International Journal of Pharmacy
Journal Homepage: http://www.pharmascholars.com

Review Article **CODEN: IJPNL6**

Potential of Floating Drug Delivery System as an Innovation

Riffat Latif[1]*, Irum Latif[2], Zulcaif Ahmad[3], Iftikhar Khan[4]

[1]Department of Pharmaceutical Sciences, Riphah International University, Lahore, Pakistan
[2]Department of Chemistry, Islamia University Bahawalpur, Bahawalpur, Pakistan
[3]Department of Pharmaceutical Sciences, University of Lahore, Lahore, Pakistan
[4]Department of Pharmaceutical Sciences, COMSATS University Islamabad, Abbotabad Campus, Islamabad, Pakistan

***Corresponding author email: silentchemist5@gmail.com**

Received on: 21-05-2021; Revised on: 04-06-2021; Accepted on: 11-06-2021

ABSTRACT

The current research related to the formulation of the floating matrix tablets planned to enhance the drug bioavailability, extend the gastric residence time and reduce the side effects of irritating drugs, which are attained after oral administration. Gum arabic, sodium alginate, carrageenan, corn starch, gum guar, hydroxypropyl methylcellulose (HPMC), and polyacrylates were different types of matrix-forming polymers studied. As the type of matrix former the relative importance of drug diffusion, polymer swelling tablet erosion for the resulting release patterns varied significantly. The tablets eroded upon contact with the release medium. The purpose of this article is to evaluate modern technology used in the development of floating drug delivery system as well as summarizes the applications the advantages and disadvantages, characterization, estimation methods and future potential, principle of floating drug delivery system for floating tablets.

Keywords: FDDS, HPMC, Swellable system, Migrating Myloelectric Cycle (MMC), Polyacrylates, Polystyrene.

INTRODUCTION

Oral dosage forms are the most common and convenient drug delivery systems and must have the property to deliver directly to target site for prolonged period of time. Previously many studies have been conducted by the scientists in whom they aimed for the increase in time of gastric emptying. In humans the average gastric emptying time after meal must be within 2-6 hours [1]. This prolongation results in the increased retention time of drug in the stomach resulting in better bioavailability of drug in the body. Drug targeting and delayed stomach emptying are the two reasons that revealed to the discovery of controlled release delivery systems in oral dosage forms [2]. Solid oral dosage forms are more stable among which tablets are the most common solid oral dosage forms. Among oral route 90% of the drugs are administered today which provides good systemic effects [3].

There are two mechanisms that are involved in the principle of floating drug delivery systems including, first is the system with effervescent characteristics and the second with non-effervescent properties [4]. The tablets formed by using non-effervescent systems uses the matrix system formed by hygroscopic polymer like Hydrocollides and polysaccharides etc. and the materials causing effervescence like reaction of carbonated with acids (e.g., sodium bicarbonate with citric acid) [5,6]. The entrapment of air molecules or air spaces is due to swelling of polymer matrix that is an aid for buoyancy for floating delivery systems. This will control the diffusion of drug from polymer matrix [7,8]. As a result of drug comes out of matrix and form a gel structure that causes buoyantic effect in the gastric juice and helps in prolongation of gastric emptying [9]. Similarly tablets formed by effervescent systems uses matrices that are synthesized by swellable polymers like polysaccharides such as chitosan and other excipients that causes effervescence of the final dosage form.

Now a days a variety of drug delivery systems are present in market between which mainlyused for the oral drug delivery. From instantaneous release to site specific development take place in the oral drug delivery. Solid oral dosage forms are more stable during which tablets are the most common solid oral dosage forms [10].

Among oral route 90% of the drugs are administered today which provides good systemic effects (Figure 1).

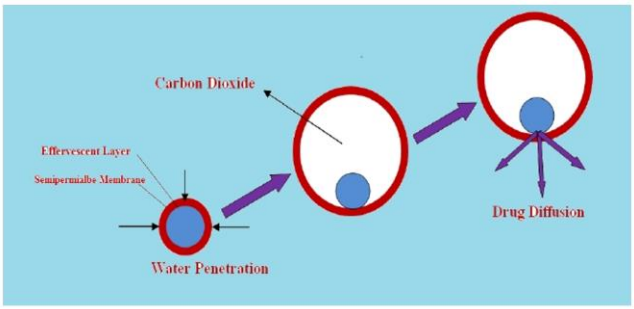

Figure 1: Mechanism of floating drug delivery systems.

