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Implementation of Quality of Design for the Development of Bilayer Tablet

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Abstract: *Different drug release properties for different drugs contained in each layer of a bilayer tablet are rarely achievable with regular tablets. Additionally, these tablets help avoid physicochemical incompatibilities between medications and excipients. The successful production of such more complicated dosage forms depends on screening the material qualities of APIs and excipients and optimizing the processing parameters of each unit operations of the manufacturing process. In order to meet safety and efficacy regulations, these operations need to be properly monitored and managed to produce a drug product with acceptable quality and performance. Blending, granulation, pre-compression, and main compression are critical stages when formulation qualities and production processes should be tuned to avoid problems like weight variation, segregation, and delamination of particular components. Bilayer tablets, as opposed to ordinary tablets, offer distinct drug release properties for certain medications that are housed in each layer. These tablets also help to avoid physicochemical incompatibilities between drugs and excipients. The successful manufacturing of such more complex dosage forms depends on screening the material attributes of API and excipients and optimizing the processing parameters of individual unit operations of the manufacturing process in order to achieve safon of layers, which is frequently encountered during the production of bilayer tablets. For the quality and performance of the medication product to be acceptable, these processes need to be properly watched over and managed. The main objective of this review is to establish the foundation for implementing the Quality by Design (QbD).*

Keywords: Optimized formulation , Layered manufacturing , Quality by design

I. INTRODUCTION

Now a days various developed and developing countries move towards a combination therapy for 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 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 better than the traditionally used dosage form.[1]

Because they circumvent the problem of drug physicochemical incompatibilities and provide unique drug rele ase profiles for each drug contained in the bilayer tablet us individual layer, bilayer tablets are thought to be a mong the best options for developing fixed-dose combination (FDC) formulations (Janczura et al., 2022; Singh et al., 2019; Won et al., 2021).

Bilayer tablets can provide unique product performance in terms of drug delivery and patient compliance sinc e they are thought to be one of the possibilities to address the oral delivery concerns of drugs, such as those fo und with conventional or matrix tablets. A bilayer tablet is necessary when prompt drug release is needed. When quick drug release is required to reduce the symptoms of illnesses such as inflammation and hypertension while maintaining the appropriate medicine blood level during the intended extended administration interv al, a bilayer tablet is necessary (Dey et al., 2012).

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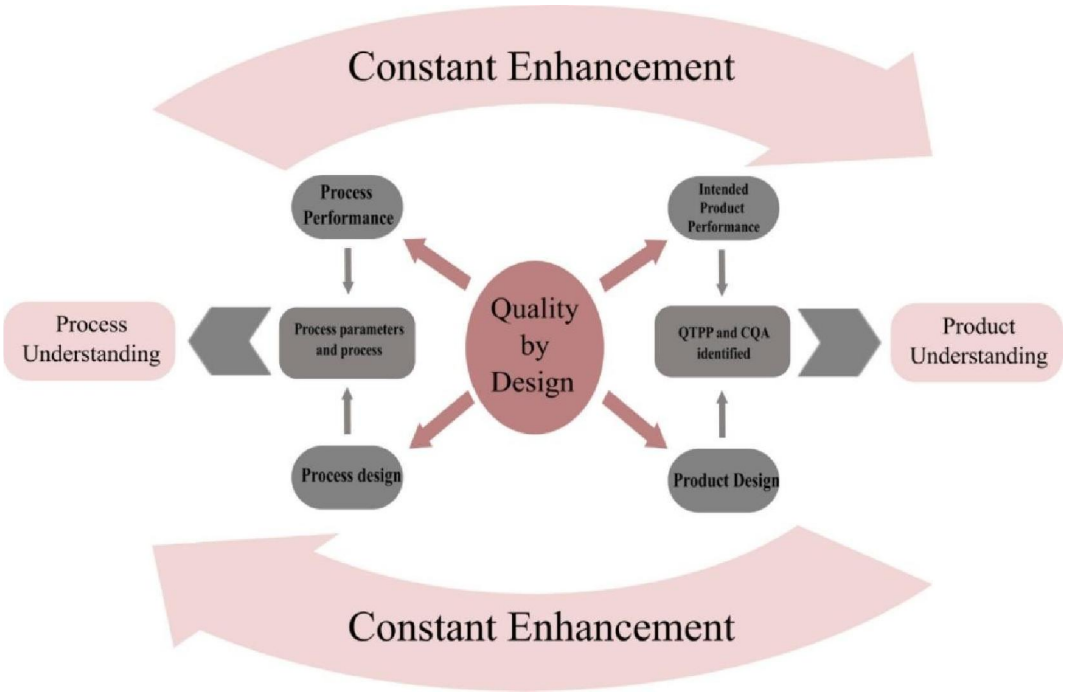
When compared to conventional tablets, bilayer tablets are anticipated to encounter a new set of challenges in terms of formulation, manufacturing parameter controls, and product performance requirements (Vaithiyalinga m and Sayeed, 2010).

