WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 5.045
Volume 4, Issue 3, 504-525. Review Article ISSN 2277– 7105

RECENT ADVANCE IN FLOATING DRUG DELIVERY SYSTEM: AN OVERVIEW

Dixit K. Prajapati*, Dr. Mukesh S. Patel, Dr. Mukesh R. Patel

Department of Pharmaceutics, Shri B. M. Shah College of Pharmaceutical Education and Research, Modasa-383315, Gujarat, India.

Article Received on
20 Dec 2014,

Revised on 14 Jan 2015,
Accepted on 08 Feb 2015

***Correspondence for Author**
Dixit K. Prajapati
Department of Pharmaceutics, Shri B. M. Shah College of Pharmaceutical Education and Research, Modasa-383315, Gujarat, India.

ABSTRACT

Oral controlled release drug delivery systems are programmed to deliver the drug in predictable time frame that will increase the efficacy, minimize the adverse effects and increase the bioavailability of drugs. This triggered an increased interest towards formulation of novel delivery systems which retained in the stomach for prolonged and predictable period of time. Oral drug delivery of nearly half of the drugs gets thwarted owing to the high lipophilic nature. Bioavailability of these drugs being function of their aqueous solubility and dissolution tends to exhibit low magnitude and high intra and inter subject variability. Many drugs have a short biological half life and thus have invents potential in ameliorating GI absorption. Recent technological and scientific research has been devoted to the development of rate controlled drug delivery systems to overcome physiological adversities such as short gastric residence times (GRT) and unpredictable gastric emptying times (GET). This review discusses overall approaches of gastro retentive drug delivery systems and limelight on floating drug delivery its formulation development, factors, and discusses various *in-vitro* and *in-vivo* evaluation parameters. The present review addresses briefly about the floating drug delivery systems.

KEYWORDS: Floating drug delivery system, Gastro Retentive system, Evaluation *in vivo* and *in vitro*, Buoyant delivery system.

INTRODUCTION

The ultimate goal of any drug delivery system is effective disease/disorder management, minimum side effects and greater patient compliance in the cost effective manner. The drug

therapeutic indices could be maximized while indices of adverse reactions or side effects could be minimized by regulating the drug release in body in a well-defined controlled manner. One of such difficulties is the ability to confine the dosage form in the desired area of the gastrointestinal tract. To overcome this physiological problem, several drug delivery systems with prolonged gastric retention time have been investigated. 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, 2]

Gastroretentive 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. Floating systems or hydrodynamically controlled systems are low-density systems that have 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. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach .This results in an increased gastric residence time and a better control of the fluctuation in plasma drug concentration.

The controlled gastric retention of solid dosage forms may be achieved by the mechanism of mucoadhesion, 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.[3]

ADVANTAGES OF FLOATING DRUG DELIVERY SYSTEM[4, 5, 6, 7]

Enhanced bioavailability

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.

Enhanced first-pass biotransformation

In a similar fashion to the increased efficacy of active transporters exhibiting capacity limited activity, the pre-systemic metabolism of the tested compound may be considerably increased when the drug is presented to the metabolic enzymes (cytochrome P450, in particular CYP3A4) in a sustained manner, rather than by a bolus input.

Sustained drug delivery/reduced frequency of dosing

For drugs with relatively short biological half life, sustained and slow input from CR-GRDF may result in a flip-flop pharmacokinetics and enable reduced dosing frequency. This feature is associated with improved patient compliance, and thereby improves therapy.

Targeted therapy for local ailments in the upper GIT

The prolonged and sustained administration of the drug from GRDF to the stomach may be advantageous for local therapy in the stomach and small intestine. By this mode of administration, therapeutic drug concentrations may be attained locally while systemic concentrations, following drug absorption and distribution, are minimal.

Reduced fluctuations of drug concentration

Continuous input of the drug following CRGRDF 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.

Improved selectivity in receptor activation

Minimization of fluctuations in drug concentration also makes it possible to obtain certain selectivity in the elicited pharmacological effect of drugs that activate different types of receptors at different concentrations.

Reduced counter-activity of the body

In many cases, the pharmacological response which intervenes with the natural physiologic processes provokes a rebound activity of the body that minimizes drug activity. Slow input of

the drug into the body was shown to minimize the counter activity leading to higher drug efficiency.

Extended time over critical (effective) concentration

For certain drugs that have non-concentration dependent pharmacodynamics, such as beta-lactam antibiotics, the clinical response is not associated with peak concentration, but rather with the duration of time over a critical therapeutic concentration. The sustained mode of administration enables extension of the time over a critical concentration and thus enhances the pharmacological effects and improves the clinical outcomes.

Minimized adverse activity at the colon

Retention of the drug in the GRDF 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 beta-lactam antibiotics that are absorbed only from the small intestine, and whose presence in the colon leads to the development of microorganism's resistance.

Site specific drug delivery

A floating dosage form is a feasible approach especially for drugs which have limited absorption sites in upper 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.

LIMITATION OF FLOATING DRUG DELIVERY SYSTEM[7, 8]

1. Floating systems are not feasible for those drugs that have solubility or stability problems in gastric fluids.
2. 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 irritative to gastric mucosa.
3. 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.
4. These systems also require the presence of food to delay their gastric emptying.

