

Review Article



A Review on Floating Drug Delivery System

Karan K. Patil *, Datta Saptarshi

Department of Pharmaceutics, S.M.B.T College of Pharmacy, Dhamangaon, Nashik, Maharashtra-422 403, India.

*Corresponding author's E-mail: karanptl397@gmail.com

Accepted on: 25-04-2013; Finalized on: 30-06-2013.

ABSTRACT

Oral delivery of drugs is by far the most preferable route of drug delivery due to the ease of administration, patient compliance and flexibility in formulation. Oral sustained drug delivery formulations show some limitations connected with the gastric emptying time. To overcome this physiological problem, several drug delivery systems with prolonged gastric retention time have been developed. The controlled drug delivery systems possessing the ability of being retained in the stomach are called gastro-retentive drug delivery systems (GRDDS). They remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Floating Drug Delivery System (FDDS) is one of the important approaches of GRDDS used to achieve prolonged gastric residence time to obtain sufficient drug bioavailability. These have a bulk density lower than the gastric content and remain buoyant in the stomach for a prolonged period of time, with the potential for continuous release of drug. The purpose of this paper is to review the concept of current technology used in the development of such system as well as summarizes evaluation method and applications of various floating dosage forms.

Keywords: Gastro retention, Floating drug delivery systems, effervescent, non-effervescent, its classification and application.

INTRODUCTION

Oral drug delivery system is the most popular route of administration due to its versatility, ease of administration and most importantly patient compliance. Oral controlled release drug delivery have recently been of increasing interest in pharmaceutical field to achieve improved therapeutic advantages, such as ease of dosing administration, patient compliance and flexibility in formulation. Since oral sustained drug delivery formulations show some limitations connected with the gastric emptying time¹. 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. Drugs with short half-lives and drugs that easily absorbed from gastrointestinal tract (GIT) are eliminated quickly from the systemic circulation.^{1,2} To overcome this physiological problem, several drug delivery systems with prolonged gastric retention time have been investigated. It is evident from the recent research and patent literature that an increased interest in novel dosage forms that are retained in the stomach for a prolonged and predictable period of time exists today. Attempts are being made to develop a controlled drug delivery system that can provide therapeutically effective plasma drug concentration levels for longer durations, thereby reducing the dosing frequency and minimizing fluctuations in plasma drug concentration at steady state by delivering drug in a controlled and reproducible manner.^{1,3}

Gastro-retentive drug delivery systems (GRDDS) 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 of drugs that are less soluble in high pH environment. The controlled gastric retention of solid dosage forms may be achieved by the mechanism of muco-adhesion, floatation, sedimentation, expansion, modified shape systems or by the administration of pharmacological agents that delaying gastric emptying. Based on these approaches, floating drug delivery systems seems to be the promising delivery systems for control release of drugs.^{2,4}

Floating Oral Drug Delivery System (FDDS) are retained in the stomach and are useful for drugs that are poorly water soluble or unstable in intestinal fluids. Floating drug delivery system have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system (Figure 1).^{4,5}

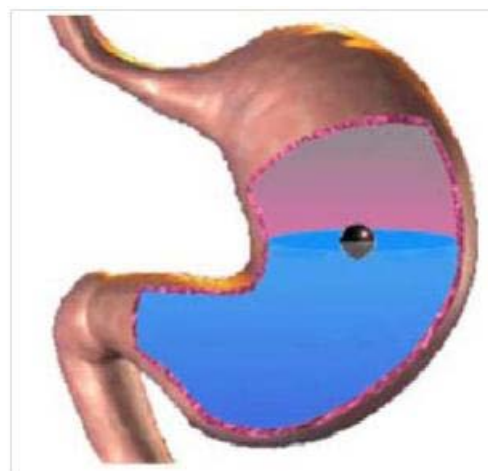


Figure 1: Intra-gastric residence positions of floating unit.⁶

After release of drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of fluctuations in plasma drug concentration.^{5,6}

BASIC ANATOMY AND PHYSIOLOGY OF GASTROINTESTINAL TRACT

Anatomically the stomach is divided into 3 regions: fundus, body, and antrum (pylorus). The proximal part made of fundus and body acts as a reservoir for undigested material, whereas the antrum is the main site for mixing motions and act as a pump for gastric emptying by propelling actions. Gastric emptying occurs during fasting as well as fed states. The pattern of motility is however distinct in the two states. During the fasting state an interdigestive series of electrical events take place, which cycle both through stomach and intestine every 2 to 3 hours. This is called the interdigestive myoelectric cycle or migrating myoelectric cycle (MMC), which is further divided into following 4 phases as described by Wilson and Washington. (Wilson CG et al., 1989) as shown in figure 2.^{3,7}

