An Elsevier Indexed Journal ISSN-2230-7346

Journal of Global Trends in Pharmaceutical Sciences

FLOATING DRUG DELIVERY SYSTEM-AREVIEW

V. Sarovar Reddy* and T. Shabanam

Department of Pharmaceutics, Annamacharya College of Pharmacy, Rajampet-516126, India

*Corresponding author E-mail: **sarovar.ancp@gmail.com**

ARTICLE INFO

Key Words

GRDDS,
Gastric residence time,
Evaluation of FDDS

ABSTRACT

Floating drug delivery system isone of the controlled targeted which focus on retention of dosage frominn the stmach to enhance the absorbtion of drugs which posses less bioavaliblity .These providesto design dosage forms both swaloling non-sweeling system by using synthetic non synthetic polymers like guar gum, pectin, chitosan ,xanthan gum,psyllium gum husk,gellan gum, Hydroxyl propyl methyl cellulose(HPMC), ethyl cellulose.The major advantage of this system is it desvers gud absorbtion as the stomach provides more volume for absorption. This review article compiles of giving detailed information on the pharmaceutical basis of their design, classification, advantages, *in vitro* and *in vivo* evaluation parameters, and the future potential of FDDS.

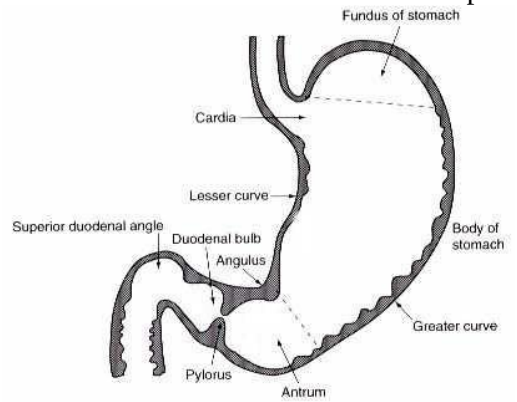
INTRODUCTION

The oral route is increasingly being used for the delivery of therapeutic agents because the low cost of the therapy and ease of administration lead to high levels of patient compliance. More than 50% of the drug delivery systems available in the market are oral drug delivery systems.1 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.2 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 GRT and a better control of the fluctuations in plasma drug concentration. However, besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal. Many buoyant systems have been developed based on granules, powders, capsules, tablets, laminated films and hollow microsphere[1]

BASIC GIT PHYSIOLOGY

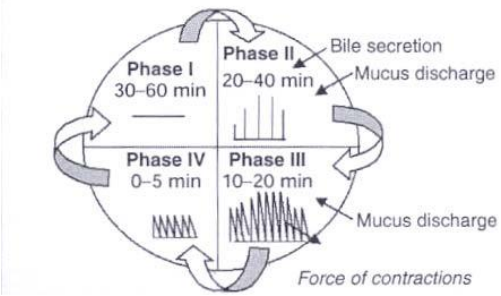
Anatomically the stomach is divided in to three regions Fundus, Body and Antrum (pylorus). The proximal part made of fundus and body acts as a reservoir for undigested materials, where as the antrum is the main site for mixing motions and acts as a pump for gastric emptying by propelling actions.3 Gastric 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.4

- Phase 1-(Basic phase)-last from 30-60 minutes with rare contractions.
- Phase 2-(Preburst phase)-last for 20-40 minutes with intermittent action potential and contractions.
- Phase 3-(Burst phase) - last for 10-20 minutes which includes intense and regular contractions for short period.
- Phase 4-last for 0-5 minutes and occurs between phase 2 and 1 of 2 consecutive cycles



Motility pattern in GIT

FACTORS AFFECTING GASTRIC RETENTION

The gastric retention time (GRT) of dosage form iscontrolled by several factors, that affect theirefficacy as a gastroretentive system.

