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Formulation and evaluation of floating drug delivery system of fosinopril

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Abstract
The present research work is an attempt to develop and evaluate floating drug delivery system of Fosinopril in order to improve drug bioavailability. A floating drug delivery system helps toimprove the buoyancy property of the drug over gastric fluids so it maintains the longer duration of action this also helps in minimizing the dosing frequency. Floating tablets of Fosinopril were prepared with solid dispersion by physical mixture by usingPEG4000.Tablets are prepared with the direct compression method by using HPMC K4M, HPMC K15M and Carbopol as polymer. Fosinopril floating tablets were prepared utilising both separate and combined polymers. Different ratios of the polymers HPMC, Carbopol 940, and guar gum were utilised. Five formulations in total (AF1–AF5) were prepared. All the formulations were subjected for the flow properties—bulk density, tap density, and angle of repose- the results were found to bewithin the acceptable range. The direct compression method was used to prepare the flotation tablets of Fosinopril. The direct compression approach is quick, easy, and labor-intensive. These formulations (AF1-AF5) were examined for a number of tests, including dissolving studies, homogeneity of content, friability, and weight fluctuation. *In vivo* studies to evaluate the performance and application of floating systems, and applications of these systems. Thesesystems are useful to several problems encountered during the development of apharmaceutical dosage form. The formulations (AF1) made with HPMC and (AF2) made with Carbopol 940 both demonstrated good floating times of 8 hours. With a floating time of 8 hours and a drug release of roughly 98.4% at the end of 24 hours, the formulation (AF1) containing hydroxypropyl methylcellulose was discovered to be the optimum formulation.

Keywords: Fosinopril, bioavailability, floating drug delivery, direct compression, HPMC

Introduction

The most promising, secure, and efficient method of drug delivery is thought to be oral. Various factors, including the gastric emptying process, the gastrointestinal transit time of the dose form, and the drug release from the oral cavity, may affect the effectiveness of oral medication delivery, dose type and location of drug absorption [1].

The majority of oral dosage forms have a number of physiological constraints, including variable gastrointestinal transit, which results in nonuni form drug release, partial drug release, and shorter dosage form resident times in the stomach [2]. This causes inadequate absorption of medications with absorption windows, particularly in the upper region of the small intestine, as the drug's remaining amount is not absorbed after it passes through the absorption site. Wide inter- and intra-subject variability are seen as a result of numerous factors affecting the stomach emptying of dose forms in humans. Such significant variability may cause non-uniform absorption as many medications are well absorbed in the upper region of the gastrointestinal track, making the bioavailability uncertain. As a result, a delivery system that can regulate and extend stomach emptying time as well as transport medications in higher concentrations to the absorption site (i.e. the upper part of the small intestine) would be useful [3].

Many FDDS have been developed recently that use a variety of technologies, each with unique benefits and drawbacks. Examples include single and multiple unit hydrodynamically balanced systems (HBS), single and multiple unit gas generating systems, hollow microspheres, and raft forming systems [4].

A drug's formulation known as FDDS uses hydrocolloids that form gels to stay buoyant in the stomach's contents. Under reasonably regulated circumstances, the pH of the stomach causes drug disintegration and release from the dose form held in the fluids. The dose form's retentive properties are not important for the medications that [5].

- Are insoluble in intestinal fluids
- Act locally
- Exhibit site specific absorption

Advantages of Gastoretentive drug delivery System

The following benefits of gastroretentive medication delivery systems are just a few;

- HBS can be used to any specific medication or set of medications.
- In contrast to medications, which are primarily absorbed via the stomach, HBS formulations are not just for medications. Due to the fact that studies have shown that these are just as effective as drugs that are absorbed from the intestine, such as chlorpheniramine maleate.
- The HBS are beneficial for medications that are absorbed via the stomach, such as ferrous salts, and for medications intended for local action in the stomach, such as those used to treat peptic ulcer disease. eg; antacids.
- It has been discovered that the site of the specific medications' site of absorption has no bearing on the effectiveness of the medications delivered using the sustained release principle of HBS.
- When a prolonged release floating dosage form tablet or capsule is taken, the medication will dissolve in the stomach juices. Following stomach emptying, the medicine that has been dissolved is ready for small intestine absorption. Therefore, it is anticipated that a

