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BILAYER TABLETS: A NOVEL TECHNOLOGY: A REVIEW

Sunitha Reddy M*, Bharath Dubashi

Department of Pharmaceutics, Centre for Pharmaceutical Sciences, Institute of Science and Technology, JNTUH, Kukatpally, Hyderabad, 500085, Telangana, India.

Corresponding author E-mail: baddam_sunitha@rediffmail.com*

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ABSTRACT

Bilayer tablets are designed for the administration of two different drugs in a single dose one for immediate release and the other for sustained release. This is a novel technology. Different types of polymers are used to alter the release of drug. Two chemically incompatible active pharmaceutical ingredients are separated. Special tablet presses are designed for their fabrication. Since last decade the use of bilayer tablets have been increased. Bilayer tablets provide several advantages over conventional release drug delivery of the same drug. Despite of their advantages, the mechanical structure of the formulation have become tricky, requiring complicated tablet architecture due to the use of different materials and complex geometric boundaries between the layers.

INTRODUCTION

Oral ingestion due to its ease of administration has been the most commonly employed and convenient route of drug delivery. It is known that modified release dosage forms have several advantages over immediate release dosage forms of same drug. Tablets are the most preferred and popular dosage forms by patients and physicians. Tablets are obtained by compression of uniform volumes of powder or granules by applying high pressure with the help of punches and dies. They may contain one or more medicaments with or without additives like diluents, lubricants, binders, glidants, disintegrating agents [1-4].Multilayered are further classified as bilayered and trilayered tablets of which the bilayered are again of two types like homogenous and heterogenous tablets. Homogenous tablets: Both the layers contains same drug. Heterogenous tablets: Each layer contains different drug. Bilayer tablets are shown in fig.1.

Fig. 1: Bilayer tablet

Bilayer tablets are the formulations intended to deliver two different drugs in a single tablet. The use of this novel technology has paced up in the past decade. Apart from separating the incompatible drugs it also controls the drug release. The main aim of developing controlled release system is to increase the drug efficiency and reduce the dosing frequency. Bilayer tablets comprises of two layers of granulation among which one is for immediate release and the other

for sustained release and both are compressed together to form single unit. Immediate release and sustained release layers are shown in fig.2.

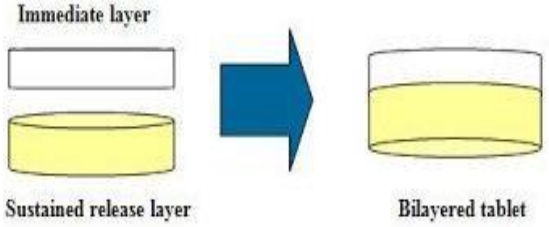


Fig. 2: Bilayer tablet showing immediate and sustained release layers

IDEAL CHARACTERISTICS [5]:

They should be free from defects like chipping, cracking, lamination, discoloration.

Should possess sufficient mechanical strength to withstand mechanical shocks during transportation.

Should maintain its chemical and physical stability throughout its shelf-life. Should release active pharmaceutical ingredient at predetermined rate.

CHALLENGES OF BILAYERED TABLETS:

If proper binding doesn't occurs between the two layers then breakage may occur. Difficult to obtain required mechanical strength.

Risk of cross-contamination between adjacent layers. Special supervision is required during punching.

ADVANTAGES [5-7]:

Improved patient compliance. Frequency of dosing is less.

Promotes greater bioavailability.

Ease of handling compared to other dosage forms. Incompatible drugs can be formulated in single unit.

Masking of unpleasant odour and bitter taste drugs can be done by coating. Stability can be enhanced.

DISADVANTAGES [6-8]:

These are expensive.

Difficult to administer to infants and unconscious patients.

Unpleasant odour, bitter taste and drugs sensitive to oxidation requires special coating or encapsulation.

PREPARATION [9-11]:

Bilayer tablets are designed in such-a-way that one layer is immediately released and the other later at predetermined rate. These two incompatible layers are separated by an inert intermediate layer.

