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PREPARATION OF HIGHLY POROUS GASTRORETENTIVE QUETIAPINE FUMARATE TABLETS BY USING A SUBLIMATION METHOD

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Abstract
The present investigation is aimed to formulate floating gastroretentive tablets containing Quetiapine Fumerate using a sublimation material. The effect of the amount of HPMC K4M on swelling and eroding of the tablets was determined. The water-uptake and erosion behavior of the gastroretentive tablets were highly dependent on the amount of HPMC K4M. The water-uptake increased with increasing HPMC K4M concentration in the tablet matrix. The weight loss from tablets decreased with increasing amounts of HPMC K4M. Camphor was used as the sublimation material to prepare gastroretentive tablets that are low-density and easily floatable.Floating properties of tablets and tablet density were affected by the sublimation of camphor. Prepared floating gastroretentive tablets floated for over 24 hrs and had no floating lag time. However, as the amount of camphor in the tablet matrix increased, the crushing strength of the tablet decreased after sublimation. The release profiles of the drug from the gastroretentive tablets were not affected by tablet density or porosity. From the Formulation, Kinetic, FTIR and DSC Studies indicated that the drug was stable in the tablets. HPMC K4M can be used as a rate controlling polymer by appropriate selection in different ratios. The release of the drug from a matrix tablet was highly dependent on the polymer concentrations.

Key words: *Gastroretentive Quetiapine fumerate floating tablets, Effervescent method, Non Effervescent method, Sublimation method.*

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INTRODUCTION:

From many decades, various drug delivery systems have been commonly used for drug administration through oral route have been known to provide a prompt release of the drug. Therefore, to achieve as well as to maintain the drug concentration within the therapeutic effective range needed for treatment, it is often necessary to take drugs several times a day. This results in a significant fluctuation in the level of drug in the blood plasma as well as dose dumping may occur [1-2].

Floating drug delivery systems are aimed to retain the drug in the stomach and are useful for drugs that are poorly soluble or unstable in the gastrointestinal fluids. The underlying principle is very simple, i.e., to make the dosage form less dense than the gastric fluids, so that it can float on them. The density of the system can be reduced by incorporating a number of low density fillers into the systems such as hydroxyl cellulose, lactates or microcrystalline cellulose. However, this system is not ideal because its performance is highly dependent on the presence of food and fluid in the stomach [3]. The basic idea behind the development of such a system was to maintain a constant level of drug in the blood plasma inspire of the fact that the drug does not undergo disintegration [4].

The drug usually keeps floating in the gastric fluid and slowly dissolves at a pre-determined rate to release the drug from the dosage form and maintain constant drug levels in the blood The concept of floating tablets is mainly based on the matrix type drug delivery system such that the drug remains embedded in the matrix which after coming in contact with the gastric fluid swells up and the slow erosion of the drug without disintegration of the tablet takes place [5].

Sometimes for generating a floating system we even need to add some effervescent or gas generating agent which will also ultimately reduce the density of the system and serve the goal of achieving a floating system [6].

These systems have a particular advantage that they can be retained in the stomach and assist in improving the oral sustained delivery of drugs that have an absorption window in a particular region of the gastrointestinal tract and continuously release the drug before it reaches the absorption window, thus ensuring optimal bioavailability [7-8].

Different approaches are currently used to prolong the gastric retention time, such as muco-adhesive, floating, sedimentation, biodegradable superporous hydrogel,and expendable systems [9]. The floating systems are floatable dosage forms that have a long-lasting intragastric buoyancy. This system offers a sustained action to the therapeutic window and better patient compliance [10].

Several technical methods have been used to prepare gastroretentive floating dosage forms such as the hydrodynamically balanced system based on hydrophilic polymers. The surface of the hydrophilic polymer of the formulation becomes swollen and hydrated when it comes in contact with the gastric fluid and then it is floated. Several researchers have investigated gas-generating systems like Effervescent, Non Effervescent and sublimation method [11–13].