- **Density** – GRT is a function of dosage form buoyancy that is dependent on the density.12
- **Size** – Dosage form units with a diameterof more than 9.5mm are reported to havean increased GRT.13
- **Shape of dosage form** – Tetrahedron andring-shaped devices with a flexuralmodulus of 48 and 22.5 kilo pounds per square inch (KSI) are reported to havebetter GRT. 90% to 100% retention at 24hours compared with other shapes.
- **Single or multiple unit formulation** –Multiple unit formulations show a morepredictable release profile and insignificant impairing of performance due to failure of units, allow coadministrationof units with different release profiles or containing incompatible substances and permit a larger margin of safety against dosage form failure compared with single unit dosage forms.
- **Fed or unfed state** – Under fasting conditions, the GI motility is characterized by periods of strong motor activity or themigrating myoelectric complex (MMC)that occurs every 1.5 to 2 hours. The MMC sweeps undigested material fromthe stomach and, if the timing ofadministration of the formulationcoincides with that of the MMC, the GRTof the unit can be expected to be very short. However, in the fed state, MMC is delayed and GRT is considerably longer.[2]
- **Nature of meal** – Feeding of indigestible polymers or fatty acid salts can change themotility pattern of the stomach to a fed state, thus decreasing the gastric emptying rate and prolonging drug release.
- **Caloric content** - GRT can be increasedby four to 10 hours with a meal that ishigh in proteins and fats.
- **Frequency of feed** – The GRT can increase by over 400 minutes whensuccessive meals are given compared with a single meal due to the low frequency of MMC.
- **Gender** – Mean ambulatory GRT in males (3.4□0.6 hours) is less compared with theirage and race-

matched female counterparts (4.6□1.2 hours), regardless of the weight,height and body surface.

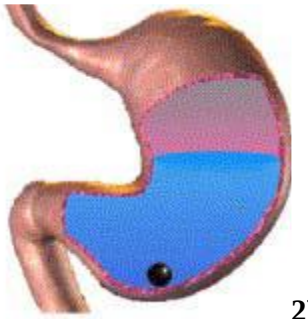
- **Age** – Elderly people, especially those over 70, have a significantly longer GRT.
- **Posture** – GRT can vary between supine and upright ambulatory states of the patient**.**15
- **Concomitant drug administration**– Anticholinergics like Atropine and Propantheline, Opiates like Codeine and Prokinetic agents like Metoclopramide and Cisapride.
- **Biological factors** – Diabetes and Crohn's disease.[3]

APPROACHES TO GASTRORETENTION

Several techniques are reported in the literature to increase the gastric retention of drugs16- 19.

1) Highdensity systems

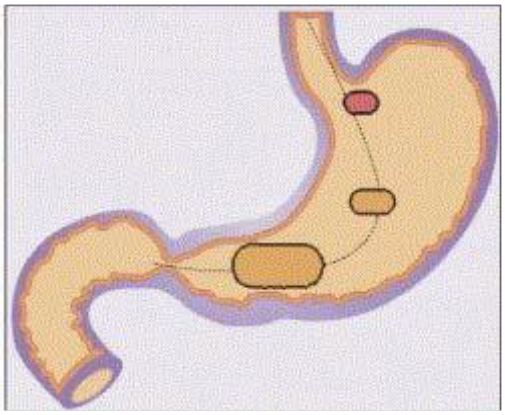
These systems, which have a density of ~3g/cm3, are retained in the rugae of stomach and capable of withstanding its peristaltic movements18, 20.The only major drawback with these systems is that it is technicallydifficult to manufacture them with a large amount of drug (>50%)and achieve required density of 2.4-2.8g/cm3. Diluents such asbarium sulphate (density= 4.9), zinc oxide, titanium oxide,and Iron powder must be used manufacture such high-densityformulation16[4]



2)

2) Swelling and expanding systems

These systems are also called as "Plug type system", since they exhibit tendency to remain logged in the pyloric sphincters. These polymeric matrices remain in the gastric cavity for several hours even in fed state 21.[5]



3) Incorporating delaying excipients

Another delayed gastric emptying approach of interest includefeeding of digestible polymers or fatty acid salts that charges themotility pattern, of the stomach to a fed stage thereby decreasing the gastric emptying rate and permitting considerable prolongation of the drug release. Prolongation of GRT of drug delivery systemconsists of incorporating delaying excipients like trietanolamine myristate in a delivery system23.[6]