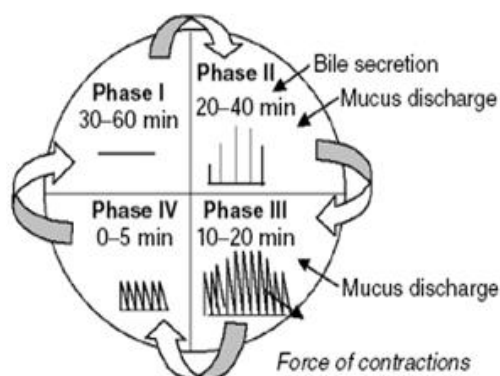


Figure 2: Motility pattern in GIT.³

1. Phase I (basal phase) lasts from 40 to 60 minutes with rare contractions.
2. Phase II (preburst phase) lasts for 40 to 60 minutes with intermittent action potential and contractions. As the phase progresses the intensity and frequency also increases gradually.
3. Phase III (burst phase) lasts for 4 to 6 minutes. It includes intense and regular contractions for short period. It is due to this wave that all the undigested material is swept out of the stomach down to the small intestine. It is also known as the housekeeper wave.
4. Phase IV lasts for 0 to 5 minutes and occurs between phases III and I of 2 consecutive cycles.^{3,7}

FACTORS AFFECTING GASTRIC RETENTION

The stomach anatomy and physiology contain parameters to be considered in the development of gastroretentive dosage forms. To pass through the pyloric valve in to the small intestine the particle size should be in the range of 1 to 2 mm.⁸ The most important parameters controlling the gastric retention time (GRT) of oral dosage forms include : density, size and shape of the dosage form, food intake

and its nature, caloric content and frequency of intake, posture, gender, age, sex, sleep, body mass index, physical activity and diseased states of the individual (e.g. chronic disease, diabetes etc.) and administration of drugs with impact on gastrointestinal transit time for example drugs acting as anticholinergic agents (e.g. atropine, propantheline), Opiates (e.g. codeine) and prokinetic agents (e.g. metoclopramide, cisapride).⁹ The molecular weight and lipophilicity of the drug depending on its ionization state are also important parameters.¹⁰

Density of dosage forms

The density of a dosage form also affects the gastric emptying rate and determines the location of the system in the stomach. Dosage forms having a density lower than the gastric contents can float to the surface, while high density systems sink to bottom of the stomach.¹¹ Both positions may isolate the dosage system from the pylorus. A density of < 1.0 gm/ cm³ is required to exhibit floating property.¹²

Shape and size of the dosage form

Shape and size of the dosage forms are important in designing indigestible single unit solid dosage forms. The mean gastric residence times of nonfloating dosage forms are highly variable and greatly dependent on their size, which may be large, medium and small units. In most cases, the larger the dosage form the greater will be the gastric retention time (GRT) due to the larger size of the dosage form would not allow this to quickly pass through the pyloric antrum into the intestine.¹³ Dosage forms having a diameter of more than 7.5 mm show a better gastric residence time compared with one having 9.9 mm.¹² Ring-shaped and tetrahedron-shaped devices have a better gastric residence time as compared with other shapes.¹⁴

Food intake and its nature

Food intake, viscosity and volume of food, caloric value and frequency of feeding have a profound effect on the gastric retention of dosage forms. The presence or absence of food in the gastrointestinal tract (GIT) influences the gastric retention time (GRT) of the dosage form. Usually the presence of food in the gastrointestinal tract (GIT) improves the gastric retention time (GRT) of the dosage form and thus, the drugs absorption increases by allowing its stay at the absorption site for a longer period. Again, increase in acidity and caloric value shows down gastric emptying time (GET), which can improve the gastric retention of dosage forms.¹⁵

Effect of gender, posture and age

Generally females have slower gastric emptying rates than male. The effect of posture does not have any significant difference in the mean gastric retention time (GRT) for individuals in upright, ambulatory and supine state. In case of elderly persons, gastric emptying is slowed down.¹⁶

DRUG CANDIDATES SUITABLE FOR FLOATING DRUG DELIVERY

Various drugs have their greatest therapeutic effect when released in the stomach, particularly when the release is prolonged in a continuous, controlled manner. Drugs delivered in this manner have a lower level of side effects and provide their therapeutic effects without the need of repeated dosages or with a low dosage frequency. Sustained release in the stomach is also useful for therapeutic agents that the stomach does not readily absorb, since sustained release prolongs the contact time of the agent in the stomach or in the upper part of the small intestine, which is where absorption occurs and contact time is limited. Under normal or average conditions, for example, material passes through the small intestine in as little as 1-3h, as shown in figure in figure 3 (a) and (b).^{17, 18}

