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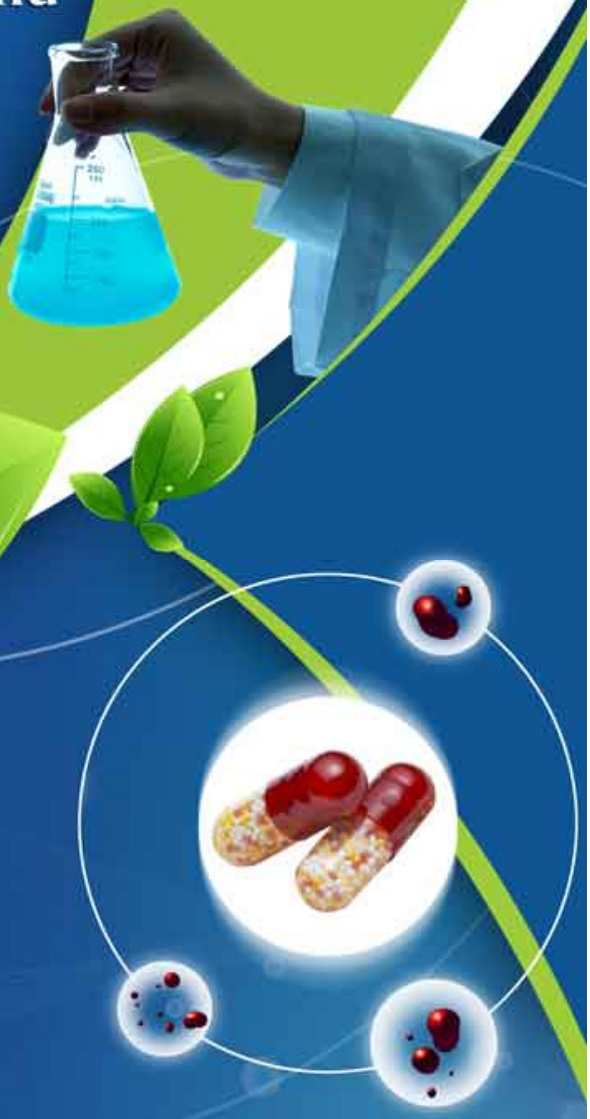

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Research Article

FORMULATION AND *IN VITRO* EVALUATION OF FLOATING DRUG DELIVERY SYSTEM OF QUETIAPINE HEMIFUMARATE

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ABSTRACT

The objective of the present investigation was to design and develop a floating drug delivery system of Quetiapine Hemifumarate using different viscosity grades of hydroxypropylmethylcellulose (HPMC K4M, HPMC K15M and HPMC K100M) in varying ratios to formulate floating tablets by direct compression method. Sodium bicarbonate and citric acid was use in the dosage form as a source of carbon-di-oxide to maintain buoyancy. The tablets were evaluated for thickness, weight variation, hardness, friability, drug content, in vitro buoyancy test, in vitro release characteristics and short term stability studies. The drug release from those tablets was sufficiently sustained (about 12 hr) and non-Fickian transport of the drug from tablets was confirmed. Formulation F1 containing HPMC K4M can be considered as an optimized formulation for gastroretentive floating tablet of Quetiapine Hemifumarate. The results of in vitro release studies showed that optimized formulation F1 could sustain drug release (99.63%) for 12 hours and remain buoyant for more than 12 hours. It was found that among the three viscosity grades i.e. HPMC K4M, HPMC K15M and HPMC K100M, HPMC K4M was found to be beneficial in improving the drug release rate and floating properties.

KEY WORDS: *Gastroretention, Floating drug delivery systems, Quetiapine Hemifumarate, HPMC, In vitro buoyancy, In vitro floating.*

INTRODUCTION

Gastro-retentive drug delivery systems (GRDDS) can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability reduces drug waste and improves solubility of drugs that are less soluble in high pH environment. The controlled gastric retention of solid dosage forms may be achieved by the mechanism of muco-adhesion, floatation, sedimentation, expansion, modified shape systems or by the administration of pharmacological agents that delaying gastric emptying. Based on these approaches, floating drug delivery systems seems to be the promising delivery systems for control release of drugs. [1- 2]. Floating Oral Drug Delivery System (FDDS) are retained in the stomach and are useful for drugs that are poorly water soluble or unstable in intestinal fluids. Floating drug delivery system 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. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of

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drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of fluctuations in plasma drug concentration. [2-4]

Quetiapine Hemifumarate (QH) is an atypical antipsychotic agent belonging to the chemical class of benzisoxazole derivatives and is indicated for the treatment of schizophrenia, bipolar disorder: including moderate to severe manic episodes in bipolar disorder, major depressive episodes in bipolar disorder and prevention of recurrence in patients whose manic or depressive episode has responded to quetiapine treatment. [5- 6] Quetiapine exhibits linear pharmacokinetic in the dosing interval. Maximum plasma concentration is reached after 1-1½ hours and the elimination half-life is approximately 7 hours. QH shows pH dependent solubility i.e. highly soluble in acidic pH and slightly soluble in basic pH. As its solubility decreases with increase in pH, it would be more beneficial to retain the drug in stomach (acidic environment) for prolonged duration so as to achieve maximum absorption and bioavailability. [7- 8]

