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A Review on an Emerging Trend Bilayer Floating Drug Delivery System

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ABSTRACT

NDDS is advanced drug delivery system which improves drug potency, control drug release to give a sustained therapeutic effect, provide greater safety, finally it is to target a drug specifically to a desired tissue. Novel drug delivery system have been developed to overcome the limitation of conventional drug delivery systems, such as of gastric retention by decreasing fluctuations in the concentration of the drug in blood,resulting in the reduction in unwanted toxicity and poor efficiency. As compared to traditional dosage forms bilayer tablets are more efficient for sequential release of two drugs that can be different or identical. Bilayer tablet is also capable of separating two incompatible substances and also for sustained release. Gastro retentive drug delivery system retains the period of dosage forms in the stomach or upper gastro intes-tinal tract ,as to improve bioavailability and the therapeutic efficacy of the drugs. Mainly the bilayer drug delivery system is suitable for drugs whose therapethic windows are narrow in the gastrointestinal tract (GIT) and also they have low elimination half life: 3-4 h. The purpose of this review is to disclose the challenges faced during the formulation of bilayer tablets.Finally, the whole article is firmly analyzed in a concluding paragraph.

Keywords: Conventional drug delivery systems, Bilayer tablet, Gastro retentive, Bioavailability.

1. INTRODUCTION

Bilayer floating tablets is an initial option to minimize chemical incompatibilities of API by separation (physical separation) & to enable the elaboration of various drug release it may be immediate release and extended release [1]. Floating DDS will be having density (bulk density) less than GIT fluids and so accumulate and afloat in the stomach fluid and will not disturbing the GIT emptying rate for an extended period. At the same time, the system is buoyant on the gastric fluid (GI fluid), the drug is liberate sluggardly at the required rate reliably afloat on the surface of the food. Many afloat systems are present depend upon the powders, granules, capsules, laminated films empty microspheres and tablets. Flotation of DDS in the drug bring out by integrating floating chamber filled with vacuum, air or inert gas from the system. When drug is released, remaining system was emptied from the stomach. This may leads to extend the gastric retention time and also having good control of variation in plasma drug concentration. Along with this side lowest gastric content required to grant proper realization of the lightning the retention, a lowest degree of floating force is also have need to keep the dosage form [2]. The whole system have the many problems due to physiologic issues like absorption index is narrow for few drugs and modification in emptying time of stomach and drug has stability problems in intestine. To control the issues regarding GRDDS was developed in which oral controlled sustained dosage form is transfer the drug in a lower rate in systemic circulation and to keep the effective plasma concentration because the drug is accumulated in stomach for a longer period of time as compare to conventional oral dosage form [3]. Tablets gives a many merits that they are the most stable dosage form until it may be dry, simple to form and cheap in cost, it gives a excellent patient compliance percentage and increase shelf life.

According to their usage they are accessible in many types in which tablets are for oral ingestion, for oral cavity, and for other administrative routes. Tablets can be manufactures by two ways i.e. wet / dry granulation and direct compression. But now a day's direct compression is most popularly used because of having increase in use of novel excipients.

