ISSN: 0976-822X

Available online on www.ijcpr.com

International Journal of Current Pharmaceutical Review and Research 2022; 14(3); 91-98

Review Article

A NOVEL APPROACH IN GASTRO RETENTIVE DRUG DELIVERY SYSTEM: FLOATING DRUG DELIVERY SYSTEM

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Received: 12-08-2022 / Revised: 30-08-2022 / Accepted: 25-09-2022
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Conflict of interest: Nil

Abstract

The purpose of writing this review on gastro retentive drug delivery systems was to compile the recent literature with special focus on various gastro retentive approaches that have recently become leading methodologies in the field of site-specific orally administered controlled release drug delivery. In this review, the current technological developments of FDDS and marketed products have been discussed. In addition, the pharmaceutical basis of their design, their advantages and future potential for oral controlled drug delivery are discussed.

Keywords: Approaches in GRDDS, Classification of FDDS, Marketed formulations

INTRODUCTION

The stomach is J-shaped organ located in the upper left hand portion of the abdomen, just below the diaphragm. It occupies a portion of the epigastria and left hydrochondriac region. The main function of the stomach is to store the food temporarily, grind it and then release it slowly into the duodenum. Due to its small surface area, it provides barrier to the delivery of drugs to small intestine.

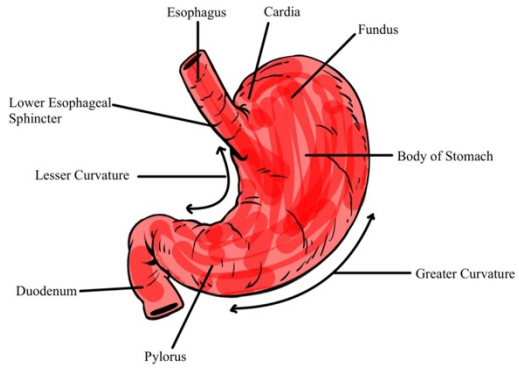


Fig 1 : Anatomy of stomach

Approaches to Gastric Retention:

A number of approaches have been used to increase the Gstric Retention Time of a dosage form in stomach by employing a variety of concepts 14, 15 These include –

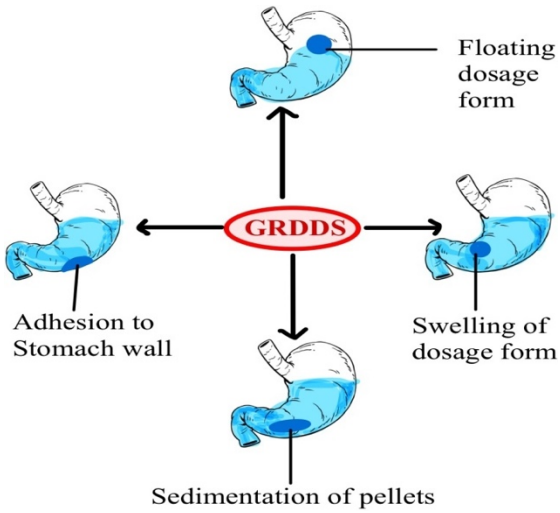


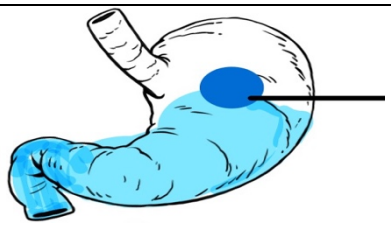
Fig 2: Approaches of Gastro Retentive Drug Delivery System

Conventional V/s Gastro retentive drug delivery system[3]

Table 1 : Conventional V/s Gastro retentive drug delivery system

Relative parameters	Conventional drug delivery system	Gastro retentive drug delivery system
Toxicity	High risk of toxicity	Very low risk of toxicity
Patient compliance	Low	Improved
Drugs with poor solubility and high pH	Not suitable for delivery of drugs with narrow absorption window in the Small intestine region	Suitable for delivery of drugs with narrow absorption window in the small Intestine region.
Drugs acting locally acting in the stomach	Not much advantageous for drugs having rapid absorption through GIT	Very much advantageous of drugs acting locally in the stomach.
Dose dumping	No risk of dose dumping.	Possibility of dose dumping

Table 2: Mechanism of Gastro Retentive Drug Delivery System

Approach	Diagram	Mechanism of action
Floating system		**Remains buoyant over gastric fluid for prolonged time as their density is less than that of gastric content, i.e. less than 1 g/ml.**
Expandable system		**Swells or unfolds and increase in size, remains lodged at sphincter. Hence exit from stomach is prevented.**
Mucoadhesive system		**Adheres to epithelial surface of GIT.**
High density/ Sedimentation system		**Retains in rugae or antrum of stomach.**

Floating Drug Delivery System:[8]

Floating drug delivery systems (FDDS) are invented to retain the drug in the stomach and applicable for drugs with poor solubility and low stability in intestinal fluids. The basis behind FDDS is making the dosage form less dense than the gastric fluids to make it float on them. FDDS are hydro-dynamically controlled low-density systems with sufficient buoyancy to float

over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. The residual system is emptied from the stomach with the release of the drug.

