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A REVIEW ON FLOATING DRUG DELIVERY SYSTEM

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ABSTRACT

Oral drug delivery is the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms. In the development of the drug delivery system many components play important role. Technological attempts have been made in the research and development of rate-controlled oral drug delivery systems to overcome physiological adversities, such as short gastric residence times (GRT) and unpredictable gastric emptying times (GET). It is known that differences in gastric physiology, such as, gastric pH and motility, exhibit both intra-as well as inter-subject variability demonstrating significant impact on gastric retention time and drug delivery behavior. This triggered the attention towards formulation of stomach specific (gastro retentive) dosage forms. FDDS are of particular interest for drugs that are locally active and have narrow absorption window in stomach or upper small intestine, unstable in the intestinal or colonic environment, and exhibit low solubility at high pH values. This particular article gives information about the approaches to design single-unit and multiple-unit floating systems, their classification, applications, advantages and limitations. These systems are useful to overcome several problems encountered during the development of a pharmaceutical dosage form.

KEYWORDS: Floating drug delivery systems, multiple unit dosage form, effervescent, swelling studies.

INTRODUCTION

Oral drug delivery is the most preferred route of drug delivery due to ease of administration and patient compliance. Oral route of administration has been received more attention in the pharmaceutical field because of the more flexibility in the designing of dosage form than drug delivery design for other routes. Most of the oral controlled drug delivery systems rely on diffusion, dissolution or combination of both mechanisms, to release the drug in a controlled manner to the Gastrointestinal tract and the drug profile data, such as dose, absorption properties and the quantity of drug needed, one can determine the desired release rate of the drug from controlled release dosage form.

Floating drug delivery system (FDDS) is a class of gastroretentive drug delivery system. FDDS is a recent advancement in pharmaceutical technology which has also several advantages over the conventional drug delivery systems. Those advantages of floating system can be used in the treatment of world's most affective diseases like cardiovascular diseases. Floating system are low density system that float over the gastric content and tending to keep afloat in the stomach without affecting gastric emptying rate for prolonged period of time. While the system floating on gastric content drug is released slowly from system at desired rate, after release of drug; system is emptied from the stomach. This results in increased in GRT and better control of fluctuation of plasma drug concentration.[1]

BASIC GIT PHYSIOLOGY

Anatomically the stomach is divided into three regions such as fundus, body and antrum (pylorus) (Fig 1).The proximal part made of fundus and body acts as a reservoir for undigested materials, where as the antrum is the main site for mixing motions and acts as a pump for gastric emptying by propelling actions. Gastric emptying occurs in both the fasting and fed states. During the fasting state an interdigestive series of electrical events take place which cycle both through stomach and intestine every 2-3 hrs, which is called as interdigestive myloelectric cycle or migrating myloelectric cycle (MMC) which is further divided in to four phases. After the ingestion of a mixed meal, the pattern of contractions changes from fasted to that of fed state which is also termed as digestive motility pattern.

- Phase 1-(Basic phase)-last from 30-60 min with rare contractions.
- Phase 2-(Preburst phase)-last for 20-40 min with intermittent action potential and contractions.

- Phase 3-(Burst phase) - last for 10-20 min which includes intense and regular contractions for short period.
- Phase 4-last for 0-5 min and occurs between phase 2 and 1 of 2 consecutive cycles.[2]

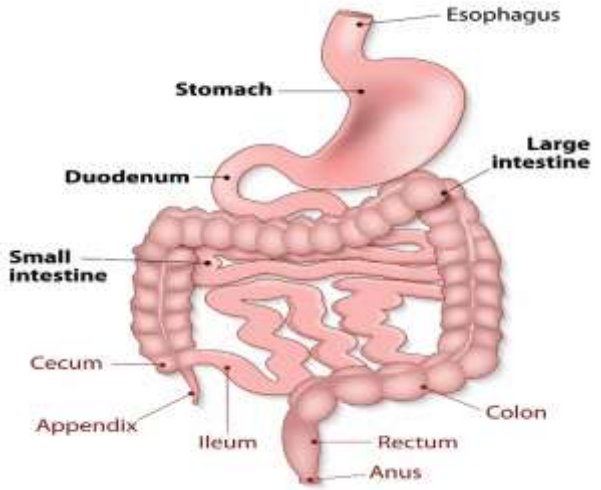

Figure 1: Human gastrointestinal tract.

