WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

A Review on Bilayer Tablet

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ABSTRACT

The development of controlled release formulations with a bilayer tablet is a revolutionary technology. Bilayer tablets are created by combining two or more active medicinal components in a single dose form. The use of bilayered tablets has increased in recent years. The progressive release of two active components in combination is better achieved with a bilayer tablet. The use of bilayered tablet technology aids in the separation of two incompatible drugs, with one layer providing quick release as a loading dosage and the other providing controlled/sustained release as a maintenance dose. By adding an inert intermediary layer, two incompatible medications can be synthesised into a bilayer tablet.

INTRODUCTION

These are created in order to produce a drug's customised release. There would be a large range of changes in the drug concentration in conventional dose forms, resulting in undesired toxicity and low efficiency [1,2].

Advantages

• Physical isolation helps to avoid chemical incompatibilities between APIs.
• Appropriate for the simultaneous delivery of two medicines [3,4].
• Traditional dose forms require repetitive dosing, which can be avoided with a bilayer tablet.• Lower dose of drug is required compared to conventional dosage forms.
• It is the most preferred & convenient route of administration.
• Chemical & microbial stability is more compared to other oral dosage forms.
• Taste & odour can be masked by coating technique.
• They show highest dose precision & low content variability.
• Easy to swallow [5,6].

Disadvantages

• Drugs with objectionable odour & with bitter taste cannot be formulated.
• Swallowing is difficult for children & for unconscious people [7,8].
• Formulation is difficult for drugs with poor wettability, slow dissolution rate & high absorption in the GIT.
• Cross contamination may occur between the 2 layers.
• Individual layer weight is inaccurate.
• Low yield, insufficient hardness & the layers gets separated [9,10].

IDEAL CHARACTERISTICS

• It should be elegant & free from chipping, cracking, discoloration and contamination [11].
• It ought to have adequate quality to with stand mechanical shock during its tablet formulation process [12].

NEED OF BILAYER TABLETS:

• To administer fixed dose combinations of diverse APIs, extend the drug product life cycle, buccal/mucoadhesive delivery systems, and construct innovative drug delivery systems such as chewing devices and floating tablets for gastro-retentive drug delivery.
• Managing the rate of administration of a single active pharmaceutical ingredient or two separate active pharmaceutical components
• To achieve swellable/erodible barriers for modified release, alter the overall surface area available for API layer by sandwiching with one or two active layers.
• To segregate incompatible active pharmaceutical ingredients (APIs) and to control API release from one layer using the functional property of the other layer (such as, osmotic property). [13-15]

BILAYER MANUFACTURING DIFFICULTIES

Bilayer tablets can be thought of as two single-layer tablets rolled into one. There are certain manufacturing obstacles in practise. When the two halves of a tablet do not entirely bind, it is known as a delamination tablet. When crushed, the two granulations should stick together.

Cross-contamination

Cross-contamination happens when the granulation of the first layer mixes with the granulation of the second layer, or vice versa. It has the potential to defeat the bilayer tablet's entire goal. Cross contamination can be greatly reduced with proper dust collection.

Yields of production

Dust collection is necessary to prevent cross contamination, which results in losses. As a result, bilayer tablets yield less than single-layer tablets.

Cost

For numerous reasons, bilayer tableting is more expensive than single layer tableting. To begin with, the tablet press is more expensive. Second, in bilayer mode, the press normally runs slower. Third, two compatible granulations must be developed, which requires more time for formulation creation, analysis, and validation. These elements, if not effectively controlled/optimized, will have an impact on bilayer compression and quality features of bilayer tablets in one way or another (Sufficient mechanical strength to maintain its integrity and individual layer weight control). As a result, gaining insight into the fundamental reasons is vital in order to build a solid product and process. [16]

TYPES OF BILAYER TABLET PRESS

1] Single sided tablet press.
2] Double sided tablet press.
3] Bilayer tablet press with displacement monitoring.

1] Single-sided press: A single-sided press is the most basic type, with both chambers of the doublet feeder separated from one another. The two distinct layers of the tablets are produced by gravity or forced feeding each chamber with various powers. The first layer powder is put into the die as it travels through the feeder, followed by the second layer powder. The tablet is then compacted in one or two stages.

Limitations of single sided press
• There is no weight monitoring or management of the individual layers, and there is no apparent division between them.
• Due to the small compression roller, the first layer dwell time is extremely short, potentially resulting in poor de-aeration, capping, and hardness issues.

Dwelling period
Dwell time is defined as the amount of time while the compression force is greater than 90% of its highest value. Longer dwell durations are crucial in making a high-quality tablet, especially when compressing a complex recipe.

Compression force
To maintain the capacity to connect with the second layer, many bilayer formulations require a first layer compression force of less than 100 daN. This capacity may be lost over 100daN, and bonding between the two layers may be insufficient, resulting in low bilayer tablet hardness and separation of the two layers.

