Available online at www.ijpsdronline.com

International Journal of Pharmaceutical Sciences and Drug Research
2017; 9(6): 315-322

Research Article

ISSN: 0975-248X
CODEN (USA): IJPSPP

Formulation and *In-vitro* Evaluation of Gastro-retentive Floating Tablets Containing Quetiapine Fumarate

P Poornima[1*], K Abbulu[2], K Mukkanti[1]

[1]*Jawaharlal Nehru Technological University, Kukatpally, Hyderabad-500072, Telangana, India*
[2]*CMR College of Pharmacy, Kandlakoya (V), Medchal Road, Hyderabad-501401, Telangana, India*

ABSTRACT

The present study was focused on Gastro-retentive tablets of Quetiapine fumarate using hydrophilic polymers HPMC K 250 PH PRM, HPMC K 750 PH PRM and HPMC K 1500 pH PRM as release retarding agents. WSR 301 was chosen as resin, Sodium bicarbonate was used as effervescent agents. FTIR studies revealed that there is no interaction between the drug and polymers used for the formulation. The tablets were prepared by direct compression method and the release rate was found to decrease with proportional increase in the ratio of polymer to drug. Quetiapine fumarate has good water solubility and is absorbed well from stomach and therefore is a very good drug to be formulated into gastro retentive floating dosage form. *In-vitro* release profile of Quetiapine fumarate and marketed product when compared, the optimized formulation F19 showed drug release of 98.61% within 24 h whereas 96.78% of the drug was released from the marketed product within 1h. The major mechanism of drug release follows zero order kinetics and non fickian transport by coupled diffusion and erosion. Such a formulation of Quetiapine fumarate with extended drug release over 24 hours probably is the best formulation for the treatment of Schizophrenia with only one oral tablet a day thus minimizing the side effects with low drug dose. The optimized formulation remained stable when subjected to accelerated stability studies.

Keywords: Quetiapine Fumarate, Floating tablets, HPMC, Schizophrenia.

DOI: 10.25004/IJPSDR.2017.090605 **Int. J. Pharm. Sci. Drug Res. 2017; 9(6): 315-322**

***Corresponding author**: Mrs. P. Poornima
Address: Jawaharlal Nehru Technological University, Kukatpally, Hyderabad-500072, Telangana, India
Tel.: +91-8328263865
E-mail ✉: pamupoornima@gmail.com
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.
Received: 09 October, 2017; **Revised:** 21 October, 2017; **Accepted**: 28 October, 2017; **Published:** 20 November, 2017

INTRODUCTION

Oral route is the most common route of administering the drug owing to the ease of formulation, low cost, convenient for the patient and simple regulatory requirement,
formulations can be changed from immediate release to extended release by using several polymers. [1] Gastro-retentive floating dosage forms are continuously

researched and developed as the stomach is a major absorption zone. The gastric emptying time which varies from 2-3 hours is a disadvantage for gastro-retentive dosage forms. Based on the formulation type and physiological condition of the patient, the gastric emptying process can vary from a few minutes to 12 hrs also. This variation may lead to unpredictable bioavailability and times to achieve peak plasma levels. [2] In addition, the relatively brief gastric emptying time in humans, through the stomach or upper part of the intestine (major absorption zone), can result in incomplete drug release from the drug delivery system, leading to reduced overall efficacy of the drug. Some drugs like Quetiapine Fumarate exhibit region-specific absorption in different regions of the intestine because of different pH conditions, various enzymes and endogenous components like bile. [3]

Some of the common approaches used to increase the gastric residence time of pharmaceutical dosage forms include Floating systems, Swelling and expanding systems, Bioadhesive systems, Unfolding and modified- shape systems, High density systems etc. Floating drug delivery systems 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. [4] Whilst the system remains afloat, the drug is released at a desired rate from the system. [5] Following drug release, the residual system gets emptied from the stomach. This results in an increased gastric retention time 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 is also required to keep the dosage form reliably buoyant on the surface of the meal. [6]

MATERIALS AND METHODS

Materials

Quetiapine Fumarate was procured from MSN Labs Ltd. Hyderabad. HPMC K 250 PRM, HPMC K 750 PRM, HPMC K 1500 PRM, and Polyox WSR 301 were obtained from Granules India Ltd, Hyderabad. Sodium bicarbonate, Avicel pH 102, PVP K 30, Talc and Magnesium Stearate were procured from Sd Fine Ltd, Mumbai and all other chemicals used were of analytical grade.

Methods

Evaluation of Final Blend

The Final blend of all formulations was evaluated for Bulk density, Tapped density, Compressibility Index (CI), Hausner's ratio and Angle of repose. [7]

Formulation Method

Accurately weighed quantities of polymers and MCC were taken in a mortar and mixed geometrically, to this required quantity of Quetiapine fumarate was added and mixed slightly with pestle. [8] Accurately weighed quantity of Sodium bicarbonate was taken separately in a mortar and powdered with pestle. The powder is passed through sieve no 40 and mixed with the drug blend which is also passed through sieve no 40. The whole mixture was collected in a plastic bag and mixed for 3 minutes. [9] To this Magnesium stearate was added and mixed for 5 minutes, later Talc was added and mixed for 2 minutes. [10] The mixture equivalent to 400 mg was compressed into tablets with 10 mm round concave punches at a hardness of 6 kg/cm^2.

Table 1: Composition of floating matrix tablets of Quetiapine fumarate with HPMC K 250 PH PRM

Ingredients (weight in mg)	Formulations						
	F1	F2	F3	F4	F5	F6	F7
Quetiapine fumarate*	230.4	230.4	230.4	230.4	230.4	230.4	230.4
HPMC K 250 PH PRM	65	70	75	80	85	90	95
WSR 301	13.6	13.6	13.6	13.6	13.6	13.6	13.6
Sodium Bicarbonate	22	24	26	28	30	32	34
Avicel pH 102	53	46	39	32	25	18	11
PVP K 30	12	12	12	12	12	12	12
Talc	2	2	2	2	2	2	2
Magnesium Stearate	2	2	2	2	2	2	2
Total Weight	400	400	400	400	400	400	400

Quetiapine Fumarate* is equivalent to 200 mg of Quetiapine

Table 2: Composition of floating matrix tablets of Quetiapine Fumarate with HPMC K 750 PH PRM

