

Overview of bilayer tablet: A Review

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Abstract: The efficiency of managing the proper plasma drug concentration in instant release in conventional dose forms is lacking. Therefore, the bilayer tablet drug delivery method is beneficial, which is based on the principle of delivering the medication quickly to provide a rapid therapeutic effect and sustain it for an extended amount of time by releasing the drug in a controlled manner. Bilayer tablet technology is one of the techniques that include both an instant and a prolonged release layer. Bi-layer tablets can be a good way to avoid chemical incompatibilities across APIs and produce distinct medication release profiles by physically separating them.

Bi-layer tablets can be monolithic, partially coated, or multilayered matrices and are used in a variety of applications. It has wide applications as an anti-inflammatory, anti-diabetic, analgesic, and antidepressant medication.

Keywords: Bilayer tablet, OROS System, L-Oros, Gemnax technology, EN SO TROL Technology, Floating drug delivery system.

INTRODUCTION

Skye Pharma PLC's Geomatrix tablet employs the bilayer tablet design.¹ Generally, a bi-layer tablet is a fixed-dose combination (FDC) intended for oral administration. The product is divided into two layers that contain the immediate release and sustained release parts; the first layer contains immediate release and the second layer contains sustained release parts.² In contrast to a single-layered tablet, the bilayer tablet addresses the briefcoming of that technology. Among other purposes, such tablets are commonly used for the physical separation of formulation components to avoid chemical incompatibilities. Different colours were used to identify the two drugs. The bi-layer tablets provide an improved method of identifying the immediate-release layer. The immediate-release layer of bi-layer tablets provides the initial dose, and the sustained release layer delivers the sustained dose. The drug is also disintegrated in a way that produces rapid onset of action and increases drug release rates. This sustained-release (retardant) action is achieved by various polymers acting as release agents, primarily hydrophilic polymers.³ Multi-layered or monolithic matrices can be used to make bi-layer tablets. If the medicine can be put in the upper non-adhesive layer of bi-layered tablets, the drug can be delivered practically unidirectionally across the oral cavity.⁴

Diclofenac is a non-steroidal anti-inflammatory medicine (NSAID) used to treat pain or inflammation caused by arthritis or ankylosing spondylitis. Paracetamol is an analgesic (pain reliever) and antipyretic (fever reducer). Patients on multiple medication therapies who require both antipyretic and analgesic action will benefit from this combo formulation.⁵ It is feasible to reduce the number of units in the daily dose, and a synergistic effect can be achieved with the proper drug combination. Patient compliance can be improved because bilayer tablets have a simple design compared to other complex-configuration dosage forms; Manufacturing is cost-effective and simple for large quantities.⁶

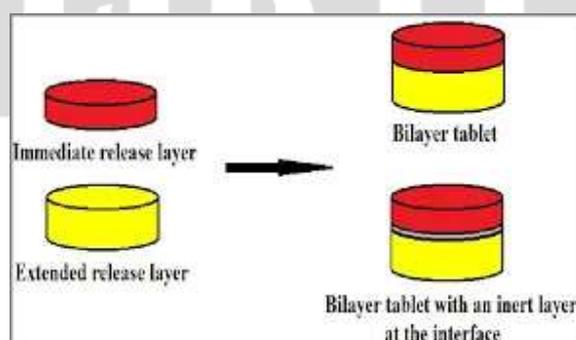


Fig 1: General appearance of bilayer tablet ⁷

NEED FOR BILAYER TABLET⁸

1. To regulate the rate of administration of a single or two active pharmacological components.
2. To segregate incompatible active pharmaceutical ingredients (APIs), and limit API release from one layer by employing a functional property of the other layer, such as the osmotic property.
3. To achieve swellable/erodible barriers for modified release, alter the overall surface area available for the API layer by sandwiching it between one or two inactive layers.
4. To provide fixed-dose combinations of multiple APIs, extend the life cycle of therapeutic products, and develop novel drug delivery systems such as chewing devices, buccal/ mucoadhesive delivery systems, and floating tablets for gastro-retentive drug delivery.⁹

General Properties of Bi-layer Tablet Dosage Forms¹⁰:

1. A bi-layer tablet should have a pleasing appearance and be devoid of flaws such as cracks, chips, contamination, and discoloration.
2. It needs to be strong enough to withstand mechanical shock during manufacture.
3. It needs to be chemically and physically stable to maintain its physical properties throughout time.
4. Chemical stability must be maintained for a long period of time.
5. The agents are released in a predictable and repeatable manner.