5. 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.
6. Drugs that cause irritation and lesion to gastric mucosa are not suitable to be formulated as floating drug delivery systems.
7. Gastric emptying of floating forms in supine subjects may occur at random and becomes highly dependent on the diameter and size. Therefore patients should not be dosed with floating forms just before going to bed.

COMPARISON BETWEEN CONVENTIONAL AND GASTRO RETENTIVE DRUG DELIVERY SYSTEM[9, 10]

Conventional drug delivery system	Gastro retentive drug delivery system
-More side effect	-No risk of dose dumping.
-Patient compliance is less.	-Improves patient compliance
-Less gastric retention time	-Improve gastric retention time
-Not appropriate for delivery of drugs with narrow absorption window in small intestine region.	-Appropriate for delivery of drugs with narrow absorption window in small Intestinal region.
-Not much beneficial for drugs exhibit local action in the stomach & degrade in the colon having rapid absorption through GIT	-Beneficial for drugs exhibit local action in the stomach & degrade in the colon having rapid absorption through GIT.
-High risk of dose dumping.	-No risk of dose dumping.

SUITABLE DRUG CANDIDATES FOR GASTRORETENTION[11, 12]

In general, appropriate candidates for FDDS are molecules that have poor colonic absorption but are characterized by better absorption properties at the upper parts of the GIT.

1. Drugs that have narrow absorption window in GI tract e.g. Riboflavin, Para-amino benzoic acid and Levadopa.
2. Primarily absorbed from stomach and upper part of GI tract e.g. Chlordiazepoxide and Cinnarizine.
3. Drugs that locally act in the stomach e.g. antacid and misoprostol.
4. Drugs that degrade in the colonic environment. E.g. Captopril, Ranitidine HCl and metronidazole.
5. Drugs that disturb normal colonic bacteria, e.g. Amoxicillin trihydrate.
6. Drugs that show low solubility at high pH values e g. Diazepam, Chlordiazepoxide, verapamil.

BASIC GASTROINTESTINAL TRACT PHYSIOLOGY

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.[13]

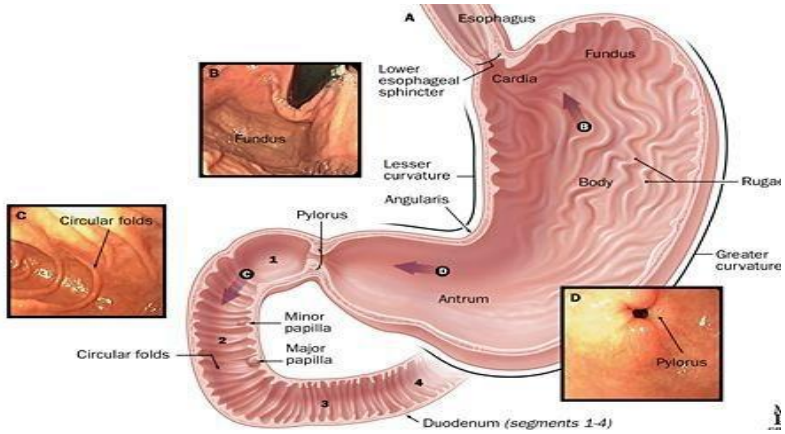

Figure 1: Gastro intestinal tract

Gastric emptying occurs in both the fasting and fed states. During the fasting state an interdigestive series of electrical events take place which cycle both through stomach and intestine every 2-3 hrs, which is called as interdigestive myloelectric cycle or migrating myloelectric cycle (MMC) which is further divided in to four phases After the ingestion of a mixed meal, the pattern of contractions changes from fasted to that of fed state which is also termed as digestive motility pattern.

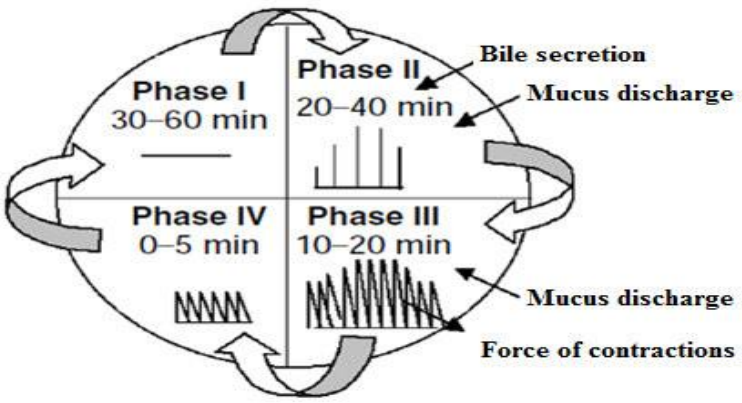

Figure 2: Motility patterns of the GIT in the fasted state

Phase I (Basal phase): It is a quiescent period lasting from 30 to 60 min with no contractions and is characterized by a lack of secretory, electrical and contractile activity.

Phase II (Preburst phase): It consists of intermittent contractions that gradually increase in intensity as the phase progresses and it lasts about 20 to 40 min. Gastric discharge of fluid and very small particles begins later in this phase.

Phase III (burst phase): This is a short period of intense distal and proximal gastric contractions (4–5 contractions per minute) lasting about 10 to 20 min; these contractions, also known as ‘‘house-keeper waves,’’ sweep gastric contents down the small intestine.