4) Modified systems

Systems with non disintegrating geometric shape molded from silastic elastomers or extruded from polyethylene blends, which extend the GRT depending on size, shape and flexural modules of drug delivery device24.[7]

5) Mucoadhesive & bioadhesive systems

Bioadhesive drug delivery systems are used to localize a delivery device within the lumen to enhance the drug absorption in a sitespecific manner. This approach involves the use of bioadhesive polymers, which can adhere to the epithelial surface in the stomach. Some of the most promising excipients that have been used commonly in these systems include polycarbophil, carbopol, lectins, chitosan, CMC and gliadin, etc25, 26.[8]

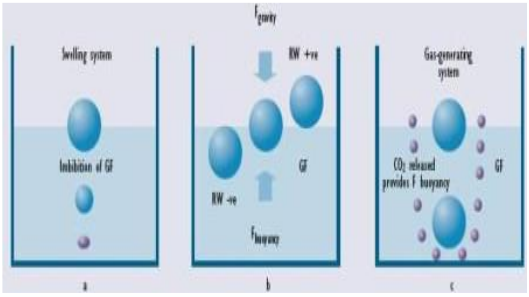
6) Floating systems

Floating drug delivery systems (FDDS) 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. After release of drug, the

residual system is emptied from the stomach27. Floatation of a drug delivery system in the stomach can be achieved by incorporating floating chamber filled with vacuum, air, or inert gas.[9]

CLASSIFICATION OF FDDS BASED ON MECHANISM OF BUOYANCY

By selection of polymer with the proper molecular weight and swelling properties controlled and sustained drug release can be achieved. Upon coming in contact with gastric fluid, the polymer imbibes water and swells. The extensive swelling of these polymersis a result of the presence of physical-chemical cross links in the hydrophilic polymer network. These cross link prevents the dissolution of polymer and thus maintain the physical integrity of the dosage form. A high degree of cross linking retards the swelling ability of the system and maintains its physical integrity for prolonged period. On the other hand, a low degree of cross linking results in extensive swelling followed by the rapid dissolution of polymer22.



MECHANISM OF BUOYANCY

A) Single unit

Single unit dosage forms are easiest to develop but suffers from the risk of losing their effects too early due to their all-or-none emptying from the stomach and, thus they may cause high variability in bioavailability and local irritation due to large amount of drug delivered at a particular site of the gastro intestinal tract28.[10]

Non effervescent systems

One or more gel forming, highly swellable, cellulosic hydrocolloids(e.g. hydroxyl ethyl cellulose, hydroxyl propyl cellulose,hydroxypropyl methyl cellulose [HPMC] and sodium carboxy methylcellulose), polysaccharides, or matrix forming polymers(e.g.,polycarbophil, polyacrylates, and polystyrene) are incorporated in high level (20-75% w/w) to tablets or capsules29, 30. For the preparation of these types of systems, the drug and the gelforming hydrocolloid are mixed thoroughly. After oral administration this dosage form swells in contact with gastric fluids and attains a bulk density of < 1. The air entrapped within the swollen matrix imparts buoyancy to the dosage form. The so formed swollen gel-like structure acts as a reservoir and allows sustained release of drug through the gelatinous mass.[11]

Effervescent systems or gas generating systems

These are matrix types of systems prepared with the help of swellable polymers such as methylcellulose and chitosan and various effervescent compounds, e.g. sodium bicarbonate, tartaric acid, and citric acid. They are formulated in such a way that when in contact with the acidic gastric contents, CO2 is liberated and gets entrapped in swollen hydrocolloids, which provides buoyancy to the dosage forms. The optimal stoichiometric ratio of citric acid and sodium bicarbonate for gas generation is reported to be 0.76:1.

B) Multiple unit

Single unit formulations are associated with problems such as sticking together or being obstructed in gastrointestinal tract, which may have a potential danger of producing irritation. Multiple unit systems avoid the ‘all-or-none’ gastric emptying nature of singleunit systems. It reduces the intersubject variability in absorption and the probability for dose dumping is lower31.

