

## REVIEW ARTICLE

### SCOPE AND SIGNIFICANCE OF FLOATING DRUG DELIVERY SYSTEM

Pattan S. R.\*, Wani N. P., Shelar M. U., Nirmal S. A., Chaudhari P. D. and Gude R. S.

(Received 24 February 2012) (Accepted 05 September 2012)

#### ABSTRACT

In recent years there have been several scientific and technological advancements in the research and development of rate-controlled oral drug delivery systems by overcoming physiological adversities, such as short gastric residence time (GRT) and unpredictable gastric emptying time (GET). Several approaches are currently utilized in the prolongation of the GRT, including floating drug delivery systems (FDDS), also known as hydrodynamically balanced systems (HBS), swelling and expanding systems, polymeric bioadhesive systems, modified-shape systems, high-density systems and other delayed gastric emptying devices. In this review, the current technological developments of FDDS including patented delivery systems and marketed products, and their advantages and future potential for oral controlled drug delivery are discussed.

**Keywords:** Bioadhesive, Gastroretentive dosage forms, Effervescent, Gastrointestinal tract.

#### INTRODUCTION

Some drugs tend to be absorbed in specific areas, principally due to their low permeability or solubility in the intestinal tract, their chemical stability, the binding of the drug to the gut contents, as well as to the degradation of the drug by the microorganisms present in the colon. Physiological factors like gastrointestinal transit time, regional pH, surface area, enzymatic activity and colonic micro flora influence drug absorption and some of these factors may be used to achieve control over drug absorption. *In vitro* receptor binding assays in drug delivery have shown to increase the proportion of lower permeability drugs developed which often results in selection of either multiplied ionized peptide mimetic or more soluble and hydrophobic drugs having improved partitioning into

the hydrophobic pockets of protein receptors. Delivery of drugs at a specific region in gastrointestinal tract, the so called absorption window needs the development of gastro retentive dosage forms. The attempts to develop gastro retentive drug delivery systems may be largely divided into two classes: those that rely on the natural physiology of the gastrointestinal tract and those that are designed to overcome it. Approaches such as size or floatation, which rely on delayed emptying from the stomach, depend on the normal physiological duration of the fed state of 4-8 h, following a meal and rather reproducible transit time through the small intestine.

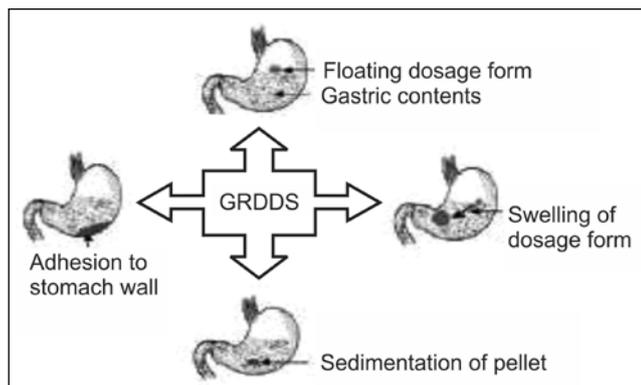
The transit time of a dosage form through the gastrointestinal tract is variable or even unpredictable, and can be of very short duration, due to this the time available for the drug absorption might be short and limits the absorption of drugs which are absorbed at certain sites along the gastrointestinal tract. There are many types of gastric retention drug delivery systems tested to overcome the limited region and times for drug absorption in gastrointestinal tract (Fig. 1). The main approaches that have been examined for gastroretentive dosage forms (GRDFs) are: low density of GRDF that cause buoyancy above

---

\*For correspondence

Pravara Rural College of Pharmacy  
Pravaranagar, A/P- Loni Bk. Tal-Rahata  
Dist-Ahmednagar 413736, (MS).  
E-mail: shashipattan@yahoo.com

gastric fluid (floating system), high density which retain the dosage form in the body of stomach, concomitant administration of drugs or excipients which slow the motility of the GIT, bioadhesion to gastric mucosa, swelling to a large size which prevent emptying of dosage form through the pyloric sphincter.



