

REVIEW ON VARIOUS ASPECTS OF GASTRORETENTIVE BILAYER FLOATING TABLET

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ABSTRACT

Floating Bi-layer tablets have been developed to achieve controlled delivery of different drugs with pre-defined release profiles. In the last decade, interest in developing a combination of two or more Active Pharmaceutical Ingredients (API) in a single dosage form has increased in the pharmaceutical industry, promoting patient convenience and compliance. GRDDS prolongs the retention time of dosage forms in the stomach or upper gastrointestinal tract, as to improve solubility, bioavailability and the therapeutic efficacy of the drugs. 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. Bilayer floating tablets offer definite advantages

over conventional release formulation of the same drug. This article explains ideal characteristics advantage, disadvantage, types and evaluations parameter of Gastroretentive bilayer floating tablets.

KEYWORDS: Bi layer, Gastroretentive, Tablets, Immediate Release, Evaluations etc.

INTRODUCTION

In recent era developed and developing countries are moving towards combination therapy for treatment of various diseases and disorders requiring long term therapy such as hypertension, Diabetes and Rheumatoid arthritics. The problem of dose dependent side effects is minimized by combination therapies and is advantageous over monotherapy In the last decade, interest in developing a combination of two or more Active Pharmaceutical Ingredients (API) in a single dosage form (bi-layer tablet) has increased in the pharmaceutical industry, promoting patient convenience and compliance.^[1]

Bilayer tablet have most advantages as compare to convetional single layer tablet. for instance, bilayer tablet are commonly used to avoid chemical incompatibility of formulation component by physical separation. In addition Such type of tablet inabled the development of controlled delivery of API'S with pre-determined release profile by combining layer with various release pattern, or combining slow –release with immediate-release layer. Bilayer tablet is suitable for sequential release of two drugs in combination, separate two incompatible substance and also for sustaine release tablet in which one layer is immediate release as a initial dose and second layer is maintenance dose. Gastroretentive drug delivery is prepared with the intention to retain drug in the gastric region for prolonged time and release incorporated drug candidates and thereby enable sustained and prolonged input of the drug to the upper part of the GIT thus leading its optimal bioavailability.^[1,2]

Gastroretentive dosage forms greatly improved the pharmacotherapy of the GIT through local drug release, leading to high drug concentrations at the gastric mucosa making it possible to treat various diseases of GI. Now days researcher are much for focusing on gastroretentive bilyer tablets. A variety of dosage forms like tablets,bilyer trilyer,thiolated tablets, patches, micropshres, pelletes, micro-particles, beads, floating ring capsule in situ gel etc have been developed for enhancing the performance attributes in the gastrointestinal drug delivery.^[3,4]

Suitable candidates for Gastroretentive bilayer floating tablet

1. Drugs that degrade in the colon, e.g., Ranitidine HCl and Metronidazole.
2. Drugs those are locally active in the stomach (e.g. misroprosol, antacids).
3. Drugs that have narrow absorption window in GIT (furosemide, riboflavin).
4. Drugs that disturb normal colonic bacteria, e.g., amoxicillin trihydrate
5. Drugs absorbed from stomach and upper part of GI-Tract, e.g., calcium supplements, chlordiazepoxide and cinnarazine.^[5,6,7]

Ideal characteristics Gastroretentive bilayer floating tablet

1. A bi-layer tablet should have elegant product identity.
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.
4. They should be free from visual defects.

