

# A review on bilayer tablet for the treatment of hypertension and diabetes

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**Abstract-** The bilayer tablet is a new technology for a successful improvement of controlled release method alongside numerous functions to ensure successful drug transport. Bilayer drugs encompass layers, which are a gradual-release layer and an instantaneous-release layer. In addition to stepped forward positive technology to overcome the shortcomings of single-layer tablet. Bi-layer tablet formulations have been required due to separate collectively incompatible lively pharmaceutical ingredients (APIs). The bilayer tablet cloth consists of both compressibility and consolidation. The cutting-edge paintings specialize in the development of a double-layer pill of empagliflozin and aliskiren inside the treatment of diabetes and hypertension. The release of aliskiren and empagliflozin was controlled with the aid of their method into a right way and sustained release layer. both layers had been prepared by moist granulation. The compatibility of polymers and excipients in conjunction with natural drugs became evaluated the use of FTIR research. tablets had been prepared and parameters earlier than and after compression, in vitro dissolution trying out, launch rate kinetics and stability studies had been evaluated. The feet-IR spectrum confirms the absence of chemical interplay among the drug and the polymers. The parameters before and after compression have been observed to be within perfect limits. For the bilayer tablet, one system of each layer changed into decided on based totally on the in vitro dissolution profile records. The cause for this constant mixture is the joint administration of drugs with extraordinary mechanisms of movement, a reduction in dosing frequency and a boom in patient compliance.

**Keywords:** Hypertension, Diabetes, Bilayer Tablet, Compression, Consolidation.

## INTRODUCTION

Based on these factors, we have suggested a bilayer pill, of which one layer is designed to provide the medication with an instantaneous release. With the intention of quickly achieving a high serum concentration. The second layer is a hydrophilic matrix with controlled release that is intended to keep the effective plasma level constant over an extended length of time. The quick increase in blood concentration that results from drug release from the fast-releasing layer is the basis for the pharmacokinetic advantage. On the other hand, as the medication is released from the sustaining layer, the blood level remains constant.

Multi-layer tablet dosage forms were created for a number of purposes, including controlling the rate at which one or two distinct active pharmaceutical ingredients (API) are delivered, separating incompatible APIs from one another, regulating the release of API from one layer by leveraging the functional property of the other layer (for example, the osmotic property), adjusting the total surface area available for API layer by sandwiching one or more inactive layers to create erodible or swellable barriers for modified release, administering fixed dose combinations of different APIs, extending the life cycle of drug products, and creating innovative drug delivery systems like chewing devices, buccal/mucoadhesive delivery systems, and floating tablets for gastro-retentive drug delivery. For example, these tablets are frequently employed to physically separate formulation components in order to prevent chemical incompatibilities. Additionally, by combining layers with different release patterns or slow-release with immediate-release layers, bilayer tablets have made it possible to design controlled administration of active medicinal ingredients with predefined release profiles. Unfortunately, due to poor mechanical and compression characteristics of the constituent materials in the compacted adjacent layers, elastic mismatch of the layers, insufficient hardness, inaccurate individual mass control, cross contamination between the layers, reduced yield, and their tendency to delaminate at the interface between the adjacent compacted layers during and after the various stages of production downstream of the compaction process, these drug delivery devices are mechanically complicated to design and manufacture, and it is harder to predict their long-term mechanical properties. Consequently, the main challenge that has to be addressed is to fully comprehend the causes of these issues at both the micro- and macroscales and to create solutions for them during the solid dose distribution design.