The aim of the study is to prepare the gastroretentive floating tablets by using different concentrations of polymer and different methods and compressed by direct compression method and analyzing the release of drug from the tablets which depending upon the concentration of polymer HPMC K4M

MATERIALS AND METHODS:

Materials

Quetiapine fumarate procured as a gift sample from Aurabindo Pharma Pvt Ltd. Hyderabad,Telangana,India,HPMC K4M purchased from Merck Specialities Pvt Ltd, Mumbai, India,Camphor purchased from Qualikem Pvt Ltd, India,Magnesium Stearate purchased from Pratham Pharma Suppliers, Janani Pharma Pvt Ltd.India. and all reagents are used in the laboratory are laboratory grades.

Methods

The Quetiapine fumarate along with excipients in three different ratios and three different methods formulated into floating tablets by Direct Compression method.

Preparation of Gastroretentive Tablets of Quetiapine Fumarate:

Effervescent method : 50 mg Quetiapine fumarate, Polymers HPMC K4M, MCC has taken in different ratios, 15mg lactose as glidant, 5mg of magnesium stearate as lubricant, 100mg of Sodium bicarbonate and 15mg of Citric acid as an effervescent agent and 10mg of Talc and mixing of powders was carried out in a blender for 15 min. 300 mg of the mixture blend was weighed for each tablet and fed manually into the die of an instrumented single punch tableting machine and directly compressed to make one tablet. The hardness was kept constant (4- 5 N) and was measured with a hardness tester (Monsanto hardness tester). The diameter and thickness of prepared tablets were maintained between 9mm and 5mm.

Non Effervescent Method: 50 mg Quetiapine fumarate, Polymers HPMC K4M, MCC has taken in

different ratios, 15mg lactose as glidant, 5mg of magnesium stearate as lubricant and 10mg of Talc and mixing of powders was carried out in a blender for 15 min. 300 mg of the mixture blend was weighed for each tablet and fed manually into the die of an instrumented single punch tablet machine and directly compressed to make one tablet. The hardness was kept constant (4- 5 N) and was measured with a hardness tester (Monsanto hardness tester). The diameter and thickness of prepared tablets were maintained between 9mm and 5mm.

Sublimation Method: 50 mg Quetiapine fumarate, Polymers HPMC K4M, MCC has taken in different ratios, 15mg lactose as glidant, 5mg of magnesium stearate as lubricant, 10mg of Talc and 100mg camphor was mixed with mixture, blend and Weighed 400mg for each tablet fed manually into the die of an instrumented single punch tableting machine and directly compressed to make one tablet. The hardness was kept constant (4- 5 N) and was measured with a hardness tester (Monsanto hardness tester). The diameter and thickness of prepared tablets were maintained between 10mm and 7mm. The tablets were sublimated in 60°C Hot air oven, and the weight of the tablets was measured at regular time intervals. Tablets with a final weight equal to the theoretical weight after complete sublimation (Table1) were selected for further experiments. In this study, camphor was completely sublimated within 24 hrs.

Table 1: Formulation Chart

Methods	**Effervescent Method**			**Non Effervescent Method**			**Sublimation Method**		
Formulations	F1	F2	F3	F4	F5	F6	F7	F8	F9
Concentrations	1:0.5	1:1	1:1.5	1:2	1:2.5	1:3	1:2	1:2.5	1:3
Quetiapine Fumerate	50mg	50mg	50mg	50mg	50mg	50mg	50mg	50mg	50mg
Hydroxy Propyl Methyl Cellulose (K4M)	25 mg	50 mg	75 mg	100 mg	125 mg	150 mg	100 mg	125 mg	150 mg
MicroCrystalline Cellulose	80 mg	55 mg	30 mg	120 mg	95 mg	70 mg	120 mg	95 mg	70 mg
Sodium Bi Carbonate	100mg	100mg	100mg	---	---	---	---	---	---
Citric Acid	15mg	15mg	15mg	---	---	---	---	---	---
Magnesium Stearate	05mg	05mg	05mg	05mg	05mg	05mg	05mg	05mg	05mg
Talc	10mg	10mg	10mg	10mg	10mg	10mg	10mg	10mg	10mg
Lactose	15mg	15mg	15mg	15mg	15mg	15mg	15mg	15mg	15mg
Camphor	---	---	---	---	---	---	100mg	100mg	100mg
WEIGHT OF THE TABLETS	300mg	300mg	300mg	300mg	300mg	300mg			
BEFORE SUBLIMATION	**No Sublimation Process for F1-F6**						400mg	400mg	400mg
AFTER SUBLIMATION							300mg	300mg	300mg

