Review Article

Floating Drug Delivery System: A Review

***Pooja Gupta, Gnanarajan, Preeti Kothiyal**

Department of Pharmaceutics, Shri Guru Ram Rai Institute of Technology & Sciences, Dehradun, (248001) Uttrakhand, India.

ABSTRACT

The purpose of writing this review on floating drug delivery systems (FDDS) was to compile the recent literature with special focus on the principal mechanism of floatation to achieve gastric retention. Drug delivery systems are those that float immediately upon contact with gastric fluids present promising approaches for increasing the bioavailability of drugs with absorption windows in stomach or upper small intestine, unstable in the intestinal or colonic environment, and exhibit low solubility at high pH values. It is new drug delivery system maximize effectiveness and compliance. The Physiological problems like short gastric residence time and unpredictable gastric emptying time were overcome with the use of floating dosage forms which provide opportunity for both local and systemic effect. Floating drug delivery system enable prolonged and continuous input of the drug to the upper part of the gastro retention tract and improve the bioavailability of medication that is characterized by a narrow absorption window. This review article is in pursuit of giving detailed information on the pharmaceutical basis of their design, classification, advantages, in vitro and in vivo evaluation parameters, and application of floating systems, and applications of these systems. These systems are useful to several problems encountered during the development of a pharmaceutical dosage form and the future potential of FDDS. At attempt has been made in this review article to introduce the readers to current development in floating drug delivery system.

Keywords: Gastric residence time, floating drug delivery system, classification, in-vitro evaluation

Received 16 June 2015 Received in revised form 2 July 2015 Accepted 21 July 2015

***Address for correspondence:**
Pooja Gupta,
Department of Pharmaceutics, Shri Guru Ram Rai Institute of Technology & Sciences, Dehradun, (248001) Uttrakhand, India.
E-mail: pooja.gupta9210@gmail.com

INTRODUCTION

The aim of drug delivery system is to afford a therapeutic amount of drug to the proper site in the body to attain promptly and then maintain desired drug concentration. 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 [1-3]. Gastric emptying of dosage forms is an extremely variable process and ability to prolong and control the emptying time is a valuable asset for dosage forms, which reside in the stomach for a longer period of time than conventional dosage forms. Several difficulties are faced in designing controlled release systems for better absorption and enhanced bioavailability. One of such difficulties is the inability to confine the dosage form in the desired area of the gastrointestinal tract. The relatively brief gastric emptying time (GET) in humans which normally averages 2-3 h through the major absorption zone, i.e., stomach and upper part of the intestine can result in incomplete drug release from the drug delivery system leading to reduced efficacy of the administered dose. Sustained releases are dosage forms that provide medication over an extended period of time. Controlled release denotes that the system is able to provide some actual therapeutic control [4]. Controlled release (modified release) dosage forms are growing in popularity. These more sophisticated systems can be used as a means of altering the pharmacokinetic

behavior of drugs in order to provide twice or once a day dosage. This is achieved by obtaining a zero-order release from the dosage form. Zero-order release includes drug release from the dosage form that is independent of the amount of drug in the delivery system [5].

The controlled gastric retention of solid dosage forms may be achieved by the mechanisms of mucoadhesion [6, 7] flotation, [8] sedimentation, [9, 10] expansion, [11, 12] modified shape systems, [13, 14] or by the simultaneous administration of pharmacological agents, [15,16] that delay gastric emptying.

Oral controlled drug release dosage forms should not be developed unless the recommended dosage interval for the controlled release dosage form is longer than that for immediate release dosage form or unless significant clinical advantages for the controlled release dosage form can be justified like the decreased side effects resulting from a lower C max with the controlled release Form as compared to the immediate release or conventional dosage form. In vivo/in vitro evaluation of FDDS has been discussed by scientists to assess the efficiency and application of such systems. Several recent examples have been reported showing the efficiency of such systems for drugs with bioavailability problems.

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 [17].

Gastric emptying occurs during fasting as well as fed states. The pattern of motility is however distinct in the 2 states. During the fasting state an interdigestive series of electrical events take place, which cycle both through stomach and intestine every 2 to 3 hours [16]. This is called the interdigestive myloelectric cycle or migrating myloelectric cycle (MMC), which is further divided into following 4 phases as described by Wilson and Washington [19].

