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Development of Bilayer Tablets as Immediate Drug Release and Sustained Drug Release

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ABSTRACT

Bilayer tablet is a new era for the successful development of controlled release formulation along with various features to provide a way of a successful drug delivery system. Bilayer tablets can be a primary option to avoid chemical incompatibilities between API by physical separation and to enable the development of different drug release profiles like the immediate release with extended release. Bilayer tablet is a very different aspect of anti-inflammatory and analgesic. Bi-layer tablet is suitable for the sequential release of two drugs in combination and also for sustained-release tablet in which one layer is immediate release as initial dose and second layer is maintenance dose. Bilayer tablet is improved beneficial technology to overcome the short coming of the single-layered tablet. There are various applications of the player tablet, it consists of monolithic partially coated or multilayered matrices.

INTRODUCTION: -

Nowadays various developed and developing countries are moving towards a combination therapy for the treatment of various diseases and disorders requiring long-term therapy such as hypertension, Diabetes and Cardiovascular diseases1. Over 90% of the formulations manufactured today are ingested orally. It shows that this class of the formulation is the most popular worldwide and the major attention of the researcher is towards this direction. The major aim of controlled drug delivery is to reduce the frequency of dosing. The design of a modified release drug product is to optimize a therapeutic regimen by providing slow and continuous delivery of drug over the entire dosing interval providing greater patient compliance and convenience. Bilayer tablet is the newer a for the successful development of controlled release formulation and is better than the traditionally used dosage forms. Bilayer tablet is suitable for the sequential release of two drugs in combination it is also capable of separating the two types of incompatible substances and also for sustained release tablet in which one layer is immediate release as initial dose and the second player is the maintenance dose. In certain cases, bilayered tablets have 2 sustained-release layers of different drugs.

Bilayer tablet is an improved technology to overcome the short coming of the single layered tablet. Player tablets contain immediate, sustained release layers, and the immediate release layer delivers the initial dose, it contains superdisintegrates, which promotes the drug release rate and attains the onset of action quickly (loading dose) whereas sustained release(maintenance dose) layer releases the drug in a sustained manner for a prolonged time period. The biphasic system isused mostly when maximum relief needs to be achieved quickly and it is followed by a sustained release phase. It also avoids repeated administration of a drug Coronary vasodilators, antihypertensive, antihistamines, analgesics, antipyretics and antiallergenic agents are mainly suitable for this type of drug delivery. Some bilayer tablets have both layers as the sustain release layers examples are certain antidiabetic agents.

THE GOAL OF DESIGNING BILAYER TABLETS:

Controlling the delivery rate of either single or two different API'S. To separate incompatible API's with each other, to control the release of one layer by utilizing the functional property of the other layer. To adapt the total surface area available for API layer either by sandwiching with one or two inactive layers in order to achieve swellable/erodible barriers for controlled release.

Bi-layer tablet is suitable for the sequential release of two drugs in combination, separate two incompatible substances and also for sustained release tablet in which one layer is immediate release as initial dose and second layer is the maintenance dose.

However, the blood level is maintained at a steady state as the drug is released from the sustaining layer.

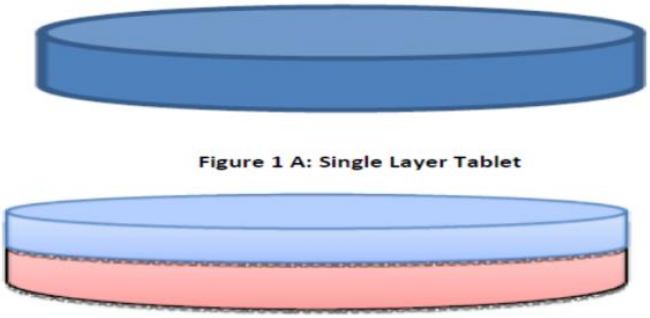


Figure 1 A: Single Layer Tablet

Fig. 1: Bilayer Tablets

NEED OF BILAYER TABLETS

For the administration of fixed-dose combinations of different APIs 13, prolong the drug product lifecycle, vocal mucoadhesive delivery systems, fabricates novel drug delivery systems such as chewing devices and floating tablets for gastro-retentive drug delivery. Controlling the delivery rate of either single or two different active API'S.