Dissolution Study

The release of quetiapine Fumerate from the GR tablets was studied using the USP dissolution apparatus II (Rotating paddle).The test for buoyancy and in vitro drug release studies are usually carried out in simulated gastric and intestinal fluids maintained at 37±0.5 ºC. In practice, floating time is determined by using the USP dissolution apparatus containing 900ml of 0.1 HCl as a testing medium maintained at

37±0.5 ºC. The rotation speed was 50rpm.The time required to float the dosage form is noted as floating time.5ml Sample was withdrawn periodically from the dissolution medium, replenished with the same volume of fresh medium each time intervals of 1 to 12hrs and the samples are analyzed for their drug contents after an appropriate dilution with 0.1 N Hydrochloric acid by using UV/Visible spectroscopy at 255nm.

Pre compression Parameters

1. Bulk density: It is a ratio of mass of powder to bulk volume. The bulk density depends on particle size distribution, shape and the cohesiveness of particles.

Bulk density = M/Vo

Where,M = mass of the powder, Vo = bulk volume of the powder

2. Tapped Density:

10gm of powder was introduced into a clean, dry 100 ml measuring cylinder. The cylinder was then tapped 100 times from a constant height and the tapped volume was read. It is expressed in gm/ml and is given by

Tapped Density = M/Vt

Where,M = mass of the powder, Vt = final tapping volume of the powder

3.Compressibility index (Carr's index):

Compressibility index is used as an important parameter to determine the flow behavior of the powder. It is indirectly related to the relative flow property rate, cohesiveness and particle size. It is Simple, fast and popular method for predicting flow characteristics. Carr's index can be represented.

Carr's Index (%) = Tapped density – Bulk density * 100

Tapped density

4. Hausner's Ratio

It is the ratio of tapped density to bulk density. It is given by

Hausner ratio = Tapped density / Bulk density

5. Angle of Repose

It is defined as the maximum angle possible between the surface of the pile of the powder and the horizontal plane. Fixed funnel method was used. A funnel was fixed to its tip at a given height 'h, above a flat horizontal surface to which a graph paper was placed. The powder was carefully poured through a funnel till the apex of the conical pile just touches the tip of the funnel. The angle of repose was then calculated using the following equation

Angle of Repose (θ)= tan-1(h/r)

Where,h=height of the pile, r=radius of the pile, θ=angle of repose.

Post Compression Parameters

Tablet density

Tablet density is an important parameter for floating tablets. The tablet would float only when its density is less than that of gastric fluid (1.004). The density is determined using following relationship.

V = r2 h d = m/v

Where,**v** = volume of tablet (cc), **r** = radius of tablet (cm)**h** = crown thickness of tablet (g/cc) and **m**= mass of the tablet

Weight Variation

To study weight variation, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight

Hardness:

Hardness or tablet crushing strength (fc) (the force required to break a tablet in a diametric compression) was measured using a Monsanto tablet hardness tester . It is expressed in kg/cm2.

Thickness: The thickness of the tablets was measured using vernier caliper. It is expressed in mm.

Friability (F):

Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at I height of 6 inches in each revolution. Preweighted sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were de dusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula.

$$F = W_{initial} - W_{final} / W_{initial} \times 100$$

Swelling Index or Water-Uptake Studies

The individual tablets were weighted accurately and kept in 50 ml of water. Tablets were taken out carefully after 60 minutes, blotted with filter paper to remove the water present on the surface and weighed accurately. Percentage swelling (swelling index) was calculated by using the formula:

$$\text{Swelling index} = W_{wet} - W_{dry} / W_{dry} \times 100$$

Floating Lag Time

The floating abilities of single tablets were determined in 500 ml pre warmed 0.1 N HCl, and shaken at 70 rpm, 37 ± 0.2°C for 24 hrs, using a shaker apparatus. The floating lag time (time at which tablets start floating) and duration were measured by visual observation.The time taken for dosage form to emerge on surface of the medium called floating Lag Time (FLT) or total duration of time (TFT).

Preformulation Studies

Preparation of Buffer Solution

Before performing the test for floating Tablets, standard curve of Quetiapine fumarate, 0.1N HCl was constructed.