**Fig. 1: Classification of gastroretentive drug delivery system**

### Floating Drug Delivery System<sup>1</sup>

The concept of floating drug delivery system was described as a method for overcoming the difficulty experienced by some people of gagging or choking while swallowing medicine pills. It was suggested that this difficulty could be overcome by providing pills having density of less than 1.0 g/mL, so that pills will float on water surface. Floating drug delivery is of particular interest for drugs that (1) act locally in the stomach, (2) are primarily absorbed in the stomach, (3) are poorly soluble at an alkaline pH, (4) have a narrow window of absorption and (5) are unstable in the intestinal or colonic environment.

### Types of Floating Drug Delivery Systems (FDDS)<sup>2</sup>

Based on the mechanism of buoyancy, two distinctly different technologies have been utilized in development of FDDS which are:

- A. Effervescent System and
- B. Non-Effervescent System

#### A. Effervescent System

Effervescent systems include use of gas generating agents, carbonates (ex. sodium

bicarbonate) and other organic acids (e.g. citric acid and tartaric acid) present in the formulation to produce carbon dioxide (CO<sub>2</sub>) gas, thus reducing the density of system and making it float on the gastric fluid. An alternative is the incorporation of matrix containing portion of liquid, which produce gas that evaporates at body temperature.

These effervescent systems are further classified into two types:

1. Gas generating systems
2. Volatile liquid/vacuum systems

#### 1) Gas-generating Systems

##### ***Intra Gastric Single Layer Floating Tablets or Hydrodynamically Balanced System (HBS)***

These are formulated by intimately mixing the CO<sub>2</sub> generating agents and the drug within the matrix tablet. These have a bulk density lower than gastric fluids and therefore remain floating in the stomach unflattering the gastric emptying rate for a prolonged period. The drug is slowly released at a desired rate from the floating system and after the complete release the residual system is expelled from the stomach. This leads to an increase in the gut and a better control over fluctuation in plasma drug concentration.

##### ***Intra Gastric Bilayer Floating Tablets***

These are also compressed tablet and contain two layers i.e.

- Immediate release layer and
- Sustained release layer

##### ***Multiple Unit Type Floating Pills***

These systems consist of sustained release pills as 'seeds' surrounded by double layers. The inner layer consists of effervescent agents while the outer layer is of swellable membrane layer. When the system is immersed in dissolution medium at body temperature, it sinks at once and then forms swollen pills like balloons, which float as they have lower density. This lower density is due to generation and entrapment of CO<sub>2</sub> within the system. The drug

reservoir compartment is enclosed by a pressure responsive collapsible bag, which is impermeable to vapour and liquid and has a drug delivery orifice. The osmotically active compartment contains an osmotically active salt and is enclosed within a semipermeable housing. In the stomach, the water in the GI fluid is continuously absorbed through the semipermeable membrane into osmotically active compartment to dissolve the osmotically salt. An osmotic pressure is then created which acts on the collapsible bag and in turn forces the bag reservoir compartment to reduce its volume and activate the drug release of a drug solution formulation through the delivery orifice. The floating support is also made to contain a bioerodible plug that erodes after a predetermined time to deflat the support. The deflated drug delivery system is then emptied from the stomach.

## **B. Non Effervescent Systems**

The non effervescent FDDS is based on the mechanism of swelling of polymer or bioadhesion to mucosal layer in GI tract. The most commonly used excipients in non effervescent FDDS are gel forming or highly swellable cellulose type hydrocolloids, polysaccharides and matrix forming material such as polycarbonate, polyacrylate, polymethacrylate, polystyrene as well as bioadhesive polymer such as chitosan and carbopol. The various types of this system are as follows:

### **1) Single Layer Floating Tablets**

They are formulated by intimate mixing of drug with gel-forming hydrocolloid, which swells in contact with gastric fluid and maintains bulk density of less than unity. The air trapped by the swollen polymer confers buoyancy to these dosage forms.