Non-effervescent systems

A little or no much report was found in the literature on noneffervescent multiple unit systems, as compared to the effervescent systems. However, few workers have reported the possibility of developing such system containing indomethacin, using chitosan as the polymeric excipient. A multiple unit HBS containing indomethacin as a model drug prepared by extrusion process.

A mixture of drug, chitosan and acetic acid is extruded through a needle, and the extrudate is cut and dried. Chitosan hydrates float in the acidic media, and the required drug release could be obtained by modifying the drug-polymer ratio.[12]

Effervescent systems

A multiple unit system comprises of calcium alginate core and calcium alginate/PVA membrane, both separated by an air compartment was prepared. 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. Freeze-drying technique is also reported for the preparation of floating calcium alginate beads. Sodium alginate solution is added drop wise into the aqueous solution of calcium chloride, causing the instant gelation of the droplet surface, due to the formation of calcium alginate. The obtained beads are freeze-dried resulting in a porous structure, which aid in floating.The authors studied the behavior of radiolabeled floating beads and compared with nonfloating beads in human volunteers using gamma scintigraphy. Prolonged gastric residence time of more than 5.5 hr was observed for floating beads. The nonfloating beads had a shorter residence time with a mean onset emptying time of 1 hr32.[13]

Floating microspheres

A controlled release system designed to increase its residence time in the stomach without contact with the mucosa was achieved through the preparation of floating microspheres. Techniques involved in their preparation include simple solvent evaporation, and solvent diffusion and evaporation. The drug release and better floating properties mainly depend on the type of polymer, plasticizer and the solvents employed for the preparation. Polymers, such as polycarbonate, Eudragit® S and cellulose acetate, are used in the preparation of hollow microspheres, and the drug release can be modified by optimizing the amount of polymer and the polymerplasticizer ratio33.

C) Raft forming systems

The basic mechanism involved in the raft formation includes the formation of viscous cohesive gel in contact with gastric fluids, wherein each portion of the liquid swells forming a continuous layer called a raft. The raft floats because of the buoyancy created by the formation of CO2 and act as a barrier to prevent the reflux of gastric Contents like HCl and enzymes into the esophagus. Usually, the system contains a gel forming agent and alkaline bicarbonates or carbonates responsible for the formation of to make the system less dense and float on the gastric fluids34. Reckitt and Colman Products Ltd. have come out with such formulation in the treatment of H.pylori infections of GIT.[14]

ADVANTAGES OF FLOATING DOSAGE FORM

1. These systems are particularly advantageous for drugs that are specifically absorbed from stomach or the proximal part of the smallintestine, e.g., riboflavin and furosemide.
2. The fluctuations in plasma drug concentration 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.
3. The efficacy of the medicaments administered utilizing the sustained release principle of floating formulation has been found to be independent of the site of particular medicaments.
4. Complete absorption of the drug from the floating dosage form is expected even at the alkaline pH of the intestine. The dissolution of the drug in gastric fluid occurs and then the dissolved drug is available for absorption in the small intestine after emptying of the stomach contents.
5. Poor absorption is expected when there is vigorous intestinal movement and a shorted transit

time as might occur in certain type of diarrhea. Under such circumstances it may be advantageous to keep the drug in floating condition in stomach to get a relatively better response.

6. Drugs that have poor bioavailability because of site-specific absorption from the upper part of the gastrointestinal tract are potential candidates to be formulated as floating drug delivery systems, thereby maximizing their absorption. A significant increase in the bioavailability of floating dosage forms (42.9%) could be achieved as compared with commercially available LASIX tablets (33.4%) and enteric-coated LASIX-long product (29.5%).[15]

DISADVANTAGES OF FDDS

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 irritant 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. Drugs that cause irritation and lesion to gastric mucosa are not suitable to be formulated as floating drug delivery systems.
6. High variability in gastric emptying time due to its all (or) non-emptying process.
7. Patients should not be dosed with floating forms just before going to bed.[16]

