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A Brief Review of Bilayer Tablet Technology: A Concept of Immediate and Sustained Drug Delivery

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Abstract
According to the literature review of the design of bilayer tablets are suitable for sequential release of two drug in which one layer is immediate release layer and the second layer is sustained release layer. Bilayer tablets have been development to achieve immediate and sustained delivery of different drugs with pre-defined release profile. Developing a combination of two or more Active Pharmaceutical Ingredients (API) in a single fixed dosage form has increase in the pharmaceutical industry, promoting patients convenience and compliance.

Keywords
Bilayer tablet, formulation, Analytical studies.

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INTRODUCTION
Bilayer Tablet is the novel technology for the development of controlled release Formulation. Developing a combination of two or more Active Pharmaceutical Ingredients (API) in a single dosage form is known as a bilayer tablet.

Now a days the use of bilayered tablets has been increased. Various developed and developing countries move towards a combination therapy for treatment of various diseases and disorders requiring long term therapy such as diabetes. Over 90% of the formation manufactured today ingested orally.

Bilayer tablet is the newer Dosage form for the successful development of controlled release formulation and better than the traditionally used dosage forms. Bilayer tablets is suitable for 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 layer is maintenance dose. In certain cases, bilayered tablet have two sustain release layers of different drugs.

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Oral route is the most commonly employed route of drug administration. Although different route of administration is used for the delivery of drugs, oral route remains the preferred mode. The popularity of the oral route is attributed patient acceptance, ease of administration, accurate dosing, cost effective

manufacturing method and generally improved shelf-life of the product. (01)

Even for sustained release systems the oral route of administration has been investigated the most, because of flexibility in dosage forms design that the oral route offers [1]. With many drugs, the basic goal of therapy is to achieve a steady-state blood level or tissue level that is therapeutically effective and non toxic for an extended period of time [2].

Bi-layer tablet concept has long been utilized to develop sustained released formulation. Such tablet has a fast releasing layer and may contain one (bi layer), to sustain the drug release. The pharmacokinetic advantage relies on the criterion that, drug release from the fast releasing layer leads to a sudden rise in the blood concentration. However, the blood level is maintained at steady state as the release from sustaining layer [3]. Extrapancreatic effects also may play a part in the mechanism of action of oral sulfonylurea hypoglycaemic drugs. [4]

ADVANTAGES AND DISADVANTAGES

Advantage [1,2,3]

- ❖ They are used as an extension of a conventional technology.
- ❖ Potential use of single entity feed granules.
- ❖ Separation of incompatible components
- ❖ Patients compliance is enhanced leading to improve drug regimen efficacy.
- ❖ Patient compliance is improved because fewer daily doses are required compared to traditional delivery system.
- ❖ Maintain physical and chemical stability.
- ❖ Retain potency and ensure dose accuracy.

Disadvantage [5,7]

- ❖ Adds complexity and bilayer rotary presses are expensive
- ❖ Insufficient hardnes,layer separation reduce yield
- ❖ Inaccurate individual layer weight control
- ❖ Cross contamination between the layer

APPLICATION [9,8]

- ❖ Bilayer tablet is suitable for sequential release of two drug in combination.
- ❖ Separate two incompatible substances.
- ❖ 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 layer tablet.
- ❖ Bilayer tablet are used to deliver the loading dose and sustained dose of the same or different drugs.
- ❖ Bilayer tablets are used for bilayer floating tablets in which one layer is floating layer another one is immediate release layer of the drug.
- ❖ Bilayer tablets are used to deliver the two different drugs having different release profiles.

NEED OF BILAYER TABLETS [5,9]

- ❖ For the administration of fixed dose combination of different API prolong the drug product life cycle buccal/mucoadhesive delivery system; fabricate novel drug delivery systems such as chewing device and floating tablets for gastro-retentive drug delivery
- ❖ Controlling the delivery rate of either single or two different active pharmaceutical ingredients.
- ❖ To modify the total surface available for API layer either by sandwiching with one or two in active layers in order to achieve swellable/erodible barriers for modified release.
- ❖ To separate incompatible 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 (such as osmotic property.

IDEAL CHARACTERISTICS [6,9]

- ❖ It should be elegant & free from chipping, cracking, discoloration and contamination [6].
- ❖ It ought to have adequate quality to with stand mechanical shock during its tablet formulation process [9].

TYPE OF BILAYER TABLETS [9,13]

- ❖ Single side tablet press
- ❖ Double sided tablet press
- ❖ Bilayer tablet press with displacement monitoring

SINGLE SIDE TABLET PRESS

The simplest design in a single sided press with both chamber of the doublet feeder separated from each other. Each chamber is gravity or forced fed with different powers, thus producing the two individual layers of the tablets. When the die passes under the feeder, it is at first loaded with the first layer powder

followed by the second layer powder. Then the entire tablet is compressed in one or two steps.