Ingredients (weight in mg)	Formulations						
	F8	F9	F10	F11	F12	F13	F14
Quetiapine fumarate*	230.4	230.4	230.4	230.4	230.4	230.4	230.4
HPMC K 750 PH PRM	65	70	75	80	85	90	95
WSR 301	13.6	13.6	13.6	13.6	13.6	13.6	13.6
Sodium Bicarbonate	22	24	26	28	30	32	34
Avicel pH 102	53	46	39	32	25	18	11
PVP K 30	12	12	12	12	12	12	12
Talc	2	2	2	2	2	2	2
Magnesium Stearate	2	2	2	2	2	2	2
Total Weight	400	400	400	400	400	400	400

Quetiapine fumarate* is equivalent to 200 mg of Quetiapine

Table 3: Composition of floating matrix tablets of Quetiapine fumarate with HPMC K 1500 PH PRM

Ingredients (weight in mg)	Formulations						
	F15	F16	F17	F18	F19	F20	F21
Quetiapine fumarate*	230.4	230.4	230.4	230.4	230.4	230.4	230.4
HPMC K 1500 PH PRM	65	70	75	80	85	90	95
WSR 301	13.6	13.6	13.6	13.6	13.6	13.6	13.6
Sodium Bicarbonate	22	24	26	28	30	32	34
Avicel pH 102	53	46	39	32	25	18	11
PVP K 30	12	12	12	12	12	12	12
Talc	2	2	2	2	2	2	2
Magnesium Stearate	2	2	2	2	2	2	2
Total Weight	400	400	400	400	400	400	400

Quetiapine fumarate* is equivalent to 200 mg of Quetiapine

Evaluation of Floating Matrix Tablets of Quetiapine fumarate

Weight Variation

Twenty (20) tablets from each batch were individually weighed in grams on an analytical balance. The average weight and standard deviation were calculated, individual weight of each tablet was also calculated using the same and compared with average weight.

Thickness

The thickness in millimeters (mm) was measured individually for 10 pre weighed tablets by using Vernier Calipers. The average thickness and standard deviation were reported.

Hardness

Tablet hardness was measured using a Monsanto hardness tester. The crushing strength of the 10 tablets with known weight and thickness of each was recorded in kg/cm^2 and the average hardness, and the standard deviation was reported.

Friability

Twenty (20) tablets were selected from each batch and weighed. Each group of tablets was rotated at 25 rpm for 4 minutes (100 rotations) in the Roche Friabilator. The tablets were then dusted and re-weighed to determine the loss in weight. Friability was then calculated as per weight loss from the original tablets. [11]

In vitro buoyancy studies

The *in vitro* buoyancy was determined by floating lag time. The tablets were placed in a 100 ml beaker containing 0.1N hydrochloric acid. The time required for the tablet to rise to the surface and float was determined as *floating lag time.* [12] The duration of time for which the dosage form constantly remained on the surface of medium was determined as the *total floating time*.

Drug Content

Twenty tablets were taken, powdered. The powder equivalent to one dose each was transferred to a 100 ml volumetric flask and 0.1N HCl was added. The volume was then made up to the mark with 0.1N HCl. The solution was filtered and diluted suitably and drug content in the samples was estimated using UV-spectrophotometer at 231 nm. [13]

In vitro Drug Release Studies [14]

The *in vitro* drug release study was performed for the single and multiple unit tablets using USP Type II dissolution apparatus using 900ml of 0.1N HCl at a temperature of 37±0.5^{o}C at 50 rpm. 5 ml of sample was collected at 0, 2, 4, 6, 8, 12, 16, 20, 24 hours and the same volume of fresh media was replenished. The drug content in the samples was estimated using UV visible spectrophotometer at 231 nm.

Analysis of *in vitro* drug release kinetics and mechanism

The *in vitro* release data from several microspheres formulations containing Quetiapine fumarate was determined kinetically using different mathematical models like Zero order, First order, Higuchi, and Korsmeyer–Peppas model. [15]

Drug-excipient compatibility studies

Fourier transform infrared spectroscopy (FTIR)

The spectral analysis can be used to identify the functional groups in the pure drug and drug-excipient compatibility. Pure Quetiapine fumarate FTIR spectra, physical mixtures and optimized formulation were recorded by using FTIR (SHIMADZU). Weighed quantity of KBr and drug-excipients were taken in the ratio 100: 1 and mixed by mortar. The samples were made into pellet by the application of pressure. [16] Then the FTIR spectras were recorded in the wavelength region between 4000 and 400 cm^{-1}.

Stability studies

Stability testing was conducted at 40°C ± 2°C/75% RH ± 5% RH for 3 months using stability chamber (Thermo Lab, Mumbai). Samples were withdrawn at predetermined intervals 0, 30, 60 and 90 days period according to ICH guidelines. [17-20] Various *in vitro* parameters like % yield, entrapment efficiency and *in vitro* release studies were evaluated.

Fig. 1: Quetiapine Fumarate floating tablets

RESULTS AND DISCUSSION

Physical parameters of prepared powder blends Quetiapine Fumarate

The results of bulk densities formulations bearing F1 to F21 were reported to be in the range of 0.50 g/cc to 0.59 g/cc. The findings of tapped density formulations F1 to F21 were reported to be in the range of 0.54 g/cc to 0.68 g/cc. The angle of repose of all the formulations was found to be satisfactory. The formulation F19 was had angle of repose value of 20.04, thus indicating good flow property. The compressibility index values were found to be in the range of 9 to 12%. These findings indicated that the all the batches of formulations exhibited good flow properties. The Hausner's ratio values in the space of 1.10 to 1.16%. These findings designated that the all the batches of formulations exhibited good flow criteria.

Physico-chemical properties of Quetiapine Fumarate floating tablets

The Quetiapine fumarate floating tablets were prepared according to the composition and shown in Figure 1. The evaluation parameters like weight variation, thickness, hardness, friability and drug content were found to be within the limits and summarized in Table 5.