Mechanism of FDDS[1]

FDDS has a bulk less than gastric fluids and so remain buoyant in the stomach with out affecting the gastric emptying rate of a prolonged period of time.

F = F buoyancy – F gravity = {Df – Ds} gv

Where,

F = Total vertical force, Df = Fluid density

Ds =Object density, v =Volume

g =Acceleration due to gravity

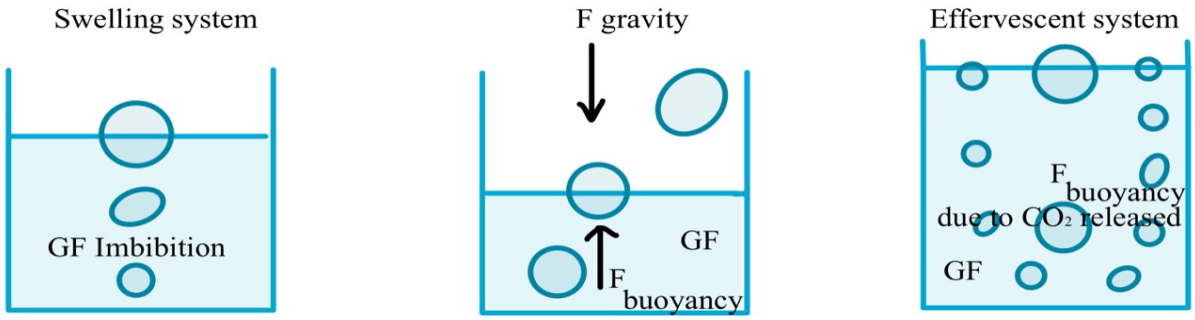


Fig 3: Mechanism of Floating drug delivery system

Criteria selection of drug candidate for the floating drug delivery system

- Readily absorption via upper gastrointestinal tract.
- Drugs with low pKa, that does exhibit unionized characters.
- Drugs are possessing lower solubility at higher pH.
- Minimizing gastric irritation as it may result in the increase of drug concentration level in the stomach.
- Drugs which get degraded in alkaline pH conditions; bioavailability of those can be enhanced by fabricating into gastro-retentive forms.
- Effect of local action of drugs e. g. treating *Helicobacter pylori* in treatment of ulcerative conditions.

Classification of floating drug delivery system (FDDS)[7]

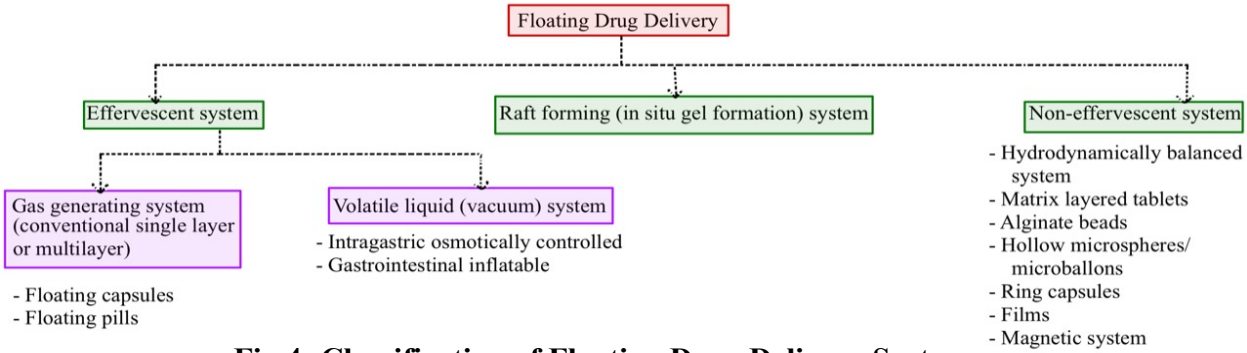


Fig 4: Classification of Floating Drug Delivery System

Gas generating systems Carbonates or bicarbonates, which react with gastric acid or any other acid (e.g. citric acid or tartaric) present in the formulation to produce CO_2 are usually incorporated in the dosage form, thus reducing the density of the system and making it float on the media[10]