medication will be completely absorbed from the floating dosage form if it stays in solution form even at the intestine's alkaline pH.
- It may be helpful to keep the medicine in a floating condition in the stomach to elicit a substantially better reaction when there is vigorous intestinal movement and a short transit period, as can occur in some types of diarrhea.
- Benefits of gastric retention include the administration of medications with limited small intestine absorption windows.
- Traditional extended-release development is difficult since many medications designated for once-daily delivery have been shown to have sub-optimal absorption due to dependence on the transit time of the dosage form. As a result, a system made for extended stomach retention will lengthen the window of time during which drugs can be absorbed in the small intestine.

Disadvantages of Gastroretentive drug delivery System
- Gastric retention is not preferred in several circumstances. It is undesirable for these medications to release slowly in the stomach since aspirin and non-steroidal anti- inflammatory drugs are known to cause gastric lesions.
- As a result, medications that could aggravate the stomach lining or become unstable in the stomach's acidic environment shouldn't be created in gastroretentive systems.
- Additionally, a gastric retention system won't help other medications that are similarly well absorbed throughout the GI tract, including isosorbide dinitrate.
- Numerous elements, including stomach motility, pH, and the presence of food, might affect gastric retention. Since these variables are never constant, it is impossible to anticipate the buoyancy precisely or accurately.
- In supine subjects, gastric emptying of floating forms may happen at random and become highly reliant on the diameter. As a result, administering floating forms to patients right before bedtime is not advised.
- Due to differences in the emptying process, there is a high degree of variability in gastric emptying time.
- Unpredictable bioavailability.

Methodology

Preformulation Studies of Fosinopril

Preformulation is the process of using biopharmaceutical principles to modify a drug's physical qualities. It is a step in the R&D process.

Primary Characterisation of active ingredients and additives, Description of Fosinopril.

5.0 mg of the sample was taken in Petri dish was spread carefully and recorded colour, odour and texture.

Melting point

Fosinopril's melting point was established using the capillary method. Finely grinded Fosinopril powder was placed in a glass capillary tube that had been previously sealed on one end. The drug-filled capillary tube was then placed inside the melting point apparatus, and the temperature at which the drug began to melt was monitored using a thermometer.

Loss on drying

10gms of Fosinopril was heated to a temperature of 105ºC in hot air oven until it remains constant weight. The formula was

$$\text{Percentage LOD} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

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. The angle of repose is designated by θ. It was determined by funnel method. The powder blend was passed through funnel so that it forms a pile. The height(h) of the pile and the radius of the pile (r) were measured and angle of repose was calculated using following formula.

$\theta = \tan^{-1}(h/r)$ **Bulk**

Density & Tapped density

Bulk density and tapped density were calculated by the formula.

$$\text{Tapped Density} = \frac{\text{Mass of Powder}}{\text{Volume of Powder (Tapped)}}$$

Hausner's ratio

It was calculated as

$$\text{Hausner's ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

Compatibility Studies

FTIR Spectroscopy

Infrared spectrum obtained for pure Fosinopril. In order to confirm that the drug and the excipients employed in the formulation development were chemically compatible, a physical combination of the drug and several polymers was used. In order to create the IR spectrum that was used for identification, 2-3 mg of sample were combined with potassium bromide and pelleted (dried at 40–50ºC). A piece of the mixture was compacted into a clear pellet using a hydraulic press and 10 tonnes of pressure. The FT-IR spectrophotometer scanned the particle. FTIR spectrometer was used to scan the material from 4000-400cm^{-1}.

Standard Graph of Fosinopril

Fosinopril standard solution in acid buffer pH 1.2, phosphate buffer pH 6.8 & pH 7.4 containing 5 to 50g was used to generate standard graphs of the medication. At 275nm, the absorbance was measured. The connection between medication concentration and absorption was linear.

