International Journal of Multidisciplinary Research and Growth Evaluation.

Formulation and Evaluation of Gastro Retentive Floating Microspheres of Semaglutide

Dr. K Mangulal [1*], CH Kantlam [2], Bhukya ragya [3], B Udaya sree [3], CH Manish [3], CH Swaroop [3], D Keerthi [3]

[1] HOD and Associate Professor, Department of Pharmaceutics, Brilliant College of Pharmacy, Abdullapurmet Village, Hayathnagar, Rangareddy, Telangana, India

[2] Principal and Professor, Department of Pharmaceutics, Brilliant College of Pharmacy, Abdullapurmet Village, Hayathnagar, Rangareddy, Telangana, India

[3] Department of Pharmaceutics, Brilliant College of Pharmacy, Abdullapurmet Village, Hayathnagar, Rangareddy, Telangana, India

* Corresponding Author: **Dr. K Mangulal**

Article Info

ISSN (online): 2582-7138
Volume: 06
Issue: 04
July - August 2025
Received: 10-05-2025
Accepted: 13-06-2025
Published: 04-07-2025
Page No: 717-722

Abstract

The objective of the present work was to formulate floating hollow microspheres of Semaglutide which is soluble and shows better absorption in gastric pH. Microspheres were prepared by emulsion solvent diffusion technique. Using various such as Tragacanth and eudragit polymers. The formulations were evaluated for micromeritics properties, in vitro buoyancy, entrapment efficiency and in vitro studies. They were characterized by FT-IR. FT-IR and studies indicated that there was no interaction between the drug and polymers. SEM photographs showed the outer surface of microspheres was smooth and dense where as internal surface was porous which helped to prolong floating to increase residence time in stomach. The results showed that floating microspheres could be successfully prepared with better yield. Results showed larger the particle size, longer was the floating time. In vitro drug release studies showed controlled release of Semaglutide for over 8 h. From the results it can be concluded that gastric floating hollow microspheres can be successfully used for the delivery of Semaglutide to control blood glucose level.

Keywords: Semaglutide, Polymers, FTIR Studies, Emulsion Solvent Diffusion Technique, Floating Time, In Vitro Drug Release Studies

Introduction

A large numbers of novel drug delivery systems are investigating day by day for drug administration through various routes. Administration of drugs by oral route is well thought-out as an appropriate and ideal route of drug delivery for increased patient compliance as compared to other drug delivery system by any other route [1]. However, oral administration of some of the drugs suffers from short term limitations such as their less oral bioavailability because of partial absorption. Degradation of drug in the gastrointestinal tract (GIT) is one of the most important cause of less oral bioavailability [2]. Various medicaments exhibit a narrow therapeutic window in the upper portion of the GIT because of proximal part of the small intestine shows prolonged absorption properties (including larger gaps between the tight junctions and dense active transporters). The extent of absorption is limited at these sites as the drug passage is rapid through these regions despite the higher absorption properties at the jejunum and duodenum [3].The net absorption of the drugs exhibiting narrow therapeutic window can significantly be improved by increasing the gastric residence time (GRT) of the medicament [4]. The oral bioavailability of the therapeutic ingredients can be expressively increased which could get metabolized in the upper portion of GIT by these gastro-retentive drug delivery approaches in contrast to the administration of non-gastro-retentive drug delivery. Several different issues exist which relate to absorption and transit of the medicament in the gastric region, which act naturally to effect the extent of medicament absorption [5]. For medicaments with short biological half-life, sustained release (SR) action may turn out the flip- flop pharmacokinetics model. They inbuilt an advantage in compare to the conventional system that it can be utilized to sort out the problem of GRT

along with the GET [6]. The objective of the present work was to formulate floating hollow microspheres of Semaglutide which is soluble and shows better absorption in gastric pH. Microspheres were prepared by emulsion solvent diffusion technique.

