WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 7.523
Volume 6, Issue 13, 238-247. Review Article ISSN 2277– 7105

FORMULATION AND EVALUATON OF FLOATING TABLET

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Article Received on
31 August 2017,

Revised on 21 Sept. 2017,
Accepted on 12 Oct. 2017

DOI: 10.20959/wjpr201713-9832

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ABSTRACT

Floating drug delivery Systems has received considerable interest in the past few decades as they can overcome the drawbacks of conventional drug delivery system like frequent dosing, low bioavailability etc. relative to fast gastric-emptying time. An optimum floating drug delivery System can be defined as a systemthat remains in the stomach for sufficient interval of time and releases the active medicament in a sustained manner. These remain floating on the gastric contents. Thus resulting in prolonged pharmacological effect thus improving the bioavailability of drug. The aim of writing this review on gastro retentive and floating Tablet was to compile the new literature with the principle, Advantages and classification of the floating tablets, method of preparation, evaluation techniques, list of drugs formulated as floating tablets, formulation evaluation and future scope of floating tablets.

KEYWORDS: Floating tablets, bioavailability, Gastro retentive, prolong release.

INTRODUCTION

Floating tablet is a class of gastroretentive drug delivery system. Gastroretentive systems are able to increase residence time of dosage forms in the stomach there by increase the bioavailability of drugs with narrow absorption window, drugs with less water solubility in alkaline pH of small intestine or drugs with poor stability in the intestinal or colonic environment.[1,2] The important point in the development of oral controlled release dosage forms is not just to prolong the delivery of the drug more than 12 hours, but to prolong the presence of the dosageforms in the stomach or upper gastrointestinal tract unit all the drug is released for desire period of time. Rapid GI transit could result in incomplete drug release from the drug delivery device in the absorption zone leading to diminished efficacy of the administered dose. A rational approach to enhance bioavailability and improve

pharmacokinetic and pharmacodynamic profile is toretain the drug reservoir above its absorption area, i.e. In the stomach and to release the drug in a controlled manner, so as to achieve zero order kinetics for a prolonged period of time, one of the most feasible approaches for achieving a prolonged and predictable drug delivery profile is to control the gastric residence time in GIT.[3,4,5] The floating drug delivery is applicable for drugs having poor bioavailability because of the narrow absorption window in the upper part of the gastrointestinal tract.[6,7] It retains the dosage form at the site of absorption and thus enhances the bioavailability.[8,9,10]

The design of floating tablets and floating drug delivery Systems (FDDS) should be primarily aimed to achieve more predictable and increased bioavailability. Now-a-days most of the pharmaceutical scientist is involved in developing the ideal FDDS. This ideal system should have advantage of single dose for the whole duration of treatment and it should deliver the active drug directly at the specific site. Scientists have succeeded to develop a system and it encourages the scientists to develop control release tablet. Control release implies the predictability and reproducibility to control the drug release, drug concentration in target tissue and optimization of the therapeutic effect of a drug by controlling its release in the body with lower and less frequent dose.

Advantages including improved bioavailability, therapeutic efficacy and possible reduction of the dose size. Gastric emptying of dosage forms is an extremely variable process and ability to prolong and control the emptying time is a valuable asset for dosage forms, which reside in the stomach for a longer period of time than conventional dosage forms. Several difficulties are faced in designing controlled release systems for better absorption and enhanced bioavailability.

Classification of Floating tablets

Floating tablets are classified depending on the use of 2 formulation variables: effervescent and non-effervescent system.

I. Effervescent Floating tablets: These are matrix types of systems prepared with the help of swellable polymers such as methylcellulose and chitosan and various effervescent compounds, e.g., sodium bicarbonate, tartaric acid, and citric acid. They are formulated in such a way that when in contact with the acidic gastric contents, CO2 is liberated and gets entrapped in swollen hydrocolloids, which provides buoyancy to the dosage forms.

II. Non-Effervescent Floating tablets: Non-effervescent floating tablets use a gel forming or swellable cellulose type of hydrocolloids, polysaccharides, and matrix-forming polymers like polycarbonate, polyacrylate, polymethacrylate, and polystyrene. The formulation method includes a simple approach of thoroughly mixing the drug and the gel-forming hydrocolloid. After oral administration. This dosage form swells in contact with gastric fluids and attains a bulk density of < 1. The air entrapped within the swollen matrix imparts buoyancy to the dosage form. The so formed swollen gel-like structure acts as a reservoir and allows sustained release of drug through the gelatinous mass.[11]

MATERIALS AND METHODS

I. Floating tablets were prepared by the wet granulation method by using hydroxyl propyl methyl cellulose (HPMC K4MCR), carbopol 934P, lactose and sodium bicarbonate.

Preparation of granules:- Granules were prepared by wet granulation method. All ingredients were accurately weighed. Then accurately weighed quantities of drug, HPMC-K4MCR, lactose, sodium bicarbonate were mixed homogeneously using glass –mortar and pestle. The wet granulation was done with ethanol (95%). Wet mass was passed through a 40-mesh screen and dried in a hot air oven at 40°C over night. The dried granules were sized through 40/60, mesh and blended with magnesium stearate (approx,1% w/w). Lactose was used as filler and channeling agent. Sodium bicarbonate was used was used as a gas generating agent, here ethanol is used as granulating agent.

