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Review Article

A REVIEW: FLOATING DRUG DELIVERY SYSTEM AS A TOOL TO IMPROVE DISSOLUTION RATE IN GASTRIC

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ABSTRACT

Floating drugs are an effective way to lift the absorption of the drug in the stomach. Drugs made drugs last longer in the stomach so that the solubility process will occur effectively in the stomach. This review-journal was created by extracting indexed journals with the floating drug as journal keywords of 40 journals. This assessment of a floating drug for a new drug delivery system (NDDS) is established to elucidate the floating drugs delivery system (FDDS) based on existing literature. The most recent progress of FDDS includes the formulation and physiological variables that could affect gastric retention and formulation are dealt with in detail. This review also summarizes some approaches to prepare a floating system, evaluation methods and characterization for FDDS pharmaceutical dosage form and also its classification.

Keywords: Floating drug, Gastric Retentive, Dissolution

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INTRODUCTION

Unique of the target drug delivery systems is to reach a therapeutic concentration of medicine to the fix target and to ensure the optimum drug level [1]. Drugs that absorbed in the gastrointestinal route easily will dissolve quickly from the systemic circulation. If an inadequate drug release preparation of drug and the residence time at the upper gastrointestinal (a prominent place for the absorption of many drugs) very fast will make bioavailability become low. Thus, prolonged gastric maintenance is very important at the control of gastroprotection time to formulate a system of controlled release in the stomach for elongated periods of time and could be estimated [2]. Anticipation depends on the state of the subject and design of formulation itself, the maintenance activity can last from several minutes until hours (usually 12 h). The scheme of the drug delivery system is controlled oral (DDS) is usually referred to get bioavailability of the drug that is more probable and repaired [3]. The typical drug has the development of oral drug delivery systems that make up of the optimization of dosage form and GI physiology habits [4]. Floating drug-delivery system (FDDS) is a gastro retentive pharmaceutical preparation that could delay the gastric residence time to obtain adequate bioavailability of a drug [5]. The system is floating in the gastric fluid for a low substance density than the aqueous medium [6].

Definition

Floating systems are low-density systems that have sufficient resistance to float on the stomach and stay afloat in the gastric without creat? an effect on the gastric emptying rate for a long period time. While the system floats on the gastric contents, the drug will be released slowly at the desired concentration in the system. Thus, the residue will be cleared from the stomach. These results will conduct to GRT elevation and be better control of flux in plasma drug concentrations. Even so, furthermore, to the content of the stomach minimally required to enable the achievement of the right of retention of the principle of buoyancy, floating style minimal level (F) also required to give a reliable dosage form floats on the surface of foods [7]. It also useful for proximal gastrointestinal (GI) tracts local drugs, for example, antibiotics for Helicobacter pylori on the manage for a peptic ulcer [8], and for drugs that difficult to dissolve or not stable in intestinal fluids [9].

Anatomi and physiology the stomach

Topographically, the stomach has five regions (fig. 1): (1) the cardia and gastroesophageal (GE) junction, (2) the fundus, (3) the antrum, (4), the corpus and (5) the pylorus.

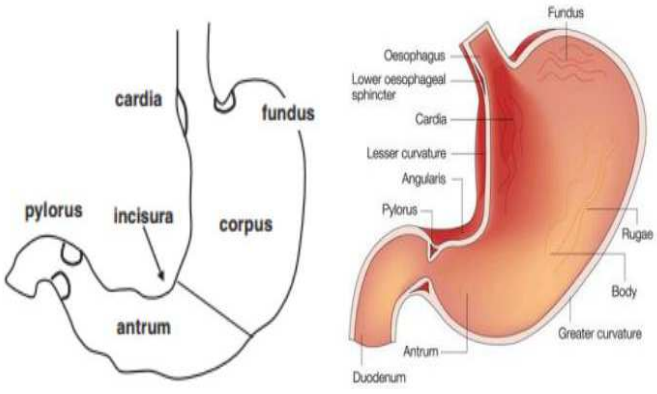

Fig. 1: Structure of gasrtics [10]

