WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 8, Issue 6, 1294-1302. Review Article ISSN 2277– 7105

A REVIEW ON FLOATING DRUG DELIVERY SYSTEMS

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Article Received on
15 March 2019,

Revised on 05 April 2019,
Accepted on 26 April 2019,

DOI: 10.20959/wjpr20196-14899

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ABSTRACT

Various novel drug delivery systems are being developed to increase effectiveness of the drug in terms of therapeutic action, reduced dosing frequency, improved patient compliance, increased bioavailability, minimal degradation of the drug and reduced adverse effects. Floating drug delivery system is one such dosage form. Floating drug delivery systems (FDDS) have a bulk density lesser than gastric fluids and float for a prolonged period of time and releases the drug slowly at the desired rate. As the gastric residence time of drug is increased, bioavailability is also improved. This review article gives a bird's eye view of floating drug delivery systems.

KEYWORDS: Novel drug delivery systems, Floating drug delivery systems, Bioavailability.

INTRODUCTION

Various novel drug delivery systems are being developed to increase effectiveness of the drug in terms of therapeutic action, reduced dosing frequency[1,2], improved patient compliance, increased bioavailability, minimal degradation of the drug and reduced adverse effects.[3]

Cost efficiency and easy administration makes the oral route most commonly used route of drug administration which is associated with superior patient compliance.[4] However, oral administration has limited use for some drugs, because of poor oral bioavailability due to incomplete absorption and/or degradation in the gastrointestinal (GI) tract. Duodenum and jejunum has good absorption characteristics, but the extent of absorption at these sites is limited, as the passage of drug through this region is rapid. Increasing the gastric residence time, can improve the absorption of drug. The gastric retention of solid dosage forms may be increased by mechanisms of mucoadhesion[5], flotation[6], sedimentation[7], expansion[8],

modified shape systems[9] or by the simultaneous administration of pharmacological agents[10] that delay gastric emptying. This present article concentrates on floating drug delivery systems.

Floating Drug Delivery Systems

Floating drug delivery systems (FDDS) are those systems which have a bulk density less than gastric fluids and because of this, these systems remains floating for a prolonged period of time in the stomach.[11] This dosage form floats over the gastric contents and releases the drug slowly at the desired rate, prolonging the gastric retention time of drug in the stomach. As the gastric residence time of drug is increased, bioavailability is also improved.

Classification of Floating Drug Delivery System

Floating drug delivery systems are classified as

I. Effervescent Floating Dosage Forms.

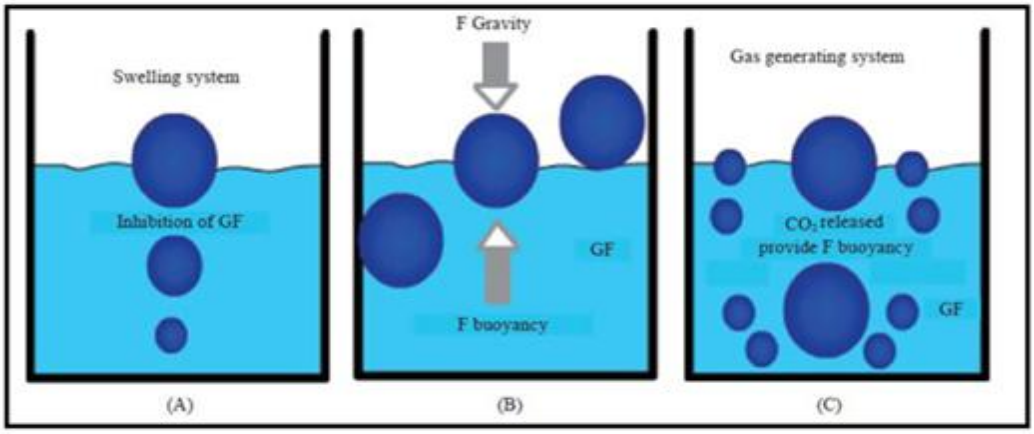
1. Gas generating systems
2. Volatile liquid containing systems

II. Non-Effervescent Floating Dosage Forms

I. Effervescent systems

These are matrix type systems. They are prepared with the help of a swellable polymer such as methylcellulose and chitosan and various effervescent compounds like sodium bicarbonate, tartaric acid, and citric acid. These are designed in such a way that, when they come in contact with gastric content, CO_2 is liberated. This liberated gas, gets entrapped in swollen hydrocolloid polymer which produces upward motion of the dosage form and helps the system to float in the gastric fluids.

