WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 6.041
Volume 5, Issue 11, 476-525 Review Article ISSN 2278 – 4357

AN UPDATE ON GASTRORETENTIVE FLOATING SYSTEMS

R. Santosh Kumar* and T. Naga Satya Yagnesh

GITAM Institute of Pharmacy, GITAM University, Rushikonda, Visakhapatnam, A.P-530045.

Article Received on
06 Sept. 2016,
Revised on 26 Sept. 2016,
Accepted on 16 October 2016
DOI: 10.20959/wjpps201611-7973

***Corresponding Author**
R. Santosh Kumar
GITAM Institute of Pharmacy, GITAM University, Rushikonda, Visakhapatnam, A.P-530045.

ABSTRACT

Gastric emptying is a complex process and makes in vivo performance of the drug delivery systems uncertain. In order to avoid this variability, efforts have been made to increase the retention time of the drug-delivery systems for more than 12hours. The floating or hydrodynamically controlled drug delivery systems are useful in such application. Floating drug delivery system enable prolonged and continuous input of the drug to the upper part of the gastro retentional tract and improve the bioavailability of medication that is characterized by a narrow absorption window. This review summarizes advantages, disadvantages, approaches, formulation and applications of floating systems.

KEYWORDS: Floating drug delivery system, hydrodynamically balanced system, effervescent, non-effervescent.

INRODUCTION

Over the past 30 years, as the expense and complications involved in marketing new drug entities have increased, with concomitant recognition of the therapeutic advantages of controlled drug delivery, greater attention is being paid on development of oral controlled drug delivery systems. The goal in designing controlled release drug delivery system is to reduce the frequency of the dosing, reducing the dose and providing uniform drug delivery. So, controlled release dosage form is a dosage form that releases one or more drugs continuously in predetermined pattern for a fixed period of time, either systemically or locally to specified target organ.

Controlled Release Drug Delivery System

Controlled release system means any drug delivery system that maintains adequate and desired release of drug over an extended period of time. The majority of these formulations are designed for oral administration, however recently such devices also been introduced for parentral administration, ocular insertion and trasdermal applications.

Advantages of Controlled Drug Delivery System

1) Reduced dosing frequency.
2) Decreased incidence and intensity of adverse effects and toxicity.
3) Improved patient compliance.
4) Controlled rate and site of release.
5) Constant level of drug concentration in blood plasma.
6) More uniform blood concentration.
7) More consistent and prolonged therapeutic effect.
8) Greater selectivity of pharmacological activity.

Disadvantages of Controlled Release Drug Delivery System

1) Toxicity due to dose dumping.
2) Increased variability among dosing units.
3) Stability problems.

Classification of Controlled Release Drug Delivery Systems

1) Based on route of Administration :	Per oral dosage forms 1) Dental systems 2) Ocular systems 3) Vaginal systems 4) Injections and implants
2) Based on Formulation Aspect :	1) Polymer based controlled released technology (dissolution/ diffusion controlled) 2) Osmotic pumps 3) Mechanical pumps 4) Biodegradable carrier based CR system 5) Ion-exchange system 6) Prodrug approach 7) Micro emulsion/ multiple emulsions

Floating Drug Delivery Systems

Floating systems, first described by Davis in 1968, have bulk density lower Than that of the gastric fluid and thus remain buoyant in stomach for a prolonged period. Floating systems

can be of effervescent or non effervescent in nature. In effervescent gas generating excipients, e.g., bicarbonate salts and acidic ingredients are used that can form CO_2 in the presence of gastric acid. Also, volatile organic solvents have been introduced into the floating chamber to generate gas at physiological temperature. Gastro retentive dosage forms extend significantly the period of time over which the drugs may be released. Thus, they not only prolong dosing intervals, but also increase patient compliance beyond the level of existing controlled release dosage forms. This application is especially effective in delivery of sparingly soluble and insoluble drugs. It is known that, as the solubility of a drug decreases, the time available for drug dissolution becomes less adequate and thus the transit time becomes a significant factor affecting drug absorption. To address this, oral administration of sparingly soluble drugs is carried out frequently, often several times per day. As a mechanism to override this problem, erodible, gastro retentive dosage forms have been developed that provide continuous, controlled administration of these drugs at the absorption site. In addition, these dosage forms are useful for delivering drugs incorporated into vesicles such as liposomes, Nanoparticles, proteinoid microspheres and pharmacosomes etc. The drugs that may irritate the stomach lining or are unstable in its acidic environment should not be formulated in gastroretentive systems. Furthermore, other drugs, such as isosorbide dinitrate, that are absorbed equally well throughout the GI tract, drugs undergoing first pass metabolism will not benefit from incorporation into a gastric retention system. It requires sufficient high level of fluids in the stomach for the drug delivery to float.

Gastric emptying of dosage forms is an extremely variable process and ability to prolong and control 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. Drug absorption from the gastrointestinal tract is a complex procedure and is subject to many variables. It is widely acknowledged that the extent of gastrointestinal tract drug absorption is related to contact time with the small intestinal mucosa.[1] Thus small Intestinal transit time is an important parameter for drugs that are incompletely absorbed.

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.

The controlled gastric retention of solid dosage forms may be achieved by the mechanisms of mucoadhesion[2], flotation[3], sedimentation[4], expansion modified shape systems[5] or by the simultaneous administration of pharmacological agent[6,7] that delay gastric emptying.

Anatomy of Stomach

The main function of the stomach is to process and transport food. It serves as a short-term storage reservoir, allowing a rather large meal to be consumed quickly. Substantial enzymatic digestion is initiated in stomach, particularly of proteins. Vigorous contractions of gastric smooth muscle mix and grind foodstuffs with gastric secretions, resulting in liquefaction of food. As food is liquefied in the stomach, it is slowly released into the small intestine for further processing.[8]

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.[9]

It has been reported that the mean value of pH in fasted healthy subjects is 1.1± 0.15. But when food comes into the stomach, the pH may rise to levels in the 3.0 to 4.0 level due to the buffering capacity of proteins. However, in fasted state, basal gastric secretion in women is slightly lower than that of men.[10]

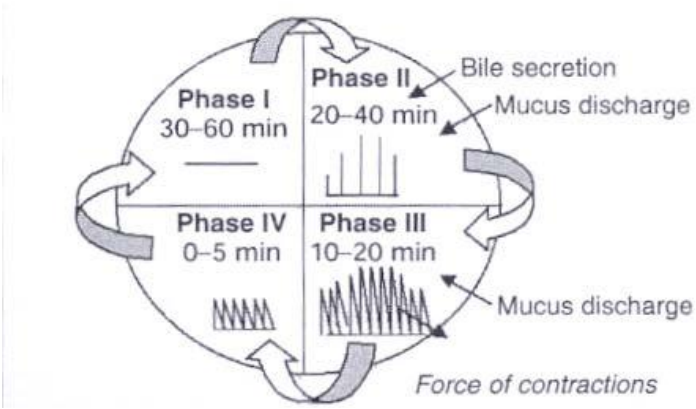
Gastric emptying occurs during fasting as well as fed states. The pattern of motility is however distinct in the 2 states. During the fasting state an interdigestive series of electrical events take place, which cycle both through stomach and intestine every 2 to 3 hours.

This is called the interdigestive myloelectric cycle or migrating myloelectric cycle (MMC), which is further divided into following 4 phases

1. Phase I (Basal phase) lasts from 30 to 60 minutes with rare contractions.
2. Phase II (Preburst phase) lasts for 20 to 40 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 10 to 20 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.



Motility Pattern in GIT

After the ingestion of a mixed meal, the pattern of contractions changes from fasted to that of fed state. This is also known as digestive motility pattern and comprises continuous contractions as in phase II of fasted state. These contractions result in reducing the size of food particles (to less than 1 mm), which are propelled toward the pylorus in a suspension form. During the fed state onset of MMC is delayed resulting in slowdown of gastric emptying rate.[11]

Factors Effecting Gastric Residence Time

a) Formulation Factors

Size of Tablets

Retention of floating dosage forms in stomach depends on the size of tablets. Small tablets are emptied from the stomach during the digestive phase, but large ones are expelled during the house keeping waves.[12]

Floating and nonfloating capsules of 3 different sizes having a diameter of 4.8 mm (small units), 7.5 mm (medium units) and 9.9 mm (large units), were formulated and analyzed for their different properties. It was found that floating dosage units remained buoyant regardless of their sizes on the gastric contents throughout their residence in the gastrointestinal tract, while the nonfloating dosage units sank and remained in the lower part of the stomach.

Floating units away from the gastro-duodenal junction were protected from the peristaltic waves during digestive phase while the nonfloating forms stayed close to the pylorus and were subjected to propelling and retropelling waves of the digestive phase.[13]

Density of Tablets

Density is the main factor affecting the gastric residence time of dosage form. A buoyant dosage form having a density less than that of the gastric fluids floats, since it is away from the pyloric sphincter, the dosage unit is retained in the stomach for a prolonged period. A density of less than 1.0g/ml i.e. less than that of gastric contents has been reported. However, the floating force kinetics of such dosage form has shown that the bulk density of a dosage form is not the most appropriate parameter for describing its buoyancy capabilities.[14]

Shape of Tablets

The shape of dosage form is one of the factors that affect its gastric residence time. Six shapes (ring tetrahedron, cloverleaf, string, pellet and disk) were screened *in vivo* for their gastric retention potential. The tetrahedron (each leg 2cm long) rings (3.6 cm in diameter) exhibited nearly 100% retention at 24 hr.[15]

Viscosity Grade of Polymer

Drug release and floating properties of FDDS are greatly affected by viscosity of polymers and their interaction. Low viscosity polymers (e.g., HPMC K100 LV) were found to be more beneficial than high viscosity polymers (e.g., HPMC K4M) in improving floating Properties. In addition, a decrease in the release rate was observed with an increase in polymer viscosity.[16]

B) Idiosyncratic Factors

Gender

Women have slower gastric emptying time than do men. Mean ambulatory GRT in meals (3.4±0.4 hours) is less compared with their age and race-matched female counterparts (4.6±1.2 hours), regardless of the weight, height and body surface.[17]

Age

Low gastric emptying time is observed in elderly than do in younger subjects. Intrasubject and intersubject variations also are observed in gastric and intestinal transit time. Elderly people, especially those over 70 years have a significantly longer GRT.[18]

Posture

i) Upright Position

An upright position protects floating forms against postprandial emptying because the floating form remains above the gastric contents irrespective of its size.[18]

Floating dosage forms show prolonged and more reproducible GRTs while the conventional dosage form sink to the lower part of the distal stomach from where they are expelled through the pylorus by antral peristaltic movements.[19]

ii) Supine Position

This position offers no reliable protection against early and erratic emptying. In supine subjects large dosage forms (both conventional and floating) experience prolonged retention. The gastric retention of floating forms appear to remain buoyant anywhere between the Lesser and greater curvature of the stomach. On moving distally, these units may be swept away by the peristaltic movements that propel the gastric contents towards the pylorus, leading to Significant reduction in GRT compared with upright subjects.[20]

Concomitant Intake of Drugs

Drugs such as prokinetic agents (e.g., metoclopramide and cisapride), anti Cholinergics (e.g., atropine or propantheline), opiates (e.g., codeine) may affect the performance of FDDS. The co administration of GI-motility decreasing drugs can increase gastric emptying time.[20]

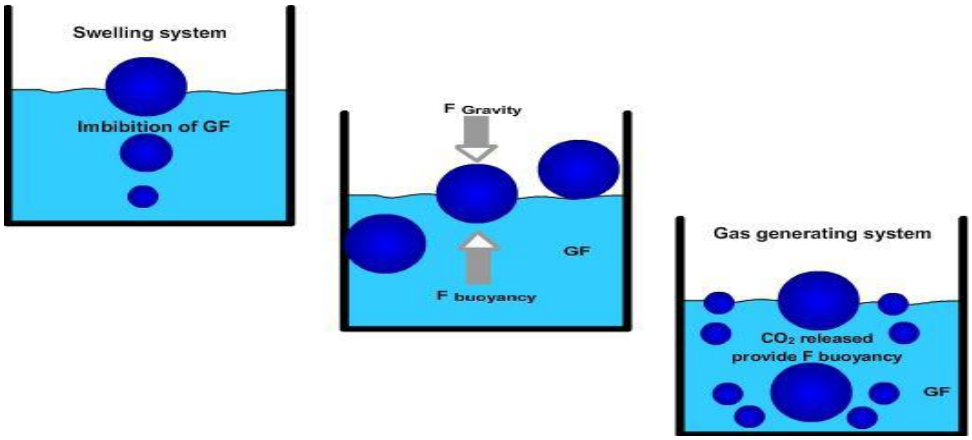
Feeding Regimen

Gastric residence time increases in the presence of food, leading to increased drug dissolution of the dosage form at the most favorable site of absorption. A GRT of 4-10 h has been reported after a meal of fats and proteins.[21]

Floating Drug Delivery Systems

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 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 (Fig 1). Many buoyant systems have been developed Based on granules, powders, capsules, tablets, laminated films and hollow microspheres.