Phase IV: This is a short transitory period of about 0 to 5 min and the contractions dissipate between the last part of phase III and quiescence of phase I.[14]

FACTORS AFFECTING GASTRIC RETENTION[15, 16, 17, 18]

Size- Dosage form units with a large diameter having large volume. If volume increases density will be decreases, low density help in floating. So that larger size devices are reported to have an increased GRT compared with small diameter.

Shape of dosage form – Tetrahedron and ring shaped devices are reported to have better GRT compared with other shapes.

Density – Low density system tend to float on the gastric fluid surface while high density system sink to bottom of stomach.

Single or Multiple unit formulation- Multiple unit formulations show a more predictable release profile and allow co-administration of units with different release profiles and permit a larger margin of safety against dosage form failure compared with single unit dosage forms.

Fed or Unfed state-The migrating myoelectric complex (MMC) occurs every 1.5 to 2 hours under fasting conditions i.e. gastric motility is higher in fasting condition which shows lesser GRT. However, in the fed state, MMC is delayed and GRT is considerably longer.

Caloric content - A meal that is high in proteins and fats, GRT can be increased by 4 to 10 hours.

Gender - GRT in males (3.4±0.6hours) is less compared with their age and race matched female (4.6±1.2 hours), (regardless of the weight, height and body surface).

Age – Geriatric patient have a significantly longer GRT as compared with children.

Posture – GRT can vary between supine and upright ambulatory position of the patient.

Disease state- GRT is altered during disease state.

The time, at which the drug is taken- When a single unit system is taken during phase III of the MMC, the powerful peristaltic waves increase the chances of expelling the drug into the duodenum.

Rate of dissolution of drug- A drug which dissolving fast will quickly evacuate with water through the pylorus.

Nature of drug- If drug is taken during meal, water soluble drug leave the stomach with water, while lipid soluble drug leave it with lipids and fats are evacuated last.

APPROACHES TO GASTRORETENTION

1. High density approach

These systems have density higher than the stomach fluid (1.004 g/cm^3). It would be at least 1.50 g/cm3. These systems are able to withstand peristaltic movement and retained in the stomach for several hours. This system can be manufacture by coating the drug with a heavy inert material such as barium sulphate, zinc oxide, titanium dioxide, iron powder, etc.[19]

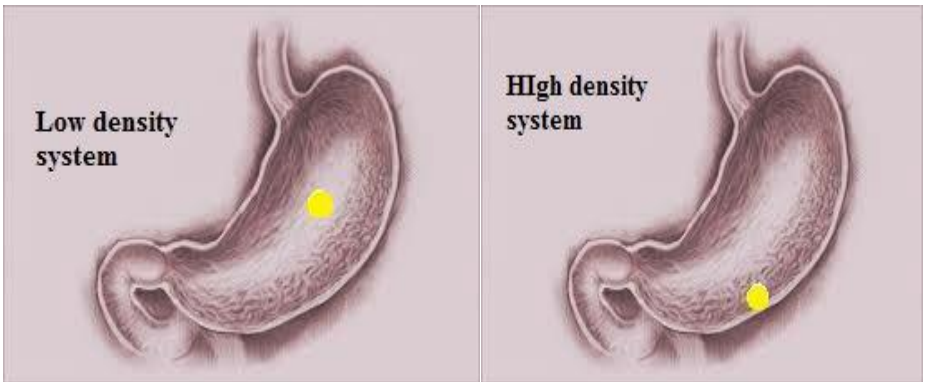

Figure 3: Low density system and High density systems

2. Mucoadhesive Drug Delivery System

Mucoadhesive drug delivery systems are designed to localize a delivery device within the lumen to increase the absorption and retention time of drugs in a specific site. Mucoadhesive drug delivery system offer drug release at controlled manner. They bypass the first pass metabolism and avoid degradation of GI enzymes and have good surface area so that they give rapid absorption and good bioavailability. The concept of mucoadhesive polymer to

extend the GI transit time is shown in figure 4. Bio adhesive or mucoadhesive polymers are natural or synthetic polymers capable of producing an adhesive interaction with a biological membrane or with the mucus lining on the GI mucus membrane. Some Bioadhesive or mucoadhesive polymers are- Polycarbophil, Carbopol, Pectins, Chitosan, HPMC, CMC and Gliadin, etc.[20]

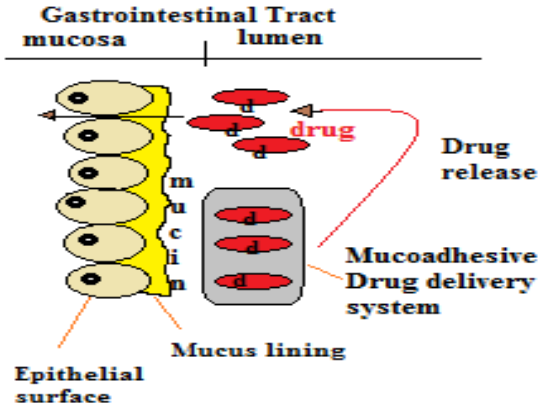

Figure 4: Interaction of a mucoadhesive drug delivery system with the mucus layer on the gastrointestinal surface epithelium.