Advantage^{11, 12}

1. By physically separating APIs, helps to avoid chemical incompatibilities.
2. Compared to other oral dose forms, it has the best chemical and microbiological stability.
3. Coating technology can cover up unpleasant odors and tastes.
4. Traditional dosing forms necessitate repetitive dosing, which can be avoided with a bilayer tablet.
5. It Provides the highest level of precision.
6. It's easy to swallow with a minimal hang-up.
7. Packing and stripping are easier and less expensive because they are lighter and more compact.
8. A bi-layer tablet is useful for limiting direct contact between two medications and so maximizing the efficacy of a drug combination.
9. Due to their synergistic action, the active ingredients' efficacy is increased.
10. Bi-layer tablets can be constructed to alter release by keeping one layer prolonged and the other immediate.
11. Single entity feed grains could be used in the future.
12. Patient compliance improves, which improves the efficacy of the treatment regimen.
13. A single bilayer tablet can provide two APIs or the same API with two different release profiles (for example, medications with extended and immediate release profiles).¹³
14. When using an embossed or monogrammed punch face, product identification is simple and quick, needing no additional processes.

Disadvantages of Bi-layer Tablet Dosage Form are:

1. Children and unconscious patients will find it difficult to swallow.
2. Some drugs resist compression into dense compacts, owing to their amorphous nature and low-density character.
3. Drugs having poor wetting qualities, slow dissolution properties, and optimum absorption high in the GIT may be challenging to synthesize or manufacture as tablets that provide adequate or full drug bioavailability.
4. Individual layer weight management isn't as accurate as it should be.
5. layer-to-layer cross-contamination.
6. Some solids have irritative effects on the mucosa of the gastrointestinal tract (e.g. aspirin).
7. Slow breakdown and dissolution may cause bioavailability issues.
8. Encapsulation may be required for bitter tasting medications, drugs with an unpleasant odor, or drugs that are oxygen sensitive.
9. Add complexity, and bi-layer tablet presses are expensive.

Types of bilayer tablets¹⁴

Bilayer tablets can be the same (homogeneous) or different (heterogeneous).

1. Homogeneous type:

Bilayer tablets have the same drug in two layers, but the drug release profile is different from one another. These bilayer tablets contain one layer of immediate release and the second layer is in an extended-release manner.

2. Heterogeneous type:

Bilayer tablet is suitable for continuous release of two drugs in combination, separating two incompatible substances.

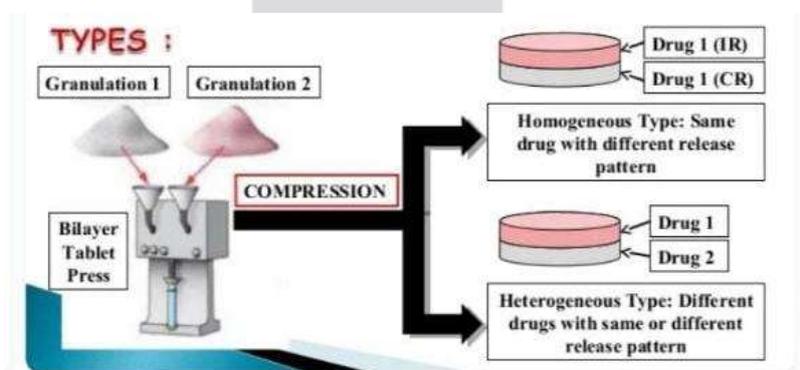
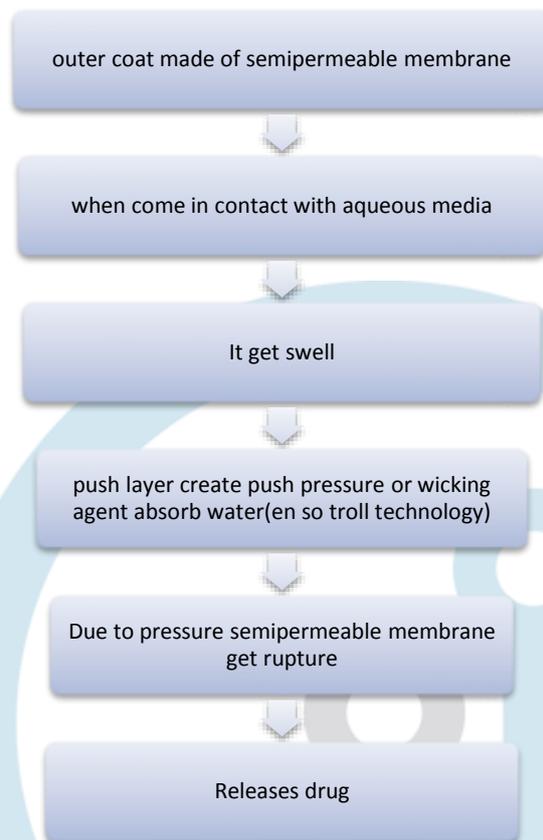