Formulation of Floating Tablets of Fosinopril

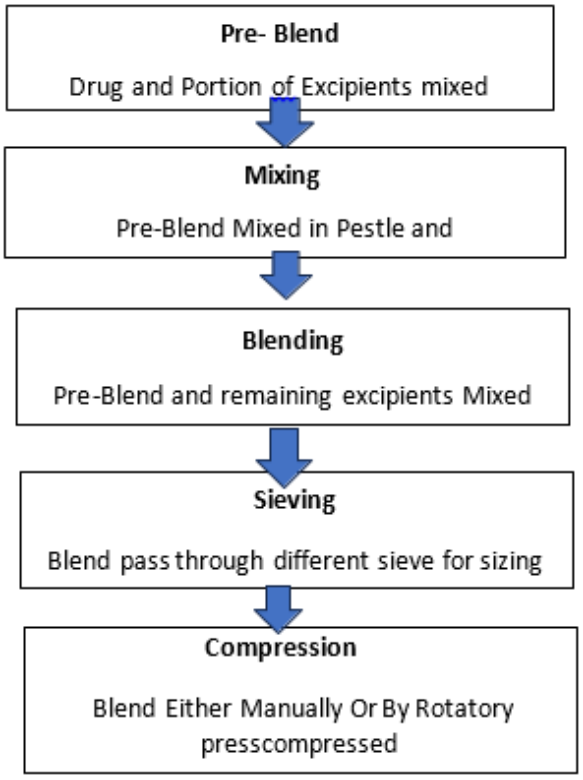

Fig 1

Differential Scanning Calorimetry studies of Fosinopril.
To investigate the physical and chemical interactions between the medicine and the applied excipients, differential scanning calorimetry (DSC) was used. On the DSC-60 equipment, DSC spectra of pure drugs and drug composite mixtures were captured. The drug-excipient mixture was scanned in a nitrogen-filled environment between 50 and 400°C. All samples were prepared in aluminium pans with aluminium covers.

***In vitro* Dissolution Studies**
In vitro dissolution carried out using USP Dissolution Testing apparatus (paddle) type. The dissolution test performed using 900 ml of 0.1 N HCL maintaining normal body temperature, 10 ml of the sample withdrawn at predetermined interval for 12 hours and fresh volume introduced and its absorbance is measured and cumulation percentage drug release is measured.

Description of Active ingredients

Table 1

Sl.no	Components	Fosinopril
1	Colour	White
2	Odor	Odourless
3	Texture	Powder

Identification test.
Identification was carried out as described in Table 5. The observed results were presented in Table 10. Additives that were used in the preformulation studies, for which identification test were performed (IP 2006). Ugwoke *et al*., 2005 states that before the development of formulation excipients quality is must be identified.

Table 1: Identification test of Fosinopril

Sl. No	Ingredients	Observation	Inference
1	Carbopol	A white precipitate immediately forms.	Carbopol may be confirmed.
2	Hydroxy Propyl Methyl Cellulose	No precipitate appears	Hydroxy Propyl Methyl Cellulose may be confirmed.

FTIR studies of Fosinopril.