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

Floating Drug Delivery Systems and Its Mechanism

Floating drug delivery systems: Floating systems are low density systems that have sufficient buoyancy to float over the gastric contents and remain in the stomach for a prolonged period. While the system floats over the gastric contents, the drug is released slowly at the desired rate, which results in increased gastro-retention time and reduces fluctuation. 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. To measure the floating force kinetics, a novel apparatus for determination of resultant weight has been reported in the literature. The apparatus operates by measuring continuously the force equivalent to F (as a function of time) that is required to maintain the submerged object. The object floats better if F is on the higher positive side as shown in fig. This apparatus helps in optimizing FDDS with respect to stability and durability of floating forces produced in order to prevent the drawbacks of unforeseeable intragastric buoyancy capability variations [20].

F = F buoyancy – F gravity

= (DF – Ds) gv--- (1)

Where, F= total vertical force, DF = fluid density,

Ds= object density, v = volume and g = acceleration due to gravity.

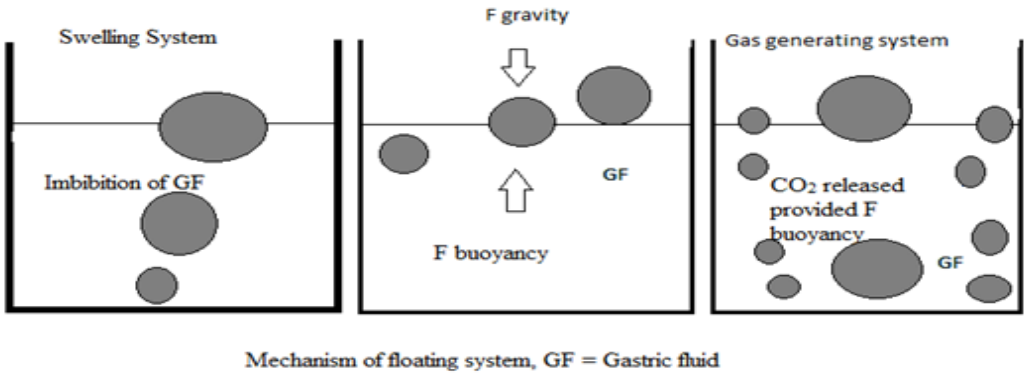

Figure 1: Mechanism of floating system

Classification of Floating Drug Delivery Systems (FDDS)

(A) Effervescent FDDS

(I) Gas generating system (II) volatile liquid containing system

(B) Non- Effervescent FDDS

(I) Colloidal gel barrier system

(II) Microporous compartment system

(III) Floating microsphere

(IV) Alginate floating beads.

(C) Raft forming system

(A) Effervescent System FDDS

These are matrix type of system. Prepared with the help of swellable polymer such as methylcellulose and Chitosan and various effervescent compounds.

Ex: sodium bicarbonate, tartaric acid, citric acid.

These are formulated in such a way that when they come in contact with gastric content, co2 is liberated and gets entrapped in swollen hydrocolloid which provides buoyancy to dosage form. The design of delivery system was based on swellable asymmetric triple layer tablet approach [21].

(I) Gas Generating Systems

These are low density FDDS is based on the formation of co2 within the device following contact with body fluids. The materials are fabricated so that upon arrival in stomach, co2is librated by acidity of the gastric content and is entrapped in the gellified hydrocolloid this produce upward motion of the dosage form and maintain its buoyancy. Decrease in specific gravity cause dosage form to float on the chyme .the co2 generating components may be intimately mixed within the tablet matrix in which case a single layer or bilayered is produced which contain the gas generating mechanism in one hydrocolloid containing layer and the drug in the other layer formulated for a sustained release effect [22- 24].

