World Inventia Publishers

Journal of Pharma Research

http://www.jprinfo.com/

Vol. 8, Issue 7, 2019 ISSN: 2319-5622 USA CODEN: JPROK3

Review Article

FLOATING DRUG DELIVERY - A REVIEW

Alagu Manivasagam [1], Sarath kumar S.J [1]*, Shaiju S. Dharan [2], Mathan S [3], Merlin N.J [4], Snigdha S. Babu [5]

[1] Assistant Professor, Department of Pharmacy, Annamalai University, Chidambaram, TN, INDIA.

*[*1] Assistant Professor, Department of Pharmaceutics, Ezhuthachan College of Pharmaceutical Sciences, Marayamuttom PO, Neyyattinkara, Thiruvananthapuram, Kerala, INDIA.*

[2] Principal, Ezhuthachan College of Pharmaceutical Sciences, Marayamuttom PO, Neyyattinkara, Thiruvananthapuram, Kerala

[3] Professor and Head, Department of Pharmaceutics, Ezhuthachan College of Pharmaceutical Sciences, Marayamuttom PO, Neyyattinkara, Thiruvananthapuram, Kerala, INDIA.

[4] Director of PG studies, Ezhuthachan College of Pharmaceutical Sciences, Marayamuttom PO, Neyyattinkara, Thiruvananthapuram, Kerala, INDIA.

[5] Assistant Professor, Department of Pharmaceutics, Ezhuthachan College of Pharmaceutical Sciences, Marayamuttom PO, Neyyattinkara, Thiruvananthapuram, Kerala, INDIA.

Received on: 12-02-2019; Revised and Accepted on: 09-07-2019

ABSTRACT

Oral controlled release dosage form has been developed over the past three decades due to their considerable therapeutic advantages such as ease of administration, patient compliance and flexibility in formulation. One of the most feasible approaches for achieving a prolonged predictable drug delivery profile is floating drug delivery system (FDDS) which prolongs the gastric residence time and increases the overall bioavailability of the dosage form. Gastric floating drug delivery system can remain in the gastric region for several hrs and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility of drug that is less soluble in high pH environment. It is also suitable for local drug delivery in stomach and proximal small intestine.

KEYWORDS: *FDDS, CRDDS and Gastrointestinal Retention.*

INTRODUCTION

Pharmaceutical dosage forms are the physical nature or form in which the drug is administered into the human body. There are many dosage forms which include tablet, capsule, pill, powder, mixture, syrup, cream, injections, suppositories etc. The different dosage forms are administered into the body via different routes of administration which includes oral, parenteral, transdermal etc. The development of a dosage form is highly based on the principles of Biopharmaceutics which gives the informations about drug kinetics which includes absorption, distribution, metabolism and elimination. Among this oral route is considered as the most important route due to its ease of administration. Conventional drug administration has many disadvantages like less bioavailability, drug leakage etc.

*** Corresponding author:**

Sarath kumar S.J.

Assistant Professor,

Department of Pharmaceutics,

Ezhuthachan College of Pharmaceutical Sciences,

Marayamuttom PO, Neyyattinkara, Thiruvananthapuram,

Kerala, INDIA.

** E-Mail: sarathkumarsj123@gmail.com*

DOI: https://doi.org/10.5281/zenodo.3357191

To avoid these disadvantages, novel drug delivery methods were developed. A drug delivery system refers to the technologies or methods which are used to present the drug at the site of action and release the drug in a predetermined rate which last for the specified time intervals.

The oral route is increasingly being used for the delivery of therapeutic agents because the low cost of the therapy and ease of administration lead to high levels of patient compliance. More than 50% of the drug delivery systems available in the market are oral drug delivery systems.

Controlled-release drug delivery systems (CRDDS) provide drug release at a controlled, predictable and predetermined rate. Controlled-release drug delivery system is capable of achieving the benefits like maintenance of optimum therapeutic drug concentration in blood with predictable and reproducible release rates for extended time period; enhancement of activity of duration for short half-life drugs; elimination of side effects; reducing frequency of dosing and wastage of drugs; optimized therapy and better patient compliances.

The successful development of oral controlled drug delivery systems requires an understanding of three aspects of the system namely,

1. The physiochemical characteristics of the drug

2. Anatomy and physiology of GIT and characteristics of dosage forms [1].

Drugs with short half lives and drugs that easily absorbed from gastrointestinal tract (GIT) are eliminated quickly from the systemic circulation. For these types of drugs, the development of oral sustained-controlled release formulations is an attempt to release the drug slowly into the gastrointestinal tract and maintain an effective drug concentration in the systemic circulation for a long time. After oral administration, such a drug delivery would be retained in the stomach and release the drug in a controlled manner, so that the drug could be supplied continuously to its absorption sites in the gastrointestinal tract. But oral sustained drug delivery formulations show some limitations connected with the gastric emptying time; variable and too rapid gastrointestinal transit could result in incomplete drug release from the device into the absorption window leading to diminished efficacy of the administered dose [3].

