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BILAYER TABLETS: A NOVEL DRUG DELIVERY SYSTEMS

K. Divya Laxmi*, Avula Kavya, Bakkareddy Apoorva, Bange Vinod, Banothu Vennela, Battulwad Shrivani

Teegala Krishna Reddy College of Pharmacy, Medbowli, Meerpet, Hyderabad.

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***Corresponding Author**
K. Divya Laxmi
Teegala Krishna Reddy College of Pharmacy, Medbowli, Meerpet, Hyderabad.

ABSTRACT

Bilayer tablets are medications that combine two drugs, either the same or different ones, in a single dose to treat a disease effectively. The goal of this review is to reveal the difficulties that arise during the preparation of bilayer tablets, as well as to propose solutions to these difficulties. Furthermore, types such as single side press, double side press, and bilayer tablet displacement press are discussed, as well as applications, pros, and cons of bilayer tablets. Furthermore, in order to gain a thorough understanding of bilayer tablets, the review article discusses the various methods and techniques used in their production.

KEYWORDS: Bilayered tablets, tablet press.

System for Oral Drug Delivery

The oral route of drug delivery has gained popularity and widespread acceptance. It is the most practical and preferred route because it is simple to use, readily available, pain-free, precise in dosage, and flexible in formulation. Reduced dosing frequency is the main goal of controlled drug delivery. The majority of pharmaceutical products designed for oral administration are intended for systemic delivery. This demonstrates that oral formulation is the most widely used around the world, and the researcher is primarily focused in this direction.

Introduction to Tablets

Tablets are solid dosage forms that each contain a single dose of a pharmaceutical ingredient They are created by compressing drug and excipients. Tablets are designed to be taken orally. Some are ingested whole, some after chewing, some are administered after being dissolved or dispersed in water, and some are kept in the mouth where the active ingredient is released.

Tablets have the following benefits.

Self-administration is possible

Accurate dosing

Physical and chemical stability

Patient compliance

Ease of transport

Readily available at low cost

Need for storage space is reduced

Ease of dispensing.

Types of Tablet

A) Oral Tablets for Ingestion

1. Single compressed tablets
2. Multiple compressed tablets

Layered tablets

Compression coated tablets

Inlay tablets

3. Modified release tablets
4. Delayed tablets
5. Targeted tablets

a. Floating tablets

b. Colon targeted tablets

6. Chewable tablets

B) Tablets used in Oral Cavity

1. Buccal tablets
2. Sublingual tablets
3. Troches and lozenges
4. Dental cones

C) Tablets administered by other Routes

1. Implantation tablets
2. Vaginal tablets

D) Tablets used to prepare Solution

1. Effervescent tablets
2. Dispersible tablets
3. Hypodermic tablets
4. Tablet triturates

Layer Tablets

Layered tablets contain two portions, one portion delivers a loading dose that releases right away, and another portion delivers a maintenance dose that releases gradually. By placing an inert barrier between two incompatible substances, we can separate them, and we can combine the immediate and sustained release portions of a medication to decrease the number of doses needed. Nowadays, controlled release formulations are frequently made using bilayered tablets. The bilayer tablet is superior to the dosage form that is typically used. These tablets have layers for both immediate and sustained release. When super disintegrating agents are added to an immediate release layer, the initial dose is immediately released, hastening the onset of action. The second layer contains the maintenance dose, which releases the drug gradually over an extended period of time. The majority of medications that are appropriate for this type of drug delivery include vasodilators, antihypertensives, antihistamines, analgesics, antipyretics, and antiallergenic agents.

Bilayer tablets' benefits

- A third layer of an inert substance can be used to separate incompatible materials.

Modifying drug release is possible.

- It is possible to combine therapies.
- Cheaper than other dosage forms.
- The highest level of microbial and chemical stability when compared to other oral dosage forms.
- Coating technologies can hide offensive odor and taste.
- Flexible idea.
- The product's grace.
- Offer the least uniform content and the highest level of precision.
- Less likely to cause hangups and easy to swallow.
- Capable of mass production.
- A bi-layer tablet can maximize the effectiveness of a drug combination by preventing

direct contact between the two medications.

- The design of bi-layer tablets allows for the modification of release because one layer can be kept as extended release and the other as immediate release.

Bilayer Tablet Drawbacks

- It may be challenging to formulate or manufacture a tablet for a drug with poor wetting, slow dissolution, or optimal absorption that is high in the GIT while maintaining adequate or complete drug bioavailability.
- Difficult for patients who are unconscious or children to swallow.
- Makes things more complicated, and bilayer rotary presses are pricey. Due to their amorphous and low density characteristics, some drugs resist compression into dense compacts.
- Layer-to-layer contamination.
- Low yield, layer separation, and insufficient hardness.
- Inaccurate control of individual layer weight
- Drugs that are sensitive to oxygen, have an offensive odor, or are bitter may need encapsulation or coating.
- It must have a long chemical stability shelf life to avoid altering the therapeutic agents.