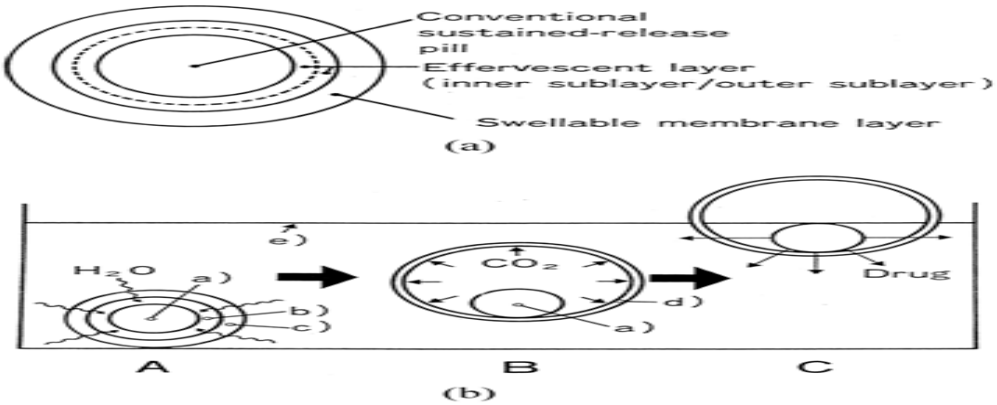

Figure 2: Mechanism of floatation via CO_2 liberation

(II) Volatile Liquid Containing Systems (Osmotically Controlled DDS)

As an Osmotically controlled floating system, the device comprised of a hallow deformable unit that was convertible from a collapsed position after an extended period of time. A housing was attached to the deformable unit and it was internally divided into a first and second chamber with the chambers

separated by an impermeable, pressure responsive movable bladder. The first chamber contain an active drug , while the second chamber contain a volatile liquid, such as cyclopentane or ether that vaporises at physiological temperature to produce a gas, enabling the drug reservoir to float. To enable the unit to exit from the stomach, the device contained a bioerodible plug that allowed the vapour to escape [25].

(B) Non-Effervescent FDDS

Non-Effervescent FDDS use a gel forming (or) swellable cellulose type of hydrocolloids,

Polysaccharide, matrix forming polymer like polycarbonate, polymethacrylate and polystyrene. One of the formulation methods involves the mixing of the drug with gel forming hydrocolloids which swell in contact with gastric fluid after oral administration and maintains integrity of shape and a bulk density barrier, the air trapped by swollen polymer confer buoyancy to the dosage forms [26].

(I) Colloidal Gel Barrier Systems (Hydrodynamic Balanced Systems)

Such system contains drug with gel-forming hydrocolloids meant to remain buoyant on the stomach content. This prolongs GRT and maximizes the amount of drug that reaches its absorption site in the solution form for ready absorption, this system incorporates a high level of one or more gel-forming highly soluble cellulose type hydrocolloid e.g.(HPMC),polysaccharides and matrix forming polymer such as polycarbophil, polystyrene and polyacrylate. On coming in the contact with GI fluid, the hydrocolloid in the system hydrates and forms a colloid gel barrier around its surface [27].

(II) Microporous Compartment Systems

This technology is based on the encapsulation of a drug reservoir inside a Microporous compartment with pores along its top and bottom walls. The peripheral wall of the drug reservoir compartment is completely sealed to prevent any direct contact of gastric surface with the undissolved drug. In the stomach, the floatation chamber containing entrapped air causes the floatation chamber containing entrapped air causes the delivery system to float over the gastric content. Gastric fluid enters through the aperture, dissolves the gastric fluid to an extent that it prevents their exist from the drug and carrier the dissolved drug for continuous transport across the intestine for absorption [28].

(III) Floating Microspheres / Micro balloons

Hallow microspheres are considers as most promising buoyant system as they are more advantageous because of central hallow space inside the microsphere. Hallow microsphere is loaded with drug in their outer polymer shelf were prepared by a novel emulsion solvent Diffusion method [29].

(IV) Alginate Beads / Floating Beads

Multi-unit floating dosage forms have been developed from freeze calcium alginate [30]. Spherical beads of approximately 2.5 mm in diameter can be prepared by dropping sodium alginate solution into aqueous solution of calcium chloride. Causing the precipitation of calcium alginate. The beads are than separated, snap-frozen in liquid nitrogen and freeze-dried at 400C for 24 h, leading to the formation of a porous system, this can maintain a floating force for over 12 h. these floating beads gave a prolonged residence time of more than 5.5 h.