Table 4: Physical properties of prepared powder blends of Quetiapine Fumarate

Formulation	Bulk density (g/cc)	Tapped density (g/cc)	Angle of repose(θ)	Carr's index (%)	Hausner's ratio
F1	0.56 ± 0.02	0.59 ± 0.01	24.34 ± 0.4	11.23 ± 0.8	1.13 ± 0.02
F2	0.58 ± 0.12	0.60 ± 0.04	21.67 ± 0.3	10.23 ± 1.0	1.12 ± 0.07
F3	0.59 ± 0.04	0.64 ± 0.05	26.54 ± 0.1	10.12 ± 0.7	1.13 ± 0.09
F4	0.51 ± 0.06	0.54 ± 0.03	21.56 ± 0.2	09.74 ± 1.0	1.11 ± 0.06
F5	0.65 ± 0.02	0.65 ± 0.02	22.56 ± 0.1	11.23 ± 0.8	1.13 ± 0.05
F6	0.57 ± 0.21	0.66 ± 0.12	23.30 ± 0.1	10.23 ± 0.5	1.12 ± 0.06
F7	0.54 ± 0.04	0.63 ± 0.04	23.89 ± 0.2	11.34 ± 0.6	1.16 ± 0.03
F8	0.53 ± 0.01	0.68 ± 0.03	24.67 ± 0.3	10.11 ± 0.8	1.12 ± 0.03
F9	0.57 ± 0.01	0.61 ± 0.01	23.56 ± 0.3	11.45 ± 0.7	1.13 ± 0.02
F10	0.58 ± 0.13	0.67 ± 0.06	21.66 ± 0.2	11.45 ± 0.5	1.15 ± 0.01
F11	0.53 ± 0.09	0.68 ± 0.12	25.34 ± 0.2	10.23 ± 0.5	1.13 ± 0.01
F12	0.51 ± 0.04	0.56 ± 0.07	21.09 ± 0.2	09.88 ± 0.4	1.11 ± 0.03
F13	0.54 ± 0.01	0.67 ± 0.04	25.14 ± 0.3	10.67 ± 0.4	1.13 ± 0.02
F14	0.57 ± 0.06	0.64 ± 0.21	22.99 ± 0.5	11.34 ± 0.5	1.12 ± 0.01
F15	0.53 ± 0.01	0.63 ± 0.04	22.78 ± 0.4	10.45 ± 0.3	1.13 ± 0.02
F16	0.54 ± 0.02	0.61 ± 0.07	22.45 ± 0.4	10.68 ± 0.2	1.13 ± 0.02
F17	0.59 ± 0.21	0.68 ± 0.03	25.09 ± 0.3	11.47 ± 0.8	1.12 ± 0.02
F18	0.58 ± 0.03	0.67 ± 0.08	23.05 ± 0.2	11.99 ± 0.3	1.14 ± 0.02
F19	0.50 ± 0.07	0.55 ± 0.03	20.04 ± 0.4	09.09 ± 0.4	1.11 ± 0.02
F20	0.59 ± 0.06	0.64 ± 0.10	24.78 ± 0.1	12.12 ± 0.5	1.14 ± 0.01
F21	0.56 ± 0.02	0.61 ± 0.12	25.06 ± 0.2	11.45 ± 0.6	1.13 ± 0.01

Above parameters are communicated as Average ± Standard Deviation; (n=3)

Table 5: Physicochemical parameters of Quetiapine Fumarate floating tablets

Formulation Number	*Weight variation (mg)	#Thickness (mm)	#Hardness (Kg/Cm²)	#Friability (%)	#Content uniformity (%)	Floating Lag time (sec)	Total floating time (hrs)
F1	401.65 ± 1.2	6.4 ± 0.12	6.3 ± 0.12	0.57 ± 0.01	95.23 ± 0.63	47	>24
F2	398.69 ± 0.8	6.3 ± 0.06	6.1 ± 0.06	0.55 ± 0.02	97.04 ± 0.06	45	>24
F3	398.04 ± 0.5	6.3 ± 0.06	6.1 ± 0.06	0.63 ± 0.03	95.56 ± 0.14	43	>24
F4	400.05 ± 0.0	6.2 ± 0.12	6.2 ± 0.12	0.72 ± 0.01	98.11 ± 1.01	40	>24
F5	401.54 ± 0.4	6.3 ± 0.00	6.3 ± 0.00	0.62 ± 0.02	94.23 ± 1.08	38	>24
F6	400.78 ± 0.4	6.3 ± 0.10	7.1 ± 0.06	0.66 ± 0.01	95.45 ± 0.31	36	>24
F7	400.65 ± 0.3	6.1 ± 0.10	6.3 ± 0.10	0.53 ± 0.02	98.91 ± 0.49	34	>24
F8	399.57 ± 0.2	6.3 ± 0.25	6.3 ± 0.40	0.69 ± 0.01	97.23 ± 0.51	46	>24
F9	400.76 ± 0.35	6.3 ± 0.06	6.3 ± 0.06	0.58 ± 0.00	96.13 ± 0.56	44	>24
F10	400.49 ± 0.2	6.2 ± 0.20	6.2 ± 0.42	0.79 ± 0.02	95.23 ± 0.24	41	>24
F11	401.53 ± 0.4	6.2 ± 0.06	6.3 ± 0.06	0.76 ± 0.01	97.97 ± 0.21	39	>24
F12	400.58 ± 0.3	6.2 ± 0.00	6.4 ± 0.06	0.73 ± 0.02	98.45 ± 0.76	37	>24
F13	401.34 ± 0.2	6.3 ± 0.26	6.8 ± 0.35	0.72 ± 0.02	97.45 ± 0.48	36	>24
F14	400.67 ± 0.3	6.1 ± 0.21	6.4 ± 0.21	0.54 ± 0.03	98.98 ± 0.23	37	>24
F15	399.65 ± 0.2	6.4 ± 0.06	7.0 ± 0.23	0.75 ± 0.02	96.45 ± 0.36	48	>24
F16	400.65 ± 0.3	6.2 ± 0.25	6.4 ± 0.23	0.78 ± 0.01	96.45 ± 0.69	46	>24
F17	401.79 ± 0.4	6.5 ± 0.15	6.8 ± 0.32	0.79 ± 0.01	96.34 ± 0.35	43	>24
F18	401.87 ± 0.1	6.4 ± 0.25	6.7 ± 0.35	0.82 ± 0.01	97.56 ± 0.23	41	>24
F19	400.16 ± 0.8	6.0 ± 0.10	6.2 ± 0.21	0.52 ± 0.89	99.78 ± 0.23	31	>24
F20	399.32 ± 0.2	6.2 ± 0.12	6.5 ± 0.2	0.63 ± 0.03	97.18 ± 0.81	37	>24
F21	399.65 ± 0.2	6.4 ± 0.06	7.0 ± 0.23	0.75 ± 0.02	96.45 ± 0.36	38	>24

*Values are expressed in mean ± SD: (n=20) #Values are expressed in mean ± SD: (n=3)

Tablets of all batches had floating lag time below 1 minute regardless of viscosity and content of HPMC because of evolution of CO_2 resulting from the interaction between sodium bicarbonate and dissolution medium; entrapment of gas inside the hydrated polymeric matrices enables the dosage form to float by lowering the density of the matrices. Total Floating time for the HPMC formulations were between 12 to 24 hours.