3. Swelling and Expandable systems

If a dosage form is bigger than the pyloric sphincter it will withstand the gastric transit. But the dosage form must be small to be swallowed. There is three configuration are required a small size for swallowing, An expanded form for gastro retention and finally a small form for evaluation. After swallowing these systems are swells to an extent that prevent their exit from the stomach through the pylorus. These systems are also called as "Plug type systems", since they have tendency to remain logged at the pyloric sphincters. Polymers selected with the proper molecular weight and swelling properties then controlled and sustained drug release can be achieved. When polymers come in contact with gastric fluid, the polymer imbibes water and swells. The swelling of these polymers is due to presence of physical-chemical cross links in the hydrophilic polymer network.

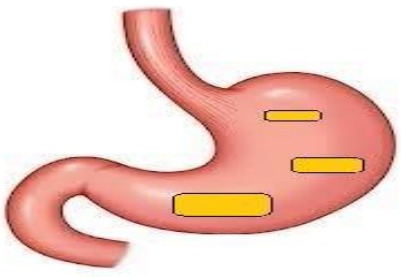

Figure 5: **Swellable tablet in stomach**

4. Magnetic Systems

In Magnetic systems dosage forms hold a small internal magnet and another magnet positioned on the abdomen externally. The problem in this system is that, the external magnet must be placed at the right position with a degree of precision.

5. Superporous Hydrogel

They are swellable system. They have average pore size >100 micro meter, absorption of water is very fast by capillary wetting, with the help of pores, so that they swell and reach to an equilibrium size within a minute. They have adequate mechanical strength to withstand the pressure by gastric contraction. They are formulated by hydrophilic particulate material Ac-Di-Sol (Crosscarmellose sodium).

FLOATING DRUG DELIVERY SYSTEM

FDDS are significantly used for drugs that are locally act in stomach and small intestine and have narrow absorption window in small intestine region, unstable in the intestinal or colonic environment and shows low solubility at alkaline environment. FDDS have density lower than gastric fluid, due to which they have tendency to float over gastric contents for prolonged period of time without affecting gastric emptying rate. As the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. Conventional controlled release dosage forms go downwards to the bottom of the stomach once ingested because their density is higher than that of gastric contents. Prolonged gastric retention improves bioavailability, reduces drug waste and improves solubility for drugs which are less soluble in alkaline pH. Floating drug delivery also used in sustained drug delivery, delivery of drug at specific site and in enhancement of absorption.[21]

APPROACES TO FLOATING DRUG DELIVERY SYSTEM

Various types of floating system have been developed which may involve generation of effervescent or non effervescent.

1. Hydrodynamically Balanced System

The hydrodynamically balanced system in either capsule or tablet form, is designed to prolong GI residence time. Hydroxypropyl Methyl Cellulose (HPMC), Hydroxy Ethyl Cellulose (HEC), Hydroxypropyl Cellulose (HPC), Sodium Carboxy Methyl Cellulose (NaCMC), Agar, Carrageenans or Alginic acid are the excipients used in the formulation of HBS. The drug and polymer mixed together and administered in gelatin capsule. The capsule

is rapidly dissolve when comes in contact with gastric fluid and the hydrocolloids in the floating device start to become hydrate and form a colloidal gel barrier around its surface with thickness growing with time. These gel barrier controls the rate of fluid penetration into the device and consequent drug releases from the barrier. The gel barrier act as a reservoir for sustained release of drug as the exterior surface of the dosage form dissolve, the gel layer is maintained by the hydration of the adjacent hydrocolloid layer. The air trapped by the swollen polymer lowers the density less than 1 and remain buoyant in the stomach for up to six hours. The working principle of HBS is shown in figure 6.[22]

