IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)
An International Open Access, Peer-reviewed, Refereed Journal

A Review On Bilayer Tablet :A Novel Pharmaceutical Drug Delivery System

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ABSTRACT:
The development of controlled release formulations with many features to guarantee effective drug administration has entered a new era with the introduction of the bi-layer tablet. By physically separating APIs, bi-layer tablets might be the best way to prevent chemical incompatibilities and create unique drug release patterns. With one layer for quick release as a loading dosage and the second layer for maintenance dose, a bi-layer tablet can be used for both the sustained release of a tablet and the sequential release of two drugs in combination. Because combination therapy is often used for anti-hypertensive, diabetic, anti-inflammatory, and analgesic drugs, the use of bi-layer tablets is significantly different. Bi-layer tablets are now being developed by several pharmaceutical companies for a variety of reasons. Both compressibility and consolidation are involved in the material of bilayer tablets. Several methods, including OROS® push pulls, L-OROSTM, EN SO TROL, DUREDASTM, and DUROS technologies, are used to prepare the bilayer tablets. There are several kinds of bilayer tablet presses on the market right now, as well as different methods for creating bilayer tablet systems and methods for characterizing and assessing them. Atorvastatin, Atenolol, Nifedipine, Aspirin, Isosorbide 5-mono-nitrate, Pioglitazone HCl, Gliclazide, Losartan potassium, trimetazidine hydrochloride, and clopidogrel bisulphate are among the medications that are now packaged in bilayer tablets.

KEYWORDS: OROS® push pull technology, sustained release, Nifedipine, and bilayer tablets.

INTRODUCTION:
Many industrialized and developing nations are now turning to combination therapy to treat a range of illnesses and conditions that call for long-term care, including diabetes, cardiovascular disease, and hypertension.One Nowadays, more than 90% of the formulations produced are taken orally. It demonstrates that this formulation class is the most widely used globally and that researchers are mostly focused on this area. The primary goal of controlled drug administration is to decrease the frequency of dosage. Modified release medication products are designed to maximize a treatment regimen by delivering the drug gradually and continuously across the whole dose interval, increasing patient comfort and compliance. The more recent option for the effective creation of a controlled release formulation is the bilayer tablet, which is superior to the despite their benefits, the mechanical structures of this drug delivery system have grown quite complex due to the use of various materials and intricate geometric boundaries between adjacent layers. This necessitates complex tablet architectures and patient-friendly administration, which present significant challenges for pharmaceutical scientists and engineers.Because oral consumption is so simple to administer, it has long been the most practical and widely used method of drug delivery. It is commonly known that compared to immediate release formulations of the same medication, variable release dose forms may provide one or more benefits. Modified release dosage forms for oral administration can be designed in a variety of methods, ranging from film-coated pellets, tablets, or capsules to more intricate and complex delivery systems including osmotically driven systems and ion-controlled systems. Pharmacological treatments either necessitate or profit from the sequential

administration of medications. By using a single dosage form, these combination formulations streamline treatment and lessen or completely eliminate the possibility of incorrect administration. Bilayer formulations include many drugs and distribute each one at its own rate of delivery (immediate, timed, or sustained) without pharmacokinetic or dynamic interactions. The disadvantage of the single-layered tablet has been addressed by the development of bilayer tablet technology.Conventional dose forms typically result in significant variations in the drug's concentration in the blood and tissues, which leads to unfavorable toxicity and ineffectiveness. The idea of regulated drug delivery systems was inspired by factors including recurrent dosage and variable absorption. Taking these factors into account, we have developed a bilayer tablet, where the first layer is designed to release the medication instantly, allowing for a rapid rise in serum concentration. The second layer is a hydrophilic matrix with controlled release that is intended to sustain an efficient plasma level for an extended amount of time. The pharmacokinetic advantage depends on the fact that a rapid increase in blood concentration occurs when the medication is released from the fast-releasing layer. As the medication is discharged from the sustaining layer, the blood level is kept constant [1].

For a number of reasons, multi-layer tablet dosage forms were created, including regulating the pace. Numerous alternatives in pharmaceutical development and manufacturing are becoming available in the modern day due to ongoing scientific research into disease regions and multi-targeted methodologies. The development and production of bilayer tablets have been going on for a while. For stacked tablets, the matrix-type technique is usually employed. Multilayer tablet technology helps polypharmacy. A significant area of focus in the medical world is polypharmacy. When at least five medications are administered at regular intervals, it finds a successful solution in multilayer tablets. Formulations designed with this goal in mind may employ high-potency active pharmaceutical ingredients (HPAPI), which are materials with smaller but more powerful concentrations. In order to give more effective medications, multilayer tablet technology uses these complex formulas. Disintegrants made specifically are more effect. Double-layer tablets: Also known as multilayered tablets or bilayer tablets, these tablets include two or more medications into one tablet, which is why they are also known as controlled-release tablets. Two medications are contained in double-layered tablets: a loading dosage in the form of an instant release layer and a maintenance dose in the form of a controlled release layer. By including an insert intermediate layer, two medications can be immediately synthesized into a bilayer. Tablets are designed to overcome a number of drawbacks, such as high cost, layer combination, and enough hardness.

