

# Formulation of Floating Drug Delivery System of Loratadine Using Guar Gum, Xanthan Gum, and HPMC K35M

P. Sravanthi  
Assistant Professor  
Department of pharmaceuticals  
Sri vasavi institute of pharmaceutical sciences, Tadepalligudem, Andhra Pradesh

Navya S  
Student pursuing B.pharm 4th year  
Department of pharmaceuticals  
Sri vasavi institute of pharmaceutical sciences, Tadepalligudem, Andhra Pradesh

P. Manju Sri Keerthi  
Student pursuing B.pharm 4th year  
Department of pharmaceuticals  
Sri vasavi institute of pharmaceutical sciences, Tadepalligudem, Andhra Pradesh

P. Rijvana  
Student pursuing B.pharm 4th year  
Department of pharmaceuticals  
Sri vasavi institute of pharmaceutical sciences, Tadepalligudem, Andhra Pradesh

K. Vivek  
Student pursuing B.pharm 4th year  
Department of pharmaceuticals  
Sri vasavi institute of pharmaceutical sciences, Tadepalligudem, Andhra Pradesh

K. Lavanya  
Student pursuing B.pharm 4th year  
Department of pharmaceuticals  
Sri vasavi institute of pharmaceutical sciences, Tadepalligudem, Andhra Pradesh

**Abstract** -Loratadine, a long-acting tricyclic antihistamine with selective peripheral histamine H1-receptor antagonistic activity, is widely used for the symptomatic relief of allergic conditions such as allergic rhinitis and chronic urticaria. It exhibits pH-dependent solubility, being more stable in acidic conditions, and possesses a narrow absorption window in the upper gastrointestinal tract. Therefore, the present study was aimed at formulating and evaluating gastroretentive floating tablets of Loratadine to prolong gastric residence time, thereby enhancing drug absorption and bioavailability.

In this study Loratadine floating tablets were prepared by using two different techniques like Effervescent floating tablets and non-effervescent floating tablets using HPMC K35, Guar gum and Xanthan Gum as polymers and sodium bicarbonate is a gas generating agent. The tablets prepared by direct compression technique were evaluated in terms of their pre-compression parameters and post compression characteristics such as physical characteristics, total buoyancy, buoyancy lag time, swelling index and in vitro release. The best formulation showed no significant change in physical appearance, drug content, total buoyancy time, buoyancy lag time or in vitro release after storage at 40°C /75% RH for three months. Based on the results with all polymers, the order of the drug release was dependent on the type of polymer and polymer proportion. HPMCK35M showed more retardation than Xanthan Gum than Guar gum.

**Keywords** : Antihistamine, buoyancy, swelling index, gastroretentive

## INTRODUCTION

### Modified Release Oral Drug Delivery Systems <sup>[1,8,13]</sup>

The oral route represents the predominant and most preferable route for drug delivery. Unlike the majority of parenteral dosage forms, it allows ease of administration by the patient and it's the natural, and therefore a highly convenient way for substances to be introduced into the human body.

Oral drug delivery systems (DDS) are divided into

- Immediate release and
- Modified release systems.

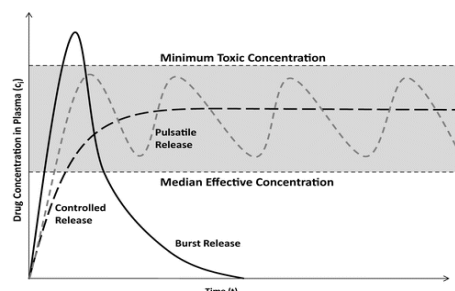
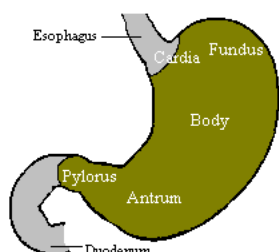