Controlled drug delivery is gaining importance these days because oral controlled drug delivery intends to deliver drug for an extended period of time which provide good bioavailability and which makes the dosage form reproducible [11]. Due to physiological problems, the system gets many difficulties like alteration in emptying time of stomach, drugs have stability issues in intestine and absorption window is narrow for some drugs [12]. Floating Drug Delivery System (FDDS) is designed to overcome these difficulties. It provide oral controlled sustained dosage form drug is retained in stomach for a prolonged period of time as compare to conventional oral dosage form and delivers the drug at slow rate in systemic circulation and maintains effective plasma concentration [13].Currently most of the pharmaceutical scientist is struggling in mounting the ideal FDDS. The purpose of Floating Drug Delivery Systems (FDDS) should be mainly aimed to attain more expected and increased bioavailability. It deliver the active drug directly at the particular site, the benefit of this ideal system is to deliver the single dose for the whole period of treatment [14].

Physiological structure of gastrointestinal tract

Fundus, body, and antrum (pylorus) are 3 regions to which Stomach is divided anatomically. Fundus covers the proximal part and body acts as a tank for undigested material, whereas the antrum act as a pump for gastric emptying by propelling actions and it is the central site for assimilation motions. During fasting as well as fed states Gastric emptying occurs. The motility pattern though distinctive in the two forms [15]. An interdigestive series of electrical events take place during the fasting state. Interdigestive myloelectric cycle or migrating myloelectric cycle (MMC), is the place, which cycle both through stomach and intestine every 2 to 3 hours.

Phases

a) Basal phase (Phase I) ends in forty to sixty minutes with exceptional contractions.

b) Preburst phase (Phase II) ends in forty to sixty minutes with contractions and irregular action potential. the amount and incidence increases slowly as the phase steps forward.

c) Burst phase (Phase III) ends in four to six minutes. It consists of strong and normal contractions for small period. All the undigested material is brushes of out of the stomach down to the small intestine due to a wave which is called housekeeper wave.

d) Phase IV ends in zero to five minutes and take place among phases three and one of 2 following cycles. Digestive motility pattern is the pattern of contractions changes from fasted to that of fed state after the ingestion of a mixed meal. It consists of continuous contractions as in phase II of fasted state. During the fed state start of MMC is late follow-on in delaying of gastric emptying rate. These contractions result in decreasing the size of food particles which are propelled toward the pylorus in a suspension form [16].

GASTRORETENTION TECHNIQUES

Many approaches used to enhance the drug retention within stomach.

Floating systems

In Floating Drug Delivery Systems (FDDS) drug remain float within stomach without disturbing the gastric emptying time for extended period because Floating Drug Delivery Systems (FDDS) have a bulk density lower than gastric fluid [17]. The drug is released gradually at the desired rate from the system at the same time as system is floating on the gastric stuff. The residual system is unfilled from the stomach subsequent to release of drug. By including floating chamber packed with vacuum, air, or inert gas, the floatation of a drug delivery system within stomach can be accomplished [18].

High density systems

These highly compactness systems are remaining in the rugae of stomach and accomplished to endure its peristaltic movements and they have a density of ~3 g/cm^3. These High density formulation prepared by using diluents such as titanium oxide, zinc oxide, barium sulphate (with density 4.9), and iron powder [19].

Larger amount of drug formulation and achievement of necessary density of 2.4-2.8 g/cm^3 is technically complex to manufacture by this system. This is the single main disadvantage with these systems [20].

Tablet swellable in stomach

The polymer absorbs water and swells up when come in contact with gastric fluid. Due to the presence of physical-chemical cross links in the hydrophilic polymer network, extensive swelling of these polymers take place [21]. Physical reliability of these dosage form retain by cross link which inhibit the dissolution of polymer. Continuous drug release can be attained by selection of polymer with the appropriate molecular weight and controlled swelling characteristics. The swelling property of the system is hinder by high extent of cross linking it assist to retain its physical integrity for extended period. Low level cross linking outcome is in widespread

bulge pursuing by the fast dissolution of polymer (Figure 2).

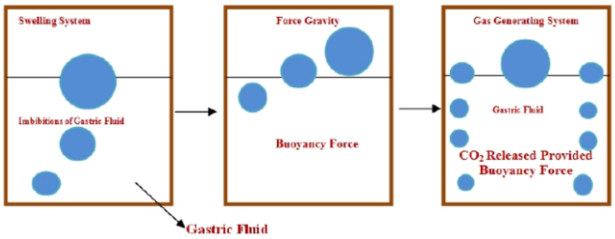

Figure 2: Mechanism explaining the swelling and expanding of floating drug delivery system.

Swelling and expanding systems

They show propensity to stay logged in the pyloric sphincters, hence, these system are also known as "Plug type system. For many hours these polymeric matrices stay in the gastric cavity yet in fed condition [19] (Figure 3).