Mechanism of Floating Systems, GF = Gastric Fluid

Advantages of Floating Drug Delivery Systems[22,23]

1. The gastroretensive systems are advantageous for drugs absorbed through the stomach. E.g. Ferrous salts, antacids.
2. Acidic substances like aspirin cause irritation on the stomach wall when come in contact with it. Hence HBS formulation may be useful for the administration of aspirin and other similar drugs.
3. Administration of prolonged release floating dosage forms, tablet or capsules, will result in dissolution of the drug in the gastric fluid. They dissolve in the gastric fluid would be available for absorption in the small intestine after emptying of the stomach contents. It is therefore expected that a drug will be fully absorbed from floating dosage forms if it remains in the solution form even at the alkaline pH of the intestine.
4. The gastroretensive systems are advantageous for drugs meant for local action in the stomach. E.g. antacids.
5. When there is a vigorous intestinal movement and a short transit time as might occur in certain type of diarrhea, poor absorption is expected. Under such circumstances it may be advantageous to keep the drug in floating condition in stomach to get a relatively better response.

Disadvantages of Floating Drug Delivery System

1. Floating system is not feasible for those drugs that have solubility or stability problem in G.I. tract.

2. These systems require a high level of fluid in the stomach for drug delivery to float and work Efficiently-coat, water.

3. The drugs that are significantly absorbed through out gastrointestinal tract, which undergo significant first pass metabolism, are only desirable candidate.

4. Some drugs present in the floating system causes irritation to gastric mucosa.

Classification of Floating Drug Delivery Systems

1). Single Unit Floating Dosage Systems

a) Effervescent system

b) Non-effervescent Systems

2). Multiple Unit Floating Dosage Systems

a) Effervescent Systems

b) Non-effervescent Systems

c) Hollow microspheres

3). Raft forming system

1). Single Unit Floating Dosage Systems

A) Effervescent Systems

Effervescent floating drug delivery systems generate gas (CO2), thus reduce the density of the system and remain buoyant in the stomach for a prolonged period of time and release the drug slowly at a desired rate. The main ingredients of effervescent system include swellable polymers like chitosan, methyl cellulose and effervescent compounds such as citric acid, sodium bicarbonate, citric acid and tartaric acid.[24]

Penners et al prepared an expandable tablet containing mixture of polyvinyl lactams and polyacrylates that swells rapidly in an aqueous environment and thus, stays in stomach over an extended period of time. In addition to this, gas-forming agents were also incorporated so as soon as the gas formed, the density of the system was reduced and thus, the system tended to float in the gastric environment.[25]

M.Jaimini et al. prepared the effervescent floating tablet of famotidine. They found that the addition of gel-forming polymer methocel (K100 and K15M) and gas-generating agent sodium bicarbonate along with citric acid was essential to achieve in vitro buoyancy. The drug release from the tablets was sufficiently sustained and non-Fickian transport of the drug from tablets was confirmed.[26]

B) Non- Effervescent System

Non-effervescent systems commonly use gel-forming or highly swellable cellulose type hydrocolloids, polysaccharides and matrix forming polymers such as polycarbonate, polyacrylate, polymethacrylate and polystyrene. The formulation method includes a simple approach of thoroughly mixing the drug and the gel-forming hydrocolloid. After oral administration, this dosage form swells in contact with gastric fluids and attains a bulk density of less 1 g/ml. The air entrapped within the swollen matrix imparts buoyancy to the dosage form.

Iannuccelli *et al* prepared air compartment multiple unit system for prolonged gastric residence. These units were composed of a calcium alginate core separated by an air compartment from membrane of calcium alginate. The porous structure generated by leaching of polyvinyl alcohol (PVA), which was employed as water soluble additive in coating composition, was found to increase the membrane permeability preventing the air compartment shrinkage. The ability of floatation increases with increase in PVA, molecular weight.[27]

Wu et al prepared floating sustained release tablets of nimodipine by using HPMC and PEG 6000. Prior to formulation of floating tablets, nimodipine was incorporated into poloxamer-188 solid dispersion after which it was directly compressed into floating tablets. It was observed that by increasing the HPMC and decreasing the PEG 6000 content, a decline in *in vitro* release of nimodipine occurred.[28]

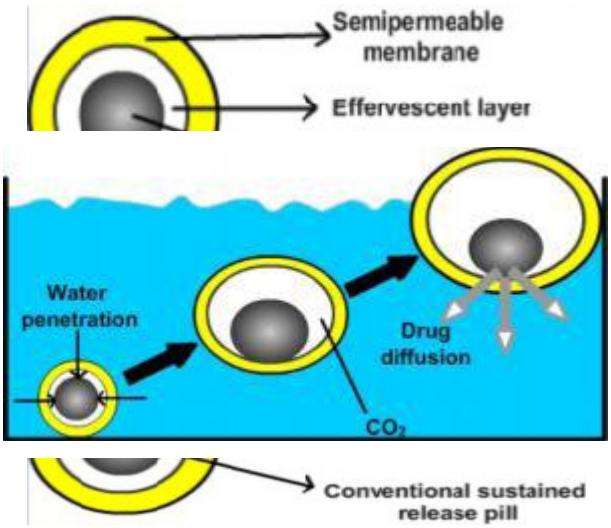
Single-unit formulations are associated with problems such as sticking together or being obstructed in the gastrointestinal tract, which may have a potential danger of producing irritation. The main drawback of such system is “all or none” phenomenon. In such cases, there is a danger of passing of the dosage form to intestinal part at the time of house-keeper waves. To overcome this difficulty multiple, unit dosage forms are designed.

2). Multiple Unit Floating Systems

Multiple unit dosage forms may be an attractive alternate since they have been shown to reduce inter and intra-subject variability's in drug absorption as well as to lower the possibility of dose dumping. Various multiple unit floating systems have been developed in different forms and using principles such as air compartment multiple unit system, hollow microspheres prepared by emulsion solvent diffusion method, beads prepared by emulsion gelation method. Use of effervescent and swellable polymer is another approach for preparing multiple unit FDDS.

A) Effervescent System

Ichikawa et al developed a new multiple type of floating dosage system composed of effervescent layers and swellable membrane layers coated on sustained release pills. The inner layer of effervescent agents containing sodium bicarbonate and tartaric acid was divided into two sub layers to avoid direct contact between the two agents. These sub layers were surrounded by a swellable polymer membrane containing polyvinyl acetate and purified Shellac. When this system was immersed in the buffer at 37ºC, it settled down and the solution permeated into the effervescent layer through the outer swellable membrane. CO2 was generated by the neutralization reaction between the two effervescent agents, producing swollen pills (like balloons) with a density less than 1.0 g/ml. It was found that the system had good floating ability Independent of pH and viscosity and the drug (Para-amino benzoic acid) released in a sustained manner as shown in fig.3 (a), (b).[29]



A) B)

A) Different Layers, B) Mechanism of Floatation via CO_2 Liberation

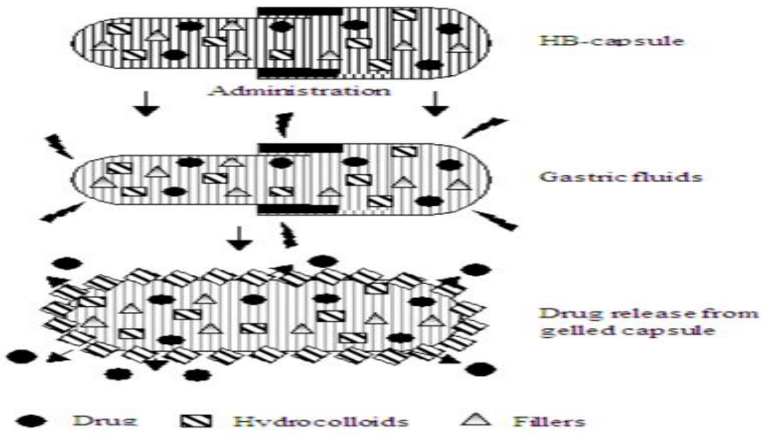
Chen et al studied the effect of formulation variables on in vitro performance of floating sustained release of verapamil. The formulations were comprised of variables like polymers excipients, polymer content, density of capsule and amount of effervescent agents.[30]

B) Non-Effervescent Systems

Not many reports were found in the literature on non-effervescent 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 is reported. A mixture of drug, chitosan and acetic acid is extruded through a needle and The extrudate is cut and dried. Chitosan hydrates and floats in the acidic media and the required drug release could be obtained by modifying the drug-polymer ratio.[31]

Thanoo et al. developed polycarbonate microspheres by solvent evaporation technique. Polycarbonate in dichloromethane was found to give hollow microspheres that floated on water and simulated biofluids, as evidenced by scanning electron microscopy (SEM). High drug loading was achieved and drug-loaded microspheres were able to float on gastric and intestinal fluids. It was found that increasing the drug-to-polymer ratio increased both their mean particle size and release rate of drug.[32]

Sheth et al. developed hydrodynamically balanced capsules containing mixture of drug and hydrocolloids containing a homogeneous mixture of drug and the hydrocolloid in a capsule, which upon contact with gastric fluid acquired and maintained a bulk density of less than 1, thereby being buoyant on the gastric contents of stomach, until all the drug was released as shown in Bellow figure.[33]



Working Principle of Hydrodynamically Balanced System

C) Hollow Microspheres

Both natural and synthetic polymers have been used to prepare floating microspheres.

Joseph et al. developed a floating dosage form of piroxicam based on hollow polycarbonate microspheres. The microspheres were prepared by the solvent evaporation technique. Encapsulation efficiency of ~95% was achieved. In vivo studies were performed in Healthy male albino rabbits. Pharmacokinetic analysis was derived from plasma concentration versus time plot and revealed that the bioavailability from the piroxicam microspheres alone was 1.4 times that of the free drug and 4.8 times that of a dosage form consisting of microspheres plus the loading dose and was capable of sustained delivery of the drug over a prolonged period.[34]

3) Raft Forming System

Raft forming systems have received much attention for the drug delivery for gastrointestinal infections and disorders. The 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. This raft floats on gastric fluids because of low bulk density created by the formation of CO_2. Usually, the system ingredients includes a gel forming agent and alkaline bicarbonates or carbonates responsible for the formation of CO_2 to make the system less dense and float on the gastric fluids.

Jorgen et al described an antacid raft forming floating system. The system contains a gel forming agent (e.g. sodium alginate), sodium bicarbonate and acid neutralizer, which forms a foaming sodium alginate gel (raft), which when comes in contact with gastric fluids, the raft floats on the gastric fluids and prevents the reflux of the gastric contents (i.e. gastric acid) into the esophagus by acting as a barrier between the stomach and esophagus.[35]

Table 1.1: Drugs That Can Be Formulated Into Floating Drug Delivery Systems

List of Drugs Formulated as Single and Multiple Unit Forms of Floating Drug Delivery Systems:

S.No	Category	Drugs that Can Be Formulated in to Floating Drug Delivery Systems
1	Analgesics	Tramadol
2	Antiamoebics	Metronidazloe
3	Antianginal dugs	Trimetazidine dihydrochloride
4	Antibiotics	Amoxicillin, Ciprofloxacin, Cefuroxime, Clarithromycin, Cefixime, Cephalexin, Cefpodoxime, Levofloxacin,

		Oflaxcin, Norfloxacin
5	Anticonvulsant	Carbamzepine
6	Anticancer	5-Flurouracil
7	Antidiabetic	Metformin, Repaglinide, Glipizide
8	Antiemetic	Domperidone, Itopride
9	Antiepileptic	Carbamzepine
10	Antihypertensive	Aenolol,Captopril, Diltiazem, Nitrendepine, Propronolol, Verapamil
11	Antilipidemics	Atorvastatin
12	Antispasmodics	Fenoverine, Tizanizide
13	Antiulcers	Famotidine, Ranitidine Lansoprazole
14	Antivirals	Acyclovir
15	Bronchodilators	Salbutamol, Theophylline,
16	Diuretics	Furosemide
17	NSAIDS	Aceclofenac, Ketorolac, Nimesulide, Loraxicam

Approaches to Design Floating Dosage Forms

The following approaches have been used for the design of floating dosage forms of single and multiple unit systems.[36]

Single-Unit Dosage Forms

In low density approaches[37], the globular shells apparently having lower density than that of gastric fluid can be used as a carrier for drug for its controlled release. A buoyant dosage form can also be obtained by using a fluid-filled system that floats in the stomach. In coated shells[38] popcorn, poprice and polystyrol have been exploited as drug carriers. Sugar polymeric materials such as methacrylic polymer and cellulose acetate phthalate have been used to undercoat these shells. These are further coated with a drug-polymer mixture. The polymer of Choice can be either ethylcellulose or Hydroxypropyl cellulose depending on the type of released desired. Finally the product floats on the gastric fluid while releasing the drug gradually over a prolonged duration.

