ingredients (APIs) that are incompatible from one another and to regulate API release from one layer by making use of a functional property of the other layer (such as an osmotic property).

Bilayer tablet manufacturing problems:

Although these drug delivery methods are mechanically challenging to produce, it can be challenging to predict their long-term effectiveness. The elastic disparity of the layers, insufficient hardness, inaccurate individual mass control, cross-contamination among the layers, decreased yield, and their propensity to delaminate at the interface between the layers during and after the various production stages following the compaction process all contribute to the layers' poor mechanical and compression characteristics. Therefore, the first problem that has to be solved in the development of proper and detailed understanding of the primary causes of the issues in both macro and micro scales and the creation of effective remedies for their resolution during the solid dose distribution design. One of the main problems is the insufficient adhesion and bonding between the adjacent compacted layers, which is primarily brought on by an interfacial crack that causes residual stresses in the tablet. These residual stresses spread over a finite distance in the tablet and cause delamination, or layer separation, which is not immediately apparent after compaction, such as during packaging, storage, or shipping. Additionally, the layers won't be able to adhere strongly if they are too hard or too soft, which could lead to compromised mechanical integrity. The determination of the layer sequence order, the elastic disparity of the neighbouring layers, layer weight ratio, damping force of the first layer, and cross-contamination between layers are some additional problems in the development process. If these variables are not under control, in some way they will have an impact on the bilayer compression process as a whole (an uncontrolled or ineffective process) as well as the quality features of the bilayer tablets, i.e., sufficient mechanical strength to maintain its usefulness and the weight control of the individual layer. In order to enable the creation of a reliable process and product, it is crucial to properly gain a complete understanding of the major factors. Understanding the factors affecting the stress state, the mechanical characteristics of each layer and the entire bilayer tablet, and compression parameters, as well as specialised methods for predicting failure as a function of compression conditions and layer properties, are fundamental because adjacent compacted layers within a bilayer tablet mechanically adhere to one another.

Areas to be addressed during the formulation of bilayer drugs:

- Material properties
- Compression forces

- Lubricant
- Layer ratio and layer sequence
- Environmental conditions
- Layer weight control
- Bilayer tablet characterization

Various approaches to bilayer tablets [6-10]:

Floating drug delivery system:

These are designed to have a lower density so they can float over the contents of the stomach after administration. Alternatively, the device can absorb the fluid until its density and buoyancy are reduced, thereby making it easier for it to pass from the stomach through a motility wave that causes emptying of the stomach. The bilayer pill is designed such that one layer delivers the medicine instantly, resulting in a quicker beginning of action, while the other layer is the floating layer, which floats inside the stomach. Intra-gastric bilayer floating tablets and multiple-unit type floating pills are the two main methods for producing floating dosages.

Intra gastric bilayer floating tablet:

These tablets have two major compressed layers: the immediate layer, which influences the target area right away, and the sustained release layer, which influences the target area after the immediate layer has done working.

Multiple unit types floating pills:

These tablets are double-layered seeds with expanded/sustained release technology. Chemically speaking, the outside layer is made up of a swellable membrane layer, while the inner layer is made up of effervescent agents. Due to their low density, these types of tablets first sink to the bottom of a solution when dissolved in it at body temperature, then swell up like a balloon and float on the surface.

Polymeric bio-adhesive system:

These are created in a way that allows them to absorb the liquid after administration. The outer layer then becomes sticky and viscous, sticking to the mucus-based stomach layer. As a result, stomach preservation is encouraged to tilt as its adhesiveness deteriorates. These have two layers, one of which is for quick dosing and the other of which has the property of bioadhesion. However, this kind of dosage has never been used on people and has only been given to animals. This results from the fundamental differences between the physiologies of the human and animal bodies, in which the quantity and nature of mucous vary greatly.

Swelling system:

These are made to be significantly smaller when administered to make taking the dose easier. These quickly decompose, swell, or unfold after ingestion to a size that blocks the pylorus channel until the drug release progresses to the desired level. It exits the stomach after gradually eroding away or disintegrating into smaller pieces. A straightforward bilayer tablet may have one layer for fast release and a second layer for longer or conventional release.

Techniques of bilayer tablets [11-13]:

To produce bilayer tablets with the necessary quality, a variety of bilayer tablet processes are used. Osmotic-release oral system (OROS) push-pull technology, En so troll technique, L-OROS Tm technology, DUROS Technology, Duredas Technology/Elan Drug Technology, Geomatrix Technologies, Geminix Technologies, programmable oral drug absorption system (Prodas), and erodible multilayer drug system are among the techniques used in this process.