To modify the total surface area available for API layer either by sand washing with one or two inactive layers in order to achieve swellable (or) erodible barriers for modified release. To separate in compatible Active pharmaceutical ingredients (APIs) from each other, to control the release of API from one layer by utilizing the functional property of the other layer.

OBJECTIVES OF BILAYER TABLETS

To control the delivery rate of either a single or two different active pharmaceutical ingredients. To separate incompatible Active pharmaceutical ingredients from each other, to control the release of API from one layer by utilizing the functional property of the outer layer.

To modify the total surface area available for API layer either by sand washing with one or two inactive layers in order to achieve swellable or erodible barriers for modified release. To administer fixed-dose combinations of different active pharmaceutical ingredients, prolong the drug product lifecycle, fabricaten ovel drug delivery systems such as chewing device buccal mucoadhesive delivery systems, and floating tablets for gastro-retentive drug delivery.

ADVANTAGES

Bi-Layer execution with optional single-layer conversion kit.

The cost is lower compared to all other oral dosage forms.

Greatest chemical and microbial stability overall oral dosage forms.

Objection able odor and bitter taste can be masked by coating technique.

Flexible Concept.

They are a unit dosage form and offer the greatest capabilities of all oral dosage forms for the greatest dose precision and the least content variability.

Easy to swallow with less tendency to hang up.

Suitable for large-scale production

DISADVANTAGES

Drugs with poor wetting, slow dissolution properties, optimum absorption high in GIT may be difficult to formulate

Difficult to swallow in the case of children and unconscious patients.

Adds complexity and bilayer rotary presses are expensive.

Some drugs resist compression into dense compacts, owing to amorphous nature, low density character.

Cross contamination between the layers.

Insufficient hardness, layer separation, reduced yield.

Imprecise individual layer weight control.

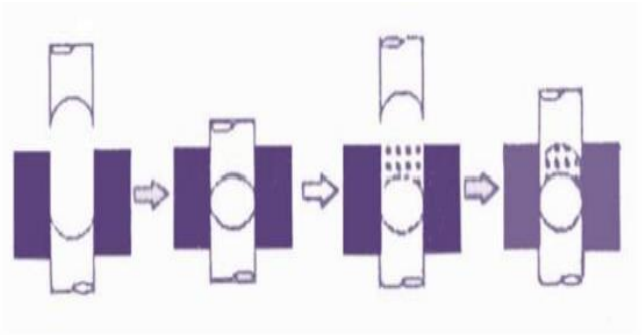
PREPARATION

Bilayer tablets are prepared with one layer of the drug for immediate release with the second layer designed to release drug later, either as a second dose or in an extended release form. The bilayer tablets with two incompatible drugs can also be prepared by compressing separate layers of each drug so as to minimize the area of contact between the two layers.

Compaction:- To produce an adequate tablet formulation, certain requirements such as sufficient mechanical strength and desired drug release profile must be met. At times, this may be a difficult task for the formulator to achieve these conditions, especially in the bilayer tablet formulation where the double compression technique is involved, because of Poor flow and compatibility characteristics of the drug which will result in capping and/or lamination. The compaction of a material involves both compressibility and consolidation.

Compression:- It is defined as a reduction in bulk volume by eliminating voids and bringing particles into closer contact.

Consolidation:- It is the property of the material in which there is increased mechanical strength due to interparticulate interaction(bonding). The compression force on layer1 was found to be a major factor influencing tablets' delaminating.



Preparation Of Bliayer Tablets.

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:- Various types of bilayer presses have been designed over the years. The simplest design is a single-sided press with both chambers of the double feeder separated from each other. Each chamber in gravity fed or force-fed with a different powder,thus producing the 2 individual layers of the tablet. When the dye passes under the feeder, it is at first loaded with the first layer of powder followed by the second layer powder then the entire tablet is compressed in one or two step. The two layers in the dye mix slightly at their interface and in most cases bond sufficiently so that no layer separation occurs when the tablet is produced this is the simplest way of producing a bilayer tablet.