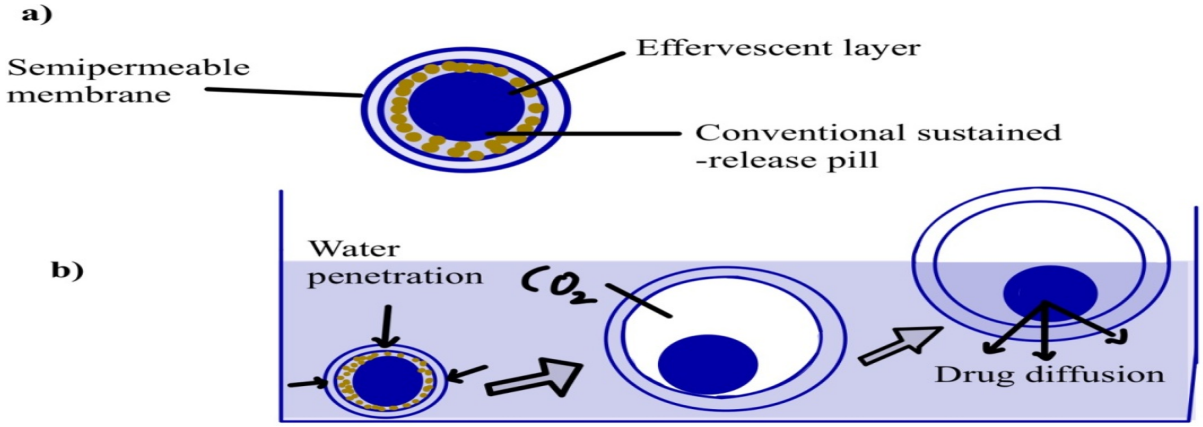


Fig 5: Gas-generating systems

Volatile liquid/vacuum containing systems

These system contain an inflatable chamber, which contains a liquid (ether, cyclopentane), that gasifies at body temperature to cause infatuation of the chamber in stomach. These devices are osmotically controlled floating system containing a hollow deformable unit that can convert from a collapsed to an expanded position, and returns to collapsed position after an extended period.

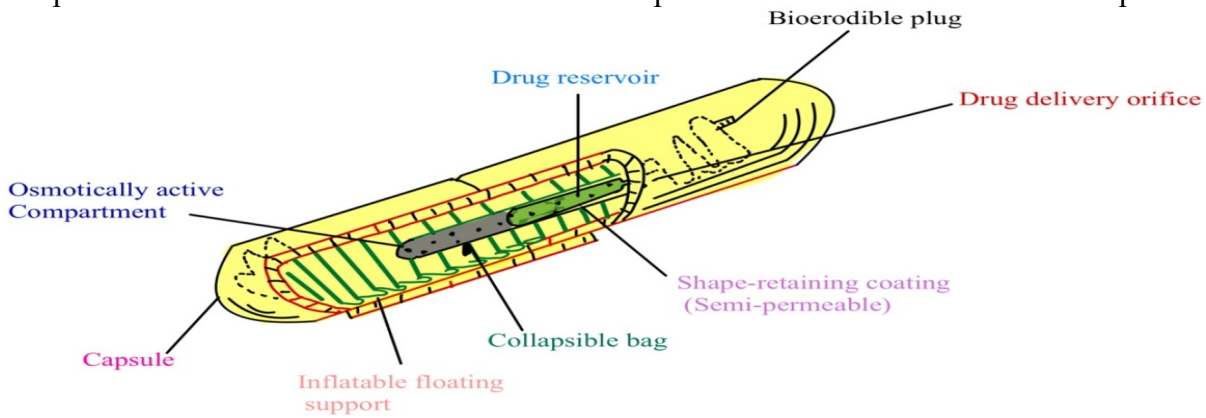


Fig 6: Volatile liquid/vacuum containing systems

Hydrodynamically balanced systems[16]

HBS/ Colloidal barrier system contain drugs with gel forming hydrocolloids to float on stomach contents. This prolongs GI residence time and maximizes drug reaching its absorption site. These are prepared by incorporating a high level (20-75% w/w) gel forming hydrocolloids e.g. hydroxyethylcellulose, hydroxypropylcellulose, HPMC etc. into the formulation and then compressing these granules into a tablets or capsules

