A REVIEW ON: FLOATING DRUG DELIVERY SYSTEM

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ABSTRACT

The oral route is the most appropriate and widely used for the delivery of drugs to the systemic circulation. This route has high acceptability for patients, particularly due to the ease of administration. Over the years oral dosage forms have become increasingly world-wise in the pharmaceutical field, with controlled release drug delivery systems that release the drug at a predetermined rate playing a major role. Various approaches have been designed and utilized to achieve efficient drug delivery for those drugs that have poor bioavailability and shorter gastric residence time. On the other hand floating drug delivery system, one of the most extensively used approaches of the Gastro retentive drug delivery system has an advantage for the drugs that are absorbed primarily in the upper segments of the Gastrointestinal tract i.e., stomach, duodenum, and jejunum. The types of floating drug delivery systems, the principle, and mechanism of floating action to achieve gastric retention. The In-vitro and In-vivo studies used to evaluate the potential, performance, and application of floating systems in to overcome various problems encountered during the development of a dosage form innovative drug delivery technologies are being used and are available for clinical use. Floating Drug Delivery Systems (FDDS) is one of the gastro- retentive dosage forms used to achieve extended duration of gastric residency. Floating drug delivery systems (FDDS) was to compile the recent literature with particular focus on the main floating mechanism to achieve gastric retention. Sustained oral release of gastrointestinal dosage types provides many benefits for drugs with absorption from the upper sections of the gastrointestinal tract and those that function locally throughout the stomach. The physiology, factors controlling gastric retention time, excipient variables influencing gastric retention, approaches to designing single-unit, hydro-dynamically balanced system and multi-unit floating structure, and aspects of their classification, formulation and evaluation.

Keywords*: floating drug, bioavailability , sustained oral gastro intestinal .*

INTRODUCTION

Most of the drug are available in market are in the form of oral drug delivery system (1) because of its cost effectiveness, compliance of patient and easy to administer (2) but due to some poor bioavailability problems and very high gastric emptying rate its use is very limited for gastric region disease and the disease whose treatment needs good plasma concentration of drug. Some of the drug is narrow absorption window at upper level of gastrointestinal. Dosage of gastric emptying time (3) is prolong or control emptying time. The distribution of the medicine must offer an extended duration of action during stomach residency in order to get over this obstacle. The time of medication release is improved, drug waste is reduced, and drug solubility is improved for drugs that are less soluble in high ambient pH to gastro retention (4) this type of drug delivery method would have comparatively less side effect and would eliminate the need for repeated dosages. Gastro retentive system remains in gastric environment for respective hours and hence prolonged the gastric retention time of the drug. Bioavailability and solubility of the drug and reduces the wastage of drug.(5) A system which is a part of gastro retentive system known as floating drug delivery system is a miserable system that works based on buoyancy system in stomach which increases the gastric residence time of drug hence increases the drug effectiveness. Because of its working based on buoyancy principle this system also called as hydro dynamically controlled system because of it provides a continuous flow and release of drug which gives a hike in the absorption of certain drug. Floating drug delivery

system explains about system that have low density, results having more buoyancy to float over gastric fluid and helps in maintaining drugs gastric residence time hence make drug more prone to give longer action. (6)Buoyant system is developed on the basis of granules, powder, capsules ,tablet, laminated films, and hollow microsphere. Drugs that have specific absorption in upper intestinal region specifically and having very high solubility in the acidic condition are more suitable for designing in form of floating system. floating multi particulate are gastro retentive drug free flowing proteins having size smaller than 200 micrometer .floating multi particulate are gastro retentive drug delivery system design as effervescent and non-effervescent floating drug delivery system. Floating drug delivery can be made in the fork of tablet and capsule .drug slowly releases at a steady rate from the system.

CLASSIFICATION

1. Single Unit Floating Dosage Systems

   Non –effervescent systems (Hydro dynamically balanced system)
   Effervescent Systems (Gas –generating System)
2. Multiple Unit Floating Dosage Systems

   Non-effervescent Systems (Hydro dynamically balanced systems)
   Hollow Microspheres
3. Raft Forming SYSTEM

ADVANTAGES OF FDDS (7.8.9.10.11.12.13)