To produce a tablet certain specifications have to be met such as the mechanical strength and the drug release profile. In case of bilayer tablets achieving mechanical strength and drug release profile may be difficult as it involves double compression and compression of two different layers. Basic concept is shown in fig.3.

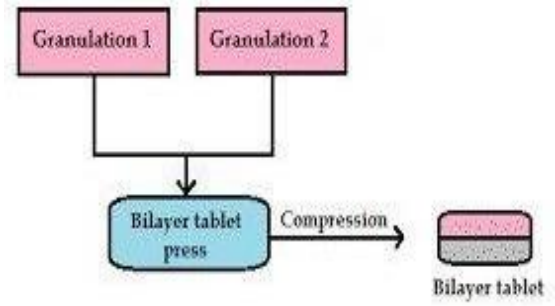


Fig. 3: Basic concept of Bilayer tablet

Compaction involves compression and consolidation.

Compression can be defined as elimination of void spaces and packing the material closer. Mechanical strength is increased due to consolidation. Manufacturing process is shown in fig.4.

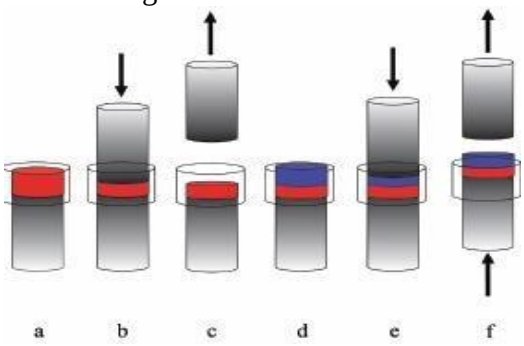


Fig. 4: Manufacturing Process of Bilayer tablet First layer b) First layer tamping c) Upper punch withdrawal d) Second layer fill e) Main compression f) Ejection

TECHNIQUES [13]:

- En So Trol Technology
- L-Oros Tm Technology
- Duros Technology
- Oros® push pull Technology
- PRODAS
- DUREDAS™

- Rotab Bilayer
- Erodible molded multilayer tablet

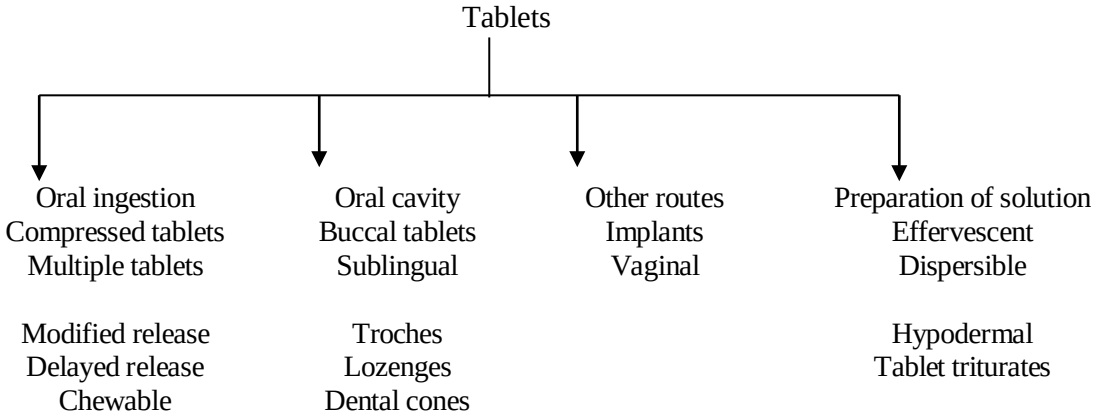
TYPES OF BILAYER TABLET PRESS:

Single Sided Tablet Press: This design comprises of two different chambers separated from one another in which different types of powders are fed. Thus, producing two different layers of tablet. When the die reaches the feeder first the first layer powder is fed then the second layer powder.

Double Sided Tablet Press: In this, the bilayer tablet undergoes four compression stages before ejecting from the die cavity. It contains separate filling points for each powder and each layer of powder undergoes pre-compression and main compression.

CHARACTERIZATION [12-14]:

Particle Size Distribution: Measured using sieving method.