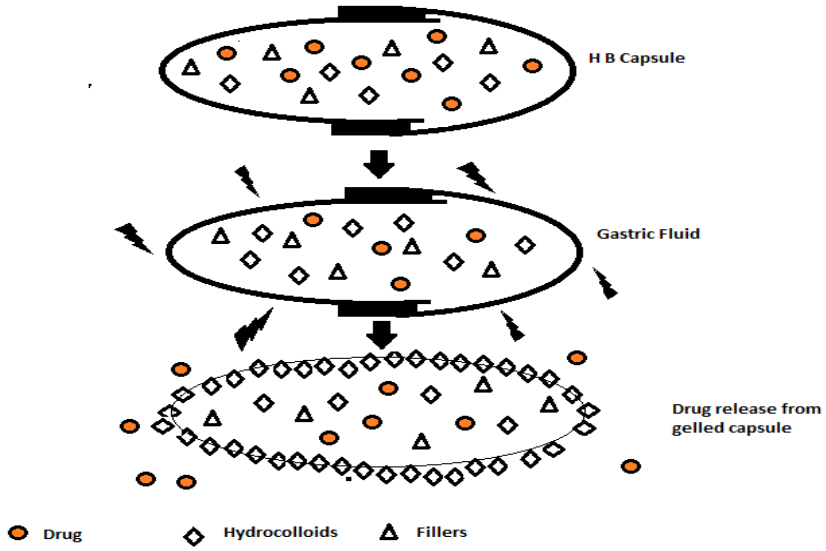

Figure 6: Working Principles of Hydrodynamically Balanced System

2. Gas generating system (Effervescent System)

These systems are prepared with swellable polymer such as methylcellulose, chitosan and various effervescent compounds, e.g., sodium bicarbonate, tartaric acid, and citric acid. When they are come in contact with gastric fluid CO2 is librated and get entrapped in swollen polymer which provide buoyancy to the system. The system consisted of sustained release pills and the pill surrounded by two layers (Fig. 7). The inner layer was an effervescent layer containing sodium bicarbonate and tartaric acid. The outer layer was a swellable membrane layer containing mainly polyvinyl acetate and purified shellac. Furthermore, the effervescent layer was separated into two sub layers to avoid direct contact between tartaric acid and sodium bicarbonate. Tartaric acid was contained in the outer sub layer and sodium bicarbonate was contained in the inner sub layer. When the system was immersed in a buffer solution at 37^0C, a swollen pill was formed, having a density less than 1 g/ ml. The

neutralization reaction occurs between effervescent layers, and CO2 gas evolved. The system was found to float completely within 10 min.[23]

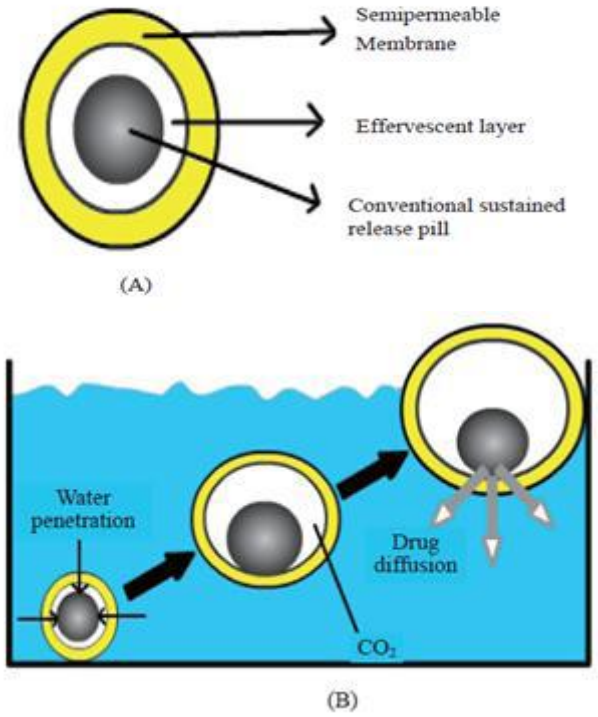

Figure 7: Gas Generating System.

(A) A multiple-unit oral floating dosage system,
(B) Stages of floating mechanism

3. Raft forming system

In Raft forming system, a gel forming solution (e.g. sodium alginate solution containing carbonates or bicarbonate) when comes in contact with gastric fluid, swell and form a viscous cohesive gel and forming a continuous layer called a raft. Because of low bulk density created by the formation of CO2, this raft floats on gastric fluids. Floating raft act as a barrier to prevent the reflux of gastric contents into oesophagus so that they are used for gastro esophageal reflux treatment.

4. Low density system

The limitation of the gas generating system is that, they have a lag time before floating on the gastric fluid, so that dosage form may undergo premature evacuation from the stomach. Therefore, low density system (<1 g/cm3) have been developed, which exhibit immediate

floating. They are composed of low density material entrapping oil or air. In this approach, the density of the device should be less than the density of gastric fluid i.e. 1 g/ml, so as to float in the gastric fluid of stomach for a prolong period of time without affecting the gastric emptying rate. As the system is floating on the gastric contents, the drug is released slowly for longer period of time. After release of drug, the left over system is emptied from the system.

TYPES OF FLOATING DRUG DELIVERY SYSTEM:

1. Single unit system

Single unit system (e.g. hydrodynamically balanced system) may cause high variability in bioavailability and local irritation due to large amount of drug delivered at a particular site of the gastro intestinal tract. These systems are unreliable in prolonging the GRT owing to their 'all-or-nothing' emptying process.

2. Multiple unit system

Multiple-unit systems (e.g. microspheres) are passing through the GIT uniformly. They avoid the 'all-or-none' gastric emptying nature of single unit system. They reduce inter subject variability in absorption and risk of local irritation. A variety of multiple-unit floating systems are based on various principles, such as air compartment multiple-unit system, micro particles based on porous carriers, hollow microspheres (micro balloons), oil-entrapped gel beads prepared by gelation method.[24]

TYPES OF FDDS BASED ON BUOYANCY

1. Non-effervescent FDDS

General approach for preparation of such system involves thoroughly mixing the drug and the gel-forming hydrocolloid. On contact with gastric fluid this dosage form swells and attains a bulk density of less than gastric fluid. The air entrapped within the swollen matrix help in buoyancy to the dosage form. Gel-forming or highly swellable cellulose type hydrocolloids, polysaccharides, and matrix forming polymers such as polycarbonate, Polyacrylate, polymethacrylate and polystyrene are common excipients used in non effervescent FDDS.