Good fundamental understanding of the anatomic and physiological characteristics of the human GIT is required to modulate the gastrointestinal transit time of a drug through FDDS for maximal gastrointestinal absorption of drugs and site specific delivery [1].

1.2. Gastrointestinal Retention:

Gastro retentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment It has applications also for local drug delivery to the stomach and proximal small intestines. Gastro retention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patients to successfully modulate the gastrointestinal transit time of a drug delivery system through floating drug delivery system (FDDS) For maximal gastrointestinal absorption of drugs and site-specific delivery, one needs to have a good fundamental understanding of the anatomic and physiological characteristics of the human GIT [2].

Gastro Retentive Drug Delivery System:

Dosage forms that can be retained in the stomach are called GRDDs. GRDDSs can improve the controlled delivery of drugs that have an absorption window by continuously releasing the drug for a prolonged period of time before it reaches its absorption site.

Prolonging the gastric retention of the drugs are sometimes desirable for achieving therapeutic benefits of drug that are absorbed from the proximal part of the GIT or those are less soluble in or are degraded by alkaline pH or they encounter at the lower part of the GIT. GRDDS are beneficial for such drugs by improving their [4].

- Bioavailability
- Therapeutics efficiency and
- Possible reduction of the dose.

Apart from these advantages, these systems offer various pharmacokinetic advantages like, maintenance of constant therapeutic levels over a prolonged period and thus reduction in fluctuation in the therapeutic levels.

Floating Drug Delivery System:

Floating systems was first described by Davis in 1968. FDDS is an effective technology to prolong the gastric residence time in order to improve the bioavailability of the drug. FDDS are low density systems that have sufficient buoyancy to float over the gastric contents and remain in the stomach without affecting the gastric emptying rate for a prolonged period. While the system floats over the gastric contents, the drug is released slowly at the desired rate, which results in increased GRT and reduces fluctuation in plasma drug concentration [4].

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 meal. Many buoyant systems have been developed based on granules, powders, capsules, tablets, laminated films and hollow microspheres.

These considerations have led to the development of oral floating dosage forms possessing gastric retention capabilities. Thus when a drug possesses a narrow 'absorption window' design of sustained release preparation require both prolongation of gastrointestinal transit time of dosage forms and controlled drug release. Floating dosage form with prolonged residence time in stomach is highly desirable for drug.

- That is locally active in stomach.

- That have absorption window in stomach or in upper small intestine.

- That is unstable in intestinal or colonic environment.

- Have low solubility at high pH value [5].

Classification of FDDS:

Floating systems can be classified as effervescent and non -effervescent systems.

i) Effervescent systems:

These buoyant delivery systems utilize matrices prepared with swellable polymers such as methocel or polysaccharides, e.g., chitosan, and effervescent components, e.g., sodium bicarbonate and citric or tartaric acid or matrices containing chambers of liquid that gasify at body temperature . Flotation of a drug delivery system in the stomach can be achieved by incorporating a floating chamber filled with vacuum, air or an inert gas. Gas can be introduced into the floating chamber by the volatilization of an organic solvent (e.g., ether or cyclopentane) or by the CO2 produced as a result of an effervescent reaction between organic acids and carbonate–bicarbonate salts. The matrices are fabricated so that upon arrival in the stomach, carbon dioxide is liberated by the acidity of the gastric contents and is entrapped in the gellified hydrocolloid. This produces an upward motion of the dosage form and maintains its buoyancy. A decrease in specific gravity causes the dosage form to float on the chime [5].

ii) Noneffervescent systems:

The Non effervescent FDDS is based on mechanism of swelling of polymer or bioadhesion to mucosal layer in GIT. The most commonly used excipients in non-effervescent FDDS are

gel forming or highly swellable cellulose type hydrocolloids, polysaccharides and matrix forming material such as polycarbonate, polyacrylate, polymethacrylate, polystyrene as well as bioadhesive polymer such as chitosan and carbopol. In one approach, gel forming hydrocolloid swells in contact with gastric fluid after oral administration and maintains a relative integrity of shape and the bulk density of less than unity within gastric environment.

Drug Candidates Suitable for FDDS:

- Drugs that have narrow absorption window in GIT (e.g. L-DOPA, Paminobenzoic acid, Furosemide, Riboflavin).
- Drugs those are locally active in the stomach (e.g. Misroprostol, Antacids).
- Drugs those are unstable in the intestinal or colonic environment (e.g. Captopril, Ranitidine HCl, Metronidazole).
- Drugs that disturb normal colonic microbes (e.g. antibiotics used for the eradication of Helicobacter pylori, such as Tetracycline, Clarithromycin, Amoxicillin).
- Drugs that exhibit low solubility at high pH values (e.g. Diazepam, Chlordiazepoxide, Verapamil) [6].

