

## FORMULATION AND EVALUATION OF BILAYER TABLETS FOR SUSTAINED RELEASE

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### Abstract

Bi-layer tablet is a new era for successful development of controlled release formulation along with various features to provide successful drug delivery. Bilayer layer tablets consist of two layers which are slow release and immediate release layers. It is an improved technology to overcome the shortcoming of the single layer tablets and offer more benefits. The bilayer tablet helps to separate incompatible active pharmaceutical ingredient (APIs) from each other. Bilayer tablets material involves both the compressibility and consolidation. Bilayer formulations carry different drugs in each layer and deliver each of them without any pharmacokinetic or dynamic interactions, with their individual rate of delivery. Controlled release dosage forms have been extensively used to improve therapy with several important drugs.

**Keywords:** Glimpiride, Metformin HCl, Sustained Release, Bilayer tablet.

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### INTRODUCTION

Diabetes mellitus, often simply referred to as diabetes, is a group of metabolic diseases in which a person has high blood sugar, either because the body does not produce enough insulin or because cells do not respond to the insulin that is produced. Diabetes is one of the major causes of death and disability in the world[1,2]. Non-insulin dependent (Type 2) diabetes mellitus is a heterogeneous disorder characterized by an underlying insufficiency of insulin. This insufficiency results from defective insulin utilization and can be corrected by administration of one or more of the currently available oral hypoglycemic agents[7]. Combination therapies have various advantages over monotherapy such as problem of dose-dependent side effects is minimized, a low dose combination of two different agents reduces the dose-related risk, the

addition of one agent may counteract some deleterious effects of the other, using low dosage of two different agents minimize the clinical and metabolic effects that occur with maximal dosage of individual component of the combined tablet[5].

Metformin is an oral biguanidine first-line choice of drug. Metformin has an oral bioavailability of 50–60% under fasting conditions and is absorbed slowly[11]. Glimpiride is orally administered sulfonyl urea agent and highly selective agonist for the sulfonyl urea receptor (SUR) are found in pancreas, which are target sites of insulin secretion. Activation of the SUR receptors activate the secretion of insulin involved in the control of glucose and lipid metabolism[1].

**Need of Bilayer Tablets[5,9]:**

- For the administration of fixed dose combinations of different APIs, prolong the drug product life cycle, buccal/mucoadhesive delivery systems, fabricate novel drug delivery 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 ingredient(s).
- To modify the total surface area available for API layer either by sandwiching with one or two inactive 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).

**Various Techniques for Bilayer Tablet[15,18]****Duredas or Dual Release Drug Absorption System Technology**

Duredas or Dual Release Drug Absorption System (Elm Corporation) utilizes bilayer tableting technology which has been specifically developed to provide two different release rates or dual release of a drug from a single dosage form. The tablets are prepared by two separate direct-compression steps that combine and immediate release granulate (for rapid onset of action) and a controlled-release hydrophilic matrix complex within one tablet. The controlled-release matrix remains intact and slowly absorbs fluid from the GI tract, which causes the matrix to expand and transforms the hydrophilic polymers into a porous, viscous gel that serves as a hammer between the drug and the surrounding fluid. As the gel continues to expand, fluid Penetrates further into the dosage form, dissolving the drug and

allowing the resulting solution to diffuse out in a controlled manner.

**Geomatrix Technology**

Geomatrix system is a multilayer tablet with a matrix core containing the active ingredient and one or more modulating layers (barriers) applied to the core during the tableting process. The function of these barriers is to delay the interaction of the core with the dissolution medium. Eight Geomatrix technologies are designed to meet a wide range of therapeutic objectives: Zero-order release provides a constant rate of drug release over a defined period of time; binary release is used to provide the controlled release of two different drugs in a single tablet, quick-slow release provides a quick burst of drug release followed by a constant rate of release over a defined period of time; slow-quick release provides an initial constant rate of release followed by a quick burst of drug release at a predetermined time; positioned release delivers the drug to a predetermined position in the digestive system before it begins to release the active drug compounds, accelerated release provides a constantly accelerating rate of drug release; delayed release provides a predetermined time lag before it begins releasing drug molecules; multiple pulse provides an initial quick burst of drug release followed by a predetermined period of no release. Some of the drugs that are marketed based on this technology are diltiazem hydrochloride, nifedipine and diclofenac sodium.

**Oros Push Pull Technology[10]**

This system consists of mainly two or three layers among which the one or more layer are essential of the drug and other layer are consist of push layer (Fig.-1) The drug layer mainly consists of 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.