In the stomach, part of the proximal made by fundus. The body acts as a reservoir for undigested materials and the antrum is the principal site for mixing gestures and acts as a pump for gastric emptying by propelling actions [11, 12]. Gastric emptying is present in both the fasting and fed states' time. During the fasting state, the inner digestive myoelectric cycle or migrating myoelectric cycle (MMC) occurs during 2-3 h, which are further divided into four phases [13].

a. Period 1 (Basic phase)
Last from 30-60 min with infrequent contractions.
b. Period 2 (Preburst phase)
Last for 20-40 min with recurrent action potential and contractions.
c. Period 3 (Burst phase)
Last for 10-20 min, which includes powerful and regular contractions for a short period.
d. Period 4
Last for 0-5 min and happens between stage 2 and 1 of 2 repeated cycles (fig. 2).

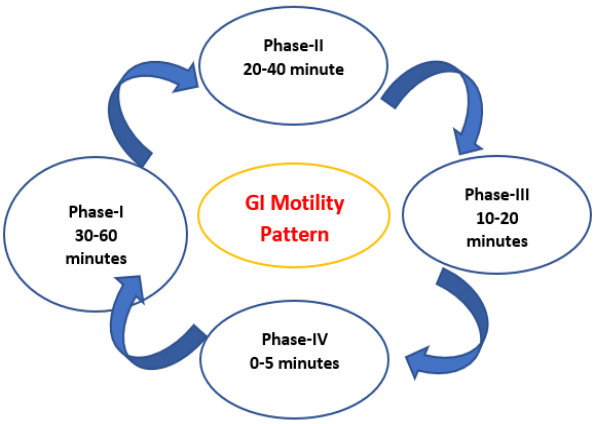

Fig. 2: Gastrointestinal motility model

The stomach has three layers of muscular a circular inside layer, a mid longitudinal layer, and an outside but incomplete oblique layer. Motor functions in the stomach are isolated by region. The fundus relaxes as fluids and solids enter the esophagus, a response known as accessible relaxation, and further, as food enters the funds, a process is known as adaptive relaxation [14, 15]. This response permits the liquid to pool in the fundus bag while the solid components of the meal remain in the mainstream of the flow to the pylorus. After the ingestion of a mixed meal, the pattern of contractions varies from fast to that of the fed state, which is also termed as digestive motility pattern.

Advantages of floating drug delivery systems

1. Tablets or capsules in the floating tablet forms will remain in the liquid for a prolonged time, even at the high pH of the intestine region.

2. In the stomach, Floating Drug

Delivery Systems are advantageous for local action, ex: Antacids

3. Floating drugs delivery system dosage forms are advantageous in the case essential of intestinal movement and in diarrhea to keep the drug in the floating state in the stomach to obtain a relatively better response.

4. Acidic stuffs like aspirin cause annoyance on the stomach barrier when coming in contact with it hence; HBS/FDDS formulations may be valuable for the administration of aspirin and other similar drugs.

5. The FDDS are advantageous for drugs absorbed by the stomach ex: Antacids and Ferrous salts [16].

Disadvantages of floating drug delivery systems

1. Floating systems are not viable for those drugs that have solubility or stability problems in gastric fluids.

2. Nifedipine, which is well absorbed along the entire GI tract and which undertake significant first-pass metabolism, may not be appropriate candidates for Floating Drug Delivery Systems since the slow gastric clearing may cause reduced systemic bioavailability (BA). Also, there are limitations to the applicability of FDDS for drugs that are irritant to the gastric mucosa.

3. FDDS needs a sufficiently high level of fluids in the stomach so that the drug dosages form float within and work efficiently.