1. **Gas generating systems:** These systems utilize effervescent reactions between carbonate / bicarbonate salts and citric / tartaric acid to liberate CO_2. This CO_2 gets entrapped in the jellified hydrocolloid which decreases specific gravity of the system and makes it to float over gastric fluids.[12]



a. **Multiple unit floating pill**[13]**:** This system consists of two layers, inner effervescent layer containing sodium bicarbonate and tartaric acid which generate carbon dioxide in aqueous media. The inner layer is further divided into two sub layers to avoid physical contact between sodium bicarbonate and tartaric acid. The outer layer is composed of a swellable membrane that traps the liberated carbon dioxide. This entrapment results in flotation of the system. The system starts floating within 10 minutes and remains floated over a period of 5 hours.

b. **Floating capsules:** This system consists of an inner layer of gas generating agents. This layer is further divided into 2 sub layers, the outer containing sodium bicarbonate and the inner containing tartaric acid. This layer is surrounded by an expansive polymeric film (composed of poly vinyl acetate [PVA] and shellac), which allows gastric juice to pass through it. The gas-generating agents in presence of gastric juices produce foam which causes swelling of outer layer. This swellable membrane layer plays an important role in maintaining the buoyancy of the pills for an extended period of time.[14]

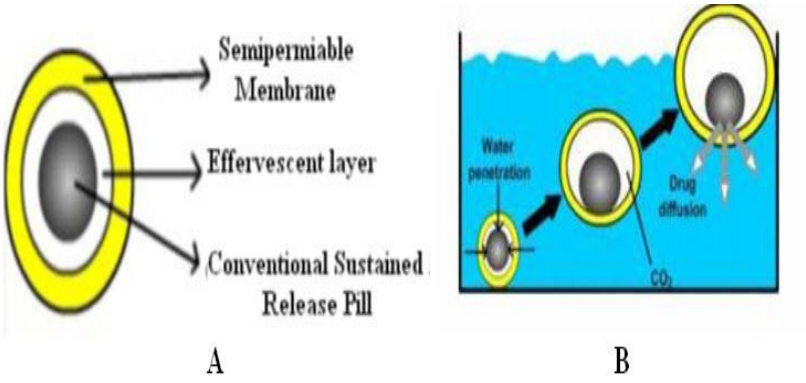
c. **Floating systems with ion exchange resins**[15]: In this system, ion exchange resin beads are prepared and loaded with bicarbonate by mixing the beads with sodium bicarbonate solution. These beads are coated with a semi permeable membrane of Eudragit- RS. When this system comes in contact with gastric contents, an exchange of chloride and bicarbonate ions takes place. This results in generation of carbon dioxide which helps the beads to float over the gastric contents and releases the drug at a predetermined rate.

d. **Floating tablets**

i. Single layer: In this system, gas (CO_2) generating agents and the drug are mixed to form a tablet matrix. When it comes in contact with the gastric juice, CO_2 is generated which makes the tablet to float over the gastric contents increasing the gastric residence time of the drug.

ii. Bi-layer tablet[16]: Bilayer tablet is composed of two layers. One layer contains the polymers and the drug. The second layer contains the effervescent mixture of sodium bicarbonate and citric acid.

iii. Triple layer tablet[17]: This tablet includes three layers. Outer layer is a semi permeable membrane, second is gas generating layer and third layer has the drug.