2] Double sided tablet press
Compression force is used to monitor and control tablet weight in most double-sided tablet presses with automated production control. The control system measures the effective peakcompression force exerted on each individual tablet or layer at the layer's primary compression. The signa is the

peak compression force that was measured.

3] Bilayer tablet press with displacement

The principle of displacement pill weight management is significantly different from the compression force principle. The sensitivity of the control system for monitoring displacement is determined by the applied pre-compression force rather than the tablet weight. [17-18]

Bilayer Tablet Characteristics: -

• Particle size distribution: Using the sieving method, the particle size distribution was determined.
• Photomicroscope study: TGG and GG were photographed using a photomicroscope (X450 magnifications).
• Angle of repose: Using the following equation, the angle of repose was computed by measuring the diameter of the powder cone.

Tan ø=h/r

Where, h = Height, r = Radius of the powder cone
• Moisture sorption capacity: All disintegrates have the ability to absorb moisture from the environment, which has an impact on moisture-sensitive medications. 1 g of disintegration was used to test moisture sorption capacity. For 2 days, uniformly dispersed in petri-dishes were kept in a stability chamber at 37±1°c and 100 percent relative humidity, and the amount was measured.

• **Density:** The loose bulk density (lbd) and tapped bulk density (tbd) were determined and calculated using the following formulas.
LBD ¼ weight of the powder=volume of the packing ð2þ
TBD ¼ weight of the powder=tapped volume of the packing ð3þ

• **Compressibility:** The compressibility index of the disintegrate was determined by Carr's compressibility index.C = 100 x (1-þb/þt) [19-20]

EVALUATION OF BI-LAYER TABLETS

•Dissolution study
•Size and shape
•Wetting time
•Water absorption ratio
•Hardness
•Uniformity of weight
•Thickness
• Friability

Thickness-

Tablet thickness and diameter were crucial factors in maintaining tablet size uniformity. A venire calliper was used to measure thickness and diameter. [21]

Hardness-

To promote early dissolution in the mouth, the hardness limit of MDT is usually kept in the lower range. A hardness tester can be used to determine the hardness of MDTS (Monsanto Hardness tester). It is measured in kilogrammes or pounds. [22]

Dimensions and form-

Dimensionally describing, monitoring, and controlling the tablet's size and shape is possible.

Uniformity of weight:

A systematic approach is followed to conduct a weight variation test. Using an electronic balance, ten tablets from each formulation are weighed and the average weight is computed.

Friability-

Friability is a term used to describe the strength of a tablet. Twenty pills were precisely weighed and placed in the tumbling equipment, which rotates at 25 rpm and drops the tablets six inches with each revolution. The tablets were weighed after 4 minutes to assess the percentage drop in tablet weight. [(Initial wt. of tablets – Final wt. of tablets)/ Initial wt. of tablets] = percent loss ×100[23]

Wetting time-

In a Petri dish with a diameter of 10 cm, five circular tissue papers with a diameter of 10 cm are arranged. In a Petri plate, ten millimetres of water-containing Eosin, a water-soluble dye, is introduced. A tablet is gently placed on the tissue paper's surface. Wetting time is the amount of time it takes for water to reach the tablet's upper surface. [24]

Water Absorption Ratio-

In a small Petri dish holding 6 ml of water, a folded piece of tissue paper was inserted twice. A tablet was placed on the paper, and the time it took to completely wet it was recorded. After that, the wetted pill was weighed. The following equation was used to calculate the water absorption ratio (R).

$R = 10 (Wa /Wb)$

Where- Wb is weight of tablet before water absorption &

Wa is weight of tablet after water absorption [25].

Dissolution Study-

To examine their capacity to provide the desired controlled medication delivery, bilayer tablets were exposed to in vitro drug release tests in simulated stomach and intestinal fluids. Since the usual gastric emptying duration is around 2 hours, drug release tests were conducted using USP dissolution test apparatus I at 100 rpm, 370.5℃, and pH 1.2 buffer (900 ml) (i.e., 0.1 N HCl) for 2 hours. The dissolution medium was changed with 900 mL of pH 6.8 phosphate buffer, and the experiment was extended for another 10 hours. 5ml of the samples were withdrawn and replaced with 5ml of drug-free dissolving media at various time intervals. The samples withdrawn were analysed by UV spectrophotometer using multi component mode of analysis [26].

CONCLUSION

When compared to single-layered tablets, bilayer tablets are the better option. Even incompatible medications can be compacted into a single pill using this method. The bilayer pill aids in the sequential release of two medicines, one of which is immediate and the other is regulated. Bilayer tablet quality and GMP criteria differ greatly. This explains why several types of tablet presses, ranging from single-sided presses to extremely sophisticated machinery, are utilised to make bilayer tablets.

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