ADVANTAGES OF FDDS

- Floating dosage forms such as tablets or capsules will remain in the solution for prolonged time even at the alkaline pH of the intestine.
- FDDS are advantageous for drugs meant for local action in the stomach eg: Antacids.
- FDDS dosage forms are advantageous in case of vigorous intestinal movement and in diarrhea to keep the drug in floating condition in stomach to get a relatively better response.
- Acidic substance like aspirin causes irritation on the stomach wall when come in contact with it hence; HBS/FDDS formulations may be useful for the administration of aspirin and other similar drugs.
- The FDDS are advantageous for drugs absorbed through the stomach eg: Ferrous salts, Antacids.[3]

DISADVANTAGES OF FDDS

- Floating systems are not feasible for those drugs that have solubility or stability problems in gastric fluids.
- Drugs such as Nifedipine, which is well absorbed along the entire GI tract and which undergo significant first-pass metabolism, may not be suitable candidates for FDDS since the slow gastric emptying may lead to reduced systemic bioavailability. Also there are limitations to the applicability of FDDS for drugs that are irritant to gastric mucosa.
- They require a sufficiently high level of fluids in the stomach, so that the drug dosages form float therein and work efficiently.
- These systems require the presence of food to delay their gastric emptying.[4]

MECHANISM OF FLOATING DRUG SYSTEMS

Various attempts have been made to retain the dosage form in the stomach as a way of increasing the retention time. These attempts include introducing floating dosage forms (gas-generating systems and swelling or expanding systems), mucoadhesive systems, high-density systems, modified shape systems, gastric-emptying delaying devices and co-administration of gastric emptying delaying drugs (Fig 2). Among these, the floating dosage forms have been most commonly used. Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the 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. To measure the floating force kinetics, a novel apparatus for determination of resultant weight has been reported in the literature. The apparatus operates by measuring continuously the force equivalent to F (as a function of time) that is required to maintain the submerged object. The object floats better if F is on the higher positive side. This apparatus helps in optimizing FDDS with respect to stability and durability of floating forces produced in order to prevent the drawbacks of unforeseeable intragastric buoyancy.[5]

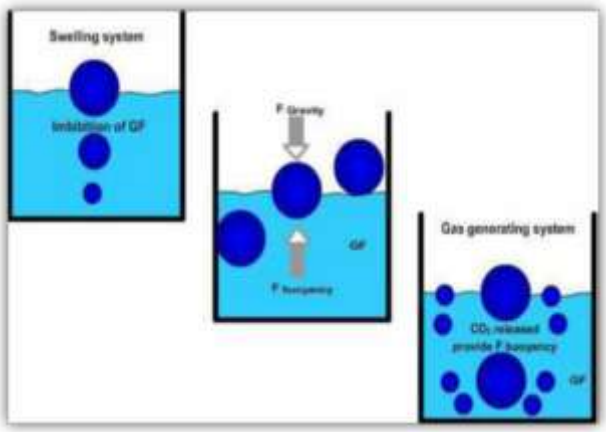

Figure 2: Mechanism of floating systems.

APPROACHES TO DESIGN FLOATING DOSAGE FORMS

Single unit dosage forms

In low density approaches the globular shells apparently having lower density than that of gastric fluid can be used as a carrier like popcorn, poprice, polystrol for the drug for its controlled release. The polymer of choice can be either Ethyl cellulose or HPMC. 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 micro porous component that houses as a reservoir having apertures present at top and bottom walls through which the gastrointestinal tract fluid enters to dissolve the drug.

