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Formulation and Evaluation of Floating Drug Delivery System Using an Anti-Asthmatic Drug

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ABSTRACT

Floating tablets using different mixture of cellulose and natural gum were prepared in order to obtain new formulation containing Montelukast sodium for management of chronic asthma. Seven different formulations of floating tablets of Montelukast sodium were prepared, which contain polymers such as hydroxy propyl methyl cellulose (K4M, K15M), xanthan gum and effervescent agent sodium bicarbonate along with drug and other excipients in various combinations. Tablets were prepared by direct compression method. The formulated tablets were subjected to thickness, hardness, weight variation, floating capacity, floating lag time, friability, and drug content. Further, the tablets were evaluated for in-vitro release characteristics for twenty four hours. All the formulations showed the satisfactory result in terms of thickness, hardness, weight variation, floating capacity, floating lag time, friability, and drug content. Drug release from the tablets was dependant on the ratio and type of the polymer used in the formulation. Swelling studies indicated significant water uptake and contributed in drug release and gastro retention. The higher viscosity polymer had been seen to inhibit the release of montelukast sodium from the FDDS. From among all the developed formulations, formulation F3 prolonged the drug release for longer period of time of 24 h and it showed a drug release of 94.09 ± 0.20 %. So, it was selected as the best formulation. Best formulation was checked for stability at 30 ± 2 °C / 65 ± 5 % RH and at 40 ± 2 °C / 75 ± 5 % RH, which showed no significant change for 2 months.

Keywords: Montelukast sodium, Floating tablets, Xanthan gum, Hydroxyl propyl methyl cellulose K4M and K15M.

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INTRODUCTION

ASTHMA

Asthma is a disease of airways that is characterized by increased responsiveness of the tracheobronchial tree to a variety of stimuli resulting in widespread spasmodic narrowing of the air passages which may be relieved spontaneously or by therapy. Asthma is an episodic disease manifested clinically by paroxysms of dyspnoea, cough and wheezing [1].

Extrinsic (atopic, allergic) Asthma

This is the most common type of asthma. It usually begins in childhood or in early adult life. Most patients of this type of asthma have personal and/or family history of preceding allergic diseases such as rhinitis, urticaria or infantile eczema. Hypersensitivity to various extrinsic antigenic substances or allergens is usually present in these cases. Most of these allergens cause ill-effects by inhalation e.g. house dust, pollens, animal dander's, moulds etc.

Intrinsic (idiosyncratic, non-atopic) Asthma

This type of asthma develops later in adult life with negative personal or family history of allergy, negative skin test and normal serum levels of IgE. Most of these patients develop typical symptom-complex after an upper respiratory tract infection by viruses. Associated nasal polypi and chronic bronchitis are commonly present. There are no recognizable allergens but about 10% of patients become hypersensitive to drugs, most notably to small doses of aspirin (aspirin-sensitive asthma).

Mixed Type

Many patients do not clearly fit into either of the above two categories and have mixed features of both. Those patients who develop asthma in early life have strong allergic component, while those who develop the disease late tend to be non-allergic. Either type of asthma can be precipitated by cold, exercise and emotional stress.

Drug-Induced asthma

Several pharmacologic agents provoke asthma. Aspirin sensitive asthma is an uncommon yet fascinating type, occurring in patients with recurrent rhinitis and nasal polyps. These individuals are sensitive to small doses of aspirin, and they experience not only asthmatic attacks but also urticaria.

It is probable that aspirin triggers asthma in these patients by inhibiting the cyclooxygenase pathway of arachidonic acid metabolism without affecting the lipoxygenase route, thus tipping the balance toward elaboration of the bronchoconstrictor leukotrienes [2].

Exercise-Induced Asthma

The typical attack of exercise-induced asthma (EIA) is provoked by 4 to 6 minutes of moderately severe to severe continuous exercise such as running 1000 meters. During the exercise the child feels well as there is some bronchodilatation which gives way to bronchospasm towards the end of the run, and the really pronounced fall in lung function only occurs some 3 to 5 minutes after stopping the exercise. EIA is post exercise asthma, and it is unusual for the attack to develop so rapidly that the child has to stop in the middle of the exercise. [3]

Montelukast sodium

Montelukast is a selective leukotriene receptor antagonist. It is used as the sodium salt, but doses are expressed in terms of the base; montelukast sodium 10.37 mg is equivalent to about 10 mg of montelukast. The mean bioavailability of montelukast is 64% and it is more than 99% bound to plasma proteins. [4]

Controlled Release Drug Delivery System through Gastric Retention

Controlled release drug delivery systems that can be retained in stomach for a long time are important for drug that are degraded in intestine or for drugs like antacids or certain enzymes that should act locally in the stomach. If the drugs are poorly soluble in intestine due to alkaline pH, gastric retention may increase solubility before they are emptied, resulting in improved gastrointestinal absorption of drugs with narrow absorption window as well as for controlling release of drugs having site-specific absorption limitation. [5]

Factors Affecting Gastric Retention [6].