Fig. 2: At time 0

Fig. 3: After 31 sec

***In vitro* buoyancy lag time of the optimized formulation F19**

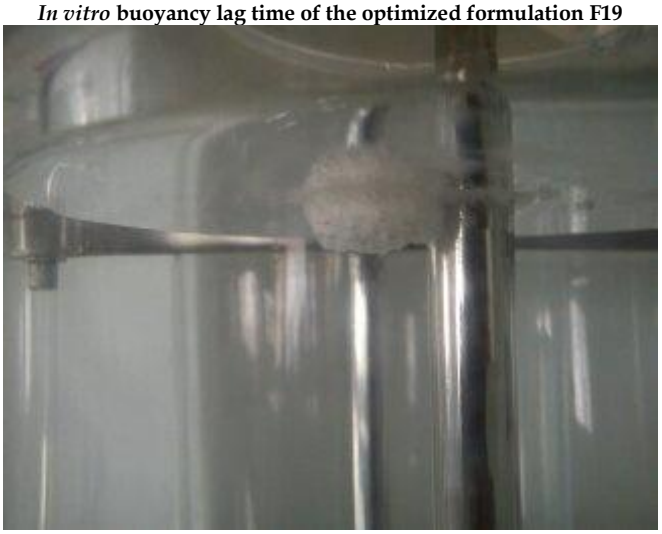

Fig. 4: Quetiapine fumarate floating tablets after 24 hours

In vitro dissolution studies

From the above figures (Figure 5, 6 and 7) it can be observed that the polymer HPMC K 1500 PH PRM has controlling effect on the release of drug from the floating matrix tablet of Quetiapine fumarate compared to HPMC K 250 PH PRM and HPMC K 750 PH PRM.

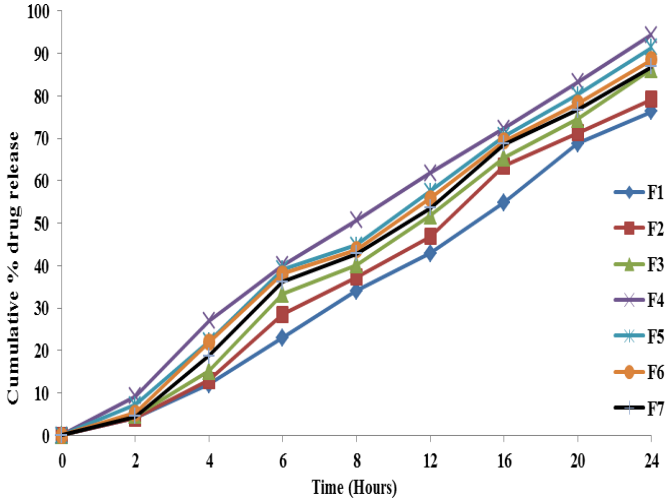

Fig. 5: *In vitro* Drug Release Profile of Quetiapine fumarate floating tablets F1-F7

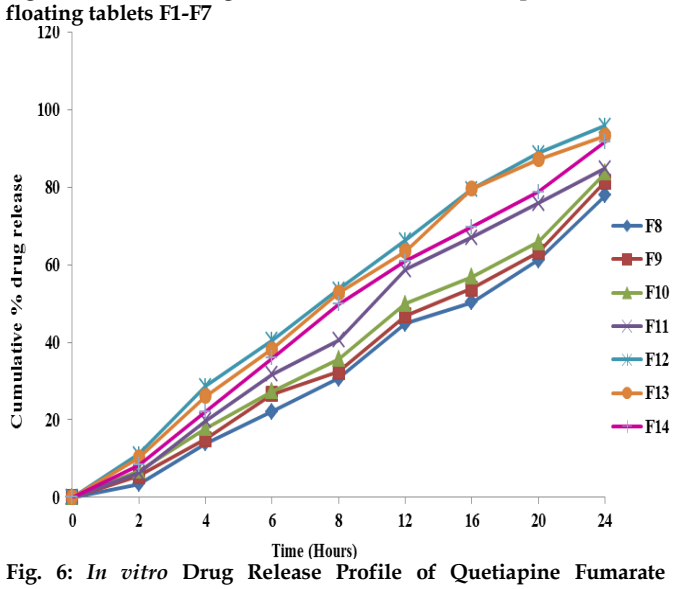

Fig. 6: *In vitro* Drug Release Profile of Quetiapine Fumarate floating tablets F8-F14

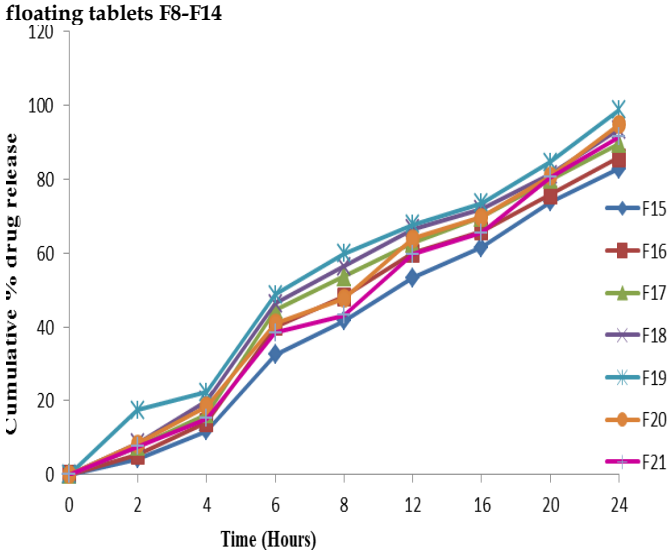

Fig. 7: *In vitro* Drug Release Profile of Quetiapine Fumarate floating tablets F15-F21

The difference in the drug release profiles of various formulations was due to the presence of different concentrations of polymer HPMC K 1500 PH PRM. The concentration of polymer was added in increasing order to check its drug release retarding ability and F19 was considered as best formulation among the all the formulations. F19 showed good buoyancy properties and controlled the drug release for desired period of time (24 hours). The release profiles from all these formulations followed diffusion controlled release, complying with higher correlation coefficient values of Higuchi and Peppas equations.

In vitro drug release studies for optimized formulation and marketed product

An *in vitro* release profile of Quetiapine fumarate and marketed product was conducted; the optimized formulation F19 was shown drug release of 98.61% within 24 h and 96.78% of the drug was released from the marketed product within 1 h.