LIMITATIONS OF FLOATING DRUG DELIVERY SYSTEMS

1. A high level of fluid in the stomach is required for drug deliver to float and work efficiently.
2. Drugs which have stability and solubility problems in GIT are not suitable candidates for these types of systems.
3. Drugs such as nifedipine, which under goes first pass metabolism may not be desirable for the preparation of these types of systems
4. Drugs which are irritant to Gastric mucosa are also not desirable.
5. The drug substances that are unstable in the acidic environment of the stomach are not suitable candidates to be incorporated in the systems[17]

FORMULATION OF FLOATING DOSAGE FORM

Following types of the ingredients can be incorporated in to floating dosage form

a. Hydrocolloids
b. Inert fatty materials
c. Release rate accelerants
d. Release rate retardant
e. Buoyancy increasing agents
f. Low density material
g. Miscellaneous

a. Hydrocolloids: Suitable hydrocolloids are synthethics, anionic or non ionic like hydrophilic gumes, modified cellulose derivatives. E.g. Accasia, pectin, agar, alginates, gelatin, casein, bentonite, veegum, MC, HPC, HEC, and Na CMC can be used. The hydrocolloids must hydrate in acidic medium i.e. gastric fluid is having pH 1.2.Although the bulk density of the formulation may initially be more than one, but when gastric fluid is enter in the system, it should be hydrodynamically balanced to have a bulk density of less than one to assure buoyancy.

b. Inert fatty materials: Edible, pharmaceutical inert fatty material, having a

specific gravity less than one can be added to the formulation to decrease the hydrophilic property of formulation and hence increases the buoyancy. Example: Purified grades of beeswax, fatty acids, long chain alcohols, glycerides, and minaral oils can be used.

c. Release rate accelerants: The release rate of the medicament from the formulation can be modified by including excipient like lactose and/or mannitol. These may be present from about 5-60% by weight

d.Release rate retardant: Insoluble substances such as dicalcium phosphate, talc, magnesium strearete decresesd the solubility and hence retard the release of medicaments.

e.Buoyancy increasing agents: Materials like ethyl cellulose, which has bulk density less than one, can be used for enhancing the buoyancy of the formulation. It may be adapted up to 80 % by weight.

f.Low density material: Polypropylene foam powder. **E**g.Miscellaneous: Pharmaceutically acceptable adjuvant like preservatives, stabilizers, and lubricants can be incorporates in the dosage forms as per the requirements. They do not adversely affect the hydrodynamic balance of the systems[18]

EVALUATION PARAMETERS OF FDDS

Different studies reported in the literature indicate that pharmaceutical dosage forms exhibiting gastric residence in vitro floating behavior show prolonged gastric residence in vivo. However, it has to be pointed out that good in vitro floating behavior alone is not sufficient proof for efficient gastric retention in vivo. The effects of the simultaneous presence of food and of the complex motility of the stomach are difficult to estimate. Obviously, only in vivo studies can provide definite proof that prolonged gastric residence is obtained.[19]

Floating time:

The test for floating time is usually performed in simulated gastric fluid or 0.1 mole.lit^{-1} HCl maintained at 37°C, by using USP dissolution apparatus containing 900 ml of 0.1 molar HCl as the dissolution medium. The time taken by the dosage form to float is termed as floating lag time and the time for which the dosage form floats is termed as the floating or flotation time.[20]

Drug release: Dissolution tests are performed using the dissolution apparatus. Samples are withdrawn periodically from the dissolution medium with replacement and then analyzed for their drug content after an appropriate dilution.[21]

Drug loading, drug entrapment efficiency, particle size analysis, surface characterization (for floating microspheres and beads):

Drug loading is assessed by crushing accurately weighed sample of beads or microspheres in a mortar and added to the appropriate dissolution medium which is then centrifuged, filtered and analyzed by various analytical methods like spectrophotometry. The percentage drug loading is calculated by dividing the amount of drug in the sample by the weight of total beads or microspheres. The particle size and the size distribution of beads or microspheres is determined in the dry state using the optical microscopy method. The external and cross-sectional morphology (surface characterization) is done by scanning electron microscope (SEM).[22]

Measurement of buoyancy capabilities of the FDDS:

The floating behaviour was evaluated with resultant weight measurements as shown in Figure 8[5]. The experiment was carried out in two different media like deionised water and simulated meal, in order to monitor possible difference. The results showed that higher molecular weight polymers with slower rate of hydration had enhanced floating behaviour and which was more in simulated meal medium compared to deionised water.[23]

Content uniformity, Hardness, Friability (Tablets):

These tests are performed as per described in specified monographs.