2. Effervescent System

Effervescent floating drug delivery systems prepared by swellable Polymers like chitosan, methyl cellulose and effervescent compounds such as citric acid, sodium bicarbonate, and

tartaric acid. On contact with gastric fluid they generate gas (CO2), thus reduce the density of the system, and remain buoyant in the stomach for a prolonged period of time.[25]

EVALUATION PARAMETER[26, 27, 28]

IN-VITRO EVALUATION OF FLOATING TABLETS

Evaluation was performed to assess the physicochemical properties and release characteristics of the developed formulations.

1. Pre-compression parameters

- **Bulk density**

It is the ratio of total mass of powder to the bulk volume of powder. It was determined by pouring a weighed quantity of tablet blend into graduated cylinder and measuring the height. Bulk density is the ratio of mass of tablet blend to bulk volume.

$$\text{Bulk Density} = \frac{\text{Mass}}{\text{Apparent volume}}$$

- **Tapped density**

It is the ratio of the total mass of the powder to the tapped volume of the powder. Accurately weighed amount of tablet blend poured in graduated cylinder and height is measured. Then cylinder was allowed to 100tap under its own weight onto a hard surface. The tapping was continued until no further change in height was noted.

$$\text{Tapped Density} = \frac{\text{Mass}}{\text{Tapped volume}}$$

- **Carr's index**

Compressibility is the ability of powder to decrease in volume under pressure using bulk density and tapped density the percentage compressibility of powder were determined, which is given as Carr's compressibility index. It is indirectly related to the relative flow rate. Carr's compressibility index was determined by the given formula.

$$\text{Carr's Index} = \frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Tapped Density}} \times 100$$

- **Hausner's ratio**

Hausner's ratio indicates the flow properties of powder and measured by the ratio of tapped density to bulk density. Hausner's ratio was determined by the given formula.

$$\text{Hausner's Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

- **Angle of repose**

Angle of repose was determined by using funnel method. The accurately weighed blend was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of blend. The drug excipient blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation.

$\theta = \tan^{-1} (h/r)$

Here;

h = Height of pile

r = Radius of pile

θ = Angle of repose

2. Post-compression parameters

- **Shape of Tablets**

Compressed tablets were examined under the magnifying lens for the shape of the tablet.

- **Tablet Dimensions**

Thickness and diameter were measured using a calibrated varniear caliper. Three tablets of each formulation were picked randomly and thickness was measured individually.

- **Hardness**

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It was expressed in kg/cm^2. Three tablets were randomly picked and hardness of the tablets was determined.

- **Friability test**

The friability of tablets was determined by using Roche Friabilator. It was expressed in percentage (%). Ten tablets were initially weighed (W initial) and transferred into friabilator. The friabilator was operated at 25rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again (W final). The % friability was then calculated by –

$F = W_{initial} - W_{final}/W_{initial} \times 100$

- **Tablet Density**

Tablet density was an important parameter for floating tablets. The tablet would floats only when its density was less than that of gastric fluid (1.004). The density was determined using following relationship.

$V = r^2hd = m/v$

V = volume of tablet (cc)

r = radius of tablet (cm)

h = crown thickness of tablet (g/cc)

m = mass of tablet

- **Weight Variation Test**

Ten tablets were selected randomly from each batch and weighed individually to check for weight variation. A little variation was allowed in the weight of a tablet by U.S. Pharmacopoeia. The following percentage deviation in weight variation was allowed showed in table

Average weight of a tablet	Percent deviation
130 mg or less	10%
>130mg and <324mg	7.5%
324 mg or more	5%

- **Buoyancy / Floating Test**

The time between introduction of dosage form and its buoyancy on the simulated gastric fluid and the time during which the dosage form remain buoyant were measured. The time taken for dosage form to emerge on surface of medium called Floating Lag Time (FLT) or Buoyancy Lag Time (BLT) and total duration of time by which dosage form remain buoyant is called Total Floating Time (TFT).

- **Swelling Study**

The swelling behavior of a dosage form was measured by studying its weight gain or water uptake the dimensional changes could be measured in terms of the increase in tablet diameter and/or thickness over time. Water uptake was measured in terms of percent weight gain, as given by the equation.

WU = (Wt – W0) x 100/WO

Wt = Weight of dosage form at time t.

W0 = Initial weight of dosage form.

- ***In-vitro* drug release studies**

The test for buoyancy and *in vitro* drug release studies are usually carried out in simulated gastric and intestinal fluids maintained at 37^{o}C. In practice, floating time is determined by using the USP dissolution apparatus containing 900ml of 0.1 HCl as a testing medium maintained at 37^{o}C. The time required to float the HBS dosage form is noted as floating (or floatation) time.

- **Surface topography**

The surface topography and structures were determined using scanning electron microscope operated with an acceleration voltage of 10k.v, Contact angle meter, Atomic force microscopy (AFM), Contact profiliometer.

- **Determination of the drug content**

Percentage drug content provides how much amount of the drug that was present in the formulation. It should not exceed the limits acquired by the standard monographs. Drug content was determined by using HPLC, HPTLC methods, near infrared spectroscopy (NIRS), Microtitrimetric methods, Inductively Coupled Plasma Atomic Emission Spectrometer (ICPAES) and also by using spectroscopy techniques.