Table 6: Comparison of marketed product of Quetiapine fumarate with optimized formulation (F19)

Time (Hrs)	Optimized formulation (F19)	Marketed
0	0.00 ± 0.00	0.00 ± 0.00
1	10.78 ± 1.35	96.78 ± 1.56
2	15.46 ± 1.58	-
4	22.34 ± 1.85	-
6	46.57 ± 1.81	-
8	57.25 ± 1.86	-
12	66.86 ± 1.32	-
16	75.56 ± 2.22	-
20	81.65 ± 2.16	-
24	98.61 ± 2.29	-

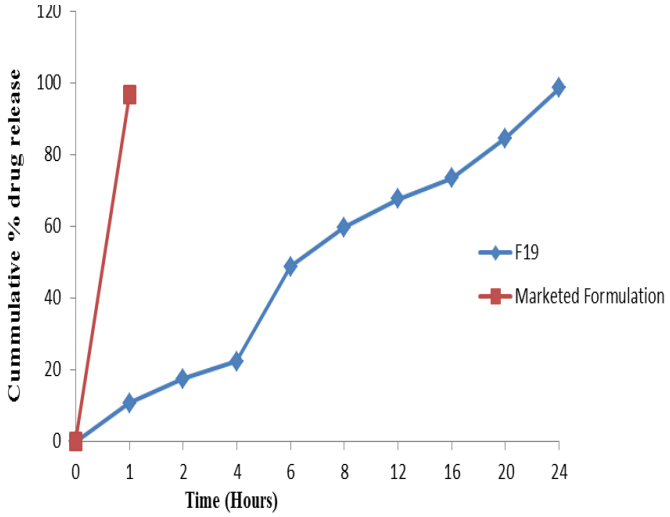

Fig. 8: Comparison of marketed product of Quetiapine fumarate with optimized formulation (F19)

Mathematical modelling of optimized formula (F19) of Quetiapine fumarate floating tablets

In vitro drug release order kinetics for optimized (F19) Formulation

In the present study drug release Mechanism of optimized Quetiapine Fumarate tablets F19 were best fitting to zero order and Higuchi model because regression coefficient was seen closest to 1. Thus the mechanism of drug release is by diffusion. Further the

n value obtained from the Korsmeyer-Peppas plots i.e. 0.833 indicating non Fickian (anomalous) transport. Thus the active ingredient is being released by coupled diffusion and erosion. The reference standard (marketed product) drug release was explained by first order kinetics as the plot showed highest linearity as the drug release was best fitted in first order kinetics. The results are summarized in Table 7.

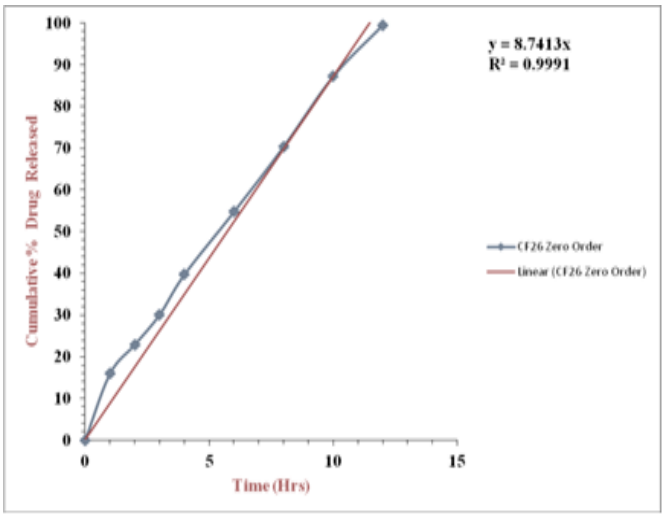

Fig. 9: Zero order plots for the optimized formulation (F19)

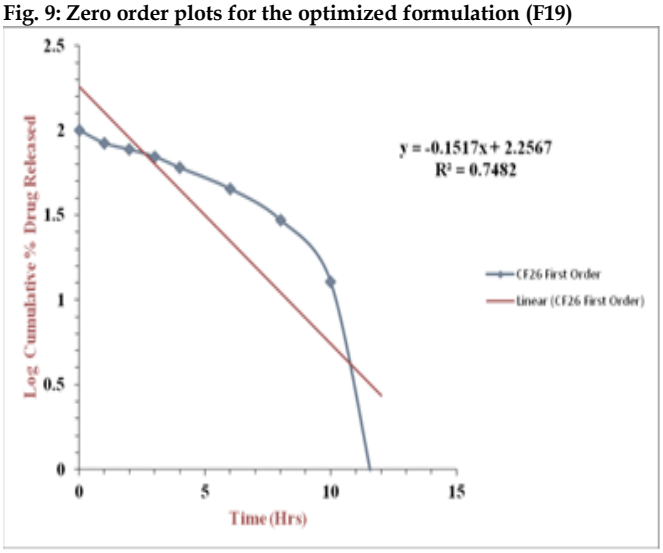

Fig. 10: First order plots for the optimized formulation (F19)

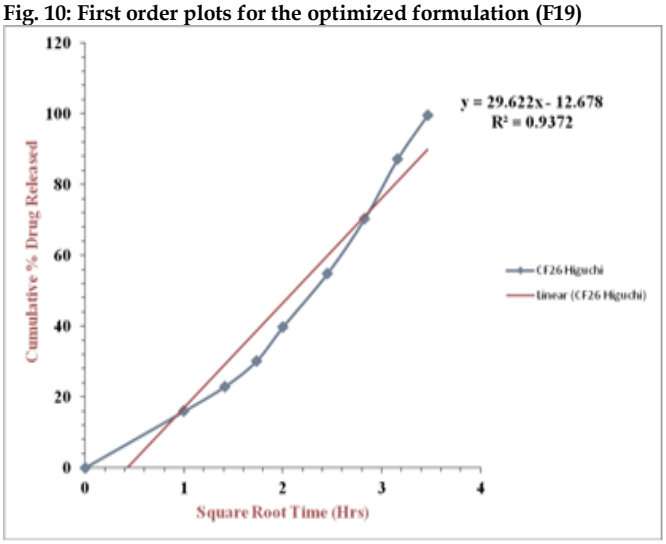

Fig. 11: Higuchi plots for the optimized formulation (F19)

