Formulation And Evaluation of Bilyer Tablet

Achal G. Mahalle[1], Shivani Suryawanshi[2], Dr. M. D. Kitukale[3]
[1,2,3]*P. Wadhwani College of Pharmacy Yavatmal*

I.INTRODUCTION

Oral route of drug administration is the most important method of administering drugs for systemic effects. Nevertheless, it is probable that at least 90% of all drugs for systemic effects are administered by the oral route. When a new drug is discovered, one of the first questions a pharmaceutical company asks is whether or not the drug can be effectively administered for its intended effect for the oral route. If patient self-administration cannot be achieved, the sale of the drug constitutes only small fraction of what the market would be otherwise of drugs that are administered orally, solid oral dosage forms represent the preferred class of product. Tablets and capsules represent unit dosage form in which one usual dose of the drug has been accurately placed [1]

Now a day's various developed and developing countries are moving towards combination therapy for treatment of various diseases and disorders requiring long term therapy such as hypertension, Diabetes and Rheumatoid arthritics. The problem of dose dependent side effects is minimized by combination therapies and is advantageous over mono therapy from last few years, interest in developing a combination of two or more active pharmaceutical ingredients in a single dosage form has increased in pharmaceutical industry. Bi-layer tablets can be a primary option to avoid incompatibilities between APIS by physical separation [2]

Bilayer tablet is suitable for sequential release of two drugs in combination, separate two incompatible substances and also for sustained release tablets in which one layer is immediate release which act as loading dose and second layer is sustained release which act as maintenance dose. Bilayer tablet is the most recent form of tablet which comprises of combination of immediate release tablets and sustained release tablets. It is a type of once-a-day oral dosage form which acts immediately upon administration and provides the action for prolonged period of 12-24hrs. [3]

A. Advantages of bi-layer tablets: [3,4]

1. Bi-layer execution with optional single layer conversion kit.
2. Low cost compared to other dosage forms.
3. Greatest chemical and microbial stability compared to other oral dosage forms.
4. Objectionable odor and taste can be masked by coating technologies.
5. Flexible concept.
6. Offer greatest precision and the least content uniformity.
7. Easy to swallow with least hang up problems.

B. Disadvantages of bi-layer tablets: [3,4]

1. Complexity and bi-layer rotary presses are expensive.
2. Insufficient hardness, layer separation, reduced yield.
3. Imprecise individual layer weight control.
4. Cross contamination between the layers.
5. Difficult to swallow in case of children and unconscious patients.
6. Some drugs resist compression into dense compacts, due to amorphous nature, low density nature.

C. Different types of bilayer tablet:

1. Bilayer modified release tablet
2. Bilayer floating tablet
3. Bilayer buccoadhesive tablet

C. Bilayer modified release tablet

This type of bilayer tablet consists of two different types of release profile layers. One layer is immediate release layer in which drug will release 90% of concentration within 30 minutes.

Other layer is sustained release layer where drug will release slowly up to 12-24 hrs.

e.g. Metaclopramide HCI+ Ibuprofen.

D. Bilayer floating tablet

This type of bilayer tablet consists of such type of combination of drugs which are sensitive to gastrointestinal PH. One layer of drug gets metabolized in stomach, while another layer gets degraded in intestine. RT

e.g. Rosiglitazone Maleate.

E. Bilayer buccoadhesive tablet

This type of bilayer tablet consists of drugs which have mucoadhesion and have the property to get attached to mucous membrane of buccal region and sustain the release of drug. e.g. Propanolol HCI

F. Schematic Presentation for Compression of Bi-Layer Tablet

1. Filling of first layer.
2. Compression of first layer.
3. Ejection of upper punch.
4. Filling of second layer.
5. Compression of both layer
6. Ejection of bi-layer table. [5]