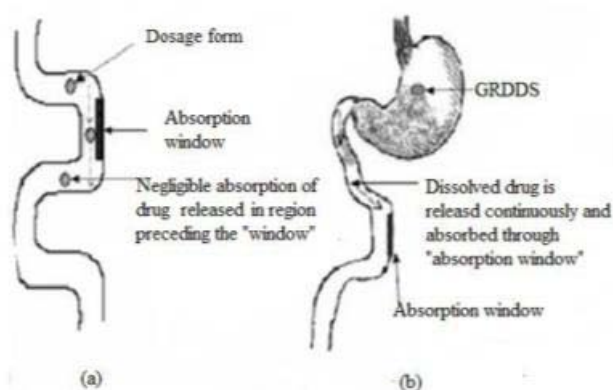


Figure 3: Drug absorption in the case of (a) Conventional dosage forms (b) Gastroretentive drug delivery systems.¹⁷

Drug Candidates Suitable for FDDS-

- Drugs that have narrow absorption window in GIT (e.g. L-DOPA, paminobenzoic acid, furosemide, riboflavin).¹⁹
- Drugs those are locally active in the stomach (e.g. misoprostol, antacids).²⁰
- Drugs those are unstable in the intestinal or colonic environment (e.g. captopril, ranitidine HCl, metronidazole)²¹
- Drugs that disturb normal colonic microbes (e.g. antibiotics used for the eradication of *Helicobacter pylori*, such as tetracycline, clarithromycin, amoxicillin)²²
- Drugs that exhibit low solubility at high pH values (e.g. diazepam, chlordiazepoxide, verapamil)²³

CLASSIFICATION OF FLOATING DRUG DELIVERY SYSTEM

The concept of FDDS was described in the literature as early as 1968, when Davis disclosed a method for overcoming the difficulty experienced by some persons of gagging or choking while swallowing medicinal pills. The author suggested that such difficulty could be overcome by providing pills having a density of less than 1.0 g/ml so

that pill will float on water surface. Since then several approaches have been used to develop an ideal floating delivery system. The various buoyant preparations include hollow microspheres ('microballoons'), granules, powders, capsules, tablets (pills), and laminated films. Most of the floating systems reported in literature are single-unit systems, such as the HBS and floating tablets. These systems are unreliable and irreproducible in prolonging residence time in the stomach when orally administered, owing to their fortuitous ('all-or-nothing') emptying process. On the other hand, multiple-unit dosage forms appear to be better suited since they are claimed to reduce the inter-subject variability in absorption and lower the probability of dose-dumping.^{24, 25, 26}

Based on the mechanism of buoyancy, two distinctly different technologies, i.e., non-effervescent and effervescent systems have been utilized in the development of FDDS. The various approaches used in and their mechanisms of buoyancy are discussed in the following subsections.

1. Effervescent Systems:

a. Volatile liquid containing systems

The gastro-retention time (GRT) of a drug can be sustained by incorporating an inflatable chamber, which contains a liquid e.g. ether, cyclopentane, that gasifies at body temperature to cause the inflation of the chamber in the stomach. The device may also consist of a bio-erodible plug made up of PVA, Polyethylene etc. that gradually dissolve causing the inflatable chamber to release gas and collapse after a predetermined time to permit the spontaneous ejection of the inflatable systems from the stomach.²³

b. Gas-generating Systems

Floatability can be achieved by generation of gas bubbles. These buoyant systems utilize matrices prepared with swellable polymers such as polysaccharides (e.g. chitosan), effervescent components (e.g. sodium bicarbonate, citric acid or tartaric acid). The optimal stoichiometric ratio of citric acid and sodium bicarbonate for gas generation is reported to be 0.76: 1.^{27, 28}

In this system carbon dioxide is released and causes the formulation to float in the stomach (Figure 4). Other approaches and materials that have been reported are a mixture of sodium alginate and sodium bicarbonate, multiple unit floating dosage forms that generate gas (carbon dioxide) when ingested, floating mini capsules with a core of sodium bicarbonate, lactose and polyvinyl pyrrolidone (PVP) coated with hydroxypropyl methylcellulose (HPMC), and floating system based on ion exchange resin technology etc. Bilayer or multilayer system has also been designed. Drugs and excipients can be formulated independently and the gas generating material can be incorporated in to any of the layers. Further modifications involve coating of the matrix with a polymer which is permeable to water, but not to carbon

dioxide. The main difficulty of these formulations is finding a good compromise between elasticity, plasticity and permeability of the polymers.²⁹