I. Density

The density of a dosage form also affects the gastric emptying rate. A buoyant dosage form having a density of less than that of the gastric fluids (≅ 1.004 gm/ml) floats. Since it is away from the pyloric sphincter, the dosage unit is retained in the stomach for a prolonged period.

II. Size and shape

To pass through the pyloric valve into the small intestine the particle size should be in the range of 1 to 2 mm. Floating dosage form with a diameter of 7.5 mm or less than that are reported to have an increased GRT as compared to those with a diameter of 9.9 mm. The dosage form with a shape tetrahedron and ring shape devices with a flexural modulus of 48 and

22.5 kilo pound per square inch (KSI) are reported to have better GIT (≅ 90 to 100 %) retention at 24 hours.

III. Fasting or fed state

Under fasting conditions, the GI motility is characterized by periods of strong motor activity or the migrating myoelectric complexes (MMC) that occur every 1.5 to 2 hours. The MMC sweeps undigested material from the stomach and if the timing of administration of the formulation coincides with that of the MMC, the GRT of the unit can be expected to be very short. However, in the fed state, MMC is delayed and GRT is considerably longer. The pH of the stomach in fasting state is ~1.5 to 2.0 and in fed state it is 2.0 to 6.0. A large volume of water administered with an oral dosage form raises the pH of stomach contents to 6.0 to 9.0. Stomach doesn't get time to produce sufficient acid when the liquid empties the stomach; hence, generally basic drugs have a better chance of dissolving in fed state than in a fasting state.

Studies have revealed that gastric emptying of a dosage form in the fed state can also be influenced by its size. Small-size tablets leave the stomach during the digestive phase while the large-size tablets are emptied during the housekeeping waves.

IV. Nature of the meal

The rate of gastric emptying depends mainly on viscosity, volume, and caloric content of meals. Nutritive density of meal helps determine gastric emptying time. It does not make any difference whether the meal has high protein, fat, or carbohydrate content as long as the caloric content is the same. However, increase in acidity and caloric value slows down gastric emptying time. Feeding of indigestible polymers of fatty acid salts can change the motility pattern of the stomach to a fed state, thus decreasing the gastric emptying rate and prolonging the drug release.

V. Effect of liquid, digestible solid and indigestible solid type food

It has been demonstrated using radio labeled technique that there is a difference between gastric emptying times of a liquid, a digestible solid, and an indigestible solid. It was suggested that the emptying of large (>1 mm) indigestible objects from stomach was dependent upon interdigestive migrating myoelectric complex. When liquid and digestible solids are present in the stomach, it contracts ~3 to 4 times per minute leading to the movement of the contents through partially opened pylorus. Indigestible solids larger than the pyloric opening are propelled back and several phases of myoelectric activity take place when the pyloric opening increases in size during the housekeeping wave and allows the sweeping of the indigestible solids. Studies have shown that the gastric residence time (GRT) can be significantly increased under the fed conditions since the MMC is delayed.

VI. Biological factors

Biological factors such as age, body mass index (BMI), gender, posture, and diseased states (diabetes, Chron's disease) influence gastric emptying. In the case of elderly persons, gastric emptying is slowed down. Generally females have slower gastric emptying rate than males. Stress increases gastric emptying rates while depression slows it down.

VII. Frequency of feed

The gastroretentive time can increase by over 400 minutes when successive meals are given compared with a single meal due to the low frequency of MMC.

VIII. Gender

Mean ambulatory GRT in males (3.4 ± 0.4 h) is less compared with their age and race-matched female counterparts (4.6 ± 1.2 h), regardless of the weight and body surface.

IX. Posture

Gastroretentive time can vary between supine and upright ambulatory states of patients.

X. Volume of liquids

The resting volume of the stomach is 25 to 50 ml. Volume of liquids administered affects the gastric emptying time. When volume is large, the emptying is faster. Fluids taken at body temperature leave the stomach faster than colder or warmer fluids.