Whenever it comes to patient compliance, the oral route is the most preferred delivery method. Numerous pharmaceutical companies have focused their research efforts on repurposing current medications in novel dosage formulations. The oral film is one such relatively recent dosage form. It is a thin film made of hydrophilic polymers that dissolves quickly on the tongue or in the buccal cavity. Formulation development for youngsters has proven to be a difficult undertaking. One of the most important variables affecting adherence to treatment plans, among other things, is how well paediatric oral drug formulations taste. While older children and teenagers generally accept solid dosage forms, younger children typically choose liquid formulations since they are simpler to ingest<sup>3</sup>. Keeping the ease of administration and swallowing in mind, pharmaceutical research has led to the development of Oral Disintegrating Tablets (ODTs). ODTs have been defined as “A solid dosage form containing medicinal substances which disintegrate rapidly, usually within a matter of seconds, when placed upon the tongue”. United States Food and Drug Administration further defines ODTs as solid oral preparations that disintegrate rapidly in the oral cavity, with an *In vitro* disintegration time of approximately 30s or less, when based on the United States Pharmacopeia (USP) disintegration test method or alternative. The lower bioavailability, long onset time and Dysphagia patients because of this the manufacturer shifted towards parenteral and liquid orals. But the liquid orals like syrup, suspension, emulsion etc. have the issue of perfect dosing mainly and parenteral are painful drug delivery, which result in patient noncompliance. Every pharmaceutical company has the desire to formulate an innovative oral dosage form which has higher bioavailability, rapid action and most patient compliance. Tablets and capsules are the most popular solid dosage forms. Many patients have a problem swallowing tablets and hard gelatin capsules, especially geriatric and pediatric patients, and do not take their medicine as prescribed. In the present situation the major focus has turned towards combination therapy for the treatment of different diseases and disorders. Combination therapy has an edge over monotherapy because it reduces the dose dependent side effects and improves the total clinical performance of the drugs. Bi-layer tablets are innovative drug delivery systems where mixing of two or more drugs in a single unit having various release profiles which increases patient compliance, prolongs the drug action. Two-layer tablets may be developed for sustained release, one layer for the immediate release of the drug and the second layer for extended release thus controlling a prolonged blood level. Layers may be colored differently to find the product.



**Fig.no.1 Bilayer tablets**

### **Aliskiren**

Aliskiren is the primary drug inside the renin inhibitor drug elegance and is used for the remedy of high blood pressure. It turned into developed by using Speeded and Novartis and started with permission by way of the FDA in early 2007. Aliskiren has been confirmed to be powerful in reducing blood stress when used alone or alongside other antihypertensive sellers. Aliskiren is used for the remedy of high blood pressure in kids above 6 years and adults. This drug can also be used along with antihypertensive inclusive of calcium channel blockers and thiazides in merchandise shape to provide extra blood pressure control. Aliskiren is a renin inhibitor. Renin is secreted by means of the kidneys when blood quantity and renal perfusion lower. It usually cleaves the protein angiotensinogen to form angiotensin I. Angiotensin I is then converted to angiotensin II, an energetic protein. Angiotensin II is an effective vasoconstrictor that causes the release of Catecholamines into the movement. It also promotes the secretion of aldosterone further to sodium reabsorption, increasing blood stress. Moreover, angiotensin II acts at the adrenal cortex in which it stimulates aldosterone release. Aldosterone will increase sodium reabsorption and potassium excretion within the nephron. Aliskiren prevents the above process thru binding to renin at its lively web site, preventing the cleavage of angiotensin, in flip inhibiting the formation of angiotensin I. This ends the cascade of angiotensin II mediated mechanisms that normally boom blood pressure.

### **Empagliflozin**

Empagliflozin is an inhibitor of sodium-glucose co-transporter (SGLT2), the transporters mostly answerable for the reabsorption glucose inside the kidney. its miles used clinically as an accessory to food plan and exercising, often in mixture with different drug remedies, for the control of type 2 diabetes mellitus. the primary acknowledged inhibitor SGLTs, polarizing, was isolated from the bark of apple timber in 1835 and researched drastically into the twentieth

century but become in the long run deemed inappropriate for clinical use given its loss of specificity and vast gastrointestinal facet effects.

#### **Advantages**

1. They are used as an extension of conventional technology.
2. Potential use of single entity feed granules.
3. Separation of incompatible components.
4. Patient compliance is enhanced leading to improved drug regimens efficacy.
5. Patient convenience is improved because fewer daily doses are required compared to traditional delivery system.
6. Maintain physical and chemical stability.
7. Retain potency and ensure dose accuracy.

#### **Disadvantages**

1. Adds complexity and bilayer rotary presses are expensive.
2. Insufficient hardness, layer separation, reduced yield.
3. Inaccurate individual layer weight control.
4. Cross contamination between the layers.

#### **NEED OF BILAYER TABLETS:**

- For the management of constant dose combinations of various APIs, lengthen the drug product existence cycle, buccal/mucoadhesive transport systems; fabricate novel drug shipping systems inclusive of chewing device and floating capsules for gastro-retentive drug shipping.
- Controlling the delivery rate of both single and two exceptionally energetic pharmaceutical components.
- To regulate the overall surface location available for API layer either through sandwiching with one or two in lively layers to attain swellable/erodible boundaries for modified release.
- To separate incompatible energetic pharmaceutical substances (APIs) from each other, to govern the discharge of API from one layer by way of making use of the practical assets of the opposite layer (along with, osmotic assets).