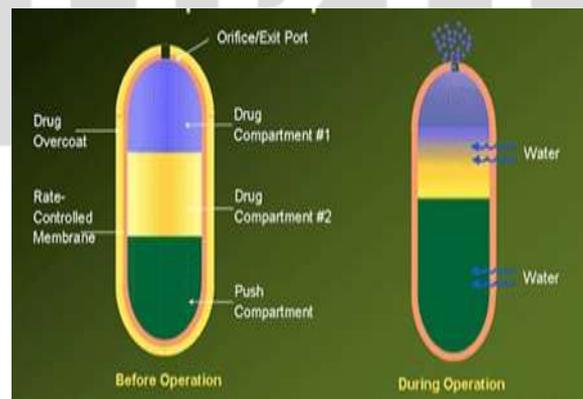
Fig 2: Types of bilayer tablet¹⁵

VARIOUS TECHNIQUES FOR BILAYER TABLET

GENERAL MECHANISM OF RELEASE OF DRUG OF ALL TECHNIQUES:

**OROS PUSH-PULL TECHNIQUE¹⁶**

OROS® Developed by Alza. It is a bilayer tablet coated with a semipermeable membrane. The OROS® system contains two or three layers; it consists of mainly two or three layers, one or more of which is responsible for delivering the drug, and the other two are responsible for delivering the push. The drug layer consists of a drug along with two or more other agents. The drug in the layer is poorly soluble, so it can be seen in the drug layer as a poorly soluble substance. The tablet is surrounded by a semipermeable membrane along with a suction and osmotic agent.

**Fig 3:** Bilayer and trilayer OROS Push pull technology**LIQUID OROSTABLET (L-OROS)¹⁷**

Liquid Oral Osmotic System (L-OROS) to overcome the drug solubility issue Alza developed the L-OROS system where the liquid soft gelatin product containing the drug in a dissolved state is initially manufactured and then coated with a barrier membrane, then the osmotic push layer, and then semi-permeable membrane containing a drilled orifice. Liquid OROS is designed to deliver drugs as liquid formulations and combine the benefits of extended release with high bioavailability.

Each of these systems includes a liquid drug layer, an osmotic engine or push layer, and a semi-permeable membrane coating. When the system is in contact with the aqueous environment water permeates across the rate-controlling membrane and activates the osmotic layer. The expansion of the osmotic layer results in the development of hydrostatic pressure inside the system, thereby

forcing the liquid formulation to be delivered from the delivery orifice (Whereas L OROS hard cap or soft cap systems are designed to provide continuous drug delivery, the L OROS delayed liquid bolus drug delivery system is designed to deliver a pulse of liquid drug. The delayed liquid bolus delivery system comprises three layers: a placebo delay layer, a liquid drug layer, and an osmotic engine, all surrounded by a rate-controlling semi-permeable membrane. The delivery orifice is drilled on the placebo layer end of the capsule-shaped device. When the osmotic engine expands, the placebo is released first, delaying the release of the drug layer. Drug release can be delayed from 1 to 10 hours, depending on the permeability of the rate-controlling membrane and thickness of the placebo layer.

L-OROS ARE OF THREE TYPES:

1. L- OROS hard cap: Design to provide continuous drug delivery.
2. L- OROS soft cap: Design to provide continuous drug delivery.
3. Delayed liquid bolus delivery system: Deliver pulse type of drug delivery.

Delayed Liquid Bolus Delivery System: It contains three layers:

- a) Placebo delay layer
- b) Liquid drug layer
- c) Osmotic engine: It is surrounded by a rate-controlling semipermeable membrane. It is a capsule shape & Delivery orifice drilled on a placebo layer.