5. The bi-layer tablet must be able to release the medicinal agents in a predictable and reproducible manner.
6. It must have a chemical stability shelflife, so as not to follow alteration of the medicinal agents.^[8,9]

Advantages Gastroretentive bilayer floating tablet

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. Bi-layer execution with optional single layer conversion kit.
3. Low cost compared to other dosage forms.
4. Greatest chemical and microbial stability compared to other oral dosage forms.
5. Objectionable odor and taste can be masked by coating technologies.
6. Offer greatest precision and the least content uniformity.
7. Easy to swallow with least hang up problems.
8. Fit for large scale production.
9. Bi-layer tablet is suitable for preventing direct contact of two drugs and thus to maximize the efficacy of combination of two drugs.
10. Bi-layer tablets can be designed in such a manner as to modified release as either of the layers can be kept as extended and the other as immediate release.
11. Expansion of a conventional technology.
12. Prospective use of single entity feed granules.
13. Separation of incompatible components.
14. Patient compliance is improved leading to improve drug regimen efficiency.
15. Easiest and cheapest to package and strip.^[10,11,12,13]

Disadvantages of Gastroretentive bilayer floating tablet

1. Drugs with poor wetting, slow dissolution properties, optimal absorption high in GIT may difficult to manufacture as a tablet that will still provide ample drug bio availability.
2. Capping is the major problem in bilayer tablets
3. Adds complexity and bilayer rotary presses are expensive.
4. Difficult to swallow in case of children and unconscious patients.
5. Some drugs resist compression into dense compacts, owing to amorphous nature, low density character.
6. Cross contamination between the layers.

7. Increased fluid levels are required in the stomach so that the system float properly.^[14-15]

Applications of Gastroretentive bilayer floating tablet

1. For the administration of fixed dose combinations of different drugs, prolong the drug product life cycle, buccal/mucoadhesive delivery systems; fabricate novel drug delivery systems such as chewing device and floating tablets for gastro-retentive drug delivery.
2. Controlling the delivery rate of either single or two different active pharmaceutical ingredient(s) is possible with bilayer tablets.
3. To modify the total surface area available for API layer either by sandwiching with one or two in active layers in order to achieve swellable/erodible barriers for modified release.
4. To separate incompatible Active pharmaceutical ingredient from each other, to control the release of API from one layer by utilizing the functional property of the other layer.
5. Promoting Patient Convenience and Compliance.
6. Bilayer tablet is improved beneficial technology to overcome the shortcoming of the single layered tablet.
7. Bilayer tablets are used to deliver the loading dose and sustained dose of the same or different drugs.
8. Bilayer tablets are used for bilayer floating tablets in which one layer is floating layer another one is immediate release layer of the drug.
9. Bilayer tablets are used to deliver the two different drugs having different release Profiles.
10. The cost is lower compared to all other oral dosage forms.^[6,17,18]

Types of Gastroretentive bilayer floating tablet

1. Single sided tablet press.
2. Double sided tablet press.
3. Bilayer tablet press with displacement monitoring.
4. Multilayer compression basics.^[19,20]

Various techniques for Gastroretentive bilayer floating tablet

1. Oros ® Push Pull Technology.
2. L-Oros Tm Technology.
3. DUROS Technology.
4. Elan Drug Technologies' Dual Release Drug Delivery System
5. EN SO TROL Technology.
6. Rotab Bilayer.

7. Geminex Technology.^[21,22,23]

Characterization of Gastroretentive bilayer floating tablet^[24,25,26]

A) Pre-compression parameters

1. Particle Size Distribution

Sieving is used to determine particle size distribution.

2. Angle of Repose

Angle of repose was calculated by measuring the diameter of the powder cone. $\tan \theta = h/r$

Where “r” is the radius and “h” is height of the powder cone.

Moisture Sorption Capacity Disintegrates is capable of absorbing moisture from the atmosphere and thus affects the hygroscopic drugs. Moisture sorption capacity is carried out by taking 1g of disintegrate in a petridish by distributing evenly over it and is placed in stability chamber at $37 \pm 1^\circ\text{C}$ with 100% relative humidity for about 2 days. Moisture uptake is measured by calculating the difference in weights.

3. Density

Ratio of mass to volume for an untapped powder is known as the bulk density. A graduated cylinder containing sample is tapped mechanically until volume changes and thus tapped density is obtained.

4. Compressibility

It is the indirect measure of bulk density. To determine compressibility of the disintegrate carrs compressibility index.