1. Drugs for FDDS, like antacids, act locally in the stomach.
2. Simple and conventional approach to formulation.
3. Because FDD can stay in the stomach for several hours, it can prolong the period that different medications are retained in the stomach.
4. Medications that are crucial for the stomach, such as antacids.
5. To keep the medicine in a floating form in the stomach, FDDS are helpful for diarrhea and intestinal motility.
6. FDDS enhances patient compliance by lowering the dose.
7. Helpful in the treatment of digestive diseases.
8. FDDS formulations may be helpful for the administration of aspirin and other similar drugs since acidic substances like aspirin create irritation on the stomach wall when they come into contact with them.
9. Drugs can benefit from the FDDS.at the alkaline PH of the intestine, floating dose forms like tablets or capsules will stay in the solution for extended periods of time.
10. FDDS medications work locally in the stomach, such as antacids.
11 FDD can remain in the stomach for several hours and thereby it can extend the gastric retention time of various drug.
12. FDDS are useful in intestinal movement and in diarrhea to hold the drug in floating state in the stomach.
13. By decreasing the dose FDDS improves patient compliance.
14. Useful in treatment of gastro intestinal disorders.
15. Acidic substance like aspirin causes irritation on the stomach wall when come in contact with FDDS formulations may be useful for the administration of aspirin and other similar drug.
16. The FDDS are useful for drugs absorbed through the stomach example: Ferrous salts, Antacids.

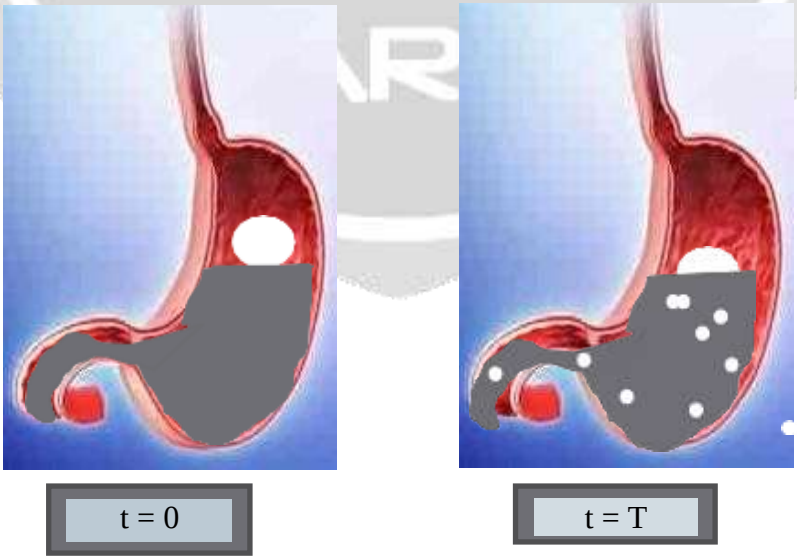
DISADVANTAGES OF FDDS (14.15.16)

1. Floating systems are not feasible for those drugs that have solubility or stability problems in gastric fluids.
2. Drugs such as Nifedipine (calcium channel blocker) which is well absorbed along the entire GI tract and which undergo significant first-pass metabolism, may not be suitable candidates for FDDS.
3. since the slow gastric emptying may lead to reduced systemic bioavailability. Also there are limitations to the applicability of FDDS for drugs that are irritant for stomach lines.
4. One of the disadvantages of floating that they require a sufficiently high level of fluids in the stomach, so that the drug dosages form float there in and work efficiently
5. Not suitable form medicines with GIT solubility or stability issues.
6. A full glass of water should be administered in the dosage form with (200-250 ml)
7. These systems need a high amount of fluid in the stomach to float and function effectively for drug delivery.

MECHANISM OF FLOATING SYSTEMS (17)

Floating drug delivery systems (FDDS) float in the stomach without slowing down the gastric emptying rate since their bulk density is lower than that of gastric fluids. Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. however ,besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the eal. To measure the floating force kinetics, a novel apparatus for determination of resultant weight has been reported in the literature. To apparatus operates by measuring continuously the force equivalent to F(as a function of time)that is required to maintain the submerged object. To object floats better if F on the higher positive side .this apparatus helps in optimizing FDDS with respect to stability and durability of floating forces produced in order to prevent the drawbacks of unforeseeable intragastric buoyancy capability variations.

Fig: 1



Comparison between Conventional and Floating Drug Delivery System

Conventional Drug Delivery System	Floating Drug Delivery System
Less gastric retention time	Improves gastric retention time
Patience compliance is less	Improves patient compliance
More side effect	No risk of dose dumping
Not appropriate for delivery of drugs with narrow absorption window in small intestine region.	Appropriate for delivery of drugs with narrow absorption window in small intestine region.