In the present work, floating drug delivery system of Quetiapine Hemifumarate was prepared by effervescent gas generating system approach using three grades of HPMC (K4M, K15M, and K100M). In this work, the effect of gel-forming polymer methocel on floating properties and release characteristics of Quetiapine Hemifumarate tablets was evaluated. [9-11]

EXPERIMENTAL

Materials

Quetiapine Hemifumarate was generously gifted from Lupin Pharmaceuticals, Pune. HPMC (K4M, K15M & K100M) were obtained from colorcon asia Ltd, Goa. PVP K-30 was obtained from Merk India Ltd, Mumbai. All other chemicals used were of analytical grade and were used without further purification.

Methods

Drug-excipient compatibility

The infrared spectra of pure drug (QH), binary mixture of drug and HPMC K4M, K15M, K100M, PVP K-30 (1:1), and optimized formulation were recorded between 600 and 4000 cm-1 by FT-IR spectrometer using KBr pellet technique. [11-12]

Preparation of tablets

Effervescent floating tablets containing Quetiapine Hemifumarate were prepared by direct compression technique. Sodium bi-carbonate and citric acid were used as a gas generating agents which causes liberation of CO_2 when tablets come in contact with acidified dissolution medium (0.1 N HCl). Lactose was used as a diluent while magnesium stearate and talc were used as lubricants. All the ingredients were weighed accurately, passed through sieve #60 and transferred to clean porcelain mortar except magnesium stearate and talc, to mix geometrically. After lubrication, the lubricated blend was compressed into tablets using tablet compression machine fitted with 8 mm punches. The tablet weight was adjusted to 200mg. Nine formulations were prepared coded from F1 to F9. The detail of composition of each formulation is presented in Table 1**.** [12-14]

Evaluation of tablets [11, 15-23]

The prepared tablets were evaluated for parameters like hardness (Monsanto hardness tester), friability, weight variation, thickness, water uptake, *in vitro* drug release, *in vitro* buoyancy study.

Hardness test

The hardness (kg/cm2) of tablets was determined by using Monsanto hardness tester. Six replicate determinations were taken, and the results are given in table 3.

Friability test

The results are given in Table 3. The friability of tablets was determined using Roche Friabilator. It is expressed in percentage (%). Ten tablets were initially weighed (Initial) and transferred into friabilator. The friabilator was operated at 25rpm for 4 minutes or run up to

100 revolutions. The tablets were weighed again (Final). The % friability was then calculated by,

% Friability = 100 (1-Winitial/ Wfinal)

% Friability of tablets less than 1% are considered acceptable.

Table 1: Formulation composition of floating tablets of Quetiapine Hemifumarate

(Quantity in mg)	*F1*	*F2*	*F3*	*F4*	*F5*	*F6*	*F7*	*F8*	*F9*
Quetiapine Hemifumarate	50	50	50	50	50	50	50	50	50
HPMC K4M	70	80	90	-	-	-	-	-	-
HPMC K15M	-	-	-	70	80	90	-	-	-
HPMC K100M	-	-	-	-	-	-	70	80	90
Sodium bicarbonate	20	20	20	20	20	20	20	20	20
Citric acid	10	10	10	10	10	10	10	10	10
PVP K-30	8	8	8	8	8	8	8	8	8
Magnesium stearate	1	1	1	1	1	1	1	1	1
Talc	2	2	2	2	2	2	2	2	2
Lactose	39	29	19	39	29	19	39	29	19
Total	200	200	200	200	200	200	200	200	200

Weight variation

To study the weight variation, 20 tablets of each formulation were weighed using an electronic digital balance. The average weight of each tablet was calculated and the percentage deviation in weight was calculated.

Water uptake study

The swelling properties of HPMC matrices containing drug were determined by placing the tablet matrices in the dissolution test apparatus, in 900 ml of 0.1 N HCL at 0 37± 0.5°C. The tablets were removed periodically from dissolution medium. After draining free from water by blotting paper, these were measured for weight gain. Swelling characteristics were expressed in terms of percentage water uptake (WU %) show relationship between swelling index and time.

$$WU\ \% = \frac{\text{Weight of swollen tablet} - \text{Initial weight of the tablet}}{\text{Initial weight of the tablet}} \times 100$$

Drug content

Five tablets were weighed individually and powdered. The powder equivalent to average weight of tablets was weighed and drug was extracted in 0.1 N HCl, the drug content was determined measuring the absorbance after suitable dilution using a Shimadzu UV/Vis double beam spectrophotometer.

***In vitro* Buoyancy Study**

The *in vitro* buoyancy study was characterized by floating lag time and total floating time. The time taken for tablet to emerge on the surface of the medium is called the floating lag time (FLT) or buoyancy lag time (BLT) and duration of time the dosage form constantly remains on the surface of the medium is called the total floating time (TFT). The test was performed using a USP type II paddle apparatus using 900 ml of 0.1 N HCL at paddle rotation of 50 rpm at 37 ± 0.5 °C. The time of duration of floatation was observed visually.