4. These systems also afect to the presence of food to delay their gastric emptying [17, 18].

Classification of the floating mechanism

Floating drug delivery systems (NDDS) are characterized based on two varieties of preparation variables: effervescent and Non-effervescent system such as fig. 3

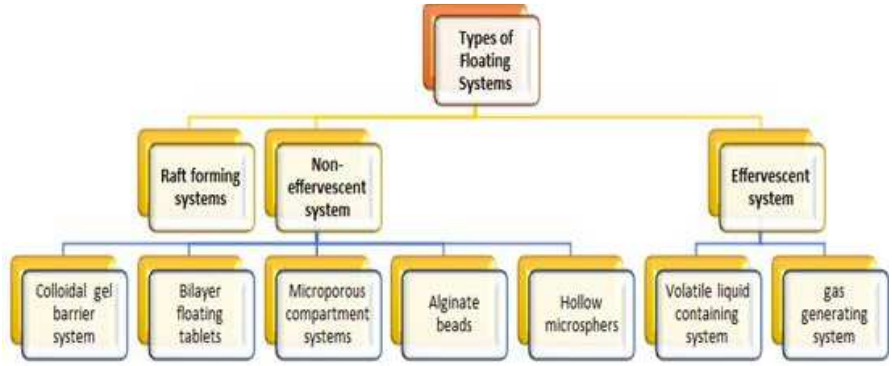

Fig. 3: Classificaction of floating system [13, 19]

Non-effervescent system

The non-effervescent FDDS primarily based on the system of swelling of the polymer or the adhesion to the mucosal layer of the gastrointestinal tract. Two of the most common excipient for non-effervescent FDDS are gel-forming or highly swellable cellulose type of hydrocolloid, polysaccharides and also matrix-forming material such as polycarbonate, polyacrylate, polystyrene, polymethacrylate as well as a bio-adhesive polymer such as chitosan and carbopol [20].

Colloidal gel barrier system

Sheth and Tossounian original design the Hydrodynamically Balanced System (HBS) that contains drugs with gel-forming

hydrocolloid, back in 1975. The system corporation a high level of gel-forming around 20-75% w/w, highly swellable, cellulose type hydrocolloids, polysaccharides and also matrix-forming polymers. When coming into contact with gastric fluid, these hydrocolloids in the system will hydrate and forming a colloidal gel barrier around the surface. These gel barriers monitor the rate of penetration of the fluid to the device and the release of the drug [21].

Bilayer floating tablet

Bilayer floating tablet contain of two-layer of immediate-release tablet that release the first dose of the system while the sustained release layer absorb the gastric fluid and form a colloidal gel barrier on the superficial, it preserves the bulk density to less than one and will remain floating in the stomach [12].

Micro-porous compartment system

A Microporous section has pores placed on the top and bottom of the wall containing a packed medicine reservoir. The peripheral wall drug reservoir is completely sealed to seal the insoluble drug in the stomach surface. The entrapped in the room will be utilized to float the system on the stomach contents and into the fluid hole that will dissolve the drug to be absorbed in the intestine [22].

Alginate beads

Multi-unit floating dosage forms are made from freeze-dried calcium alginate. Round beads with 2.5 mm diameter can be equipped with dripping sodium alginate soluble to a calcium chloride solution; this process will result in precipitation of calcium alginate which can form a porous system that can reinforce the capacity to float for more than 12 h and have some more time long [23].

Hollow microspheres

Hollow microspheres are micro-balloons occupied with medication in the outer shell of the polymer and applied by the emulsion solvent diffusion method. Ethanol solution: aqueous dichloromethane and enteric solution of PVA of a turn temperature of 400 °C. The resulting gas phase is spread into polymer droplets by vaporization of dichloromethane, forming an internal hollow in a polymeric microsphere with the drug formed an internal cavity in the microsphere of polymer with the drug. The micro balloons will float constantly over the surface of acidic dissolution media that keep a surfactant for more than 12 h (*in vitro*) [24].

Effervescent system

In an effervescent system, preparation is designed to produce carbon dioxide gas. Among them are carbonates, generating gas, and other organic acids. The design of the formulation is intended to decrease the density system that can be floating in the gastric fluid [25]. The free CO_2 gas can mix rapidly in the tablet matrix in the case of single-layered tablets [17]. The other way is through combining a matrix that contains a part of liquid, were later from the fusion, will produce gas that will evaporate at body temperature [26]. This effervescent system can be categorized into two groups, gas-producing system and volatile liquid containing the system.