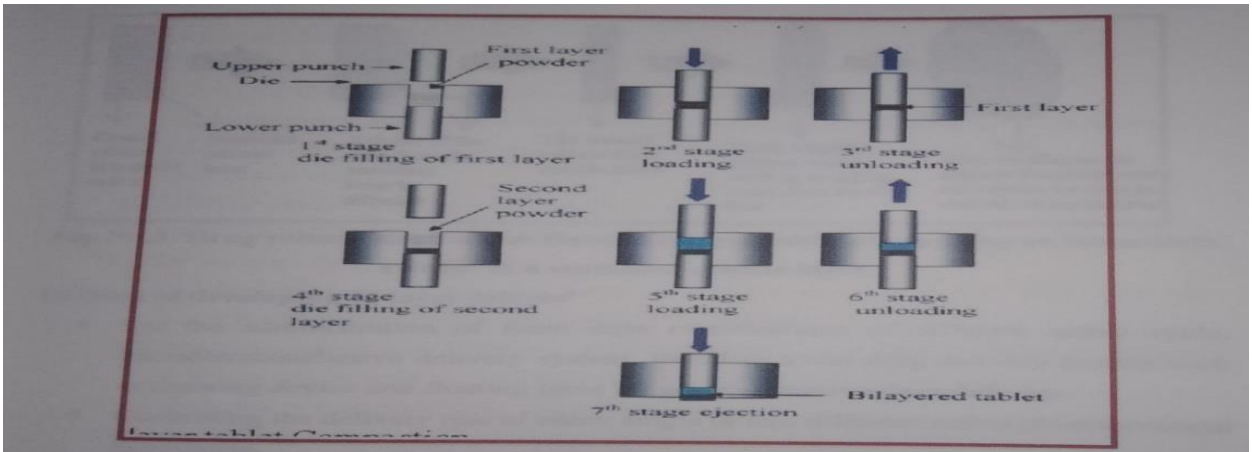

Fig.No.2 schematic presentation for compression of bi-layer tablet

G. General purpose: [3,4]

1. It should have graceful product identity free of defects like chips, craVarious techniques of bilayer tablet
2. Should have sufficient strength to with stand mechanical shock during its production, packaging, shipping and dispensing.
3. Should have physical and chemical stability.
4. The bi-layer tablet must release drug in a expectable and reproducible manner.
5. Must have a chemical stability shelf life, so as not to follow alteration of the medicinal agents.
6. Formulation of bilayer tablet:

Bilayer tablet is formulated by mainly two methods: -

1. Wet granulation method
2. Direct compression method

1. Wet granulation method

Weigh all drugs and excipients accurately and pass through sieve# 100. Prepare binder solution. Wet massing of mixture with the binder solution is done in a pestle mortar. Screen wet mass with the help of sieve# 10. Dry the granules. After drying blend with the help of lubricants and disintegrants to produce running powder. Compress the mixture into tablets with the help of flat punch.

2. Direct compression method

Weigh accurately all the excipients and drugs and pass through sieve# 100. Mix all the components in a pestle mortar and compress them in the form of tablet directly

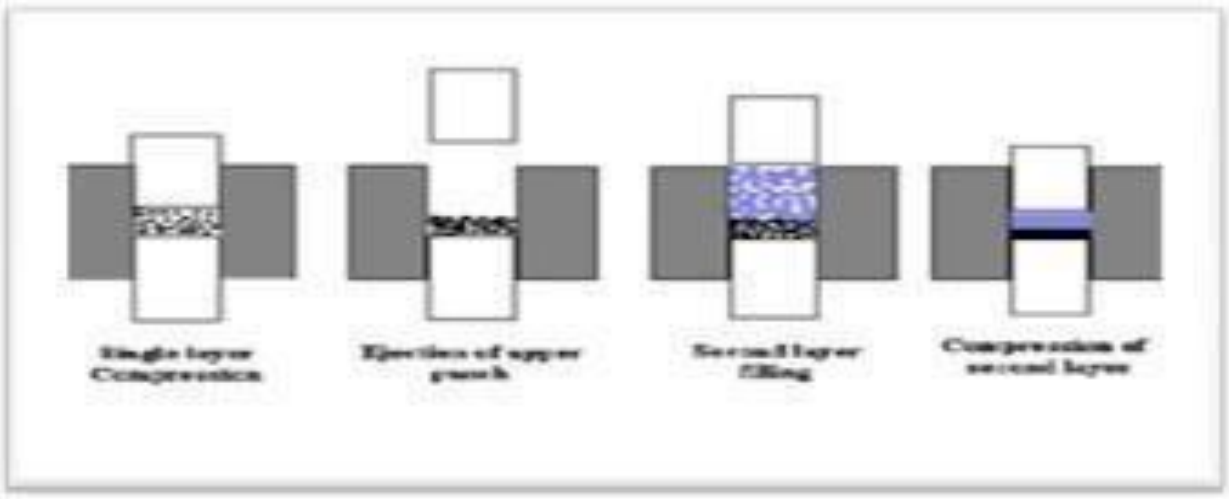

Fig:Bilayer tablet Compresion Cycle

H. Applications of bilayer tablet:

- Hypertension e.g. Propanolol hydrochloride and hydrochlorothiazide
- Diabetes e.g. Metformin and glimepiride, Metformin and glipizide
- Analgesics e.g. aceclofenac and COX inhibitors
- Antipyretics e.g. ibuprofen and Metaclopramide HCI [6]