Carr's Index = $(\text{tapped density} - \text{bulk density}) \times 100 / \text{tapped density}$.

5. Hausner's ratio

It is used to determine powder flow.

Hausner's ratio = $\text{tapped density} / \text{pour density}$.

B) Post compression parameters

1. Tablet Thickness and Size

Diameter & thickness are important for tablet uniformity. Vernier calipers are used for the determination of tablet thickness & diameter.

2. Tablet Hardness

Tablet hardness is measured by using Monsanto hardness tester. It is performed to find out the tablet breaking point and to test the structural integrity during handling, storage & transportation.

3. Friability

It is used to measure the mechanical strength of the tablet or granules. The equipment used for determining friability is friabilator. 20 tablets are accurately weighed and placed in the friabilator which revolves at 25rpm by dropping the tablets from a height of 6" in each revolution. Tablets are then weighed after 4min to determine the percentage loss.

4. Floating Lag Time

It is the time interval taken by the tablets to start floating. It should be less than one minute. It is measured by dissolution test apparatus containing 0.1 N HCl (900ml).

5. Floating Time

It is the total time taken by which the tablets remain floating in the media.

6. Drug Content Uniformity

Ten tablets are taken and powdered equivalent weight of drug dose is taken and is transferred to volumetric flask and then buffer is added and absorbance is determined using U.V spectrophotometer.

7. Swelling Study

Initially tablet is weighed (W₁) and placed in a glass beaker, containing 200 mL of 0.1 N HCl, maintained in a water bath at 37 ± 0.5 C. At different time intervals, the tablet is removed and the excess of liquid is carefully removed by a filter paper. The swollen tablet is reweighed (W₂). The swelling index (SI) is calculated using the formula.

$$SI = \frac{W_t - W_0}{W_0} \times 100$$

W_t = (Weight of swollen tablet), W₀ = (Initial weight of tablet).

8. Dissolution Studies

Tablets are subjected to in vitro drug dissolution studies in simulated gastric & intestinal fluid to evaluate the controlled drug delivery potential.^[60] Dissolution studies are carried out using USP I dissolution apparatus at 100 rpm at 37±0.5°C with 900ml pH 1.2 buffer for 2 hours. Later on the dissolution medium is replaced with 900ml of pH 6.8 phosphate buffer. This is

continued for other 10 hour. Drug samples of about 5ml are withdrawn and replaced with the drug free dissolution medium. The samples are analyzed using UV spectrophotometer.

9. Weight Variation Test

Twenty tablets are selected and weighed individually. Then the average weight and standard deviation is calculated. Test passes when not more than two tablets deviate from average weight.

B) In-vivo evaluation.

In vivo studies

- a) Radiology.
- b) Scintigraphy.
- c) Gastroscopy.
- d) Magnetic Marker Monitoring.
- e) ¹³C octanoic acid breath test.
- f) Pharmacokinetic study.

Future potential for Gastroretentive bilayer floating tablet

Bilayer floating tablets can be useful in comorbid conditions like Hyperlipidemia & hypertension & other diseases as immediate response can be achieved by using loading dose as one layer along with sustained release layer which will maintain the concentration of the drug in plasma for prolonged period of time. Bilayer floating tablets by using natural's polymers can be prepared. This concept of bilayer floating approach can be used for combination of one/ two herbal drugs.

CONCLUSION

Gastroretentive bilayer floating tablet is improved beneficial technology to overcome the shortcoming of single layered tablet. Bilayer tablets provide one of the important design approaches where incompatible drugs, with different indication, and same drug with different release rate can be incorporated in a single unit. 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. In the last decade, interest in developing a combination of two or more Active Pharmaceutical Ingredients in a single dosage form has increased in the pharmaceutical industry, promoting patient convenience and compliance. Drugs which has

narrow absorption window such as anti- viral, antibiotic and antifungal can be given in floating bilayer dosage form. Using Gastroretentive bilayer floating tablet approach combination of two herbal drugs can be also given for more therapeutic effect.

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