Fig 1: Hypothetical CR Plasma concentration of drug versus Time Profile

### Gastroretentive Drug Delivery Systems

The retention of oral dosage forms in the upper GIT causes prolonged contact time of drug with the GI region, leading to higher bioavailability, and hence therapeutic efficacy, reduced time intervals for drug administration, potentially reduced dose size and thus improved patient compliance. Therefore, controlled release DDS possessing gastric retention properties may be potentially useful. [5,9]

Fig 2: Anatomy of stomach



#### ➤ Physiological Factors Affecting Gastric Retention

- The Gastric pH
- The Gastric Emptying Process

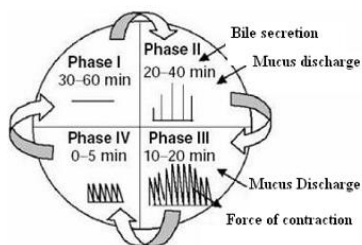


Fig 3: Phases of gastric emptying (fasting)

#### Approaches to Increase Gastric Retention [1, 2, 6]

Various approaches have been pursued over the last three decades, to increase the retention of oral dosage forms in the stomach. The most common approaches used to increase the gastric residence time of pharmaceutical dosage forms include

- Bio (Muco) adhesive systems
- Swelling and expanding systems
- Modified shape systems
- Delayed gastric emptying devices
- Density controlled systems
  - High density systems
  - Floating systems (non-effervescent or effervescent FDDS) [4,5]

#### Floating Systems [3,7]

The concept of floating DDS was first described in the literature in 1968 (Davis, 1968), when Davis developed a method for overcoming the difficulty experienced by persons of gagging or choking while swallowing medicinal pills. He suggested that such difficulty could be overcome by providing pills with a density of less than 1 g/cm<sup>3</sup>, so that the pill will float

on water surface. Since then, several approaches have been used to develop an ideal floating system. Floating DDS or hydrodynamically balanced systems (HBS) have a bulk density lower than the gastric fluids ( $\leq 1.004 \text{ g/cm}^3$ ), and thus 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 a desired rate from the system. After the release of the drug, the residual system is emptied from the stomach. This results in an increase in gastric retention time and a better control of fluctuations in plasma drug concentrations.

#### Types of Floating drug delivery systems:

Based on the principle and technology used in development of FDDS they are 2 types.

- Non effervescent systems with inherent low density or low density due to swelling;
- Effervescent systems with low density due to gas generation and entrapment.

S.No	Product	Active ingredient
1	Madopar	Levodopa and benserzide
2	Valrelease	Diazepam
3	Topalkan	Aluminium magnesium antacid
4	Almagate FlatCoat	Antacid
5	Liquid Gavison	Alginic acid and NaHCO <sub>3</sub>

Table 1: FDDS available in the market

#### I. AIM AND OBJECTIVE

**Aim:** To formulate sustained release effervescent floating tablet dosage form of Loratadine (10 mg) using various polymers and to study the drug release characteristics.

✓ To study the effect of various factors like –

- Effect of sodium bicarbonate
- Drug polymer ratio
- Effect of polymer grade or viscosity
- Nature of the polymer

#### Objective:

Loratadine, an H1 receptor blocker, is absorbed mainly in the proximal gastrointestinal tract, is stable in acidic pH, and shows enhanced bioavailability in the presence of food, making it suitable for a floating multiple-unit dosage form. However, its short half-life (~8 hours), low bioavailability (40%), and high protein binding make maintaining steady-state plasma concentration with conventional tablets difficult. Therefore, a sustained-release gastroretentive formulation is needed to

improve bioavailability and maintain therapeutic levels. The formulation aims to achieve stable in vitro and in vivo buoyancy for at least 12 hours

### Plan of work

To achieve the above objectives, the experimental work was framed as below.