II. LITERATURE REVIEW

1. Shivani Madhukarrao Suryawanshi et al 2023,[7] Bilayer tablets are prescription medications that combine two of the same or different medications in a single dose to effectively treat an illness. The purpose of this review is to identify the difficulties encountered in the production of bilayer tablets and to suggest solutions. Moreover, styles like single-side applications, benefits, and drawbacks of bilayer tablet displacement presses, double side presses, and to better comprehend the bilayer tablet, other tablets are mentioned. In addition, to fully understand the bilayer numerous procedures and methods used in the production of these types of tablets are also talked about in the review article. A final paragraph provides a critical analysis of the entire essay.

2. Swati Saxena et al 2020,[8] Bi-layer tablets are presently being developed by several pharmaceutical companies for a number of purposes, including marketing, therapeutic efficacy, patent extension, and so on. Capital investment has been decreased with the use o f this technology. Bilayer tablets have been created using modified tablet presses to address issues with tablets such as yield reduction, insufficient hardness, inaccurate individual layer weight control, cross-contamination between the layers, and layer separation. An I tablet press that has been adapted is utilized when high manufacturing output is needed. Keywords: novel drug delivery method, sustained release, tablet, bilayer

3. Mr. Vivek M. Satpute et al 2020,[9] Bilayer tablets are designed to deliver different medications with pre-defined releases in an instantaneous and sustained manner. The last few decades have seen a rise in the pharmaceutical industry's creation of active pharmaceutical ingredients (API) in a single set dosage form, which also encourages patient compliance and convenience. It can be argued that bi-layer tablets are a preferable choice for minimizing chemical incompatibilities that occur between active pharmaceutical ingredients and for facilitating the development of different drug release profiles. A bilayer tablet is ideal for combining two incompatible chemicals into one tablet or for the sequential release of two medications in combination.

4. B. Siva Sai Kiran et al 2015,[10] The creation of the bilayer tablet, which combines several properties with a controlled release formulation, is a new chapter in the successful story of drug delivery systems. In order to prevent chemical incompatibilities between API through physical separation and to facilitate the development of distinct drug release profiles, such as immediate release and prolonged release, bilayer tablets may be the principal choice. An entirely

different kind of analgesic and anti-inflammatory is the bilayer pill. A bi-layer tablet can be used for both sustained release,A bilayer tablet is a technologically advanced solution that addresses the shortcomings of a single-layered tablet. There are several

5. Prasanthi Teella et al 2015,[11] the development of a Le Bi layer tablet, a single dose form containing two active pharmaceutical ingredients (API), is of interest to those in the pharmaceutical industry. A bilayer table serves as both a loading dosage and a maintenance dose while concurrently administering two pharmaceuticals at once in a controlled and rapid manner, hence preventing incompatibility between two active APIs by physical separation. In this case, the medicine is delivered by Eactitrabe acting as an immediate release layer and Metformin HC acting as a sustained release layer. Both immediate release and sustained release polymers (HPMC K15M, HPMC KAM, and HPMC K100M) are used in this approach.

6. Verma Rameshwar et al 2014,[12] Bi-layer tablet is a new era for effective creation of controlled release formulation combined with numerous features to ensure successful medication delivery. Two layers make up bilayer layer tablets: an immediate release layer and a gradual release layer. Additionally, more advantageous technology was developed to address the drawbacks of the single-layer tablets. Due to different active pharmaceutical ingredients (APIs) that were incompatible with one another, bilayer tablet formulations were necessary. The composition of bilayer tablets includes both consolidation and compressibility. Different bilayer tablet press kinds that are now on the market, different bilayer tablet system techniques

7. M Namrata et al 2013,[13] A further benefit to the pharmaceutical industry is the fact that drug delivery systems with modified geometric configurations—especially tablets—have demonstrated encouraging outcomes in drug delivery technology and ease of manufacture. Drug delivery technology has been shown to benefit from geometrically aberrated drug delivery methods, particularly bilayered tablets. Bi-layer tablet development is now underway at several pharmaceutical companies for a number of purposes, including marketing, therapeutic, patent extension,and capital investment reduction. In the last ten years, there has been interest in creating a single Active Pharmaceutical Ingredient (API) that combines two or more Active Pharmaceutical Ingredients (API). Bi-layer tablets were created to accomplish controlled administration of various medications with pre-defined release patterns.