- **Fourier transform infrared analysis**

Fourier transform infrared spectroscopy is a technique mostly used to identify organic, polymeric, and some inorganic materials as well as for functional group determination. Fourier Transform Infrared Analysis (FT-IR) measurements of pure drug, polymer and drug loaded polymer formulations were obtained on FTIR. The pellets were prepared on KBr-press under hydraulic pressure of 150kg/cm^{2}; the spectra were scanned over the wave number range of 3600 to 400 cm-1 at the ambient temperature.

- **Differential Scanning Calorimetry (DSC)**

DSC used to characterize water of hydration of pharmaceuticals .Thermo grams of formulated preparations were obtained using DSC instrument equipped with an intercooler. Indium/Zinc standards were used to calibrate the DSC temperature and enthalpy scale. The sample preparations were hermitically sealed in an aluminum pan and heated at a constant rate of 10°C/min; over a temperature range of 25° C – 65°C. Inert atmosphere was maintained by purging nitrogen gas at the flow rate of 50ml/min.

IN-VIVO EVALUATION PARAMETER

Although many animal models including rabbits have reported for in vivo behavior, human studies are easily and widely acceptable. Type of the study determines the tracing element to be incorporated. We have even reduced the size of the dosage form in order to avoid congestion of the narrow trachea if rabbits are used.

- **Radiology**

X- ray is widely used for examination of internal body systems. Barium sulphate is widely used Radio opaque marker. So, drug s replaced by BaSO4 and x-ray images are taken at various intervals to view Gastro retention. It is advisable to prepare different concentration of BaSO4 and find out which ratio gives the comparable *in vitro* floatation. Our research experience shows that 20% of the drug if substituted will give satisfactory results. The corresponding author has performed *in vivo* studies on rabbits of a mucoadhesive anticancer single unit dosage form and is in pipeline for patent.

- **Scintigraphy**

Similar to X-ray, emitting materials are incorporated into dosage form and then images are taken by scintigraphy. Widely used emitting material is 99Tc (technetium).

- **Gastroscopy**

Gastroscopy is peroral endoscopy used with fiber optics or video systems. Gastroscopy is used to inspect visually the effect of prolongation in stomach. It can also give the detailed evaluation of GRDDS.

- **Magnetic marker monitoring**

In this technique, dosage form is magnetically marked with incorporating iron powder inside, and images can be taken by very sensitive bio-magnetic measurement equipment. Advantage of this method is that it is radiation less and so not hazardous.

- **Ultrasonography**

Used sometimes, not used generally because it is not traceable at intestine.

- **13C Octanoic acid breath test**

13C Octanoic acid is incorporated in to GRDDS. In stomach due to chemical reaction, octanoic acid liberates CO_2 is replaced with 13C isotope. So time up to which $13CO_2$ gas is

observed in breath can be considered as gastric retention time of dosage form. As the dosage form moves to intestine, there is no reaction and no CO_2 release.

MARKETED FORMULATION OF FLOATING DRUG DELIVERY SYSTEM[29]

Brand name	Drug	Delivery system	Manufacturer
Cifran O.D.	Ciprofloxacin	Gas generating floating tablet	Ranbaxy, India
Oflin O.D.	Ofloxacin	Gas generating floating tablet	Ranbaxy, India
Conviron	Ferrous sulphate	Colloidal gel forming FDDS	Ranbaxy, India
Liquid Gavison	Alginic acid and sodium bicarbonate	Effervescent floating liquid alginate preparation	GlaxoSmithKline, India
Almagate float Coat	Al-Mg Antacid	Floating liquid form	-
Glumetza	Metformin HCl	Tablet	Depomed
Topalkan	Al-Mg	Floating liquid alginate preparation	Pierre Fabre Drug, France
Valrelease	Diazepam	Floating Capsule	Hoffman-LaRoche, USA
Madopar HBS	Benserazide and L-dopa	Floating CR Capsule	Roche Product, USA
Cytotec	Misoprostol	Bi layer floating Capsule	Pharmacia, USA

CONCLUSION

The FDDS become an additional advantage for drugs that are absorbed primarily in the upper part of GI tract. 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 they can be delivered efficiently thereby maximizing their absorption and enhancing absolute bioavailability. The control of gastro intestinal transit could be the focus of the next decade and may result in new therapeutic possibilities with substantial benefits for patient. Now, a lot of work is running to develop different types of gastroretentive delivery systems of various drugs. In the future, it is expected that they will become of increasing importance, ultimately leading to improved efficiencies of various types of pharmacotherapies.

ACKNOWLEDGEMENTS

The author would like to thank Dr. M. S. Patel for his comments on this article.