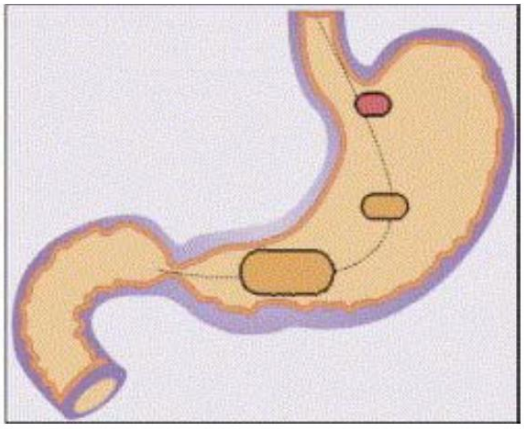

Figure 3: Swelled tablet in stomach.

FDDS CATEGORIZATION DEPEND ON MECHANISM

Multiple units

It decrease the inter subject unevenness in absorption and the possibility for dose removal is lesser. Single unit formulations are related to problems such as sticking mutually or being hindered in gastrointestinal tract, which may have a potential hazard to manufacture. Multiple unit systems avoid the 'all-or-none' gastric emptying nature of single unit systems [22].

Single unit

Single unit dosage forms are unproblematic to manufacture but owing to huge quantity of drug distribute at a particular place of the gastro intestinal tract they might cause elevated unpredictability in bioavailability and local irritation and they endure from the danger of losing their properties also early on due to their all-or-none emptying from the stomach [23-25].

Effervescent systems or gas generating systems

They are prepared in such a method that while in contact with the acidic gastric contents, carbon dioxide is released and acquire ensnared in swollen hydrocolloids, which gives buoyancy to the dosage forms [1-3]. For gas production the optimal stoichiometric proportion of citric acid and sodium bicarbonate is reported to be 0.76:1. These are matrix form of systems formulated with the assist of swellable polymers diverse effervescent compounds, e.g., tartaric acid, sodium bicarbonate, and citric acid and other than effervescent compound chitosan and methylcellulose [4-6].

Systems non-effervescent

Following oral administration this dosage form bulge in gastric fluids and reached to bulk density of less than one. The air ensnare inside the inflamed matrix gives buoyancy to the dosage form [7]. The so produced swollen gel-like composition works as a pool and permit continuous release of drug through the gelatinous mass [8]. For the formulation of these types of systems, the drug and the gel forming hydrocolloid are mixed systematically. Matrix forming polymers (e.g., polycarbophil, polystyrene and polyacrylates), are included in high level (20%-75% w/w) to tablets or capsules, or One or more gel forming, extremely swellable, cellulosic hydrocolloids (e.g., hydroxypropyl methyl cellulose, hydroxyl ethyl cellulose, sodium carboxy methyl cellulose, hydroxyl propyl cellulose), polysaccharides [9].

Floating microspheres

A controlled release system formulated to increase its residence time in the stomach with no contact with the mucosa was attained by the preparation of floating microspheres [10,11]. Solvent diffusion, evaporation, and solvent evaporation are the method involved in the formulation of floating microspheres [12]. Plasticizer, the solvents employed for the preparation and the type of polymer are the major properties on which drug release and floating depend. The drug release can be altered by optimizing the quantity of polymer and the polymer plasticizer ratio, Polymers, such as polycarbonate, Eudragit® S and cellulose acetate, are used in the preparation of hollow microspheres (Figure 4).

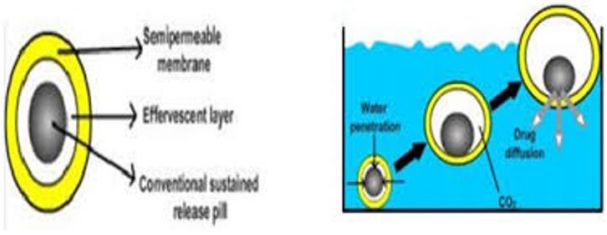

Figure 4: Controlled release system of floating microspheres.

Raft forming systems

The basic mechanisms drawn in the raft development comprise the formation of thick cohesive gel in contact with gastric fluids, where every part of the liquid swells forming an uninterrupted coat called a

raft [15]. By the development of CO_2, buoyancy produced and because of this raft floats and it is act as a barrier to stop the reflux of gastric stuffing like HCl and enzymes into the esophagus. To formulate the system of low density and float on the gastric mucosa, the system contains a gel forming agent and alkaline bicarbonates or carbonates [16].

FLOATING DRUG DELIVERY SYSTEMS LIMITATIONS

- Drugs which are annoyance to Gastric mucosa are not enviable.
- Drugs which under goes first pass metabolism may not be enviable for the preparation of these types of systems [17].
- Drugs with solubility and stability problems in GIT are not appropriate aspirant for these sorts of systems.
- Elevated level of fluid in the stomach is necessary for drug delivery to float and work competently.
- The most inappropriate aspirant to be incorporated in the systems is the drug substances that are breakdown in the acidic environment of the stomach [18,19].