2. **Volatile liquid containing systems**[18]: In this system, inflatable chambers are used to increase the gastric residence time of the drug. These chambers contain a liquid such as ether, cyclo pentane. This liquid changes to gaseous state at body temperature and causes expansion of this system, which makes it float over the gastric contents. This device also contains a bio erodible plug made up of PVA, Polyethylene, etc. This plug dissolves gradually and releases gas which finally collapses after a predetermined time.

II. Non-effervescent systems

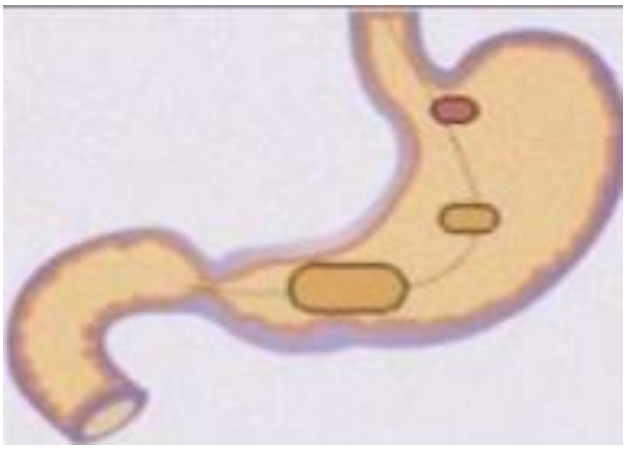
After entering the stomach these systems absorb gastric fluid and swells unrestrictedly.[19] They swell to such an extent that it cannot exit from the stomach. The air trapped by swollen polymer gives buoyancy to the dosage forms. These systems are also known as the "plug type system" as they have a tendency to get stuck near the pyloric sphincter. In these systems, gel forming swellable cellulose type of hydrocolloids, polysaccharides, matrix forming polymers like polycarbonate, poly methacrylate and polystyrene are used. The various types of this system are discussed below:

a. **Colloidal gel barrier systems**[20]: This system contains drug along with gel forming hydrocolloids. When this system comes in contact with gastric fluid, the hydrocolloid in the system hydrates and forms a colloidal gel barrier around the drug core. The air trapped by the swollen polymer maintains a density less than one and provides buoyancy to this dosage forms.

b. **Micro porous Compartment System[21]:** In this system, drug is encapsulated inside a micro porous compartment. This compartment has aperture along its top and bottom wall and the peripheral walls of the compartment are completely sealed to prevent direct contact with gastric mucosal surface. The entrapped air in the compartment causes the system to float over the gastric contents. Gastric fluid enters through the apertures to dissolve the drug.

c. **Alginate beads**: These are multi-unit floating dosage forms. In this system freeze-dried calcium alginate has been used. The beads are produced by drop wise addition of alginate into calcium chloride solution[22], followed by precipitation of calcium alginate and freeze-drying. This alginate beads are porous which can maintain a floating force over 12 h.

d. **Hollow microspheres**: Hollow microspheres are also known as micro balloons. These systems are considered as most favourable buoyant system as they are more advantageous because of central hollow space inside the microsphere. These systems are loaded with drug in their outer polymer layer. These are prepared by emulsion solvent diffusion method.[23]



Characteristics of drugs that can be formulated as floating drug delivery systems[24]

- ✓ Drugs which are locally active in the stomach. Eg. Misoprostol, antacids etc.
- ✓ Drugs which have narrow absorption window in the GIT. Eg. Furosemide, L-dopa, Para-amino benzoic acid, riboflavin. etc.
- ✓ Drugs that exhibit low solubility at high pH values. Eg. Diazepam, Chlordiazepoxide, Verapamil hydrochloride.
- ✓ Drugs which are unstable in the intestinal or colonic environment. E.g. Captopril, ranitidine HCl, Metronidazole.

- ✓ Drugs having a specific site of absorption in the upper part of small intestine.