Limitation of single sided press

- ❖ No weight monitoring/control of the individual layers
- ❖ No distinct visual separation between the two layers
- ❖ Very short first layer dwell time due to the small compression roller, possibly resulting in poor de-aeration, capping, and hardness problems.

DOUBLE SIDED TABLET PRESS

Most double-sided tablet presses with automated production control use compression force to monitor and control tablet weight. The effective each compression force exerted on each individual tablet or layer is force is the by the control system at the main compression of the layer. This measured peak compression force is the signal used by the control system to reject out of tolerance tablets and correct the die fill depth when required.

BILAYER TABLET PRESS WITH DISPLACEMENT MONITORING

The displacement tablet weight control principle is fundamentally different from the principle based upon compression force. When measuring displacement, the control. System sensitivity does not depend on the tablet weight but depends on the applied pre-compression force.

VARIOUS STEPS INVOLVED IN THE BILAYER TABLET FORMULATION ARE AS FOLLOWS [14,15,16]

- ❖ Filling of first layer
- ❖ Compression of first layer
- ❖ Ejection of upper punch
- ❖ Filling of second layer
- ❖ Compression of second layer
- ❖ Ejected fully bilayer tablet

EVALUATION OF BILAYER TABLETS [9,10]

GENERAL APPEARANCE

The general appearance of tablets is visual identity and overall elegance is essential for consumer acceptance for the production process.

SIZE AND SHAPE

The shape and dimensions of compressed tablets are determined by the type routing during the compression process.

THICKNESS AND DIAMETER

The diameter of the tablets is determined. Thickness and diameter of tablets were important for uniformity of tablet size. Thickness and diameter were measured using venire caliper.

WEIGHT VARIATION TEST

For weight variation test, twenty tablets are selected randomly, and the average weight is calculated there after the weight variance is calculated and weight variation is compared with IP standard. Twenty tablets were selected at random and the average weight was calculated. Weight Variation was calculated and was compared with I. P. standards (Singh and Kim., 2000).

FRIABILITY

Friability will be measured by taking randomly 10 tablet which is weighed and placed in a friabulator and rotated at 25 rpm for a period of 4 minutes after resolution the tablets can be dusted and weighed. Friability is the measure of tablet strength. Electrolab EF2 friabilator (USP) was used for testing the friability using the following procedure. Twenty tablets were weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution. After 4 min, the tablets were weighed and the percentage loss in tablet weight was determined.

% loss = [(Initial wt. of tablets – Final wt. of tablets)/ Initial wt. of tablets] ×100

HARDNESS

The hardness of the tablet will be carved out using Monsanto type hardness tester. The hardness of the tablet is measured in kg/cm^2. The resistance of tablets to shipping or breakage under conditions of storage, transportation and handling before usage depends on its hardness. The hardness of tablet of each formulation was measured by Monsanto hardness tester.

***IN VITRO* DISSOLUTION STUDIES**

The bilayer formulation is subjected to invitro drug release studies in simulate gastric and intestinal fluids to assess their ability in providing the desired controlled drug delivery. Bilayer tablets were subjected to in vitro drug release studies in simulated gastric and intestinal fluids to assess their ability in providing the desired controlled drug delivery. Drug release studies were carried out using USP dissolution test apparatus I at 100 rpm, 37±0.5°C, and pH 1.2 buffer (900 ml) (i.e. 0.1 N HCl) for 2 hours, since the average gastric emptying time is about 2 hours. The dissolution medium was replaced with pH 6.8 phosphate buffer (900ml) and experiment continued for another 10 hours. At different time intervals, 5ml of the samples were withdrawn and replaced with 5ml of drug-free dissolution medium.

The samples withdrawn were analyzed by UV spectrophotometer using multi component mode of analysis (Atram et al., 2009).

STABILITY STUDIES (ICH Geneva 2003)

Stability study of the bilayer tablet can be evaluated as per ICH guideline Q1C. The optimized formulation was subjected for two-month stability study according to ICH guidelines. The selected formulations were packed in aluminium foils, which were in wide mouth bottles closed tightly. They were then stored at Room Temperature 40ºC / 75% RH for 2 months and evaluated for their permeation study.