- 1) Formulation of effervescent floating matrix tablets of Loratadine
  - a) Determination of effect of sodium bicarbonate concentration on floating lag time and optimizing its concentration.
- 2) Formulation of Loratadine (10 mg) effervescent floating matrix tablets with different concentrations of polymers HPMC K 35, Guargum and Xanthan Gum
- 3) Evaluation of effervescent floating matrix tablets of Loratadine
  - a) Construction of standard calibration curve of Loratadine in 0.1N HCl.
  - b) To determine floating lag time and total buoyancy time.
  - c) To evaluate formulated matrix tablets for various physical parameters like weight variation, thickness, hardness and friability.
  - d) Determination of in vitro drug release from the formulations in 0.1N HCl.
  - e) Determination of % swelling of all formulations.
  - f) To determine content uniformity of effervescent floating matrix tablets.
  - g) In vitro release data was fitted into various kinetic models for suggesting the suitable mechanism of drug release.
- 4) Construction of theoretical release profile.
- 5) Selection of the best batch of tablets based on the in-vitro release kinetic data
- 6) Determination of drug-excipients interaction by Fouriertransform infrared spectroscopy

## II. MATERIALS AND EQUIPMENTS

The following raw materials and equipments were used in the preparation of floating matrix tablets of Loratadine.

**Table 2:** List of materials used in the present study

S.No	Material	Supplied by
1	Loratadine	Aurobindo Pharma Ltd
2	Sodium bicarbonate	Merck
3	HPMC K35	Signet Corporation USA
4	Guargum	Himedia

5	Xanthan Gum	Himedia
6	Micro crystalline cellulose	Signet Corporation USA
7	Aerosil	Himedia
8	Talc	Loba Chem
9	Magnesium stearate	Loba Chem
10	Barium sulphate	Loba chem
11	Hydrochloric acid	Merck

**Table 3:** List of equipments used in the present study

S.No	Name of the Instrument	Manufacturer
1	Electronic weighing balance	Shimadzu
2	16 station Tablet compression machine	Cadmach, Ahmedabad
3	Monsanto Hardness tester	Pharma labs, Ahmedabad
4	Digital Vernier Calipers	Mitutoyo corp., Kawasaki, Japan
5	Tablet dissolution tester	Lab India (DS 8000)
6	UV/Visible Spectrophotometer	Lab India (UV 3092)
7	Sonicator	Power sonic 405
8	Hot air oven	Ambala
9	Sieve	Remi

## Methods

- Construction of Standard calibration curve <sup>[15]</sup>
- Preparation of 0.1NHCl
- Standard graph of Loratadine in 0.1N HCl
- Preparation of standard stock solution
- Plotting of Standard Curve for Loratadine

### III. PROCEDURE FOR PREPARATION OF EFFERVESCENT FLOATING MATRIX TABLET

Floating matrix tablets containing Loratadine were prepared by direct compression technique using varying concentrations of sodium bicarbonate and different grades of polymers in a standard procedure.

#### Direct Compression method <sup>[10]</sup>:

- Weighing:**  
Loratadine, gas generating agent (sodium bicarbonate), polymer (Carbopol 934, HPMC K4M, HPMC K15M, and HPMC K100M), lactose, lubricants (aerosol, talc and magnesium stearate) were accurately weighed.
- Milling (sieving):**  
All the weighed ingredients were passed through 44# sieve.
- Mixing:**  
All the ingredients were mixed in a polybag and again passed through 44# sieve.
- Compression:**  
The blend was weighed into individual tablet weights and compressed into tablet using required (8mm/9mm) punch in 16 station tablet compression machines.

#### Evaluation of tablets <sup>[11]</sup>

- Physicochemical properties of tablets
  - Weight variation
  - Tablet Thickness
  - Tablet Hardness
  - Friability
  - Drug Content Estimation
  - Buoyancy / Floating test <sup>[14]</sup>

### IV. RESULTS AND DISCUSSION

#### Standard calibration curve of Loratadine

UV spectrophotometric method was developed for the Loratadine. The method obeyed Beer-Lambert's law in the concentration of 5-30µg/ml with regression coefficient of 0.999. Thus, the said method was found to be suitable for the estimation of Loratadine in *In vitro* dissolution studies.