Hydro dynamically balanced systems (HBS) are designed to prolong the stay of the dosage forms in the gastric intestinal tract and aid in enhancing the absorption. Drugs having a better solubility in acidic environment and also having specific site of absorption in the upper part of small intestine is achieved by these HBS systems. To retain in stomach for a prolonged period of time the dosage form must have bulk density of <1 and has to maintain its structural integrity and release drug constantly from the dosage form. Among all the advantages single-unit formulations are associated with some limitations such as sticking together or being obstructed in the GIT which may lead to potential danger of producing irritation.

Multiple unit dosage forms

Multiparticulate dosage forms are gaining much favor over single unit dosage forms. The potential benefits include increased bioavailability; predictable, reproducible and generally short gastric residence time, no risk of dose dumping; reduced risk of local irritation, and the flexibility to blend pellets with different compositions or release patterns. Because of their smaller particle size these systems are capable of passing through the GI tract easily, leading to less inter and intrasubject variability. However, potential drug loading of a Multiparticulate system is lower because of the proportionally higher need for excipients (e.g., sugar cores). Most Multiparticulate pulsatile delivery systems are reservoir devices coated with a reputable polymeric layer. Upon water ingress, drug is released from the core after rupturing of the surrounding polymer layer, due to pressure build up within the system. The pressure necessary to rupture the coating can be achieved with swelling agents, gas producing effervescent excipients or increased osmotic pressure. Water permeation and mechanical resistance of the outer membrane are major factors affecting the lag time. Water soluble drugs are mainly released by diffusion; while for water insoluble drug, the release is dependent on dissolution of drug.[6]

POLYMERS USED IN FLOATING DRUG DELIVERY SYSTEM

Polymers are used in floating system so as to target the drug delivery at specific region in the GI tract i.e. stomach. Polymers are the macromolecule compound containing many monomer units joined to each other by bonds. Both synthetic and natural polymers are used in the floating drug delivery. Natural polymers used in floating system are guar gum, chitosan, xanthum gum, gellan gum, sodium alginate, etc. Synthetic polymers used for the floating drug delivery are HPMC, eudragit, ethyl cellulose, etc.

Natural polymers

Natural gums (obtained from plants) are hydrophilic carbohydrate polymer of high molecular weight. They are generally insoluble in organic solvents like hydrocarbon and ether.

Guar gum

Guar gum is naturally occurring galactomannan polysaccharide. Guargum hydrates and swells in cold water forming viscous colloidal dispersions or sols. This gelling property retard the drug release and make it a flexible carrier for extended release dosage forms.

Chitosan

Chitosan is natural polymer obtainer by deacetylation of chitin. It has favorable biological properties such as non-toxic, biodegrable, biocompatible. It is a bioadhesive polymer and have anti-bacterial properties thus make it suitable for site specific delivery. Chitosan is high molecular weight polycationic weak base with pka value of 6.2-7. On addition to acidic pH of 1.2 or neutral media it become buoyant in nature and provide control release. By increasing thickness of chitosan film release rate can be decreased.

Xanthum gum

Xanthan gum is a high molecular weight extracellular polysaccharide produced by pure culture aerobic fermentation of carbohydrate. Xanthan is a long chained polysaccharide with large number of trisaccharide side chains. Gum also has an excellent solubility and stability under acidic and alkaline conditions and in the presence of salts and resists common enzymes.

Gellan gum

Gellan gum is an anionic, high molecular weight, deacetylated extracellular, linear polysaccharide. This gum has an outstanding flavor release, high gel strength, an excellent stability, process flexibility, high clarity, good film former and thermally reversible gel characteristics. Gellan gum is produced as a fermentation product from S*pingomonas elodea.*

Sodium alginate

Sodium alginate consists chiefly of the sodium salt of alginic acid, which is a mixture of polyuronic acids composed of residues of d-mannuronicacid and L-guluronic acid.

Synthetic polymers

Synthetic polymers are becoming increasingly important in pharmaceuticals. Use of synthetic polymers ranges from binder, film coating agent, etc. Synthetic polymers are either purely synthetic or they are modified form of natural polymer known as semi-synthetic.