Fluid-filled floating chamber type of dosage forms includes incorporation of a gas-filled floatation chamber into a microporous component that houses a drug reservoir.[39] Aperture or opening are present along the top and bottom walls through which the gastrointestinal fluid enters to dissolve the drug. The other two walls in contact with the fluid are sealed so that the undissolved drug remains therein. The fluid present could be air, under partial vacuum or any other suitable gas, liquid, or solid having an appropriate specific gravity and an inert behavior. The device is of swallowable size, remains afloat within the stomach for a prolong time and after the complete release the shell disintegrates, passes off to the intestine and is

eliminated. Hydrodynamically balanced systems (HBS) are designed to prolong the stay of the dosage form in the gastro intestinal tract and aid in enhancing the absorption. Such systems are best suited for drugs having a better solubility in acidic environment and also for the drugs having specific site of absorption in the upper part of the small intestine. To remain in the stomach for a prolong period of time the dosage form must have a bulk density of less than 1. It should stay in the stomach, maintain its structural integrity and release drug constantly from the dosage form. Single unit formulations are associated with problems such as sticking together or being obstructed in the gastrointestinal tract, which may have a potential danger of producing irritation.

Multiple-Unit Dosage Forms

The purpose of designing multiple-unit dosage form is to develop a reliable formulation that has all the advantages of a single-unit form and also is devoid of any of the Above mentioned disadvantages of single-unit formulations. In pursuit of this endeavor many multiple unit floatable dosage forms have been designed. Microspheres have high loading capacity and many polymers have been used such as albumin, gelatin, starch, polymethacrylate, polyacrylamine and poly alkyl cyanoacrylate. Spherical polymeric microsponges also referred to as "microballoons" have been prepared. Microspheres have a characteristic internal hollow structure and show an excellent in vitro floatability.[40] In Carbon dioxide-generating multiple-unit oral formulations several devices with features that extend, unfold, or are inflated by carbon dioxide generated in the devices after administration have been described. These dosage forms are excluded from the passage of the pyloric sphincter if a diameter of ~12 to18 mm in their expanded state is exceeded.

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. Acacia, 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 mineral 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 Retardants

Insoluble substances such as Dicalcium phosphate, talc, magnesium stearate decreased 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.

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.[41]

Evaluation of Floating Drug Delivery Systems

1) Evaluation of Powder Blend For

a) Angle of Repose

b) Bulk Density

c) Percentage porosity

2) Evaluation of Tablets For

a) Buoyancy capabilities

b) In vitro floating and dissolution behavior

c) Weight variation

d) Hardness & friability

e) Particle size analysis, surface characterization (for floating microspheres and beads):

f) X-Ray/Gamma Scintigraphy

g) Pharmacokinetic studies

1) Evaluation of Powder Blend[42]

a) Angle of Repose

Angle of repose is defined as "the maximum angle possible between the surface of the pile of powder and the horizontal plane." Lower the angle of repose, better the flow properties. The angle of repose may be calculated by measuring the height (h) of the pile and the radius of the base(r) with ruler.

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

b) Bulk Density

Bulk density denotes the total density of the material. It includes the true volume of interparticle spaces and intraparticle pores. The packing of particles is mainly responsible for bulk. Bulk density is defined as:

$$\text{Bulk density} = \frac{\text{Weight of the powder}}{\text{Bulk volume of powder.}} \quad \text{---- (2)}$$

When particles are packed, it is possible that a large amount of gaps may be present between the particles. Therefore, trapping of powder allows the particles to shift and remove the voids to minimum volume. The volume occupied by the powder in this condition represents the bulk volume. Substituting this volume for a given weight of powder in equation (2) gives the bulk density.

C) Percentage Porosity

Whether the powder is porous or nonporous, the total porosity expression for the calculation remains the same. Porosity provides information about hardness, disintegration, total porosity etc.

$$\% \text{ porosity, } \epsilon = \frac{\text{Void volume}}{\text{Bulk volume}} x100 \text{ ---- (3)}$$

$$\% \text{ porosity, } \epsilon = \frac{(\text{Bulk volume-true volume})}{\text{True density x100}} x100 \text{ ----- (4)}$$

2) Evaluation of Floating Tablets

a) Measurement of Buoyancy Capabilities of the FDDS

The floating behavior is evaluated with resultant weight measurements. The experiment is carried out in two different media, deionised water and simulated meal. The results showed that higher molecular weight polymers with slower rate of hydration had enhanced floating behavior and it was observed more in simulated meal medium compared to deionised water.

b) *In Vitro* Floating and Dissolution Behavior

The dissolution tests are generally performed on various drugs using USP dissolution apparatus. USP 28 states "the dosage unit is allowed to sink to the bottom of the vessel before rotation of the blade is started". A small, loose piece of nonreactive material with Not more than a few turns of a wire helix may be attached to the dosage units that would otherwise float. However, standard USP or BP methods have not been shown to be reliable predictors of in vitro performance of floating dosage forms.[43]

Pillay *et al* applied a helical wire sinker to the swellable floating system of theophylline, which is sparingly soluble in water and concluded that the swelling of the system was inhibited by the wire helix and the drug release also slowed down. To overcome this Limitation, a method was developed in which the floating drug delivery system was fully

submerged under a ring or mesh assembly, and an increase in drug release was observed. Also, it was shown that the method was more reproducible and consistent. However, no significant change in the drug release was observed when the proposed method was applied to a swellable floating system of Dilitiazem, which is a highly water-soluble drug. It was thus concluded that the drug release from swellable floating systems was dependent upon uninhibited swelling, surface exposure and the solubility of the drug in water.[44]

c) Weight Variation

In practice, composite samples of tablets (usually 10) are taken and weighed throughout the compression process. The composite weight divided by 10, however provides an average weight but contains a problem of averaged value. To help alleviate this problem, the United States pharmacopeia (USP) provides limits for the permissible variations in the weights of individual tablets expressed as a percentage of the average weight of the sample. The USP provides the weight variation test by weighing 20 tablets individually, calculating the average weight and comparing the individual tablet weights to the average. The tablets meet the USP test if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.[45]

d) Hardness & Friability

Hardness is defined as the "force required to break a tablet in diametric compression test." Hardness is hence, also termed as the tablet crushing strength. Some devices which are used to test hardness are Monsanto tester, strong Cobb tester, Pfizer tester, etc. The laboratory friability tester is known as the Roche Friabilator. This consists of a device which subjects a number of tablets to the combined effects of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm & drop the tablet to a distance of six inches with each revolution. Normally, a pre-weighed tablet sample is placed in the friabilator which is then operated for 100 revolutions. Conventional compressed tablets that lose less than 0.5 to 1.0% of their weight are generally considered acceptable. Most of the effervescent tablets undergo high friability weight losses, which accounts for the special stack packaging that may be required for these types of tablets.[45]

e) Particle Size Analysis, Surface Characterization (for Floating Microspheres and Beads)

The particle size and the size distribution of beads or microspheres are 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).[43]

f) X Ray/Gamma Scintigraphy

X-Ray/Gamma Scintigraphy is a very popular evaluation parameter for floating dosage form nowadays. It helps to locate dosage form in the gastrointestinal tract (GIT), 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 radionuclide in a formulation allows indirect external observation using a γ-camera or scintiscanner. In case of γ-Scintigraphy, the γ-rays emitted by the radionuclide are focused on a camera, which helps to monitor the location of the dosage form in the GIT.[43]

g) Pharmacokinetic Studies

Pharmacokinetic studies are an integral part of the in vivo studies and several works have been reported on these. Sawicki studied the pharmacokinetics of verapamil, from the floating pellets containing drug, filled into a capsule and compared with the conventional verapamil tablets of similar dose (40 mg). The T_{max} and AUC (0- infinity) values (3.75 h and 364.65ng/ml -1h respectively) for floating pellets were comparatively higher than those obtained for the conventional verapamil tablets. (Tmax value 1.21 h and AUC value 224.22 mg/ml-1h).[43]

Applications of Floating Drug Delivery Systems

Floating drug delivery offers several applications for drugs having poor bioavailability because of the narrow absorption window in the upper part of the gastrointestinal tract. It retains the dosage form at the site of absorption and thus enhances the bioavailability. These are summarized as follows.

1. Sustained Drug Delivery

HBS systems can remain in the stomach for long periods and hence can release the drug over a prolonged period of time. The problem of short gastric residence time encountered with an oral CR formulation hence can be overcome with these systems. These systems have a bulk

density of <1 as a result of which they can float on the gastric contents. These systems are relatively large in size and passing from the pyloric opening is prohibited.

Eg. Sustained release floating capsules of Nicardipine hydrochloride were developed and were evaluated in vivo. The formulation compared with commercially available MICARD capsules using rabbits. Plasma concentration time curves showed a longer duration for administration (16 hours) in the sustained release floating capsules as compared with conventional MICARD capsules (8 hours).[46]

2. Site-Specific Drug Delivery

These systems are particularly advantageous for drugs that are specifically absorbed from stomach or the proximal part of the small intestine, e.g., riboflavin and Furosemide.

Eg. Furosemide is primarily absorbed from the stomach followed by the duodenum. It has been reported that a monolithic floating dosage form with prolonged gastric residence time was developed and the bioavailability was increased. AUC obtained with the floating tablets was approximately 1.8 times those of conventional Furosemide tablets.[47]

3. Absorption Enhancement

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.

Eg: A significantly 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%).[48]

Table 1.2: Recent Literature Work Done on Floating Drug Delivery Systems

S.no	Name of the drug	Category	Reason for gastroretentive drug delivery	Technology used	Polymers that enhances the buoyancy	Result	Ref No
1	Tramadol	Analgesic	To improve the controlled drug delivery of drugs and to improve the bioavailability	3^2 central composite design, Effervescent system.	HPMC K-100 LV, CP 971, Carbopol.	HPMC K-LV and carbopol were showed desired floating properties and less floating lag time to attain a desired action of the dosage form	[49]
2	Metronidazloe	Anti Amoebic	To improve local therapy in the gastrointestinal tract, optimize the systemic absorption and minimize the premature drug degradation.	Ionsitol gelation technique, 3^2 full factorial design.	Chitosan, Sodium alginate, α-Carragenum, HPMC E5.	Sodium alginate can be used as gelling agent and HPMC E5 can be used as release retarding agent to achieve the optimum drug delivery	[50]
3	Trimetazidne dihydrochloride	Antianginal drug	To enhance the gastrointestinal transit time and bioavailability	Dry coating technique	HPMC 4000 CPS, Carbopol 971p, polycarbophil, Guar gum	HPMC 15 cps can be used to retard the drug release, sodium bicarbonate can be used as a gas generating agent	[51]
4	Ciprofloxacin	Antibiotic	Prolong the GI transit time to improve the bioavailability	Effervescent system.	MethocelK4M, MethocelK15M, Methocel K-100M	After comparison of various concentrations of methocel the methocel -100M was showed desired duration of floating time in 10 hours and percent drug release.	[52]
5	Cefuroxime Axetil	Antibiotic	To enhance the gastrointestinal absorption of formulation.	3^2 factorial design by direct compression technique.	HPMC K-4M, HPMC K-100LV, SLS.	The ratio of HPMC K-4M to HPMC K-100LV and the content of SLS can be used for optimum floating drug delivery by 3^2 factorial design	[53]
6	Clarithromycin	Antibiotic	To enhance the encapsulation efficiency and particle size.	Emulsion gelation method.	HPMCK100M, Sodium alginate, Sunflower oil.	Sodium alginate can be used as thickening and gelling agent, it was reduced interfacial tension	[54]

						between oil and water phase, HPMC K-100M was used to achieve the controlled release of the drug.	
7	Cefixime	Antibiotic	To increase the gastric residence time and bioavailability	Effervescent system	Xanthan gum, guar gum, crosslinked PVP, Sodium alginate, HPMC K-4M, HEC.	Increased concentration of sodium bicarbonate from 30-60 mg per tablet resulted in the increased floating time & drug release. HPMC K-4M and HEC showed maximum drug released.	[55]
8	Cefuroxime Axetil bilayer tablets	Antibiotic	Prolong the GI transit time to enhance the bioavailability.	Hydrodynamically balanced system.	HPMC K-4M, Sodium bicarbonate, sodium citrate.	HPMC K-4M was the polymer of choice and sodium bicarbonate can be used as a gas generating agent for desired in vitro floating time and dissolution rate	[56]
9	Cefpodoxime proxetil	Antibiotic	To prolong the gastric residence time.	Effervescent system.	Guar gum, HPMC, Carbopol 934-P.	High viscosity HPMC can be used to prolong the drug delivery, carbopol 934-P can be used to avoid the gastric emptying and to achieve the desired floating property.	[57]
10	Cefixime	Antibiotic	To prolong the gastric residence time and improve the bio availability.	Effervescent system.	HPMC K- 4M, Sodium CMC, Carbopol 934.	Sodium bicarbonate can be used as gas generating agent in the presence of 0.1N HCL. The combination of sodium bicarbonate and citric acid provide desired floating time of Cefixime.	[58]
11	Cefuroxime Axetil	Antibiotic	To enhance the gastric transit time and enhance the bio availability	Diffusion and polymer erosion.	HPMC15M, HPMCE5LV, sodium lauryl sulphate, $NaHCO_3$	Sodium bicarbonate can be used as gas generating agent. SLS was used to enhance the solubility. HPMCK 15M, HPMC E 5L V can be used as gel forming agent	[59]