TABLE -1

EVALUATION OF FLOATING DRUG DELIVERY SYSTEM (18.19.20.21)

- **Bulk Density:**

  It is the ratio of total mass of powder (m) to the bulk volume (Vo) of powder.

  Db=m/Vo

- **Tapped Density:**

  It is the ratio of total mass of powder (m) to the tapped volume (Vi) of powder.

  Dt = m/Vi

- **Compressibility Index:**

  The flow ability of powder can be evaluated via evaluating the bulk density (so) and tapped density (at) of powder and the rate at which it packed down. Compressibility index calculated bymeans of
  Where,

  so= Bulk density g/ml,

  at= Tapped density g/ml.

- **Hausner's Ratio:** It is evaluated by means of taking Tapped density and it divided by Bulkdensity by the usage of following formula.
  Hausner's Ratio= Tapped density / Bulk density

- **Angle of Repose:**

  The frictional forces in a loose powder or granules can be measured via angle of repose. This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane. The granules are allowed to flow through the funnel fixed to a stand at fixed height (h).

  The angle of repose, then calculated by measuring the height and radius of the heap of granulesformed.
  Tan θ = (h/r) θ= tan-1 (h/r)
  θ = angle of repose

  h = height of the heapr = radius of the
  heap

- **Hardness:**

  Hardness shows the capability of a tablet to face up to mechanical shocks while handling. The hardness of the

tablets was evaluated using Monsanto hardness tester. It was expressed in kg/cm2. Three tablets have been randomly picked and hardness of the tablets was decided.

- **Friability test:**

The friability of tablets was evaluated by using Roche Friabilator. It was expressed in percent (%). Ten tablets had been to start with weighed (W) and transferred into friabilator. The friabilator were operated at 25 rpm for 4 minutes or run as much as 100 revolutions. The tablets have been weighed again (Wo). The % friability was then calculated by using formula

%F = 100 (1-Wo/W)

% Friability of tablets less than 1% was considered desirable.

- **Tablet Density:**

Tablet density was an excellent parameter for floating tablets. The tablet could floats most effectivewhen its density turned into much less than that of gastric fluid (1.004). The density was determined by the usage of following formula.
V = лr2hd = m/v Where,
v = volume of tablet (cc)r = radius of
tablet (cm)
h = crown thickness of tablet (g/cc)m = mass of
tablet

- **Weight Variation Test:**

Ten tablets were selected randomly from each batch and weighed separately to test for weightvariation. A little variation was allowed in the weight of a tablet through U.S. Pharmacopoeia.

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- **Determination of Buoyancy lag time**:

The buoyancy lag is the time required for tablet to come out towards surface & float. The buoyancy of tablets was studied at 37±0.5ºc in 900ml of simulated gastric fluid. The buoyancy lagtime was determined by the usage of stop watch and overall floating time was observed visually.

- **Floating time:**

Floating time was measured by the use of USP dissolution apparatus-II at 50 rpm using 900ml of0.1N HCl and temperature was set at 37±0.5ºC, throughout the study. The duration of floating (floating time) is the time the tablet floats within the dissolution medium (including floating lag time, which is the time required for the tablet to rise to the surface) is measured by visual observation.

- **Swelling Index:**

Swelling study was carried out for the floating sustained release layer tablets. The accurately Weighed tablets were placed in USP dissolution apparatus II containing 900ml of 0.1N HCl maintained at 37±2ºC and allowed to swell up to constant weight. The tablets had been removed, blotted with filter paper, and changes in weight were determined. The experiments were performed in triplicate. The degree of swelling (Swelling index) was then determined from theformula.

SWELLING INDEX= Wg-W0/Wo=100

Where,

Wo is the initial weight of tablet and Wg is the weight of tablet at equilibrium swelling in themedium.

- **Drug Content:**

Five tablets were chosen randomly from a batch, weighed and powdered in a mortar. An accurately weighed quantity of powdered tablets equivalent to 100 mg was taken in a standard flask and the volume was filled up to the mark with 0.1 N HCL; the solution was filtered through a 0.45 um membrane paper. Analysis was done by the usage of spectrophotometric method.

APPLICATION OF FLOATING DRUG DELIVERY SYSTEM (22)

- **Enhanced Bioavailability:**

The bioavailability of riboflavin CR-GRDF is substantially increased compared with the administration of non GRDF CR polymeric formulations.

- **Sustained delivery of drugs:**

Oral CR formulations experienced problems in the GIT like gastric residence time. HBS systems that can stay in the stomach for prolonged period of time and having a bulk density of less than 1 and can float on the gastric contents can usually overcome these problems.