Hydroxy propyl methyl cellulose

Hydroxypropyl methylcellulose ethers belong to an extensive family of white to off-white, odorless, water soluble polymers that bind, retain water, thicken, form

films, lubricate. It is a semi synthetic, inert, viscoelastic polymer, used as an excipient and controlled-delivery component in oral medicaments, found in a variety of commercial products.

Eudragit
Polymethacrylates (Eudragit) are primarily used in oral capsule and tablet formulations as film-coating agents. Depending on the type of polymer used, films of different solubility characteristics can be produced. It is soluble in gastric fluid below pH 5. In contrast, Eudragit L, S and FS types are used as enteric coating agents because they are resistant to gastric fluid. Different types of enteric coatings are soluble at different pH values: e.g. Eudragit L is soluble at pH >6 whereas Eudragit S and FS are soluble at pH >7.

Ethyl cellulose
Ethocel has been widely used in the pharmaceutical industry for over 50 years. Ethyl cellulose has been used for choice in pharmaceutical formulations for various purposes, such as taste-masking of bitter actives, moisture protection, stabilizer, extended release multiparticulate coating, micro-encapsulation of actives, extended release binder in inert matrix systems, solvent and extrusion granulation. The application of EC in wet extrusion processes is limited, since the polymer has considerable elastic properties, but can be successfully used as matrix former in combination with some plasticizing agents.[7]

CLASSIFICATION OF FLOATING DRUG DELIVERY SYSTEMS

Floating drug delivery systems are classified depending up on the two formulations variables

- **Non-effervescent systems**

This type of system, after swallowing, swells via imbibition of gastric fluid to an extent that it prevents their exit from the stomach. The formulation methods of such type dosage forms involves the mixing of the drug with a gel, which swells when comes in contact with gastric fluid and maintains a relative integrity of shape and a bulk density of less than one within the outer gelatinous barrier. The air trapped by the swollen polymer provides buoyancy these dosage forms. The most commonly used excipients in these systems include hydroxypropyl methyl cellulose (HPMC), polyacrylate polymers, polyvinyl acetate, carbopol agar, sodium alginate, calcium chloride, polyethylene oxide and polycarbonates. This system can be further classified into four sub-types such as:

Colloidal gel barrier system
These types of systems contain drug with gel forming hydrocolloids which allow them to remain buoyant on the stomach content. This prolongs GRT and maximizes the amount of drug at its absorption sites in the solution form for ready absorption. This system incorporates a high level of one or more gel forming highly soluble cellulose type hydrocolloid as hydroxypropyl cellulose, hydroxyethyl cellulose. This hydrocolloid hydrates and forms a colloid gel barrier around its surface after coming in contact with gastric fluid and also helps in sustain releasing of drug.

Microporous Compartment system
In this technology, a drug reservoir is encapsulated inside a microporous compartment with pores along its top and bottom walls. The peripheral walls of the drug reservoir compartment are completely sealed. This sealing prevents any direct contact of gastric surface with the undissolved drug. The flotation chamber containing the delivery system to float over the gastric content entrapped air allows, in the stomach. Gastric fluid enters through an aperture, dissolves the drug and carries the dissolved drug for continuous transport across the intestine for absorption.

Alginate beads
To develop multi unit floating dosage forms, the freeze dried calcium alginate has been used. Spherical beads of approximately 2.5 mm in diameter can be prepared by the precipitation of calcium alginate via dropping sodium alginate solution into aqueous solution of calcium chloride. The beads are then separated, snap-frozen in liquid nitrogen, and freeze-dried at-40ºC for 24 hours, it leads to the formation of a porous system which can maintain a floating force for over 12 hours. These floating beads prolonged residence time for more than 5.5 hours.

Hollow Microspheres/Microballons
A novel emulsion solvent diffusion method used to prepare hollow microspheres loaded with drug in their outer polymer shelf ethanol/ dichloromethane solution of the drug and an enteric acrylic polymer was poured into an agitated solution of poly vinyl alcohol (PVA) that was thermally controlled at 40ºC. The gas phase is generated in the dispersed polymer droplet by the evaporation of dichloromethane formed in the internal cavity of microsphere of the polymer and drug. The microballoon floated continuously over the surface of an acidic dissolution media containing surfactant for more than 12h.