### **2) Bilayer Floating Tablets**

A bilayer tablet contains two layers, immediate release layer which releases initial dose from system while the another sustained release conventional tablets. Eg: A bilayer floating capsule of misoprostol,

which is a synthetic analog of prostaglandin E1, which is used as a protectant of gastric ulcers caused by administration of NSAIDs.

Various approaches for preparation of gastroretentive drug delivery system include floating systems, swellable and expandable systems, high density systems, bioadhesive systems, altered shape systems, gel forming solution or suspension system and sachet systems. Among these, the floating dosage form has been used most commonly. The floating systems include gas-generating systems, non effervescent systems and raft forming systems. The floating oral delivery system is expected to remain buoyant in a lasting way upon the gastric contents and enhance bioavailability of all drugs which are well absorbed from the GI tract.

### **3) Alginate Beads**

Multi unit floating dosage forms are developed from freeze dried calcium alginate. Spherical beads of approximately 2.5 mm diameter can be prepared by dropping a sodium alginate solution into aqueous solution of calcium chloride, causing precipitation of calcium alginate leading to formation of porous system, which can maintain a floating force for over 12 h. When compared with solid beads, which gave a short residence time of 1 h, these floating beads gave a prolonged residence time of more than 5.5 h.

### **4) Hollow Microspheres**

Hollow microspheres (microballoons), loaded with drug in their outer polymer shells were prepared by a novel emulsion solvent diffusion method. The ethanol:dichloromethane solution of drug and enteric acrylic polymer was poured into an agitated aqueous solution of PVA that was thermally controlled at 400°. The gas phase generated in dispersed polymer droplet by evaporation of dichloromethane formed an internal cavity in microsphere of polymer with drug. The microballoons floated continuously over the surface of acidic dissolution media containing surfactant for more than 12 h *in vitro*.

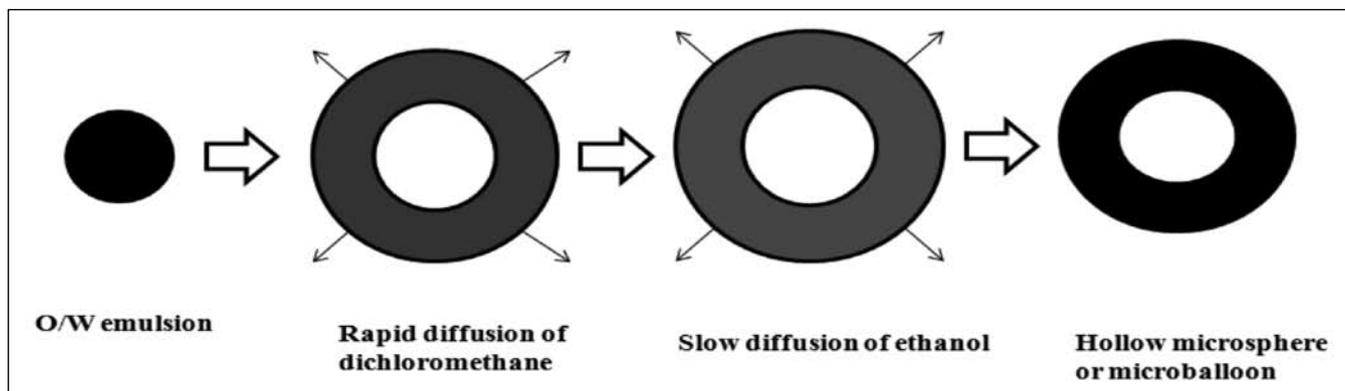


Fig. 2: Formulation of floating hollow microsphere or microballoon

### Optimization Parameters<sup>3,4</sup>

**IR Spectra:** FTIR spectra of pure drug, polymer and microspheres is obtained in KBr pellets at moderate scanning speed between 4000-400  $\text{cm}^{-1}$  in a Perkin-Elmer FTIR spectroscope.

**Yield of Microspheres:** The prepared microspheres with a particular size range are collected and weighed. The measured weight is divided by the total amount of all non-volatile components which are used for the preparation of the microspheres.