Two distinct APIs can be released sequentially and simultaneously on a bilayer tablet. The layer is designed to provide the drug's instant release. Due to repeated administration, there may be little control over the drug release in conventional dosage forms, which can lead to unpredictable and frequently hazardous plasma concentrations and serious side effects. Furthermore, the bioavailability of conventional dose forms may change depending on a number of physiological parameters, excipients, and the drug's physiochemical characteristics. Compared to traditional dosage forms, controlled drug delivery systems (CDDS) offer a number of benefits, including consistent and repeatable release rates, extended action, particularly for medications with short half-lives, decreased toxicity, and enhanced drug bioavailability because of localized activity (Divya, 2011). However, dose dumping, burst release, and site-specific drug delivery prevented CDDS from achieving these benefits. Bilayer tablets were developed as a result of these factors. delivery of one or two different active pharmaceutical ingredients (API); separating incompatible APIs from one another; controlling the release of API from one layer by utilizing the other layer's functional property (such as osmotic property); modifying the total surface area available for the API layer by sandwiching it with one or two inactive layers to create erodible/swellable barriers for modified release; giving different APIs fixed dose combinations; prolonging the drug products' life cycle; and developing novel drug delivery systems like chewing devices, buccal/mucoadhesive delivery systems, and floating tablets for gastro-retentive drug delivery [2]. There are a few noteworthy advantages when comparing bilayer tablets to traditional monolayer tablets. To prevent chemical incompatibilities, for instance, these tablets are widely employed to physically separate formulation ingredients. Manufacturers of pharmaceutical drugs have focused their product development efforts in recent years on fixed dose combos (FDCs) for the treatment of various conditions, including HIV/AIDS, type 2 diabetes, hypertension, and pain, to name a few. FDC products are delivered to patients using a variety of methods, including compression coating, active coating (Desai et al., 2013; Charlton and Nicholson, 2010), bilayer floating tablets (Ranade et al., 2012; Lalita et al., 2013), multilayer tablets

(Benkerrour et al., 2004), and buccal/mucoadhesive delivery systems (Park and Munday, 2002; Yedurkar et al., 2012).

Because of its ease of administration, patient compliance, minimal sterility requirements, and adaptable dosage form design, the oral route is the most practical and favored method of delivering drugs to the systemic circulation. Nevertheless, a number of physiological challenges face the development process, including the inability to confine and localize the drug delivery system within specific GIT regions, an unpredictable gastric emptying rate that differs from person to person, a short gastrointestinal transit time, and the existence of an absorption window in the upper small intestine for a number of drugs. The emptying process may take a few minutes to twelve hours, depending on the subject's physiological condition and the pharmacological formulation's design.[1] The instance of tablets with two layers If the medicine can be integrated into the upper non-adhesive layer, its administration into the entire oral cavity can be made nearly unidirectional.
In order to obtain CDDS for various medications with predetermined release patterns, bi-layer tablets have been designed. Conventional dose forms typically result in a large range of variations in the drug's concentration in the tissues and systemic circulation, which leads to unfavorable effects and ineffectiveness. The idea of controlled medication delivery systems was born out of these dynamics, which include irregular absorption and repeated dosage. Reducing the frequency of dosage or increasing medication effectiveness through localization at the site of action, lowering the amount needed, or ensuring uniform drug distribution are the goals of formulation sustained or controlled delivery systems. Sustained release drug delivery aims to increase patient compliance, ensure drug safety, and increase drug effectiveness. A tablet with two layers is appropriate.

ADVANTAGE:
1. They are unit dosage form and offer the greatest capabilities of all oral dosage form for the greatest dose precision and the least content variability.
2. Cost is lower compared to all other oral dosage form.
3. Lighter and compact.
4. Easiest and cheapest to package and strip.
5. Easy to swallowing with least tendency for hang-up.
6. Objectionable odour and bitter taste can be masked by coating technique.
7. Suitable for large scale production.
8. Greatest chemical and microbial stability over all oral dosage form.
9. Product identification is easy and rapid requiring no additional steps when employing an embossed and/or monogrammed punch face.
10.They are used as an extension of a conventional technology.
11.Potential use of single entity feed granules.
12.Separation of incompatible components.
13 .Patient compliance is enhanced leading to improved drug regimen efficacy.
14. Patient convenience is improved because fewer daily doses are required compared to traditional delivery system.
15. Maintain physical and chemical stability.
16. Retain potency and ensure dose accuracy.

Disadvantage:
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.
5.Difficult to swallow in case of children and unconscious patients.
6. Some drugs resist compression into dense compacts, owing to amorphous nature, low density character.
7.Drugs with poor wetting, slow dissolution properties, optimum absorption high in GIT may be difficult to formulate or manufacture as a tablet that will still provide adequate or full drug bioavailability.
8.Bitter testing drugs, drugs with an objectionable odour or drugs that are sensitive to oxygen may require encapsulation or coating.

Application:

1.Bi-layer tablet is suitable for sequential release of two drugs in combination.