Preparation of floating tablet:- The homogeneously lubricated granules with magnesium stearate (1% w/w) were then compressed in to tablet using single punch tablet compression machine. Compression force was adjusted to obtain tablet with hardness in the range of 6.2-6.9 kg/cm^2 on a Monsanto tablet hardness tester. Evaluation of blends before compression.

II. Floating tablets can be prepared by directcompression method. Here pure drug was mixed with required quantity of HPMC K4M, sodium CMC, carbopol 934P, sodiumbicarbonate and lactose by geometric mixing inmortar and pestle for 10 min. The above powderwas lubricated with magnesium stearate inmortar and pestle for 2min. The lubricated blendwas compressed into tablets using 12 mm flat faceround tooling on CLIT Pilot Press rotarytablet machine.

III. The dry granulation method (slugging method)

The ingredients in the formulation are intimately mixed and precompressed on heavy duty tablet machines. The slug which is formed is ground to a uniform size and compressed into the finished tablet.

METHOD OF EVALUATION

- **Bulk density**[12-15]

It is a ratio of mass of powder to bulk volume. The bulk density depends on particle size distribution, shape and cohesiveness of particles. Accurately weighed quantity of powder was carefully poured in to graduated measuring cylinder through large funnel and volume was measured, which is called initial bulk volume. It is expressed in gm/ml and is given by the formula:

$$\text{Bulk density} = M/Vo$$

Where,

M = mass of the powder

Vo = bulk volume of the powder.

- **Tapped density**[12-15]

10 gm of powder was introduced into a clean, dry 100 ml measuring cylinder. The cylinder was then tapped 100 times from a constant height and the tapped volume was read. It is expressed in gm/ml and is given by:

$$\text{Tapped density} = M/Vt$$

Where,

M = mass of the powder

Vt = final tapping volume of the powder.

- **Angle of repose (θ)**[12-15]

It is defined as the maximum angle possible between the surface of the pile of the powder and the horizontal plane. Fixed funnel method was used. A funnel was fixed with its tip at a given height ‘h, above a flat horizontal surface to which a graph paper was placed. Powder was carefully poured through a funnel till the apex of the conical pile just touches the tip of the funnel. The angle of repose was then calculated using following equation:

$$\text{Angle of repose } Ø = \tan 1(h/r)$$

Where,

h=height of the pile

r=radius of the pile.

- **CompressibiltyIndex (carr'sIndex)**[12-15]

Compressibilty Index is used as an important parameter to determine the flow behavior of the powder. It is indirectly related to the relative flow property rate, cohesiveness and particle size. It is simple, fast and popular method for predicting flow characteristic. Carr's index can be represented by equation:

$$Carr's\ Index\ (\%) = \frac{Tapped\ density - Bulk\ density}{Tapped\ density} \times 100 \qquad (1)$$

- **Hausner's ratio**[12-15]

Hausner's ratio is used to predict the flowability of the powders. This method is similar to compressibility index. Hausner's ratio can be represented by equation:

Hausner's ratio = Tapped density / bulk density

- **Floating lag time and total floating time**[16]

Floating lag time (FLT) and total floating time (TFT) of floating tablets were measured visually in dissolution apparatus type II containing100 mL 0.1 N HCl with a paddle rotated at 50 rpm (pH 1.2) at 37 ± 0.5 °C.

- **Swelling index**[17]

The prepared tablets were placed in a glass containing 200 ml of 0.1 N HCl at 37 ± 0.5°C. The percentage of swelling at different time interval was calculated by the following equation.

$$SI(\%) = \frac{W_t - W_o}{W_o} \times 100 \qquad (3)$$

Where, SI is swelling index, $W_t$is weight of tablet at time t, w_o is weight of the dry tablet before placing in the glass.

- **Dissolution Study**

In vitro drug release of the formulation was carried out using USP dissolution apparatus type II paddletype under sink condition with rotating speed of 50 rpm and at temperature of37 ± 0.5 °C. The dissolution medium used was 900ml 0.1NHCl. The samples were withdrawn at predetermined time intervals for period of 6hours and replaced with the fresh medium, suitably diluted and were analyzed using UV/Visible spectrophotometer.

- **Dimensionl Analysis**

The thickness and diameter of tablets was determined using vernier caliper. Twenty tablets from each batch were used and average values were calculated.

- **Hardness**[19]

Tablet hardness and strength are the essential to see that the tablet can with the shock and stress during manufacturing packing and transportation, and while handled by the patient.

To test the hardness of the tablet Monsanto tester, Strong-cobb tester, the Pfizer tester, the Erweka tester, the Schleuniger tester are used.

- **Friability**[20]

Friability is the tested for a tablet to see weather the tablet is stable to abrasion or not, it is tested by using Roche friabilator. This is made up of a plastic drum fixed with a machine which rotated at 25 rpm for 100 revolutions. And then the twenty tablets which were weighed prior to the test are taken out of the drum and cleaned with a cloth and weighed once again, the weight variation must not be less than 0.5 to 1.0% for an conventional tablet.