***In vitro* Dissolution Studies**

The release rate of Quetiapine Hemifumarate floating tablets was determined by using Dissolution testing apparatus USP type II (Paddle type). The dissolution testing was performed using 900ml of 0.1N HCl at 37± 0.5 °C temperature and speed 50 rpm. A sample (10ml) of the solution was withdrawn from the dissolution testing apparatus hourly for 12 hours and the samples were replaced with fresh dissolution medium. The samples were filtered through a 0.45µ membrane filter & Absorbance of these solutions was measured at 248 nm wavelength using a Shimadzu UV/Vis double-beam spectrophotometer. Analysis of data was done by using 'PCP Disso V-3' software, India.

Stability study

The stability of optimized formulations was tested according to ICH guidelines. The formulations were stored at accelerated (40±2 °C/75±5 % RH) test conditions in stability chamber (Remi, CHM-6S) for three month. At the end of month, tablets were tested for drug content and percent drug released.

Drug release kinetics [24-26]

In order to investigate the mode of release from both the developed tablet formulations the release data were analyzed with the following mathematical models:

Zero-order kinetic: $Q0 = Qt + k0t$

Where, Qt is amount of drug release at time t

k0 is zero order release rate constant.

Q0 is amount of drug present initially at t = 0

First-order kinetic: $\ln (100 – Q) = \ln Q0 – k1t$

Where, Q = amount of drug release at time t

Q0 = amount of drug present initially

K1 = first order release rate constant

Higuchi equation: $Q = kH\ t1/2$

Where, Q = amount of drug release at time t

KH = Higuchi dissolution constant

Korsmeyer- Peppas model: $Q = kPtn$

Where, kPis constant incorporating structural and geometric characteristics of the release device.

n is the release exponent indicative of the mechanism of release.

This equation was further simplified and proposed by Ritger and Peppas

$Mt / Minf = atn$

Where, Mt / Minf = fractional release of drug

a = constant depending on structural and geometric characteristics of the drug dosage form.

n = release exponent

The value of "n" indicates the drug release mechanism. For a slab the value n = 0.5 indicates Fickian diffusion and values of n between 0.5 and 1.0 or n = 1.0 indicate non-Fickian mechanism. In case of a cylinder n = 0.45 instead of 0.5, and 0.89 instead of 1.0.

This model is used to analyze the release from polymeric dosage forms, when the release mechanism is not well known or when there is

a possibility of more than one type of release phenomenon being involved.

Table 2: Interpretation of diffusional release mechanisms from dosage forms

Release exponent (n)	*Drug transport mechanism*
0.5	Fickian diffusion
0.5 < n < 1.0	Anomalous transport (non-Fickian)
1.0	Case-II
> 1.0	Super case-II transport

RESULTS AND DISCUSSIONS

FT-IR studies for drug-polymer compatibility

The IR spectra of QH showed the principle peaks at wave numbers 3750, 3080, 2880, 2380, 1600, 1340, 1030, 791 cm−1. Broad peak at 3750 cm-1 may be due to O-H stretching, 3080 cm-1Ar-H stretching and 2880 cm-1 C-H stretching, 2380 cm-1 may be due to aromatic C=C stretching, 1600 cm−1 may be due to C-N stretching, 1340 cm-1 may be due to C-H bending, 1030 cm-1 may be due to –C-O-C group, 791 cm-1 may be due to substituted benzene ring. (Fig. 1)

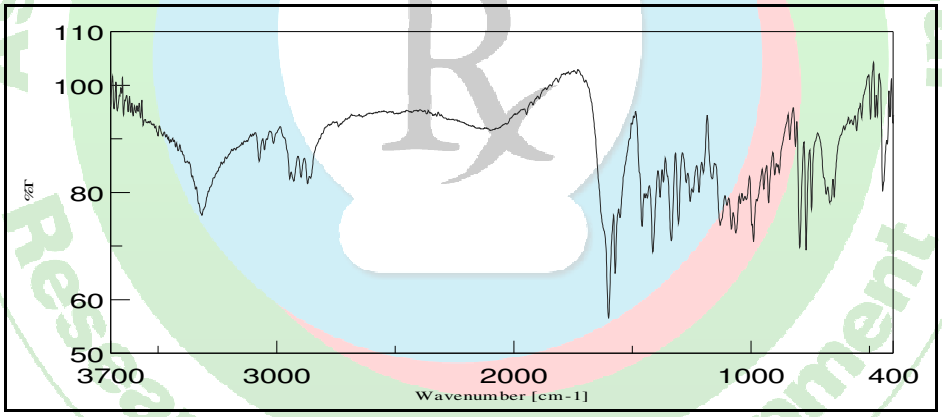

Figure 1: FT-IR spectrum of Quetiapine Hemifumarate

From FTIR spectra (Figure 2) of HPMC K4M, HPMC K15M and HPMC K100M, the characteristic peaks at 1647.75, 1652.89, 1647.65 27cm-1 respectively can be assigned to the C=C stretching in the aromatic ring and a peaks at 1455.41, 1455.98, 1456.81 27cm-1 respectively can be assigned to the C-H deformation.