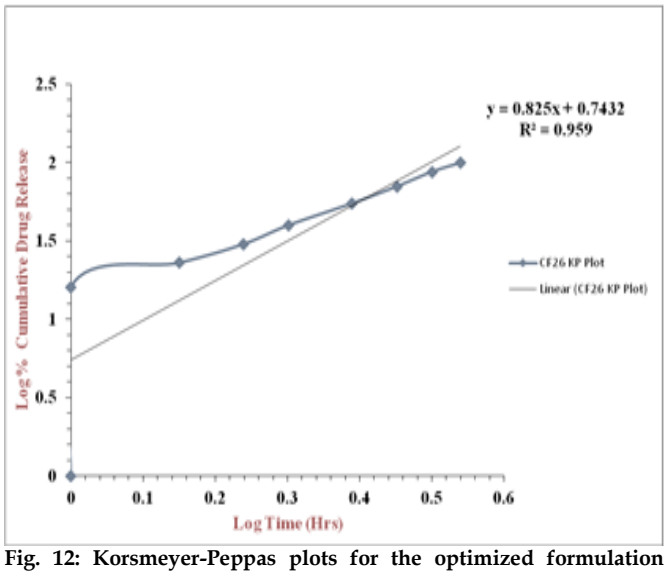

Fig. 12: Korsmeyer-Peppas plots for the optimized formulation (F19)

In vitro drug release order kinetics for marketed product

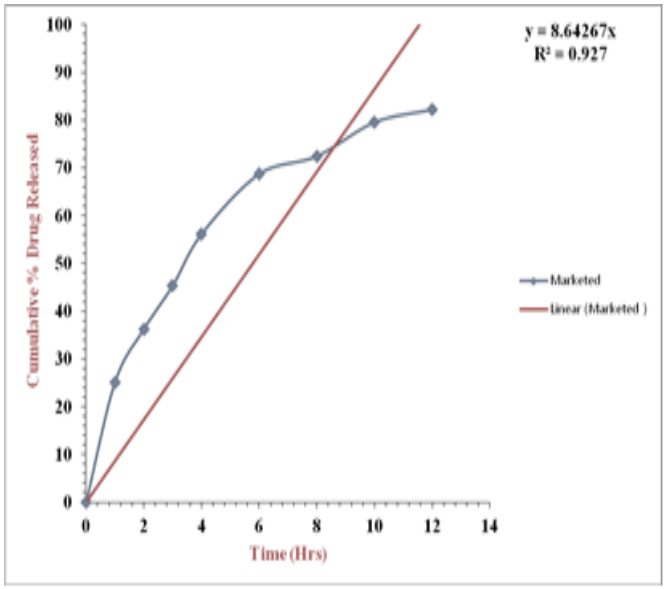

Fig. 13: Zero order plots for the marketed product

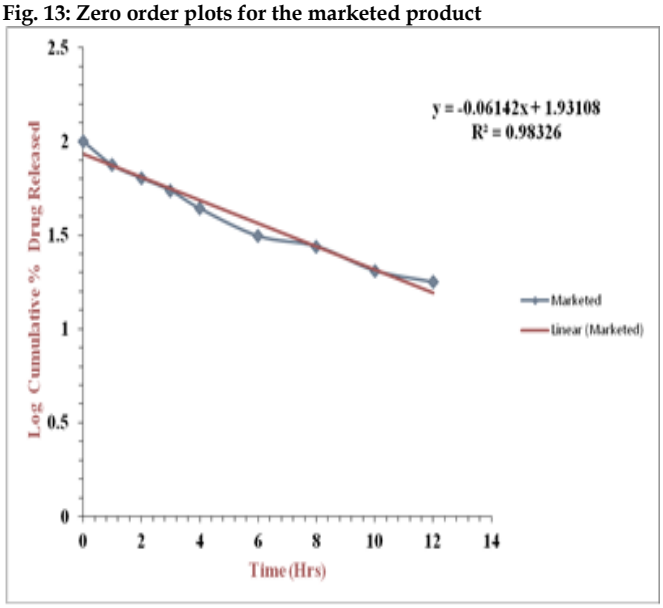

Fig. 14: First order plot for the marketed product

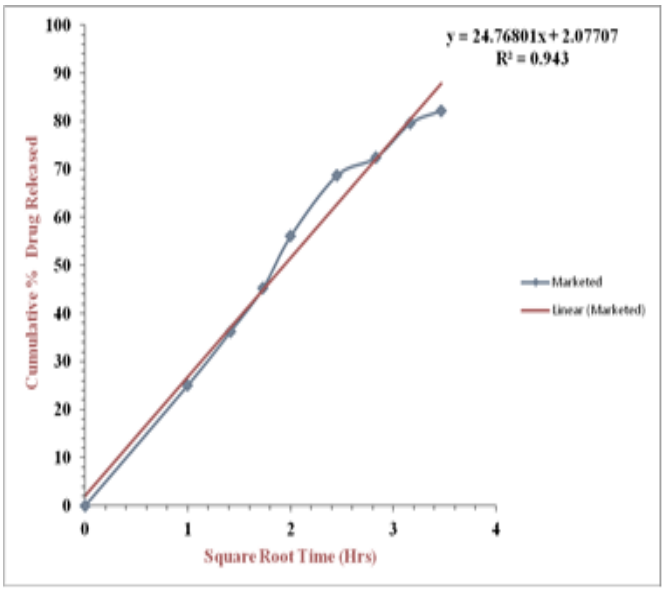

Fig. 15: Higuchi plot for the marketed Formulation

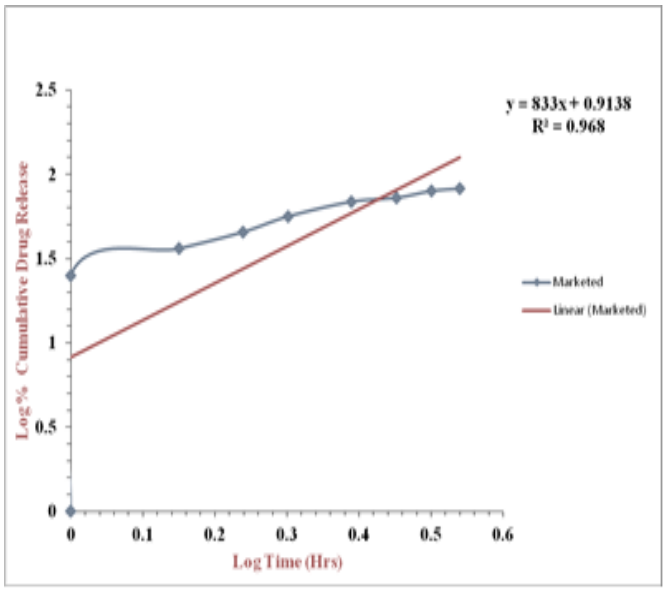

Fig. 16: Korsmeyer-Peppas plot for the marketed product

Table 7: Release order kinetics of F19 and Marketed Product

Formulation Code	Zero Order		First Order		Higuchi		Korsmeyer-Peppas	
	R^2	N	R^2	N	R^2	n	R^2	n
Marketed	0.927	8.642	0.994	0.061	0.954	24.76	0.971	0.833
F19	0.999	8.741	0.748	0.151	0.937	29.62	0.959	0.825