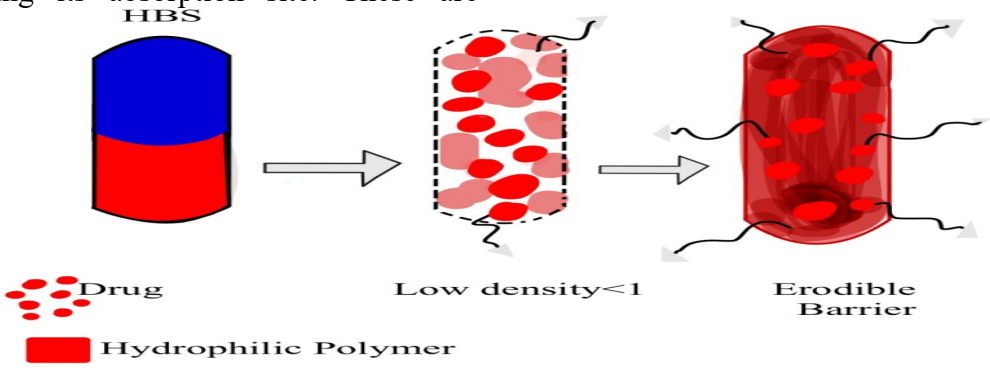


Fig 7: Hydrodynamically balanced systems

Hollow microspheres/microballons

Polymers used commonly: Polycarbonates, Cellulose acetate, Calcium alginate, Eudragit Class, Agar, Methoxylated pectin etc.

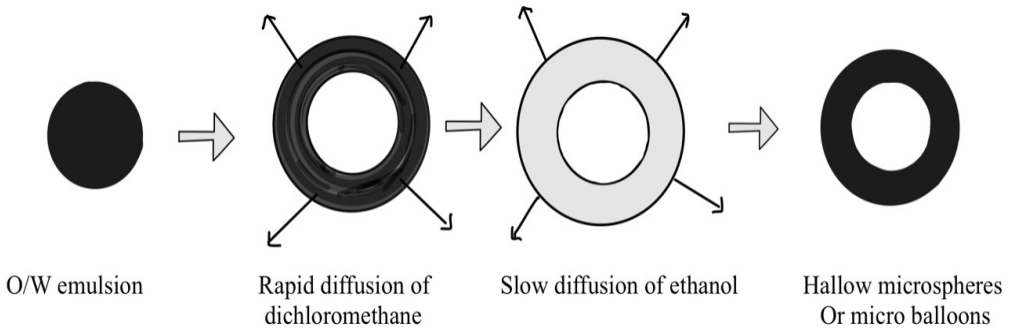


Fig 8: Hollow microspheres/microballons

Alginate beads[11]

Prepared by dropping sodium alginate solution into aqueous solution of calcium chloride, causing the precipitation of calcium alginate. Freeze dry in liquid nitrogen at 40°C for 24 hrs. Beads of 2.5 mm in diameter spherical in shaped will be prepared.

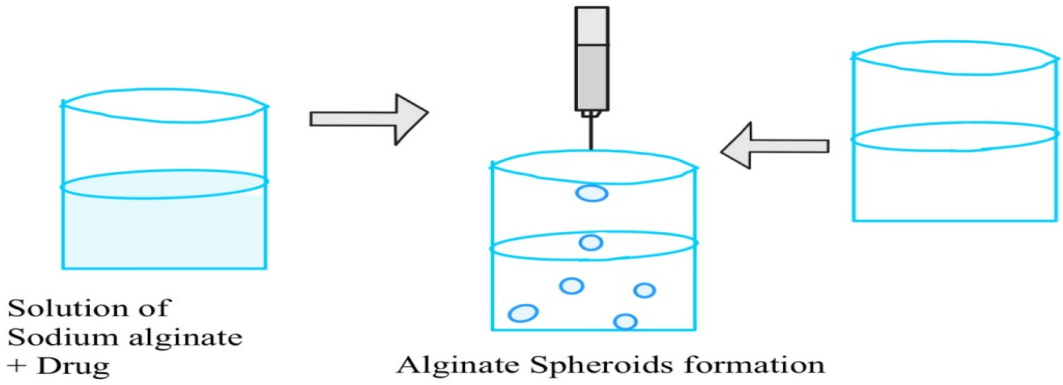


Fig 9: Alginate beads

Raft forming systems

This system is used for delivery of antacids and drug delivery for treatment of GI infections and disorders. The mechanism involved in this system includes the formation of a viscous cohesive gel in contact with gastric fluids, forming a continuous layer called raft.