(C) Raft forming systems

Raft forming system have received much attention for the delivery of antacid and drug Delivery for gastro infection and disorders on contact with gastric fluid a gel forming Solution swells and forms a viscous cohesive gel containing entrapped co2 bubbles. Which Forms raft layer on top of gastric fluid which releases drug slowly in stomach. (Often used For gastro esophageal reflux treatment [31].

Advantages of FDDS

FDDS is highly advantageous in the treatment of the disorders related to the stomach. As the prime objective of such systems is to produce a gastro retentive product or a product which has an enhanced retention time in the stomach [32].

- Drugs with considerably short half life can be administered in this manner to get an appreciable therapeutic activity.
- Enhancement of the bioavailability for drugs which can metabolized in the upper GIT.
- They also have an advantage over the conventional system as it can be used to overcome the adversities of gastric

retention time as well as the gastric emptying time.
- The duration of treatment through a single dose, which releases the an active ingredient over an extended period of time.
- The active entity is delivered specifically to the site of action, thus minimizing or eliminating the side effects.

Disadvantages of FDDS:

The major disadvantage of floating system is requirement of a sufficient high level of fluids in the stomach for the drug delivery to float. However this limitation can be overcome by coating the dosage form with the help of bioadhesive polymers that easily adhere to the mucosal lining of the stomach [33].

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.

Drugs that cause irritation and lesion to gastric mucosa are not suitable to be formulated as floating drug delivery systems.

High variability in gastric emptying time due to its all (or) non-emptying process.

Patients should not be dosed with floating forms just before going to bed.

Floating system is not feasible for those drugs that have solubility (or) stability problem in gastric fluids.

The dosage form should be administered with a minimum of glass full of water (200-250 ml).

The drugs, which are absorbed throughout GIT, which under go first-pass metabolism (Nifedipine, Propranolol etc.), are not desirable candidate.

Drug Candidates Suitable for FDDS [34-36]:

a. Drugs that have narrow absorption window in GIT (e.g. L-DOPA, paminobenzoic acid, furosemide, riboflavin).

b. Drugs those are locally active in the stomach (e.g. misroprostol, antacids).

c. Drugs those are unstable in the intestinal or colonic environment (e.g. captopril, ranitidine HCl, metronidazole).

d. Drugs that disturb normal colonic microbes (e.g. antibiotics used for the eradication of Helicobacter pylori, such as tetracycline, clarithromycin, amoxicillin).

e. Drugs that exhibit low solubility at high pH values (e.g. diazepam, chlordiazepoxide, verapamil).

Factors affecting Floating Drug Delivery System:

a) Density: Density of the dosage form should be less than the gastric contents (1.004gm/ml).

b) Size and Shape: Dosage form unit with a diameter of more than 7.5 mm are reported to have an increased GRT competed to with those with a diameter of 9.9 mm. The dosage form with a shape tetrahedron and ring shape devises with a flexural modulus of 48 and 22.5 kilo-pond per square inch (KSI) are reported to have better GIT for 90 to 100 % retention at 24 hours compared with other shapes.

c) Fed or Unfed State: Under fasting conditions, the GI motility is characterized by periods of strong motor activity or the migrating myoelectric complexes (MMC) that occurs every 1.5 to 2 hours. The MMC sweeps undigested material from the stomach and if the timing of administration of the formulation coincides with that of the MMC, the GRT of the unit can be expected to be very short. However, in the fed state, MMC is delayed and GRT is considerably longer.

d) Nature of the Meal: Feeding of indigestible polymers of fatty acid salts can change the motility pattern of the stomach to a fed state, thus decreasing the gastric emptying rate and prolonging the drug release.

e) Caloric Content: GRT can be increased between 4 to 10 hours with a meal that is high in proteins [37, 38].