Table 8: Parameters after Accelerated Stability Study of optimized Formulation F19

Parameters	Temperature Maintained at 40 ± 2°C ; Relative Humidity (RH) Maintained at 75% ± 5% RH			
	Initial	After 1 month	After 3 months	After 6 months
Drug Content (%)	99.78 ± 0.14	99.26 ± 0.68	98.73 ± 0.37	99.12 ± 0.22
***In vitro* Drug Release (%)**	98.65 ± 1.15	98.10 ± 1.53	97.82 ± 1.42	97.50 ± 1.35
Floating lag time	31	32	33	33

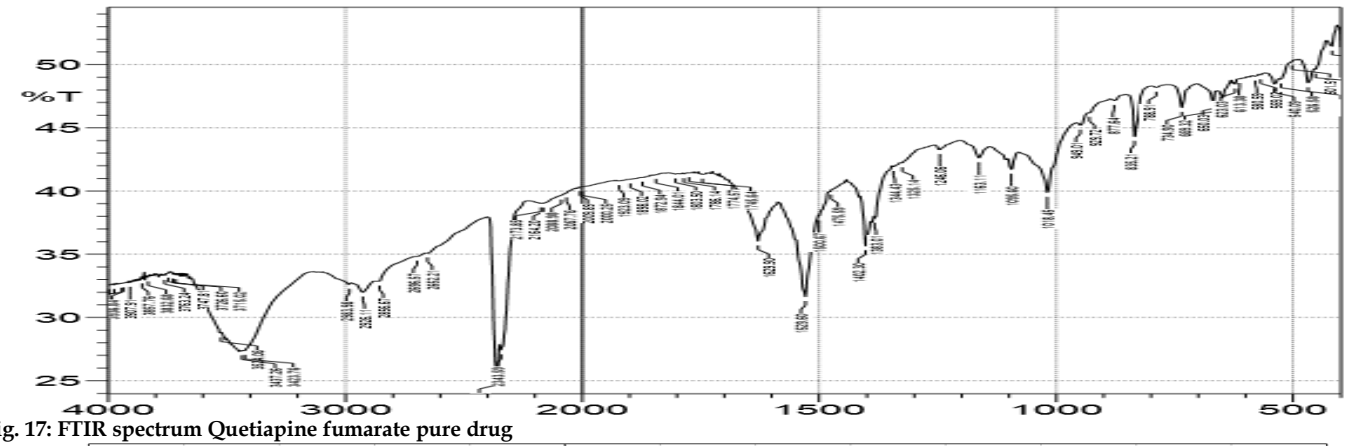

Fig. 17: FTIR spectrum Quetiapine fumarate pure drug

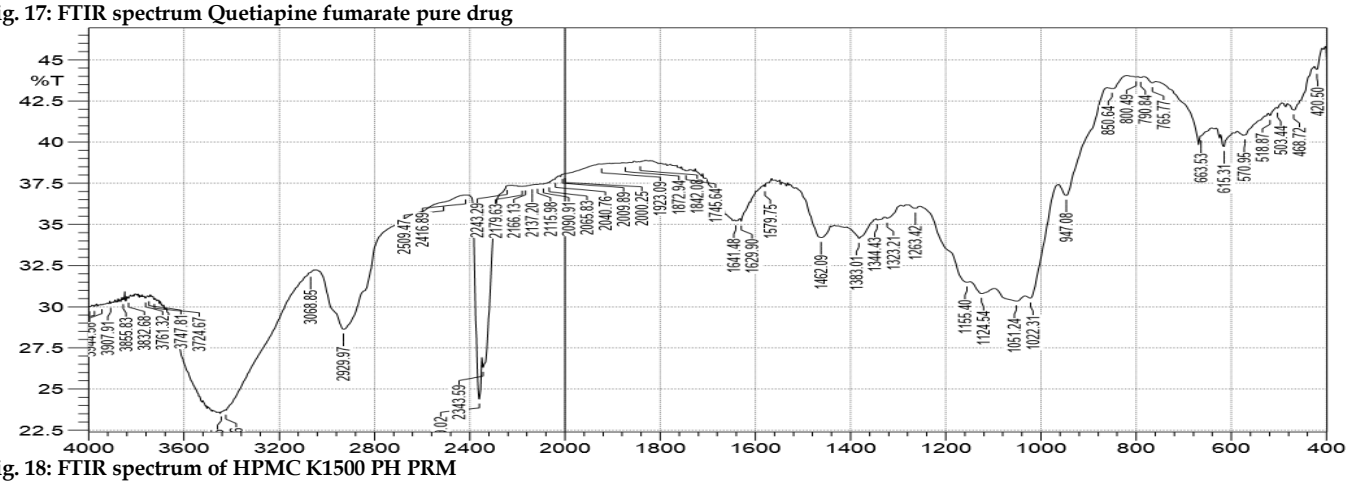

Fig. 18: FTIR spectrum of HPMC K1500 PH PRM

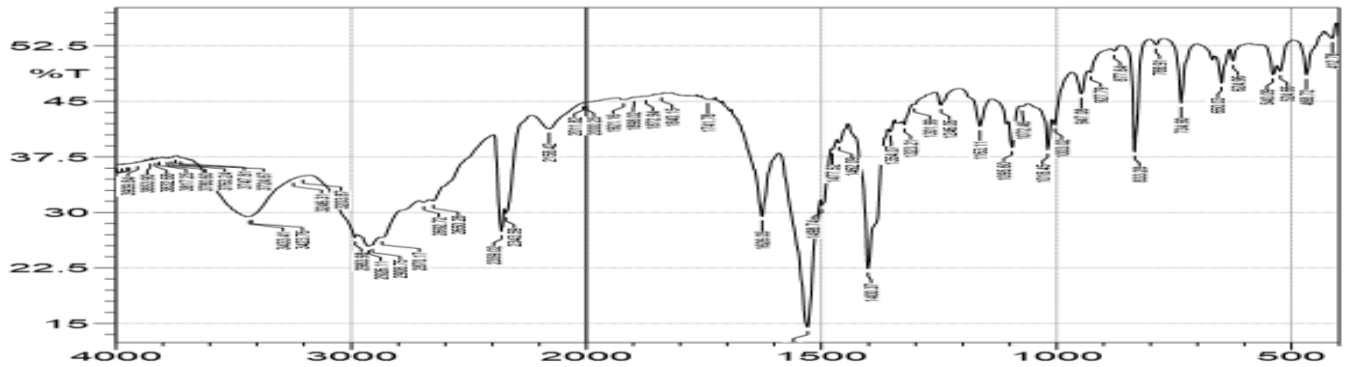

Fig. 19: FTIR spectrum of Quetiapine fumarate optimized formulation (F19)