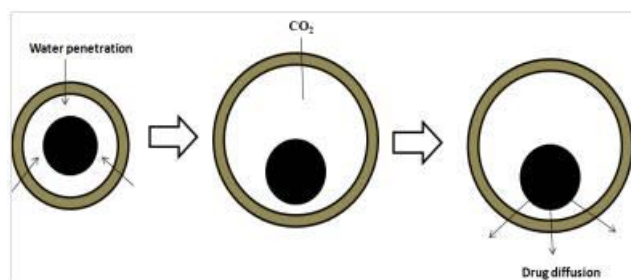


Figure 4: Drug release from effervescent (gas generating) systems.²⁹

2. Non-effervescent systems

a. Colloidal gel barrier systems

These systems contain drug with gel-forming hydrocolloids meant to remain buoyant on the stomach content. These are single-unit dosage form, containing one or more gel-forming hydrophilic polymers. Hydroxypropyl methylcellulose (HPMC), hydroxethyl cellulose (HEC), hydroxypropyl cellulose (HPC), sodium carboxymethyl cellulose (NaCMC), polycarboxophil, polyacrylate, polystyrene, agar, carrageenans or alginic acid are commonly used excipients to develop these systems. The polymer is mixed with drugs and usually administered in hydrodynamically balanced system capsule. The capsule shell dissolves in contact with water and mixture swells to form a gelatinous barrier, which imparts buoyancy to dosage form in gastric juice for a long period. Because, continuous erosion of the surface allows water penetration to the inner layers maintaining surface hydration and buoyancy to dosage form. Incorporation of fatty excipients gives low-density formulations reducing the erosion. Madopar LP®, based on the system was marketed during the 1980's. Effective drug deliveries depend on the balance of drug loading and the effect of polymer on its release profile. Several strategies have been tried and investigated to improve efficiencies of the floating hydrodynamically balanced systems.²⁹⁻³¹ The working principle of the HBS is more clearly illustrated in Figure 5.

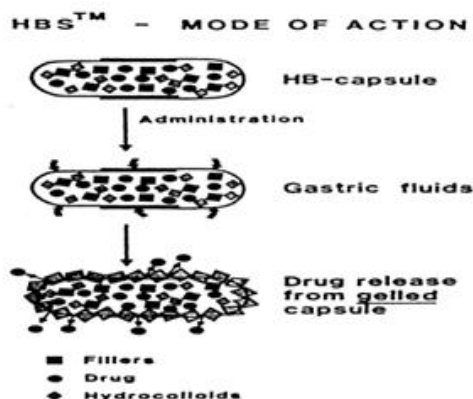


Figure 5: Working principle of the hydrodynamically balanced system (HBS). The hard gelatin capsule contains

a special formulation of hydrocolloids, which swell into a gelatinous mass upon contact with gastric fluids.²⁴

b. Microporous Compartment System:

This technology is based on the encapsulation of drug reservoir inside a Microporous compartment with aperture along its top and bottom wall. The peripheral walls of the drug reservoir compartment are completely sealed to prevent any direct contact of the gastric mucosal surface with the un-dissolved drug. In stomach the floatation chamber containing entrapped air causes the delivery system to float over the gastric contents. Gastric fluid enters through the apertures, dissolves the drug and carries the dissolved drug for continuous transport across the intestine for absorption.²⁴ The Microporous Compartment System is shown in figure 6.