Bilayer Tablets are Required

- To extend the lifespan of drug products,
- Todevelop novel drug delivery systems like chewing devices and floating tablets for gastro-retentive drug delivery.
- To administer fixed dose combinations of various APIs.
- To regulate the rate at which one or more active pharmaceutical ingredients are delivered.
- To create swellable/erodible barriers for modified release by modifying the total surface area available for the API layer by sandwiching it with one or two active layers.
- 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.

Ideal Bilayer Tablet Characteristics

- It should be strong enough to withstand mechanical shock while being produced, packaged, shipped, and administered.
- The product should be elegantly crafted and free from flaws like chips, cracks,

discoloration, and contamination.

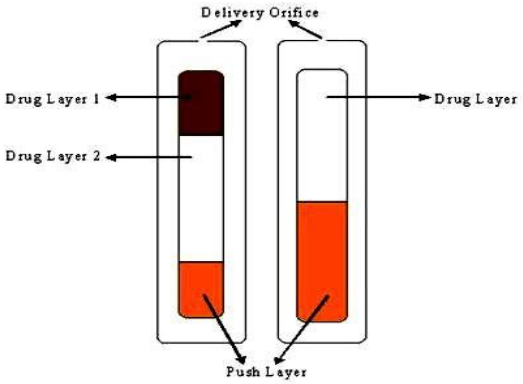
- Must have a long chemical shelf life to avoid causing the medicinal agents to change.
- The bilayer tablet's drug release must be predictable and repeatable.
- It must be stable on both a physical and chemical level to maintain its physical properties over time.

Bilayer Tablet Manufacturing Challenges

- Bilayer tablets can be conceptualized as a combination of two single-layer tablets. Manufacturing presents some practical difficulties.
- Delamination: When the two tablet halves do not completely bond, the tablet breaks apart. When compressed, the two granulations ought to stick together.
- Cross-contamination: This occurs when the first layer's granulation mixes with the second layer's granulation, or the other way around
- Production yields: Dust collection is necessary to prevent cross-contamination, which results in losses. Bilayer tablets are therefore less productive than single-layer tablets.
- Price: For several reasons, bilayer tableting is more expensive than single layer tableting. For starters, the tablet press is more expensive. Second, in bilayer mode, the press generally runs slower. Third, two compatible granulations must be developed, which means more time spent on formulation development, analysis, and validation. If these factors are not well controlled/optimized, they will have an effect on the bilayer compression and the quality attributes of the bilayer tablets (sufficient mechanical strength to maintain its integrity and individual layer weight control). As a result, it is critical to gain insight into the root causes in order to design a robust product and process.

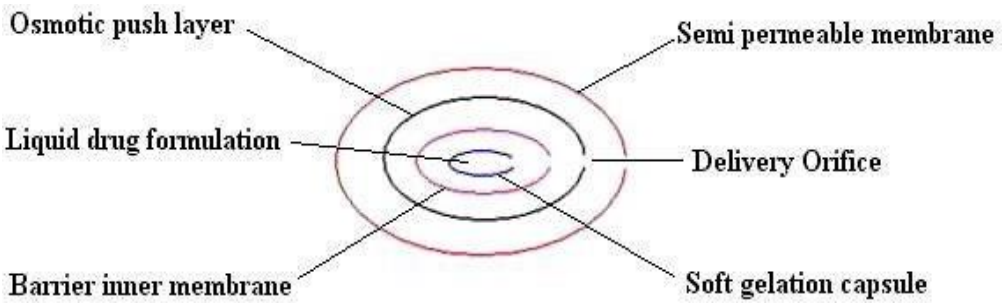
Various Bilayer Tablet Techniques

OROS® Push Pull Technology This system primarily consists of two or three layers, one of which acts as a push layer and contains the drug and other ingredients. The primary components of the drug layer are drugs and two or more diverse agents. As a result, the medication in this layer is in a poorly soluble form. Osmotic and a suspending agent have also been added. The core of the tablet is encased in a semi-permeable membrane.



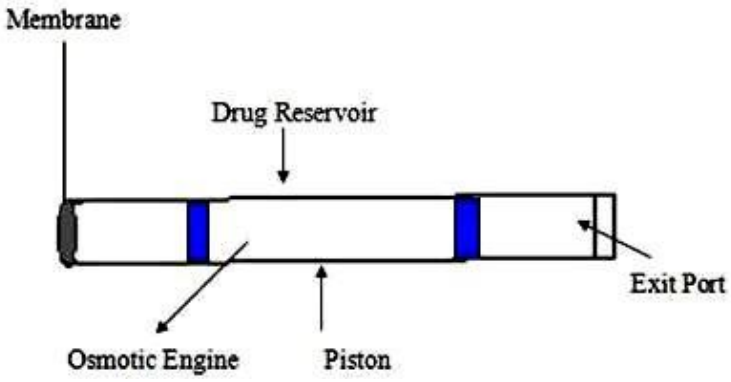
Technology L-OROS

This system was employed due to the solubility issue. The L-OROS system was created by A1za. Once the lipid soft gel product with the drug in solution has been created, it is coated with a barrier membrane, an osmotic push layer, and then a semi-permeable membrane with an exit orifice.



