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A Review on Bilayer Tablets

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ABSTRACT

A bi-layer tablet is a new era for the successful development of controlled release formulation along with various features to provide successful drug delivery. Bilayer tablet technology, an excellent improved technique for providing combine release patterns of drug i.e. immediate release and sustained release. In this system two incompatible drugs combined in the single dosage form. 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 (immediate release with extended-release). There is the various application of the bilayer tablet it consists of monolithic partially coated or multilayered matrices. This review explains the fundamentals of the bilayer tablet system along with its fabrication techniques, different approaches, characterization, challenges in Bilayer tablet manufacturing, Quality & GMP requirements, for their production and recent developments in the field of bilayer technology. Bilayer tablet is improved beneficial technology to overcome the shortcoming of the single-layered tablet. In the case of bilayered tablets, drug release can be rendered almost unidirectional if the drug can be incorporated in the upper nonadhesive layer its delivery occurs into the whole oral cavity.

INTRODUCTION

Based on these considerations, we have proposed a bilayer tablet, in which the one layer is formulated to obtain the immediate release of the drug, to reach a high serum concentration in a short period. The second layer is a controlled release hydrophilic matrix, which is designed to maintain an effective plasma level for a prolonged period.[1]

Bi-layer tablets can be a primary option to avoid chemical incompatibilities between APIS by physical separation and to enable the development of different drug release profiles (immediate release with extended-release). 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 the second layer is maintenance dose.[2]

Figure No. 1: Bilayer tablets

APPLICATION OF BILAYER TABLETS

- ❖ Separate two incompatible substances.
- ❖ A bilayer tablet is suitable for the sequential release of two drugs in combination.
- ❖ Promoting patient convenience and compliance.
- ❖ Bilayer tablet is improved beneficial technology to overcome the shortcoming of the single-layered tablet.
- ❖ Bilayer tablets are used to deliver the two different drugs having different release profiles.[3]

ADVANTAGES OF BILAYER TABLETS

- They are used as an extension of conventional technology.
- Low cost compared to another dosage form.
- Greatest chemical and microbial stability compared to other oral dosage forms.
- Objectionable odor and taste can be masked by coating technology.
- Easy to swallow with least hang-up problems.[4]

DISADVANTAGES OF BILAYER TABLETS

- Bi-layer rotary presses are expensive.
- Cross-contamination between the layers.
- Difficult to swallow in case of children and unconscious patients.

IDEAL CHARACTERISTICS OF BILAYER TABLETS

- A bi-layer tablet should have elegant product identity while free of defects like chips, cracks, discoloration, and contamination.
- It should have sufficient strength to stand mechanical shock during its product packaging, shipping and dispensing.
- It should have the chemical and physical stability to maintain its physical attributes over time. The bi-layer tablet must be able to release the medicinal agents in a predictable and reproducible manner.[5]

TYPES OF BILAYER TABLET

Bilayer tablet is of two types:

- Homogenous type
- Heterogenous type

HOMOGENOUS TYPE

These are preferred when drug showing release profiles different from each other. These are developed in such a manner that one layer acts as a loading dose for immediate release and another layer for giving maintenance dose or extended-release.

HETEROGENEOUS TYPE

These are formulated with two incompatible substances in a single dosage form separated from each other. Two drugs providing sequential release in combination are the example of this type.[6]

TYPES OF BILAYER TABLET PRESS

A. Single-sided tablet press

B. Double-sided tablet press

C. Bilayer tablet press with displacement monitoring

SINGLE-SIDED TABLET PRESS

❖ The simplest design is a single-sided press with both chambers of the double feeder separated from each other.

❖ Two individual layers of the tablet produced as each chamber have gravity or forced fed with a different powder.

❖ When the die passes under the feeder, it is at first loaded with the first-layer powder followed by the second-layer powder.

❖ Then the entire tablet is compressed in one or two (pre and main- compression) steps.

Figure No. 2: Single-sided press

Limitations of the single-sided press are;

❖ No weight control/monitoring of the individual layer.

❖ No distinct visual separation between the two layers.

❖ Very short first layer dwell time due to the small compression roller, possibly resulting in poor de-aeration, capping and hardness problem.

B) DOUBLE SIDED TABLET PRESS

❖ A double-sided press has an individual fill station, pre-compression and main compression for each layer.