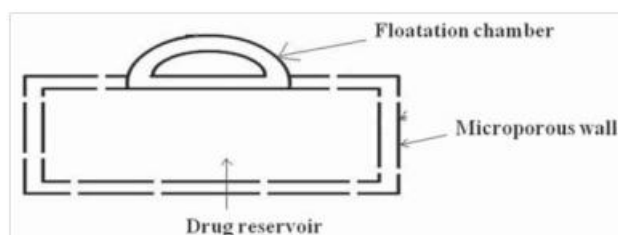


Figure 6: Microporous Compartment System³²

c. Alginate beads

Alginates have received much attention in the development of multiple unit systems. Alginates are nontoxic, biodegradable linear copolymers composed of L-glucuronic and L-mannuronic acid residues.⁶ Multiple unit floating dosage forms have been developed from freeze-dried calcium alginate. Spherical beads of approximately 2.5 mm in diameter can be prepared by dropping a sodium alginate solution into aqueous solutions of calcium chloride, causing precipitation of calcium alginate. The beads are then separated, snap and frozen in liquid nitrogen and freeze dried at -40°C for 24 hours, leading to the formation of porous system, which can maintain a floating time over 12 hours.^{30, 31} A multiple unit system can be developed comprising of calcium alginate core and calcium alginate/PVA membrane, both separated by an air compartment. Air compartment provides buoyancy to beads. In presence of water, the PVA leaches out and increases the membrane permeability, maintaining the integrity of the air compartment. Increase in molecular weight and concentration of PVA, resulted in enhancement of the floating properties of the system.^{6, 31}

d. Hollow microspheres

Hollow microspheres are considered as one of the most promising buoyant systems, as they possess the unique advantages of multiple unit systems as well as better floating properties, because of central hollow space inside the microsphere (Figure 7).⁶

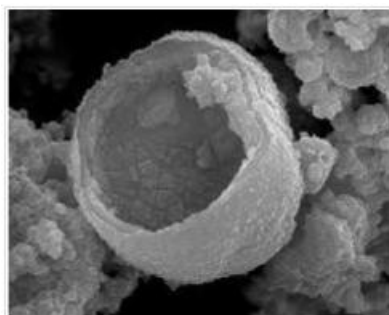


Figure 7: Micro balloons⁶

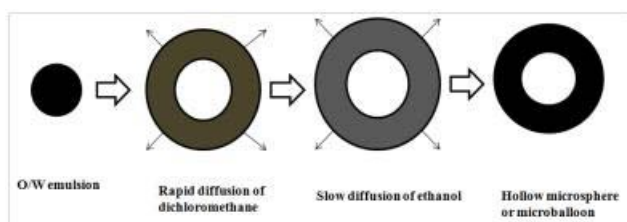


Figure 8: Formulation of floating hollow microsphere or microballoon.²⁹

Hollow microspheres (microballons), loaded with active drug in their outer polymer shells were prepared by a novel emulsion-solvent diffusion method. The ethanol: dichloromethane solution of the drug and an enteric acrylic polymer was poured in to an agitated aqueous solution of PVA that was thermally controlled at 40°C. The gas phase generated in dispersed polymer droplet by

evaporation of dichloromethane formed in internal cavity in microspheres of the polymer with drug. The microballons floated continuously over the surface of acidic dissolution media containing surfactant for greater than 12 hours in vitro (Figure 8).³²

LIST OF DRUGS EXPLORED FOR VARIOUS FLOATING DOSAGE FORMS⁴

Microspheres Tablets/Pills: Chlorpheniramine maleate, Aspirin, griseofulvin, Acetaminophen, p-nitroaniline, Acetylsalicylic acid, Ibuprofen, Amoxycillin trihydrate, Terfenadine, Ampicillin, Tranilast, Atenolol, Theophylline, Captopril, Isosorbide di nitrate, Sotalol, Isosorbide mononitrate.

Films: P-Aminobenzoic acid, Cinnarizine, Piretanide, Prednisolone, Quinidine gluconate.

Granules: Cinnarizine, Diclofenac sodium, Diltiazem, Indomethacin, Fluorouracil, Prednisolone, Isosorbide mononitrate, Isosorbide dinitrate.

Powders: Riboflavin, phosphate, Sotalol, Theophylline.

Capsules: Verapamil HCl, Chlordiazepoxide HCl, Diazepam, Furosemide, L-opa and benserazide, Misoprostol, Propranolol HCl, Ursodeoxycholic acid, Nicardipine

MARKETED PRODUCTS OF FDDS²³

Dosage Form	Active Ingredients	Products	Company, Country
Floating Controlled Release Capsule	Levodopa and benserzide	Madopar	Roche Products, USA
Floating Capsule	Diazepam	Valrelease	Hoffmann-LaRoche, USA
Effervescent Floating Liquid alginate Preparation	Aluminium hydroxide, Magnesium carbonate	LIQUID GAVISON	Glaxo Smith Kline, INDIA
Floating Liquid alginate Preparation	Aluminium -Magnesium antacid	TOPALKAN	Pierre Fabre Drug, FRANCE
Colloidal gel forming FDDS	Ferrous sulphate	CONVIRON	Ranbaxy, INDIA
Gas-generating floating Tablets	Ciprofloxacin	CIFRAN OD	Ranbaxy, INDIA
Bilayer floating Capsule	Misoprostal	CYTOTEC	Pharmacia, USA