Drug excipient compatibility studies [7]

FTIR is a useful technique to check and confirm any interaction that may occur between excipients and drug. The FTIR spectra of drug, excipients, briefly, solid sample (1 mg) along with 100 mg dried potassium bromide was compressed into a disc. For liquid sample, few drops of the sample were dripped onto NaCl or KBr aperture plate and sandwiched it under another aperture plate, such that no gas bubbles were trapped. The sample allowed formation of a thin liquid membrane between the two aperture plates. Thereafter, sample was scanned for absorbance over the range from 4000 to 400 (cm-1) wave numbers.

Materials and Methods

Semaglutide was collected as a gift sample from Hetero labs, Hyderabad and various excipients and polymers were purchased from AR chemicals, Hyderabad.

Methodology

Formulation development

Preparation and evaluation of Semaglutide floating microspheres

Table 1: Formulation development of Semaglutide floating microspheres

F. no	Polymer	Drug and polymer ratio	Stirring speed
F1	Tragacanth	1:1	800
F2	Tragacanth	1:2	800
F3	Eudragit RS100	1:1	800
F4	Eudragit RS100	1:2	800

Method

Emulsion-solvent diffusion technique with some modifications was used to prepare Eudragit, Tragacanth microspheres containing Semaglutide. Briefly Semaglutide was dissolved in 5 ml distilled water. Polymers was dissolved in Dichloromethane at various drug - polymer ratios (1:1 and 1:2). Then these drug and polymer solutions were mixed and emulsified using a Remi Lab Magnetic stirrer at 500 rpm for about 10 min to form stable w/o emulsion. This stable w/o emulsion was slowly added to 200 ml aqueous solution containing 1 % PVA and stirred at 1000 rpm by a mechanical stirrer equipped with a three bladed propeller (Remi motors, India) at room temperature for 2 h to allow the solvent to evaporate completely. Microspheres were isolated by filtration and washed with distilled water several time to remove PVA. The produced microspheres were dried at ambient temperature for 24 h and dried in vacuum chamber at 25 ^{0}C for 2 h to remove any residual solvent.

Evaluation of floating microspheres [8,9,10]

Particle size analysis

Particle size analysis plays an important role in determining the release characteristics and floating property. The sizes of floating microspheres were measured by using a set of standard sieves ranging from 14, 16, 18, 22, 30 and pan. The sieves were arranged in increasing order from top to bottom. The floating microspheres were passed through the set of sieves and amount retained on each sieve was weighed and the % weight of floating microspheres retained by each sieve was calculated.

Mean particle size for all formulation was determined by dividing the total weight size of formulation to % total weight of floating microspheres.

Percentage Yield

The percentage yield of different formulations was determined by weighing the floating microspheres after drying. The percentage yield was calculated as follows.

$$\text{Total weight of \% Yield} = \frac{\text{floating microspheres}}{\text{Total weight of drug and polymer}} \times 100$$

Surface Characterization by SEM

From the formulated batches of floating microspheres, formulation which showed an appropriate balance between the buoyancy and the percentage release were examined for surface morphology and shape using scanning electron microscope. Sample was fixed on carbon tape and fine gold sputtering was applied in a high vacuum evaporator. The acceleration voltage was set at 20KV during scanning. Microphotographs were taken on different magnification and higher magnification (200X) was used for surface morphology.

Floating Property of Floating microsphere

100 mg of the floating microsphere were placed in 0.1 N HCl (300 ml) containing 0.02% tween 20. The mixture was stirred with paddle at 100rpm. The layer of buoyant microspheres was pipetted and separated by filtration at 1, 2, 4 and 6 hours. The collected microspheres were dried in a desiccator overnight. The percentage of microspheres was calculated by the following equation:

$$\text{\% Floating microsphere} = \frac{\text{Weight of floating microsphere}}{\text{Initial weight of floating microsphere}} \times 100$$