Limitations

No weight monitoring or control of the individual layers.

No distinct visual separation between the 2 layers.

Dwell time due to the small compression roller possibly resulting in poor deaeration capping and hardness problems.

2) Double sided tablet presses:- Most of the double sided tablet press, which automates production control use compression force to monitor and control the weight of the tablet weights. The effective compression force exerted on each individual tablet with the help of the compression system at the main compression of the layer. This system helps into reject out the tolerance tablets and correct the die fill depth when required.

Advantages

Low compression force exerted on the first layer to avoid chapping and separation of the individual layer.

Increased dwell time at pre-compression of both first and second layer to provide sufficient hardness at maximum turret speed.

Maximum prevention of cross-contamination between two layers.

A clear visual separation between the two layers.

Displacement weight monitoring for accurate and independent weight control of the individual layer.

Maximized yield.

Separation of the two individual layers is due to insufficient bonding between the two layers during final compression of bilayer tablet.

Limitations

Correct bonding is only obtained when the first layer is compressed at a low compression force so that this layer can still interact with the second layer during a final compression.

Bonding is too restricted if the first layer is compressed at a high compression force.

The low compression force required when compressing the first layer, unfortunately, reduces the accuracy of the weight monitoring/control of the first layer in the case of tablet presses with compression force measurement.

3) Bi-Layer Tablets Presses with Displacement:- The principle of bilayer tablet press is fundamentally different from the principle of compression force. In this case, the accuracy increases with reduced compression force. At higher production speeds the risk of capping and separation increases, but can be reduced by sufficient dwell time a tall four compression stages.

Advantages

Displacement weight monitoring /control for accurate independent weight control of the individual layers.

Low compression force is exerted on the first layer to avoid chapping and separation of the 2 individual layers.

Increased dwell time at pre-compression of both first and second layer to provide sufficient hardness at maximum turret speed.

Maximum prevention of cross contamination between the layers.

A clear visual separation of the layers.

Maximized yield.

4) Multilayer Compression Basics:- Presses can be designed specifically for multi layer compression or a standard double press can be converted for multipliers. The multilayer tablet concept has been long utilized to develop sustained release formulations such tablets

have fast releasing layers and may contain players or triple layers to sustain the drug release from the tablet. The pharmacokinetics advantage relies on the fact that drug release from fast releasing granules leads to sudden rise in blood concentration, however the blood level is maintained at a steady state as the drug is released from the sustained granules.

VARIOUS APPROACHES OF BILAYER TABLETS

A) Floating drug delivery system:- These are designed to have a low density and thus float on gastric contents after administration until the system either disintegrates or the device absorbs fluid to the point where its density is such that it loses buoyancy and can pass more easily from the stomach with a wave of Motility responsible for gastric emptying. The bilayer tablet is designed in such a manner that, one layer gives the immediate dosing of the drug which gives a faster onset of action while another layer is designed as a floating layer that floats in the stomach.

B) Polymeric Bioadhesive System:- These are designed to imbibe fluid following administration, such that the outer layer becomes a viscous, tacky material that adheres to the gastric mucosa/mucus layer. This should encourage gastric retention until the adhesive forces are weakened. These are prepared as one layer with immediate dosing and other layer with bioadhesive properties.

C) Swelling System These are designed to be sufficiently small on administration so as not to make ingestion of the dosage form difficult. On ingestion they rapidly swell or disintegrate or unfold to a size that precludes passage through the pylorus until after drug release has progressed to a required degree Gradual erosion of the system or its breakdown into smaller particles enables it to leave the stomach. The simple bilayer tablet may contain an immediate release layer with the other layer as extended-release or conventional release.

TECHNIQUES OF BILAYER TABLETS

1) OROS® push pull technology:- This system consists of mainly two or three layers among which the one or more layer is essential of the drug and other layer are consist of push layer. The drug layer mainly consists of drugs a long with two or more different agents. So this drug layer comprises of a drug which is poorly soluble form. There is a further addition to suspending agent and osmotic agent. A semipermeable membrane surrounds the tablet core.