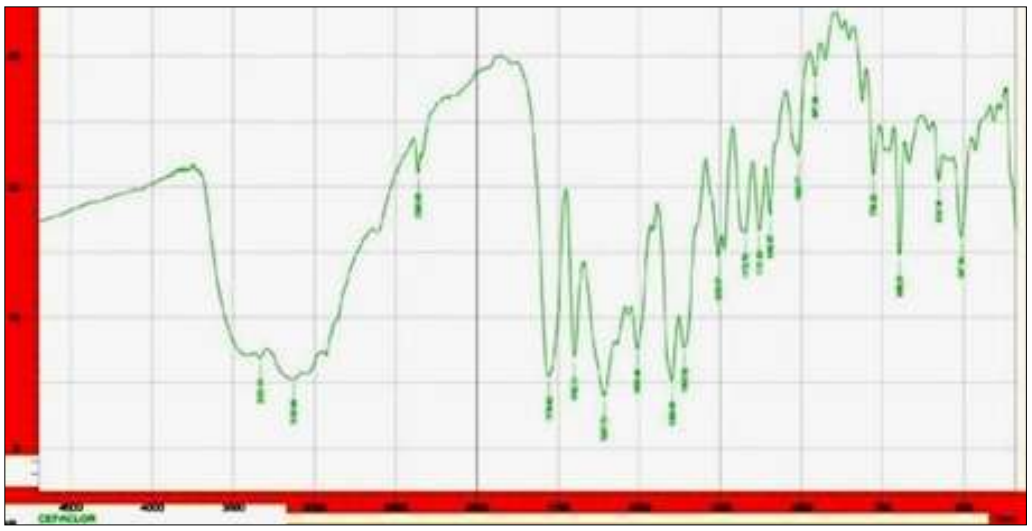

Fig 2: FTIR Spectra of Fosinopril

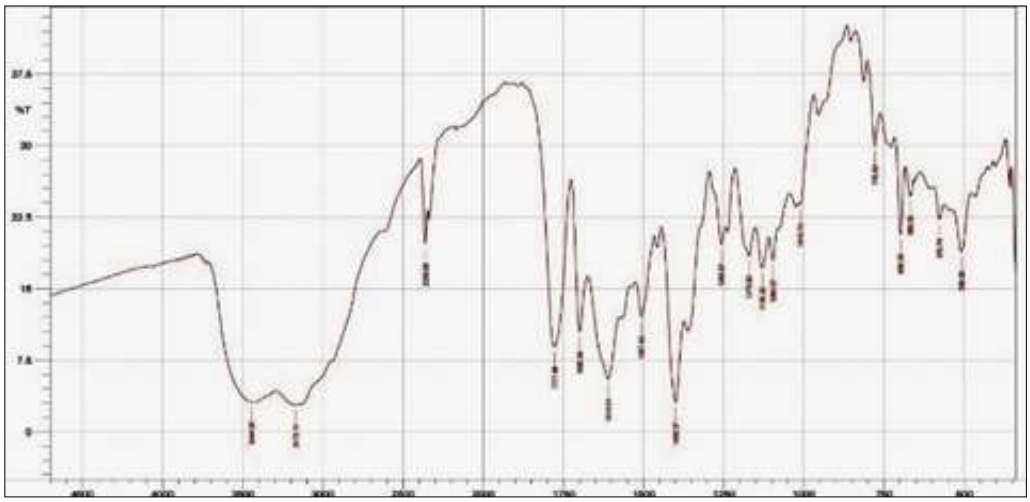

Fig 3: FTIR Spectra of Fosinopril + Carbopol 940

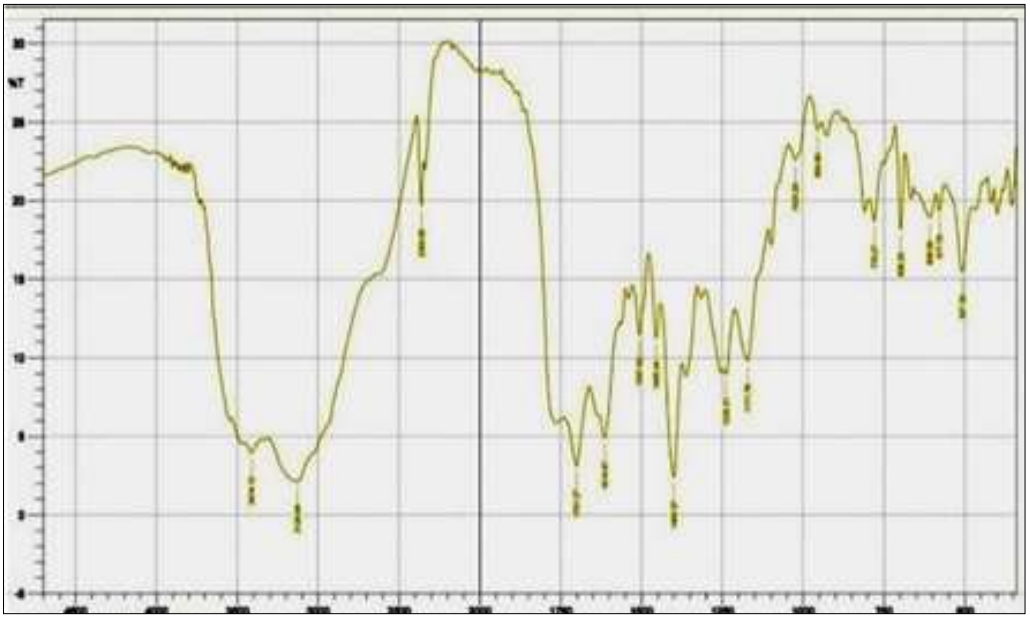

Fig 4: FTIR Spectra of Fosinopril + Guar gum

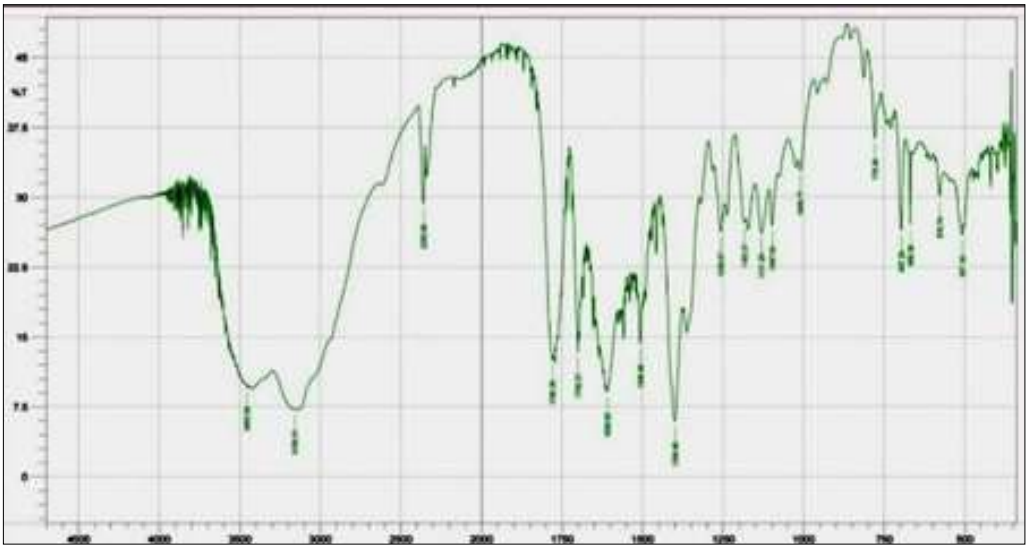

Fig 5: FTIR Spectra of Fosinopril + HPMC

In an effort to investigate the possible chemical interaction of drug with polymer, that have been analyzed (a) Fosinopril; (b) Carbopol 940; (c) Guar gum;(d) HPMC. Fosinopril has shown a characteristic peak at 1778.43 cm^{-1}, which shows C=C, broad band at 3333.10 cm^{-1}, shows a

characteristic peak at 3128.64 cm^{-1}, which is responsible for C-NH, a sharp peak at 1360.62 cm^{-1} due to the presence of C-N.

Table 2: Characteristics of final blend of Fosinopril floating matrix tablets

Formulations	Angle of repose (θ)	Bulk density (g/ml)	Tapped density (g/ml)	Hausner's ratio
F1	21º.32'	0.365	0.386	13.53
F2	22^0.15′	0.345	0.412	13.79
F3	21^0.23′	0.343	0.417	13.98
F4	23^0.36′	0.351	0.387	13.45
F5	24^0.18′	0.344	0.415	12.31

Differential Scanning Calorimetry studies of Fosinopril.
Thermograms for pure Fosinopril and mixed matrix floating tablets comprising Fosinopril and other excipients were both obtained. This depicts the melting endotherm for pure powdered Fosinopril, which occurred at 327.30 °C. In neither sample did the drug's melting point alter noticeably. It proves the substance existed in its distinctive physical and molecular form.