Resultant weight: The in vitro measuring apparatus has been conceived to determine the real floating capabilities of buoyant dosage forms as a function of time. It

operates by force equivalent to the force F required to keep the object totally submerged in the fluid This force determines the resultant weight of the object when immersed and may be used to quantify its floating or non floating capabilities. The magnitude and direction of the force and the resultant weight corresponds to the Victoria sum of buoyancy (F_{buoy}) and gravity (F_{grav}) forces acting on the objects as shown in the equal [24]

$$F = F_{buoy} - F_{grav}$$
$$F = dfgV - dsgV = (df-ds) gv$$
$$F = (df - M/V) gV$$

In which the F is total vertical force (resultant weight of the object), g is the acceleration due to gravity, df if the fluid density, ds is the object density is the object mass and V is the volume of the object.[25]

X-Ray/Gamma Scintigraphy:

X-Ray/Gamma Scintigraphy is a very popularly used evaluation parameter for floating dosage form these days. It helps to locate dosage form in the GIT and by which one can predict and correlate the gastric emptying time and the passage of dosage form in the GIT. Here the inclusion of a radio- opaque material into a solid dosage form enables it to be visualized by X-rays. Similarly, the inclusion of a γ-emitting radio nucleide in a formulation allows indirect external observation using a γ-camera or scinti scanner.[26]

Pharmacokinetic studies:

Pharmacokinetic studies are the integral part of the in vivo studies. Sawicki et al studied the pharmacokinetics of Verapamil, from the floating pellets containing drug, filled into a capsule, and compared with the conventionalerapamil tablets of similar dose (40 mg). The t_{max} and AUC (0- infinity) values (3.75 h and 364.65 $ng.ml^{-1}h$ respectively) for floating pellets were comparatively higher than those obtained fo the conventional Verapamil tablets. (t_{max} value1.21 h, and AUC value 224.22 ng.ml-1h). No much difference was found between the C_{max} values of both the formulations, suggesting the improved bioavailability of the floating pellets compared to the conventional tablets. The microspheres showed about 1.4 times more bioavailability, and the elimination half-life was increased by about three times than the free drug.[27][28]

Specific Gravity

Specific Gravity of the floating system can be determined by the displacement benzene as a displacing medium[29]

CONCULSION:

Floating drug delivery system technique is used for various active drug substance which are used in curing viral,fungal,bacterial infections.This drug delivery system focus on drug absorption in the stomach by retaning dosage for longer period of time compared to main other dosage forms.

REFERENCE:

1. Vishal Bhardwaj Nirmala, S.L. Harikumar, floating drug delivery system: a review Pharmacophore 2013 ,Vol. 4 (1), 26-38.
2. Natasha Sharma*, Dilip Agarwal, M.K. Gupta and Mahaveer Pr. Khinchi A Comprehensive Review on Floating Drug Delivery System ISSN: 2229-3701,450-451.
3. Arora S, Ali A, Ahuja A, Khar RK, Baboota S. Floating drug delivery systems: A review. AAPS PharmSciTech 2005; 6(3): E372-E390.
4. Chien YW. Rate-control drug delivery systems: controlled releasevs. sustained release. Med Prog Techn 1989; 15: 21-46.
5. Chien YW. Oral drug delivery and delivery system in novel drugdelivery Systems, ed, 50, Marcel Dekker publication, New York,1992.