Types of bilayer tablets [14-17]:

Bilayer tablets come in three different varieties with different production mechanisms. The first variety, known as a single side press, is the simplest design and is created using a basic pressing technique that uses force or gravity sometimes. The second type is the double-sided press, which is created through compression, and the final type is the bilayer tablet press, which is created through displacement. The following describes each of the three types:

Single sides press:

The single-sided press, which includes discrete chambers for the doublet feeder, is thought to be the simplest in terms of design. Two distinct tablet layers are produced by forcing or using gravity to feed each of the two chambers, respectively. Following the die's passage beneath the feeder, the first layer's filling with medication powder is completed, followed by the second layer. After that, one or two steps are taken to connect the entire tablet. The risk of the two layers separating is minimised since the two films of the tablet pass through the die and gently mix at their interface, creating a strong link between the two layers.

Double-sided tablet press:

This kind of bilayer pill has a separate fill station and a core compression for each film. The bilayer tablet goes through four different steps before being ejected through the press. The compression force is used by a majority of the double-sided tablet presses having automatic production control for monitoring and controlling the tablet weight. The control system

calculates the effective peak compression force that is applied to each tablet or tablet layer at the main layer compression.

Bilayer tablet press with displacement:

The displacement control principle used by tablets differs from others that depend on compressive force. The applied pre-compression force affects the control system sensitivity during displacement measurement, but not the tablet weight. Therefore, the pre-compression force is reduced to improve the monitoring process, which will improve the bonding between the first and second layers. The upper pre-compression roller and lower pre-compression roller are the two compressors that make up the bilayer tablet press. The former is connected to an air piston, while the latter controls the compression height and is situated on a yoke.

Preparation of bilayer tablets [18-22]:

Bilayer tablets are made with a layer of medication intended for immediate release and a second layer intended for delayed release, either as a second dose, or in a shape for a prolonged release. It is also possible to produce bilayer tablets with two incompatible medications by compressing individual layers of each drug to reduce the area of contact between two layers. There may also be a further inert layer added in the middle. Certain conditions, including the required mechanical strength and desirable drug release profile, must be satisfied in order to manufacture an appropriate tablet formulation. While making bilayer tablets using the double compression process, it might be challenging for the formulator to accomplish these parameters because of the drug's poor flow and compatibility characteristics, which can lead to capping and/or lamination. A substance's compressibility and consolidation are both factors in its compaction.

Advantages of bilayer tablets:

- It can be a supplement to traditional technology.
- Use of single-entity feed grains is conceivable.
- Enhanced patient convenience because fewer daily doses are required compared with the standard administration system, which improves the effectiveness of the treatment regimen.
- It is in charge of preserving chemical and physical stability as well as separating incompatible parts.
- Alternative benefits include maintaining potency and guaranteeing dose accuracy, having superior chemical and microbiological stability compared to other oral dosage forms, and providing the least uniform content and highest precision.

- Bilayer tablets prevent two medications from coming into direct contact with one another, yet by combining the two pharmaceuticals, they become more effective.

Disadvantages:

- Due to their amorphous and low density characteristics, several medications resist compression into dense compacts.
- Drugs that have an unpleasant taste, an offensive odour, or are oxygen-sensitive may need to be coated or encapsulated.
- In the case of youngsters and people who are unconscious, swallowing is difficult.
- It may be challenging to construct or manufacture a tablet for a medicine with poor wetting, sluggish dissolution, or optimal absorption that is high in the GIT while maintaining adequate or complete drug bioavailability.

Applications:

- Bilayer tablets are suitable for the combined sequential administration of two medicines.
- It separates the two inconsistent medications.
- The instantaneous drug release occurs in the first layer of sustained-release tablets while the sustained dose is present in the second layer.
- The constraints of a single-layered tablet are overcome by a bilayer tablet, a cutting-edge technology.
- It facilitates patient compliance and convenience while delivering both the initial and maintenance dose of one or more medicines.
- Bilayer floating tablets are two-layer tablets with a floating layer on top and an instantaneous medication release on the bottom.
- Bilayer tablets provide the simultaneous administration of two distinct medications with various release patterns.
- Bilayer tablets provide the simultaneous administration of two distinct medications with various release patterns. These tablets are used to deliver fixed dosages of various APIs. Erodible or swellable barriers are used to expand and alter the surface area for active medicinal components for customised release.

CONCLUSION:

Manufacturers have a great opportunity to differentiate themselves from adversaries, increase the effectiveness of their products, and safeguard against counterfeit items. GMP regulations and bilayer tablet quality can vary greatly. This explains why a wide variety of presses, from straightforward

single-sided presses to highly complex equipment, are utilised to create bi-layer tablets. Compression force-controlled presses are obviously limited when a high-quality bi-layer tablet is to be made together with precise weight control of both layers due to their inadequate sensitivity and, consequently, lack of accuracy at low compression pressures necessary to secure interlayer bonding.

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