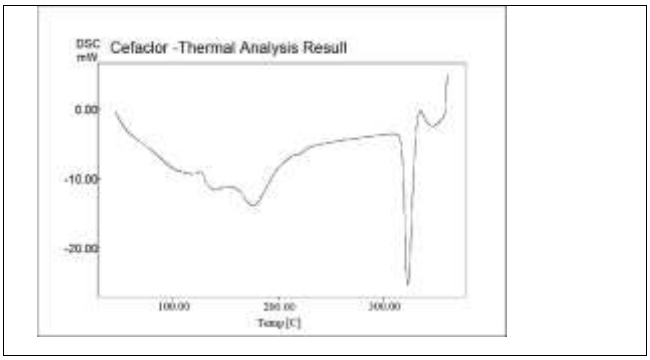

Fig 6: DSC thermogram of Fosinopril

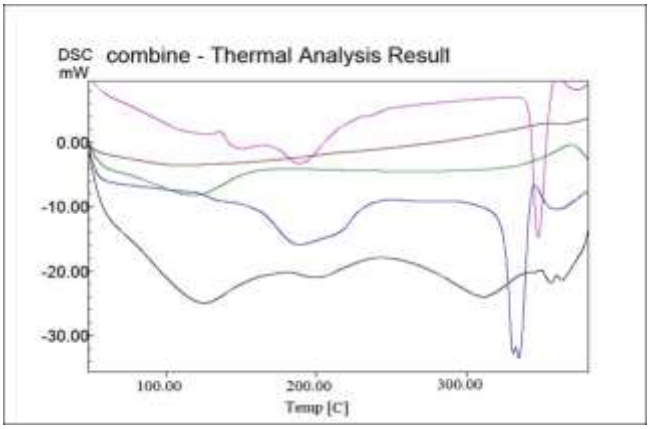

Fig 7: DSC thermogram of Fosinopril and polymers

Standard graph of Fosinopril.
The floating tablet's dissolution tests must be carried out in 0.1N HCl. So, using an Elico spectrophotometer, the UV spectra of Fosinopril in 0.1N HCl was captured. The peak in the spectrum at 275 nm was chosen to build the standard graph of Fosinopril in 0.1N HCl. There is a perfect correlation between drug concentration and absorbance, as shown by the plot of absorbance vs. concentration of Fosinopril in 0.1N HCl, which is linear in the concentration range of 20–50g/ml.

Table 3: Standard plot of Fosinopril

Concentration	Absorbance
0	0
10	0.201
20	0.346
30	0.501
40	0.654
50	0.799

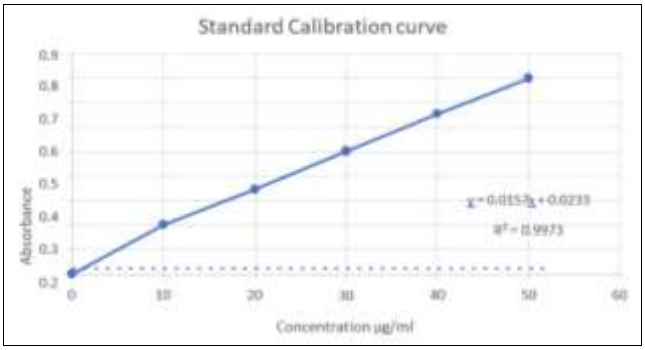

Fig 8: Calibration curve of Fosinopril *In-vitro* Dissolution Study.

Each dissolution vessel of the dissolving paddle apparatus contained 900ml of newly prepared dissolution medium, i.e. 0.1N HCl, and was rotated at 75 rpm while being kept at a temperature of 37+/-0.50C. Fosinopril pills were dissolved in a solution. Every 0, 1, 2, 4, 8, 12, 16, 20 and 24 hours, about 5 ml of the dissolution liquid were pipetted out, and the volume was adjusted by substituting 5 ml of 0.1N HCl. The aforementioned samples, totaling 5ml (7 samples), were gathered in a volumetric flask and diluted with 0.1N HCl to generate 10ml. Finally, a UV spectrometer set to 275 nm was used to measure the solution's absorbance.

Conclusion
Fosinopril floating tablets were prepared utilising both separate and combined polymers. Different ratios of the polymers HPMC, Carbopol 940, and guar gum were utilised. Five formulations in total (AF1–AF5) were prepared. All the formulations were subjected for the flow properties—bulk density, tap density, and angle of repose- the results were found to be within the acceptable range. The direct compression method was used to prepare the flotation tablets of Fosinopril. The direct compression approach is quick, easy, and labor-intensive. These formulations (AF1-AF5) were examined for a number of tests, including dissolving studies, homogeneity of content, friability, and weight fluctuation.