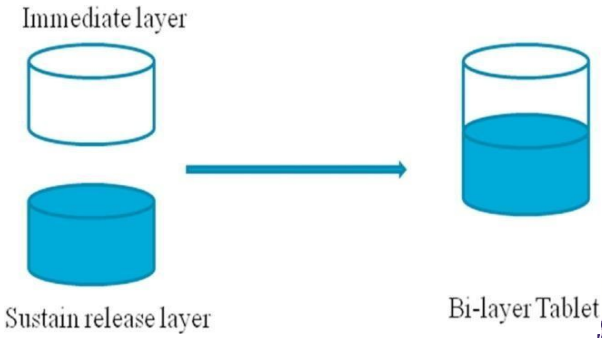
Quality by Testing (QbT) formulation development ensures the quality of the drug product only after analytica l testing in a quality control laboratory, but it is not assured throughout the design and development phase itsel f.

The Quality by Design (QbD) concept has been embraced by pharmaceutical development as a systematic app roach to strategy, offering several advantages when quick medication release is required to reduce the sympto ms of diseases including inflammation and hypertension.



Difference between bilayer and normal tablet

Normal tablet	Bilayer tablet
1. Design: single layer, immediate release 2. Release mechanism- immediate release of active ingredient 3. Short duration 4. Low Production Cost	1. Design: two layer each with the different release profile 2. Release mechanism: sustained release And immediate - release layer. 3. Prolong drug release 4. High Production Cost



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Classification of bilayer tablet

Based on Release Mechanism:

- Immediate Release Bilayer Tablets: Designed to release the active ingredient quickly.
- Sustained Release Bilayer Tablets: Formulated to release the drug over an extended period.
- Delayed Release Bilayer Tablets: Release the drug after a specific time delay, often using enteric coatings

Based on Composition:

- Single Active Ingredient: Contains one active pharmaceutical ingredient (API) in both layers.
- Multiple Active Ingredients: Contains different APIs in each layer, allowing for combination therapy

Mechanism of bilayer tablet :-

Layer Composition:

- Immediate Release Layer: Usually contains a fast-dissolving excipient, allowing for rapid release of the drug.
- Sustained Release Layer: Formulated with slower-dissolving materials, controlling the rate of drug release over time.

Layering Process:

- The two layers are compressed together, often using specialized tablet presses designed for bilayer formulations.

Drug Release:

- Upon ingestion, the immediate release layer dissolves quickly, providing a rapid therapeutic effect.
- The sustained release layer then gradually releases the remaining drug, maintaining its therapeutic effects over a long period

Plan of work :

1. Literature review

2. Collect necessary solvent and reagent ,chemical, materials needed for experimentation

3. Formulation of bilayer tablet :

Step 1: Weighing and Dispensing (Time: 30 minutes)

1. Weigh API 1 (immediate release) and API 2 (sustained release).
2. Dispense excipients (diluents, binders, disintegrants, lubricants) for Layer 1 and Layer 2.
3. Record weights and verify against batch record.

Step 2: Mixing (Time: 30 minutes)

1. Mix Layer 1 ingredients (API 1, diluent, binder, disintegrant) in V-blender.
2. Mix Layer 2 ingredients (API 2, matrix former, diluent, binder) in separate V-blender.
3. Verify mix uniformity.

Step 3: Granulation (Time: 2 hours)

1. Granulate Layer 1 mixture using high-shear granulator.
2. Granulate Layer 2 mixture using high-shear granulator.
3. Verify granule size and density.

Step 4: Milling (Time: 1 hour)

1. Mill Layer 1 granules to desired particle size.
2. Mill Layer 2 granules to desired particle size.
3. Verify particle size distribution.

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Step 5: Compression - Layer 1 (Time: 2 hours)

1. Load Layer 1 mixture into tablet press.
2. Compress Layer 1 using rotary or single-punch press.
3. Verify tablet thickness and hardness.

Step 6: Compression - Layer 2 (Time: 2 hours)

1. Load Layer 2 mixture on top of Layer 1.
2. Compress both layers together using rotary or single-punch press.
3. Verify tablet thickness and hardness.