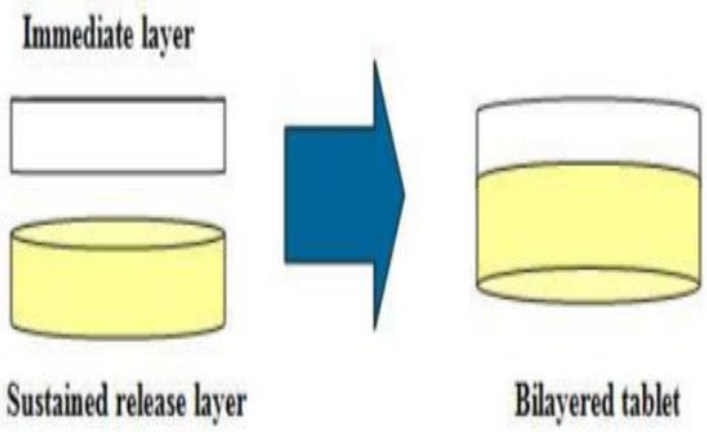

Fig.1 Bilayer floating tablet

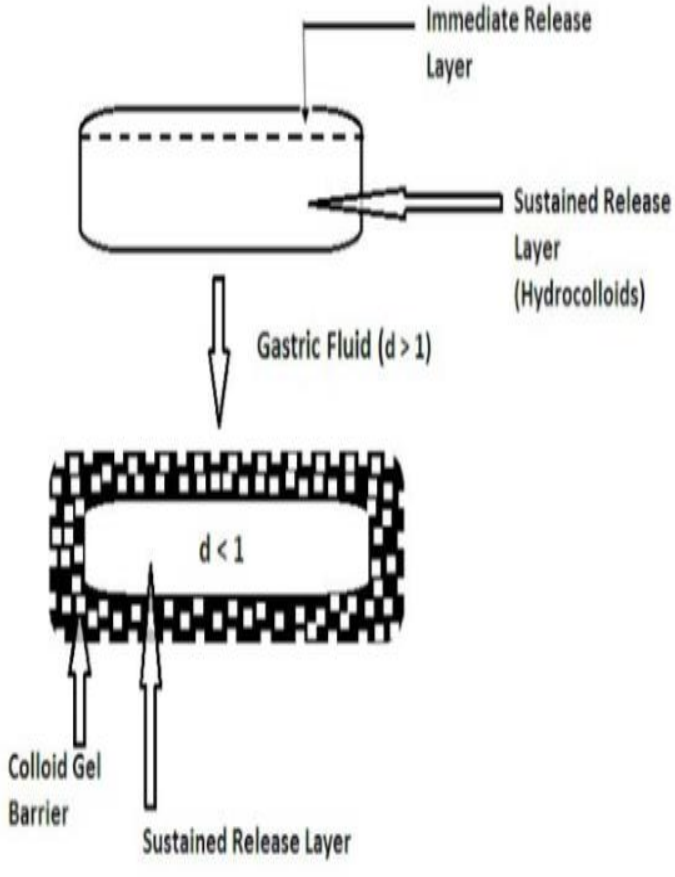

Fig.2 Bilayer floating tablet

2. BASIC GASTROINTESTINAL TRACK

2.1 Anatomy

An atomically, the stomach is divided into three regions: Fundus, body, and antrum (pylorus). The distal portion is made-up of fundus & body perform like a storage cabin for non-digested material and on the other hand antrum is work like a pump to expelled out the content from stomach and the major site for mixing motions. In both the conditions like during fasting and fed Gastric emptying will be occurred The graph in the motility regarding is the main two states. In fasting condition interdigestive phase of electrical performance will occurred, in which both the cycle in stomach or in intestine at every 2-3 h. This is also called the interdigestive myloelectric cycle or migrating myloelectric cycle and this is sub divided into following four phases.

- **Phase I i.e basal phase occurs from 40 min to 1 h** having rare contractions.
- **In pre-burst phase i.e Phase II occurs for 40 min to 1 h** with sporadic electrical potential and contractions. When the development in phase occurs, subsequently the intensity and frequency will be extend.
- **Phase III i.e burst phase occurs for 4-6 min.** It involves extreme and regular contractions for a short period. This is because of the nondigested material is excreted out from stomach down to small intestine. This term is coined as a housekeeper wave.
- **Phase IV occurs for 0-5 min** and comes between Phases III and I of two consecutive cycles.

After the consumption of a mixed food, the graph of contractions varies from fasted to the non-fasted. This is also known as digestive motility pattern and involves constant contractions as in Phase II of fasted state. The contractions having result in lowering the size of meal particles (to <1 mm), which are expelled toward the pylorus in a suspension form. During the fed state onset of MMC was slow down the result of gastric emptying rate. Gastric residence time (GRT) and unpredictable gastric emptying rate [4].

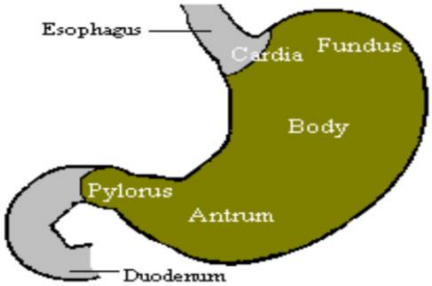

Fig.3 Stomach Overview

3. FLOATING DRUG DELIVERY SYSTEM

Different approaches are applied to increase the GR (Gastric Retention) Time for oral dosage form. Floating system having low bulk density and it will be the floating state in the stomach. They can reserve drug for longer period of time. such type of system can increase drug's safety as well as minimize side effect as result the bioavailability of the drug will be increases [5].

3.1 Mechanism of Floating Systems

To evaluate the floating force kinetics, a unique apparatus for determination of all the evaluation parameters of the dosage form has been reported in the literature. The equipments and apparatus are used to measure the continuous force equivalent to F (as a function of time) which is used to manage the all object. The object is floats excellent if F will be high in the positive side. This apparatus guiding in the evaluation of FDDS in the form of stability and durability forces developed in order to prevent the risk of unforeseeable intra gastric buoyancy capability variations .FDDS having a bulk density less than gastric fluids and maintain a floating property in the stomach without affecting the gastric emptying rate for a prolonged period of time [6].