❖ Most of the double-sided tablet presses with automated production control use compression force to monitor and control tablet weight.

❖ The effective peak compression force exerted on each tablet or layer is measured by the control system at the main-compression of that layer.

❖ Measured peak compression force (under constant thickness) is the signal used by the control system to reject out-of-tolerance tablets and correct the die fills depth when required.

Figure No. 3: Double-sided tablet press

C) BILAYER TABLET PRESS WITH DISPLACEMENT MONITORING

❖ The displacement tablet weight control principle is fundamentally different from the principle-based upon the compression force.

❖ When measuring displacement, the control system sensitivity does not depend on the tablet weight but depends on the applied pre-compression force.

❖ This double-sided tablet press has been specifically designed and developed for the production of quality bilayer tablets and provides.

❖ 'Displacement' weight monitoring/control for accurate and independent weight control of the individual layers.

❖ Low compression force exerted on the first layer to avoid capping and separation of the two individual layers.

❖ Increased dwell time at pre-compression of both first and second layers to provide sufficient hardness at maximum turret speed.

❖ Maximum prevention of cross-contamination between the two layers - a clear visual separation between the two layers – maximized yield.[7]

Figure No. 4: Bilayer tablet press

VARIOUS TECHNIQUES FOR BILAYER TABLET

A) OROS® push-pulls technology

This system consists of mainly two or three-layer among which the one or more layer is essential of the drug and other layers are consist of push layer. The drug layer mainly consists of the 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 semi-permeable membrane surrounds the tablet core.[8]

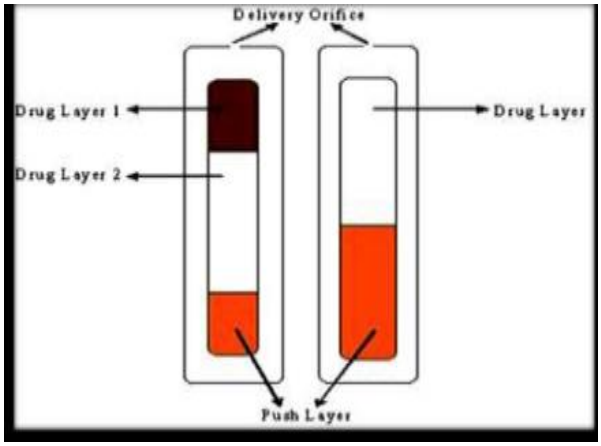

Figure No. 5: OROS® push-pulls Technology

B) L-OROSTM technology

This system used for the solubility issue Alza developed the L-OROS system where a lipid soft gel product containing the drug in a dissolved state is initially manufactured and then coated with a barrier membrane, then osmotic push layer and then a semi-permeable membrane, drilled with an exit orifice.[9]

C) EN SO TROL technology

Solubility enhancement of an order of magnitude or to create optimized dosage form Shire laboratory uses an integrated approach to drug delivery focusing on identification and incorporation of the identified enhancer into controlled release technologies.[10]

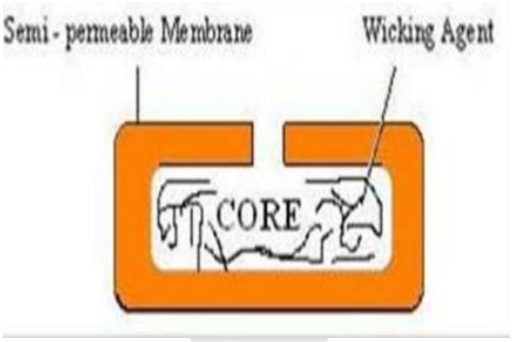

Figure No. 6: EN SO TROL Technology

D) DUREDAS™ technology

This system is also known as Elan drug technologies' Dual release drug delivery system. DUREDAS™ Technology is a bilayer tablet that can provide immediate or sustained release of two drugs or 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 within the one tablet. The modified-release properties of the dosage form are provided by a combination of hydrophilic polymers.[11]

E) DUROS technology

The system consists of an outer cylindrical titanium alloy reservoir. This reservoir has a 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 releases minute quantity of concentrated form in continues and consistent from over months or year.[12]