- **Effervescent Systems**

These buoyant systems utilize matrices prepared with swellable polymers such as methocel polysaccharides (e.g., chitosan) and effervescent components (e.g., sodium bicarbonate, citric acid or tartaric acid). The system is so prepared that when it arrives in the stomach carbon dioxide is released, causing the formulation to float in the stomach.[8]

EVALUATION OF FLOATING DRUG DELIVERY SYSTEMS

Various parameters that need to be evaluated in gastro retentive formulations which includes floating duration, dissolution profiles, specific gravity, content uniformity,

hardness and friability in case of solid dosage forms. In case of multi particulate drug delivery systems, differential scanning calorimeter, particle size analysis, flow properties, surface morphology, mechanical properties and x-ray diffraction studies are performed.

Size and shape evaluation

The particle size and shape plays a major role in determining solubility rate of the drugs and thus potentially its bioavailability**.** The particle size of the formulation was determined using sieve analysis, air elutriation analysis, photo analysis, optical microscope, electro résistance counting methods (coulter counter), sedimentation techniques, laser diffraction methods, ultrasound attenuation spectroscopy, air pollution emissions measurements.[9]

Floating properties

Effect of formulation variables on the floating properties of gastric floating drug delivery system was determined by using continuous floating monitoring system and statistical experimental design.

Surface topography

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

Determination of moisture content

The water content per seldom of interest. Rather, it shows whether a product intended for trade and production has standard properties such as

- Storability
- Agglomeration in the case of powders
- Microbiological stability
- Flow properties, viscosity
- Dry substance content
- Concentration or purity
- Commercial grade (compliance with quality agreements)

Thus moisture content of the prepared formulations was determined by Karl fisher titration, vacuum drying, Thermo gravimetric methods, Air oven method, Moisture Meters, Freeze drying as well as by physical methods.[10]

Swelling studies

Swelling studies were performed to calculate molecular parameters of swollen polymers**.** Swelling studies was determined by using dissolution apparatus, optical microscopy and other sophisticated techniques which include H_1NMR imaging, confocal laser scanning microscopy, cryogenic scanning electron microscopy, light scattering imaging. The swelling studies by using dissolution apparatus was calculated.[11]

Table 1: Drugs tried in the formulations of stomach specific floating dosage forms.

Stomach Specific Floating Dosage Forms	Drugs
Floating microspheres	Aspirin, Griseofulvin, p-nitroaniline, Ibuprofen, Ketoprofen, Piroxicam, Verapamil, Cholestyramine, Theophylline, Nifedipine, Nicardipine, Dipyridamol, Tranilast and Terfinadine
Floating granules	Diclofenac sodium, Indomethacin and Prednisolone
Films	Cinnarizine , Albendazole
Floating tablets and pills	Acetaminophen, Acetylsalicylic acid, Ampicillin, Amoxycillin trihydrate, Atenolol, Fluorouracil, Isosorbide mononitrate, Para- aminobenzoic acid, Piretanide, Theophylline, Verapamil hydrochloride, Chlorpheniramine maleate, Aspirin, Calcium Carbonate, Fluorouracil, Prednisolone, Sotalol, pentoxyfilline and Diltiazem HCl, Atenolol, ciprofloxacin.
Floating capsules	Chlordiazepoxide hydrogen chloride, Diazepam , Furosemide, Misoprostol, L-Dopa, Benserazide, Ursodeoxycholic acid and Pepstatin, and Propranolol.[12]

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.[13] It retains the dosage form at the site of absorption and thus enhances the bioavailability. These are summarized as follows.

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.

Enhanced bioavailability

The bioavailability of riboflavin CR-GRDF is significantly enhanced in comparison to the administration of non-GRDF CR polymeric formulations. There are several different processes, related to absorption and transit of the drug in the

gastrointestinal tract, that act concomitantly to influence the magnitude of drug absorption.

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, eg, riboflavin and furosemide.

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.

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.