Concept of Floating Drug Delivery System [7].

Gastric emptying of dosage forms is an extremely variable process and ability to prolong and control the emptying time is a valuable asset for dosage form, which resides in the stomach for a longer period of time than conventional dosage forms.

Several difficulties are faced in designing controlled release system for better absorption and enhanced bioavailability. One of such difficulties is the inability to confine the dosage form in the desired area of GIT. Gastro-retentive system can remain in the stomach for several hours and so significantly prolong gastric residence time of drug.

Prolonged gastric retention improves bioavailability, reduces drug wastage, and improves solubility of drugs. Gastro-retention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patients.

Advantages of Floating Dosage Form

- Improved absolute bioavailability of drugs that have poor bioavailability because of their limited absorption to the upper gastrointestinal tract absorption and improving their absolute bioavailability.
- Buoyant delivery system is considered beneficial for the treatment of gastric and duodenal cancers.
- Floating concept can be utilized in development of various anti-reflux formulations.
- To explore the eradication of H. pylori by using the narrow spectrum antibiotics.

Disadvantages of Floating Dosage Form

- These systems require a high level of fluid in stomach for drug delivery to float.
- Not suitable for drugs that have solubility or stability problem in GIT.
- Not be desirable for drugs such as nifedipine which is well absorbed along the entire GIT and which undergoes first pass metabolism.
- Drugs which are irritant to gastric mucosa are also not desirable or suitable.
- The drug substances that are unstable in the acidic environment of the stomach are not suitable candidates to be incorporated in the systems.
- The dosage form should be administered with a full glass of water (200-250 ml).

OBJECTIVES

1. To carry out preformulation studies for possible drug-polymer interactions by FTIR.
2. To develop and formulate controlled release floating tablets (gastro-retentive) for Montelukast Sodium.
3. To evaluate the formulated dosage forms based on…
    - Physicochemical parameters like…
        - Weight variation
        - Thickness
        - Hardness
        - Friability
    - Uniformity of drug content
    - Floating lag time
    - Floating time

- In vitro release studies.

4. To carry out short term stability studies of the most satisfactory formulation as per ICH guidelines for two months.

Table 1 - List of material used

Materials	Source
Montelukast Sodium	Matrix laboratories limited, Secunderabad.
Hydroxy propyl methyl cellulose (K4M, K15M)	Colorcon Asia Pvt. Ltd. Goa.
Xanthan gum	Loba chem. Pvt. Ltd. Mumbai.
Sodium bicarbonate	Karnataka fine chem. Bangalore.
PVP K-30	Karnataka fine chem. Bangalore.
Citric acid	Karnataka fine chem. Bangalore.
Talc	Karnataka fine chem. Bangalore.
Magnesium stearate	Karnataka fine chem. Bangalore.
Lactose	Karnataka fine chem. Bangalore.

Table 2: List of equipments

Equipments	Model/ Company
UV-visible spectrophotometer	Spectrophotometer UV-1700, Shimadzu
Electronic analytical balance	Shimadzu UX420H, Japan.
Fourier transform infrared Spectrophotometer	Bruker optics, Tensor 27.
Tablet compression machine	Mini Press-I, Rimek, Karnavati.
Screw Gauze	BioAids.
Hardness tester	Techno Scientific, Pfizer hardness tester
USP dissolution apparatus	Dissolution tester (USP), Labindia DS 8000
Tablet Friabilator	Electolab, EF-2
Digital pH Meter	Eutech Instruments
Tap Density Tester	Electrolab, ETD-1020

METHODOLOGY

PREFORMULATION STUDY

Preformulation study is one of the important prerequisite in development of any drug delivery system. Thus, a preformulation study was carried out to check the compatibility between drug and selected polymers and development of analytical method of drug.

UV SPECTRUM ANALYSIS OF MONTELUKAST SODIUM:

The solution was scanned in the range of 200 to 400 nm to fix the maximum wavelength and UV spectrum was obtained.

PREPARATION OF STANDARD CURVE

Standard stock solution of Montelukast Sodium in methanol

Accurately weighed 50 mg of Montelukast sodium was made to dissolve in methanol and the solution was made up to 50 ml with methanol. From this stock solution 10 ml was withdrawn and transferred into 100 ml volumetric flask. Volume was made with methanol in order to get standard stock solution containing 100 µg/ml.