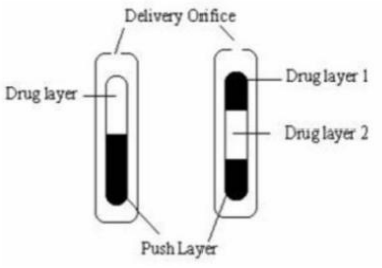


Fig. 2: OROS® Push Pulls Technology

2) L-ORO time technology:- This system is used for the solubility issue also developed the L-OROS system a lipid soft gel product containing a drug in a dissolved state is initially manufactured and then coated with a barrier membrane, than osmotic push layer and then a semi-permeable membrane, drilled with an exit orifice.

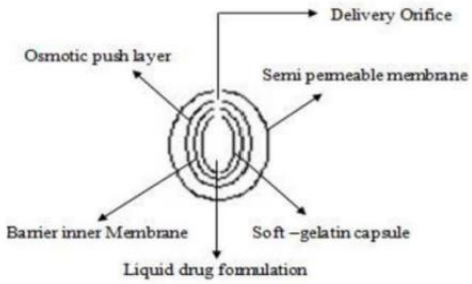


Fig 3: L-ORO Time Technology

3) ENSOTROL technology Solubility enhancement of an order of magnitude or creates optimized dosage forms hire laboratory to use an integrated approach to drug delivery, focusing on identification and incorporation of the identified enhancer into controlled release technologies.

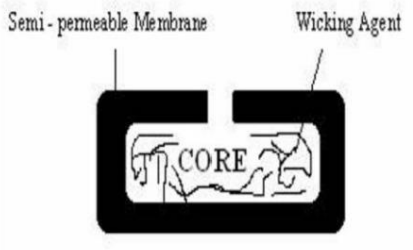


Fig.4: ENSOTROL Technology

4) DUROS Technology The system consists of an outer cylindrical titanium alloy reservoir. This reservoir has high impact strength and protects the drug molecules from enzymes. The

DUROS technology is the miniature drug dispensing system that opposes a miniature syringe and regions minute quantity of concentrated form in continuing and consistent from over months or years.

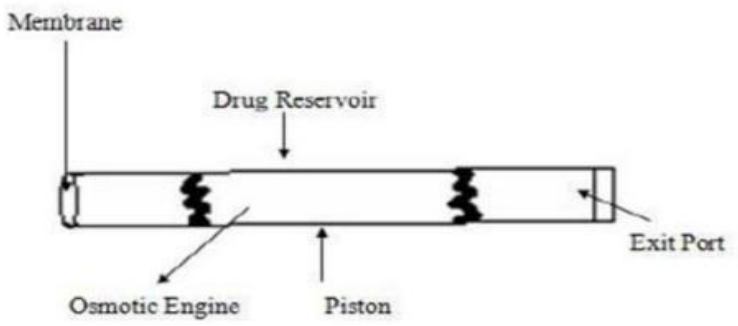


Fig.5: DURO Technology

5Elan Drug. Technologies Dual Release Drug Delivery System

DUREDAS™ Technology is a bilayer tablet that can provide immediate or sustained release of two drugs or different release rates of the same drug in one dosage form. The tableting process can provide an immediate release granulate and a modified release hydrophilic matrix, complex as separate layers with in one tablet. The modified-release properties of the dosage form are provided by a combination of hydrophilic polymers.

Benefits:-

Bilayer tableting technology.

Tailored release rate of two drug Components.

Capability for immediate release and modified release components in one tablet.

Unit dose tablet.

Evaluation of Bilayer Tablet

1) General Appearance:- The general appearance of a tablet, its visual identity and overall elegance is essential for consumer acceptance. Includes in are tablets size, shape, color, presence or absence of an odor, taste, surface texture, physical flaws and consistency and legibility of any identifying marking.

2) Size and Shape:- The size and shape of the tablet can be dimensionally described monitored and controlled.