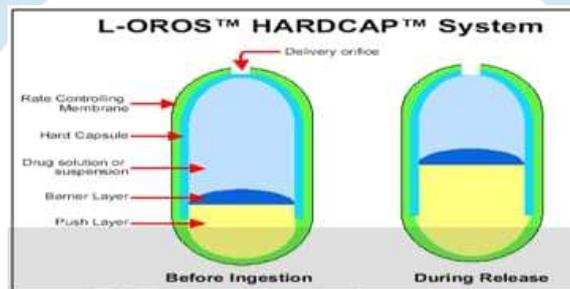


Fig.10: L-OROS hardcap™ System

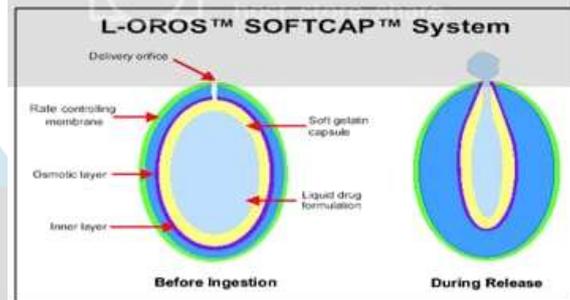


Fig 4: L – OROS tm technology¹⁸

En so troll technology

Shire Laboratory uses an integrated approach to drug delivery focused on the identification of the identified enhancers and incorporation of them into controlled release technologies to improve solubility by a factor of several or create an optimized dosage form. In these techniques, the outer membrane is semipermeable and the inner core contains a drug along with a wicking agent. Wetting agents enable water to be absorbed into the porous structure of a delivery device. Specifically, wicking agents can either swell or not swell. Wicking agents are used to draw water to surfaces inside the core of a tablet, creating channels or a network of increased surface area and drug release rate through orifice enhancement.

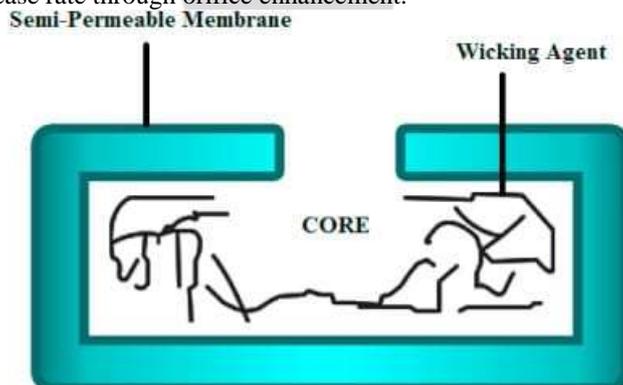


Fig 5: EN SO TROL Technology

PRODAS¹⁹

The Programmable Oral Drug Absorption System is a multi-particulate drug delivery system that encapsulates controlled-release mini-tablets ranging from 1.5 to 4 mm in diameter. This technology combines multiparticulate drug delivery techniques with controlled-release nanotechnology, and the mini-tablet provides the benefit of both hydrophilic matrix and microporous matrix. Tablets can thus integrate both technologies into a single dosage form. Different release rates can be combined into the same dosage form to obtain desired release rates. These combinations may include immediate-release, delayed-release, and controlled-release mini-tablets. Combinations of these forms can ultimately include immediate-release mini-tablets, delayed-release tablets, and controlled-release mini-tablets. In addition to controlled absorption over a specific period and targeted delivery of drugs to specific absorption sites, PRODAS technology also enables targeted delivery of drugs throughout the gastrointestinal tract. Mini-tablets formulated with different active ingredients can also be used to form combination products.

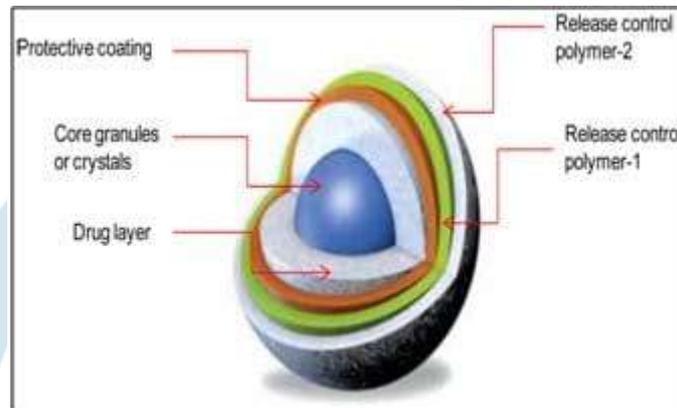


Fig6: PRODAS ® Technology: Programmable Oral Drug Absorption System

GEMINEX TECHNOLOGY¹⁹

Geminex provide the independent release of a single active ingredient or multiple active ingredients in a bilayer tablet. The active ingredient release can be determined by two or more different controlled release profiles or by an individually controlled release profile. The TIMERx matrix is used in controlled release layers in the bilayer tablet, which gives a controlled release and immediate release profile simultaneously.

ERODABLE MOLDED MULTILAYER TABLET

Erodible molded tablets in an erosion-based platform have the advantage of delivering zero or delayed-release with little to no impact on gastrointestinal conditions. To control drug release, the matrix, coat, and geometry must be altered to achieve either a zero-order release or a modified release. Through alterations to the matrix, coat, and geometry, the rate and mode of release can be designed and engineered to suit the end-user. With a zero-order, the drug is dispersed through the matrix in a coat that is biodegradable but has low water permeability to prevent penetration. If the matrix comes into contact with water, the matrix starts to erode. This matrix erosion is caused by GI fluids and is promoted by gut movement. Because the dosage form is designed so that water diffusion into the matrix is slowed, almost all drug release is caused by erosion. Advantageous for drugs that have chemical and physical stability issues after contact with water. Using standard plastic injection molding technology. Egalet delivery technology is accurate, reproducible, and low in cost.