Preparation of 0.1N HCl

A 8.65 ml of Conc. HCl was placed in a 1000 ml volumetric flask and the volume was made up with water and the pH was adjusted to 1.2.

Preparation of Standard Solution Quetiapine fumarate: Accurately weighed 100mg of Quetiapine fumarate was placed in a 100ml volumetric flask and 50ml of 0.1 N HCl was added to dissolve the drug. The volume was made up to 100ml HCl to give 1000 µg/ml of solution (stock solution -I).

A 10ml aliquot from stock solution -I was taken and diluted to 100ml within a volumetric flask to get 100µg/ml (stock solution -II)

Determination of Absorption Maxima (λ_{max}) for Quetiapine Fumarate:

A 1ml aliquot of standard solution standard solution stock solution-II was diluted to 10ml to give 10 µg/ml standard solutions of Quetiapine fumarate 0.1 N HCl. This solution was scanned on a UV-Visible spectrophotometer against the respective media blank. An absorption maximum (λ_{max}) of 255nm was obtained for all solutions and was selected to prepare standard curve.

Preparation of Standard curve of Quetiapine Fumarate

Aliquotes of 0.2, 0.4, 0.6, 0.8, and 1ml of Quetiapine fumarate standard solution of 100 µg/ml (stock solution-II) was taken and diluted to 10ml to obtain concentrations from 0.2 to 1µg/ml with 0.1 N HCl. The absorbances of solutions were determined at 255nm against respective media solutions as blank and a standard curve was plotted

RESULTS AND DISCUSSION:

Calibration Curve Values

The absorbance was measured in a UV spectrophotometer at 255nm against 1.2 pH buffer. The absorbance so obtained were tabulated as in table 2.Calibration curve was plotted and shown in figure 1 and regression value R^2 of 0.999 was obtained.

Table 2: Calibration Curve Values

S.No	Conc µg/ml	Absorbance
1	0	0
2	2.0	0.061
3	4.0	0.119
4	6.0	0.179
5	8.0	0.240
6	1.0	0.310

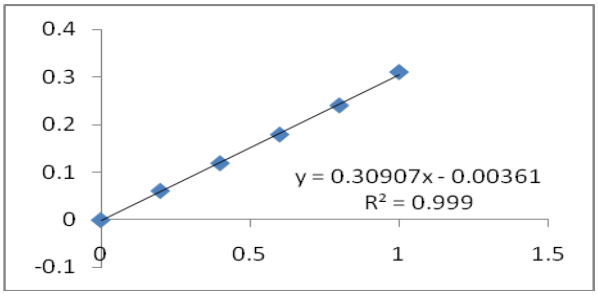


Fig 1: Standard graph of Quetiapine Fumerate in 0.1N HCl

Pre Compression Parameters

Table 3 represents the physical properties of the powder used for the preparation of tablets. The flow properties such as angle of repose, Bulk density, Tapped density, Carr's index, and Hausner's ratio are considered as indirect measurements of powder flowability. Hausner's ratio is indicative of inter-particular friction; the Carr's index shows the propensity of a material to diminish in volume. As the values of these indices increase, the flow of the powder decreases. All parameter values are within the satisfactory limit compared with the standard values.

Post Compression Parameters:

The results of the physical characterization of tablets are summarized in Table 4 . All the formulations hardness, weight variation, friability, thickness, Diameter and Floating Lag Time were found to be within pharmacopoeia limits. The swelling behavior is important for bioadhesion. Water sorption increases with an increase in the concentration of hydrophilic polymer and there is no floating lag time for the formulations F7-F9 because the tablets composite was highly porous due to sublimation with camphor as sublimation material.

Dissolution Profiles of Different Concentration Formulation

The ex-vivo residence time was determined using USP dissolution apparatus with different methods of formulations such as Effervescent(F1-F3), Non Effervescent(F4-F6), Sublimation method(F7-F9). Among F9 showed maximum residence time of 10 Hrs. It was found that an increase in concentration of the polymer increases the residence time. This was mainly due to the strong mucoadhesion nature of the polymer used. The results of in vitro drug release studies of different formulations were shown in Table 5,6 and Figure 2,3and 4. The initial burst release decrease with increase in concentration of polymer. To ascertain the mechanism of drug release, the dissolution data were analyzed by Zero order, first order, Higuchi and Peppas equations. Amount of percentage of drug release versus time curves exhibited straight line for the formulations and confirmed that the release rate followed zero order release kinetics, the percentage of drug release versus the time curves shows linearity and proves that all the formulations followed Zero order as shown Figure 5.