Calibration curve of Montelukast Sodium in methanol

From standard stock solution, a series of dilutions of 0.5, 1.0, 1.5, 2.0 and 2.5 ml were taken in separate 10 ml volumetric flasks and the volume was made up by methanol. Absorbance of these solutions was measured against blank of methanol at 344.5 nm for Montelukast Sodium.

PREPARATION OF STANDARD CURVE

Standard stock solution of Montelukast Sodium in Simulated gastric fluid (pH 2) with 0.1% w/v SLS

Accurately weighed 10 mg of Montelukast sodium was made to dissolve in 100 ml of simulated gastric fluid with 0.1% w/v SLS. Volume was made with simulated gastric fluid with 0.1% w/v SLS in order to get standard stock solution containing 100 µg/ml.

Calibration curve of Montelukast Sodium in Simulated gastric fluid with 0.1% w/v SLS

From standard stock solution, a series of dilutions of 0.3, 0.6, 0.9, 1.2 and 1.5 ml were taken in separate 10 ml volumetric flasks and the volume was made up by simulated gastric fluid with 0.1% w/v SLS. Absorbance of these solutions was measured against blank of simulated gastric fluid with 0.1% w/v SLS and methanol at 344 nm for montelukast sodium.

DRUG POLYMER COMPATIBILITY STUDIES

a) Drug polymer compatibility studies were carried out using FTIR.
b) Infrared spectrum of pure drug was seen in between 600 to 3800 cm^{-1}.
c) The study was carried out on individual pure drug and its physical mixture with the selected polymers under study.

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FORMULATION DEVELOPMENT OF FLOATING TABLETS

Various formulations of floating tablets were developed for Montelukast sodium using selected polymers like HPMC K4M, HPMC K15M and Xanthan gum. Sodium bicarbonate and citric acid were selected as gas generating agents. Talc and Magnesium stearate were used as glidant and lubricant respectively.

Table 3: Formulation chart

INGREDIENTS	F1(mg)	F2(mg)	F3(mg)	F4(mg)	F5(mg)	F6(mg)	F7(mg)
DRUG	10.4	10.4	10.4	10.4	10.4	10.4	10.4
HPMC K4M	-	26.66	53.30	13.35	13.35	40	40
HPMCK15M	40	26.66	13.35	53.30	13.35	-	40
XANTHAN GUM	40	26.66	13.35	13.35	53.30	40	-
SODIUM BICARBONATE	60	60	60	60	60	60	60
CITRIC ACID	10	10	10	10	10	10	10
PVP	25	25	25	25	25	25	25
MAGNESIUM STEARATE	1	1	1	1	1	1	1
TALC	1	1	1	1	1	1	1
LACTOSE	12.6	12.6	12.6	12.6	12.6	12.6	12.6

METHOD OF PREPARATION OF FLOATING TABLETS

Floating tablets of Montelukast sodium were prepared by direct compression technique using varying concentrations of different grades of polymers with sodium bicarbonate and citric acid. All the ingredients were accurately weighed, and except Magnesium stearate all other ingredients were blended uniformly in a glass mortar. After sufficient mixing of drug as well as other ingredients, Magnesium stearate was added, as post lubricant, and further mixed for 2-3 minutes. Lubricated powder was compressed to tablets by 8 mm punch using rotary tablet machine.

EVALUATION OF FLOATING TABLETS OF MONTELUKAST SODIUM

MICROMERITIC PROPERTIES [8]

1. ANGLE OF REPOSE

The angle of repose of powder was determined by the funnel method. The accurately weighed powder was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of the powder. The powder was allowed to flow through funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation.

$$\text{Angle of repose } (\theta) = \tan^{-1}(h/r)$$

2. BULK DENSITY

Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. Powder from each formulation, previously lightly shaken to break any agglomerates formed was introduced into a 10 ml measuring cylinder. After the initial volume was observed, the sample is then tapped on a mechanical tapper apparatus. The tapping was continued until no further change in volume was noted.

Bulk density is calculated by using formula:

Bulk density =mass/volume

Tapped density = Tapped volume/ wt. of powder

3. CARR'S INDEX

The Carr's index of the powder was determined by using formula:

$$\text{Carr's index (\%)} = [(TBD - LBD) \times 100]/TBD$$

EVALUATION OF PHYSICOCHEMICAL PARAMETERS OF FLOATING TABLETS

TABLET THICKNESS

Thickness of tablets was important for uniformity of tablet size. Thickness was measured using screw gauze on randomly selected samples.