POLYMERS AND OTHER INGREDIENTS USED IN PREPARATIONS OF FLOATING DRUGS¹

Polymers: HPMC K4 M, Calcium alginate, Eudragit S100, Eudragit RL, Propylene foam, Eudragit RS, ethyl cellulose, poly methyl methacrylate, Methocel K4M, Polyethylene oxide, β Cyclodextrin, HPMC 4000, HPMC 100, CMC, Polyethylene glycol, polycarbonate, PVA, Polycarbonate, Sodium alginate, HPC-L, CP 934P, HPC, Eudragit S, HPMC, Metolose S.M. 100, PVP, HPC-H, HPC-M, HPMC K15, Polyox, HPMC K4, Acrylic polymer, E4 M and Carbopol.

Inert fatty materials (5%-75%) : Edible, inert fatty materials having a specific gravity of less than one can be used to decrease the hydrophilic property of formulation

and hence increase buoyancy. e.g. Beeswax, fatty acids, long chain fatty alcohols, Gelucires 39/01 and 43/01.

Effervescent agents: Sodium bicarbonate, citric acid, tartaric acid, Di-SGC (Di-Sodium Glycine Carbonate, CG (Citroglycine).

Release rate accelerants (5%-60%): e.g. lactose, mannitol

Release rate retardants (5%-60%): e.g. Dicalcium phosphate, talc, magnesium stearate.

Buoyancy increasing agents (upto80%): e. g. Ethyl cellulose.

Low density material: Polypropylene foam powder (Accurel MP 1000).

ADVANTAGES OF FDDS^{4, 6, 24, 30, 31}

- Floating dosage forms such as tablets or capsules will remain in the solution for prolonged time even at the alkaline pH of the intestine.
- FDDS are advantageous for drugs meant for local action in the stomach eg: Antacids.
- FDDS dosage forms are advantageous in case of vigorous intestinal movement and in diarrhea to keep the drug in floating condition in stomach to get a relatively better response.
- Acidic substance like aspirin causes irritation on the stomach wall when come in contact with it hence; HBS/FDDS formulations may be useful for the administration of aspirin and other similar drugs.
- The FDDS are advantageous for drugs absorbed through the stomach e.g.: Ferrous salts, Antacids.

DISADVANTAGES OF FDDS^{6, 24 30, 31}

- Floating systems are not feasible for those drugs that have solubility or stability problems in gastric fluids.
- Drugs such as Nifedipine, which is well absorbed along the entire GI tract and which undergo significant first-pass metabolism, may not be suitable candidates for FDDS since the slow gastric emptying may lead to reduced systemic bioavailability. Also there are limitations to the applicability of FDDS for drugs that are irritant to gastric mucosa.
- One of the disadvantages of floating systems is that they require a sufficiently high level of fluids in the stomach, so that the drug dosages form float therein and work efficiently.
- These systems also require the presence of food to delay their gastric emptying.

APPLICATION OF FLOATING DRUG DELIVERY SYSTEM^{24, 29, 32}

- **Enhanced Bioavailability:** The bioavailability of therapeutic agents can be significantly enhanced especially for those which get metabolized in the upper GIT by gastroretentive drug delivery approaches in comparison to the administration of non-gastroretentive drug delivery. The bioavailability of riboflavin CR-GRDF is significantly enhanced in comparison to the administration of non-GRDF CR polymeric formulations. There are several different processes, related to absorption and transit of the drug in the gastrointestinal tract, that act concomitantly to influence the magnitude of drug absorption. (Cook JD et al., 1990)
- **Sustained Drug Delivery:** Oral CR formulations are encountered with problems such as gastric residence time in the GIT. Drug absorption from oral controlled release dosage forms often limited by the short GRT available for absorption. These problems can be

overcome with the 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. Gastroretentive dosage forms can produce prolonged and sustained release of drugs from dosage forms.

- **Site Specific Drug Delivery Systems:** The controlled, slow delivery of drug from gastroretentive dosage form provides sufficient local action at the diseased site, thus minimizing or eliminating systemic exposure of drugs. These systems are particularly advantageous for drugs that are specifically absorbed from the stomach or the proximal part of the small intestine. The controlled, slow delivery of drug to the stomach provides sufficient local therapeutic levels and limits the systemic exposure to the drug. This reduces side effects that are caused by the drug in the blood circulation. In addition, the prolonged gastric availability from a site directed delivery system may also reduce the dosing frequency. Eg: Furosemide and Riboflavin. (Menon A et al., 1994)
- **Absorption Enhancement:** Drugs which are having poor bioavailability because of site specific absorption from the upper part of the GIT are potential candidates to be formulated as floating drug delivery systems, thereby maximizing their absorption. (Rouge N et al., 1998)
- **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 GRDF 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.
- **Reduced Fluctuations of Drug Concentration:** Continuous input of the drug following controlled release gastroretentive delivery produces systemic drug concentrations within a narrower range compared to the immediate release oral 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.