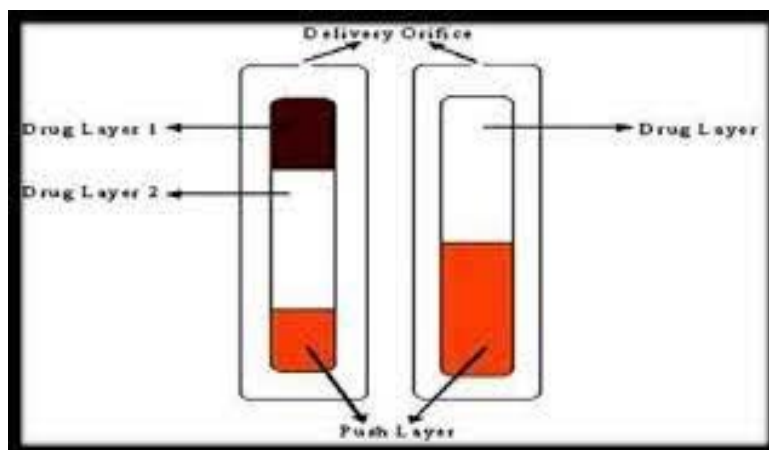


Figure-1: Oros Push Pull Technology

### Ensotrol Technology

Solubility enhancement of an order of magnitude or to create optimized dosage form Shire laboratory use an integrated

approach to drug delivery focusing on identification and incorporation of the identified enhancer into controlled release technologies (Fig.-2).

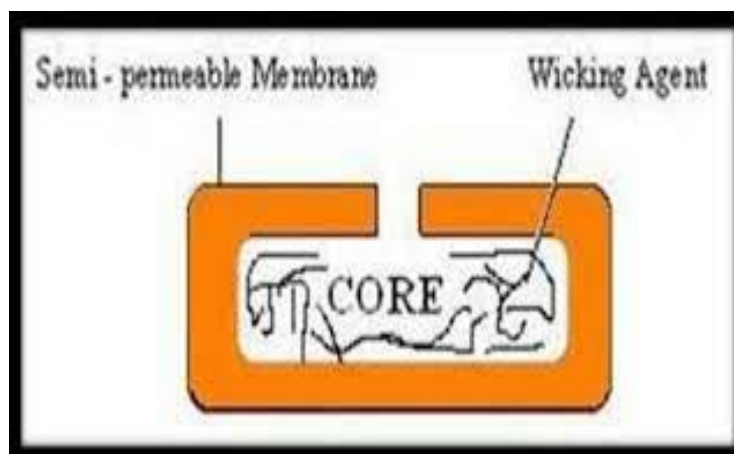


Figure-2: Ensotrol Technology

### PRE- EVALUATION OF BILAYER TABLETS<sup>3,12</sup>

- **Bulk density:**

**Method:** Both loose bulk density (LBD) and tapped bulk density (TBD) are determined. A quantity of accurately weighed powder (bulk) from each formula, previously shaken to break any agglomerates formed is introduced into a 25 ml measuring cylinder. After the initial volume is observed, the cylinder is allowed to fall under its own weight onto a hard

surface from the height of 2.5 cm at 2 second intervals. The tapping is continued until no further change in volume is noted. LBD and TBD are calculated using following formula.

- **Tapped density:** Weight of powder to the total volume of powder after tapping.
- **Carr's Index:** The Carr's index is frequently used in pharmaceuticals as an indication of the flowing ability of a powder. In a free-flowing powder, the bulk density and tapped density would

be close in values; therefore, the Carr's index would be small. On the other hand, in a poor-flowing powder where there are greater interparticle interactions, the difference between the bulk and tapped density observed would be greater; therefore, the Carr's index would be larger. A Carr's index greater than 25 is considered to be an indication of poor flowing ability, and below 15, of good flowing ability.

#### POST-EVALUATION OF BILAYER TABLETS[5,19]

- **Tablet thickness:** Thickness of each sample should be measured using a vernier caliper and the mean thickness is calculated by adding the thickness of each sample and then dividing it by the no. of samples.
- **Friability:** Friability is defined as the percentage of weight loss of powder from the surface of the tablets due to mechanical action and the test is performed to measure the weight loss during transportation. It is a supplement test for uncoated / compressed tablets other than physical measurement e.g. hardness (tablet breaking force).
- **Weight variation test:** The United States Pharmacopoeia (USP) as well as Indian Pharmacopoeia (IP) provides criteria for tablet weight variation of intact dosage units. All the brands complied with the compendial specification for uniformity of weight which states that tablets weighing 130 mg or less, weights of not more than two tablets should differ from the average weight by more than 10% and none deviates by more than twice that percentage.
- **Dissolution test:** Dissolution testing measures the extent and rate of solution formation from a dosage form such as tablet, capsule, ointment, etc. The dissolution of a drug is important for its bioavailability and therapeutic

effectiveness. Dissolution and drug release are terms used interchangeably.

#### CONCLUSION

Bi-layer tablet is improved beneficial technology to overcome the shortcoming of the single layer 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 second is maintenance dose[2]. The preparation of tablets in the form of multi layers is used to provide systems for the administration of drugs, which are incompatible and to provide controlled release tablet preparations by providing surrounding or multiple swelling layers. Bi-layer tablets offer an excellent opportunity for manufacturers to separate themselves from their competitors, improve their products efficacy and protect against impersonator products[20]. Bilayer tablets consist of two layers which are a slow release and an immediate release layer. In a bilayer tablet, one layer is formulated to obtain immediate release of the drug, with the aim of reaching a high serum concentration in a short period of time. The second layer is a controlling release hydrophilic matrix, which is designed to maintain an effective plasma level for a prolonged period of time. A bi-layer tablet may be prepared with various combinations, which is useful for various ailments. Thus, bi-layer formulation is a dosage form that is safe and possess greater advantages to both patient and clinician that it may be administered as a single tablet once a day.

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