TABLET HARDNESS

The resistance of tablet for shipping or breakage, under conditions of storage, transportation and handling, before usage, depends on its hardness. The hardness of tablet of each formulation was measured by Pfizer hardness tester.

FRIABILITY

Friability is the resistance of the tablet to withstand the effect of abrasion and shock. Roche friabilator was used for testing the friability using the following procedure. Twenty tablets were weighed accurately and placed in the friabilator. The friabilator was operated at 25 rpm for 4 min or run up to 100 revolutions. The tablets were weighed again and the percentage loss in tablet weight was determined.

$$\% \text{ loss} = \frac{\text{Initial wt. of tablets} - \text{Final wt. of tablets}}{\text{Initial wt. of tablets}} \times 100$$

WEIGHT VARIATION [9]

Twenty tablets were weighed individually and the average weight was determined. Then percentage deviation from the average weight was calculated. According to IP standards, not more than two of the individual tablets deviate from the average weight by more than the percentage shown in the table 6 and none deviates by more than twice that percentage.

UNIFORMITY OF DRUG CONTENT [10]

Ten tablets were weighed and average weight was calculated. All tablets were crushed and powder equivalent to 10.4 mg drug was dissolved in methanol and the volume was made up to 100 ml with methanol. The solution was shaken for 30 minutes and filtered. From this 1 ml of solution was taken into a 10 ml volumetric flask and the volume was made with methanol. Absorbance was measured spectrophotometrically at 344.5 nm against methanol as a blank. Amount of drug present in one tablet was calculated.

FLOATING LAG TIME [11]

The floating lag time was carried out in a beaker containing 100 ml of 0.1 N HCl as a testing medium maintained at 37 ºC. The time required for the tablet to rise to the surface and float was determined as floating lag time.

FLOATING TIME

Floating time was the time, during which the tablet floats in 0.1 N HCl dissolution medium (including floating lag time).

SWELLING CHARACTERISTICS

The swelling properties of floating tablets containing drug were determined by placing the tablets in the USP dissolution testing apparatus II, in 900 ml of 0.1 N HCl at 37 ± 0.5 ºC, rotated at 50 rpm. The tablets were removed periodically from dissolution medium, blotted to remove excess water and weighed. Swelling characteristics were expressed in terms of percentage water uptake (WU %).

$$WU\ \% = \frac{\text{Wt. of swollen tablet} - \text{Initial wt. of the tablet}}{\text{Initial wt. of the tablet}} \times 100$$

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DISSOLUTION STUDIES [12]

The release rate of montelukast sodium from floating tablets was determined using USP dissolution testing apparatus II (paddle type). The dissolution test was performed using 900 ml of simulated gastric fluid containing 0.1% w/v SLS at 37 ± 0.5 ºC and 75 rpm. Aliquot volume was withdrawn from the dissolution apparatus hourly for 24 h and the samples were replaced with fresh dissolution medium. After filtration, the amount of drug released was determined from the standard calibration curve of pure drug.

Details of dissolution test:

1. Apparatus : USP type II
2. Volume of medium : 900 ml
3. Temperature : 37 ± 0.5 ºC
4. Paddle speed : 75 rpm
5. Dissolution medium used : Simulated gastric fluid with 0.1% w/v SLS
6. Aliquot taken at each time interval: 9 ml

Kinetic study [13-15]

In order to analyse the release mechanism, several release models were tested such as:

$$\text{Higuchi: } Qt = K_H\sqrt{t} \quad \text{---------- 1}$$

Where Qt is the amount of drug released at time t and K_H is the higuchi release rate; this is the most widely used model to describe drug release from pharmaceutical matrices.

$$\text{Zero order: } Q_t = Qo + Kot \quad \text{---------- 2}$$

Where Q_t is the amount of drug released at time t, Ko is the apparent dissolution rate constant or zero order release constant and Qo is the initial concentration of the drug in the solution resulting from a burst effect; in this case the drug release runs as a constant rate.

$$\text{First order: } \ln Q_t = \ln Qo + K_1 t \quad \text{---------- 3}$$

Where K_1 is the first order release constant; in this case the drug released at each time is proportional to the residual drug inside the dosage form.

CONCLUSION

- Montelukast sodium showed maximum absorption at wavelength 344.5 nm in methanol. The value of correlation coefficient was found to be 0.999, which showed

linear relationship between concentration and absorbance. Preformulation study for drug-polymer compatibility by FTIR gave confirmation about their purity and showed no interaction between drug and selected polymers.