DUROS TECHNOLOGY

An exterior cylindrical titanium alloy reservoir forms the basis of the system. The drug molecules are protected from enzymes by this reservoir's high impact strength. The DUROS technology is a micro medicine distribution system that works in the same way as a syringe and dispenses a small amount of concentrated medication regularly and continuously for months or years.

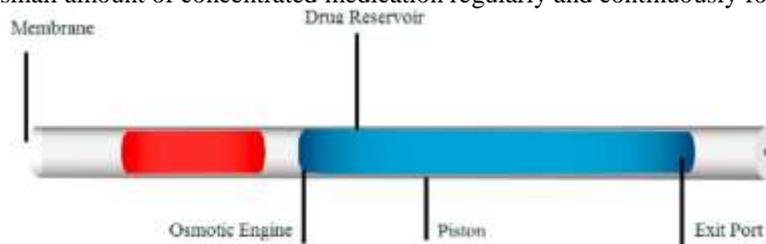


Fig 7: DUROS Technology

DURADAS TECHNOLOGY

DUREDAS technology is a bi-layer tablet that can deliver an immediate or sustained release of two medications or multiple release rates of the same drug in a single dose form. Within one tablet, the tableting technique can produce different layers of immediate-

release granulate and modified-release hydrophilic matrix complex. A mixture of hydrophilic polymers provides the dosage form with modified-release features.

MANUFACTURING PROCESS OF BILAYER TABLET²⁰

Bi-layer tablets are prepared with one layer of a drug for immediate release, with the second layer designed to release the drug later, either as a second dose or in an extended-release form. The bi-layer tablets with two incompatible drugs can also be prepared by compressing separate layers of each drug to minimise the area of contact between the two layers. The inclusion of an additional layer of inert material is also possible.

The manufacturing process is mainly divided as:

A. COMPACTION:

A good tablet formulation should meet certain requirements, such as mechanical strength and the desired drug release profile. Sometimes, it may be difficult to achieve these conditions even in bi-layer tablet formulation when the double compression technique is used, due to the poor flow and compatibility characteristics of the drug, which will result in capping or lamination. Compression and consolidation are two aspects of compaction.

B. COMPRESSION

Compression is a process of reducing bulk volume by eliminating voids and bringing particles closer together.

Bilayer Tablet Compression consists of the following steps:

1. Filling of the first layer
2. Compression of the first layer
3. Ejection of the upper punch
4. Filling of the second layer
5. Compression of the second layer
6. Ejection of a bi-layer tablet

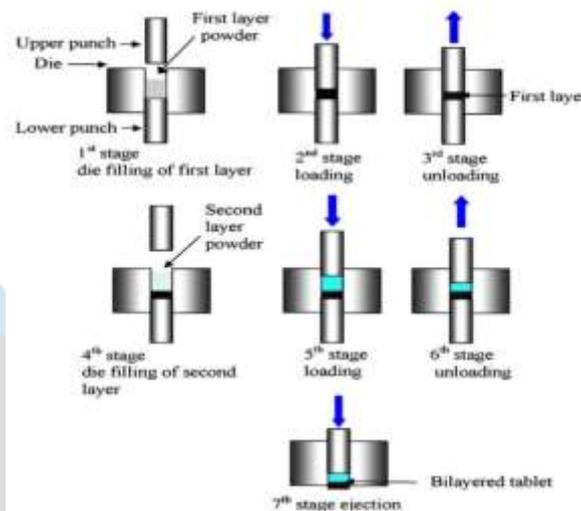


Fig 8 : Manufacturing process of bilayer tablet²¹

C. CONSOLIDATION

This means that there is an increase in the mechanical strength of the material due to inter-particulate interactions (bonding). It was found that a strong compression force on layer one contributed to tablet delamination.

BILAYER TABLET: QUALITY AND GMP REQUIREMENT²²

A quality bi-layer tablet will only be produced by a press that can manufacture it in a validated and GMP-compliant manner.

- A) Protect the bi-layer tablets from capping and separation into their layers.
- B) The separation of the two layers is achieved by using a clear visual separation.
- C) Assuring adequate tablet hardness.
- D) Avoiding cross-contamination within the two layers
- E) Weight control of individual layers, high yield, and accuracy.
- F)

TYPES OF BILAYER TABLET PRESS

1. Single-sided tablet press.
2. Double-sided tablet press
3. Bilayer tablet press with displacement monitoring

1. Single-sided press

A single-sided press with both chambers of the doublet feeder separated from one another is the most basic design. The two distinct layers of tablets are produced by gravity or force-feeding each chamber with varying power. The first layer of powder is put onto the die as it travels through the feeder, followed by the second layer of powder. After that, in one or two steps, the entire tablet is compressed.