Table 4: Standard Graph of Loratadine in 0.1N HCl at 280nm

Concentration (µg/ml)	Absorbance
0	0
5	0.125
10	0.243
15	0.371
20	0.495
25	0.617
30	0.733

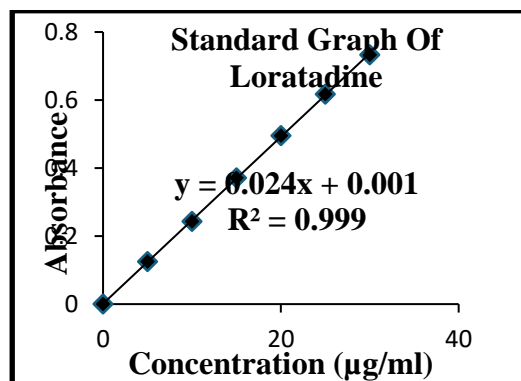


Figure:4 Standard calibration curve of Loratadine in 0.1N HCl

#### Formulation development of Loratadine effervescent floating matrix tablets with Guar gum

Formulation composition:

Ingredients	F-1	F-2	F-3
	mg/tab		
Loratadine	10	10	10
Guar gum	20	30	40
Sodium bicarbonate	25	25	25
Microcrystalline cellulose	36	26	16
Aerosil	5	5	5
Talc	3	3	3
Magnesium stearate	1	1	1
Total weight	100	100	100

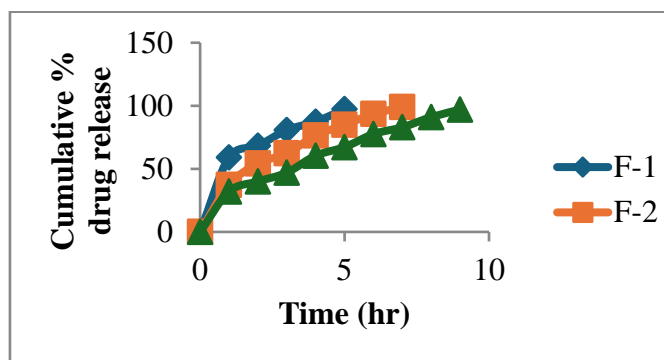
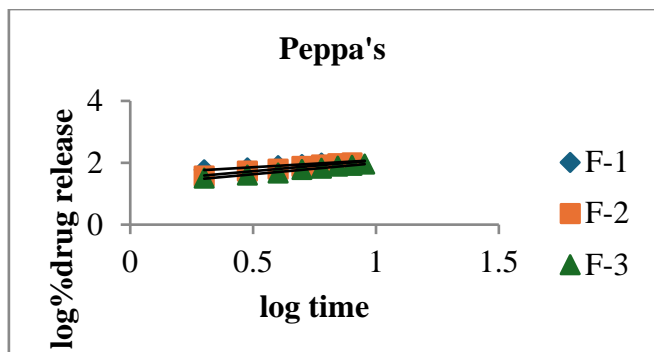


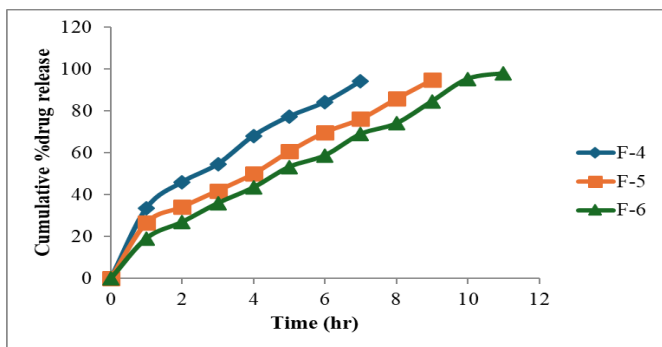
Figure 5: Cumulative percentage drug release of formulations prepared with Guar gum.