Drug Entrapment efficiency

The various formulations of the floating microspheres were subjected for drug content. 50 mg of floating microspheres from all batches were accurately weighed and crushed. The powdered microspheres were dissolved with 10ml ethanol in 100ml volumetric flask and the volume was made up with 0.1 N HCl. This resulting solution is than filtered through Whatmann filter paper No. 44. After filtration, from this solution 10 ml was taken out and diluted up to 100 ml with 0.1 N HCl. Again from this solution 2 ml was taken out and diluted up to 10 m1 with 0.1 N HCI and the absorbance was measured at 280 nm against 0.1 N HCl as a blank. The percentage drug entrapment was calculated as follows.

$$\text{\% Drug entrapment} = \frac{\text{- Calculated drug concentration}}{\text{Theoretical drug concentration}} \times 100$$

In vitro drug release study [11]

In vitro drug release studies for all formulations were carried out using the USP type –II dissolution basket assembly. Microspheres equivalent to 100 mg of Semaglutide were taken. The dissolution media of 900 ml of stimulated gastric fluid (pH1.2) was maintained at 37±0.5 ºC and stirred at 100 rpm. 1 ml aliquots were withdrawn at a predetermined

intervals and equal volume of dissolution medium was replaced to maintain sink conditions. The necessary dilutions were made with 1.2 pH buffer and the solution was analyzed for the drug content spectrophotometrically using UV-Visible spectrophotometer.

Stability Study [12]

From the prepared floating microspheres which showed appropriate balance between the buoyancy and the percentage release was selected for stability studies. The prepared formulation were placed in borosilicate screw capped glass containers and stored at room temperature (27 ± 2° C), oven temperature (42±2° C) and in refrigerator (5-8° C) for a period of 30 days. The samples were assayed for drug content at regular intervals for two weeks.

Results & Discussion

FT-IR Spectrum of Semaglutide

FT-IR Spectra of Semaglutide and F4 formulation were recorded. All these peaks have appeared in formulation and physical mixture, indicating no chemical interaction between Semaglutide and polymer. It also confirmed that the stability of drug during microencapsulation process.