8. Sandesh Kumar et al 2013,[14] In order to improve the oral bioavailability of glimepiride hydrochloride, bilayer tablets of the medicine are to be formulated and assessed for oral sustained drug release in pharmaceutical systems. decrease in the toxicity of drugs. decrease in the frequency of pharmacological dosages. The drug releases quickly at first, followed by a steady rate of release, which is known as biphasic release. The medication delivered during the first pulse rapidly reaches therapeutic plasma drug levels and lessens the sustained release layer's delayed onset of action. Due to the patient's prompt relief, this improves patient compliance. For as long as the system is in use, these kinds of drug delivery systems are made to distribute the medication in a way that keeps the drug level inside the therapeutic window. 9] C. Gopinath et al 2013,[15] The creation of the bi-layer tablet, which combines several qualities with a controlled release formulation, is a new chapter in the successful delivery of medication. -layer tablets may be the best way to prevent physical separation of APIs that are chemically incompatible and to allow for the creation of various drug release profiles. A bi- layer tablet, with one layer for immediate release as the loading dosage and a second layer for maintenance, is appropriate for both far-reaching sustained release and the sequential release of two medication doses in combination. For anti-hypertensive, diabetic, anti-inflammatory, and analgesic medications—drugs where combination therapy is frequently used—using high-layer tablets is therefore a totally different matter. For a number of reasons, several pharmaceutical

9. Divya A. K. Kavitha et al 2011,[16] Over the past 30 years as t the expense and complications involved in marketing new drug entities have increased, with concomitum mcognition ncognition of of the therapeutic advantages of of controlled drug delivery, greater attention has been focused on development of sustained or comrolled release drag delivery systems. Bilayer tablet is new era for the successtal development of controlled release formadation along with various features to provide a way of successful drug delivery system

10. Need Of Study:

- For the administration of fixed dose.

- Combinations of different APIs, prolong the drug product life cycle, buccal/ muco- adhesive delivery systems; fabricate novel drug deliver systems such as chewing device and floating tablets for gastro-retentive drug delivery.
- Controlling the delivery rate of either single or two different active pharmaceutical ingredients to modify the total surface area available for API layer either by sandwiching with one or two in active layers in order to achieve swellable/erodible barriers for modified release.
- To separate incompatible Active pharmaceutical ingredient (APIs) from each other, to control the release of API from one layer by utilizing the functional property of the other layer (such as, osmotic property)

III. AIM AND OBJECTIVE

Aim: Formulation and evaluation of bilayer tablet (immediately and sustained release layers) study

Objective:

- To improve therapeutic efficacy, maintain uniform drug levels
- To control the delivery rate of either single or two different Ingredientis active pharmaceutical
- To carry out the stability studies for optimized formulation
- Formulation and process optimization of bilayer tablets
- Formulation of such a bilayered tablet that is resistant to capping with good crushing strength, superior integrity and delivering the two active ingredients in the desired manner.
- To control weight variation during tableting
- To carry out pre formulation studies and drug-excipients compatibility study.
- To study the effect of different polymer in the formulation

A. Plan of work:

- Present proposed research work has been planned as follow-
- Literature survey
- Selection of drug and polymer& other excipients
- Procurement of drug and polymer& other excipients Preformulation study (compatibility and flowability study) Drug polymer compatibility study.
- Formulation of bilayer tablet
- Preliminary study of drug and polymer Evaluation of bilayer tablet:

1. Thickness
2. Hardness
3. Frability
4. Disintegration test
5. In-vitro dissolution studies
6. Drug content
7. Stability studies

IV. FUTURE SCOPE

- Improved Drug Delivery: Bilayer tablets allow for the delivery of two different drugs or different release profiles in a single dosage form. This is useful for optimizing therapeutic effects and patient compliance.
- Customization: Bilayer tablets can be designed to separate incompatible drugs, offer controlled release of drugs over time, or combine immediate and sustained release for enhanced treatment.
- Manufacturing Advancements: Development of more advanced technologies and materials will improve the precision and efficiency of bilayer tablet formulation.
- Challenges in Evaluation: Quality control of bilayer tablets involves ensuring uniform layer distribution, adhesion between layers, and stability. Evaluation also includes tests for dissolution, mechanical strength, and release profile.
- Formulating various formulations using different polymers those extended the drug release.

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