F = F buoyancy - F gravity = (Df - Ds) gv

Where, Df = fluid density ,F= total vertical force, Ds = object density ,g = acceleration due to gravity, v = volume

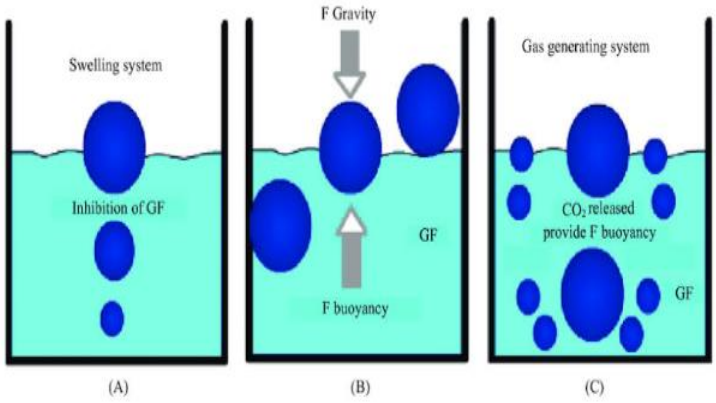

Fig.4 Mechanism of Floating Systems

4. NEED FOR GASTRIC RETENTIVE DRUG DELIVERY SYSTEMS

To prolong the drug release and to reduce the variable gastric emptying process. When When the drug is administered orally so, after oral administration of dosage form would be retained in the stomach for the prolong period of time & release the drug there in such a manner that the release of drug is prolonged, So that the drug could be release continuously to its absorption sites i.e. in the upper gastro retentive part. Dosage form can store in the gastric region for longer period of time and hence significantly prolong the (gastric residence time) GRI of drugs . The requirment for gastro retentive dosage forms (GRDFs) has led to great efforts in both the fields academia as well as industry towards the expansion of such delivery systems. These efforts resulted in GRDFs that were designed, in large part, based on the following approaches.

(a) High density dosage form that is remain for the longer period of time in the lower part of the stomach.

(b) Low density form of the dosage form that causes float in (gastric fluids)GF. (c) Adhesion to stomach mucosa [7].

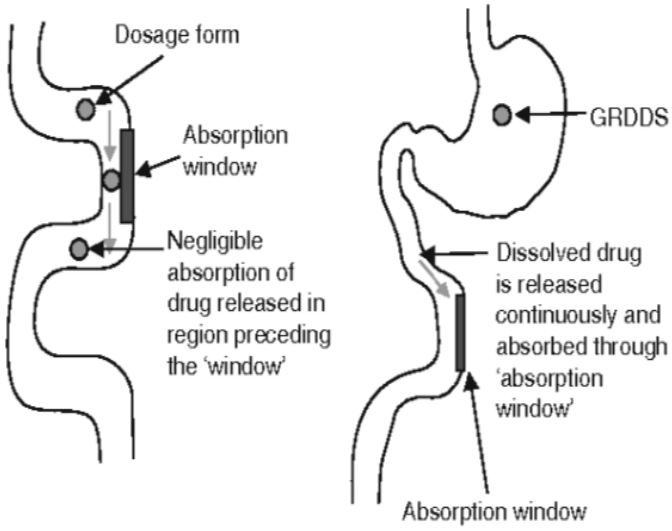

Fig.5 Conventional Dosage Form shows negligible absorption whereas in GRDDS drug is continuously absorbed

5. Bilayer floating drug delivery system

5.1 Needs of Bilayer Floating Tablet

1. Prolong the drug product life cycle.
2. For giving fixed dose combinations of different APIs.
3. To separate incompatible active pharmaceutical ingredients from each other, to control the release of API from one layer by utilizing the functional property of other layer (such as osmotic property).
4. .Fabricate novel drug delivery systems such as chewing [8].
5. To modify the total surface area available for API [9,10,11]
6. To control the delivery rate of either single or two different active pharmaceutical ingredients.System provid

the floating tablets for gastroretentive drug delivery systems. [12,13,14]

5.2 Advantages of the bilayered tablet dosage form

1. Bi-layer implementation is considered with the single-layer conversion kit.
2. Cost for oral dosage form was higher as compare to other dosage form.
3. Higher stability was measured in chemicals and microbes as compare to other dosage form.
4. coating techniques was applied to cover the bitter taste and odor
5. Flexible Concept.
6. It is the unit dosage form having good dose precision and also having the lower content variability.
7. It was easy to swallowed with lower ability for hangup [15]

5.3 Disadvantages of floating bi-layer tablets

1. 1.fluid levels should be higher in the stomach to attained floating system properly.
2. 2.Separation of layer occurs due to insufficient bonding and reduction in yield occurs.
3. 3.There are chances of cross contamination between two layers. [16,17]

5.4 Limitations of bilayer floating drug delivery system

1. The drug which are not stable in the acidic medium are not good to be incorporated. [18].
2. There is a chance of interfacial crack and layer separation , there fore it is an One of the main challenge in bilayer formulation to adhesion between adjacent compacted layer. [19]

5.5 The major requirements for bilayer floating drug delivery system

The content release are should be very slow to provide a reservoir.