3) Tablet thickness:- Tablet thickness is an important characteristic in reproducing appearance and also in counting by using filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Ten tablets were taken and their thickness was recorded using a micrometer.

4) Weight variation:- Standard procedures are followed as described in the official books.

5) Friability:- Friction and shock are the forces that most often cause the tablets to chip, chop or break. The friability test is closely related to tablet hardness and is designed to evaluate the ability of the tablet to with stand abrasion in packaging, handling and shipping. It is usually measured by the use of the Roche friabilator. A number of tablets are weighed and placed in the apparatus where they are exposed to rolling and repeated shocks as they fall 6inches in each turn within the apparatus. After four minutes of this treatment or 100 revolutions, the tablets are weighed and the weight is compared with the initial weight. The loss due to abrasion is a measure of the tablet friability. The value is expressed as a percentage. A maximum weight loss of not more than 1% of the weight of the tablets being tested during the friability test is considered generally acceptable and any broken or smashed tablets are not picked up. Normally, when capping occurs, friability values are not calculated. A thick tablet may have fewer tendencies to cap as thin tablets of large diameter, often show extensive cupping, thus indicating that tablets with greater thickness have reduced internal stress the loss in the weight of the tablet is the measure of variability and is expressed in percentage as:

%Friability=1-(loss in weight/Initial weight)X100

6) Hardness:- The resistance of tablets to capping, abrasion or breakage under conditions of storage, transportation and handling before usage depends on their hardness. The small and portable hardness tester was manufactured and introduced by Monsanto in the Mid 1930s. It is now designated as either the Monsanto or Stokes hardness tester. The instrument measures the force required to break the tablet when the force generated by a coil spring is applied diametrically to the tablet. The strong-Cobb Pfizer and Schleuniger apparatus which were later introduced measures the diametrically applied force required to break the tablet. Hardness, which is now more appropriately called crushing strength determinations are made during tablet production and are used to determine the need for pressure adjustment on tablet

machine. If the tablet is too hard, it may not disintegrate in the required period of time to meet the dissolution specifications, if it is too soft, it may not be able to withstand handling during subsequent processing such as coating or packaging and shipping operations. The force required to break the tablet is measured in kilograms and a crushing strength of 4 kg is usually considered to be the minimum for satisfactory tablets. Oral tablets normally have a hardness of 4to10 kg however, hypodermic and chewable tablets are usually much softer (3kg) and some sustained release tablets are much harder(10- 20kg). Tablet hardness has been associated with other tablet properties such as density and porosity. Hardness generally increases with normals to a rage of tablets and depends on the shape, chemical properties, binding agent and pressure applied during compression.

7) Stability Study:- The bilayer tablets are packed in suitable packaging and stored under the following conditions for a period as prescribed by ICH guideline for accelerated studies. The tablets were withdrawn after a period of 15days and analysed for physical characterizations Visualdefects, Hardness, Friability and Dissolution and drug content. The data obtained is fitted into first or derequations to determine the kinetics of degradation. Accelerated stability data are plotted according Arrhenius equation to determine the shelf life at 25°C.

CONCLUSION

Bilayer tablet is improved beneficial technology to overcome the short coming of the single layered tablet. There are various application of the bilayer tablet, it consist of monolithic partially coated or multilayered matrices. Bilayer tablet is suitable for sequential release of two drugs in combination, separating two incompatible substances and also for sustained-release tablet in which one layer is immediate release as initial dose and the second layer is the maintenance dose. The preparation of tablets in the form of multilayer is used to provide systems for the administration of drugs, which are incompatible and to provide control release tablet preparations by providing surrounding or multiple swelling layers. Bilayer tablet quality and GMP requirements can vary widely. This explains why many different types of presses are being used to produce bilayer tablets, ranging from simple single-sided presses to highly sophisticated machines.

REFERENCES

1. Mohideen S and Satyanarayana T. Development and evaluation of two layered tablet of glimepiride and metformin hydrochloride for the treatment of hyperglycemia. Inter JBio Pharma. 2011;2(1):31-35.