#### **CHALLENGES IN BILAYER MANUFACTURING:**

Conceptually, bilayer pills can be seen as unmarried-layer capsules compressed into one. In exercise, there are some production demanding situations.

##### **Delamination**

The tablet falls aside when the 2 halves of the pill no longer bond absolutely. the two granulations need to adhere whilst compressed.

##### **Cross-contamination**

Whilst the granulation of the first layer intermingles with the granulation of the second layer or vice versa, go-infection happens. It could triumph over the very motive of the bilayer pill. Proper dirt collection goes a protracted way toward stopping cross contamination.

##### **Production yields**

To prevent infection, dirt collection is needed which leads to losses. therefore, bilayer drugs have decrease yields than single-layer drugs.

##### **Cost**

Bilayer tableting is greater costly than single layer tableting for several motives. First, the pill press charges greater. Second, the clicking normally runs extra slowly in bilayer mode. Third, improvement of two like-minded granulations is an ought to, which means greater time spent on system development, analysis and validation. those factors, if now not properly controlled/optimized, in a single way or every other will affect the bilayer compression according to see and the nice attributes of the bilayer capsules (enough mechanical strength to keep its integrity and man or woman layer weight manipulate). Consequently, it's essential to obtain an insight into the root reasons to permit the design of a robust product and manner.

#### **PREPERATION OF BILAYER TABLETS**

Bilayer capsules are prepared with one layer of drug for fast release with the second layer designed to release drug later, both as a second dose or in an extended-launch shape. The bilayer pills with incompatible tablets also can be organized with the aid of compressing separate layers of every drug to reduce vicinity of touch among two layers. an extra intermediate layer of inert material will also be blanketed. To provide ok pill method, certain requirements consisting of sufficient mechanical energy and the favored drug release profile need to be met. At instances, this could be tough mission for formulator to gain these situations especially in bilayer pill components wherein double compression technique is worried, due to terrible waft and compatibility function of the drug so that it will bring about capping and/or lamination. The compaction of a fabric entails both compressibility and consolidation.

### Compression

It's defined as reduction in bulk extent with the aid of casting off voids and bringing debris into nearer contacts. Creating a bi-layer pill includes compressing two formulations right into a unmarried stable oral pill. The procedure keeps a physical separation of the formulations via layering one on top of the opposite. It allows for the controlled shipping of a single or more than one energetic pharmaceutical substance in a single tablet.

### Consolidation

It's far from the belongings of the cloth in which there is multiplied mechanical power because of interparticulate interaction (bonding). The compression force on layer 1 turned into observed to be a major thing influencing tablet delamination.

### CONCLUSION

Bi-layer capsules provide an excellent opportunity for producers to separate themselves from their competition, improve their merchandise efficacy and defend against impersonator products. Bilayer layer tablets had been which include two layers which is slow launch and immediately release layer proposed a bilayer pill, in which the one layer is formulating to attain on the spot release of the drug, with the aim of attaining a high serum concentration in a brief time frame. the second layer is a controlling release hydrophilic matrix, that is designed to maintain an powerful plasma level for a extended time frame. The blessings of bilayer tablet technology outweigh the drawbacks of unmarried layered pill generation. The pharmaceutical enterprise's adoption of bilayer capsules has made it possible to combine incompatible energetic components into a single unit dosage shape and construct pre-planned launch profiles for active chemicals. one of the key design strategies for combining incompatible medicines with wonderful warning signs and the identical medicinal drug with various release fees right into a single unit is offered via bilayer tablets. Bilayer drugs may be used for sustained launch drugs, wherein the first layer is added at once because the preliminary dose and the second one layer is the preservation dose, as well as for the sequential launch of medications in combination. Bilayer pills improve affected person compliance, extend the drug(s) motion and may deliver incompatible capsules in a unmarried formulation. Bilayer tablets have one layer of active factor for immediate launch and a 2d layer for not on time release, both as a second dose or in an extended-release fashion. Bilayer tablets are advancing helpful technologies to overcome the disadvantages of single-layered tablets.

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