Step 7: Coating (Optional) (Time: 2 hours)

1. Prepare coating solution.
2. Load tablets into coating pan.
3. Apply coating using spray or dip coating.

Step 8: Drying (Time: 2 hours)

1. Dry coated tablets in tray or fluid-bed dryer.
2. Verify moisture content.

Step 9: Quality Control (Time: 2 hours)

1. Assay (API content).
2. Dissolution (release rate).
3. Hardness.
4. Friability.
5. Uniformity of dosage units.
6. Stability (shelf-life).

Step 10: Packaging (Time: 1 hour)

1. Package tablets in blister packs or bottles.
2. Label and package inserts.

Evaluation test for bilayer tablet :

Physical Inspection

Appearance: Check for uniformity in size, shape, and color. Surface Texture: Look for any defects like cracks or chips.

Thickness and Diameter Measurement

Use a calibrated micrometer to measure thickness and diameter, ensuring consistency across the batch.

Hardness Testing

Employ a hardness tester (e.g., Monsanto or Strong-Cobb) to determine the tablet's mechanical strength.

Friability Test

Use a friabilator to assess the tablet's resistance to abrasion. A loss of weight under 1% is typically acceptable.

Disintegration Test

Measure the time taken for the tablet to disintegrate in a specified fluid (usually water or stimulate gastric fluid)

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Dissolution Test

Conduct dissolution testing to evaluate the release profile of the active ingredients over time. Use appropriate media and conditions.

Factor affecting on bilayer tablet

1. Material Selection: Choice of excipients (binders, disintegrants, lubricants) can impact the tablet's mechanical properties and release profile.
2. Compression Force: The pressure applied during tablet compression affects hardness, dissolution rates, and overall stability.
3. Layer Thickness: Variation in layer thickness can affect drug release and tablet integrity.
4. Moisture Content: The presence of moisture can influence stability and dissolution rates.
5. Granulation Method: Whether wet or dry granulation is used can affect the homogeneity and flow properties of the powder blend.
6. Coating : If a coating is applied, its material and thickness will also impact release characteristics.
7. Storage Conditions: Temperature and humidity during storage can affect the tablet stability and efficiency

II. CONCLUSION

Bilayer tablets represent a significant advancement in pharmaceutical formulation, allowing for the controlled release of multiple active ingredients. Their design enables distinct release profiles, improving therapeutic efficacy and patient compliance. The bilayer structure facilitates the combination of immediate and sustained-release mechanisms, catering to diverse treatment needs. Overall, bilayer tablets offer a promising approach to enhancing drug delivery systems, optimizing performance, and addressing specific therapeutic goals

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 Pharama . 2011;2(1):31-35.
[2]. Yadav A and Jain DK. Formulation development and in vitro characterization of player and floating [10/16, 8:44 PM] Bala: bioadhesive tablets of propranolol hydrochloride. Asia J Phar Life Scie.2011;1(1):2.
[3]. Dey S and Chatto PS. Formulation and evaluation o 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 diltiazemhcl. 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] Aulton ME. 2nd ed. London: Churchill Livingstone; 2002. Aulton's Pharmaceutics: The Design and Manufacture of Medicines; pp. 397–441. [Google Scholar]
[9]. Sanghavi S, Polara M, Patel J, Shah N. Bilayer tablets — A review on state of art. Res J Pharm Dosage Forms Tech. 2012;04:160–6. [Google Scholar]
[10].Despande RD, Gowda DV. Bilayer tablets-An emerging trend: A review. Int J Pharm Sci. 2011;2:2534–44.
[11].Remya PN, Damodharan N. Formulation and evaluation of bilayered tablets of Ibuprofen and methocarbamol. Int J PharmTech Res 2010;2:1250-5.
[12]. Karthikeyan D, Karthikeyan M. Effect of different viscosity grades of HPMC on drug Release profi le. J Pharm Res 2008;1:23-8.
[13].Enayatifard R, Saeedi M, Akbari J, Tabatabaee YH. Effect of hydroxypropyl methylcellulose and ethyl cellulose content on release profi le and kinetics of diltiazem HCl from matrices. Trop J PharR2009;8:42532.

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[14]. Phillips SJ, Whisnant JP. Hypertension and stroke. In: Laragh JH, Brenner BM, editors. Hypertension: Pathophysiology, Diagnosis, and Management. 2nd ed. New York: Raven Press; 1995. p. 465-78.
[15]. Florey K. Analytical Profi les of Drug Substances. 1st ed. Vol. 10. Philadelphia: Academic Press, An Imprint of Elsevier; 2005. p. 405-43.