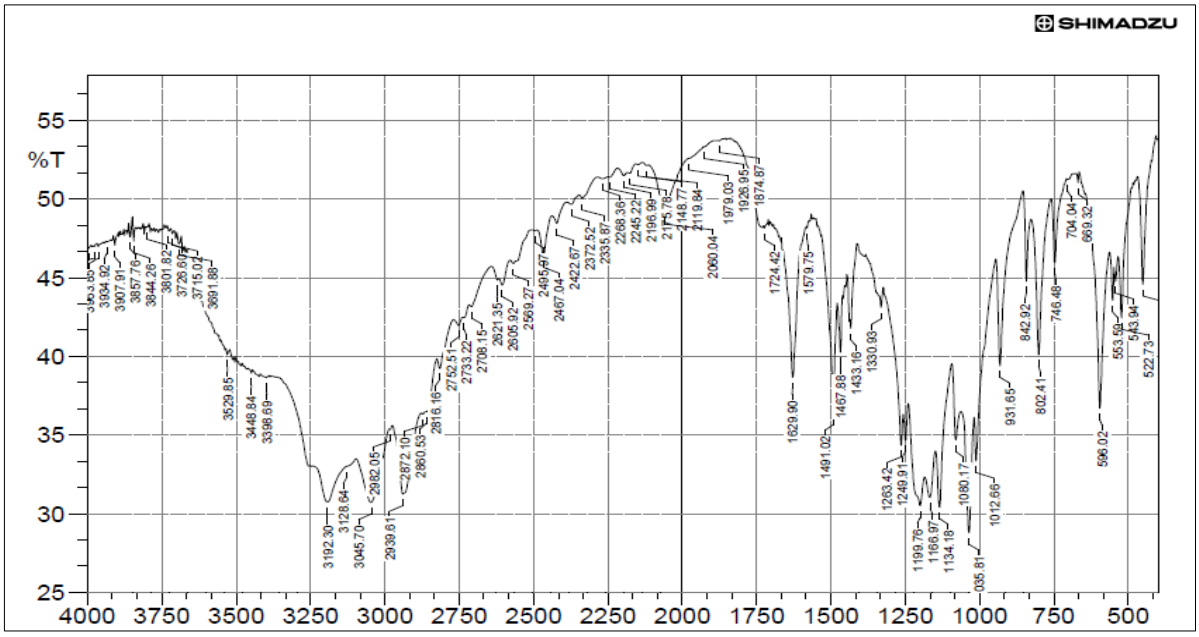

Fig 1: FTIR Studies of Semaglutide

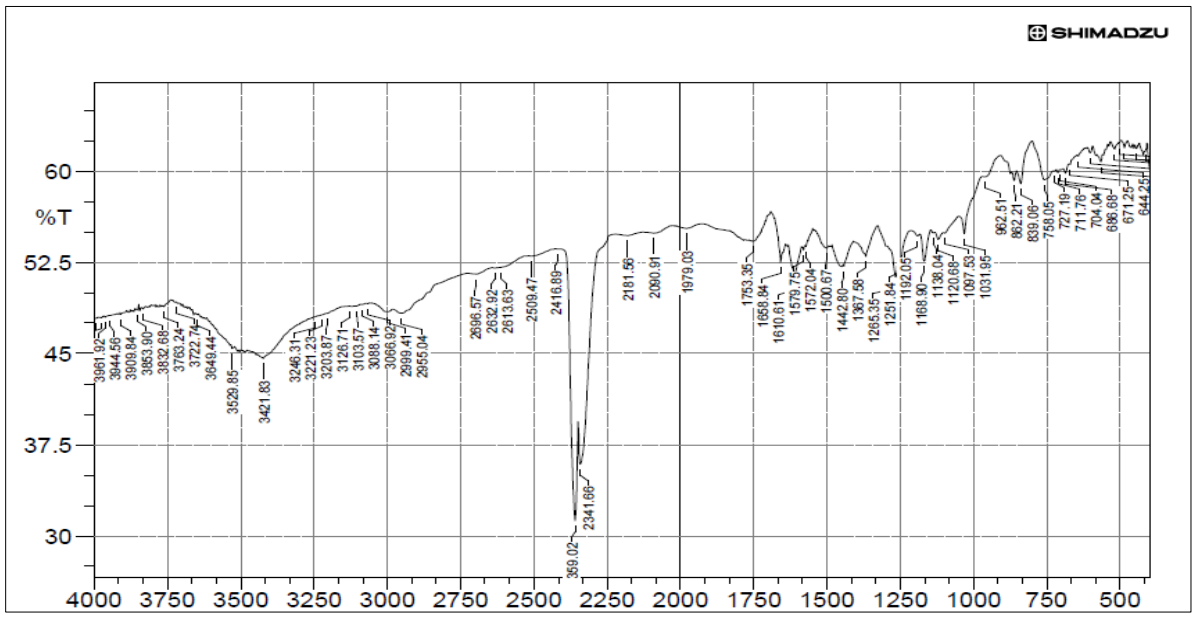

Fig 2: FTIR Studies of optimized formulation

Evaluations of floating microspheres

Particle size analysis

Particle size was determined by sieving method it plays important role in floating ability and release corrected of drug from Floating microspheres. If size of Floating microspheres less than 500 µm so release rate of drug will be high and floating ability will reduce, while Floating microspheres range between 100 µm – 1000 µm, floating ability will be more and release rate will be in sustained manner.