Volatile liquid

The volatile liquid containing systems Inflatable chamber with a liquid can be included which provides sustained gastric retention of the drug delivery system [27]. Liquids in this system include cyclopentane, either that gasifies at body temperature, which can result in inflammation of the chamber in the stomach. They contain a deformable hollow unit which osmotically controls floating systems. The system is differed into two compartments; the first section contains a drug and there is a volatile liquid in the second compartment [28]. It contains polymers that gasify at body temperatures effervescent compounds such as swellable polymers like methodical and polysaccharides tartaric acid, sodium bicarbonate, and citric acid. Resin beads loaded with bicarbonate and coated with ethylcellulose are the most common approach for the preparation of these systems. The ethylcellulose coating is permeable to water, which releases CO2 owing to which it floats [29].

Raft forming systems

Raft forming systems consume a fundamental mechanism by forming a thick interconnected gel in contact with gastric fluid, in which apiece part of the portion of the liquid forms a continuous layer called a raft. The formation of carbon dioxide gas can take this raft afloat. Also, carbon dioxide can avoid the discharge of gastric fluid into the esophagus [30]. This system usually contains a gelling agent, a carbonate or a bicarbonate base to make a less dense system and can make it float in the gastric solution [31].

Factors affecting gastric retention time of the preparation

1. Density-should be lower than that of the gastric fluidal contents (1.004 g/ml)

2. Size-the diameter of more than 7.5 mm [32].

3. Incidence of feeding-GRT can rise by more than 400 min when consecutive foods are dispense compared to a single meal due to low-frequency MMC.

4. Caloric content can be increased by 4-10 with foods high in protein and fat.

5. Gender-average outpatient GRT in men (3.4 h) less than age and race matching with women (4.6 h) regardless of height, body weight and surface [33].

Evaluation of floating tablet

Drug content

Five tablets for each group were taken and ground. The powder equal to 100 mg of the drug was weighed and moved to a beaker glass and then 0.01 N HCl was added and then shaken for 5 min and added 0.01 N HCl to make up to 100 ml and the solution was then produced for 15 min and filtered through the filter paper Whatman. Finally, a solution was diluted appropriately and then measured spectrophotometrically at 203 nanometers using a UV-Visible spectrophotometer (Jasco V530 with 0.01N HCl blank) [34].

Hardness

Tablets are sited between two anvils of hardness tester and the force (kg) is slowly increased to get a proper reading. Readings on a noticeable scale are recorded for the pressure, which is required to break the tablet [35].

Determination of the drug content uniformity

The portion of drug content provides how much volume of drug is in the formulation. It should not exceed the limits obtained by standard monographs. The drug content is determined using HPLC, NIRS, HPTLC, Microtitrimetric method, and ICPAES [36].

Swelling index

The swelling behavior of the measuring unit is determined by the weight assignment. The tablet swelling index corresponds to the tablet site in the dissolution tool basket (type 1) using a pH 6.8 buffer dissolution medium at 37±0.5 °C. The trials were conducted in triplicate for each time point; the swelling index was calculated using the following formula [37].

Test of disintegration time

The time of tablet disintegration was carried out by using a terminate tablet disintegration test device [38].

Floating properties

The effect of formulation variables on the floating properties of gastric drug delivery systems is determined by using a continuous floating monitoring system and statistical trial design [32, 38].

***In vitro* dissolution studies**

The rate of release of ondansetron hydrochloride from floating tablets is established using the USP Dissolution Testing Apparatus 2 (paddle method). The dissolution test was made using 900 ml 0.1 N HCl for 12 h. The sample (5 ml) of the solution was quite from the dissolution apparatus every hour and the sample was changed with a new dissolution medium. The sample was filtered through a 0.45µ

membrane filters and diluted to a concentration corresponding to 0.1 N HCl for 12 h. The transmitter or absorbance of this solution was quantified at 310 nm [37, 39, 40].