2.Separate Two Incompatible Substances.

3.Sustained release tablet in which one Layer is immediate release as initial dose and second layer is maintenance dose.

4.Promoting Patient Convenience and Compliance.

5.Bilayer tablet is improved beneficial technology to overcome the shortcoming of the single layered tablet.

6.Bilayer tablets are used to deliver the loading dose and sustained dose of the same or different drugs.

7.Bilayer tablets are used for bilayer floating tablets in which one layer is floating layer another one is immediate release layer of the drug.

8.Bilayer tablets are used to deliver the two different drugs having different release.

Ideal Characteristic:

1.A bi-layer tablet should have elegant product identity while free of defects like chips, cracks, discoloration and contamination.

2. It should have sufficient strength to with stand mechanical shock during its production packaging, shipping and dispensing.

3. It should have the chemical and physical stability to maintain its physical attributes over time. The bi-layer tablet must be able to release the medicinal agents in a predictable and reproducible man.

4. It must have a chemical stability shelf-life, so as not to follow alteration of the medicinal agents.

Objective:

1.To control the delivery rate of either single (Bogan et al., 2008) or two different active pharmaceutical ingredients(s) (Kulkarni et al.,

2009; Nirmal et al., 2008).

2. To separate incompatible APIs from each other, to control the release of one API from one layer by utilizing the functional property of other layers (such as osmotic properties).

3. To modify the total surface area available for API layer by sandwiching with one or two inactive layers in order to achieve

swellable/erodible barriers for modified release (Efentakis et al., 2008; Phaechmud et al.,2008).

Bilayer tablet types include:

a. Homogenous Type:Bilayer tablets are recommended when the medications' release profiles differ from one another. It enables the disintegration and release characteristics to be designed and modulated. One layer is prepared for immediate release, while the other layer is intended to provide extended release or a second dose.

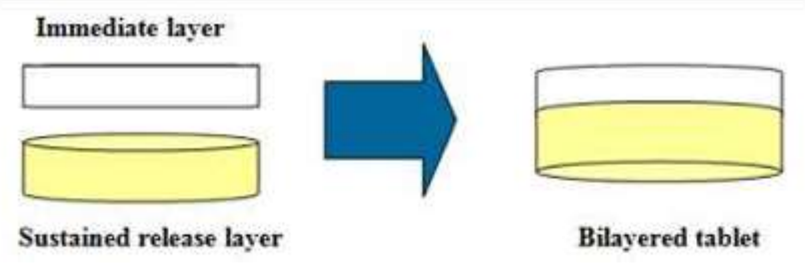


Fig .Bilayer Tablets (the same drug with different release pattern) homogeneous)

b. Heterogenous Type: Bilayer Tablets can be used to segregate two incompatible substances or to release two medications in combination sequentially.

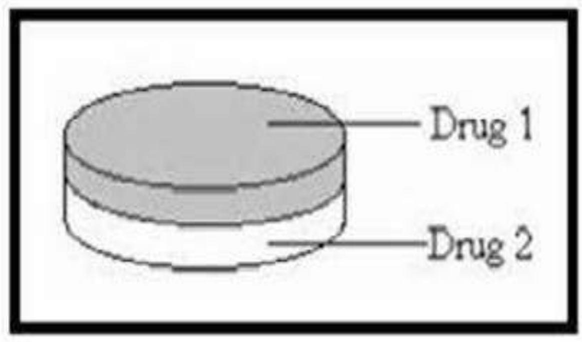


Fig . Bilayer Tablets (with two drugs heterogenous)

General characteristics:

1.A bi-layer tablet should be devoid of flaws such as contamination, chips, cracks, and discolouration, and it should have a stylish product identity.
2. It must be strong enough to endure mechanical shock while being manufactured, packaged, shipped, and dispensed.
3. It must be physically and chemically stable in order to hold onto its physical characteristics throughout time.The release of the therapeutic ingredients from the bi-layer tablet must be consistent and repeatable.
4. The shelf-life must be chemically stable to prevent the therapeutic substances from changing.

Bilayer manufacturing challenges:
Bilayer tablets are conceptually equivalent to two single-layer tablets that have been squeezed into one. There are several production obstacles in practice.
1. Delamination: When the tablet's two halves do not fully fuse together, the tablet breaks apart. When crushed, the two granulations ought to stick together.
2. Cross-contamination: This happens when the first layer's granulation mixes with the second layer's granulation, or vice versa. It might defeat the bilayer tablet's primary function. Cross contamination can be avoided in large part by collecting dust properly.
3. Production yields: Dust collection is necessary to avoid cross-contamination, which results in losses. As a result, yields from bilayer tablets are lower than those from single-layer tablets.
4. Cost: Compared to single-layer tableting, bilayer tableting is more costly.

Types of Bilayer tablets:
1. Single sided tablet press.
2. Double sided tablet press
3. Bilayer tablet press with displacement monitoring.
4. Multilayer compression basics.