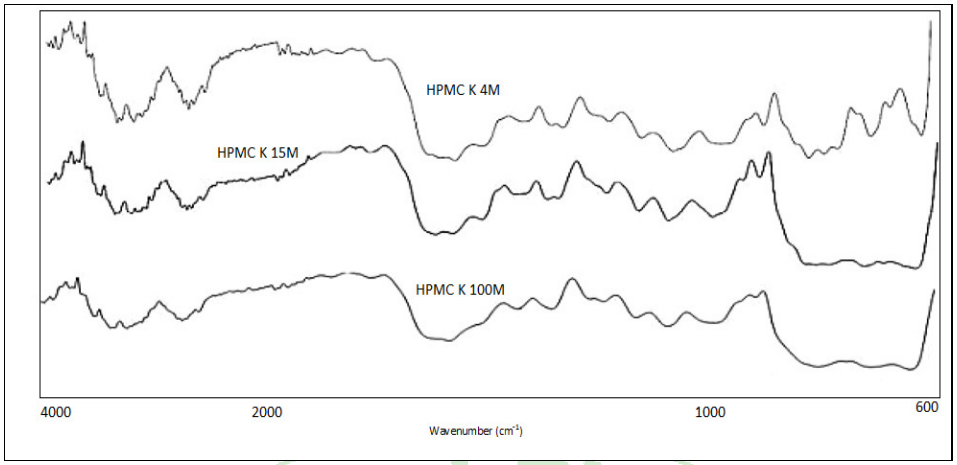

Figure 2: FT-IR spectrum of HPMC K4M, K15M and K100M

The IR spectra of binary mixture of drug and HPMC K4M, K15M and K100M (1:1), and optimized formulation did not show any changes. The principle peaks obtained for the combinations were almost same as that of pure drug. Since there is no change in the position and nature of the bands in the formulation, it is concluded that the drug maintains its identity without any chemical interaction with polymer and excipient used. The FT-IR spectra of QH, binary mixture (1:1) of QH with polymers and optimized formulation are shown in Fig. 3 and 4 respectively.

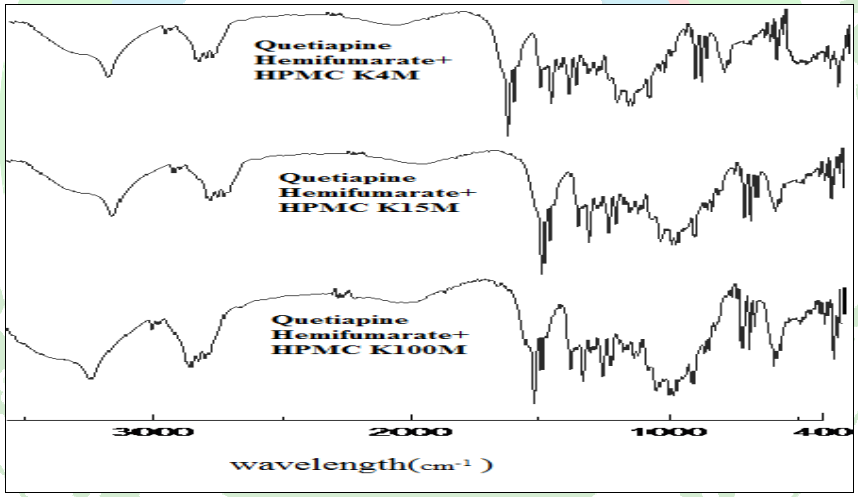

Figure 3: FT-IR spectrum of binary mixture of drug with HPMC K4M, K15M and K100M

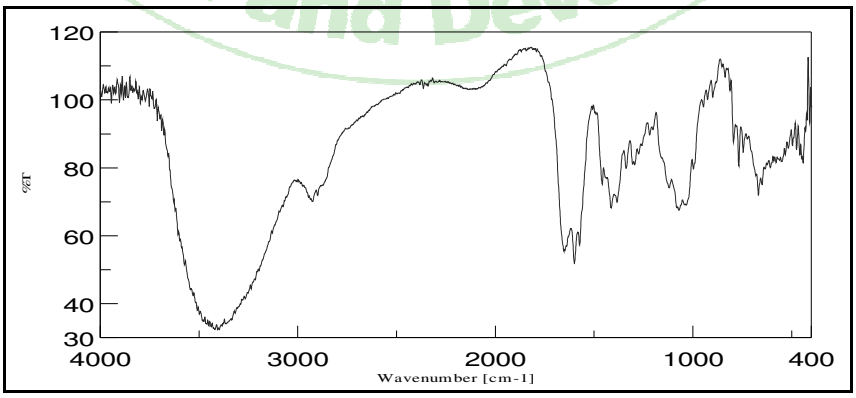

Figure 4: FT-IR of floating matrix tablet (F1)

Precompression parameters

All the formulations of QH showed good flow property as shown in table 3. Bulk density and tapped density observed in the ranged of 0.61 to 0.69 and 0.76 to 0.88 respectively, while compressibility index ranged from 16.04 to 19.73 %. Angle of repose ranged from 24.23 to 27.86, Hausner ratio ranged from 1.15 to 1.24. (Table 3)