$\% \text{ Yield} = (\text{Actual weight of product} / \text{Total weight of excipient and drug}) \times 100$

**Particle Size Analysis:** Size distribution is determined by sieving the microparticles using a nest of standard BSS sieves as well as by optical microscopy.

**DEE (Drug Entrapment Efficiency):** Microspheres equivalent to the potency of the drug is to be taken for evaluation. The amount of drug entrapped was estimated by crushing the microspheres and extracting with aliquots of 0.1N HCl repeatedly. The extract is transferred to a 100 mL volumetric flask and the volume is made up using 0.1N HCl. The solution is filtered and the absorbance is measured after suitable dilution spectrophotometrically (UV, Shimadzu, Japan) at a certain wavelength against appropriate blank. The amount of drug entrapped in the microspheres is calculated by the following formula:

$DEE = (\text{Amount of drug actually present} / \text{Theoretical drug load expected}) \times 100$

**Surface Topography (SEM):** The surface morphology of the microspheres is examined by scanning electron microscopy.

**Weight Variation and Hardness:** Weight variation test is done according to USP and hardness is measured with Monsanto hardness tester.

**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 remains buoyant is 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 floatation i.e. as long the dosage form remains buoyant is called total floating time (TFT).

**Tablet Density:** Tablet density is an important parameter for floating tablets. The tablet will float only if its density is less than that of gastric fluid (1.004). Density (d) is determined using the relationship:

$$d = m/v \text{ where } v = \pi r^2 h$$

**In Vitro Release Study:** The *in vitro* release study for all the formulations is to be carried out by USP dissolution test apparatus type-II. The temperature of the dissolution medium (0.1 M HCl, 900 mL) is maintained at  $37 \pm 1^\circ$  with a constant stirring rate. The

tablets are to be placed inside the dissolution vessel. And sampling is done at suitable intervals.

$\% \text{ Floating microspheres} = (\text{weight of floating microspheres} / \text{initial weight of floating microspheres}) \times 100$

### Factors Affecting Gastric Retention

There are several factors that can affect gastric emptying of an oral dosage form which include density, size and shape of dosage form, feeding state, biological factors such as age, gender, posture, body mass index, disease state etc.

#### 1. Effect of Dosage Form Size & Shape<sup>5-8</sup>

Small size tablets are emptied from the stomach during the digestive phase while large size units are expelled. It is found that floating unit with a diameter equal or less than 7.5 mm has larger gastric residence time (GRT) compared to non floating units but the GRT is similar for floating and non-floating units having a large diameter of 9.9 mm. Moreover, in supine subjects, size influences GRT of floating and non-floating form. Tetrahedron and ring shaped devices have a better GRT as compared with other shapes.

#### 2. Gender, Posture & Age<sup>9-11</sup>

Mean ambulatory GRT in males (3.4±0.6 h) is less compared with their age and race-matched female counterparts (4.6±1.2 h) regardless of their weight, height and body surface. Women empty their stomach at a lower rate than men even when hormonal changes due to menstrual cycle are minimized. The mean GRT in the supine state (3.4±0.8 h) is not statistically significant from that in the upright, ambulatory state (3.5±0.7 h). In case of elderly, the GRT is prolonged especially in subject more than 70 years old (mean GRT – 5.8 h).

#### 3. Effect of Food & Specific Gravity<sup>12, 13</sup>

To float FDDS in the stomach, the density of dosage form should be less than gastric content i.e. 1.0 g/cm<sup>3</sup>. Since, the bulk density of a dosage form is

not a sole measure to describe its buoyant capabilities because the magnitude of floating strength may vary as a function of time and gradually decrease after immersing dosage form into fluid as a result of development of its hydrodynamic equilibrium. Presence of food is the most important factor affecting GRT than buoyancy. GRT is significantly increased under fed condition since onset of MMC is delayed. Studies show that GRT for both floating and non-floating single unit are shorter in fasted subjects (less than 2 h), but significantly prolonged after a meal (around 4 h).

#### 4. Nature of Meal & Frequency of Food<sup>14, 15</sup>

Feeding of indigestible polymers or fatty acid salts can change the motility pattern of the stomach to fed state, to increase gastric emptying rate and prolonging the drug release. Diet rich in protein and fat can increase GRT by 4-10 h.