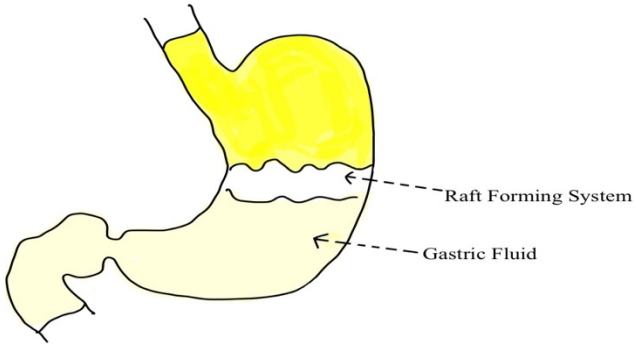


Fig 10: Raft forming systems

Advantages of floating drug delivery System[26]

1.Simple and conventional technique for formulation.
2.Site-specific drug delivery
3.Controlled delivery of drugs.
4.Delivery of drugs for residual action at a specific site in the stomach.
5.Improved drug absorption with increased GRT and excess duration of contact of dosage regimen at its target site.
6.Ease of administration with higher patient compliance.
7.In treating gastro esophageal reflux disorders (GERD).
8.Minimizing irritation of GIT mucosa by the drugs with slow release rate

Disadvantages of floating drug delivery system

1.Gastric emptying of floating systems may occur at random and highly dependent on its dimensions. Therefore patients should not have dosage prior going to bed.
2.Certain drugs present in the floating system may causes irritation to gastric mucosal linings.
3.The drugs those get significantly absorbed throughout gastrointestinal tract, with significant first-pass metabolism, are desirable candidate predominantly.

Applications of floating drug delivery system[8]

1.FDDS are perfect HBS dosage form to provide better delivery of drugs and reduced its GI side effects.
2.FDDS served as an excellent drug delivery system in the eradication of Helicobacter pylori, blamed for chronic gastritis and peptic ulcers.
3.FDDS is site-specific drug delivery: These systems are particularly advantageous for drugs that are specifically absorbed from the stomach or the proximal part of the small intestine, e. g., Riboflavin and Furosemide.
4.In case of Parkinson patient, FDDS is effective in absorption of the drug over a period of 6-8 h and maintained substantial plasma concentration.
5.FDDS are claimed for the increased efficacy of drugs as recent studies show that the administration of Diltiazem floating tablets twice a day would be more effective compared to normal tablets in hypertensive patients.

Evaluation Parameters of Floating Drug Delivery System[9,12]

1.Floating duration
2.Dissolution profiles
3.Specific gravity
4.Content uniformity
5.Differential scanning calorimetry
6.Particle size analysis
7.Flow Properties

List of Drugs Explored in Floating Dosage Forms

Table 3: List of Drugs Explored in Floating Dosage Forms

Types of dosage forms	Drugs explored in floating dosage forms
Microspheres	Aspirin, Griseofulvin, P-nitroaniline, Ibuprofen, Ketoprofen, Terfenadine, Tranilast.
Granules	Diclofenac sodium, Indomethacin, Prednisolone.
Films	Cinnarizine
Capsule	Chlordiazepoxide, Daizepam, Furosemide, Levodopa, Benserazide, Misoprostol, Propanolol
Tablet/ Pills	Acetaminophen, Amoxicillin, Atenolol, Cinnazirine, Diltiazepam, Flourouracil, P-aminobenzoic acid, Prednisolone, Quinidine, Sotalol, Theohpylline, Verapamil

Marketed preparations of floating drug delivery system[17]

Table 4: Marketed preparations of floating drug delivery system

Product	Active Ingredient
Madopar	Levodopa, Benserzide
Valrelease	Diazepam
Topalkan	Aluminum magnesium antacid
Liquid Gavison	Alginic acid and sodium bicarbonate
Cifran	Ciprofloxacin
Rantac	Ranitidine
Creon 1000	Pancreatin
Dompan SR	Panatoprozole and Domperidone

CONCLUSION

Drug absorption in the gastrointestinal tract is a highly variable procedure and prolonging gastric retention of the dosage form that leads to extend the time for drug absorption. FDDS promises to be a potential approach for gastric retention. Numbers of commercial products and patents issues in these fields are the evidence of it. The aim is to improve the bioavailability of the drug with narrow absorption window in gastrointestinal tract region and to acheive prolong effect. By prolonging the drug resident time in GI region improves the solubility of drug that is less soluble in high pH and reduces drug waste, reduction in plasma level fluctuation. Although there are a number of difficulties to be worked out to achieve prolonged gastric retention, a large number of companies are focusing toward commercializing this technique.

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