Table 3: Powder blend properties

Formulation	*Bulk Density ± SD (gm/ml)*	*Tapped Density ± SD (gm/ml)*	*Compressibility Index ± SD (%)*	*Angle of Repose ± SD (θ)*	*Hausner Ratio ± SD*
F1	0.61 ± 0.01	0.76 ± 0.01	19.73± 0.25	25.65 ± 0.82	1.24 ± 0.05
F2	0.62 ± 0.005	0.76 ± 0.01	18.42 ±0.55	27.28 ± 0.79	1.24 ± 0.01
F3	0.63 ± 0.014	0.78 ± 0.015	20.25 ± 0.79	28.3 ± 1.52	1.22 ± 0.05
F4	0.63 ± 0.01	0.79 ± 0.015	19.23 ±0.42	24.23 ± 0.35	1.21 ± 0.005
F5	0.65 ± 0.015	0.79 ± 0.026	17.72 ± 0.90	25.84 ± 1.13	1.22 ± 0.011
F6	0.64 ± 0.015	0.81 ± 0.015	18.98 ± 0.39	25.46 ± 0.53	1.23 ± 0.01
F7	0.68 ± 0.01	0.80 ± 0.01	15.0 ± 0.27	25.12 ± 0.79	1.23 ± 0.005
F8	0.68 ± 0.01	0.81 ± 0.01	16.04 ± 0.58	24.54 ± 0.61	1.23 ± 0.020
F9	0.73± 0.015	0.88± 0.026	17.04±0.88	27.86±1.31	1.159±0.014

[Note- All values are given as mean ± SD, n=3]

Evaluation of tablets

Hardness and Friability test

The hardness of prepared QH tablets was found to be in the range of 5 to 6.33 kg/cm2 and friability of tablets was found in the range of 0.10 to 0.47 (< 1%), as shown in Table 4.

Thickness and Weight variation

All the prepared tablets were evaluated for thickness and weight variation and results are shown in Table 4. The percent deviation from the average weight was found to be within the official limits.

Drug content

The drug content uniformity studies revealed that drug content between 91.38 ± 2.3% and 99.97 ±2.8% is acceptable. (Table 4)

Water uptake study

Tablets composed of polymeric matrices which forma gel layer around the tablet core when they come in contact with water and this gel layer affects the drug release properties. Penetration of water causes the swelling of polymeric matrix which is very important factor to insure floating and drug dissolution. The formulation with HPMC K4M, HPMC K15M, and HPMC K100M showed significant swelling and good tablet integrity. It is shown that the concentration of sodium bicarbonate and citric acid has not affected the swelling of tablets. From the results it is observed that, HPMC K100M showed higher swelling compared to HPMC K 15M and HPMC 4M which states that swelling index increase with increase in polymer viscosity grades. The results of water uptake study of all formulations are shown in Fig. 5.

Table 4: Evaluation of tablets parameters

Formulation code	Hardness (kg/cm2)	Friability (%)	Weight variation (mg)	Thickness (mm)	Drug content (%)
F1	5±0.81	0.255	198.31±1.60	4.45±0.52	97.56±0.79
F2	5.33±0.94	0.187	200.58±1.53	4.25±0.21	99.97±0.64
F3	6±0.81	0.275	200.62±2.34	4.28±0.09	98.95±0.85
F4	5.33±0.47	0.476	201.90±2.31	4.23±0.04	95.85±0.75
F5	6.33±0.47	0.104	201.44±1.51	4.26±0.16	91.38±0.23
F6	5.66±0.47	0.329	199.34±1.56	4.29±0.061	93.06±0.56
F7	5±0.81	0.149	202.03±1.56	4.42±0.21	98.41±0.12
F8	5.66±0.47	0.335	203.35±1.33	4.51±0.29	92.21±0.45
F9	5±0.81	0.288	200.12±2.93	4.37±0.13	97.93±0.32

[Note- All values are given as mean ± SD, n=3]

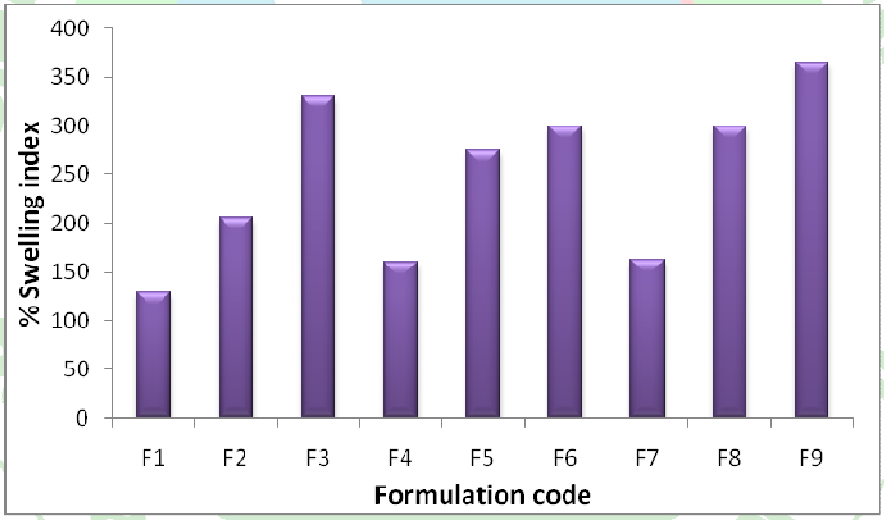

Figure 5: Swelling indices of formulations.