Drug - excipient compatibility studies

FTIR spectra of Quetiapine fumarate showed peaks of 3410, 2941, 1629, 1530, 1400 and 1060 cm^{-1} due to –OH stretching, C-H stretching, C=O stretching, N-H bending, C-H bend in plane and C-C stretching respectively. FTIR Spectra of HPMC K 1500 PH PRM showed peaks of 2929, 1462, 1163, 1022, 947 and 850 cm^{-1} due to C-H stretching, O-H stretching and C-C stretching respectively. FTIR spectra of optimized formulation showed both characteristics peaks of drug and polymer indicating no drug-polymer interaction.

Stability Studies

There were no changes observed in % drug content, In vitro drug release studies and floating lag time during storage of the optimized formulation and the results are tabulated in Table 8. Hence the optimized formulation was found to be stable.

In the present work, it can be concluded that the Quetiapine fumarate floating tablets can be an innovative and promising approach for the delivery of Quetiapine fumarate as extended drug release over 24 hours which is the best formulation for the treatment of Schizophrenia with only one oral tablet a day thus minimizing the side effects with low drug dose, which improves patient compliance.

REFERENCES

1. Whitehead, L, Fell JT, Collett JH. Development of a Gastroretentive Dosage Form. European Journal of Pharmaceutical Sciences. 1996; 4 (1): 182.
2. Mojaverian P, Vlasses PH, Kellner PE, Rocci ML Jr. Effects of gender, posture and age on gastric residence time of an indigestible solid: pharmaceutical considerations. Pharm. Res. 1988; 5(10): 639–644.
3. Deshpande AA, Rhodes CT, Shah NH, Malick AW. Controlled release drug delivery system for prolonged gastric residence: an overview. Drug Dev. Ind. Pharm. 1996; 22(6): 531- 539.
4. Hwang SK, Park H, Park K. Gastric retentive drug delivery systems. Crit. Rev. Ther. Drug Carrier Syst. 1998; 15(3): 243–284.
5. Gruber P, Rubinstein A, Li VH, Bass P, Robinson JR. Gastric emptying of non-digestible solids in the fasted dog. J. Pharm. Sci. 1987; 76(2): 117–122.
6. Desai S, Bolton S. A Floating Controlled Release Drug Delivery System: In vitro–In vivo Evaluation. Pharma. Res. 1993; 10 (9):1321-1325.
7. Li S, Lin S, Chien TW, Daggy BP, Mirchandani HL. Statistical optimization of gastric floating system for oral controlled delivery of calcium. AAPS PharmSciTech. 2001; 2(1):E1.
8. Li S, Lin S, Daggy BP, Mirchandani HL, Chien TW. Effect of formulation variables on the floating properties of gastric floating drug delivery system. Drug Dev Ind Pharm. 2002; 28(7):783-793.
9. Martindale – The Complete Drug Reference -35th Edition, Chicago Pharmaceutical Press, London, 2007.
10. Rama Rao T, Bala Krishna K, Hussain MA, Anjum M, Azizurrahman M. Formulation and Evaluation of Gastroretentive Floating Tablets of Quetiapine Fumarate. RJPBCS. 2014; 5 (5): 380-389.
11. Nasrin N, Asaduzzaman M, Mowla R, Rizwan F, Alam A. A Comparative Study of Physical Parameters of Selected Ketorolac tromethamine tablets available in the Pharma Market of Bangladesh. Journal of Applied Pharmaceutical Science. 2008; 1(8): 101-103.
12. Penners G, Lustig K, Jorg PVG, inventors. Expandable pharmaceutical forms. US patent 5 651-985. July 29, 1997.
13. Phuapradit W, Bolton S. Influence of tablet density on oral absorption of sustained release acetaminophen matrix tablets. Drug Dev Ind Pharm. 1991; 17:1097-1107.
14. Phuapradit W. Influence of Tablet Buoyancy on Oral Absorption of Sustained Release Acetaminophen Matrix Tablets [dissertation]. [Thesis]. Jamaica, NY: St John's University; 1989.
15. Małgorzata W, Marcin Z, Aleksandra A. Tasting cetirizine-based microspheres with an electronic tongue. Sensors and Actuators B Chemical. 2016; 238: 1190-1198.
16. Janssen M, Timur UT, Woike N, Welting TJ, Draaisma G, Gijbels M, van Rhijn LW, Mihov G, Thies J, Emans PJ. Celecoxib-loaded PEA microspheres as an auto regulatory drug-delivery system after intra-articular injection. J Control Release. 2016 Dec 28; 244(Pt A):30-40.
17. Tyagi LK, Kori ML. Stability Study and In-vivo Evaluation of Lornoxicam Loaded Ethyl Cellulose Microspheres. Int. J. Pharm. Sci. Drug Res. 2014; 6(1): 26-30.
18. Singh K, Kumar A, Langyan N, Ahuja M . Evaluation of mimosa pudica seed mucilage as sustained-release excipient. AAPS PharmSciTech 2009; 10: 1121-1127.
19. Peppas NA Analysis of Fickian and non-Fickian drug release from polymers. Pharm ActaHelv. 1985; 60: 110-111.
20. Siepmann J, Kranz H, Bodmeier R, Peppas NA. HPMC-matrices for controlled drug delivery: a new model combining diffusion, swelling, and dissolution mechanisms and predicting the release kinetics. Pharm Res. 1999; 16: 1748-1756.

HOW TO CITE THIS ARTICLE: Poornima P, Abbulu K, Mukkanti K. Formulation and *In-vitro* Evaluation of Gastro-retentive Floating Tablets Containing Quetiapine Fumarate. Int. J. Pharm. Sci. Drug Res. 2017; 9(6): 315-322. **DOI: 10.25004/IJPSDR.2017.090605**