1. Single-sided tablet press: Over time, a variety of bilayer presses have been developed. A single-sided press with both chambers of the press is the most basic design.The double feeders were isolated from one another. The two distinct tablet layers are

created by gravity feeding or force feeding a separate powder into each chamber. The dye is loaded with the first layer of powder as it passes beneath the feeder, then the second layer of powder, and finally the complete tablet is squeezed in one or two steps. The simplest method of creating a bilayer tablet involves the two layers of dye slightly mixing at their interface and, in most circumstances, bonding sufficiently to prevent layer separation during tablet production.

Limitations**:**

No visual differentiation between the two layers

• No weight monitoring or management of the individual layers.
• The small compression roller may cause dwell time, which could lead to issues with hardness and poor deaeration capping.

2.Double-sided tablet press: The majority of double-sided tablet presses that automate production control gauge and regulate tablet weights using compression force. the efficient compression force applied to every tablet using the compression system at the layer's primary compression. When necessary, this mechanism assists in rejecting the tolerance tablets and adjusting the dies' fill depth.

Advantage:
1. The initial layer is subjected to a low compression force to prevent chapping and layer separation.
2. Extended dwell time for both the first and second layer precompression to ensure adequate hardness at the highest turret speed.
3. The highest level of protection against cross-contamination between two layers.
4.The two layers are visually distinct from one another.
5.Displacement weight monitoring for precise and autonomous layer-by-layer weight control.

6. A higher yield.
7. When the bi-layer tablet is finally compressed, the two distinct layers separate because there is not enough bonding between them.

Limitations:

If the first layer is compressed at a high compression force, bonding is too limited; correct bonding can only be achieved when the first layer is compressed at a low compression force, allowing it to still interact with the second layer during a final compression.

3.Bilayer Tablet Presses with Displacement: The compression force principle and the bilayer tablet press principle are essentially distinct. In this instance, as the compression force is decreased, the accuracy rises. The risk of capping and separation rises with increased production speed, although it can be decreased with enough dwell time between the four compression phases.

Advantage:
1. Accurate independent weight control of the separate layers using displacement weight monitoring and control.
2. To prevent chapping and the separation of the two distinct layers, a low compression force is applied to the first layer.
3. Extended dwell time during first and second layer precompression to ensure adequate hardness at maximum turret speed.
4. Maximum protection against inter-layer cross-contamination.
5. A distinct visual division of the layers.
6. Maximum production.

4.Multilayer Compression Basics: A regular double press can be modified for multipliers, or presses can be made especially for multilayer compression. Long used to create prolonged release formulations, the multilayer tablet concept may have players or triple layers to prolong the drug release from the tablet in addition to a fast-releasing layer.The benefit of pharmacokinetics is based on the fact that although drug release from fast-releasing granules causes a sharp increase in blood concentration, drug release from sustained granules keeps blood levels stable.

Manufacturing process of bilayer tablet :

Production methods like wet granulation/roller compaction and the inclusion of binders make it more difficult to comprehend the crucial elements influencing compression and tablet breaking force. Therefore, it is important to pay close attention to the tablet's breaking force and tendency to delaminate or cap throughout production or storage. The tablet press has a significant impact on the production of multilayer tablets, aside from the crucial material characteristics of the individual ingredients and the finished blend. Pre-compression force level, punch velocity, consolidation time (the period of time when punches change vertically with respect to the rolls as the distance between the punch tips decreases), dwell time (the period of time during which punches do not change vertically with respect to the rolls), and relaxation time.

1. Ignoring first layer compression: As previously mentioned, the number of compressions used in the production of multi-layer tablets is equivalent to the number of layers the tablet has. Granules from the first layer may mix uncontrollably with those from the second layer at the interface if the first layer is not crushed before the second layer is added. Furthermore, if the first layer is not compressed prior to the second layer being added, because the first layer's granules may move toward the die cavity's outer edge due to centrifugal

force during turret rotation, creating an angled (skewed) contact. In addition to being aesthetically pleasing, a distinct separation between the two layers also visually ensures that there is no cross-contamination.

2. Tablet breaking force: The force necessary to cause the tablets to shatter in a certain plane is defined by the current USP. Usually, the tablets are positioned between two platens, one of which moves to give the tablet enough force to fracture it. Conventional, round tablets with a circular cross-section experience loading throughout their diameter (also known as diametrical loading), and fracturing happens in that plane. Tensile strength takes into account the tablet's geometry and offers a more basic indicator of the mechanical strength of the device. The following 19 is used to determine tensile strength.

$2F/\pi Dh$ is the tensile strength.
where "D" and "h" are tablet positions, and "F" is the load necessary to break the tablet diametrically (as opposed to de-laminating or capping). The reported adhesion strength was 23. Pharmaceutical companies typically test the tablet breaking force, which is basically the load required to break the tablet, even though tensile strength measurement is suitable for evaluating tablet strength. The crushing strength-friability ratio is an additional metric for mechanical strength (CSFR). No matter how the tablet's strength is assessed, a measure to gauge this crucial quality needs to be thoroughly examined, and the formulation and manufacturing process must complement the test method selection. During the stability investigations, the tablet's integrity must be evaluated to ensure that environmental factors and age have not adversely affected the layers' adherence.