						to obtain a desirable floating drug delivery.	
12	Levofloxacin hemihydrate	Antibiotic	To Enhance the gastrointestinal transit time and bio availability	Effervescent system.	Sodium alginate, sodium bicarbonate, methyl cellulose, potassium bicarbonate.	Pore Volume of sodium bicarbonate was found to be higher than potassium carbonate beads. Hence sodium bicarbonate is having lesser density and more buoyancy, sodium bicarbonate beads shoed faster release and potassium carbonate beads showed sustained release.	[60]
13	Levofloxacin hemihydrate	Antibiotic	To enhance the gastric residence time and bioavailability.	Effervescent system.	HPMC K-4M, Gelucire 43/01. Sodium bicarbonate.	Gelucire 43/01 can be used release retarding agent, HPMC K-4M can be used as matrix agent, sodium bicarbonate was used as gas generating agent for optimum floating drug delivery	[61]
14	Clarithromycin	Antibiotic	To achieve the prolonged and predictable drug delivery profile in the GI tract so as to control the gastric residence time	D-optimal mature design, effervescent system.	HPMCK4M, HPMC K 100 LV, Sodium Carboxy methyl cellulose, NaHCO3	Sodium bicarbonate can be used as a gas generating agent, HPMC K4M, HPMC K 100LV are used to obtain the optimum floating drug delivery	[62]
15	ciprofloxacin	Antibiotic	To prolong the gastric residence time and increase the bioavailability	Effervescent system.	HPMC, Carbomer, NaHCO3.	Sodium bicarbonate can be used as a gas generating agent. Increase the proportion of polymer (HPMC K 4M and Carbomer), was associated with decreased in the overall cumulative drug release.	[63]
16	Cefpodoxime proxeil	Antibiotic	Prolong the gastric residence time and increase the	Effervescent system	HPMC, Carbopol 934p, NaHCO3,	Sodium bicarbonate has predominant effect on the buoyancy lag time. While HPMC	[64]

			bioavailability.		Hydroxypropyl cellulose.	K 100M, HPMC has predominant effect on total floating time and drug release.	
17	Ciprofloxacin	Antibiotic	To increase the stay period of drug in the absorption area and decrease the dosing interval by increasing the bioavailability	Effervescent system	HPMC, Sodium CMC, Carbopol, NaHCO3	Sodium bicarbonate can be used as gas generating agent. HPMC AND sodium CMC can be used to achieve the desired floating drug delivery.	[65]
18	Amoxicillin	Antibiotic	To increase the gastric residence time and enhance the bioavailability.	3^2 factorial design, in-situ gelling system.	Sodium alginate, calcium chloride, sodium citrate, HPMC K100M	Sodium alginate can be used as gelling polymer to sustain release for 10-12 hours with zero order release kinetics and HPMC K 100M is used as thickening agent.	[66]
19	Cefixime	Antibiotic	To prolong the gastric residence time and increase drug absorption and bioavailability	Effervescent system.	HPMC K 4M, NaHCO3, Xanthan gum	15%w/w of HPMC k4M can be used to achieve the optimum floating drug delivery (94.7 ±0.2%) buoyancy was also achieved by effervescent mixture of NaHCO3 and citric acid.	[67]
20	Cephalexin	Antibiotic	To ensure the optimum bioavailability and prolong the gastric retention time.	3^2 factorial design, effervescent system	HPMC K 100 M, citric acid.	High concentration of viscosity polymer induces the formation of strong viscous gel layer that retard the rate of water diffusion into the tablet matrix which resulted in the retardation of drug release.	[68]
21	Clarithromycin	Antibiotic	Prolonged gastric residence time with the desired in-vitro release profile for localized action in the stomach.	Effervescent system.	HPMC K-4M, $NaHCO_3$, Carbopol 934P, Xanthan gum.	HPMC 4 M showed better drug release and floating properties when compared to other polymers,	[69]
22	Amoxicillin	Antibiotic	To obtain a site specific	Effervescent	HPMC K-100M,	Sodium bicarbonate can be used	[70]

	trihydrate		drug delivery for stomach and to extend its duration of action.	system.	HPMC K-15M, sodium bicarbonate.	as gas generating agent, HPMC K-4M and HPMC-K 100M, retarded drug release to attain desired floating drug delivery.	
23	Cefpodoxime proxetil	Antibiotic	To increase the gastric residence time.	Effervescent system and hydrodynamically balanced system.	HPMC K-4M, HPMC K-15M, HPMC K-100M, $NaHCO_3$.	HPMC K 4M show better controlled release and floating properties compared with other HPMC grades.	[71]
24	Ciprofloxacin	Antibiotic	To prolong the gastric residence time of the drug and enhance bioavailability	Effervescent system	HPMC K -4M, Ethyl cellulose, $NaHCO_3$	$NaHCO_3$ can be used as gas generating agent. Ethyl cellulose can be used to enhance the floating property.	[72]
25	Oflaxcin	Antibiotic	To Increase the gastric retention time of dosage form and enhance the bioavailability	Effervescent system.	Poly ehyleneoxide, sodium bicarbonate, gumkaraya.	The addition of sodium bicarbonate as gas generating agent to achieve the in-vitro buoyancy, poly ethylene oxide and gum karaya are suitable polymers to achieve the desired floating drug delivery.	[73]
26	Norfloxacin	Antibiotic	To prolong the gastric residence time and to increase the bioavailability.	Effervescent system, wet granulation technique.	HPMC K-4M, HPMC K-100M, Xanthan gum.	HPMC K-4M and HPMC K-100M has good floating properties and less floating lag time.	[74]
27	Oflaxcin	Antibiotic	To prolong the gastric residence time and increase bioavailability.	Effervescent system.	HPMC K-100M, locust bean gum, sodium bicarbonate.	Increase in the HPMC K-100M concentration will decrease the floating lag time.	[75]
28	Ciprofloxacin	Antibiotic	To prolong the gastric residence time and to increase the bioavailability.	Effervescent system.	HPMC K-100M, cross povidone, sodium bicarbonate, sodium starch Glycolate.	HPMC K- 100M grade can show optimum swelling properties and floating properties than other HPMC grades. Cross povidone resulted in good swelling and floating drug delivery systems.	[76]

29	Carbamzepine	Anti convulsant	To improve the gastrointestinal transit time and bioavailability	Effervescent system.	HPMC K-4M, Ethyl cellulose, sodium bicarbonate.	HPMC is used as a matrix agent, and sodium bicarbonate is a gas generating agent and ethyl cellulose is act as a floating enhancer.	[77]
30	5-Flurouracil	Anti cancer	To enhance the gastrointestinal transit time and bioavailability.	Effervescent system.	HPMC4M, HPMCKV600, HPMCK50, PEG 6000, $NaHCO_3$.	Sodium bicarbonate used as gas generating agent, HPMC K4M, HPMCKV600, HPMCK50 used as gel forming agents.	[78]
31	Metformin HCL	Ant diabetic	To prolong the gastric residence time and enhance the bioavailability.	Non aqueous emulsification solvent evaporation.	Petroleum ether, ethyl cellulose.	Microspheres having low density are suitable for prolong the gastric residence time and bioavailability.	[79]
32	Repaglinide	Antidiabetic	To increase the gastric residence time and bioavailability of the drug.	Emulsion Solvent diffusion technique.	Calcium silicate, Eudragit S.	Calcium silicate based floating microspheres showed good controlled release of oral administration of Repaglinide when compared with the Eudragit S.	[80]
33	Glipizide	Antidiabetic	To increase the bioavailability and reduction in dosing frequency.	Hydrodynamic ally balanced system, 2^3 factorial design.	HPMC, methyl cellulose, ethyl cellulose.	Methyl cellulose can be used for binding property and HPMC is used for imparting the floating property o he dosage form.	[81]
34	Metformin HCL (sodium alginate beads)	Antidiabetic	To improve the bioavailability, to prolong the gastric residence time.	Ionotropic gelation technique, 3^2 factorial design.	HPMC E-50, Ethyl cellulose, Calcium alginate.	Sodium bicarbonate can be used as a gas forming agent, ethyl cellulose and calcium chloride as gelling agent.	[82]
35	Glipizide	Antidiabetic	To increase the bioavailability and reduction in dosing frequency.	Effervescent system.	Carbopol-940p, Sodium bicarbonate, Citric acid.	Sodium bicarbonate used as gas generating agent and carbopol was used to formulate the matrix system for optimum floating drug delivery,	[83]

36	Domperidone	Antiemetic	To prolong the gastrointestinal time and enhance the bioavailability.	Effervescent system.	Polyethylene oxide, HPMC K-15M, Sodium bicarbonate.	HPMC can be used as a gelling agent and polyethylene oxide was selected as matrix agent and sodium bicarbonate was used as a gas generating agent for optimum controlled release.	[84]
37	Carbamzepine	Antiepileptic	To prolong the gastric residence time and to increase bioavailability.	Effervescent system and simple lattice design.	HPMC K-4M, Ethyl cellulose, Sodium bicarbonate.	HPMC K-4M can be used as matrix agent, it has excellent gelling activity and ethyl cellulose can be used as floating enhancer.	[85]
38	Itopride	Antiemetic	To prolong the gastric residence time and bioavailability.	Effervescent system.	HPMC K-100M, HPMC K- 15M, Carbopol 934P, sodium bicarbonate.	Carbopol 934P along with HPMC K-15 M and HPMC K-100 M showed better result when compared with carbopol 934P alone, Sodium bicarbonate can be used as a gas generating agent.	[86]
39	Domperidone	Antiemetic	To prolong the gastric residence time and enhance the drug bioavailability.	Effervescent system.	HPMC K-4M, Carbopol 934P, Sodium alginate.	HPMC K-4M and carbopol 934P, and sodium alginate exhibit desired floating and prolonged release.	[87]
40	Captopril	Anti hypertensive	To improve the gastric residence time and bioavailability.	Effervescent system.	HPMC K-100M, HPMC K-15M, HPMC K-4M.	Tablets having low viscosity HPMC swell more rapidly than tablets with high viscosity HPMC to achieve the desired floating property.	[88]
41	Diltiazem	Anti hypertensive	To prolong the gastric residence time and improve bioavailability	Effervescent system.	Methocel K-100M, compritol888, Sodium bicarbonate.	Methocel K-100M can be used as gel forming agent and sodium bicarbonate is a gas generating agent. And compritol 888 can be used as floating controlled release polymer.	[89]
42	Nitrendepine	Anti	To prolong the gastric	Emulsion solvent	Ethyl cellulose,	The gastric residence time of	[90]

		hypertensive.	residence time and increase the oral bioavailability.	diffusion method.	Anhydrous Silicic acid (aerosil), polyvinyl alcohol.	microballons of Nitrendepine was over 5hrs when compared to the non-floating microspheres.	
43	Nimodipine	Anti hypertensive	To enhance the solubility and dissolution rate and prolong the gastric residence time.	Effervescent system.	Methocel K-4M, Methocel K-15M, Eudragit RSPO, HPMC E-15.	HPMC can be used as swellable polymer and Eudragit RSPO can be used as drug release retarding agent.	[91]
44	Diltiazem HCL	Anti hypertensive	To prolong the gastric residence time and improve the bioavailability.	Melt granulation.	HPMC K-4M, Ethyl cellulose, gelucire 43/01.	Gelucire 43/01 can be used as carrier for design of multi-unit floating drug delivery system like Dilitiazem and ethyl cellulose can be used to enhance the floating time.	[92]
45	Propranlol	Anti hypertensive	To prolong the gastric residence time and to improve the bioavailability.	Gas formation technique.	HPMC K-15M, Dicalcium phosphate, Sodium CMC, Carbopol 934P.	HPMC can be used as floating polymer and reduction Dicalcium phosphate concentration is found to be optimum for floating delivery	[93]
46	Verapamil	Anti hypertensive	To enhance the elimination half life and to prolong gastric residence time.	3^2 factorial design, response surface methodology, effervescent system.	HPMC K-15M, carbopol 934.	HPMC K-15m and carbopol 934 can be used as gel forming agent and sodium bicarbonate can be used as gas generating agent.	[94]
47	Propronolol HCL microballons	Anti hypertensive	To prolong the gastrointestinal time and enhance the bioavailability.	Solvent evaporation technique.	Eudragit S-100, Calcium silicate, Polyvinyl alcohol.	The microballons containing calcium silicate were showed better floating drug delivery systems than Eudragit S-100 microballons.	[95]
48	Atenolol	Anti hypertensive	To enhance the bioavailability and to improve the gastric residence time.	Effervescent system.	HPMC K-4M, HPMC K-100M, Guar gum, Xanthan gum.	HPMC K-4M can be used as gel forming agent, natural polymer and sodium bicarbonate can be used as gas generating agent.	[96]