- **Site specific drug delivery systems:**

The controlled, gradual drug delivery to the stomach provides appropriate local therapeutic ratesand reduces the systemic exposure of the drug. The dosing frequency can be decreased by extended gastric availability from a site driven drug delivery system. E.g. Furosemide and Riboflavin.

- **Improvement of Absorption:**

Drugs with low bioavailability due to site specific absorption from the upper part of the GIT arepossible candidates to be developed as floating drug delivery systems, by optimizing their absorption.

- **Minimized adverse reaction at the colon:**

Retention of the drug in the stomach in HBS minimizes the amount of drug entering the colon.Unwanted drug activity in the colon region can thus be avoided.

- **Reduced drug concentration fluctuation:**

  Continuous input of the drug following CR-GRDF administration creates concentrations of theblood drug within a narrower range compared with types of immediate release dosage forms.

Marketed products of floating drug Delivery system.(23)

Brand Name	Delivery system	Drug	Company
Modopar ® HBS)	Floating CR capsule	Benserazide and L-Dopa	Roche Products USA
(Prolopa® HBS)			
Topalkan®	Floating liquid alginate Preparation	Al-Mg antacid	Pierre Fabre Drug,France
Liquid	Effervescent floating	Aluminum Hydroxide ,	Glaxo

TABLE-2

RECENT ADVANCES IN FLOATING DOSAGE FORMS

The process of floating and drug release behavior of poly(vinyl acetate)-based floating tablets with membrane controlled drug delivery were studied by. Strubing et al (24)investigated the mechanism of floating and drug release behaviour of poly(vinyl acetate)- based floating tablets with membrane controlled drug delivery. Tablets containing propranolol HCl with Kollidon® SR as an excipient for direct compression and different Kollicoat® SR 30 D/Kollicoat® IR coats, varying from 10 to 20 mg polymer/cm2 , were investigated with regard to drug release in 0.1 mol/l HCl. Furthermore, the onset of floating, the floating duration and the floating strength of the device were determined. Additionally, bench top MRI tests on a few chosen materials were carried out. In addition, bench top MRI studies of selected samples were performed. Coated tablets with a 10 mg polymer/cm2 SR/IR, and an 8.5: 1.5 coating exhibited the shortest lag-times prior to drug release and the onset of floating, and also the fastest increase in and the highest maximum values of the floating strength. The drug release was delayed significantly with a time interval of 24 h as shown by the linear drug release characteristics prepared a gastro-retentive drug delivery system of DA-6034, a new synthetic flavonoid derivative, for the treatment of gastritis using an effervescent floating matrix system (EFMS).The EFMS was created to enable the tablets to float in gastric fluid and release the medication constantly, overcoming the therapeutic limitations of DA-6034 caused by its poor solubility in acidic conditions.

CONCLUSION

Drug absorption in the gastrointestinal tract is a highly variable procedure and prolonging gastric retention of the dosage form extends the time for drug absorption. FDDS promises to be a potential approach for gastric retention. Dosage forms with a prolonged GRT will bring about new and important therapeutic options. The currently available polymer-mediated Non effervescent and effervescent FDDS, designed on the basis of delayed gastric emptying and buoyancy principles, appear to be a very much effective approach to the modulation of controlled oral drug delivery. Number of commercial products and patents issued in this field are the evidence of it. The FDDS become an additional advantage for drugs that are absorbed primarily in the upper part of GI tract i.e. the stomach, duodenum, and jejunum. Some of the unresolved, critical issues like the quantitative efficiency of floating delivery systems in the fast edand fed states, role of buoyancy in enhancing GRTof FDDS and more than that formulation of an ideal dosage form to be given locally to eradicateH.Pylori, responsible for gastric ulcers worldwide. Due to the

complexity of pharmacokinetic and pharmacodynamic parameters, in vivo studies are required to establish the optimal dosage form for a specific drugs. As an important way to boost the bioavailability and controlled delivery of many medication , gastro-retentive floating drug delivery systems have emerged. FDDS and research will continue until an optimal solution that can be applied on industrial scale is found.