CONCLUSION [6,9]

Bilayer Tablets often an excellent opportunity for manufacturers to separate themselves from their competitors, improve their products efficacy and protect against impersonator product. Bilayer layer tablets have been consisting of two layers which is slow release and immediate release of the drug, with the aim of reaching a sign serum concentration in a short period of time. Now a day,s bilayer tablets are prepared. Bilayer tablet is improved beneficial technology to overcome the shortcoming of the single layered tablet. There is various application of the bi-layer tablet it consists of monolithic partially coated or multilayered Matrices. Bilayer tablet is suitable for sequential release of two drugs in combination, separate two incompatible substances and also for sustained release tablet in which one Layer is immediate release as initial dose and second layer is maintenance dose. The preparation of tablets in the form of multi layers is used to provide systems for the administration of drugs, which are incompatible and to provide controlled release tablet preparations by providing surrounding or multiple swelling layers. Bilayer tablet quality and GMP-requirements can vary widely.

REFERENCES

1. Atram SC, Udavant YK, Salunke RJ, Neb GB, Shahi SR, Gulecha BS, Padalkar AN. Formulation and evaluation of bilayer tablet containing Metoprolol succinate and Amlodipine besylate as a model drug for anti-hypertensive therapy. J Pharm Res 2009;2(8):1335-47.
2. Shukla A, Bansal S and Mishra MK: Formulation and evaluation of mucoadhesive buccal tablets of glipizide, research article. International Journal of Pharmaceutical Science Letter 2015; 5 (6): 636-643.
3. Sandhan S, Sapra K and More J: Formulation and evaluation of sustained release matrix tablets, original research article. International Journal of Pharmceutical and Biological Research 2013; 1(4): 89-94.
4. Mandal U, Gowda VK, Ghosh A and Selvan PS, Sam Solomon VD, Pal TK: Development of dissolution medium. Asian Journal of Chemistry 2008; 20 (4): 2651-2656
5. Venkateswarlu K and Shanthi A: Formulation and evaluation of sustained release matrix. Journal of Pharmaceutical and Biological Science 2012; 5(2): 17-23.
6. Radhika PR, Pal TK and Sivakumar T: Formulation and evaluation of sustained release matrix tablets, original article. Iranian Journal of Pharmaceutical Science 2009; 5(3): 205-214.
7. Lakshmana-Murthy G, Hareesha CH, Gargei P and Nanthiswaran S: Drug release and swelling kinetic studies sustained release matrix tablets, original review. International Journal of Pharmaceutical and Industrial Research 2011; 1(1): 43-50.
8. Badugu LR and Gunti R: Estimation in commercial drugs by RP-HPLC, research article. International Journal of Atoms and Molecules, 2012; 2(1): 103-108.
9. Goyal S, Gupta A, Bhatt N and Rani R: Development and validation of RP-HPLC method for estimation in bulk drug and pharmaceutical formulation. International Journal of Pharmaceutical Technology and Research 2013; 5(1): 183-188.
10. Atif M, Khalid SH, Kit GL, Sulaiman SS and Chandersekaran A: Development and validation of RP-HPLC method. Journal of Young Pharmacists 2013; 5: 26-29.
11. Momin JG, Dubey S, Nayak N and Kumar H: Development and validation of HPLC method for the estimation in pharmaceutical dosage forms, Research Article. International Journal of Applied Pharmaceutical and Biological Research 2016; 1(2): 87-91.
12. Atif M, Ahmad M, Qamar UZ, Syed AS, Asrul AS, Usman M and Najam US: pharmacokinetics in healthy and diabetic volunteers, research article. Tropical Journal of Pharmaceutical Research 2011; 10 (2): 147-152.
13. Dhawan S and Singla AK: Performance liquid chromatographic analysis: application to *in-vitro* and *in-vivo* Journal of Chromatographic Science 2003; 41: 295-300.
14. Review of Literature: development and validation of LC method for the estimation in pharmaceutical dosage form and serum.
15. Shaikh R and Karigar A: Reverse phase high performance liquid chromatography method for analysis of glipizide in pharmaceutical dossage forms, research article. International Journal of Research in Aurvedic Pharmacy 2010; 1(2): 455-458
16. Lahoti SR, Puranik PK, Heda AA and Navale RB: Development and validation of RP-HPLC method for analysis in guinea pig plasma and its application to pharmacokinetic study. a review, International Journal of Pharmaceutical Technology and Research 2010; 2(3): 1649-165.

17. Review of Literature: development and validation of LC method for the estimation of in pharmaceutical dosage form and serum.
18. Shaikh R and Karigar A: Reverse phase high performance liquid chromatography method for analysis of glipizide in pharmaceutical dossage forms, research article. International Journal of Research in Aurvedic Pharmacy 2010; 1(2): 455-458
19. Lahoti SR, Puranik PK, Heda AA and Navale RB: Development and validation of RP-HPLC method for analysis of glipizide in guinea pig plasma and its application to pharmacokinetic study. a review, International Journal of Pharmaceutical Technology and Research 2010; 2(3): 1649-165.