Moisture sorption capacity: Disintegrates absorb moisture from atmosphere that effects the moisture sensitive drugs. Moisture sorption capacity is determined by taking 1gm of disintegrate in petri-dish and uniformly spread and stored for 48hrs at 37±1ºc and 100%RH in stability chamber. The difference between the weights gives the amount of moisture uptake.

Density: Mass of a unit volume material. d = m/v

Bulk density = weight of the powder / Bulk volume Tapped density = weight of the powder / True volume

Angle of repose: It is a measurement of powder flow property, as shown in table 1. It is calculated using the equation,

$\Theta = \tan^{-1}(h/r)$

Compressibility: It is calculated using the formulae, Carr's index (%) = (true density – bulk density / true density) 100

Flow property of powder depends on carr's index as shown in table 2.

Hausner's ratio: It is calculated using the equation, Hausner's ratio = true density / bulk density

Type of powder flow depends on hausner's ratio as shown in table 3.

EVALUATION TESTS [15-18]:

General Appearance: It includes visual identity and overall elegance is essential.

The visual identity involves the measurements of attributes like size, shape, color, odour, taste and surface texture.

Size and shape: The size and shape can be monitored, controlled and dimensionally described.

Thickness: It is the only variable related to process. The variation in thickness of tablets may occur due to change in die fill and particle size distribution and packing of particles.

Thickness can be measured by vernier calipers and micrometer. The thickness should be controlled within a variation of ±5% of standard values.

Hardness: It generally measures the tablet crushing strength. Tablet is placed between two jaws that crush the tablet and the machine measures the force applied on the tablet and detects when it fractures.Hardness of 4-5kg/sq.cm is satisfactory.

Table 1: Flow Property Of Powders Based On Angle Of Repose

Angle of repose (ɵ)	Type of flow	Type of powder
<25	Excellent	Non-cohesive
25-30	Good	Non-cohesive
30-40	Passable	Cohesive
>40	Very poor	Very fine

Table 2: Carr's Index

Carr′s index (%)	Flow property
≤10	Excellent
12-16	Good
18-21	Fair
23-28	Passable
28-35	Poor
35-38	Very poor
>40	Extremely poor

Table 3: Hausner's Ratio

Hausner's ratio	Type of flow
<1.25	Good flow
1.25-1.5	Moderate flow
>1.5	Poor flow

Various devices used to measure the hardness are Monsanto tester, Pfizer tester and Strong-cobb tester.

Friability: Few tablets are selected randomly and weighed, subjected to friabilator. After friabilation tablets are reweighed, tablets that lose <0.5-1% tablet weight are acceptable.

Weight variation: 20 tablets were randomly picked, weighed individually and average weight is calculated. Compare the individual weights to average weight. Tablet pass the test if NMT two individual weights deviate more than 1% from the average weight.

Stability Study: Bilayer tablets are packed well with suitable packing materials and stored under specific conditions for certain prescribed time as per the guidelines if ICH for accelerated stability studies. The storage conditions and time period are shown in table 4.Some of the marketed products are shown in table 5

Table 4: Stability Study

Study	Storage Conditions	Time period
Long term	25ºc ±2ºc /60%RH±5%RH	12 months
Intermediate	30ºc ±2ºc /65%RH±5%RH	6 months
Accelerated	40ºc ±2ºc /75%RH±5%RH	6 months

Table 5: Marketed Products

Product Name	Active pharmaceutical ingredient	Manufacturer
Unistar	Rosuvastatin, Aspirin	Unichem Laboratories Ltd.
Glimeto-MP	Glimepride, Pioglitazone	RPG Life Sciences Ltd
Istamet	Sitagliptin, Metformin hydrochloride	Ranbaxy Pharmaceuticals Ltd.
Pioglu	Pioglitazone, Metformin hydrochloride	Emcure Pharmaceuticals Ltd.

CONCLUSION:

Bilayer tablets, the novel technology aid the delivery of incompatible drugs in a single unit. The release of the active pharmaceutical ingredient can be controlled and predetermined. This technology reduces the dosing frequency. Now a days this technology is used for the administration of anti-diabetics, anti-pyretic, anti-inflammatory, anti-hypertensive drugs.

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