3. Lubrication effect: The amount of lubricant may have an effect on the interfacial contacts between the first layer and the second layer because the first layer compression makes the first layer surface homogeneous and maybe less rough. As the amount of lubricant, like magnesium stearate, is increased, the tablet's surface becomes smoother 24. For instance, Dietrich et al. (2000) found that modest compression pressures and a relatively low lubricant concentration (practically achievable) are necessary for first layer tableting in order to improve the interfacial interaction between the layers. However, as part of the product development process, the amount of lubricant required to prevent the initial layer from picking and sticking needs to be evaluated. The combined lubricant in the bulk of the granules. Research has been done to determine how lubricant affects the crucial tablet quality attributes by adding it to the dies and punches rather than the granules directly. In the literature, this procedure is known as external lubrication. The lubricant used in external lubrication is rather to introducing it to the bulk powder mixture 25, have demonstrated that the external lubricant can boost crushing strength by 40% without delaying tablet disintegration when sprayed onto the die and punches for every compression cycle. It is verified by using a scanning electron microscope to view a layer of magnesium stearate on the tablet. Despite its apparent benefits for mono-layer tablets, this new technology may also be used to better understand how lubricant affects the quality aspects of bilayer tablets.

4. Coating: To enhance appearance, shield the cores from environmental factors, or regulate the release profile, multi-layered tablets are frequently coated. In either scenario, the development of the product must take into account the effects of loads, high temperatures, and solvent exposure on the multilayered tablets. The coefficients of thermal expansion of the tablet layers and the effect of this variation on the tablet integrity are crucial for preventing layer-separation during the coating process. As previously mentioned, when bi-layered tablets were coated, cracks only developed on the surface of one layer within a few minutes of the coating process, leaving the other layer intact. Testing revealed that there was a considerable difference in the thermal expansion coefficient between the tablet's two layers. There was no sign of cracking when the control coating was applied, with each layer being run independently at 40–55 °C. The product was reformulated with nearly identical coefficients of thermal expansion for each layer in order to reduce cracking. Therefore, extra attention that may not be required for drug products that do not require coating is necessary for multilayer drug products that are meant to go through the coating process.

5. Stability: To guarantee that drug products maintain their integrity over the course of their shelf life and function predictably, stability studies require regular testing and close observation. The treatment routine is made simpler by the convenience of bi-layer tablets made with a mixture of two therapeutic substances. Over the past 27 years, there has been a steady growth in the usage of two APIs in combination or the same API with a variable release rate to maximize therapy and enhance patient compliance. Maintaining the bi-layer tablets' performance and quality throughout their expiration time is essential to

achieving this goal. The ICH recommendations and the generated supporting stability data must be followed when conducting the stability investigations.

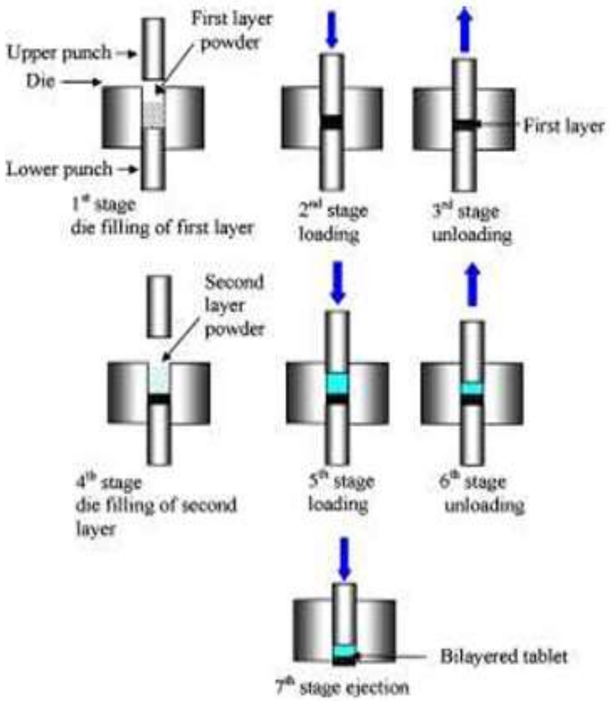
6. In vitro performance: Depending on the planned dosage design and the physico-chemical properties of the medication in each layer, the bi-layer tablets will require different in vitro dissolution tests. Developing a meaningful disintegration process for bi-layer medicinal products is made more difficult by this diversity, particularly if the bi-layer tablets contain medications with varying water solubilities. Generally speaking, the bi-layer tablets need to have characteristics like swelling and water absorption rates evaluated. For instance, the separation of these layers in the disintegration media may not matter if the purpose of the bi-layer instant tablet is to deliver two incompatible APIs because it would not affect the functionality of the product. The integrity of the layers in the dissolution media is crucial to the drug product's performance (in vivo) if the bi-layer tablet is a modified release product with the ability to adjust the release rate of the API layer by compacting with a placebo layer. When assessing the quality and performance of bi-layer medicinal products, bio-relevant dissolving test circumstances would be more significant. For instance, substantial usage of simulated fluids on both fresh tablets and long-term stability samples is required for in vitro dissolving testing of bi-layer tablets manufactured with water-insoluble APIs.