REFERENCES

1. Gupta P and Gnanarajan PK. Floating Drug Delivery System: A Review.Int. J Pharm Res Rev. 2015; 4(8): 37-44.
2. Shyama SK and Sivakumar R. Floating Drug Delivery System: An Updated Review. Int J Curr Pharm Clinical Res. 2014; 4(3):150-53.
3. Parma PD, Pande S, Shah HS, Sonara SN and Patel GH. Floating Drug Delivery System:A Novel Approach to Prolong Gastric Retention. World J Pharma Pharma Sci. 2014; 3(4): 418-44.
4. Veerareddy PR, Bajjuri S, Sanka K, Jukanti R, Bandari S and Ajmeru RK. Formulation and Evaluation of Gastroretentive Dosage Form of Ofloxacin. Stamford J Pharma Sci. 2011; 4(1): 09-18.
5. Nirmal J, Saisivam S, Peddanna C, Muralidharan S, Godwinkumar S and Nagarajan M. Bi- layer tablets of Atorvastatin Calcium and Nicotinic acid; Formulation and evaluation. Chem Pharm Bulletin. 2008; 56(10): 1455-58.
6. Hamza Yassin El-Said and Mona HA. Design and *In Vitro* Evaluation of Novel Sustained- Release Double-Layer Tablets of Lornoxicam: Utility of Cyclodextrin and Xanthan Gum.
7. http://www.pharmabiz.com, BasakS,Chronicle Specials, Floatable Gastroretentives: Emerging Potentials, Mar-2006.
8. Deshpande A.A., Shah N.H., Rhodes C.T.,MalickW.,Development of a novel controlled release system for gastricretention, Pharm. Res. 1997; 14: 815-819.
9. Joseph N.H. Laxmi S., Jayakrishnan A. floating type oral dosage from for piroxicam based on hollow.
10. Bharkatiya M, Kitawat S and Ojha A. Floating drug delivery system: A review. J Drug DelivTher. 2014.
11. http://www.pharmabiz.com, BasakS,Chronicle Specials, FloatableGastroretentives: Emerging Potentials, Mar- 2006.
12. Deshpande A.A., Shah N.H., Rhodes C.TMalickW.,Development of a novelcontrolled release system for gastricretention, Pharm. Res. 1997; 14: 815-819.
13. Joseph N.H. Laxmi S., Jayakrishnan A. floating type oral dosage from for piroxicam based on hollow.
14. Kawashinia Y, Niwa T. Takcuchi H. Hino T, Itoh Y. Hallow microspheres for use as a floating controlled drug delivery system in the stomach. J.Pharm.Sci.1992; 81(2): 135-140.
15. Joseph N.H. Laxmi S., Jayakrishnan A. A floating type oral dosage from for piroxicam based on hollow Microspheres: in vitro and in vivo evaluation in rabbits. J. Cont. Rel. 2002; 79:71-79
16. Mukhi,U.,& Mohanty , S.(2013) . Formulation and evaluation of floating tablets of Cefuroxime axetil. International Journal of Pharmacy and Pharmaceutical Sciences, 5(SUPPL..4), 156-161.

17. Talukder, Fassinir R. Gastro retentive delivery system: Hollow beads. Drug DevInd Pharm. 2004; 4: 405-412
18. Tomar P, Shukla V, Kharia AA and Chatterjee DP. Floating drug delivery system: an updated review. J Med Pharm Allied Sci. 2013; 04: 31-42.
19. Sharma N, Agarwal D, Gupta MK and Khinchi MP. A Comprehensive Review on Floating Drug Delivery System.Int J Res Pharm Biomed Sci. 2011; 2(2): 428-41.
20. Gadhve MV, Lende LK, Tajane TS and Gaikwad DD. Formulation and Development of Bilayer Floating Tablet of Nifedipine using surface solid dispersion technique. Int J Adv Pharm. 2016; 5(5): 117-26.
21. Reddy RS, Ramachandra CT, Hiregoudar S, Nidoni UK, Kammar M, and Ram J. influence of processing conditions on functional and reconstitution properties of milk powder made from Osmanabadi goat milk by spray drying. Small Ruminant Res. 2014; 119: 130–137.
22. Arunachalam A, Karthikeyan M, Kishore K, Prasad PH, Sethuraman S, Ashutosh kumar S and Manidipa S.
23. Pal, P., Sharma, V., & Singh, L. (2012). A REVIEW ON FLOATING TYPE GASTRORETENTIVE DRUG DELIVERY SYSTEM Pallavi Pal*, Vijay Sharma , Lalit Singh. 3(4), 37-43
24. S. Strübing, T. Abbouda, C. Renata, et al. New insights on poly(vinyl acetate)-based coated floating tablets: characteri- zation of hydration and CO2 generation by benchtop MRI and its relation to drug release and floating strength. Eur. J. Pharm. Biopharm., 2008, 69: 708-717.