49	Metoprolol	Anti hypertensive	To improve the oral bioavailability of the drug and prolong the gastric residence time.	2^3 factorial design.	HPMC K-4M, HPMC K-10M, Carbopol 934P, Sodium Carboxy methyl cellulose.	HPMC K-4M, HPMC K-10M can be used as swellable polymer and sodium CMC is a swellable polymer.	[97]
50	Captopril	Anti hypertensive.	To improve the oral bioavailability of the drug and prolong the gastric residence time.	Gas formation technique.	Eudragit RL 30D, RS 30D, $NaHCO_3$	$NaHCO_3$ can be used as a gas generating agent and Eudragit RL 30D, RS 30D enhance the floating property.	[98]
51	Cinnarizine	Anti histamine.	To enhance the gastric transit time and bioavailability.	3^2 full factorial design, in-situ gelling suspension.	Sodium alginate, Polysorbate 80, Sodium citrate, Calcium carbonate.	Polysorbate 80 can be used as wetting agent and sodium citrate outside the gastric environment to obtain a desirable floating drug delivery.	[99]
52	Labetalol	Anti Hypertensive	To improve the bioavailability and patient compliance and to increase the gastric residence time.	Simplex centroid design, effervescent system.	HPMC K-M, Carbopol 934P, Sodium Carboxy methyl cellulose, $NaHCO_3$.	HPMC K4M can be used as gel forming polymer and sodium bicarbonate can be used as gas generating agent.	[100]
53	Verapamil	Anti hypertensive	To increase the gastric retention time and control the drug release from the dosage form.	Effervescent system.	HPMC, Carbopol, Xanthan gum, $NaHCO_3$	Sodium bicarbonate can used as to achieve the optimum buoyancy and HPMC, carbopol and Xanthan gum can be used as gelling agent.	[101]
54	Captopril	Anti hypertensive	To enhance the bioavailability and to improve the gastric residence time.	Hydrodynamically balanced system.	HPMC K 15M, PVPK 30, Carbopol 934P, $NaHCO_3$.	Carbopol 934P acts as physical barrier to drug release. Increased in polymer concentration resulted in optimum floating drug delivery.	[102]
55	Atenolol	Anti hypertensive	To increase the gastric residence time and to increase the drug bioavailability.	Effervescent system.	Guar gum, Sodium alginate, HPMC 100 CPS, Carbopol 940	Among the four polymers sodium alginate showed the best result to achieve the optimum floating drug delivery.	[103]

56	Metoprolol succinate	Anti hypertensive	To increase the gastric residence time and to improve the bioavailability.	Effervescent system	HPMC K-4M, HPMCK15M, Sodium CMC, Carbopol 934P.	HPMC K-4M shoed best swelling nature when compared with other polymers, maximum drug is released is observed in formulation containing sodium CMC.	[104]
57	Atenolol	Anti hypertensive	To prolong the gastric residence time and to improve bioavailability.	Effervescent system.	Xanthan gum, HPMC K-4M, HPMC K-100M, Dica. Phosphate.	Dicalcium phosphate is a channeling agent and HPMC K-4M and HPMC K-100M, Xanthan gum retarded release	[105]
58	Metoprolol tartrate.	Anti hypertensive	To prolong the gastric residence time and to improve the bioavailability.	3^2 full factorial design, pulsatile system.	HPMC E-5, HPMC E-15, HPMC E-50, HPMC K-15M.	A chronotherapy based floating pulsatile release tablet of matrix tablet was successfully developed to achieve the optimum floating drug delivery.	[106]
59	Propronolol	Anti hypertensive	To improve the bioavailability and to improve the gastric residence time.	Effervescent system	HPMC K-4M, HPMC – E 15 LV, Xanthan gum, Sodium alginate.	Tablets formulated with HPMC and sodium alginate, HPMC E-15 LV failed to produce matrix of required strength, where as formulation containing Xanthan gum showed good drug retaining abilities but floating tablets were found to be poor.	[107]
60	Atorvastatin	Anti lipidemic	To prolong the gastric residence time and to improve the bioavailability.	Melt granulation technique.	HPMC K-4M, Ethyl cellulose, sodium bicarbonate.	Ethyl cellulose can be used to enhance the floating property, and sodium bicarbonate can be used as gas generating agent.	[108]
61	Orlistat	Anti obesity	To prolong the gastric residence time and to enhance the elimination half life.	Solvent evaporation system, emulsion solvent diffusion technique.	Eudragit –S, Calcium silicate, polyvinyl alcohol.	Calcium silicate based floating microspheres showed better release when compared with the Eudragit-S for optimum floating drug delivery.	[109]
62	Dipyridamole	Anti- platelet	To prolong the gastric	Effervescent	Methocel K-4M,	HPMC can be used as matrix	[110]

		drug	residence time and to improve the bioavailability.	system.	Methocel K-15M, Methocel K-100M.	forming material. Content of HPMC plays an important role in drug release initially and in the later phase viscosity of HPMC is important for the release of drug.	
63	Fenoverine	Anti spasmodic	To maintain a constant plasma concentration and enhance the gastric residence time.	Effervescent system.	HPMC K-4M, HPMC 100 LV, $NaHCO_3$.	HPMC K-4M, HPMC 100 LV can be used to obtain a desirable buoyancy property and sodium bicarbonate can be used as a gas generating agent.	[111]
64	Tizanizide	Anti spastic (muscle relaxant)	To prolong the gastric residence time and overcome its low bioavailability.	Effervescent system.	HPMC K-4M, HPMC K-15M, HPMC K-100M.	The optimized formulation of F-9 containing high concentration of HPMC K-15M showed excellent buoyant ability and suitable drug release pattern. This is helpful for improve bio availability.	[112]
65	Famotidine	Anti ulcer	To increase the gastro intestinal transit time and enhance the bioavailability.	Solvent evaporation method	Eudragit L-100, PEG 6000.	Eudragit L-100 microspheres can be used to enhance the floating property and PEG 6000 can used as pore forming agent.	[113]
66	Ranitidine	Anti ulcer	To enhance the bioavailability and increasing the gastric residence time of a drug.	3^2 full factorial design, effervescent system.	Guar gum, Xanthan gum, HPMC K-4M.	Guar gum and Xanthan gum and HPMC K-4M can be used to achieve the optimum floating drug delivery and sodium bicarbonate can be used as gas generating agent.	[114]
67	Famotidine	Anti ulcer	To enhance the bioavailability and prolong the gastric residence time.	Effervescent system.	HPMC K-100 LV, HPMC K-4MCR, $NaHCO_3$.	HPMC K-100 LV and HPMC K-4MCR can be used to attain a better control release; $NaHCO_3$ used to achieve the desired in-vitro buoyancy.	[115]
68	Ranitidine hydrochloride	Anti ulcer	To enhance the gastric residence time and	Melt granulation, 3^2 factorial design.	Ethyl cellulose, Methyl cellulose,	Compritol was able to float the granules more than 12 hours,	[116]

			bioavailability.		HPMC, Compritol.	ethyl cellulose can be used to enhance the floating property and low viscosity grade HPMC is suitable for optimum drug delivery.	
69	Famotidine	Antiulcer	To improve the gastric residence time of drug and enhance the bioavailability.	Effervescent system.	HPMC K-100M, HPMC K-15M.	HPMC K-100M was found to float longer duration when compared to HPMC K-15M. NaHCO3 can be used to get a desired in vitro buoyancy of famotidine.	[117]
70	Famotidine	Anti ulcer	To achieve the optimum gastric residence time and enhance bioavailability.	Effervescent system.	Chitosan, Xanthan gum, $NaHCO_{3.}$	Sodium bicarbonate can be used as gas generating agent and chitosan; Xanthan gum can be used as to obtain a desirable floating property.	[118]
71	Famotidine	Anti ulcer	To prolong the gastro intestinal residence time and to improve the bioavailability.	Effervescent system.	HPMC K4M, HPMC K100M, $NaHCO_3$, Citric acid.	Citric acid and sodium bicarbonate can be used as gas generating agent. HPMCK4M and HPMCK100M can be used as gel forming agents to achieve optimum buoyancy.	[119]
72	Lansoprazole	Anti ulcer	To improve bio availability and enhance the gastric residence time.	Effervescent system.	Chitosan, HPMCK4M, $NaHCO_{3.}$	Viscosity of HPMCK4M is responsible for slow release of drug from the tablet. Chitosan can be used to improve the floating time of tablets. Sodium bicarbonate can be used as gas generating agent.	[120]
73	Famotidine	Anti ulcer	To enhance the gastric residence time and to improve the bio availability.	Direct compression technique, effervescent	Poly propylene, HPMCE4, HPC, Xylo glucan, Gellan gum.	Polypropylene foam powder was incorporated into the tablets to get an optimum floating delivery. HPMC E4, HPC can be used as	[121]

				system.		gelling agents.	
74	Famotidine	Anti ulcer	To prolong the gastric residence time and increase the bioavailability.	Emulsion gelation method.	Sodium alginate, carbopol 934P, HPMC K-15M.	Sodium alginate alone could not sustain drug release for sufficient period of time where as incorporation of rate controlled polymers such as carbopol 934P and HPMC sustained drug release from beads for more time.	[122]
75	Ranitidine	Anti ulcer	To prolong the gastric residence time and to improve the bio availability.	Effervescent system.	HPMC K4M, Carbopol 934P.	The tablets prepared by HPMC K4M and carbopol 934P to prolong the gastric residence time and bioavailability of ranitidine drug release was found to be follow zero order kinetics.	[123]
76	Ranitidine	Anti ulcer	To increase the gastric residence time and to improve the bio Availability.	Effervescent system.	Methocel K15M, Methocel K 100M, PVP K-30.	The tablets with methocel K 100M, were found to be float longer duration of time as compared to the formulation containing the methocel K-15M, combination of citric acid and sodium bicarbonate was found to be achieve the optimum in-vitro buoyancy.	[124]
77	Acyclovir	Anti viral	To enhance he bioavailability and to prolong the gastric residence time.	3^2 full factorial design, effervescent system.	HPMC K-4M, Sodium bicarbonate, PVP-K30.	Sodium bicarbonate can be used as gas generating agent. The tablets were prepared with HPMC K-4M to produce a good gel strength entrapping carbon dioxide gas and impart stable buoyancy.	[125]
78	Acyclovir	Anti viral	To prolong the gastric residence time and to improve the	Effervescent system.	$CaCO_3$, HPMC, Chitosan,	Sodium alginate solution containing CaCO3 used as gas generating agent, chitosan can	[126]

			bioavailability.		Sodium alginate.	used as to improve the floating floating property.	
79	Acyclovir	Anti viral	To prolong the gastric residence time and to improve the bio availability.	Effervescent system.	HPMC K-100M, HPMC K-15M.	HPMC K-100M and HPMC K-15M can be used as gel forming agents. Sodium bicarbonate and citric acid as gas generating agents for desired in –vitro floating time and dissolution rate.	[127]
80	Salbutamol	bronchodilator	To prolong the gastrointestinal transit time and enhance the bioavailability.	Effervescent system.	HPMCK-100M, Microcrystalline cellulose, sodium bicarbonate, citric acid.	HPMC K-100M can be used as gel forming agent and sodium bicarbonate can be used as gas generating agent.	[128]
81	Theophylline	Bronchodilator	To improve the bioavailability and to prolong the gastric residence time.	Effervescent system.	HPMC K-4M, HPMC K-15M, HPC, carbopol 934 P.	Carbopol 934 can be used as retard the drug release. HPMC K-4M, showed floating time to better release when compared with other polymers.	[129]
82	Salbutamol sulphate	Bronchodilator	To control the gastric residence time of drug delivery.	3^2 full factorial design, effervescent system.	HPMC K-4M, HPMC K-100M, Sodium bicarbonate, Polyvinyl Pyrrolidone.	Sodium bicarbonate can be used as gas generating agent. The combination of sodium bicarbonate, HPMC, stearic acid can be used to increase the gastric residence time.	[130]
83	Theophylline	Bronchodilator	To achieve the in vitro buoyancy and enhance the bioavailability.	3^2 factorial design, Effervescent system.	Poly ethylene oxide.	The addition of gel forming polymer poly ethylene oxide and gas generating agent sodium bicarbonate was essential to achieve the optimum floating drug delivery.	[131]
84	Furosemide	Diuretic	To improve the gastrointestinal transit time and bioavailability.	3^2 full factorial design, Effervescent	HPMC K-4M, HPMC K-100M.	Lowest viscosity grade of HPMC K-4M is suitable for desired in-vitro floating drug delivery,	[132]