BILAYER TABLET PREPARATION.

Bilayer tablets are made with one layer of medication that releases immediately and the second layer that releases the medication later, either as an extended release form or as a second dose. In order to reduce the area of contact between two layers, distinct layers of each medicine can also be compressed to create bilayer tablets containing two incompatible pharmaceuticals. It is also possible to incorporate an extra inert layer in between. Certain specifications, like acceptable mechanical strength and the intended drug release profile, must be fulfilled in order to create an appropriate tablet formulation. Sometimes, the formulator may find it challenging to meet these requirements, particularly when using the double compression approach in the formulation of bilayer tablets, due to inadequate flow.

Compression: It is described as a decrease in bulk volume achieved by removing voids and putting particles closer together.

Combination: It is the characteristic of the material whereby interparticulate interaction (bonding) results in greater mechanical strength. One of the main factors affecting tablet delamination was discovered to be the compression stress on layer 1.



Pharmacokinetics factor :

1.Biological half-life: Since this can lower the frequency of dosing, drugs with a biological half-life of 2–8 hours are thought to be good candidates for sustain release dosage forms. This is constrained, though, because medications with extremely brief biological half-lives can need disproportionately high dosage levels per unit to have long-lasting effects, making the dosage form itself restrictive.

2.Absorption rate: Intake The drug's release rate constant from the dosage form determines the rate of absorption of a sustained formulation; absorption is restricted to the intestine for medications absorbed via active transport.

3.Distribution: The way that medications are distributed across tissues may have a significant impact on the kinetics of drug clearance as a whole. The apparent volume of distribution takes on varying values based on the time course of drug disposition since it not only reduces the concentration of the drug in circulation but also has the potential to be rate limiting in its equilibrium with blood and extravascular tissue. Therefore, knowledge of drug disposition is necessary for designing sustain release products.

4.Metabolism: Before changing into a different form, the metabolic conversion to a medicine must be taken into account. A successful sustain release product can be created as long as the location, rate, and extent of metabolism are known (Kumar et al., 2012).

B). Drug properties relevant to sustain release formulation:

1. Dosage size: For a traditional dosage form, a dose size of 500–1000 mg is regarded as the maximum. This also applies to dose forms with sustained release. Given that the safety of administering big doses with a limited therapeutic range is influenced by dose size consideration.

2. Ionization, PKA, and Aqueous Solubility: Since most medications are weak acids or bases, they must dissolve in the aqueous phase surrounding the delivery site before partitioning into the absorbing membrane to be absorbed.

3. The partition coefficient: Because the biological membrane is lipophilic, a drug's partition coefficient has a significant impact on its bioavailability. The drug's capacity to move across the membrane is largely dependent on its partition coefficient. Because they will be confined in the aqueous phase, drugs with low partition coefficients are regarded as poor candidates for the sustain release formulation.

4. Drug stability: When medications are taken orally, they encounter enzymatic destruction and acid-base hydrolysis. In this situation, a drug release system that administers medication over a longer length of time is desirable if the drug is unstable in the stomach; on the other hand, a drug that is unstable in the intestine will have issues with reduced bioavailability. Islam et al. (2011), Kumar et al. (2012)

Design or oral sustained release of drug:

Because of its convenient dose form, design, and patient care, the oral route of administration is the most often used method. Before creating a sustain release dosage form, a number of factors should be considered, such as the gastrointestinal motility, the enzyme system and its impact on the medication and dosage form, and the different pH levels in the GIT. The mechanism of diffusion, dissolution, or a combination of both is used by the majority of sustained release dosage forms to generate a slow release of the drug at a predefined rate. The following are the plasma drug concentration profiles for a sustained release formulation, a zero order sustained release formulation, and a standard tablet or capsule formulation (Lachman et al., 2009).

MERITS:

a)Drug therapy is brought under control.
b) It is possible to alter the rate and degree of drug absorption.
c) Drug administration occurs less frequently.
d) It is possible to increase patient compliance.
e) It is possible to make drug administration convenient.
f) Making the medicine as widely available as possible at the lowest possible dosage.
g) It is possible to expand the high potency drug's safety margin.

Drawbacks:

a) It does not allow for the early conclusion of treatment.

b) Less freedom to change the dosage.

c) The average biological half-life is the basis for the creation of these dosage forms.

d) According to Lachman et al. (2009), they are expensive.

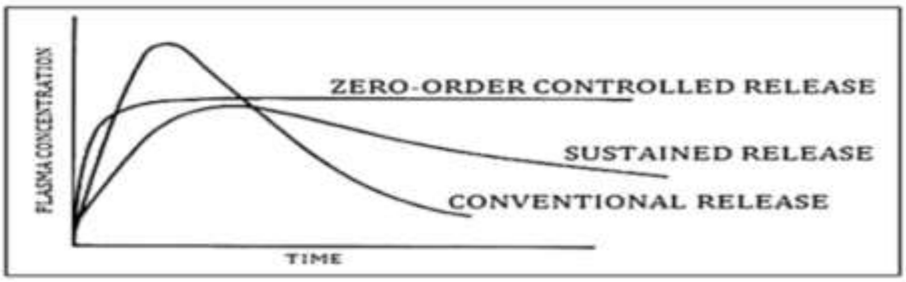


Fig:Plasma drug concentration profile for conventional release, sustained release and zero order.