**Figure 6:** Graph showing Korasmeier & Peppas kinetics of formulations prepared with Guar gum (F-1 to F-3)

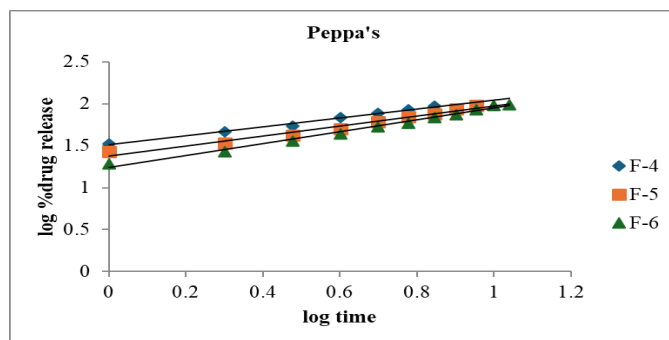
**Formulation development of Loratadine floating matrix tablets prepared with Xanthan gum**

Ingredients	F-4	F-5	F-6
	mg/tab		
Loratadine	10	10	10
Xanthan Gum	20	30	40
Sodium bicarbonate	25	25	25
Microcrystalline cellulose	36	26	16
Aerosil	5	5	5
Talc	3	3	3
Magnesium stearate	1	1	1
Total weight	100	100	100



**Figure 7:** Cumulative percentage drug release of formulations prepared with Xanthan Gum

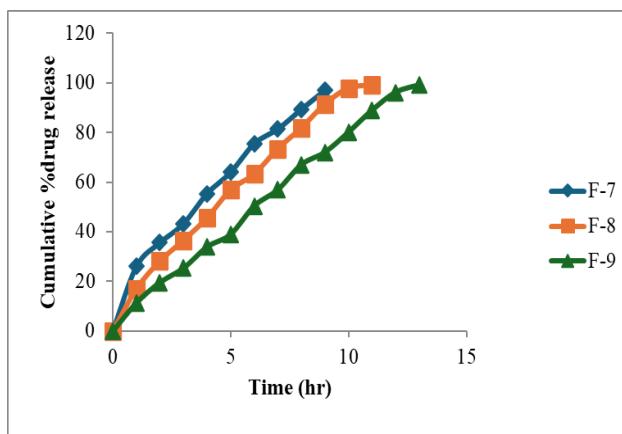
**Fig 8:** Graph showing Peppas kinetics of formulations prepared



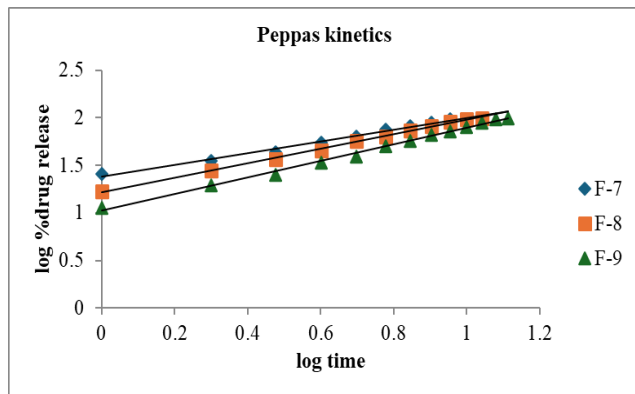
with Xanthan Gum (F-4 to F-6)

**Formulation development of Loratadine floating matrix tablets prepared with HPMC K 35**

Ingredients	F-7	F-8	F-9
	mg/tab		
Loratadine	10	10	10
HPMC K 35	20	30	40
Sodium bicarbonate	25	25	25
Lactose	36	26	16
Aerosil	5	5	5
Talc	3	3	3
Magnesium stearate	1	1	1
Total weight	100	100	100