Technology DUROS

An outer cylindrical titanium alloy reservoir makes up the system High impact strength and enzyme protection are provided by this reservoir. The DUROS technology is a tiny drug dispensing system that dispenses concentrated medication in continuous and reliable doses over the course of months or years, much like a miniature syringe.



ENSOTROL Technology

To Enhance solubility by an order of magnitude or developing an optimized dosage form Shire laboratory employs an integrated approach to drug delivery that focuses on identifying and incorporating the identified enhancer into controlled release technologies.

Programable Oral Drug Absorption System (PRODAS)

The foundation of PRODAS, a multi-particulate drug delivery system, is the encapsulation of controlled release mini tablets with a diameter ranging from 1.5 to 4 mm. This technology offers the desired release rates because it combines multi-particulate and hydrophilic matrix tablet technologies. These factors might include mini tablets with controlled release, delayed release, and/or immediate release. The PRODAS technology allows for targeted drug delivery to specific absorption sites throughout the GI tract in addition to controlled release absorption over a predetermined period. Utilizing mini tablets made with various ingredients allows for the creation of combination products.

Technologies GEMINEX

With this drug delivery system, multiple drugs can be delivered at various times. By reducing the drug's side effects, this technology essentially increases the therapeutic efficacy of the drug. Because it offers drug delivery at various rates in a single tablet, it benefits both the industry and the patient.

Multilayer Erodible Molded Tablet

Egalet erodible molded tablets in a platform based on erosion. It has the advantage of delivering zero order or delayed release with minimal gastrointestinal impact. Egalet erodible molded multi-layered tablets are made using injection molding egalet technology, which includes a coat and a matrix. The gradual erosion of the matrix part controls drug release. The mode and rate of release are designed and engineered by changing the matrix, the coat, and the geometry to achieve either a zero order release or a delayed release. A drug is dispersed

throughout the matrix for a zero order. The coat is biodegradable, but its water permeability is low, preventing it from penetrating. When exposed to available water, the matrix erodes. The matrix is eroded by GI fluids and promoted by gut movements in the GI tract. Because the dosage form is designed to slow water diffusion into the matrix, drug release is almost entirely mediated by erosion. It is unquestionably preferable for drugs that have chemical and physical stability issues after contact with water. Egalet delivery technology is built on standard plastic injection molding techniques to ensure accuracy, reproducibility, and low production costs.

Bilayer Tablet Press

A tablet multiple layer press is simply a tablet press that has been modified so that each press revolution includes two die-filling and compression cycles. To summarize, each punch compresses twice, once for the first layer of a two-layer tablet and again for the second layer. Three compression cycles are available on three-layer presses. There are currently two types of layer presses in use: one in which each layer can be ejected from the press separately for weight checking, and one in which the first layer is compressed so hard that the second layer does not bond to it, or bonds so poorly that the layers can be easily separated for weighing upon ejection.

Types of Bilayer Tablet Press

A) Single sided tablet press.
B) Double sided tablet press
C) Bilayer tablet press with displacement monitoring.
D) Multilayer compression basics.
E) Piccola bilayer
F) RoTab Bilayer

Single Sided Press

Over the years, numerous types of bilayer presses have been developed. The most basic design is a single-sided press with two separate chambers for the double feeder. The two distinct layers of the tablet are created by forcing or gravity-feeding a different powder into each chamber. The first layer of powder and the second layer of powder are loaded into the die as it moves beneath the feeder. The entire tablet is then compressed in one or two steps (two pre and main compression). This is the simplest method because the two layers in the

die barely mix at their interface and, in most cases, sufficiently bond to prevent layer separation when the tablet is produced.

Double Sided Tablet Presses

The majority of double-sided tablet presses that use automated production control track and regulate tablet weights using compression force. The compression system's effective compression force applied to each individual tablet during the layer's primary compression. This system assists in correcting the die fill depth when necessary and rejecting out the tolerance tablets.

Advantages

- The first layer was compressed gently in order to prevent capping and layer separation.
- Extended dwell time at first and second layer pre-compression to ensure adequate hardness at top turret speed.
- Maximum cross-contamination prevention between two layers.
- The two layers are visibly separated from one another.
- Displacement weight monitoring for precise and independent layer-by-layer weight control
- Maximum yield.

Piccola Bilayer

To meet the requirements of new product development, this rotary press was created to simulate small-scale two-layer tablet production conditions. The Piccola Bi-layer Press complies with CGMP standards and is capable for type D or type B tooling that complies with TSM or EU standards, allowing the use of the same production punches. There are completely independent systems for weight, height, and hardness adjustment, both for the first and second layers, for an appropriate adjustment in tablet production. With the aid of a PLC system with a touch screen and software for Galenic Development and Production Control, all parameters, including production rate and, separately, the rate of each star forced feeder, can be controlled simultaneously. There are numerous add-ons and choices for the software.

CONCLUSION

In conclusion, the bilayer tablets are a type of modern medicine that binds various substances together to treat illnesses. The main goal of this drug delivery system is to ensure that the medication is efficient, has a minimal number of side effects, and was properly manufactured while taking into account all GMP guidelines in order to maintain its quality over the course of its shelf life. Different methods and presses are used to meet these requirements in order to maximize their effectiveness.