Immediate Release:

By providing patients with a convenient dose form or regimen, an immediate release dosage form enables a producer to maintain market exclusivity. The term "immediate release" refers to tablets that are made to dissolve and release their medication without the need for additional rate-controlling elements like coatings or other methods.Because they are simple to use, act quickly, are affordable, and improve patient compliance, instant release tablets have recently begun to acquire acceptance and appeal as a medication delivery method. The pace and degree of medication absorption in instant release (IR) solid oral dose forms are primarily determined by three factors:
1. Rate of dissolution.
2. Solubility.
3. Permeability of the intestinal wall.
When it comes to IR dosage forms with highly soluble active pharmaceutical ingredients (APIs).

TECHNIQUES OF BILAYER TABLETS:

1.Push pull technology by O R O S:
This system is mostly composed of two or three layers, of which one or more are necessary for the medicine and the remaining layers are push layers. The medication and two or more distinct agents make up the majority of the drug layer. Thus, this drug layer contains a drug in a form that is weakly soluble. In addition to the osmotic and suspending agents, there is another addition. The tablet core is encased in a semipermeable membrane.

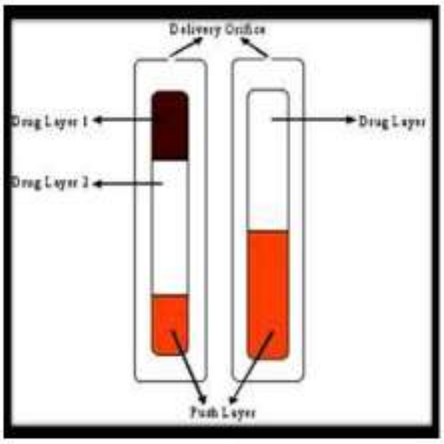


Fig:OROS®PushPullsTechnology

2.L-ORO timetechnology: This system was created to address the solubility issue. It starts with a lipid soft gel product that contains a drug in a dissolved state. It is then coated with a barrier membrane, followed by an osmotic push layer, a semi-permeable membrane, and an exit orifice.

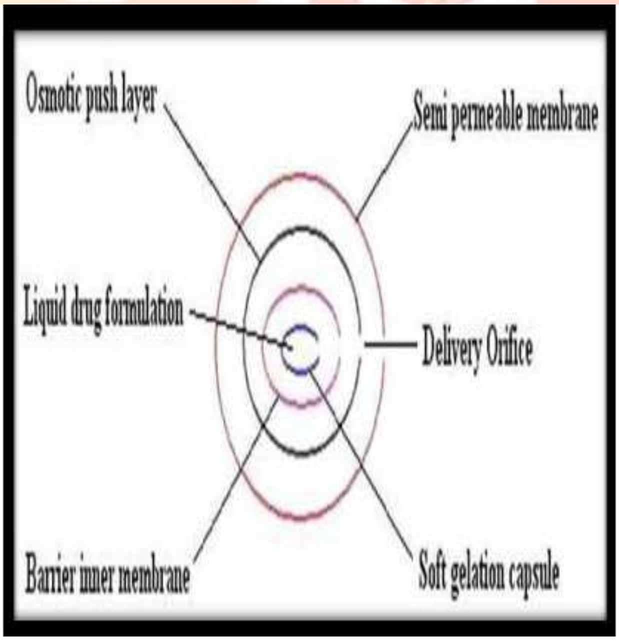


Fig:L-ORO TimeTechnology

3.ENSOTROL technology: A laboratory that employs an integrated strategy to drug delivery, concentrating on the identification and integration of the identified enhancer into controlled release technologies, can provide optimum dosage forms or boost solubility by an order of magnitude.

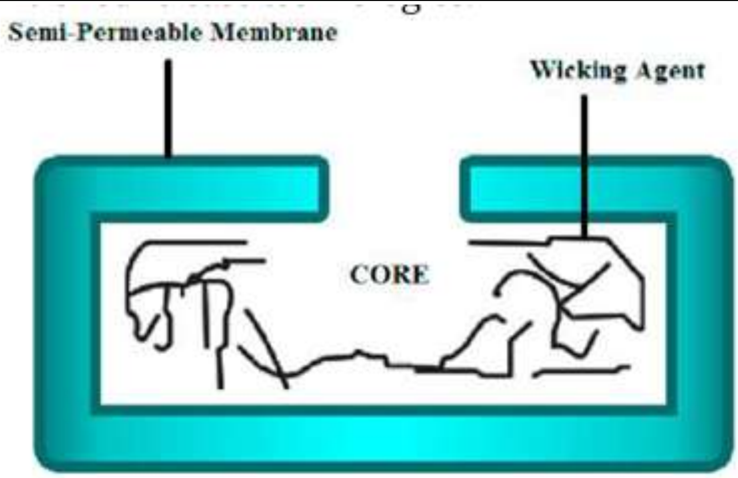


Fig: ENSOTROLTechnology

4.DUROS Technology: An exterior cylindrical reservoir made of titanium alloy makes up the system. This reservoir shields the medication molecules from enzymes and has a high impact strength. The DUROS technology is a tiny medicine delivery device that functions similarly to a tiny needle that continuously and consistently distributes minuscule amounts of concentrated form over the course of months or years.