Advantages of Floating dosage form :

1. These systems are particularly advantageous for drugs that are specifically absorbed from stomach or the proximal part of the small intestine, e.g., Riboflavin and Furosemide.
2. The fluctuations in plasma drug concentration are minimized, and concentration-dependent adverse effects that are associated with peak concentrations can be prevented. This feature is of special importance for drugs with a narrow therapeutic index.
3. The efficacy of the medicaments administered utilizing the sustained release principle of floating formulation has been found to be independent of the site of particular medicaments
4. Complete absorption of the drug from the floating dosage form is expected even at the alkaliine pH of the intestine. The dissolution of the drug in gastric fluid occurs and then the dissolved drug is available for absorption in the small intestine after emptying of the stomach contents.
5. Poor absorption is expected when there is vigorous intestinal movement and a shorted transit time as might occur in certain type of diarrhea. Under such circumstances it may be advantageous to keep the drug in floating condition in stomach to get a relatively better response.
6. Drugs that have poor bioavailability because of site-specific absorption from the upper part of the gastrointestinal tract are potential candidates to be formulated as floating drug delivery systems, thereby maximizing their absorption. A significant increase in the bioavailability of floating dosage forms (42.9%) could be achieved as compared with commercially available LASIX tablets (33.4%) and enteric-coated LASIX-long product (29.5%).

Limitations of Floating Drug Delivery Systems:

1. A high level of fluid in the stomach is required for drug delivery to float and work efficiently.
2. Drugs which have stability and solubility problems in GIT are not suitable candidates for these types of systems.
3. Drugs such as Nifedipine, which under goes first pass metabolism may not be desirable for the preparation of these types of systems.
4. Drugs which are irritant to Gastric mucosa are also not desirable.
5. The drug substances that are unstable in the acidic environment of the stomach are not suitable candidates to be incorporated in the systems [1].

Applications of Floating Drug Delivery Systems :

1. Sustained Drug Delivery:

Problems such as gastric residence time in the GIT encountered with oral control release formulations can be overcome with the hydrodynamically balanced system (HBS) systems which can remain in the stomach for long periods and have a bulk density <1 as a result of which they can float on the gastric contents. These systems are relatively larger in size and passing from the pyloric opening is prohibited. Recently sustained release floating capsules of Nicardipine hydrochloride were developed and were evaluated in vivo.

2. Bioavailability Enhancement:

Drugs that have poor bioavailability because of site specific absorption from the upper part of the gastrointestinal tract are potential candidates to be formulated as floating drug delivery systems, thereby maximizing their absorption. The absorption of bromocriptine is limited to 30% from the gastrointestinal tract. However a hydrodynamically balanced system (HBS) of the bromocriptine can enhance the absorption

3. Site-Specific Drug Delivery:

For the drugs like riboflavin and furosemide which are specifically absorbed from stomach or the proximal part of the small intestine, this system have more advantages. The controlled, slow delivery of drug to the stomach provides sufficient local therapeutic levels and limits the systemic exposure to the drug which resulted to reduce side effects that are caused by the drug in the blood circulation. As well as the prolonged gastric availability from a site directed delivery system may also reduce the dosing frequency.

4. Minimized Adverse Activity at the Colon:

Retention of the drug in the HBS systems at the stomach minimizes the amount of drug that reaches the colon. Thus, undesirable activities of the drug in colon may be prevented. This Pharmacodynamic aspect provides the rationale for floating drug delivery formulation for betalactam antibiotics that are absorbed only from the small intestine, and whose presence in the colon leads to the development of microorganism's resistance.

5. Reduced Fluctuations of Drug Concentration:

Continuous input of the drug following control release floating drug delivery dosages form administration produces blood drug concentrations within a narrower range compared to the immediate release dosage forms. Thus, fluctuations in drug effects are minimized and concentration dependent adverse effects that are associated with peak concentrations can be prevented. This feature is of special importance for drugs with a narrow therapeutic index [1].

REFERENCES:

1. Neha Narang. An updated review on: Floating Drug Delivery System (FDDS). Int J Appl Pharm **2011**;3(1):1-7.
2. Shakti Dwivedi, Vikash Kumar. Floating Drug Delivery Systems - A Concept of Gastroretention Dosages Form. Int J Res in Pharm & Biomed Sci **2011**;2(4):1413-1426.

3. A. Badoni, A. Ojha, G. Gnanarajan, P. Kothiyal. Review on Gastro Retentive Drug Delivery System. The Pharm Innov **2012**;1(8):32-42.
4. Anand S. Surana, Rakhee K. Kotecha. An Overview On Various Approaches To Oral Controlled Drug Delivery System Via Gastroretention. Int J Pharm Sci Rev & Res **2010**;2(2): 68-72.
5. Azhar Danish Khan, Meenakshi Bajpai. Floating Drug Delivery System: An Overview. Int J PharmTech Res **2010**;2(4):2497-2505.
6. Karan K. Patil, Datta Saptarshi. A Review on Floating Drug Delivery System. Int J Pharm Sci Rev Res **2013**; 21(1):276-283.

How to cite this article:

Sarath kumar SJ, et al. FLOATING DRUG DELIVERY - A REVIEW. J Pharm Res 2019;8(7):478-481.
DOI: https://doi.org/10.5281/zenodo.3357191

Conflict of interest: The authors have declared that no conflict of interest exists.

Source of support: Nils