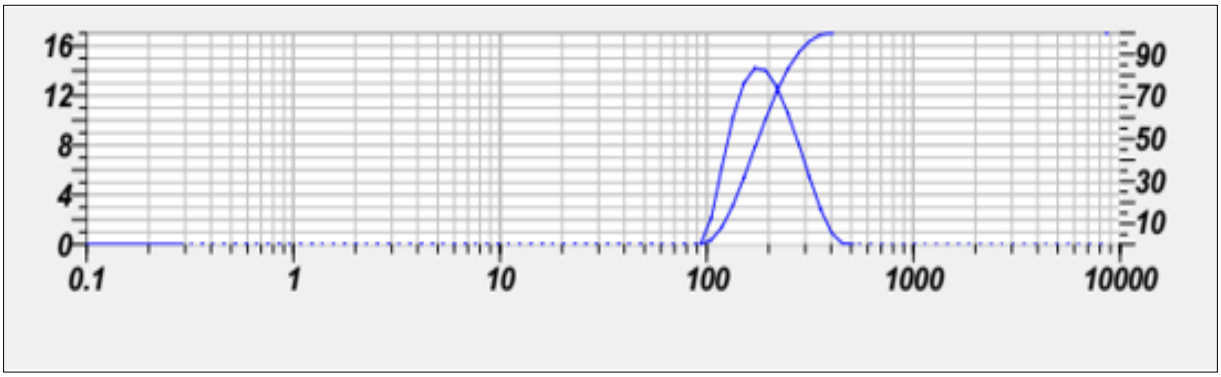

Fig 3: Particle size analysis of Optimized formulation

Table 2: Particle size of Different formulations of Floating microsphere

S. No	Formulation code	Mean particle size* (µm)
1	F1	179
2	F2	186
3	F3	145
4	F4	176

Table 3: Percentage yield for different formulation

Formulation	Percent Yield*(%)
F1	80.13
F2	78.86
F3	82.13
F4	85.50

Percentage Yield

Percentage yield of different formulation was determined by weighing the Floating microspheres after drying. The percentage yield of different formulation were in range of 78.86- 85.50 % as shown in Table.

Scanning Electronic Microscopy

Shape and surface characteristic of Floating microspheres examine by Scanning Electronic Microscopy analysis as shown in Fig. Surface morphology of F4 formulation examine at different magnification 40X and 200X, which illustrate the smooth surface of floating Floating microspheres and small Floating cavity present in microsphere which is responsible for floating property.

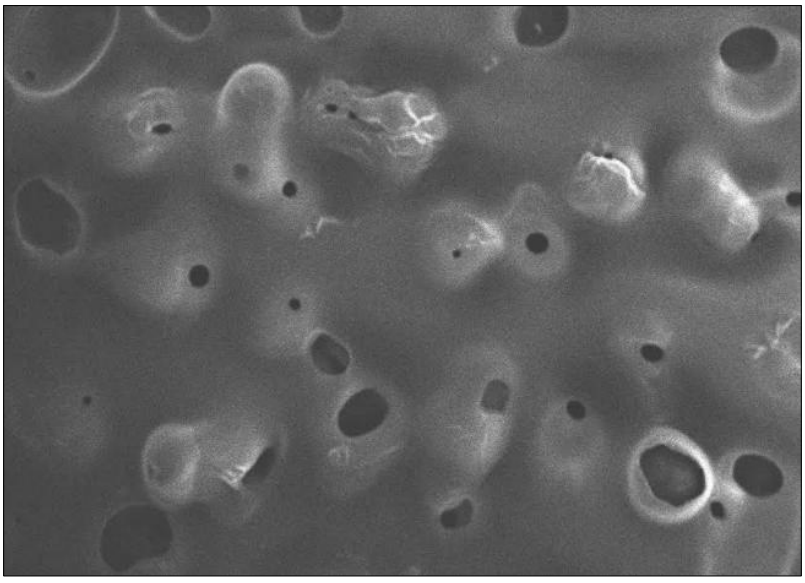

Fig 4: SEM Analysis of Optimized formulation

The optimized formulation F4 was evaluated for its surface morphology by using SEM analysis. The particle size was found to be 176 µm. The Floating microspheres were found to be smooth and spherical in shape.

Floating Property of Floating Microsphere

Floating Microsphere were dispersed in 0.1 N HCl to simulate gastric fluid. Floating ability of different formulation were found to be differed according to polymer ratio.