2. Yadav A and Jain DK. Formulation development and in vitro characterization of player and floating IJPCBS 2015, 5(3), 510-516 Raveendra Babu et al . ISSN: 2249-9504 516 bioadhesive tablets of propranolol hydrochloride. Asia J Phar Life Scie.2011;1(1):2.
3. Dey S and Chatto PS. Formulation and evaluation of fixed-dose combination of bilayer gastro retentive matrix tablet containing atorvastatin as fast release and atenolol as sustained release. BiomedRes Inter. 2014;10(1155):396106.
4. Banu H and Sahariar MR. Formulation development of bi-layer acetaminophen tablets for extended drug release.J Chem Pharm Res.2011;3(6):348-360.
5. Solanki PD. Formulation evaluation and optimization of bilayer floating tablet of repaglinide and glipizide. Inter J Pharm Rese Schoc.2012;1(3):123-134.
6. Sadhana RS and Vidya MM. Development and evaluation of bilayer floating tablets of diltiazem HCl. Inter J Pharm Pharm Scien.2014;6(2):62-65.
7. Sharma V, Nagpal M, Jain UK, Mangotia A and Kumar R. Antidiabetic drug and combination therapy. ARPB. 2013;3(2):389-394.
8. Ali SH and Reddy BR. Formulation and evaluation of bilayer tablet of atorvastatin and pioglitazone for metabolic disorder. IAJPS. 2014;1(6):448-455.
9. Balaji G, Prakash GK, Suresh K and Venkatesh B. Bilayer tablet are view. IJRRPAS. 2013;3(4):488-506.
10. Pranjal KS and Sanjoo K. Bilayer and floating bioadhesive tablets. J Drug Deliv Thera. 2011;1(1):32-35.
11. Kulkarni A and Bhatia M. Development and evaluation of bilayer floating tablets of atenolol and lovastatin for biphasic release profile. Iran J Pharm Res. 2009;8(1):15-25.
12. Gattani SG, Khabiya SS, Amrutkar JR and KushareSS. Formulation and evaluation of bilayer tablets of metoclopramide hydrochloride and diclofenac sodium. P DAJ Pharm Scien Technol. 2012;66(2):151-60.
13. Reddy RK and SrinivasN. Formulation and evaluation of bilayered tablets of losartan potassium. IP. 2014;2(1):312-320.
14. Prakash VK and Shankar UB. Formulations and evaluation of ibuprofen floating tablets. IJPCBS. 2012;2(4):47-481.
15. Sandeep N and GuptaMM. Immediate drug release dosage form a review. JDDT. 2013;3(2):155-161.
16. Pateriya A, Bhowmick M, Pandey GK, Joshi A and Dubey BR. Formulation and evaluation of player tablets of candesartan and hydrochlorothiazide for the treatment of hypertension. JDDT. 2013;3(6):21-35.
17. Kumar HG, Jaganathan K, Kumar SR and Peruma lP. Formulation and invitro evaluation of bilayer floating tablets of metformin hydrochloride and sitagliptin phosphate. Intern J Pharma Resea. 2013;5(1):53-59.
18. Kumar HA, Kavitha K,Kumar SA,Kumar RM and Singh JSD. Novel approaches of bilayer tablet technology are view. IJPCBS. 2013;3(3):887-893.
19. Sahota R, Singh G, Mankoo P, Kaur R, Singh S, Nagpal M, Upendra K and JainUK, Shelly KS and Sharma M. Development and characterization of bilayer tablets containing metformin hydrochloride sustained release layer and atorvastatin calcium in the immediate release layer. IPP. 2013;1(3):220-229.
20. Chaudhari S, Bawaskar M and Shirsat A. Formulation and evaluation of player floating tablet of carvedilol phosphate. JDDT. 2012;2(5):9-19.
21. Indian Pharmacopoeia. The Controller of Publication, Delhi. 1996; 2: 735. 22. Lachman L, Liberman H and Kanig J.The theory and practice of industrial pharmacy. Varghese Publishing House, Mumbai. 1987; 3rd Edn:297.