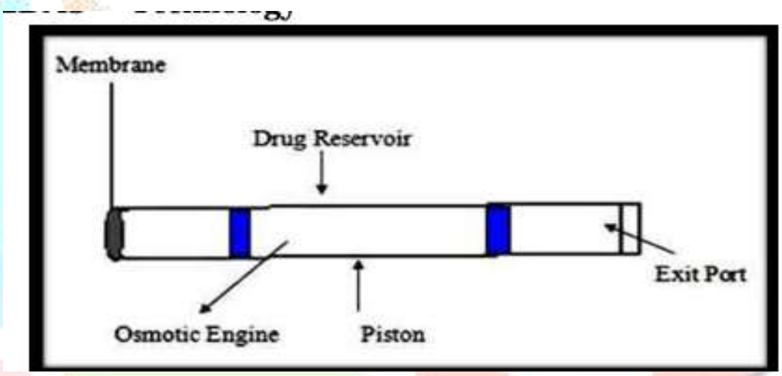


Fig: DUROTechnology

Evaluation of Bilayer tablets :

1. General Appearance: Consumer approval of a tablet depends on its overall "elegance," visual identity, and general appearance. Included are the tablet's dimensions, form, color, taste, texture, physical defects, consistency, and legibility of any identifying markings, as well as whether or not it has an odor.

2. Size and Shape: Dimensional description, monitoring, and control of the tablet's size and shape are all possible.

3. Tablet thickness: When utilizing filling equipment to count and reproduce look, tablet thickness is a crucial factor. Certain filling devices use the tablets' consistent thickness as a counting mechanism. A micrometer was used to measure the thickness of ten pills.

4. Weight varitation 32: The official books' descriptions of standard processes are adhered to.

5. Friability 32: The forces that most frequently result in tablets chipping, capping, or breaking include friction and shock. The friability test, which assesses the tablet's resistance to abrasion during handling, shipping, and packaging, is closely linked to tablet hardness. The Roche friabilator is typically used to measure it. After being weighed, many tablets are put into the device, where they are subjected to rolling and repeated shocks while falling six inches each time. The tablets are weighed and their weight is compared to the starting weight following 100 revolutions or four minutes of treatment. One indicator of tablet friability is the amount lost as a result of abrasion.

The value is stated as:
% Friability = 1- (loss in weight / Initial weight) X 100.

6. Crushing strength (hardness) 33:: The hardness of tablets determines how resistant they are to capping, abrasion, or breakage during handling, storage, and transit before to use. In the middle of the 1930s, Monsanto produced and released the compact, portable hardness tester. These days, it is known as the Stokes or Monsanto hardness tester. When the force produced by a coil spring is applied diametrically to the tablet, the device calculates the force necessary to shatter the tablet. The diametrically applied force needed to shatter the pill is measured using the Schleuniger and Strong-Cobb Pfizer equipment, which was later introduced.Determinations of hardness, or more accurately, crushing strength, are made during tablet manufacturing and are used to assess if the tablet needs to have its pressure adjusted.

7. Stability Study (Temperature dependent): In accordance with ICH recommendations for expedited research, the bilayer tablets are packaged appropriately and kept for the duration of the study under the following circumstances.

Quality and GMP standards:
Bi-layer tablet quality and good manufacturing practice (GMP) requirements 34 In order to manufacture a high-quality bi-layer tablet in a validated and GMP manner, the chosen press must be able to: • Prevent capping and separation of the two separate layers that make up the bi-layer tablet.
•Offering tablets with enough hardness.
• Preventing contamination from spreading between the two layers.
• Giving the two levels a distinct visual separation.
• A lot of yield.
• Accurate and personalized control over the two layers' weight.
As this article tries to show, these conditions are not as simple to fulfill as they may seem.
Although it may seem apparent, accurate and individual weight control of the two layers is a difficult task to do, as this essay aims to show.
• Very brief first-layer dwelling.

Marketed formulation of Bilayer tablets **:**

Conclusion:

The bilayer tablet is a new type of tablet that has several properties to offer an effective drug delivery system and is successful in developing controlled release formulations. The upgraded, useful technology of the bilayer tablet addresses the drawbacks of the single-layered tablet. Bi-layer tablets can be used to segregate two incompatible substances, release two medications in succession, or create sustained release tablets with a maintenance dose in the second layer and an immediate release dose in the first layer. For anti-hypertensive, diabetic, anti-inflammatory, and analgesic medications, where combination therapy is frequently utilized, the usage of bi-layer tablets is a completely other matter. GMP standards and the quality of bilayer tablets can differ greatly. This explains why there are so many distinct kinds of presses in use.

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