Table 4: % Buoyancy Time for different formulations

Formulation	1 hour	2 hours	3 hours
F1	94.52	93.65	92.51
F2	93.65	92.43	91.53
F3	92.65	91.20	90.25
F4	90.12	89.63	88.93

Drug Entrapment

The drug entrapment efficacy of different formulations were in range of 82.33% - 85.56 % Drug entrapment efficacy slightly increases eudragit content ratio in Floating microspheres. This is due to the permeation characteristics of

Eudragit that could facilitate the diffusion of part of entrapped drug to surrounding medium during preparation of Floating microspheres.

Table 5: Drug entrapment for different formulation

Formulation	Drug Entrapment (% w/w)
F1	82.39
F2	84.35
F3	82.33
F4	85.56

In-Vitro Drug release study

In-Vitro drug release study of Floating microspheres was evaluated in pH 1.2 buffer. Eudragit RS100 which is present in all formulation, have low permeability in acid medium. Since Eudragit is less soluble in acidic pH, release of drug in 0.1 N HCl was generally low.

Table 6: Comparative *In-Vitro* Drug Release Profile for Formulation in pH 1.2 phosphate

Time(hrs)	F1	F2	F3	F4
0	0	0	0	0
1	18.12	16.10	16.39	19.25
2	26.90	25.55	26.82	28.92
3	42.50	45.10	44.21	46.52
4	54.68	53.18	55.82	58.40
5	61.25	62.49	63.19	65.75
6	75.10	75.68	74.58	76.98
7	85.62	85.34	84.20	85.42
8	94.60	95.21	96.38	97.86

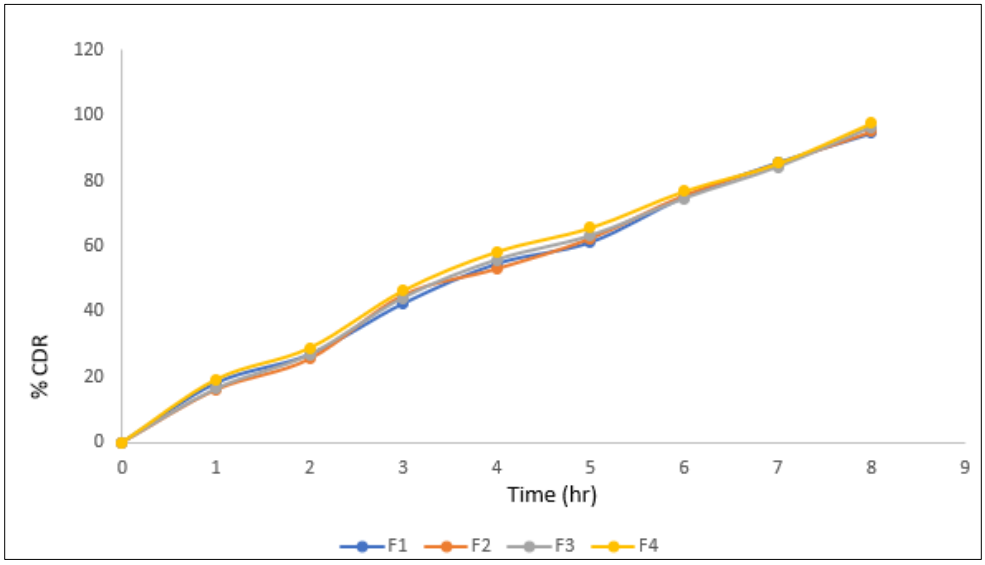

Fig 5: Comparative *In-Vitro* Drug Release Profile Of (F1-F4) formulation

All the 4 formulations of Floating microspheres were subjected to dissolution studies. Dissolution was carried out in franz diffusion cell apparatus at 100 rpm in the volume of 10 ml dissolution media of 0.1N HCL for 8 hours. F4 showed a release rate of 97.86 by end of 8th hour of dissolution study.

Stability Study

Stability study was carried out for the F4 formulation by exposing it to different temperature 25°C, 30°C and 40°C for 90 days. The sample was analyzed for drug content at the regular intervals. It was found that no remarkable change in the drug release of F4 formulation. This indicates that F4 was stable for following temperature.