Evaluation Parameters:

1. Size and Shape Evaluation: The particle size and shape plays a major role in determining solubility rate of the drugs and thus potentially its bioavailability. The particle size of the formulation was determined using Sieve analysis (Jayant, Mumbai), Air elutriation (Bahco TM) analysis, Photo analysis, Optical microscope (Olympus, India, Pvt. Ltd), Electro résistance counting methods (Coulter counter), Sedimentation techniques, Laser diffraction methods, ultrasound attenuation spectroscopy, Air Pollution Emissions Measurements etc.

2. Floating Properties: Effect of formulation variables on the floating properties of gastric floating drug delivery system was determined by using continuous floating monitoring system and statistical experimental design.
3. Surface Topography: The surface topography and structures were determined using scanning electron microscope (SEM, JEOL JSM – 6701 F, Japan) operated with an acceleration voltage of 10k.v, Contact angle meter, Atomic Force Microscopy (AFM), Contact portfolio-meter.
4. Swelling Studies: Swelling studies were performed to calculate molecular parameters of swollen polymers. Swelling studies was determined by using Dissolution apparatus, optical microscopy and other sophisticated techniques which include 1HNMR imaging, Confocal laser scanning micro- and fats scopy (CLSM), Cryogenic Scanning Electron Microscopy (Cryo-SEM), Light scattering imaging (LSI) etc. The swelling studies by using Dissolution apparatus (USP dissolution apparatus (usp-24) Lab-India Disso 2000) was calculated as per the following formula.
Swelling ratio = Weight of wet formulation / Weight of formulations
5. 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), Micro-titrimetric methods, Inductively Coupled Plasma Atomic Emission Spectrometer (ICPAES) and also by using spectroscopy techniques (Elico Limited, Hyderabad).
6. Percentage Entrapment Efficiency: Percentage entrapment efficiency was reliable for quantifying the phase distribution of drug in the pre-pared formulations. Entrapment efficiency was deter-mined by using three methods such as Micro dialysis method, Ultra centrifugation, and pressure Ultra filtration.
7. In-vitro Release Studies: In vitro release studies (USP dissolution apparatus LAB-INDIA Dissolution 2000) were performed to provide the amount of the drug that is released at a definite time period. Release studies were performed by using Franz diffusion cell system and synthetic membrane as well as different types of dissolution apparatus.
8. Fourier Transforms Infrared Analysis: Fourier transform infrared spectroscopy (FTIR, Shimadzu, Model-RT-IR-8300) is a technique mostly used to identify organic, polymeric, and some inorganic materials as well as for functional group determination. Fourier Transform Infrared Analysis (FTIR) 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 150 kg/cm2; the spectra were scanned over the wave number range of 3600 to 400 cm-1 at the ambient temperature.
9. Differential Scanning Calorimetry (DSC): Shimadzu, Model-DSC-60/DSC-50/ Metler Toldeo are generally 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 50 ml/min [39-41].

CONCLUSION

Drug absorption in the gastrointestinal tract is a highly variable procedure and prolonging gastric retention of the dosage form extend the time for drug absorption. FDDS promises to be a potential approach for gastric retention. Number of commercial products and patents issued in this field are the evidence of it. The aim is to improve the bioavailability of the drug with narrow absorption window in gastrointestinal tract region. By prolonging the drug resident time in GI region improves the solubility of drug that is less soluble in high PH and reduces drug waste, reduction in plasma level fluctuation. Although there are number of difficulties to be worked out to achieve prolonged gastric retention, a large number of companies are focusing toward commercializing this technique.

Table 1: Marketed Preparations of Floating Drug Delivery system [42]

S. no.	Product	Active Ingredient
1	Madopar	Levodopa and benserzide
2	Valrelease	Diazepam
3	Topalkan	Aluminum magnesium antacid
4	Almagate flat coat	Antacid
5	Liquid gavison	Alginic acid and sodium bicarbonate

FUTURE POTENTIAL

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. 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 and these are potential to treat the Parkinson's disease. Some of the unresolved critical issues related to the rational development of FDDS include, the quantitative efficiency of floating delivery systems in the fasted and fed states and the correlation between prolonged GRT and SR/PK characteristics. However, we are as close as we have ever been to see a greater transition of gastric retention devices from developmental level to the manufacturing and commercial level.