				system.		sodium bicarbonate can be used as gas generating agent.	
85	Zolpidem tartrate	Hypnotic sedative.	To prolong the gastric residence time and to improve bioavailability.	Gas formation technique.	HPMC 5CPS, low substituted HPC, Eudragit NE 30D	Eudragit NE 30D and sodium bicarbonate can be used as effervescent agent for desired in vitro floating drug delivery.	[133]
86	Tizanizide	Muscle relaxant	To prolong the gastric residence time and to enhance the bioavailability.	Effervescent system.	HPMC K-4M, HPMC K-15M, HPMC K-100M.	HPMC K-100M can be used for desirable floating drug delivery when compared with the HPMC K-4M and HPMC K-15M.	[134]
87	Aceclofenac	NSAID	To improve the bioavailability and to prolong the gastric residence time.	Effervescent system.	HPMC – E5M, Eudragit, PVP K-30.	In the case of HPMC, as the concentration is increased harden the tablet is increased and in the case of Eudragit decreased hardness of tablet, both polymers are used to get the desired dissolution rate.	[135]
88	Ketorolac	NSAID	To improve the bioavailability and increasing gastric residence time in the stomach.	Emulsion solvent diffusion method.	Eudragit F 100, Eudragit S 100, Ethyl cellulose, HPMC K 4M.	Ethyl cellulose and HPMC K4M based microspheres showed grater buoyancy when compared with only ethyl cellulose base microspheres.	[136]
89	Nimesulide	NSAID	To increase the bioavailability by increasing the residence time in the stomach.	Effervescent system.	HPMC, Guar gum, Carbopol, $NaHCO_3$.	Tablets prepared with the HPMC showed best drug release. Sodium bicarbonate can be used as a gas generating agent.	[137]
90	Loraxicam	NSAID	To improve the bioavailability and to prolong the gastric residence time.	Effervescent system.	HPMC K-15M, Calcium carbonate.	HPMC K-15M and calcium carbonate can be used as buoyancy initiator to achieve the optimum floating drug delivery of dosage form.	[138]
91	Tramadol	Opioid analgesic	To prolong the gastric residence time and	3^2 full factorial design,	HPMC K-4M, HPC, $NaHCO_3$.	HPMC and HPC can be used to achieve the optimum floating	[139]

			improve the bioavailability.	effervescent system.		ability.	
92	Baclofen	Skeletal muscle relaxant	To increase the residence time of drug in stomach and thereby increase the absorption.	3^2 full factorial design, In-situ gelling system.	Sodium alginate, Calcium bicarbonate.	Calcium bicarbonate can be used to increase the duration of floating time. Sodium alginate can be used for optimum floating drug delivery.	[140]

REFERENCES

1. Hirtz J, The Gut Absorption of Drugs in Man, A Review of Current Concepts and Methods of Investigation, Br J Clin Pharmacol, 1985; 19: 77S-83S.
2. Ponchel G, Irache JM, Specific and Non-Specific Bioadhesive Particulate System for Oral Drug Delivery to the Gastrointestinal Tract, Adv Drug Del Rev, 1998; 34: 191-219.
3. Deshpande AA, Shah NH, Rhodes CT, Malick W, Development of A Novel Controlled-Release System for Gastric Retention, Pharm Res, 1997; 14: 815-819.
4. 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: 208-213.
5. 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: 1087-1089.
6. Groning R, Heun G, Oral Dosage Forms With Controlled Gastrointestinal Transit, Drug Dev Ind Pharm, 1984; 10: 527-539.
7. Groning R, Heun G, Dosage Forms with Controlled Gastrointestinal Passage-Studies on the Absorption of Nitrofurantion, Int J Pharm, 1989; 56: 111-116.
8. Wilson CG, Washington N, The Stomach: It's Role in Oral Drug Delivery, 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 Delivery System Based on A Dried Gel Matrix Network [Master's Thesis], Jamaica, NY: St John's University, 1984.
10. Davis SS, Stockwell AF, Taylor MJ, The Effect of Density on the Gastric Emptying of Single- and Multiple- Unit Dosage Forms, Pharm Res, 1986; 3: 208-213.
11. Desai S, Bolton S, A Floating Controlled Release Drug Delivery System, *In Vitro- In Vivo* Evaluation. Pharm Res, 1993; 10: 1321Y1325.
12. Oth M, Franze M, Timmermans J, And Moes A, The Bilayer-Floating Capsule, A Stomach Directed Drug Delivery System For Misoprostal, Pharm Res, 1992; 9: 298-302.
13. Timmermans J, Gasnsbeka BV, Moes A, Accessing By Gammascintigraphy 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.

14. Gergogiannis YS, Rekkas DM, Dallos PP, Chailis NH, Floating and Swelling Characteristics of Various Excipients Used In Controlled Release Technology, Drug Dev Ind Pharm, 1993; 19: 1061-1081.
15. 15.Cargill R, Cadwell LJ, Engle K, Fix JA, Porter PA, Gardner CR, 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.
16. Li S, Lin S, Daggy BP, Mirchandani HL, Chien YW, Effect of HPMC and Carbopol on The Release and Floating Properties of Gastric Floating Drug Delivery System Using Factorial Design, Int J Pharm, 2003; 253: 13-22.
17. Patel GM, Floating Drug Delivery System: An Innovative Approach to Prolong Gastric Retention, Www.Pharmainfo.Net, 2007.
18. Mojaverian P, Vlasses PH, Kellner PE, Rocci ML, Effects of Gender, Posture and Age on Gastric Residence Time of Indigestible Solid, Pharmaceutical Considerations, Pharm Res, 1988; 10: 639-664.
19. Timmermans J, Moes AJ, Factors Controlling the Buoyancy and Gastric Retention Capabilities of Floating Matrix Capsules, New Data for Reconsidering the Controversy Pharm Sci, 1994; 83: 18-24.
20. 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.
21. 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.
22. Babu VBM, Khar RK, *In Vitro* And *In Vivo* Studies of Sustained Release Floating Dosage Forms Containing Salbutamol Sulphate, Pharmazie, 1990; 45: 268-270.
23. Hetal N Kikani, A Thesis on Floating Drug Delivery System, The North Gujarat University, Patan, 2000; 11-12.
24. Rubinstein A, Friend DR. Specific Delivery to the Gastrointestinal Tract, In: Domb A.J (Ed.), Polymeric Site-Specific Pharmacotherapy, Wiley, Chichester, 1994; 282-283.
25. Penners G, Lustig K, Jorg PVG. Expandable Pharmaceutical Forms.US Patent, 1997; 5: 651,985.
26. Jaimini M, Rana AC, Tanwar YS, Formulation and Evaluation of Famotidine Floating Tablets, Current Drug Delivery, 2007; 4: 51-55.
27. Innuccelli V, Coppi G, Bernabei M T, Cameroni R, Air Compartment Multiple-Unit System For Prolonged Gastric Residence,. Int. J. Pharm, 1998; 174: 47-54.

28. 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 Bao, 1997; 32: 786-790.
29. Ichikawa M, Watanabe S, Miyake Y, A New Multiple Unit Oral Floating Dosage System, Preparation and *In Vitro* Evaluation of Floating and Sustained-Release Kinetics, Pharm Sci, 1991; 80: 1062- 1066.
30. Chen GL, Hao WH, *In Vitro* Performance of Floating Sustained Release Capsule of Verapamil. Drug Dev Ind. Pharm, 1998; 24(11): 1067-1072.
31. Arora S, Ali J, Ahuja A, Khar KR, Baboota S, Floating Drug Delivery Systems, A Review. AAPS Pharm. Sci. Tech, 2005; 6(3): Article 47.
32. Thanoo BC, Sunny MC, Jayakrishnan A, Oral Sustained Release Drug Delivery Systems Using Polycarbonate Microspheres Capable of Floating on the Gastric Fluids, J. Pharm. Pharmacol, 1993; 45: 21-24.
33. Sheth PR, Tossounian JL, Sustained Release Pharmaceutical Capsules, US Patent, 1978; 4: 126,672.
34. Joseph NH, Laxmi S, Jayakrishnan A, A Floating Type Oral Dosage Form For Piroxicam Based on Hollow Microspheres, *In Vitro* And *In Vivo* Evaluation In Rabbits, J. Cont. Rel, 2002; 79: 71-79.
35. Jorgen F, Toftkjor H, Antacid Composition.US Patent 50681095, 14: 815.
36. Yang L, Fassihi R, Zero Order Release Kinetics from Self Correcting Floatable Configuration Drug Delivery System, J Pharm Sci, 1996; 85: 170-173.
37. Deshpande AA, Shah NH, Rhodes CT, Malick W, Development of A Novel Controlled-Release System for Gastric Retention, Pharm Res, 1997; 14: 815-819.
38. Burns SJ, Attwood D, Barnwell SG, Assement of A Dissolution Vessel Designed For Use With Floating and Erodible Dosage Forms, Int J Pharm, 1998; 160: 213-218.
39. Joseph NJ, Laxmi S, Jayakrishnan A, A Floating Type Oral Dosage Form For Piroxicam Based On Hollow Microspheres, *In Vitro* And *In Vivo* Evaluation In Rabbits, J Control Release, 2002; 79: 71-79.
40. Soppimath KS, Kulkarni AR, Rudzinski WE, Aminabhavi TM, Microspheres As Floating Drug Delivery System To Increase The Gastric Residence Of Drug, Drug Metab Rev, 2001; 33: 149-160.
41. Patel GM, Floating Drug Delivery System, An Innovative Approach To Prolong Gastric Retention. 2007 Feb.

42. Subrahmanyam CVS, Setty JT. Laboratory Manual of Physical Pharmaceutics, Jain MK For Vallabh Prakashan, 2002.
43. Shah SH, Patel JK, Patel NV. Stomach Specific Floating Drug Delivery System: A Review, Int. J. Pharm. Res, CODEN (USA): IJPRIF ISSN: 0974-4304. 2009; 3: 623-633.
44. Pillay, Shinde AKJ. Gastroretentive Drug Delivery System: An Overview. 2008; 13: 543-548.
45. Koner P, Saudagar RB and Daharwal SJ, Gastro-Retentive Drugs: A Novel Approach Towards Floating Therapy, 2007; 5(1): 2211-2215.
46. Fell J T, Whitehead L, Collet H, Prolonged Gastric Trtention Using Floating Dosage Forms, Pharm Technol. 2000; 24(3): 82-90.
47. Moursy NM, Afifi NH, Ghorab DM, El-Saharty Y, Formulation and Evaluation of Sustained Release Floating Capsules Of Nicardipine Hydrochloride, Pharmazie, 2003; 58: 38-43.
48. Menon A, Ritschel WA, Sakr A, Development and Evaluation of A Monolithic Floating Dosage Form For Furosemide, J Pharm Sci. 1994; 83: 239-245.
49. Bupindre Singh, Ashu Rani, Babitha, Naveen Ahuja, Rishi Kapil, Formulation Optimization of Hydrodynamically Balanced Oral Controlled Release Bioadhesive Tablets Of Tramadol Hydrochloride, Scientia Pharmacentica, April 2010; 78: 303-323.
50. Shasikanth D. Bharate, Madurabai, M.Patel, Rahul V.Deshmukh, Pradeep, K.Nimase, Formulation and Evaluation of Controlled Release Metronidazloe Loaded Floating Alginate Beads Using Natural Polymers, Journal of Pharmacy Research, Mar 2009; 2(3): 524-527.
51. Ahmed Abdelbary, Omaima N.ei-Gazayerly, nashwa A.El-Gendy, Adel A.Ali, Floating Tablets For Trimetazidine Dihydrochloride: An Approach For Extended Release With Zero Other Kinetics, AAPS Pharma Scitech, Sep 2010; 11(3): 1058-1067.
52. Bhalchandra M.Habade, Vidyasri Kambe, R.Ramesh, Millind, P.Wagh, Formulation and Evaluation of Folating Drug Delivery Systems of Ciprofloxacin International Journal of Pharmaceutical Research and Development, January 2012; 3(11): 32-40.
53. Viral F.Patel, Natavarlal M.pael, Intragastric Floating Drug Delivery System of Cefuroxime Axetil: *In-Vitro* Evaluation, AAPS Pharma Scitech, 2006 Feb 26; 7(1): 1-7.
54. Pradeep Kishan Nimase, Vidyasagar Gali, Prasant Jalandar Ghule, Preparation and Evaluation of Multiple Unit Floating Drug Delivery System of Clarithromycin,

International Journal of Pharma Research & Development, November 2010; 2(9): 139-145.