#### 5. Type of Formulation<sup>16, 17</sup>

Multiple unit formulation shows a more predictable release profile and insignificant impairing of performance due to failure of units, allow co-administration of units with different release profile or containing incompatible substances and permit a large margin of safety against dosage form failure compared with single unit dosage form.

#### Potential Drug Candidates for Gastroretentive Drug Delivery Systems<sup>1</sup>

- 1) Drugs that are locally active in the stomach e.g. misoprostol, antacids etc.
- 2) Drugs that have narrow absorption window in gastrointestinal tract (GIT) e.g. L-dopa, para aminobenzoic acid, furosemide, riboflavin etc.
- 3) Drugs that are unstable in the intestinal or colonic environment e.g. captopril, ranitidine hydrochloride, metronidazole.
- 4) Drugs that disturb normal colonic microbes e.g. antibiotics against *Helicobacter pylori*.
- 5) Drugs that exhibit low solubility at high pH values e.g. diazepam, chlorthalidone, verapamil hydrochloride.

## Applications<sup>18, 19</sup>

Floating drug delivery system (FDDS) offer several applications for drugs having poor bioavailability because of narrow absorption window in the upper part of GIT. It retains the dosage form at the site of absorption and enhances the bioavailability. Table I mentions the commercial gastroretentive floating formulations.

### 1. Sustained Drug Delivery

Hydrodynamically balanced system (HBS) type dosage forms remain in the stomach for several hours, increase the gastric residence time and thus release the drug over a prolonged period of time. These dosage forms have bulk density less than one, relatively large in size and did not easily pass through pylorus. Madopar HBS formulation has shown to release levodopa for up to 8 h *in vitro*, whereas the standard formulation released levodopa in less than 30 min.

### 2. Site Specific Drug Delivery

FDDS are particularly useful for drug having specific absorption from stomach or proximal part of the small intestine e.g. riboflavin, furosemide etc. In fact, the absorption of captopril has been found to be site specific, stomach being the major site followed by duodenum. This property prompts the development of a monolithic floating dosage form for captopril which could prolong the gastric residence time and thus increase the bioavailability. AUC obtained with the floating tablet was approximately 1.8 times that of conventional tablets. Recently, a bilayer floating capsule of misoprostol, which is a synthetic analog of prostaglandin E1, was developed and used as a protectant of gastric ulcers caused by administration of NSAIDs. By targeting slow delivery of misoprostol to the stomach, the desired therapeutic levels could be achieved and wastage of drug be reduced.

### 3. Absorption Enhancement

Drugs that have poor bioavailability because their absorption is restricted to upper GIT can be delivered specifically thereby improving their absolute

bioavailability. Eg: A significant increase in the bioavailability of floating dosage form of captopril as compared to commercial available tablet.

4. There are some cases wherein the relative bioavailability of floating dosage form is reduced as compared to conventional dosage form e.g. floating tablets of amoxicillin trihydrate has bioavailability reduced to 80.5% when compared with conventional capsules. In such cases, the reduction in bioavailability is compensated by the advantages offered by FDDS e.g. patients with advanced Parkinson's disease, experienced pronounced fluctuations in symptoms while treatment with standard L-dopa. A HBS dosage form provided a better control of motor fluctuations although its bioavailability was reduced by 50-60% of the standard formulation.

5. FDDS serve as an excellent drug delivery system for the eradication of *Helicobacter pylori*, which is believed to be the causative bacterium for chronic gastritis and peptic ulcers. The patients require high concentration to be maintained at the site of infection that is within the gastric mucosa. The floating dosage form by virtue of its floating ability was retained in stomach and high concentration of drug was maintained in the stomach. A sustained liquid preparation of ampicillin was developed using sodium alginate that spreads out and adheres to gastric mucosal surfaces whereby releasing the drug continuously.