The specific gravity should be always less than the gastric contents (1.004 — 1.01 gm/cm^3).

is required to form a cohesive gel carrier [20]

5.6 Applications of bilayer floating drug delivery system

1. The sequential release of two drugs in combination is best suitable in bilayer technology.
2. Separate Two Incompatible drug Substances.
3. Bilayer tablet was refined to overcome the shortcoming of the single layered tablet.
4. Sustained dose of the same with various drugs [21,22]

5.7 Methodology used for Bilayer Floating Tablet

1. L-Oros Tm Technology
2. Oros ® Push Pull Technology
3. Elan Drug Technologies
4. DUROS Technology Dual Release Drug Delivery System
5. Rotab Bilayer
6. EN SO TROL Technology
7. PRODAS or Programmable Oral Drug Absorption System
8. Geminex Technology [23]

6. EVALUATION TECHNIQUES OF BILAYER FLOATING TABLET

6.1 Angle of Repose

In powder frictional forces can be measured with the help of angle of repose. The higher the angle of repose that can be possible between surface of powder is the and horizontal plane i.e. height.

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

$$\theta = \tan\text{-}1h/r$$

Where, Angle of repose has to be findout with the help of hight of pile that is h and radius of pile that is r. [24]

6.2 Compressibility Index

Manly the copressibility index is an indication of the compressibility of a powder and the propensity of the powder to be compressed is manly determined by compressibility index .The settling property and interparticulate interaction is also determined with the help of compressibility index.

$$\text{Compressibility index (\%)} = \rho t - \rho 0 * 100 / \rho t$$

Where, ρt = Tapped density gram/ml

$\rho 0$ = Bulk density gram/m [25]

6.3 Thickness and diameter

The diameter of the tablets is determined with a Verneir Caliper (or) Screw Gauage. [26,27]

6.4 Weight variation test

The weight variation in which twenty tablets are selected randomly where the average weight is there after the weight variation is calculated and weight variation is compared with IP standard.[28,29]

6.5 Friability

Friability will be measured by taking randomly 10 tablets which is weighed and placed in aFriabulator (Roche Friabilator) at 25 rpm for a period of 4 mins. After resolution, the tablets can be dusted and wieghed. [26,27]

Friability is calculated by the following formula.

$$\text{Friability (\%)} = W1 - W2/W1 \times 100$$

Where, W1 = Weight of Tablets (Initial / Before Tumbling)

W2 = Weight of Tablets (After Tumbling or friability)

6.6 Disintegration Time

One tablet was put in each disintegration test apparatus testube in which the beaker containing the buffer 0.1N HCl or Phosphate buffer solution having a pH 6.8 and test is processed at 37°C. The disintegrate time of the drug is noted as disintegration time. [30]

6.7 Dissolution Studies

Dissolution test was performed with the help of USP paddle apparatus by maintain a temperature at, 37ºC for 50 rpm(Rotation per minute) rotational speed after that 0.5ml sample was withdrawn at a different time interval and the 5 ml solution was replaced with the 5 ml of buffer solution.[31]

6.8 Floating Lag Time

The time taken by the tablets to start afloat.The limit should be less than 1 minute. It was identified by dissolution apparatus having 0.1 N HCl (900ml).

6.9 Floating Time

The total time required to float a tablet in medium.[30]

6.10 Drug Content Uniformity

10 tablets are taken and transfered into a powdered form having a equivalent weight of drug dose was taken in volumetric flask and buffer is added to make it in the dissolution form. Now absorbance is determined using U.V.spectrophotometer. [31]

7. CONCLUSION

Bilayer tablet is an advanced technique to get over the drawbacks of single layered tablet. The tablets are made in the Bilayer form to provide systems for the administration of drugs. Bilayer tablet mainly provide controlled release tablet preparation by providing surroundings or multiple swelling layers in the pharmaceutical research work. The release of drug is a most important parameter. Bilayer tablet increases gastric emptying time and bioavailability which results in gastric retention. The aim of bilayer drug is to improve the bioavailability of the drug with narrow absorption window in the gastric region. Floating Drug Delivery System is a better way for gastric retention.

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