6. Patel GM. Floating drug delivery system: An innovative approachto prolong gastric retention. www.pharmainfo.net, 2007.
7. Koner P, Saudagar RB, Dharwal J. Gastro-retentive drugs anovel approach towards floating therapy inhttp://www.pharmainfo.net/exlusive/reviews/gastroretentive drugs a novel approach towards floating therapy/, 2007
8. Wilson CG, Washington N. The Stomach: its role in oral drugdelivery. In: Rubinstein, M.H., (Ed.). Physiological pharmaceutics: biological barriers to drug absorption. Ellis Harwood, Chechester, 1989: 47-70.
9. Desai S. A Novel Floating Controlled Release Drug DeliverySystem Based on a Dried Gel Matrix Network [master'sthesis], Jamaica, NY: St John's University; 1984.
10. Davis SS, Stockwell AF, Taylor MJ. The effect of density on thegastric emptying of single- and multiple-unit dosage forms, Pharm Res 1986; 3: 208- 213.
11. Oth M, Franze M, Timmermans J, Moes A, The bilayer-floatingcapsule: a stomach directed drug delivery system for misoprostol. Pharm Res 1992; 9: 298-302.
12. Timmermans J, Gasnsbeka BV, Moes A. Accessing by gammascintigraphythe *in vivo* buoyancy of dosage form having known size and floating force profiles as a function of time. Pharm Tech 1989; 1: 42-51.
13. Gergogiannis YS, Rekkas DM, Dallos PP, Chailis NH. Floatingand swelling characteristics of various excipients used in controlled release technology. Drug Dev Ind Pharm 1993; 19:1061-1081
14. Cargill R, Cadwell LJ, Engle K, Fix JA, Porter PA, Gardner CR. Controlled gastric emptying: I. Effects of physical properties ongastric residence times of non disintegrating geometric shapes in beagle dogs. Pharm Res 1988; 5: 533-536.
15. Li S, Lin S, Daggy BP, Mirchandani HL, Chien YW. Effect of HPMC and Carbopol on the release and floating properties ofgastric floating drug delivery system using factorial design. Int J Pharm 2003; 253: 13-22.
16. Mojaverian P, Vlasses PH, Kellner PE, Rocci ML. Effects ofgender, posture, and age on gastric residence time ofindigestible solid: pharmaceutical considerations. Pharm Res 1988; 10; 639- 664.
17. Timmermans J, Moes AJ. Factors controlling the buoyancy andgastric retention capabilities of floating matrix capsules: newdata for reconsidering the controversy. J Pharm Sci 1994; 83; 18-24.
18. Chawla G, Gupta P, Koradia V, Bansal AK. Gastroretention: A Means to address regional variability in intestinal drug absorption. Pharm Tech 2003; 27: 250-268.
19. Muller-Lissner SA, Blum AL. The effect of specific gravity and eating on gastric emptying of slow-release capsules. New Engl J Med 1981; 304: 1365-1366.
20. Singh BN, Kim KH. Floating drug delivery system: An approach to the controlled drug delivery via gastric retention. J Control Release 2000; 63: 235-259.
21. Shah SH, Patel JK, Patel NV. Stomach specific floating drug delivery system: A review. Int J Pharm Res 2009; 1(3): 623-633.
22. Devereux JE, Newton JM, Short MB. The influence of density on the gastrointestinal transit of pellets. J Pharm Pharmacol 1990; 42(7): 500-501.
23. Bolton S and Desai S, 1989, US 4,814,179.
24. Gupta P, Virmani K, Garg S. Hydrogels: From controlled release to pH responsive drug delivery. Drug

Discovery Today 2002; 7(10): 569-579.
25. Groning R, Heun G. Dosage forms with controlled gastrointestinal transit. Drug Dev Ind Pharm 1984; 10: 527- 539.
26. Kedzierewicz F, Thaivenot P, Lemut J, Etienne A, Hoffman M, Maincent P. Evaluation for peroral silicon dosage forms in human by gamma-scintigraphy. J Control Release 1999; 58: 195-205.
27. Patel R. Recent development in floating drug delivery system for gastric retention of drugs: an overview. 2007; http://www.swatijaininst.com/etechno/feb2007/roma.rtf
28. Asane GS. Mucoadhesive gastrointestinal drug delivery system: An overview. 2007; www.pharmainfo.net
29. Mayavanshi AV, Gajjar SS. Floating drug delivery systems to increase gastric retention of drugs: A Review. J Pharm Tech 2008; 1(14): 345-348
30. Sheth PR, Tossounian JL. 1978, US 4,126,672.

****