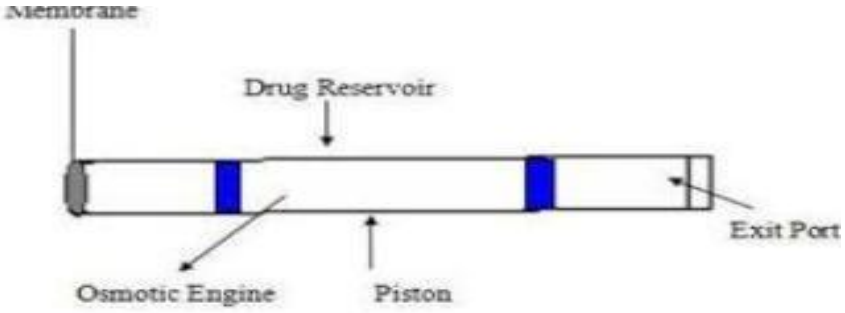

Figure No. 7: DUROS Technology

COMPRESSION STEPS OF BILAYERED TABLETS

Various steps of bi-layer tablet formulation are as follows:

- ❖ Filling of the first layer.
- ❖ Compression of the first layer.
- ❖ Ejection of upper punch.
- ❖ Filling of the second layer.[13]

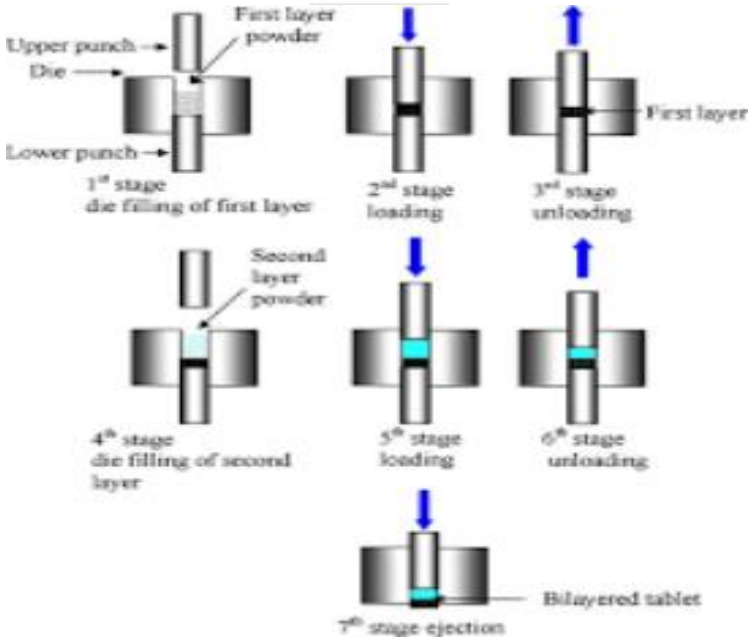

Figure no 8 Compression steps of bilayered tablets

CHALLENGES IN BILAYER MANUFACTURING

Bilayer tablets can be seen as two single-layer tablets compressed into one. In practice, there are some manufacturing challenges.

❖ Delamination: Tablet falls apart when the two halves of the tablet do not bond completely. The two granulations should adhere when compressed.[14]

❖ Cross-contamination: When the granulation of the first layer intermingles with the granulation of the second layer or vice versa, cross-contamination occurs. It may conquer the very purpose of the bilayer tablet. Proper dust collection goes a long way toward preventing cross contamination.[15]

❖ Production yields: To prevent cross-contamination, dust collection is required which leads to losses. Thus, bilayer tablets have lower yields than single-layer tablets.[16]

❖ Cost: Bilayer tableting is more expensive than single-layer tableting for several reasons. First, the tablet press costs more.[17]

EVALUATION OF BILAYERED TABLETS

❖ Tablet Thickness and Size

The thickness and diameter of tablets were important for the uniformity of tablet size. Thickness and diameter were measured using venire caliper. [18]

❖ 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 the tablet of each formulation was measured by Monsanto hardness tester.[19] The hardness was measured in kg/cm^2.

❖ 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.[20]

% loss = [(Initial wt. of tablets – Final wt. of tablets)/ Initial wt. of tablets] ×100

❖ 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.[21]

SUMMARY

Bi-layer tablets offer an excellent opportunity for manufacturers to separate themselves from their competitors, improve the efficacy of their products. A bi-layer tablet is improved beneficial technology to overcome the limitation of the single-layered tablet. 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 the second layer is maintenance dose.

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