Floating drug delivery system advantages

- Due to its easiness of administration improved patient compliance is attained.
- This system hang about in stomach intended for several hours so it gives sustained drug delivery like hydro dynamically balanced system (HBS) dosage variety altered gastric residence time [20].
- The drugs such as furosemide, for which site specific drug delivery is required, are prepared as floating system [21].
- It keeps the steady blood level.
- It achieved drug delivery with controlled released by keeping optimum therapeutic window [22].
- These are chemically and microbiologically stable from all other oral routes
- They are the mainly well-suited oral dosage form due to lesser content variation and elevated dose precision [23].
- Designed for greater level of production FDDS is most suitable.
- By coating mask the bitter taste and bad odor [24].

CONCLUSION

Gaps and innovations are always available in Noval drug delivery systems and Floating Drug Delivery Systems have their own potential in this field. Depending upon enhanced stability, increased bioavailability, improved dissolution profile and grip on controlled delivery of drug at the target site, floating tablets have a great potential in oral dosage forms. As the type of matrix former the relative importance of drug diffusion, polymer swelling tablet erosion for the resulting release patterns varied significantly. The tablets eroded upon contact with the release medium. The gas generating agent sodium bicarbonate and synthetic polymer HPMC K100M, ethyl cellulose, makes the floating drug delivery system is a potential technique to attained extended drug release and *in vitro* buoyancy. The preferred dissolution profile might be attained by choosing an appropriate opus of HPMC K100M and ethyl cellulose. The mechanism used for preparation of a buoyant drug product is just to target increased gastric resistance time. The principal control point in manufacturing of floating dosage forms is that the density of drug product should be less than that of digestive fluids. Hence Floating Drug Delivery Systems are the best choice for patients with G.I diseases.

REFERENCES

1. Dixit N. *J of current pharm. research*,2021;11(6):252-285.
2. Bhalla N, Goswami M.*Int J of Pharm Research & Allied Sci*.2021;11(6):150-155.
3. Chavanpatil M, Jain S, Chaudari S, Shear R, Vavia P. *Int J Pharm*.2021;11(6):856-864.
4. Swamy PV, Bhosale UV, Hiremath SN, Shirsand SB, Raju SA. *Int J Pharm*.2021;11(6):300-310.
5. Arora S, Ali J, Ahuja A. et al. *AAPS Pharm Sci Tech*.2021;11(6):585-590.
6. Hilton AK, Deasy PB. *Int J Pharm*.2021;11(6):464-468.
7. Krogel I and Bodmeier R. *Int J Pharm*.2021;11(6):960-986.
8. Sheth P,Tossounian J.*Drug Dev Ind Pharm*.2021;11(6):340-349.
9. Ushimaru K,Nakamichi Sito H.*Drug Dev Ind Pharm*.2021;11(6):110-115 .
10. Sumit D,Paramita S.*Int J Pharm*.2021;11(6):141-144.
11. Mayavanshi SV, Gajjar AR.*Int Drug Dev Sys*.2021;11(6):52-60.
12. Shah, S. H., Patel, J. K., Patel, N. V.*Int J Pharm Tech Res.* 2021;11(6):220-223.
13. Patel A, Subhabrata R,Ram Sharnagat T. *DARU J of Pharm Sci.*2021;11(6):57-64.
14. Desai S, Sanford B. *Int J Pharm.*2021;11(6):1321-1325.
15. Tamizharasi S, V. Rathi, J. Rathi.*Floting Drug Dev Sys.* 2021; 11(6):300-305.
16. Jain A, Sunil K. *J of controlled res.* 2021;11(6): 300-309.
17. Sungthongjeen S,Srisagul D.*Int J Pharm.*2021;11(6): 136-

143.

18. Dave E, Brijesh S, Avani F,Madhabhai M. *Aaps Pharm Sci Tech*.2021;11(6): 77-82.
19. Ahmad F, Farhan J, *Asian J of Chem*.2021;11(6):4580-4603.
20. Gohel D, Mukesh C.*Asian J of Chem*.2021;11(6): 22-26.
21. Soppimath K, Kumaresh S.*Int J Med*.2021;11(6): 149-160.
22. Patel A, Viral F, Natavarlal M P. *AAPS Pharm Sci Tech*.2021;11(6): E118-E124.
23. Oth G, Marianne K. *Pharm. J res.* 2021;11(6): 298-302.
24. Li Shoufeng. *Drug dev Ind pharm.* 2021;11(6): 783-793.
25. Chavanpatil K, Mahesh D. *Int. J Pharm.* 2021;11(6): 86-92.