CONCLUSION

Drugs with poor absorption rates in intestinal pH can be repaired using the FDDS approach. The strategy of making FDDS varies greatly depending on the physicochemical nature of the drug and the systematic approach that makes the drug last long in the stomach. The FDDT can be achieved by a non-effervescent system, colloidal gel barrier system, bilayer floating tablet, micro-porous compartment system, alginate beads, hollow microspheres effervescent system, volatile liquid, and raft forming systems and it can be evaluated according to essential floating drugs delivery parameters.

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AUTHORS CONTRIBUTIONS

All authos have contributed equally

CONFLICT OF INTERESTS

Declare none

REFERENCES

1. Ahuja G, Pathak K. Porous carriers for controlled modulated drug delivery. Indian J Pharm Sci 2009;7A:599-607.
2. Rajesh K, Usharani E, Nagaraju R, Haribabu R, Siva RPV. Design and evaluation of sustained-release floating tablets for the treatment of gastric ulcers. J Pharm Sci Res 2009;1:81-7.
3. Brahma NS, Kwon HK. Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention. J Controlled Release 2000;63:35–259.
4. Kumaresh S Soppimath, Anandrao R Kulkarni, Walter ER, Tejraj MA. Systems to increase gastric microspheres as floating drug delivery retention of drugs. Drug Metab Rev 2001;33:149–60.
5. Bardonnet PL, Faivre V, Pugh WJ, Piffaretti JC, Falson F. Gastroretentive dosage forms: overview and special case of *helicobacter pylori*. J Controlled Release 2006;111:8.
6. Meka L, Bhaskar K, Krishna MC, Venkateswarlu V, Madhusudan RY. Preparation of a matrix type multiple-unit gastro retentive floating drug delivery system for captopril based on gas formation technique: *in vitro* evaluation. AAPS PharmSciTech 2008;9:2.
7. Desai S, Bolton S. A floating controlled-release drug delivery systems: *in vitro–in vivo* evaluation. Pharm Res 1993;10:1321–5.
8. Umamaheshwari B, Jain S, Bhadra D, Jain NK. Floating microspheres bearing acetohydroxamic acid for the treatment of *helicobacter pylori*. J Pharm Pharmacol 2003;55:1607–13.
9. Jain SK, Awasthi AM, Jain NK, Agrawal GP. Calcium silicate based microspheres of repaglinide for gastroretentive floating drug delivery: preparation and *in vitro* characterization. J Controlled Release 2005;107:300–9.
10. Soybel D. Anatomy and physiology of the stomach. Surg Clin North Am 2005;85:875-94.
11. Yie WC. Novel drug delivery system 2nd ed. New York: Marcel jekker Inc;1993. p. 21-3.
12. Garg S, Sharma S. Gastroretentive drug delivery system. Business Briefing Pharmatech 2003;203:160-6.
13. Vedha H, Chaudhary J. The recent developments on gastric floating drug delivery systems: an overveiwint. J Pharmtech Res 2010;2:524-34.
14. Jahnberg T, Abrahamsson H, Jansson G. Vagal gastric relaxation in the dog. Scand J Gastroenterol 1997;12:221–4.
15. Arakawa T, Uno H, Fukuda T. New aspects of gastric adaptive relaxation, reflex after food intake for more food: involvement of capsaicin-sensitive sensory nerves and nitric oxide. J Smooth Muscle Res 1997;33:81–8.
16. Arunachalam. Floating drug delivery systems: a review. Int J Res Pharm Sci 2011;2:76-83.
17. Shweta A. Floating drug delivery systems: a review. AAPS PharmSciTech 2005;6:372-9018.
18. Gangadharappa HV, Pramod KTM, Shiva KHG. Gastric floating drug delivery systems. Indian J Pharm Educ Res 2007;41:295-306.