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References
1. Vora B, Khopade AJ, Jain VVD, Shelly, Jain NK. Targeted oral drug delivery. Indian drugs,1996:33(8):365-373.
2. Mazer N, Abisch E, Gfeller JC, Laplanche R, Bauerfeind P, Cucala M, Lukachich M, Blum A. Intragastric behavior and absorption kinetics of a normal and floating modified-release capsule of Isradipine under fasted and fed conditions. J. Pharm. Sci.1988:77:647-657.
3. Sungthongjeen S, Paeratakul O, Limmatvapirat S, Puttipipatkhachor S. Preparation and in vitro evaluation of a multiple-unit floating drug delivery system based on gas formation technique. Int.J. Pharm,2006:324:136-143.
4. Bodmeier R, Paeratakul O. Leaching of water-soluble plasticizers from polymeric films prepared from aqueous

colloidal polymer dispersions. Drug Dev. Ind. Pharm,1992:18:1865-1882.
5. Fell JT. Targeting of drugs and delivery systems to specific sites in the gastroinstestinal tract. J.Anat, 1996; 189:517-519.
6. Wilson CG, Washington N. The stomach its role in oral drug delivery. In: Rubinstein MH, ed. Physiological Pharmaceutical; Biological Barriers to Drug Absorption. Chinchester, UK, Ellis Horwood, 1989, 47-70.
7. Rahman Z, Ali M, Khar R. Design and evaluation of bilayer floating tablets of captopril Acta Pharm,2006:56:49-57.
8. Amal HEL. Magdas K, Safaa SS. Gamal AL, Naggar VF. Evaluation of Stomach protective activity of ketroprofen floating microparticles. Ind. J.Pharm.Sci., 2003, 399-401.
9. Dave BS, Amin AF, Patel MM. Gastroretentive drug delivery system of Ranitidine hydrochloride: Formulation and Invitro evaluation. AAPS Pharm. Sci. Tech,2004:5(2):34:1-6.
10. Welling PG, Dobrinska MR. Dosing considerations and bioavailability assessment of controlled drug delivery systems. Chapter,1987:7:254.
11. Sriamornsak P, Thirawong N. Morpology and buoyancy of oil entrapped calcium pectinate gel beads. AAPS,2004:6(3):24:1-7.
12. Stockwell AF, Davis SS, Walker SE. In vitro evaluation of alginate gel systems as sustained release drug delivery systems", J.control, release,1986;(3):167-175.
13. White head L, Collett, JH. Fell JT. Amoxycillin release from a floating dosage form based on alginates", Int. J.Pharm,2000:210:45-49.
14. Joseph NJ, Laxmi, Jayakrishnan A. A floating type of oral dosage form for piroxicam based on hollow microspheres: in vitro and invivo evaluation in rabbits. J. control release,2002:79:71-79.
15. Rajak PR, Bhattacharya A, Sharma NE, Kataki MS, Rajkumari AN.
16. Gastroretentive floating drug delivery system: an approach in gastroretentive drug delivery. Int J Pharm Pharm Sci,2011;3:9-16.
17. Moursy NM, Afifi NN, Ghorab DM, EL- Saharty, Y. Formulation and evaluation of sustained release floating capsules of Nicardipine hydrochloride. Pharmazie,2003:58:38-43.
18. EL-Kamale AH, Sokar MS, AL Gamalss, Naggar VF. Preparation and evaluation of ketoprofen floating oral drug delivery system. Int. J.Pharm,2001:220:13-21.
19. Kamel EK, Sokar MS, Aigamal SS, Nagger VF. Preparation and evaluation of Ketoprofen floating oral drug delivery system. Int J.Pharm,2001:220:13-21.
20. Du Q, Zhao C, Li XH. Preparation of hydrodynamic balanced system of cinnarizine capsule Chip-Pharm-J-Zhongguo-y-Yaoxue-Zazhi,1995:30:277-279.
21. Murata Y, Sasaki N, Myamoto E, Kawashima S. Use of floating alginate gelbeads for stomach specific drug delivery. Eur-J-Pharma-And- Biopharma,2000:50(2):221-226.