FUTURE PERSPECTIVES IN FDDS

Among the drugs currently in clinical use are several narrow absorption window drugs that may benefit from compounding into a FDDS. Replacing parenteral administration of drugs to oral pharmacotherapy would substantially improve treatment. It is anticipated that FDDS may enhance this possibility. Moreover, it is expected that the FDDS approach may be used for many potentially active agents with narrow absorption window,



whose development has been halted due to lack of appropriate pharmaceutical FDDS technologies. Combination therapy to treat *H. Pylori* infection in a single FDDS needs to be developed. Further investigation may concentrate on the following concept:

- Design of array of FDDS, each having a narrow GRT for use according to the clinical need e.g. dosage and state of disease. This may be achieved by compounding polymeric matrices with various biodegradation properties.
- Identification of a minimal cut-off size above that DFs retained in the human stomach for prolonged period of time. This would permit a more specific control to be achieved in gastroretentivity.
- Design and development of gastroretentive drug delivery systems as a beneficial strategy for the treatment of gastric and duodenal cancers.
- Exploring the eradication of *Helicobacter pylori* by using various antibiotics.
- Study of the effect of various geometric shapes, in a more excessive manner than previous studies, extended dimensions with high rigidity, on gastroretentivity.
- Design of novel polymers according to clinical and pharmaceutical need.

CONCLUSION

Drug absorption in the gastrointestinal tract is a highly variable procedure and prolonging gastric retention of the dosage form extends the time for drug absorption. Gastro-retentive floating drug delivery systems have emerged as an efficient means of enhancing the bioavailability and controlled delivery of many drugs. Floating drug delivery system is one of these oral dosage system forms and become an approach to prolong gastric residence time, thereby targeting site-specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effects. The increasing sophistication of delivery technology will ensure the development of increase number of gastro retentive drug delivery to optimize the delivery of molecules that exhibit absorption window, low bioavailability and extensive first pass metabolism. FDDS promises to be a potential approach for gastric retention. Although there are number of difficulties to be worked out to achieve prolonged gastric retention, a large number of companies are focusing toward commercializing this technique.

REFERENCES

1. Manoj Goyal, Rajesh Prajapati, Kapil Kumar Purohit, S.C. Mehta, 'Floating Drug Delivery System', Journal of Current Pharmaceutical Research, 5(1), 2011, 7-18.
2. Streubel A, Siepmann J, Bodmeier R, Gastroretentive drug delivery system, Expert Opinion Drug Delivery, 3(2), 2006, 217- 33.
3. Shweta Arora, Javed Ali, Alka Ahuja, Roop K. Khar and Sanjula Baboota, Floating Drug Delivery Systems: A Review, AAPS PharmSciTech, 6(3), 2005, E372-E390.
4. AV Mayavanshi, SS Gajjar, Floating drug delivery systems to increase gastric retention of drugs, Research J. Pharm. and Tech., 1(4), 2008, 345-348.
5. Rohilla ankur, Rohilla seema, Dahiya amarjeet, Khan M. U., Gastroretentive dosage form: Review on floating drug delivery systems, International research journal of pharmacy 2(5),2011, 72-78.
6. Hetangi rathod, Vishnu Patel, Moin Modasia, 'Floating drug delivery system: innovative approach of gastroretention', international journal of pharmaceutical sciences review and research, 4(3), 2010, 183-192.
7. Ekta Gurnany, Priyanka Singhai, Arti Soni, Rahul Jain, Sunil K Jain and Aviral Jain., Gastro Retentive Drug Delivery System- A Review, Journal of Pharmacy Research, 4(6), 2011, 1899-1908.
8. Wilson CG, Washington N. The stomach: its role in oral drug delivery. In: Rubinstein, MH, editors. Physiological Pharmaceutical: Biological barriers to drug absorption. Chichester, U.K.: Ellis Horwood. 1989, 47-70.
9. Streubel A, Siepmann J, Bodmeier R. Drug delivery to the upper small intestine window using Gastroretentive technologies. Curr Opin Pharmacol 2006, 501-508.
10. Larhed AW, Artursson P, Grasjo J, Bjork K. Diffusion of drugs in native and purified gastrointestinal mucus. J Pharm Sci 86(6), 1997, 660-665.
11. Dubernet C. Systèmes à libération gastrique prolongée. In: Falson-Rieg F, Faivre V, Pirot F, editors. Nouvelles formes médicamenteuses. Editions Médicales Internationales. Editions TEC and DOC. Cachan. 2004, 119-133.
12. Arora S, Ali J, Khar RK, Baboota S. Floating drug delivery systems: A review. AAPS Pharm Sci Tech, 6(3), 2005, 372-390.
13. El-Kamel AH, Sokar MS, Al Gamal SS, Naggar VF. Preparation and evaluation of ketoprofen floating oral delivery system. Int J Pharm 220, 2001, 13-21.
14. Garg S, Sharma S. Gastroretentive drug delivery systems. Business Briefing: Pharmatech 2003, 160-166.
15. Khosla R, Feely LC, Davis SS. Gastrointestinal transit of non-disintegrating tablets in fed subjects. Int J Pharm, 53, 1989, 107-117.
16. Mojaverian P, Vlasses PH, Kellner PE, Rocci Jr ML. Effects of gender, posture and age on gastric residence time of an indigestible solid: Pharmaceutical considerations. Pharm Res, 10, 1988, 639-644.
17. Coupe AJ, Davis SS, Evans DF, Wilding IR. Nocturnal scintigraphic imaging to investigate the gastrointestinal transit of dosage forms, J. Con. Rel. 20, 1992, 155-162.
18. A.R.Dhole Et Al, A Review On Floating Multiparticulate Drug Delivery System – A Novel Approach To Gastric Retention, International Journal Of Pharmaceutical Sciences Review And Research, 6(2), 2011, 205-210.
19. Garg R, Gupta GD. Progress in controlled gastroretentive delivery systems. Trop. J Pharm Res 7(3), 2008, 1055-1166.