Advantages of Fdds[25]

1) As the main objective of FDDS is to enhance the gastric retention time of the drug, these systems are highly advantageous in the treatment of the disorders related to the stomach.
2) Therapeutic activity of drugs with considerably short half life can be increased by this system.
3) Bioavailability for drugs which can metabolize in the upper GIT has been increased.
4) These are advantageous over the conventional system as they overcome the difficulties of gastric retention time as well as the gastric emptying time.
5) Side effects are minimizing as the active drug is delivered specifically to the site of action.

DISADVANTAGES OF FDDS

1) The main disadvantage of floating system is requirement of a sufficient high level of fluids in the stomach for the drug delivery to float.
2) Gastric retention is influenced by many factors such as gastric motility, pH and presence of food. These factors are never constant and hence the buoyancy cannot be predicted.
3) Drugs that cause irritation to gastric mucosa are not suitable to be formulated as floating drug delivery systems.
4) Patients should not be dosed with floating forms just before going to bed.
5) Floating system is not useful for drugs that have solubility (or) stability problem in gastric fluids.
6) The dosage form should be administered with a minimum of glass full of water (200-250 ml).

Evaluation tests

Some of the important tests to be carried out on floating drug delivery systems are given below.

1. Floating Properties: The time taken by the tablet to rise to upper one third of the dissolution vessel after introducing into the dissolution medium is called as floating lag time. The time for which the formulation constantly floats on the surface of the medium is called as the floating or flotation time. These tests are usually performed in simulated gastric fluid or 0.1 N HCL maintained at 37^{o} C, by using USP dissolution apparatus containing 900 ml 0.1 N HCL as dissolution medium.[26]

2. Drug release: Drug release studies are performed using the USP dissolution apparatus. Simulated gastric and intestinal fluids maintained at 370^{o} C are used as dissolution medium. Samples are withdrawn periodically from the dissolution medium, replaced with the same volume of fresh medium each time, and then analyzed for their drug contents after an appropriate dilution.

3. Size and Shape Evaluation: The particle size and the size distribution of beads or microspheres are determined in the dry state using the optical microscopy method. The external and cross sectional morpholgy (surface characterization) is done by scanning electron microscope (SEM). The drug release depends on the size and shape of the floating microparticles.

4. Weight gain and water uptake (WU): Weight gain or water uptake is determined by considering the swelling behaviour of floating dosage form. This is done by immersing the dosage form in simulated gastric fluid at 37^{o}C. Then changes in tablet dimensions like tablet diameter and / or thickness are measured at regular one hour time intervals up to 24 hours. The swollen tablets are then reweighed and WU is measured in terms of percent weight gain, as given by the below equation.

$$WU = (Wt - Wo) \times 100 / Wo$$

In which Wt and Wo are weights of dosage form at time t and initially respectively.[27]

Marketed Products of Gastroretentive Drug Delivery Systems[28]

Brand name	Delivery System	DRUG (dose)	Company Name
Valrelease®	Floating capsule	Diazepam (15 mg)	Hoffmann-LaRoche
Liquid Gaviscon®	Effervescent Floating liquid alginate preparations	Al hydroxide (95 mg), Mg Carbonate (358 mg)	Glaxo Smithkline, India
Topalkam®	Floating liquid alginate preparation	Al-Mg antacid	Pierre Fabre Drug, France
Almagate Flot Coat®	Floating dosage form	Al Mg antacid	Pierre Fabre Drug, France
Conviron®	Colloidal gel forming FDDS Bilyer floating capsule	Ferrous Sulphate	Ranbaxy, India
Cytotech®	Bilayer Floating Capsule	Misoprostol (100µg/200µg)	Pharmacia, USA
Cifran OD®	Gas-generating floating form	Ciprofloxacin (1 gm)	Ranbaxy, India

CONCLUSION

Oral route of drug delivery is one of the oldest and safest routes for drug delivery. Floating drug delivery system is a modified drug release system developed to overcome some disadvantages of conventional oral delivery. FDDS is a potential approach for enhancing gastric retention, thereby increasing absorption and bioavailability of drug from stomach.

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