Limitations of the single-sided press

1. Individual layer weights aren't monitored or controlled.
2. There is no clear visual distinction between the two levels.
3. Due to the small compression roller, the initial layer dwell time is quite short, perhaps resulting in poor deaeration, capping, and hardness issues.
4. This can be fixed by slowing down the turret rotation (to extend the dwell period), but this will result in reduced tablet output.

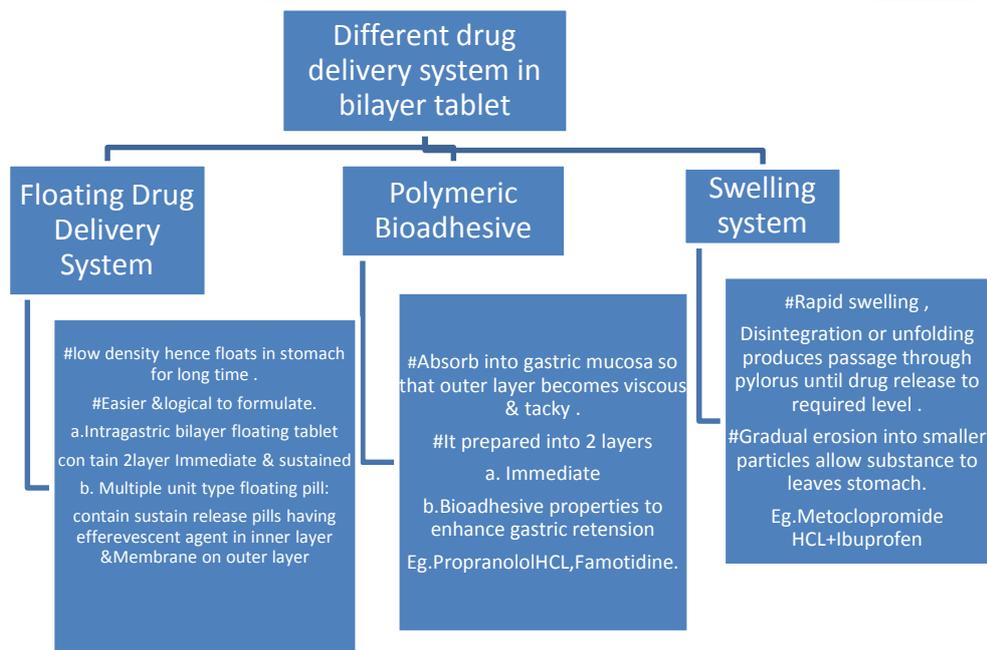
2. Double-sided tablet press:

Compression force is used to monitor and manage tablet weight in most double-sided tablet presses with automated production control. At major compression of the layer, the control system measures the effective peak compression force exerted on each tablet or layer. The control system uses this measured peak compression force to reject out-of-tolerance die fill depths and adjust them as needed.

3. Bilayer tablet press with displacement monitoring:

The principle of displacement pill weight management is significantly different from the compression force principle. The sensitivity of the control system while monitoring displacement is determined by the applied pre-compression force rather than the tablet weight.

DIFFERENT DRUG DELIVERY SYSTEMS USED IN BILAYER TABLET



Characterization of bilayer tablet²³

a) Particle size distribution

Sieving was used to measure the particle size distribution.

b) Photo microscope study

With the use of a photomicroscope, we have taken a photo of TGG and GG (X450 magnification).

c) Angle of repose

To calculate the angle of repose, we measured the diameter of the powder cone and used the following equation:

$$\tan \theta = h/r,$$

where **h** and **r** are the height and radius of the powder cone, respectively.

d) Hausner's ratio

A fixed funnel method was used to determine the angle of repose of powder blends in each layer of the formulations. Each layer was poured through the funnel separately until the apex of the pile formed at the tip touched the tip of the funnel. The angle of repose was then calculated according to a formula.

$$\text{Hausner's ratio} = \text{Tapped density} / \text{Bulk density}$$

e) Moisture sorption capacity

Disintegrates are capable of absorbing moisture from the atmosphere, which can adversely affect moisture-sensitive drugs. The amount of moisture uptake was determined by measuring the difference in weight between 2 grams of disintegrating uniformly distributed in Petri dishes kept in a stability chamber at 37°C and 100% relative humidity for two days and measured by the amount of moisture absorbed.

f) Density

i) **Bulk density:** A bulk density calculation was performed using a formula based on the following calculation:

$$\text{Bulk density (BD)} = \text{weight of powder} / \text{volume of bulk.}$$

The bulk density is calculated by placing the powder blend into a measuring cylinder; the total volume

ii) Tapped density:

A tapped density was determined by tapping the cylinder 100 times and calculating the tapped density by formula. The tapped volume was measured after 100 taps, and then the tapped density was calculated by using the formula:

$$\text{Tapped density (TD)} = \frac{\text{weight of powder}}{\text{Tapped volume}}$$

g) Compressibility:

By using Carr's compressibility index, we can determine the compressibility index of the powder.

$$\text{Carr's index (\%)} = \frac{\text{Tapped density} - \text{bulk density}}{\text{tapped density}} \times 100$$

Evaluation of Bi-layer Tablets:²⁴

- General Appearance:** Consumers accept products when they have an appealing visual identity, including their size, color, shape, odor, taste, texture, physical flaws, and legibility of any identifying mark. Other parameters include tablet size, shape, color, appearance, odor, taste, and texture of the surface.
- Size and Shape:** Dimensionally, we can describe, monitor, and control the tablet's dimensions and shape.
- Tablet Thickness:** Using filling equipment, tablets' uniform thickness can be used as a counting mechanism. Some filling machines are designed to count tablets based on their uniform thickness.
- Uniformity weight:** 20 tablets were randomly chosen, and their weights were compared to the average weight. This was accomplished by weighing each tablet and comparing them to the average weight.

Sr .no	As per USP standards	Max.% deviation allowed	As per IP/BP standards
1	130 mg or less	10%	84 mg or less
2	130 -324 mg	7.5%	80-250 mg
3	More than 324 mg	05%	More than 250mg

5. **Hardness:** Using Monsanto's hardness tester, we evaluated the hardness of the tablet, which has high impact resistance under handling, transportation, and storage conditions. kg/cm² is the unit of hardness.

6. **Friability:** The forces most often responsible for tablet chipping, cracking, and breaking is friction and shock. Twenty tablets are weighed and placed in the Roche friability apparatus where they are subjected to repeated shocks as they fall six inches on each turn. The weight of the tablets is calculated after abrasion in four minutes or 100 turns, compared to their initial weight. Abrasion results in a loss in weight, indicating the friability of the tablet. Any broken or smashed tablets should not be collected, as weight loss of less than 1% is considered generally acceptable during the friability test. The percentage friability is calculated as follows:

$$\% \text{ friability} = \left[\frac{\text{initial weight} - \text{final weight}}{\text{initial weight}} \right] \times 100$$

7. **Drug Content:** Weighing 10 tablets and calculating the average weight would be used to determine the medication content. The pills would then be triturated, resulting in a fine powder.

8. **Dissolution Studies:** Dissolution testing is the process of releasing a medication from a tablet into solution per unit time under controlled conditions. In-vitro drug release tests in the simulated stomach and intestinal fluids would be performed on bi-layer tablets to determine their potential to deliver the appropriate controlled medication delivery. The dissolution medium can be chosen based on the dissolution site.

9. **Stability Study:** The bi-layer tablets would be put in appropriate packaging and kept in the following conditions for the duration of the accelerated study, as required by ICH guidelines: After 15 days, the tablets would be withdrawn and analyzed for physical characterization (visual defects, hardness, friability, and dissolution, among other things) as well as drug content. The data is fitted into first-order equations to determine the kinetics of deterioration. At 25°C, accelerated stability data is plotted using the Arrhenius equation to determine the shelf life.

Study	Storage Condition	Period
Long term	30°C ± 2°C/65% RH ± 5% RH	12 months
Intermediate	30°C ± 2°C/65% RH ± 5% RH	6 months
Accelerated	40°C ± 2°C/75% RH ± 5% RH	6 months

10. **Buoyancy Determination:** The time it takes for the dosage form to emerge on the medium's surface is known as floating lag time, and the time it takes for the dosage form to emerge on the medium's surface continuously is known as total floating time (TFT). One tablet from each formulation batch would be placed in a dissolution unit with 900 ml of dissolution media and rotated at the required RPM. The medium's temperature would be kept at 37°C. The time it takes for the tablet to appear on the medium's surface, as well as the amount of time it stays on the medium's surface, would be recorded.

11. **Swelling study²⁵:** Individual tablets would be precisely weighed and stored in 50 mL of water. After 60 minutes, the tablets would be carefully removed, blotted with filter paper to remove any remaining water, and weighed correctly. The formula for calculating percentage swelling would be:

$$\text{Swelling study} = \frac{\text{Wet weight} - \text{Dry weight}}{\text{Dry weight}} \times 100$$

Challenges related to bilayer technology²⁶

Bilayer tablets are two single-layer tablets that have been compressed into one. When the two components of a tablet do not completely connect, it breaks into fragments. When compacted into a bilayer tablet, both granulations should adhere correctly. Some manufacturing issues exist in practice:

- Inconsistent weight control of individual layers.