6. Floating systems are particularly useful for acid stable drugs, drugs which are poorly soluble or unstable in intestinal fluids and for those which undergo abrupt changes in their pH-dependent solubility due to food, age and pathophysiological conditions of GIT. e.g. floating system for furosemide lead to potential treatment of Parkinson's disease. Approximately 30% drug was absorbed after oral administration.

## Limitations<sup>20</sup>

1. The floating system requires a sufficiently high level of fluid in the stomach for the system to float. This problem can be overcome by coating

**Table I: Commercial Gastroretentive Floating Formulations<sup>1, 19</sup>**

Name	Type and Drug	Company, Country	Remarks
Madopar HBS (Propal HBS)	Floating capsule, levodopa and benserazide	Roche Products, USA	Floating CR capsules
Valrelease	Floating capsule, diazepam	Hoffmann-LaRoche, USA	Floating capsules
Topalkan	Floating antacid, aluminum and magnesium mixture	Pierre Fabre Drug, France	Effervescent floating liquid alginate preparation
Amalgate Float Coat	Floating antacid, Floating gel	-	Floating dosage form
Conviron	Ferrous sulphate	Ranbaxy, India	Colloidal gel forming FDDS
Cifran OD	Ciprofloxacin (1 g)	Ranbaxy, India	Gas generating floating form
Cytotech	Misoprostol (100 mcg/ 200 mcg)	Pharmacia, USA	Bilayer floating capsule
Liquid Gaviscon	Mixture of alginate	Glaxo Smith Kline, India	Suppress gastro-esophageal reflux and alleviate the heart burn

the dosage form with bioadhesive polymer which adhere to gastric mucosa or administering dosage form with a glass full of water (200-250 mL).

- Floating systems are not suitable for drugs that have stability or solubility problem in gastrointestinal fluid or that irritate gastric mucosa.
- Drugs which have multiple absorption site or which undergo first pass metabolism were not desirable candidate for FDDS.
- Floating dosage form should not be given to the patients just before going to the bed as gastric emptying occurs rapidly when the subject remains in supine posture.
- The single unit floating dosage form is associated with "all or none concept". This problem can be overcome by formulating multiple unit system like floating microspheres or microballoons.

#### Future Potential<sup>19</sup>

- Floating dosage form offers various future potential as evident from several recent publications. The reduced fluctuations in the plasma level of drug results from delayed gastric emptying.

- Drugs that have poor bioavailability because of their limited absorption to the upper gastrointestinal tract can be delivered efficiently thereby maximizing their absorption and improving their absolute bioavailability.
- Buoyant delivery system considered as a beneficial strategy for the treatment of gastric and duodenal cancers.
- The floating concept can also be utilized in the development of various anti-reflux formulations.
- Developing a controlled release system for the drugs, which have the potential to treat Parkinson's disease.
- To explore the eradication of *Helicobacter pylori* by using the narrow spectrum antibodies.

#### CONCLUSION

Based on the literature survey, it may be concluded that gastroretentive drug delivery offers various potential advantages for drug with poor bioavailability because their absorption is restricted to the upper gastrointestinal tract (GIT) and they can be delivered efficiently thereby maximizing their absorption and

enhancing absolute bioavailability. Due to complexity of pharmacokinetics and pharmacodynamic parameters, *in vivo* studies are required to establish the optimal dosage form for a specific drug. Another promising area of research for gastroretentive drug delivery system is eradication of *Helicobacter pylori*, which is now believed to be causative bacterium of chronic gastritis and peptic ulcers. Indeed, the drug delivery system must remain for a sufficient time in the stomach, which is not compatible with its normal physiology. In the future, it is expected that they will become of increasing importance, ultimately leading to improved efficiencies of various types of pharmacotherapies.

### ACKNOWLEDGEMENTS

Padmabhushan Hon. Shri. Balasaheb Vikhe Patil, Ex. Union Minister, Government of India, Hon. Shri. M. M. Pulate Saheb, Vice Chairman, PRES and President PIRENS, and Hon. Shri. Rajendra Vikhe Patil, Managing Trustee, Pravara Rural Education Society, Loni for their kind support, encouragement and motivation.