19. Jose GR, Hosen O, Khalid S. Progresses in gastroretentive drug delivery systems, Pharmatech; 2013. p. 152-6.
20. Saritha D, Sathish D, Madhusudan RY. Formulation and evaluation of gastroretentive floating tablets of domperidone maleate. J Appl Pharm Sci 2012;2:68-73.
21. Sharma N, Dilip A, Gupta MK, Mahaveer PK. A comprehensive review on the floating drug delivery system. Int J Res Pharm Biomed Sci 2011;2:428–41.
22. Avinash K, Dwivedi A, Praween K, Abhinav G. Floating drug delivery system a significant tool for stomach specific release of cardiovascular drugs. Int J Drug Dev Res 2014;4:116-29.
23. Sarawade A, Ratnaparkhi MP, Chaudhari S. An overview floating drug delivery system. Int J Res Dev Pharm Life Sci 2014;3:1106-15.
24. Mayavanshi AV, Gajjar SS. Floating drug delivery systems to increase gastric retention of drugs: a review. Res J Pharm Tech 2008;1:345-8.
25. Sharma M, Chaturvedi AK, Singh UK, Gupta RD, Gulati A, Sehgal P. Floating drug delivery system: an approach to oral controlled drug delivery. Pharm Res 2007;7:1-14.
26. Bhavjit K, Shivani S, Geetika S, Rupinder S, Sukhdev S, Meenu N, *et al*. A review on floating drug delivery system. Asian J Biomed Pharm Sci 2013;3:1-6.
27. Ziayur R, Mushir A, Khar RK. Design and evaluation of bilayer floating tablets of captopril. Acta Pharm 2006;56:49-57.
28. Khavare NB. A review on key parameters and components in designing of osmotic controlled oral drug delivery systems. Indian J Novel Drug Delivery 2010;2:122-31.
29. Shila V Devtalu, Ashwini EP, Manoj M Bari, Shashikant DB. A novel approach of bilayer tablet technology. Int J Pharm Sci Rev Res 2013;21:46-52.
30. Nayak AK, Ruma M, Biswarup D. Gastroretentive drug delivery systems. Asian J Pharm Clin Res 2010;3:2-10.
31. Purnima T, Ubaidulla U, Roop KK, Vishwavibhuti. A review on floating drug delivery system. Int J Res Dev Pharm Life Sci 2012;1:1-10.
32. Meenakshi J, Ujjwal N, Jyotsana K, Devendra S. A review: gastroretentive drug delivery system (GRDDS). Indian J Pharm Biol Res 2015;3:82-92.
33. Uddin M, Rathi PB, Siddiqui AR, Sonawane AR, Gadade DD. Recent development in floating delivery systems for gastric retention of drugs an overview. Asian J Biomed Pharm Sci 2011;1:26-42.
34. Sameer S, Prajapai K, Pathak AK, Mishra A. Formulation and evaluation of floating tablet of captopril. Int J Pharm Tech Res 2011;3:333-41.
35. Rahman Z, Ali M, Khar RK. Design and evaluation floating labeled. Act Pharm 2006;56:49-57.
36. Yuvarej ST, Pushpendra SN, Garima RO. Devolpment and evaluation of floating microsperes of verapamil hydrochloride. Brazilian J Pharm Sci 2007;43:529-34.
37. Daisy CKS, Vengatesh S, Elango KR, Devi D, Deattu N, Christina P. Formulation and evaluation of floating tablets of ondansetron hydrochloride. Int J Drug Dev Res 2012;4:265-74.
38. Budaya UD, Surini S. Development of coproses excipient of xanthan gum and acacia gum as control release matrices for famotidin floating tabalet. Int J Appl Pharm 2020;23:192–6.
39. Chowdary KPR, Areefulla HS. Formulation and evaluation of floating tablets of gliclazide employing HPMC and carbopol. Int J Chem Sci 2012;10:1213-20.
40. Jassim ZE. Formulation and evaluation of furosemid liquid solid compact. Int J Appl Pharm 2017;8:39–48.
41. Muchtaridi M, Yuliani E, Sopyan I. Application off-line SPE-HPLC/UV methods in analysis of ofloxacin in human urine (*in vitro*). Int J Pharm Pharm Sci 2015;8:255–61.