In vitro Buoyancy Study

In all Tablets batches (F1 to F9) floating lag time variation from 42.33 sec to 66.66 sec was observed. All tablet formulations exhibited satisfactory floatation ability and remained buoyant for more than 14 hr in 0.1N HCl dissolution medium (Fig. 6). Formulation F9 containing highest amount of HPMC K100M has longer floating lag time. (Table 5 shows the results of buoyancy study) The optimum concentration of Sodium bicarbonate was found to be 10% to obtain low floating lag time and prolonged floatation. Floating lag time (FLT) and total floating time (TFT) were found to be depended on the concentration of gas generating agent and polymers used in the formulation. The results showed that as the molecular weight of HPMC increases the viscosities of the gel matrix around the tablet also increase which in turns increase the floating lag time.

Table 5: *In vitro* Buoyancy studies

Formulation	*Floating lag time (sec.)*	*Total floating time (hrs.)*
F1	50.66±2.5	15.66±0.57
F2	57±1	16.66±0.57
F3	62.33±2.5	18±1
F4	42.33±2.5	15.66±0.57
F5	52.66±2.08	16.33±0.57
F6	66.65±3.05	18±1
F7	43±2.64	16±1
F8	56.33±2.51	17.66±0.57
F9	66.66±1.52	18.66±0.57

[Note- All values are given as mean ± SD, n=3]

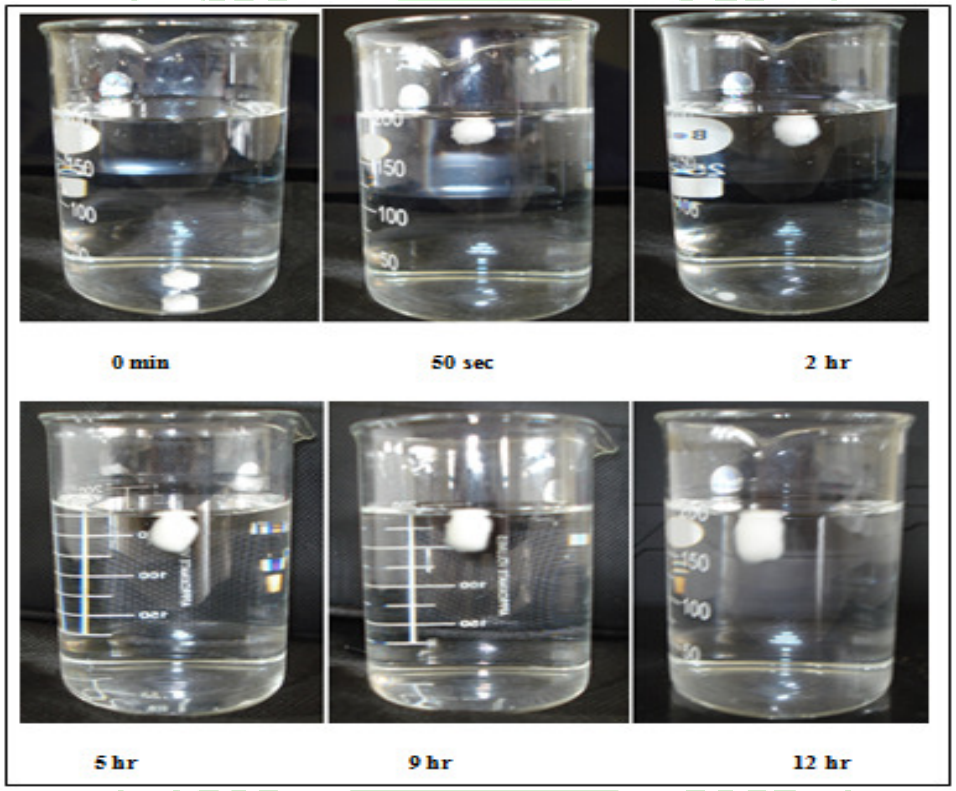

Figure 6: Floating Lag Time of Quetiapine Hemifumarate Floating Matrix Tablet F1

***In vitro* Dissolution Studies**

The *in vitro* drug release data was given in Table 6 and drug release profiles are shown in Fig. 7. Formulations F1, F2 and F3 containing HPMC K4M exhibited 99.63, 92.17 and 88.84% of drug release in 12 hours respectively. Formulations F4, F5 and F6 containing HPMC K15M exhibited 96.52, 90.52 and 86.35% of drug release in 12 hours respectively. The formulations F7, F8 and F9 were prepared with HPMC K100M exhibited 84.43, 80.52and 77.93% drug release rates in 12 hours respectively In the above results, it was observed that as the concentration of the polymers increased, there is a decrease in the drug release rates. An increase in polymer concentration causes increase in viscosity of the gel as well as the gel layer with longer diffusional path. This could cause a decrease in effective diffusion coefficient of the drug and a reduction in drug release rate.