Minimizedadverse activity at the colon
Retention of the drug in the HBS systems at the stomach minimizes the amount of drug that reaches the colon. Thus, undesirable activities of the drug in colon may be prevented. This Pharmacodynamic aspect provides the rationale for GRDF formulation for betalactam antibiotics that are absorbed only from the small intestine, and whose presence in the colon leads to the development of microorganism's resistance.

Reduced fluctuations of drug concentration
Continuous input of the drug following CRGRDF administration produces blood drug concentrations within a narrower range compared to the immediate release dosage forms. Thus, fluctuations in drug effects are minimized and concentration dependent adverse effects that are associated with peak concentrations can be prevented. This feature is of special importance for drugs with a narrow therapeutic index.

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

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

Reduced counter-activity of the body
In many cases, the pharmacological response which intervenes with the natural physiologic processes provokes a rebound activity of the body that minimizes drug activity. Slow input of the drug into the body was shown to minimize the counter activity leading to higher drug efficiency.

Extended time over critical (effective) concentration
For certain drugs that have non-concentration dependent pharmacodynamics, such as beta-lactam antibiotics, the clinical response is not associated with peak concentration, but rather with the duration of time over a critical therapeutic concentration. The sustained mode of administration enables extension of the time over a critical concentration and thus enhances the pharmacological effects and improves the clinical outcomes.[14]

CONCLUSION

Drug absorption in the gastrointestinal tract is a highly variable procedure and prolonging gastric retention of the dosage form extends the time for drug absorption. FDDS promises to be a potential approach for gastric retention. Although there are number of difficulties to be worked out to achieve prolonged gastric retention, a large number of pharmaceutical manufacturers are focusing towards commercializing this technique

REFERENCES

1. Sahil K, Akanksha M, Sudeep B,Premjeet S. Floating drug delivery system: A review. International Research Journal of Pharmacy, 2011; 2(9): 18-24.
2. Garg S, Sharma S. "Gastroretentive drug delivery systems". Pharmatech, 2003; 160-166.
3. Vedha hari b.n.et al. The recent developments on gastric floating drug delivery systems: an overview. International Journal Pharmtech res., 2010; 2(1): 524-534.
4. Gangadharappa H.V, Pramod Kumar T.M, Shiva Kumar H.G. "Gastric floating drug delivery systems." India Journal Pharmaceutical Education Research, 2007; 41(4): 295-306.
5. Abhishek S, S. P. Hiremath. Floating drug delivery system: A review. Ammerican Journal of Pharmtech Research, 2012; 2(1): 139-153.
6. Yang L, Fassihi R. Zero order release kinetics from selfcorrecting floatable configuration drug delivery system. Journal of Pharmaceutical Sciences, 1996; 85: 170-173.
7. D. P. Kulkarni,S. S. Saboo. Polymers used in floating drug delivery system: A review.European Journal of Pharmaceutical and Medical Research, 2017; 4(8): 611-616.
8. Whitehead L, Collet JH, Fell JT, Sharma HL, Smith AM. Floatingdosage forms: an in vivo study demonstrating prolonged gastric retention. Journal Control Release, 1998; 55: 3-12.

9. Choi BY, Park HJ, Hwang SJ, Park JB. Preparation of alginate beads for floating drug delivery system effects of CO2 gas forming agents. International Journalof Pharmacy, 2002; 239; 81-91.
10. Ichikawam, Watenables, Miyake Y. "A multiple unit oral floating dosage systems preparation and in–vivo evaluation of floating and sustained release characteristics. Journal of Pharmacy Sciences, 1991; 80: 1062-1066.
11. Ziayur Rahman, Mushir Ali, RK. Khar. "Design and evaluation of Bilayer floating tablets of Captopril". Acta pharm, 2006; 56: 49-57.
12. Shah SH, Patel JK, Patel NV. Stomach specific floating drug delivery system: a review. International Journal Pharmaceutical Technology Research, 2009; 1(3): 628-629.
13. Narang N. An updated review on: floating drug delivery system. International Journal of Applied Pharmaceutics, 2011; 3(1): 17.
14. 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.