ACKNOWLEDGEMENT

The authors are thankful to Mr. Gnanarajan, SGRRITS, Dehradun, India, for making available the required facilities for this work.

REFERENCES

1. Shweta Arora, Floating drug delivery systems: A review AAPS Pharm SciTech.: E372–E390, Vol-6, Issue 3, September (2005).
2. GSN Koteswara Rao, KV Ramana Murthy, Aayisha Begum, B Roja Rani, Ch Ragha Naveen, B Raj Kumar, et al. Formulation and Evaluation of Floating Drug Delivery Systems of Propranolol HCl using Modified Pulsincap Technique. International Journal of Pharma Research & Review, Sept 2014; 3(9):15-22.
3. Avaru Geetha Dutt, Ande Pratyusha, Uma Maheshwar Rao, Motor Leela Keerthi, Kalakuntla Sai Krishna, Ashok Morsu. Formulation and Evaluation of Gastro Retentive Drug Delivery System of Tizanidine Hydrochloride: A Review. International Journal of Pharma Research & Review, Oct 2014; 3(10):34-45
4. Hirtz J. The git absorption of drugs in man: a review of current concepts and methods of investigation. Br J Clin Pharmacol. 1985; 19:77SY83S.
5. Rouge N, Buri P, Doelker E. Drug absorption sites in the gastrointestinal tract and dosage forms for site specific delivery. Int J Pharm 1996; 136:117-139.
6. Gwen.M.jantezen, and Joseph.R.Robinson, Sustained and Controlled release drug delivery systems, Chapter-15, page 501-523.
7. Ponchel G, Irache JM. Specific and non-specific bioadhesive particulate system for oral delivery to the gastrointestinal tract. Adv Drug Del Rev. 1998; 34:191Y219.
8. Lenaerts VM, Gurny R. Gastrointestinal Tract-Physiological variables affecting the performance of oral sustained release dosage forms. In: Lenaerts V, Gurny R, eds. Bioadhesive Drug Delivery System. Boca Raton, FL: CRC Press; 1990.
9. Deshpande AA, Shah NH, Rhodes CT, Malick W. Development of a novel controlled-release system for gastric retention. Pharm Res. 1997; 14:815Y819.
10. Rednick AB, Tucker SJ. Sustained release bolus for animal husbandry. US patent 3 507 952. April 22, 1970.
11. Davis SS, Stockwell AF, Taylor MJ, et al. The effect of density on the gastric emptying of single and multiple unit dosage forms. Pharm Res. 1986; 3:208Y213.
12. Urguhart J, Theeuwes F. Drug delivery system comprising a reservoir containing a plurality of tiny pills. US patent 4 434 153. February 28, 1994.
13. Mamajek RC, Moyer ES. Drug dispensing device and method. US Patent 4 207 890. June 17, 1980.
14. Fix JA, Cargill R, Engle K. Controlled gastric emptying. III. Gastric residence time of a non-disintegrating geometric shape in human volunteers. Pharm Res. 1993; 10:1087Y1089.
15. Kedzierewicz F, Thouvenot P, Lemut J, Etienne A, Hoffman M, Maincent P. Evaluation of peroral silicone dosage forms in human's bygamma-scintigraphy. J Control Release. 1999; 58:195Y205.