55. Raghavendra Rao NG, Pentewar Ram, Thube Ketan, Suryakar VB, Formulation and *In-Vitro* Evalation Of Gastric Oral Floating Tablets of Cefixime For Controlled Release, Research Journal Of Pharmaceutical, Biological And Chemical Sciences, July-Sep, 2010; 1(3): 141-154.
56. Ravindra S Dhumal, Samitkumar T. Rajmana, Sanjay T Dhumal and Atmaram P Paw, Design and Evaluation of Bilayered Floating Tablets of Cefuroxime Axetil For Bimodal Release, Journal of Scientific And Industrial Research, October 2006; 65: 812-816.
57. K.Sreenivasa Rao, Rakash R.Vairagkar, Dattatreya B.Udgirkar, Praveen S.Patel, Karna Kumar V.Biarder, Gastro Retentive Floating Matrix Tablets of Cefodoxime Proxetil, International Journal of Research in Pharmacy and Chemistry, Dec 2012; 2(1): 190-194.
58. N.G. Raghavendra Rao, Harish A Panchal And Pentewar Ram, Formulation and *In-Vitro* Evaluation of Gastro Retentive Drug Delivery System of Cefixime For Prolonged Release, Der Pharmacia Sincia, 2011; 2(2): 236-248.
59. R.K. Kar, S.Mohapatra, D.Mohapatra, R.K. Dash, B.B. Barik, Preparation and *In-Vitro* Characterization of Cefuroxime Axetil Loaded Gastro Retentive Tablets, Drug Invention Today, 2010; 2(10): 457-459.
60. Vibha Krishnan, S.Sai Sasi Kumar, Febin Prabhudass, R.Vijayaraghavan, Effect of Pore Forming Agents on The Physical Characteristics And Release Kinetics of Levofloxacin Hemihydrates From Floating Alginate Drug Delivery System-An *In-Vitro* Study, Trends Biomater, Artif. Organs, 2010; 24(3): 139-145.
61. V.T.Thakkar, P.A. Shah, T.G Soni, M.Y. Parmar, M.C.Gohel, T.R. Gandhi, Goodness of Fit Model Dependent Approach For Release Kinetics of Levofloxacin Hemihydrates Floating Tablet, Dissolution Technologies, Feb 2009; 35-39.
62. Shasikanth D.Bharate, Madura Bai, M.Patel, Amol B, Patil, Sandeep R.Pawar, Sumit, R.Rathi, Formulation and Optimization of Controlled Released Floating Tablets of Clarithromycin, Joural of Pharmacy Reasearch, Mar 2009; 2(3): 445-448.
63. Ajay Bhagheawal, Dinesh Kumar Patidar, Pradeep Sharma, Studies on Formulation and Evalation of Floating Tablets of Ciprofloxacin HCL, International Journal of Comprehensive Pharmacy, 2010; 1(5): 1-4.
64. SN Borkar, R.Suresh, VA Sawant, VS Shende, VJ Mokale, G. Dama, An Approach To Formulate Bilayered Gastro Retentive Floating Drug Delivery System of Cefpodoxime Proxetil, International Journal of Chem Tech Research, June 2010; 2(2): 1229-1242.

65. Mukhopadyay S, Goswami L, Satheesh Madhav, Uppadyaya K, Formulation and Evaluation of Floating Tablets of Ciprofloxacin HCL, International Journal of Comprehensive Pharmacy, 2010; 1(5): 1-4.
66. Dasarath M.Patel, Divyesh K.Patel, Chhagan N.patel, Formulation and Evaluation of Floating Oral Insitu Gelling System of Amoxicillin, International Scholarly Research Network, 2011; 1-8.
67. Yash Paul, Manoj Kumar, Bupinder Singh, Formulation, Evaluation and Study Of Effect Of Hydrochloride Polymers on Release Rate of Cefixime Floating Tablets, International Journal of Pharma and Biosciences, Oct-Dec 2011; 2(4): 472-488.
68. Anil Kumar J.Shinde, Arun N. Waghule, Manij, B Paithane, Harinadh N More, Formulation And *In Vitro* Evaluation of Sustained Release Floating Tablets of Cephalexin Using Hydrophilic Polymers, International Journal of Pharmacy and Pharmaceutical Sciences, 2010; 2(1): 58-65.
69. Muralidhar Nama, Chandra Shekar Rao Gonugunta, Prabhakar Reddy Veera Reddy, Formulation and Evaluation of Gastro Retentive Dosage Form of Clarithromycin, AAPS Pharma Sci Tech, Mar 2008; 9(1): 231-237.
70. A. Kowal, A.K. Pathak, Formulation and Evaluation of Intra Gastric Buoyant Tablets of Amoxicillin Trihydrate, International Journal of Pharmacy And Life Sciences, Feb 2011; 2(2): 546-550.
71. Madhu Sodan Sharma, Achharish Goel, Anubhav Goswami, Design and Characterization Of Floating Tablets of Cefpodoxime Proxetil, International Journal of Biopharmaceutical & Toxicological Research, May 2011; 1(1): 9-16.
72. Ramzi Anil Kumar Arza, Chandra Shekar Rao Gonugunta, Prabhakar Reddy Veera Reddy, Formulation and Evaluation of Swellable and Floating Gastro Retentive Ciprofloxacin Hydrochloride Tablets, AAPS Pharma Sci Tech, Mar 2009; 10(1): 220-226.
73. MV Srikanth, N Sreenivasa Rao, SA Sunil, GS Sharma, MV Umwangho, KV Ramana Murthy, Formulation and Evaluation of Gastro Retentive Floating Drug Delivery System of Oflaxcin, Drug Invention Today, Feb 2011; 3(3): 7-9.
74. Ramesh Bomma, Rongalal Appalaswamy Naidu, Madhusudan Rao Yamsani, Kishna Veera Brahma, Development and Evaluation Of Gastro Retentive Norfloxacin Floating Tablets, Acta Pharma, 2009; 9: 211-221.

75. Paramod Patel, Someswar Rao B, Suresh V Kulakarni, Baswaraj, Chetan Sarpar, Anand Ammanage, Formulation and In-Vitro Evaluation of Floating Matrix Tablets of Oflaxcin Asian Journal of Res Pharma, Sci, 2011; 1(1): 17-22.
76. Ramji Anil Kumar Arza, Chandra Shekar Rao Goguntal, Prabhakar Reddy Veera Reddy, Formulation and Evaluation of Swellable And Floating Gastro Retentive Ciprofloxacin Hydrochloride Tablets, AAPS Pharma Scitech, Mar 2009; 10(1): 220-226.
77. D.M.Sarkar, R.V.Kshirsagar, R.M.deshbhratar, Studies on Formulation and *In Vitro* Evaluation of Gastro Retentive Drug Delivery System of Carbamzepine, International Journal of Chem Tech Research, Mar 2010; 2(1): 108-113.
78. Kavitha K, Design and Characterisation of Targeted Drug Delivery System of 5-Fluro Uracil, International Journal of Pharma and Biosciences, Jan-Mar 2012; 3(1): 616-623.
79. Asha Patel, Subhabrata Ray, Ram Sharanagat Thaahkur, *In-Vitro* Evaluation and Optimization of Controlled Release Floating Drug Delivery System of Metformin Hydrochloride, DARU, 2006; 14(2): 57-64.
80. Sunil K.Jain, A.M.Awashti, N.K. Jain, G.p.Agarwal, Calcium Silicate Based Microspheres of Repaglinide for Gastro Retentive Floating Drug Delivery. Preparation and *In-Vitro* Characterization, Journal of Controlled Release, 2005; 107: 300-309.
81. M Siva Balan, T Punitha Vani, Phaneendar Reddy, Vasudevaiah, Anup Joshe, and G Nigila, Formulation and Evaluation of Gastro Retentive Glipizide Floating Tablets, International Journal Of Comprehensive Pharmacy, 2011; 1(3): 1-4.
82. Masareddy RS, Bormal UB, Patil.BR, Sarat V, Metformin HCL Loaded Sodium Alginate Floating Microspheres Prepared By Ionotropic Gelation Technique: Formulation Evaluation and Optimization, Indian Journal of Novel Drug Delivery, April- June 2011; 3(2): 125-133.
83. M.Sampath Kumar, R.Senthil Selvi, P.Perumal, Chandra Shekar. Y, Zakir, Formulation and *In Vitro* Evaluation of Gastro Retentive Floating Tablets of Glipizide, International Journal of Innovative Pharmaceutical Research, 2011; 2(3): 151-155.
84. Shailesh Prajapati, Laxmanbhai. Patel, Chhaganbhai. Patel, Floating Matrix Tablets of Domperidone Formulation and Optimization Using Simplex Lattice Design, Iranian Journal of Pharmaceutical Research, 2011; 10(3): 447-455.
85. Dasarath M. Patel, Natvaralal M.Patel, Nitesh N.Pandya and Pranav D.Gogani, Gastro Retentive Drug Delivery System of Carbamzepine: Formulation Optimization Using Simplex Lattice Design: A Technical Note, AAPS Pharma Scitech, 2007; 8(1): 1-5.

86. R.Margret Chandria, Debjit Bhowmik, Chiranjib, B.Jayakr, Formulation and Evaluation of Gastro Retentive Drug Delivery System of Gasroprokinetic Drug Itopride Hydrochloride, International Journal of Pharmacy and Pharmaceutical Sciences, 2010; 2(1): 53-65.
87. ST Prajapati, LD Patel, DM Patel, Studies on Formulation and *In Vitro* Evaluation of Floating Matrix Tablets of Domperidone, Indian Journal of Pharmaceutical Sciences, 2009; 71(1): 19-23.
88. Shweta Sharma, Akhil Sharma, Kamal Kishore Jha, The Study of Captopril Floating Matrix Tablets Using Polymers as Release Retarding Agent, The Pharma Research, 2009; 01: 34-40.
89. Manooj N.Gambhire, Kshitij W.Ambade, Sushma D.Kumari, Vilasrao J.Kadam, Kishan R.Jadav, Development and *In-Vitro* Evaluation of an Oral Floating Matrix Tablet Formulation of Diltiazem Hydrochloride, AAPS Pharma Scitech, 2007; 8(3): 1-9.
90. Jiamiao Wang, Fude Cui, Kai Shi, Linlin Yang, Shuo Liqiang Zhang, *In-Vitro* Evaluation of a Sustained Release Multiple Unit Floating System Containing Nitrendepine, Asian Journal of Pharmaceutical Sciences, 2008; 3(4): 151-157.
91. Ajay Kumar Patil, Shaik Majahar, Gulam Ifrani, Floating Tablets of Nimodipine and Its Inclusion Complex With B-Cyclodextrin For Controlled Release, International Journal of Pharma Tech Research, April-June 2011; 3(2): 619-625.
92. Shyam Shimpi, Bhsakar Chauhan, K.R. Mahadik, Anant Paradkar, Preparation and Evaluation of Diltiazem Hydrochloride-Gelucire 43/01 Floating Granules Prepared By Melt Granulation, AAPS Pharma Scitech, 2004; 5(3): 1-6.
93. Kiran Chaturvedi, S.Umadevi. Subhash Vagani, Floating Matrix Dosage Form For Propronolol Hydrochloride Based on Gas Formulation Technique: Development and *In-Vitro* Evaluation Scientia Pharmaceutica, Sep 2010; 78: 927-939.
94. Gajanam Deshmukh, Deepti Ruikar, Tejas Ghelani, Hemangi Patel, Jitendran Patel, Jignesh Patel, Formulation and Statistical Optimization of Verapamil Hydrochloride Floating Drug Delivery System By Response Surface Methodology, International Journal of Pharmaceutical Sciences, July 2011; 2(3): 26-42.
95. Akash Yadav, Dinesh Kumar Jain, Formulation Development and Characterization of Propronolol Hydrochloride Microballons For Gastro Retentive Drug Delivery, African Journal Of Pharmacy and Pharmacology, Oct 2011; 5(15): 1801-1810.
96. Parikh Bhavik, Anjan Kumar, Patel Ishvarce, Jitendra Chandrasekhar Hugar, Dayakar Rao Kalakuntla, Formulation and Evaluation of Floating Tablet of Atenolol:

Functionality of Natural And Synthetic Polymers, IJPPS, Journal of Pharmaceutics and Cosmetology, 2011; 1(3): 15-19.