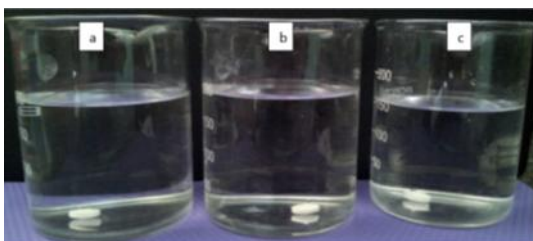
**Figure 9:** Cumulative percentage drug release of formulations prepared with HPMC K 35



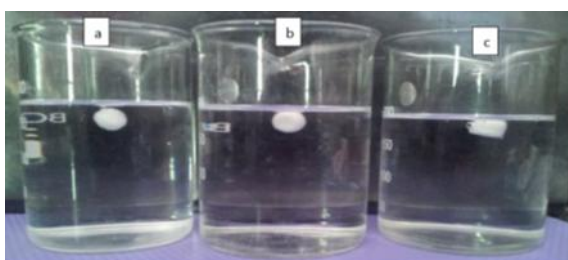
**Fig 10:** Graph showing Korasmeyer & Peppas kinetics of formulations prepared with HPMC K 35 (F-7 to F-9)

**In vitro buoyancy studies** <sup>[12]</sup>

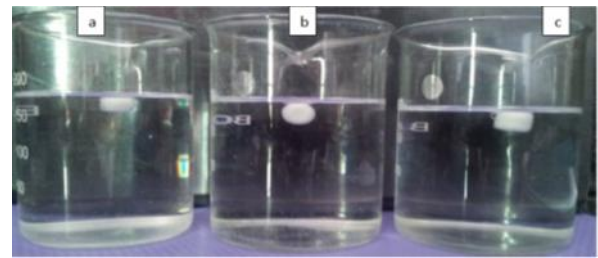
In vitro buoyancy study was evaluated for selected formulations (F-3, F-6 and F-9). The tablets were dropped into 100ml of 0.1N HCl taken in 250ml beaker. The tablets were observed for the floating time. Digital photographs were taken at initial, 3hours, 6hours and 12hours. The matrix tablets prepared with HPMCK4M floated for 10 hours in the media. The tablets prepared with HPMCK15M and HPMCK100M floated for more than 12 hours. Fig 6.33 to Fig 6.37 shows the photographs of floating property in 0.1N HCl.



**Fig 11:** In-vitro buoyancy studies: At initial time a) dosage form with HPMCK4M, b) dosage form with HPMCK15M, c) dosage form with HPMCK100M



**Fig 12:** In-vitro buoyancy studies: At 3hours a) dosage form with Guargum, b) dosage form with Xanthan Gum, c) dosage form with HPMCK35



**Fig 13:** In-vitro buoyancy studies: At 6hours a) dosage form with Guargum, b) dosage form with Xanthan Gum, c) dosage form with HPMCK35

**SUMMARY**

Loratadine effervescent floating matrix tablets were developed to prolong gastric residence time and enhance bioavailability, as the drug is better soluble in acidic pH and absorbed in the upper GIT. A standard calibration curve in 0.1N HCl at 254 nm showed good linearity (50–400 µg/mL, R<sup>2</sup> = 0.999). Matrix tablets were prepared using Guar gum, Xanthan gum, and HPMC K35M. All formulations exhibited good physicochemical properties. Polymer concentration and tablet hardness significantly influenced floating behavior and drug release. Tablets showed rapid buoyancy (<30 seconds) and remained floating for more than 8 hours. Drug release was extended up to 9 hours. Release mechanisms included diffusion, case II transport (Guar gum), and non-Fickian diffusion (Xanthan gum and HPMC K35M). Among polymers, HPMC K35M showed the highest release retardation, followed by Xanthan gum and Guar gum.