20. Dave, B. S., Amin, A. F. and Patel M., Gastroretentive drug delivery system of ranitidine HCl formulation and in vitro evaluation. AAPS Pharma Sci Tech 5, 2004, 1-10.
21. Hejazi, R. and Amiji, M., Stomach-specific anti-H. Pylori therapy. I: Preparation and characterization of tetracycline of a floating multiple-unit capsule, high-density loaded chitosan microspheres. Int J Pharm 235, 2002, 87- 94.
22. Sawicki, W., Pharmacokinetics of verapamil and nor verapamil from controlled release floating pellets in humans. Eur J Pharm Biopharm 53, 2001, 29-35.
23. S.Gopalakrishnan, Floating Drug Delivery Systems: A Review, Journal of Pharmaceutical Science and Technology 3 (2), 2011, 548-554
24. Brahma N. Singh, Kwon H. Kim, Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention, Journal of Controlled Release 63, 2000, 235–259.
25. Y. Kawashima, T. Niwa, H. Takeuchi, T. Hino, Y. Ito, Preparation of multiple unit hollow microspheres (microbal loons) with acrylic resin containing tranilast and their drug release characteristics (in vitro) and floating behavior (in vivo), J. Control. Release 16, 1991, 279–290.
26. N. Rouge, J.C. Leroux, E.T. Cole, E. Doelker, P. Buri, Prevention of the sticking tendency of floating minitablets filled into hard gelatin capsules, Eur. J. Pharm. Biopharm. 43, 1997, 165–171.
27. Sangekar, S., Evaluation of effect of food and specific gravity of the tablets on gastricretention time. Int.J.Pharm 35, 1985, 34-53.
28. Singh, B. N. and Kim, K. H., Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention. J Control Release. 63, 2002, 235-259.
29. Amit Kumar Nayak, Jadupati Malakar and Kalyan Kumar Sen, Gastroretentive drug delivery technologies: Current approaches and future potential, J Pharm Educ Res 1(2), 2010, 1-12.
30. Vyas S.P and Khar R.K. Targetted and controlled Drug Delivery Novel carrier system 1st Ed., CBS Publishers and distributors, New Delhi, 2002, 196- 217.
31. Jain N.K., Progress in Controlled and Novel Drug Delivery Systems, 1st Ed. CBS Publishers and Distributors, New Delhi, 2004, 84-85.
32. Shakti Dwivedi¹ and Vikash Kumar, Floating Drug Delivery Systems- A Concept of Gastroretention Dosages Form, International Journal of Research in Pharmaceutical and Biomedical Sciences 2(4), 2011, 1413-1426.

Source of Support: Nil, **Conflict of Interest:** None.