Thus, Formulation F1 and F4 were selected as optimized batch based on their ability to sustain drug release up to 12 hrs as shown in table 6 and figure 7. Formulation F5-F9 showed less than 91% drug release even after 12 hrs which leads to the loss of drug embedded in matrix.

Table 6: Percent drug release data.

Time	*% Drug Released*								
	F1	*F2*	*F3*	*F4*	*F5*	*F6*	*F7*	*F8*	*F9*
1hr	**25.11± 1.13**	20.10± 0.90	17.10± .90	**25.61± 0.69**	17.10± 0.69	14.59± 0.26	13.59± 0.93	10.59±1.19	11.09± 1.13
2 hr	**30.25± 0.67**	25.72± 0.68	22.20±1 .18	**31.25± 0.94**	22.20± 0.68	20.68± 1.58	19.67± 0.68	18.66±0.44	15.16± 0.95
3 hr	**37.43± 0.69**	33.87± 0.51	25.82± 1.38	**35.93± 0.95**	25.82± 0.93	27.30± 1.18	28.79± 0.52	27.77±0.94	22.25± 0.96
4 hr	**40.64± 0.45**	39.06± 1.37	34.48± 0.92	**40.14± 1.16**	34.48± 1.14	33.96± 0.69	39.97± 0.69	36.98±0.95	30.38± 0.48
5 hr	**55.88± 1.34**	42.83± 0.67	38.67± 1.19	**54.37± 1.15**	42.67± 0.69	38.15± 0.70	50.70± 0.68	42.74±0.71	41.06± 1.19
6 hr	**71.20± 0.94**	61.04± 1.35	50.39± 0.95	**66.68± 1.17**	61.93± 0.66	61.89± 0.71	64.49± 1.19	45.88±0.92	51.80± 0.66
7 hr	**85.10± 0.68**	72.38± 2.52	66.19± 0.96	**82.57± 1.61**	72.78± 0.67	68.24± 0.91	67.85± 0.95	55.64±0.65	56.59± 1.16
8 hr	**89.07± 1.19**	80.29± 0.73	75.56± 0.90	**88.02± 1.14**	77.18± 0.93	72.11± 1.61	72.22± 1.21	64.46±1.16	61.90± 1.20
9 hr	**95.06± 0.67**	86.23± 0.67	78.98± 0.67	**92.01± 0.67**	82.61± 0.67	77.01± 0.67	76.62± 0.67	67.31±0.67	69.25± 0.67
10 hr	**97.08± 1.35**	89.70± 1.35	84.41± 1.35	**93.50± 1.35**	87.06± 1.35	83.43± 1.35	81.54± 1.35	75.68±1.35	72.12± 1.35
11 hr	**98.61± 2.52**	90.69± 2.52	87.37± 2.52	**95.51± 2.52**	89.54± 2.52	85.39± 2.52	83.48± 2.52	79.10± 2.52	76.52± 2.52
12 hr	**99.63± 0.73**	92.17± 0.73	88.84± 0.73	**96.52± 0.73**	90.52± 0.73	86.35± 0.73	84.43± 0.73	80.52±0.73	77.93± 0.73

[Note- All values are given as mean ± SD, n=3]

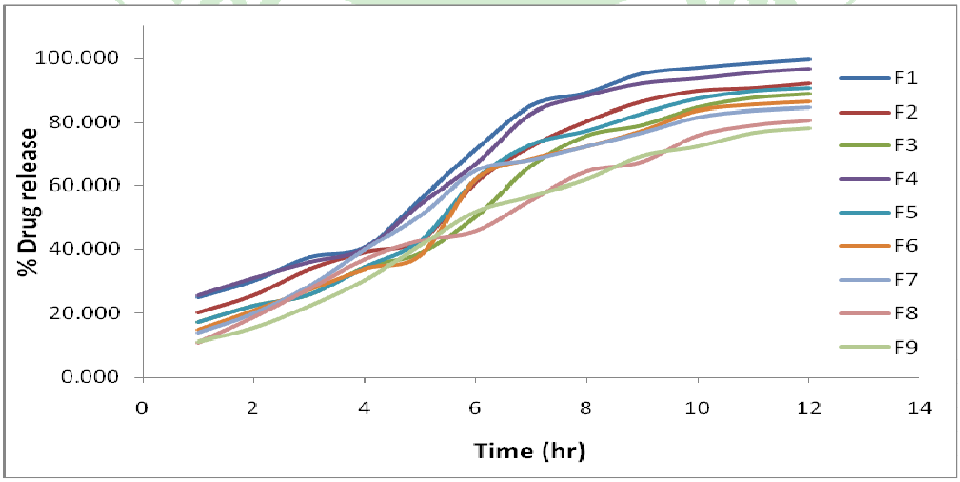

Figure 7: Comparative *in vitro* release profile of F1-F9 batches

From the *in vitro* dissolution studies, it is observed those different grades of polymer and its concentration from F1 to F9 mainly affects the drug release profile. Formulations containing higher viscosity grades of HPMC have slower drug release rates as compared to lower viscosity grades of HPMC. HPMC K15M and HPMC K100M with higher molecular weight forms a gel of higher viscosity i. e. 15000 cps and 100000 cps respectively, compared to HPMC K4M with nominal viscosity 4000 cps. Thus HPMC K4M increases the release rate and extends as compared to HPMC K15M and HPMC K100M. From the results it is also observed that as the concentration of polymer increased, there is decrease in the drug release rate. An increase in polymer concentration causes increase in viscosity of gel as well as gel layer with longer diffusional path which causes decrease in effective drug diffusion and reduction in drug release rate.