- **Size and Shape**[21]

It can be dimensionally described & controlled. The thickness of a tablet is only variables. Tablet thickness can be measured by micrometer or by other device. Tablet thickness should be controlled within a ± 5% variation of standard value.

- **Weight Variation test (U.S.P.)**[21]

Take 20 tablet and weighed individually. Calculate average weight and compare the individual tablet weight to the average. The tablet pass the U.S.P. test if no more that 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.

- **Disintegration Test (U.S.P.)**[21]

The U.S.P. device to test disintegration uses 6 glass tubes that are 3” long; open at the top and 10 mesh screens at the bottom end. To test for disintegration time, one tablet is placed in each tube and the basket rack is positioned in a 1-L beaker of water, simulated gastric fluid or simulated intestinal fluid at 37 ± 2 0 C such that the tablet remain 2.5 cm below the surface of liquid on their upward movement and not closer than 2.5 cm from the bottom of the beaker in their downward movement. Move the basket containing the tablets up and down through a

distance of 5-6 cm at a frequency of 28 to 32 cycles per minute. Floating of the tablets can be prevented by placing perforated plastic discs on each tablet.

According to the test the tablet must disintegrate and all particles must pass through the 10 mesh screen in the time specified. If any residue remains, it must have a soft mass. Disintegration time: Uncoated tablet: 5-30 minutes coated tablet: 1-2 hours.

List of Drugs Formulated of Floating Tablets

S. No.	Name of Drug	Category of Drug	Short Summary	Reference
1.	Famotidine	Histamine-2 Blocker	The results indicated that the tablet remained buoyant for 6-10 hours. Decrease in the citric acid level increased the floating lag time but tablets floated for longer duration.	[22]
2.	Ranitidine	Histamine H2-receptor Antagonist.	The studies indicate that the proper balance between a release rate enhancer and a release rate retardant can produce a drug dissolution profile similar to a theoretical dissolution profile.	[23]
3.	Cefuroxime axetil	Antibacterial	Tablets were prepared by direct compression technique. Kinetic treatment to dissolution profiles revealed drug release ranges from anomalous transport to case 1 transport, which was mainly dependent on both the independent variables.	[24]
4.	Levofloxacin hemihydrate	Antimicrobial	The tablets were prepared by melt granulation method to improve the oral bioavailability of the drug and to achieve extended retention in the stomach which may result in prolonged absorption.	[25]
5.	Atenolol	$Beta_1$-selective (cardio selective)	The floating matrix tablets of Atenolol were prepared by direct compression method. The release kinetics showed first order model and zero order model.	[26]
6.	Cefpodoxime Proxetil	beta-lactam antibiotic with bactericidal activity	The tablets were prepared by direct compression technique. The gastric residence time of Cefpodoxime Proxetil containing formulation was prolonged & floated in stomach for longer period, & increased bioavailability.	[27]
7.	Bromocriptine Mesilate	Anti Parkinson Agents (dopamine Agonist)	Formulation was Prepared by Direct Compression Method. Showed Good Physical Properties and stability. This dosage form especially caused reduction in dosing frequency and increased bioavailability.	[28]
8.	Captopril	Hypertension	Floating tablets were prepared by wet granulation method. Resulted in zero- order	[29]

			sustained release floating formulation of captopril, with enhanced oral bioavailability.	
9.	Ramipril	Hypertension	The gastro retentive drug delivery systems was retained in the stomach for a longer period of time and improve the bioavailability.	[30]
10.	Ofloxacin	Antibiotic	Ofloxacin floating tablets enhanced the bioavailability and therapeutic efficacy of the drug. All formulations possessed good floating properties with total floating time between 8- 12 hrs.	[31]
11.	Losartan Potassium	Antihypertensive	Floating tablets were prepared by wet granulation method, resulting in prolonging the gastric emptying time. The floating tablets remained in the stomach for a longer period of time with sustained drug release.	[32]
12.	Nizatidine	Histamine H2-receptor antagonist with antacid activity	The tablets were prepared by direct compression technique. The results combined excellent floating behavior and sustained drug release as compared to conventional nizatidine tablet for antiulcer activity in rabbits.	[33]
13.	Cephalexin	antibiotic	The result indicated good matrix integrity and drug release in sustain release manner and the kinetic of drug release was best fit it to Peppas model	[34]

CONCLUSION

Floating tablets have emerged as the power full means of improving the bioavailability and providing sustained release and avoiding the adverse effects of many drugs. Floating tablets have proved to be potential approach for gastric retention. These systems have special advantage for the drug that are primarily absorbed from the upper part of GIT. So with an improved knowledge of formulation development aspect, physiochemical and pharmacological prospects of drug there is lot of future scope for designing of optimum floating drug delivery system.

CONFLICT OF INTEREST

The authors of this review have no conflict of interest.

ACKNOWLEGEMENT

The authors are thank full to the institute of pharmacy Bundelkhand University Jhansi for the providing the facility to compile this review.

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