- Layer-to-layer cross-contamination.
- Misalignment of elastic modulus between adjacent layers. Inadequate layer bonding and inadequate interfacial strength could result from a high elastic modulus ratio between adjacent layers.
- Reduced production yield and a proclivity to delaminate (separation of distinct layers) at the non-planer interface between adjacent compacted layers.
- Low drug load combined with a disproportionate layers weight ratio.
- The hardness of the bilayer tablet is insufficient.
- Throughout the shelf life of the product, it maintains its physical and chemical integrity.
- Large tablet size, which may affect the unit dose's swallowability.
- High temperature and humidity have an effect on layer adhesion during storage.

Various Advancements in the Field of Bilayer Tablets

DRUG	DOSAGE FORM	RATIONALE	METHOD	reference
Statin Aspirin	Bilayer tablets	To reduce medication interactions and aspirin-related adverse effects.	Dry & wet granulation	27
Metformin Glipizide	Bilayer tablets	Drugs have a synergistic effect on diabetes.	Wet granulation	28
Cefuroxime axetil	Bilayer floating tablets	Bimodal drug release	Granulation	29
Telmisartan Simvastatin	Bilayer tablets	to reduce contact between Simvastatin & telmisartan	Wet granulation	30
Propranolol HCl	Bilayer tablets	Bimodal drug release	Wet granulation	31
Misoprostol Diclofenac	Bilayer tablets	To minimize contact b/w drug	Wet granulation	32
Diclofenac Cyclobenzaprine HCl	Bilayer tablets	Synergistic effect in pain	Wet granulation	33
Granisetron HCl	Bilayer buccal tablet	To overcome the bioavailability problem, reducing side effects	Direct compression	34
Metformin HCl Glimepiride	Bilayer tablets	Synergistic effect in diabetes	Wet granulation	35
Indomethacin	Bilayer floating tablets	Biphasic drug release	Wet granulation	36
Metformin HCl Atorvastatin Calcium	Bilayer tablets	To develop polytherapy for the treatment of NIDDS & hyperlipidemia	Wet granulation	37
Cefixime Trihydrate Dicloxacillin Sodium	Bilayer tablets	Synergistic effect in bacterial infections	Wet granulation	38
Piracetam Vinpocetine	Bilayer tablets	Synergistic effect in Alzheimer's disease	Wet granulation	39
Metformin HCl Pioglitazone	Bilayer tablets	Synergistic effect in diabetes mellitus	Wet granulation & direct compression	40
Cefuroxime Axetil Potassium Clavulanate	Bilayer tablets	Synergistic effect against microbial infections and to minimize dose-dependent side effects	Dry granulation	41
Amlodipine Besylate Metoprolol Succinate	Bilayer tablets	Synergistic effect in hypertension	Direct compression & wet granulation	42
Atorvastatin Calcium	Bilayer buccal tablets	To overcome the bioavailability problem, reducing side effects and frequency of administration	Direct compression	43
Paracetamol diclofenac	Bilayer tablets	Synergistic effect of drugs in pain	Wet granulation	44
Losartan	Bilayer tablets	Biphasic release profile	Direct compression	45
Metformin HCl Pioglitazone	Bilayer tablets	Synergistic effect in diabetes mellitus	Dry & wet granulation	46
Guaifenesin	Bilayer tablets	Biphasic release profile	Wet granulation	47
Tramadol Acetaminophen	Bilayer tablets	Synergistic effect of drugs in pain	Coacervation via temp change	48
Atenolol Lovastatin	Bilayer floating tablets	Synergistic effect in hypertension and biphasic release profile	Direct compression	49
Montelukast Levocetirizine	Bilayer tablets	To improve the stability of drugs in combination	Wet granulation	50
Salbutamol Theophylline	Bilayer tablets	Synergistic effect of drugs in asthma	Wet granulation	51

CONCLUSION

The bilayer tablet is an enhanced technology that addresses the shortcomings of the single-layered tablet. There are many uses for bilayer tablets, which can be monolithic, partially coated, or multilayered matrices. Bi-layer tablets are appropriate for the sequential release of two medications in combination, the separation of two incompatible substances, and also for sustained release tablets in which one layer is the initial dose and the second layer is the maintenance dose. Multilayer tablet preparations are utilized to create solutions for the administration of incompatible medications as well as controlled-release tablet preparations by providing surrounding or multiple swelling layers. Quality and GMP requirements for bi-layer tablets can vary significantly. This explains

why a wide range of presses, from simple single-sided presses to extremely complicated machines like the Courtoy-R292F, are utilized to manufacture bi-layer tablets. Whenever high-quality bi-layer tablets need to be produced at high speed, the use of an “air compensator” in combination with displacement control appears to be the best solution.

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