- Various formulations were developed by using release rate controlling and gel forming polymers like HPMC (K4M, K15M) and Xanthan gum by direct compression method with the incorporation of sodium bicarbonate as gas generating agent.

- Developed floating tablets possessed the required physicochemical parameters such as hardness, friability, weight variation, drug content, swelling index and floating properties. All the developed floating tablets floated up to 20 and 24 h.

- Swelling studies indicated significant water uptake and contributed in drug release and gastro retention. The higher viscosity polymer had been seen to inhibit the release of montelukast sodium from the FDDS. From among all the developed formulations, formulation F3 prolonged the drug release for longer period of time of 24 h and it showed a drug release of 94.09 ± 0.20 %. So, it was selected as the best formulation.

- The most satisfactory formulation had showed no major change in physicochemical properties, drug content, floating properties and in-vitro dissolution pattern after storage at 30 ± 2 °C / 65 ± 5 % RH and at 40 ± 2 °C / 75 ± 5 % RH, there was no change in the above parameters during stability studies for two months.

- Therefore, it was concluded that the most satisfactory formulation satisfied the physicochemical parameters, floating properties, drug content requirement, in vitro drug release profile requirements and stability requirements.

SUMMARY

- Standard calibration curve was prepared for the determination of montelukast sodium in simulated gastric fluid with 0.1 % w/v SLS (pH 2) at 344 nm and in methanol at 344.5 nm.

- FTIR spectrum of pure drug and drug-polymer mixture revealed no chemical interaction.

- Total seven batches of floating tablets using polymers such as HPMC K4M, HPMC K15M and Xanthan gum were prepared by direct compression technique.

- Various physicochemical parameters like thickness, hardness, friability, weight variation, uniformity of drug content, floating properties and swelling studies were evaluated. In-vitro dissolution studies were also performed for the drug release study.

- Stability study of F3 formulation was performed and showed no major change in physicochemical parameters, floating properties and drug release profile at 30 ± 2 °C / 65 ± 5 % RH and 40 ± 2 °C / 75 ± 5 % RH.

- The best floating performance and the best in vitro drug release profile were achieved by formulation F3 which contains polymers HPMC K4M, HPMC K15M and Xanthan gum in a ratio of 4:1:1 respectively which gave the drug release up to 24 h.

REFERENCES

[1] Harsh Mohan. Text Book of Pathology. 4th Ed. Jaypee Brothers Medical Publishers, New Delhi. 2000: 454-55.
[2] Robbins, Cotran. Pathologic Basis of Disease. 7th Ed. Elsevier Publishers, New Delhi. 2004: 726.
[3] Godfrey S. Exercise induced asthma. Arch Dis Child 1983; 58 :1-2.
[4] Sweetman S. Martindale - The complete drug reference. 35th Ed. Pharmaceutical Press, London. 2007; 1: 1011.
[5] Gastro-Retentive Drugs: A Novel Approach towards Floating Therapy [cited 2011 Mar 28]. Available at URL:http://www.pharmainfo.net/reviews/gastro-retentive-drugs-novel-approach-towards-floating-therapy.
[6] Brahma N, Kwon H. Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention. J Control Release 2000; 63: 235–59.
[7] Arora S, Ali J, Ahuja A, Khar RK, Baboota S. Floating Drug Delivery Systems: A Review. AAPS PharmSciTech 2005; 6(3): Article 47.
[8] Lachman L, Liberman HA, Kanig JL. The Theory and Practice Of Industrial Pharmacy. 3rd Ed., Mumbai: Varghese publishing house. 1990: 296-302.
[9] Indian Pharmacopoeia, Government of India, Ministry of Health and Family Welfare. Vol. II Delhi: Controller of Publications. 1996: 182.
[10] Sreekanth SK, Palanichamy S, Rajasekharan T, Thanga AT. Formulation and evaluation studies of floating matrix tablets of nifedipine. Int J Pharm Bio Sci 2010; 1(2).
[11] Patel MP, Patel MM, Patel DH, Patel KN. Formulation development, optimization and evaluation of Famotidine floating matrix tablets. Int J Pharm Sci DrugRes 2009; 1(2): 85-90.
[12] Arthur O, Marie D, Raimar L. Pharm Res 2008; 25(12): 2778-85.
[13] Costa P, Lobo JMS. Pharm Dev Tech 2001; 6(3): 343-51.
[14] Peppas NA. J Biomed Mater Res 1983; 17: 1079-87.
[15] Ritger PL, Peppas NA. J Cont Rel 1987; 5: 37-42.