Table 7: Results of stability studies of optimized formulation F-4

S.NO	Time in days	Physical changes	Mean % drug release		
			Semaglutide		
			25^{0}C/60%	30^{0}C/75%	40^{0}C/75%
1.	01	No Change	97.86	96.42	95.18
2.	30	No Change	97.86	96.53	95.25
3.	60	No Change	97.86	96.16	95.16
4.	90	No Change	97.86	96.18	95.24

The optimized formulation was stored in different conditions to check the stability. Drug release of the optimized formulation F4 initially was 97.86 %. From the above result it can be concluded that there was no significant change in physical and chemical properties of the Floating microspheres of formulation F-4 after 3 Months.

3. Conclusion

- Emulsion Solvent diffusion method used for preparation of hollow microspheres of Semaglutide.
- FT-IR studies indicated that there was no chemical interaction between the drug and the polymers used.
- The morphology of hollow microspheres was examined using SEM. The view of microspheres showed a hollow spherical structure with rough surface morphology. It was also evident that the hollow microspheres exhibited porous surfaces.
- Results of drug content determination from hollow microsphere inferred that there was proper and uniform distribution of drug. The percentage encapsulation

efficiency of microspheres also showed that the drug loading was optimum and increased with increasing amount of polymers. The prepared microspheres exhibited good micromeritic properties.

- From the results of particle size analysis, it is clear that all the process variables were within the limits and the process was reproducible. The study of micromeritic properties indicated fair to good flow of microspheres.
- All the formulations floated for more than 8 hours. In vitro test showed that larger the particle size, longer the floating time. The microspheres of all the formulations were spherical and free flowing. In vitro floating behavior studies showed that among all formulations had maximum percentage floating ability, the best being F4.
- Results of the stability studies showed that there were no significant changes in the drug content and physical appearance.

References

1. Vyas SP, Khar RK. Controlled drug delivery: concepts and advances. 1st ed. Delhi: Vallabh Prakashan; 2002. p. 196-205.
2. Singh BN, Kim KH. Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention. J Control Release. 2000;63(3):235-59.
3. Ojha G. Floating microspheres: development, characterization & application. AAPS PharmSci. 2006;8(3):E129-40.
4. Arora S, Ali J, Ahuja A. Floating drug delivery systems: a review. AAPS PharmSciTech. 2005;6(3):E372-90.
5. Yeole PG. Floating drug delivery system: need & development. Indian J Pharm Sci. 2005;67(3):265-72.
6. Sato Y, Kawashima Y, Takeuchi H, Yamamoto H. Physicochemical properties to determine the buoyancy of hollow microspheres (microballoons) prepared by the emulsion solvent diffusion method. Eur J Pharm Biopharm. 2003;55(3):297-304.
7. El-Kamel AH, Sokar MS, Al Gamal SS, Naggar VF. Preparation and evaluation of ketoprofen floating oral delivery system. Int J Pharm. 2001;220(1-2):13-21.
8. Sato Y, Kawashima Y, Takeuchi H, Yamamoto H. In vitro evaluation of floating and drug releasing behavior of hollow microspheres (microballoons) prepared by the emulsion solvent diffusion method. Eur J Pharm Biopharm. 2004;57(2):235-43.
9. Patel VF, Patel NM, Yeole PG. Studies on formulation and evaluation of ranitidine floating tablets. Indian J Pharm Sci. 2005;67(6):703-9.
10. Kale RD, Tayade PT. A multiple unit floating drug delivery system of piroxicam using Eudragit polymer. Indian J Pharm Sci. 2007;69(1):120-3.
11. Dave BS, Amin AF, Patel MM. Gastroretentive drug delivery system of ranitidine hydrochloride: formulation and in vitro evaluation. AAPS PharmSciTech. 2004;5(2):e34.
12. Vedha Hari BN, Brahma Reddy A, Punitha S, Parimala Devi D, Victor Rajamanickam G. The recent developments on gastric floating drug delivery systems: an overview. Int J PharmTech Res. 2010;2(1):524-34.