**CONCLUSION**

In conclusion, different swelling polymers like Guar gum, Xanthan Gum and HPMCK35, can be successfully employed in the preparation of controlled release floating tablets of Loratadine. The formulations were prepared with gas generating agent. The research study provided useful information for the formulation scientists on formulation, characterization during development of controlled drug delivery systems of Loratadine using these hydrophilic polymers. This dosage forms hold promise for further in vivo studies which can be explored for the further development.

### ACKNOWLEDGMENT

I would like to express my sincere gratitude to my project guide for their constant support, valuable guidance, and encouragement throughout this work. I am also thankful to the faculty members of the Department of Pharmaceutics for their suggestions and assistance.

I extend my thanks to my institution for providing the necessary facilities to carry out this research. I am grateful to my friends and classmates for their help and cooperation during the project. Finally, I would like to thank my family for their continuous support and motivation.

### REFERENCES

- [1] S.P.VYAS ROOP K.KHAR, Controlled Drug Delivery concepts and advances, 1<sup>st</sup> edition, 2002, 196-217.
- [2] Oral controlled release formulation design and drug delivery, Theory to practice, Edited by Hong Wen and Kinam Park pg: 1-20
- [3] Swetha Arora, Roop K. Khar, Floating drug delivery system; A review, AAPS Pharm SciTech; 2005. 6 (3), 372-390.
- [4] Ezra A and Hoffman A A, peptide prodrug approach for improving biphosphate oral absorption. J Med Chem. 2000; 43; 3641-3652
- [5] Klausner EA, Lavy E, Stepensky D, Friedman M, Hoffman A. Novel gastroretentive dosage forms: evaluation of gastroretentivity and its effect on riboflavin absorption in dogs. Pharm Res. 2002; 19: 1516-1523.
- [6] Javed Ali, Alka Ahuja, Roop K.Khar and Sanjula Baboota "Floating Drug Delivery Systems" A Review AAPS Pharm SciTech; 2005. 6 (3), 372-390.
- [7] AV Mayavanshi et al, Floating drug delivery systems to increase gastric retention of drugs: A Review, Research J. Pharm. and Tech, pg: 345-348
- [8] Li, S., Lin, S., Daggy, B.P., Mirchandani, H.L., Chien, Y.W., 2002. Effect of formulation variables on the floating properties of gastric floating drug delivery system. Drug Dev. Ind.Pharm. 28, 783-793.
- [9] The theory and practice of Industrial Pharmacy, Leon Lachman, Herbert A.Liberman, special Indian edition 2009, pg: 293-345
- [10] Rathod Hetangi, Patel Vishnu, Modasia Moin. Floating drug delivery system: innovative approach of gastroretention. International Journal of Pharmaceutical Sciences Review and Research. Sept–Oct 2010; 4(3): 183-192.
- [11] S. Baumgartner, J. Kristel, F. Vreer, et al. Optimisation of floating matrix tablets and evaluation of their gastric residence time. Int.J. Pharm. 2000, 195: 125-135.
- [12] Hamdani, J., Goole, J., Moës, A.J., Amighi, K., 2006a. In vitro and in vivo evaluation of floating riboflavin pellets developed using the melt pelletization process. Int. J. Pharm. 323, 86-92.
- [13] Hoichman, D., Gromova, L.I., Sela, J., 2004. Gastroretentive controlled-release drugs. Pharmaceutical Chemistry Journal 38, 621-624.
- [14] S. Baumgartner, J. Kristel, F. Vreer, et al. Optimisation of floating matrix tablets and evaluation of their gastric residence time. Int.J. Pharm. 2000, 195: 125-135.
- [15] Suhas Gurav et al, Development and Validation of Derivative UVSpectropotometric Methods for Quantitative Estimation of Loratadine in Bulk and Pharmaceutical Dosage Form International Journal of ChemTech Research, Vol.4, No.2, pp 497-501, April-June 2012