16. Groaning R, Heun G. Oral dosage forms with controlled gastrointestinal transit. Drug Dev Ind Pharm. 1984; 10:527Y539.
17. Groning R, Heun G. Dosage forms with controlled gastrointestinal passage—studies on the absorption of nitrofurantion. Int J Pharm. 1989; 56:111Y116.
18. Desai S. A Novel Floating Controlled Release Drug Delivery System Based on a Dried Gel Matrix Network [master's thesis]. 1984 Jamaica, NY, St John's University.
19. Vantrappen GR, Peters TL, Janssens J. The secretory component of interdigestive migratory motor complex in man. Scand J Gastroenterology. 1979; 14:663Y667.
20. Wilson CG, Washington N. The stomach: its role in oral drug delivery. In: Rubinstein MH, ed. Physiological Pharmaceutical: Biological Barriers to Drug Absorption. Chic ester, UK: EllisHorwood; 1989:47Y70.
21. Roop K. Khar, Controlled Drug Delivery, Gastro retentive system 4th edn. 202-203.
22. Khan F.N, Dehghan H.G., Int J Health Res 2009; 2(1): 23
23. Kamalakkannan V, Puratchikody A, Prasanth VV and Masilamani K: Enhancement of Drugs Bioavailability by Floating Drug Delivery System – A Review. International Journal of Drug Delivery 2011; 1: 558-70.
24. Suryawanshi A and Hiremath SP: Floating Drug Delivery System – A Review. American Journal of Pharmatech Research 2011; 2(1): 138-53.
25. Shubhrajit M, Thilothama LR and Shoshanna D. Formulation and in vitro evaluation of metoprolol succinate floating tablets by using two viscosity grade of HPMC. International Journal of Pharmaceutical Science and Research 2012; 3 (9): 3507-13.
26. Bardonnet PL, Faivre V, Pugh WJ, Piffaretti JC and Falson F: Gastro retentive Dosage Forms: Overview and Special case of Helicobacter pylori. Journal of Control Release 2006; 111: 1 – 18.
27. Narang N: AN Updated Review On: Floating Drug Delivery System (FDDS). International Journal of Applied Pharmaceutics 2011; 3(1): 1-7.
28. Chandiran S, Kumar BP and Narayan V: Formulation and in vitro evaluation of floating drug delivery system for salbutamol sulphate. International Journal of Pharma Biomed Sciences 2010; 1(1): 12-15.
29. Jain A: New Concept: Floating Drug Delivery System. Indian Journal of Novel Drug Delivery 2011; 3(3): 163-69.
30. Geetha A, Rajendra K, Mohan CHK, Sateesh V and Raju PN: A Review on Floating Drug Delivery Systems. International Journal of Pharmaceutical Research and Biomedical Analysis 2012; 1(1): 1-13.
31. Wu W, Zhou Q, Zhang HB, Ma GD, Fu CD. Studies on nimodipine sustained release tablet capable of floating on gastric fluids with prolonged gastric resident time. Yao Xue Xue Bao. 1997; 32:786Y790.
32. Erni W, Held K. The hydro dynamically balanced system: a novel principle of controlled drug release. Eur Neurol. 1987; 27:215Y275.
33. Sheth PR, Tossounian J. The hydro dynamically balanced systems (HBS): a novel drug delivery system for oral use. Drug Dev Ind Pharm. 1984; 10:313Y339.
34. Degtiareva H, Bogdanov A, Kahtib Z, etal. . The use of third generation antacid preparations for the treatment of patients with nonulcerous dyspeosia and peptic ulcer complicated by reflux esophagus [in Chinese]. Liakrs' ka sprava. 1994; 5 6:119Y122.
35. Fabregas JL, Claramunt J, Cucala J, Pous R, Siles A. In vitro testing of an antacid formulation with prolonged gastric residence time (Almagate flat coat). Drug Dev Ind Pharm. 1994; 20:1199Y1212.
36. Washington N, Washington C, Wilson CG, Davis SS. What is liquid Graviscon? A comparison of four international formulations. Int J Pharm. 1986; 34:105Y109.
37. Reddy L.H, Murthy R.S., Floating dosage systems in drug delivery, Crit. Rev. There. Drug Carr. Syst., 2002; 19: 553-585.
38. Klausner EA, Lavy E, Friedman M and Hoffman A, "Expandable Gastro retentive dosage form", J. Control. Rel., 2003, 90, 143-162.
39. Gastro Retentive Drugs: A review, Express Pharma Pulse, Apr 17 (2003).
40. www.pharmainfo.net.
41. Gattani YS, "Floating drug delivery system: A Review", Int. J. Pharm. and Bio Sciences 2010, V1 (2).
42. Shah SH, Patel JK, Patel NV, "Stomach specific Floating drug delivery system: A Review", Int. J. Pharm. Res., 2009, 3, 623-633.