97. C.Narendra, M.S. Srinadh, Ganesh Babu, Optimization of Bilayer Floating Tablet Containing Metaprolol Tartrate As Model Drug For Gastric Retention, AAPS Pharma Scitech, 2006; 7(2): 1-7.
98. Lingam Meka, Bhaskar Kesavan, Krishna Mohan Chinnala, Venkateswerlu Vobalabiona, Madhusudan Rao Yamsani, Preparation of Matrix Type Multiple Unit Gastro Retentive Drug Delivery System For Captopril Based on Gas Formation Technique*: In Vitro* Evaluation, AAPS Pharma Scitech, June 2008; 9(2): 612-619.
99. Supriya S.Shidyae, Anirudda S.kulakarni, Sagar B.Sutar, Vilasarao J. Kadam, Sustained Release Floating Drug Delivery System of In Situ Gelling Suspension of Cinnarizine, Journal of Pharmacy Research, Mar 2009; 2(3): 449-454.
100. Ravi K.Barde, Rahul K. Amrutkar, Minal R.Narkhade, Jitendra Y.Nehete, Optimization of Gastro Retentive Delivery System of Labetalol Hydrochloride Using Simplex Centroid Design, International Journal of Pharmaceutical Sciences and Research, June 2011; 2(9): 2439-2445.
101. Anand Patel, Moin Modasiya, Dushyant Shah, Vishnu Patel. Development and *In-Vitro* Floating Behavior of Verapamil HCL Intra Gastric Floating Tablets, AAPS Pharma Scitech, Mar 2009; 10(1): 310-315.
102. Ziyaur Rehman, Mushir Ali, RK Khar, Design And Evaluation of Bilayered Floating Tablets of Captopril, Acta Pharm, 2006; 56: 49-57.
103. G.Eswar, M. Saritha, Formulation and Evaluation of Atenolol Floating Tablets Using Different Polymers, Guargum, Sodium Alginate, HPMC 100 CPS And Captopril 940, International Journal of Pharmaceutical and Biological Archivers, 2011; 2(4): 1146-1151.
104. Rabi N Panigrahy, Arun M. Mahale, Puspendra S Dhaked, Formulation and *In-Vitro* Evaluation of Combined Floating Mucoadhesive Tablets of Metoprolol Succinate, International Journal of Pharmacy And Pharmaceutical Sciences, 2011; 3(2): 221-226.
105. VD Havaldar, AS Kulkarni, RJ Das, NH Alorkar, KK Mali, Floating Matrix Tablets of Atenolol: Formulation and *In Vitro* Evaluation, Asian Journal of Pharmaceutics, 2009; 3(4): 286-291.
106. Anuradha K. Salunke, Remeth J. Dias, Kailas K. Mali, Niranjan S. Mahajan, Viswajeet S. Ghorpade, Formulation and Evaluation of Floating Pulsatile Drug Delivery System of Metaprolol Tartarate, Der Pharmacia Letter, 2011; 3(3): 147-160.

107. Swathi C. Jagdale, Amith J. Agavekar, Sudhir V.Pandya, Bhanudas S.Kuchekar, Anirudhha R. Chabukswar, Formulation and Evaluation of Gastro Retentive Drug Delivery System of Propronolol Hydrochloride, AAPS Pharma Scitech, Sep 2009; 10(3): 1-9.
108. N. Arun Kumar, C Rani, K P Mohan Raj, Formulation and *In-Vitro* Evaluation of Oral Floating Tablets of Atorvastatin Calcium, Research Journal Pharma and Tech, Oct-Dec 2008; 1(4): 492-495.
109. Sunil K.Jain, Govind P.Agarwal, Narendra K. Jain, Evaluation of Porous Carrier Based Floating Orlistat Microspheres For Gastric Delivery, AAPS Pharma Scitech, 2006; 7(4): 1-9.
110. Viral F.Patel, Natvarlal M.Patel, Statistical Evaluation of Influence of Viscosity And Content of Polymer on Dipyridamole Release From Floating Matrix Tablets: A Technical Note: AAPS Pharma Scitech, 2007; 8(3): 1-5.
111. Suresh Bandari, Chandra Mohan Eaga, Ashok Thadishetty, Madhusudan Rao Yamsani, Formulation and Evaluation of Multiple Tablets As a Biphasic Gastro Retentive Floating Drug Delivery System For Fenoverine, Acta Pharma, 2010; 7(3): 89-97.
112. Adimoolam Sentil, Rahul Goroga Raut, Prasahant Sharad Salunke, Sonal Umesh Kulakarni, Narayana Swamy VB, Formulation and Evaluation of Floating Tablets of Tizanizide Hydrochloride, International Research Journal of Pharmacy, Sep 2011; 2(8): 124-129.
113. S.Ramachandran, S. M. Shaheedha, G. Thirumurugan, M.D. Dhanaraju, Floating Controlled Drug Delivery System of Famotidine Loaded Hollow Microspheres in the Stomach, Current Drug Delivery, 2010; 7: 93-97.
114. Brijesh S. Deve, Avani F. Amin, Madhubav Patel, Gastro Retentive Drug Delivery System of Ranitidine Hydrochloride: Formulation and *In-Vitro* Evaluation, AAPS Pharma Scitech, 2004; 5(2): 1-6.
115. S.D. Barhaate, Yogesh Rupnar, Rahul Rahane, M.M. Patel, Formulation Optimization of Bilayer Floating Tablet of Famotidine, International Journal of Pharma and Biosciences, Oct-Dec 2010; 1(4): 613-621.
116. Dasharath M.Patel, Natvaralal M.Patel, Viral F. Patel, Darshini A. Bhatt, Floating Granules of Ranitidine Hydrochloride-Gelucire 43/01 , Formulation Optimization Using Factorial Design, AAPS Pharma Scitech, 2007; 8(2): 1-7.
117. M. Jaimani, A.C. Rana, Y.S. Tanwar, Formulation and Evaluation of Famotidine Floating Tablets, Current Drug Delivery, 2007; 4: 51-55.

118. Jagat Leena S, Swathi Seema P, Mali Prabha R, Tripati Pallavi S, Deshmukh Kishore R, Formulation and Evaluation of Floating Matrix Tablets of Famotidine Using Natural Polymers, International Research Journal of Pharmacy, June 2011; 2(6): 110-115.
119. Rakesh Pahwa, Sumit Jindal, Lovely Chhabra, Himanshu Datt, Rekha Rao, Development and *In-Vitro* Characterization of Effervescent Floating Drug Delivery System of Famotidine, International Journal of Pharmaceutical Sciences and Research, 2012; 3(1): 541-546.
120. Patel Krunal M, Biswajit Biswal, Nabin, Janki Patel, Preparation and Evaluation of Gastro Retentive Floating Tablets of Lansoprazole, Journal of Pharmacy Research, 2010; 3(12): 2934-36.
121. Enas M. Elmowafy, Gehanne A.S. Awad, Samar Mansour, A. Elshamy, Release Mechanisms Behind Polysaccharides –Based Famotidine Controlled Release Matrix Tablets, AAPS Pharma Scitech, Dec 2008; 9(4): 1230-1239.
122. Bk Satish Babu, VR Sandeep, RB Ravi, R Shruthinag, Formulation and Evaluation of Floating Drug Delivery System of Famotidine, Indian Journal of Pharmaceutical Sciences, 2010; 72(6): 738-744.
123. Rohit Patel, Ravindra Pal Singh, KM Panchal, Stuhi Guptha, Lalith Kumar, Formulation and Optimization of Floating Matrix Tablets of Ranitidine Hydrochloride, International Journal of Comprehensive Pharmacy, 2011; 5(8): 1-5.
124. Prasanth Khemariya, Sachin Misra, Amith Sulka, Mohit Bargava, Sanjay K. Singhai, Sanjay Goswami, An Emerging Trend in Floating Technology- Floating Tablets of Ranitidine HCL, International Journal of Drug Delivery, 2010; 2: 154-158.
125. AA Kharia, S N Hirenath, A K Sing Hai, S K Jain, Design and Optimization of Floating Drug Delivery System of Acyclovir, Indian Journal of Pharmaceutical Sciences, 2010; 72(5): 599-606.
126. M.D. Raja, Narra Kishore, U.M. Dhanalekshmi, C. Senthil Kumar, G. Ranga Raj, P. Neelakanta Reddy, T.S. Uma,, P.K. Sehgal, Formulation and *In-Vitro* Evaluation of Floating Alginate Beads For Site Specific Delivery of Acyclovir, Journal of Global Trends in Pharmaceutical Sciences, Jan-Mar 2011; 2(1): 31-42.
127. Vidhyadhar H.Banker, Preeti, D.Gaikwad, Sunil P.Pawar, Design and Evaluation of Floating Drug Delivery Based on Matrix Tablet of Acyclovir, International Journal of Pharmaceutical Research and Development, Aug 2011; 3(6): 192-200.

128. Sharad N. Shinde, Satej S. Magdum, Shekar B. Waikar, Mahesh R.Mishra, Kamla K. Chandak, Development and Evaluation of Floating Tablets of Salbutamol Sulphate, International Journal of Pharma Research & Development, July 2010; 2(5): 1-7.
129. P.N. Kendre, S.N. Lateef, R.K. Godge, P.D. Chanduri, S.L. Fernandes, S.K. Vibhute, Oral Sustained Delivery of Theophylline Floating Matrix Tablets - Formulation and *In-Vitro* Evaluation, International Journal of Pharma Tech Research, Jan-Mar 2010; 2(1): 130-139.
130. Monica Rp Rao, Girish S. Sonar, Rachan R. Mandsaurwale, Swapnila D Vanshiv, Evaluation of Effervescent Floating Matrix Tablet Formulation of Salbutamol Sulphate Using Full Factorial Design, Asian Journal of Pharmaceuticals, 2009; 3(1): 43-49.
131. S. Sarojini, D. Ariva Jagan, R. Manavalan, V. Jayanthi, Buoyant Sustained Release Theophylline Tablets Based on Poly Ethylene Oxide, International Journal of Pharmacy and Pharmaceutical Sciences, 2010; 2(1): 144-150.
132. Deepak Jain, Sofia Verma, Shashi Barati Shulka, Alok Pal Jain, Prakash Jain, Priyanka Yadav, Formulation and Evaluation of Gastro Retentive Tablets of Furosemide, Evaluation Based on Drug Release Kinetics and Factorial Designs, Journal of Chemical and Pharmaceutical Research, 2010; 2(4): 935-978.
133. P.P. Amruthar, P.D. Chaudari, S.B.Patil, Design and *In-Vitro* Evaluation of Multi Particulate Floating Drug Delivery System of Zolpidem Tartarate, Colloids And Surfaces, Biointerfaces, 2012; 89: 182-187.
134. S.Mandal, G.N. Ratan, J.S.Mulla, J.Thimma Settee, A.Kancriya, Design and *In-Vitro* Evaluation of Gastro Retentive Sustained Release Tablets of Tizanizide Hydrochloride, Indian Journal of Novel Drug Delivery, Oct-Dec 2010; 2(4): 144-152.
135. Ambati Brahma Reddy, B. Samyukhta Rani, D. Eswar Tony, D. Siva Naga Raja, L.Sindhura, N. Sarat Kumar, Aceclofenac Floating Tablets- A Promising Sustained Release Dosage Form, International Journal of Drug Development And Research, April-June 2011; 3(2): 290-300.
136. Shasikanth D. Bharate, Yogesh S. Rupral, Rupesh M. Sonvane, Kapil R.Pawar, Rahul Kumar, D.Rahane, Formulation and Evaluation of Floating Microspheres of Ketorolac Trometamol, International Journal of Pharmaceutical Research and Development, Nov 2005; 1(9): 1-8.
137. Rajendra Jangde, Nilesh Garde, Sunil Hargude, Swarnalata Saraf, Shailendra Saraf, Monolithic Floating Tablets of Nimesulide, The Pharmaceutical Magazine, Mar 2008; 1-3.

138. S. Satiya Raj, Ramya D. Devi, Vedha BN Hari, Loranaxicam Gastro Retentive Floating Matrix Tablets: Design and *In-Vitro* Evaluation, Journal of Advanced Pharmaceutical Technology & Research, 2011; 2(3): 156-162.
139. Swathi C. Jagadale, Swapnil, A. Ghorpade, Bhanudas, S. Kuchekar, Aniruddha R. Chabukawar, Effect of Polymer and Gas Forming Agent on Floating Drug Delivery of Tramadol Hydrochloride Using Response Surface Methodology: *In-Vitro* and *In-Vivo* Evaluation, International Journal of Pharmaceutical Applications, 2011; 2(3): 181-194.
140. Rishad R. Jivani, Chhagan N. Patel, Dashrath M.Patel, Nurudin P. Jivani, Development of a Novel Floating Insitu Gelling System For Stomach Specific Drug Delivery of The Narrow Absorption Window Drug Baclofen, Iranian Journal of Pharmaceutical Research, 2010; 9(4): 359-368.