### REFERENCES:

- Jain S. K., Agrawal G. P. and Jain N. K.: Evaluation of Porous Carrier-based Floating Orlistat Microspheres for Gastric Delivery, **AAPS PharmSciTech**. 2006; 7(4) Article 90 (<http://www.aapspharmscitech.org>).
- Nayak A. K., Maji R., Das B.: Gastroretentive drug delivery systems: a review, **Asian J Pharm Clin Res**. 2010, 3 (1), 2-10.
- Patel A., Ray S., Thakur R. S.: *In vitro* evaluation and optimization of controlled release floating drug delivery system of metformin hydrochloride, **DARU** Volume 2006, No. 2, 14.
- Patel S. S., Ray S. and Thakur R. S.: Formulation and Evaluation of Floating Drug Delivery System Containing Clarithromycin For *Helicobacter pylori*, **Acta Poloniae Pharmaceutica Drug Res**. 2006, 63(1), 53-61.
- Oth M., Franze M., Timmermans J., Moes A.: The bilayer-floating capsule: a stomach directed drug delivery system for misoprostol, **Pharm Res**. 1992; 9, 298-302.
- Timmermans J., Gasnsbeka B.V., Moes A.: Accessing by gamma-scintigraphy the *in vivo* buoyancy of dosage form having known size and floating force profiles as a function of time, **Pharm Tech**. 1989; 1: 42-51.
- Gergogiannis Y. S., Rekkas D. M., Dallos P. P., Chailis N. H.: Floating and swelling characteristics of various excipients used in controlled release technology, **Drug Dev Ind Pharm**. 1993; 19: 1061-1081.
- Cargill R., Cadwell L. J., Engle K., Fix J. A., Porter P. A., Gardner C. R.: Controlled gastric emptying: I. Effects of physical properties on gastric residence times of non disintegrating geometric shapes in beagle dogs, **Pharm Res**. 1988; 5: 533-536.
- Patel G.: Floating drug delivery system: An innovative approach to prolong gastric retention. [www.pharmainfo.net](http://www.pharmainfo.net), 2007.
- Mojaverian P., Vlasses P. H., Kellner P. E., Rocci M. L.: Effects of gender, posture, and age on gastric residence time of indigestible solid: pharmaceutical considerations, **Pharm Res**. 1988; 10; 639- 664.
- Timmermans J., Moes A. J.: Factors controlling the buoyancy and gastric retention capabilities of floating matrix capsules: new data for reconsidering the controversy, **J Pharm Sci**. 1994; 83; 18-24.
- Muller Lissner S. A., Blum A. L.: The effect of specific gravity and eating on gastric emptying of slow release capsules, **New Engl J Med**. 1981; 304: 1365-1366.
- Singh S. *et al*: Gastro retentive Drug Delivery System: Current Approaches, **J Pharm Res**. 2009, 2(5), 881-886.
- Kelly K.: 'Physiology of the Gastrointestinal Tract' (Johnson, L. J. ed.), 1981, 393.
- Golub A. L., Frost R.W., Betlach C. J., Gonzalez A. J.: Physiologic considerations in drug absorption from the gastrointestinal tract, **Allergy Clin Immunol**. 1986, 78(4), 689.
- Khosla R., Feely L. C., Davis S. S.: The gastrointestinal transit of non-disintegrating tablets in fed subjects, **Int J Pharm**. 1989, 53, 117.
- Johnson R. H., Rowe E. L.: Medicinal dosage forms of unpolymerised thiolated gelatin with a cross linking accelerating agent providing a slowly released medication from a swollen matrix, U. S .Patent 3, 574, 820, 1971.
- Sonar G. S.: Bioadhesive-floating matrix tablet of salbutamol sulphate using response surface methodology: optimization and *in vitro* evaluation, **J Pharm Res**. 2009, 2(5), 908-914.
- Patil J. M.: Trends in Floating drug delivery systems, **J Sci Ind Res**. 2006, 65, 11-21.
- Basavaraj B.V.: A Multiple Unit Floating Controlled Drug Delivery System of Famotidine, **J Pharm Res**. 2009, 2(5), 826-829 .