Drug release kinetics

The dissolution data of batches F1 to F9 was fitted to Zero order, First order, Higuchi, Hixson crowell and Korsmeyer-Peppas models. The coefficient of regression (R2) value was used as criteria to choose the best model to describe drug release from the tablets. The R2 values of various models are given in Table 7.

Table 7: Kinetic treatment to dissolution data for floating matrix tablet

Formulations	*Regression Coefficient (R2)*						*Best fit Model*
	Zero order Plot	*First order Plot*	*Matrix plot*	*Korsmeyer-Peppas Plot*		*Hix. Crow Plot*	
				(R2)	*n (release exponent)*		
F1	**0.946**	**0.921**	**0.986**	**0.971**	**0.654**	**0.963**	**Matrix**
F2	0.965	0.97	0.961	0.979	0.698	0.986	Hix crow
F3	0.981	0.967	0.945	0.975	0.76	0.983	Hix crow
F4	**0.942**	**0.9677**	**0.9678**	**0.968**	**0.63**	**0.985**	**Hix crow**
F5	0.9732	0.9737	0.947	0.975	0.781	0.986	Hix crow
F6	0.973	0.979	0.949	0.983	0.8	0.987	Hix crow
F7	0.959	0.992	0.965	0.989	0.805	0.992	First order
F8	0.984	0.986	0.962	0.997	0.834	0.996	Peppas
F9	0.984	0.9905	0.95	0.9903	0.873	0.995	Hix crow

The mean diffusional exponent values **(n)** obtained from Korsmeyer equation ranged from 0.63 to 0.87 indicating that all these formulations presented a dissolution behaviour controlled by Non Fickian Diffusion (When n tends towards< 0.5) The results for formulation F1 with R2 value of 0.986 confirmed that the formulation followed Higuchi matrix model indicating Quetiapine Hemifumarate release from controlled drug delivery system were by both diffusion and erosion mechanism.

Stability study

The optimized QH floating tablet (F1) were stored at accelerated (40±2 °C/75±5 % RH) test conditions in stability chamber (Remi, CHM-6S) for three month and showed no significant changes in the physical parameters, drug content, floating characteristics and in-vitro dissolution studies. (Table 8)

Table 8: Stability studies of floating matrix tablet F1

Sr. No	Parameters	After one month Observations	After two month Observations	After three month observation
1	Physical Appearance	No change	No change	No change
2	Weight Variation(mg)	200.58±1.53	203.44±1.51	201.44±1.41
3	Thickness (mm)	4.30±0.0341	4.26±0.020	4.36±0.030
4	Hardness (Kg/cm2)	5±0.81	5.4±0.47	5.8±0.57
6	Drug Content (%)	99.54±0.32	99.24±0.75	99.10±0.75
7	Buoyancy lag time (Sec)	50.66±1.24	71±0.81	60±0.51
8	Duration of buoyancy(hr)	16.6±0.48	15.4±1.01	16.4±1.51
9	% Drug release(12 hr)	99.50±0.58	99.12±0.78	98.95±0.55

[Note- All values are given as mean ± SD, n=3]

CONCLUSION

From the data obtained, it can be concluded that effervescent floating tablets of Quetiapine Hemifumarate can be formulated as an approach to increase gastric residence time and thereby improve its bioavailability. The floating tablets of Quetiapine Hemifumarate were formulated in nine different batches F1 to F9 by using hydrophilic polymers HPMC K4M, HPMC K15M and HPMC K100M, along with effervescing agent sodium bicarbonate and citric acid. The *in vitro* drug release profiles obtained for tablets made with different polymers and their combinations allow efficient control of drug release. The type of polymer affects the drug release rate and the mechanism. Quetiapine Hemifumarate floating drug delivery system showed improved *in vitro* bioavailability and extended drug release which may favors the reduced dose frequency and patient compliance. From the results obtained, it was concluded that the floating matrix tablets formulation F1 is the best formulations as the extent of drug release was found to be around 99%. These batches also showed immediate floatation and floatation duration up to 14 hours for floating matrix tablets. The drug release model of these formulations complies with Higuchi matrix kinetics. Based on the results we can say that floating type gastro retentive drug delivery system holds a lot of potential for drug having solubility as well as stability problem in alkaline pH or which mainly absorbed in acidic pH. We can certainly explore this drug delivery which are may lead to improved bioavailability and ensured therapy with many existing drugs.

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