REFERENCES

1. Ramaiyan D., Vijaya Ratna J., Floating Drug Delivery System: A Novel Approach. International Journal of Pharmaceutical Development & Technology, *2012; 2 (1): 29-36.*
2. Arunachalam A., Karthikeyan M., Konam K. Floating Drug Delivery System: A Review. International Journal of Research And Pharmaceutical Science, 2011; 2(1): 76-83.
3. Chowdary K., Chaitanya C. Recent Research on Floating Drug Delivery System-A Review. Journal of Global trend in pharmaceutical science, 2014; 5(1): 1361-1373.
4. Garg R., Gupta G. Progress in Controlled Gastroretentive Delivery System. Tropical Journal of Pharmaceutical Research, 2008; 7(3): 1055-1066.
5. Singh B N., Kim K H. Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention. Journal of Controlled Release, 2000; 63: 235-259.
6. Klausner E A., Lavy E., Friedman M., Hoffman A. Expandable gastroretentive dosage forms. Journal of Controlled Release, 2003; 90: 143-162.
7. Vedha hari. The Recent Developments On Gastric Floating Drug Delivery Systems: An overview. International Journal of Pharmaceutical Technology And Research, 2010; 2(1): 524-534.
8. Tanwar Y., Naruka P., Ojha G. Devolpment And Evaluation Of Floating Microsperes Of Verapamil hydrochloride. Brazilian journal of pharmaceutical sciences, 2007; 43(4): 529-534.
9. Nasa P., Mahant S., Sharma D. Floating Systems: A Novel Approach towards Gastroretentive Drug Delivery Systems. International Journal of Pharmaceutical And Pharmaceutical Sciences, 2010; 2(3): 1-7
10. Bhardwaj L., Sharma P., Malviya R. A Short Review on Gastro Retentive Formulations for Stomach Specific Drug Delivery:Special Emphasis on Floating *In situ* Gel Systems. African Journal of Basic & Applied Sciences, 2011; 3(6): 300-312.
11. Singh B., Kim K. Floating drug delivery systems - an approach to oral controlled drug delivery via gastric retention. Journal of Controlled Release, 2000; 63(3): 235-259.
12. Shaha S. Gastro-retentive floating drug delivery system. Asian Journal of Pharmaceutical Sciences, 2009; 4(1): 65-80.
13. Kaur B., Sharma S., Sharma G., Sharma M. A Review of Floating Drug Delivery System. Asian Journal of Biomedical and Pharmaceutical Science, 2013; 3(24): 1-6.
14. Hirtz. The GIT absorption of drug in man: A Review of Current Concepts and method of Investigation. British Journal of Clinical Pharmacology, 1985; 19: 77-83.

15. Ware M., Tiwari S., Roy A. New Insights In to Gastro-Retentive Floating Drug Delivery System. World Journal of Pharmacy And Pharmaceutical Science, 2013; 3(1): 252-270.
16. Chanda R., Roy A., Bahadur S., Saha S., Das S. A Floating Drug Delivery: A Potential Alternative to Conventional Therapy. International Journal of Pharmaceutical Technology and Research, 2010; 2(1): 49-59.
17. Gupta G., Singh A. A Short Review on stomach specific drug delivery system. International Journal of Pharmaceutical Technology and Research, 2012; 4(4): 1527-1545.
18. Bardonnet P L., Faivre V., Pugh W., Piffaretti J., Falson F. Gastroretentive dosage forms: Overview and special case of Helicobacter pylori. Journal of Controlled Release, 2006; 111: 1 –18.
19. Nasa P., Mahant S., Sharma D., Floating Systems: A Novel Approach towards Gastroretentive Drug Delivery Systems. International Journal of Pharmaceutical and Pharmaceutical Sciences, 2010; 2(3): 1-7.
20. Narang N., An Updated Review on Floating Drug Delivery System. International Journal of Applied Pharmaceutics, 2011; 1(3): 1-7.
21. Nijamuddin M., Ahmed A., Shelar S., Patel V., Khan T. Floating microspheres of Ketoprofen: Formulation and Evaluation. International Journal of Pharmacy and Pharmaceutical Sciences, 2010; 2(2): 164-168.
22. Kawashima Y., Niwa T., Takeuchi H., Hino T., Ito Y. Preparation of multiple unit hollow microspheres (microballoons) with acrylic resins containing tranilast and their drug release characteristics *(In vivo)*. Journal of Controlled Release, 1991; 16: 279-290.
23. Jayanthi G., Jayaswal S., Srivastava A. Formulation and evaluation of terfenadine microballoons for oral controlled release. Pharmazie, 1995; 50: 769-770.
24. Patil J M., Hirlekar R., Gide P., Kadam V. Trends in floating drug delivery system. Journal of scientific and Industrial Research, 2006; 65: 11-21.
25. Tadros M. Controlled-release effervescent floating matrix tablets of ciprofloxacin hydrochloride: Development, optimization and *in vitro–in vivo* evaluation in healthy human volunteers. European Journal of Pharmaceutics and Biopharmaceutics, 2010; 74(2): 332-339.
26. Dixit N. Floating Drug Delivery System. Journal of Current Pharmaceutical Research, 2011; 7 (1): 6-20.

27. Ichikawam., Watenables., Miyake Y. A multiple unit oral floating dosage systems preparation and *in–vivo* evaluation of floating and sustained release characteristics. Journal of Pharmaceutical Science, 1991; 80: 1062-1066.
28. Sonar G., Jain D., More D. Preparation and in vitro evaluation of bilayer and floating bioadhesive tablets of Rosiglitazone Maleate, Asian Journal of Pharmaceutical sciences, 2007; 2(4): 161-169.
29. El-Nahas., Honsy K. Chitosan based Floating Microsphere of Trimetazidin Dihydrochloride: Preparation and *In vivo* Characterisation. Indian Journal of Pharmaceutical Sciences, 2011; 73(4): 355-482.