Table 3: Pre Compression Parameters

S.No	Formulation	Angle of repose	Bulk density	Tapped density	Carr's index	Hausners ratio
1	F1	24.15±0.06	0.51±0.03	0.62±0.05	17.74±0.07	1.21±0.06
2	F2	25.08±0.03	0.47±0.07	0.59±0.04	20.33±0.02	1.25±0.03
3	F3	23.28±0.12	0.48±0.05	0.59±0.06	18.64±0.02	1.22±0.03
4	F4	27.21±0.09	0.54±0.02	0.65±0.07	16.92±0.06	1.20±0.07
5	F5	28.25±0.02	0.52±0.03	0.63±0.03	17.46±0.05	1.21±0.05
6	F6	29.35±0.03	0.48±0.05	0.60±0.05	20.00±0.01	1.25±0.04
7	F7	26.75±0.05	0.47±0.04	0.56±0.06	16.07±0.06	1.18±0.08
8	F8	24.38±0.06	0.53±0.07	0.62±0.04	14.51±0.05	1.16±0.03
9	F9	25.02±0.08	0.50±0.02	0.58±0.03	13.79±0.08	1.15±0.05

Table 4: Post Compression Parameters

S.No	Formulation	Hardness (kg/cm^2)	Thickness (mm)	Diameter (mm)	Avg wt variation (mg)	Friability	Floating Lag time (Sec)	Floating Duration (hrs)	Swelling Index±SD
1	F1	4.6	0.5±0.13	0.9	299±0.13	0.44	118	>24	5.00±0.12
2	F2	5.2	0.4±0.74	0.9	300±0.16	0.49	158	>24	4.60±0.17
3	F3	5.0	0.4±0.76	0.9	300±0.16	0.45	155	>24	4.00±0.26
4	F4	4.8	0.5±0.12	0.9	301±0.25	0.50	105	>24	3.33±0.32
5	F5	4.9	0.5±0.13	0.9	300±0.17	0.48	200	>24	4.00±0.27
6	F6	4.7	0.4±0.79	0.9	299±0.12	0.43	250	>24	4.00±0.28
7	F7	4.1	0.6±0.02	0.9	300±0.17	0.47	0	>24	4.60±0.23
8	F8	4.0	0.6±0.02	0.9	302±0.10	0.52	0	>24	5.33±0.16
9	F9	4.0	0.7±0.01	0.10	300±0.25	0.46	0	>24	6.00±0.18
									n=3

Table 5: Percentage of Drug Release Profile

Time	1 hr	2hr	3hr	4hr	5hr	6hr	7hr	8hr	9hr	10hr
Formulation 1	06.32	13.87	19.84	26.89	35.95	48.15	57.19	63.93	67.68	70.12
Formulation 2	03.24	10.13	20.92	30.12	42.15	56.18	61.92	68.60	71.54	75.23
Formulation 3	04.86	11.35	21.59	30.34	45.84	52.78	59.32	65.18	71.38	78.08
Formulation 4	01.69	06.54	10.08	15.24	20.92	28.02	39.18	48.99	55.21	62.89
Formulation 5	02.23	07.18	12.62	19.59	26.63	37.83	45.87	51.32	58.41	65.81
Formulation 6	03.18	05.83	08.93	17.05	22.78	34.09	41.92	52.85	60.82	68.25
Formulation 7	05.78	10.25	17.97	26.31	38.78	45.30	57.65	70.49	76.61	82.08
Formulation 8	08.17	14.38	23.29	35.40	48.21	57.37	69.02	78.14	80.27	86.50
Formulation 9	11.96	19.38	25.53	31.35	42.27	55.34	68.27	75.36	87.28	94.18

Graphical Representation of Percentage of Drug Release

Effervescent Method:

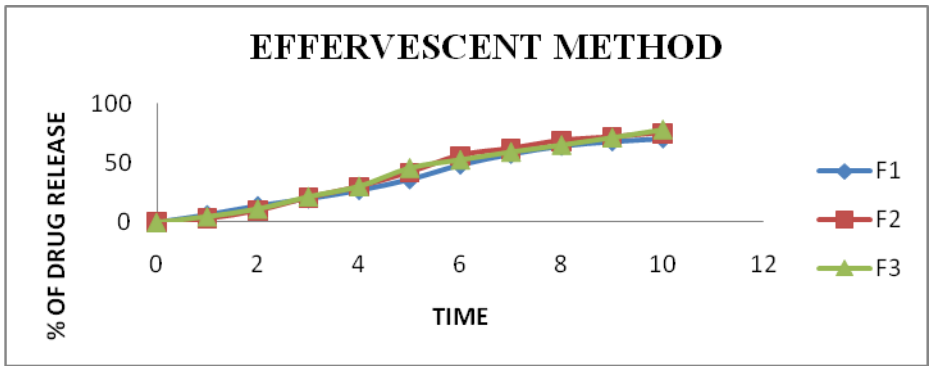


Fig 2: Graphical Representation of % Drug Release of Formulations (F1, F2 and F3)

Non Effervescent Method:

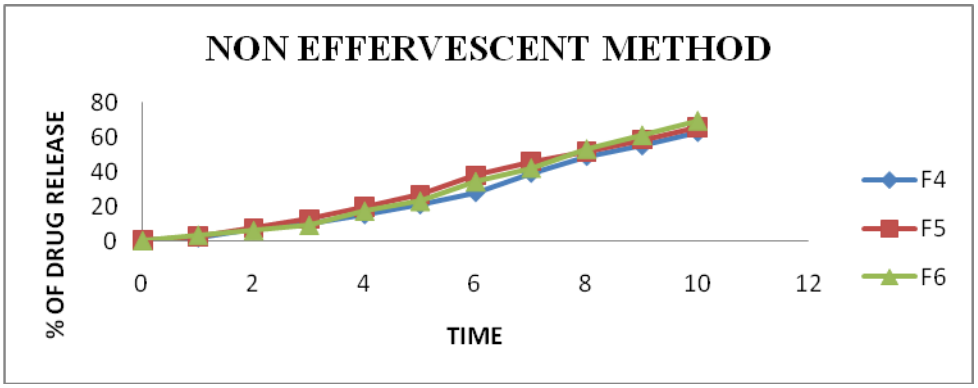


Fig 3: Graphical Representation of % Drug Release of Formulations(F4, F5 and F6)

Sublimation Method:

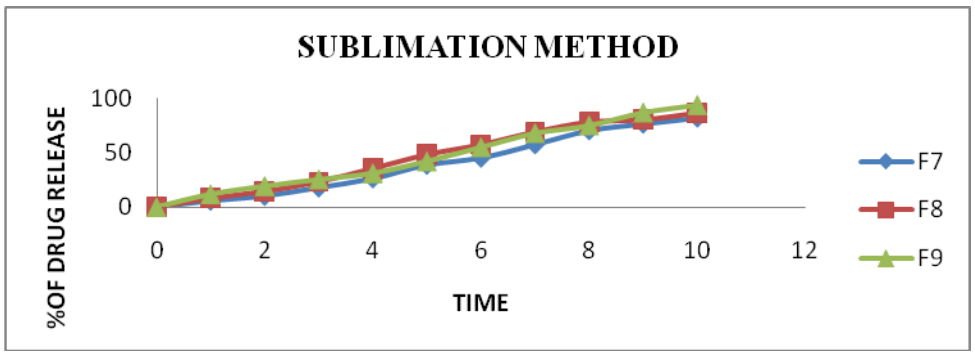
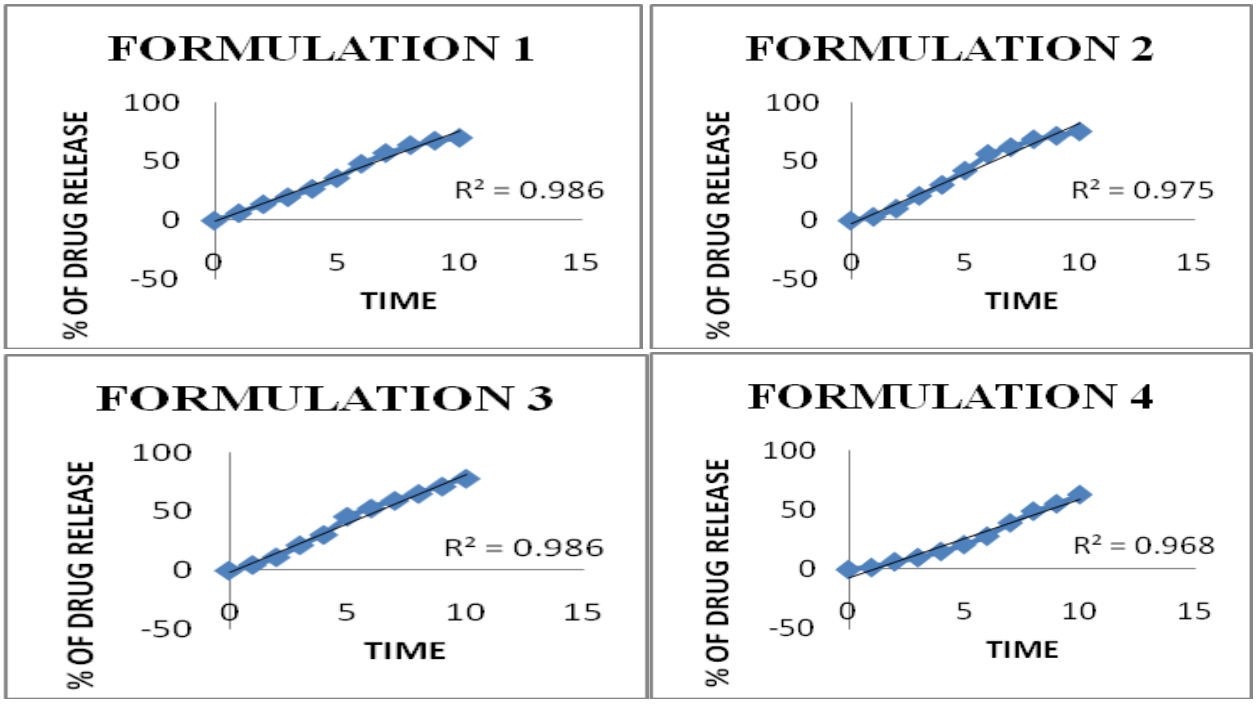


Fig 4: Graphical Representation of % Drug Release of Formulations(F7, F8 and F9)

KINETIC ANALYSIS OF DISSOLUTION DATA:



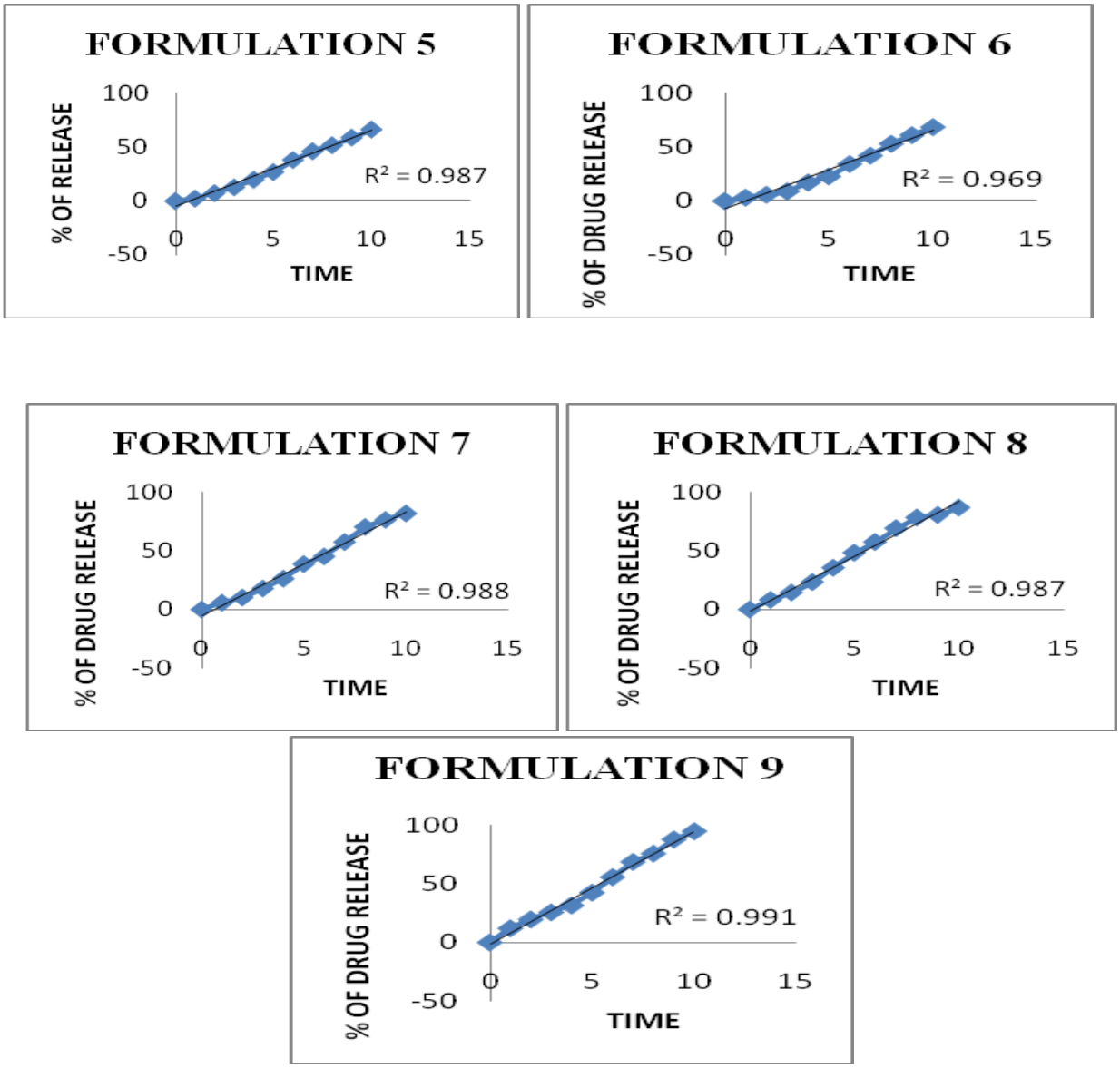


Fig 5: Graphical Representation of Kinetic Analysis Dissolution Data F1-F9 by Zero Order Kinetics

Table 6 : Release Kinetics

Formulation	Zero Order	% Of Drug Release		Higuchi's		Peppas		First Order	
	R^2	Time (Hrs)	Cumulative of %Drug release	Sq.Root Time	Cumulative of %Drug release	Log Time	Log Cum of %Drug release	Time (Hrs)	Log % of Drug remain
F1	0.9863	0	0	0	0	0	0	0	0
F2	0.9759	1	7.85	1.00	7.85	0.00	0.89	1	2.00
F3	0.9868	2	12.53	1.41	12.53	0.30	1.10	2	1.96
F4	0.9683	3	26.94	1.73	26.94	0.48	1.43	3	1.94
F5	0.9877	4	37.76	2.00	37.76	0.60	1.57	4	1.86
F6	0.9690	5	41.69	2.24	41.69	0.70	1.62	5	1.80
F7	0.9884	6	52.46	2.45	52.46	0.78	1.72	6	1.77
F8	0.9874	7	56.34	2.65	56.34	0.85	1.75	7	1.68
F9	0.9916	8	64.12	2.83	64.12	0.90	1.80	8	1.64
		9	73.58	3.00	73.58	0.95	1.87	9	1.57
		10	87.33	3.16	87.33	1.00	1.94	10	1.42

FTIR Study

FTIR spectrum of quetiapine fumarate (Figure 6,7 and 8) shows a broad peak at 3750 cm-^{1}may be due to O-H stretching,3080 cm-^{1} Ar-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, 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. The FTIR spectrum of the best formulation obtained during the from the results, it is clear that, there is no appreciable change in the positions of the characteristic bands of the drug along with the FTIR spectrum of the best formulation derived during the present investigation. Since there is no change in the nature and position of the bands in the formulation, it can be concluded that the drug maintains its identity without going any chemical interaction with the polymer.

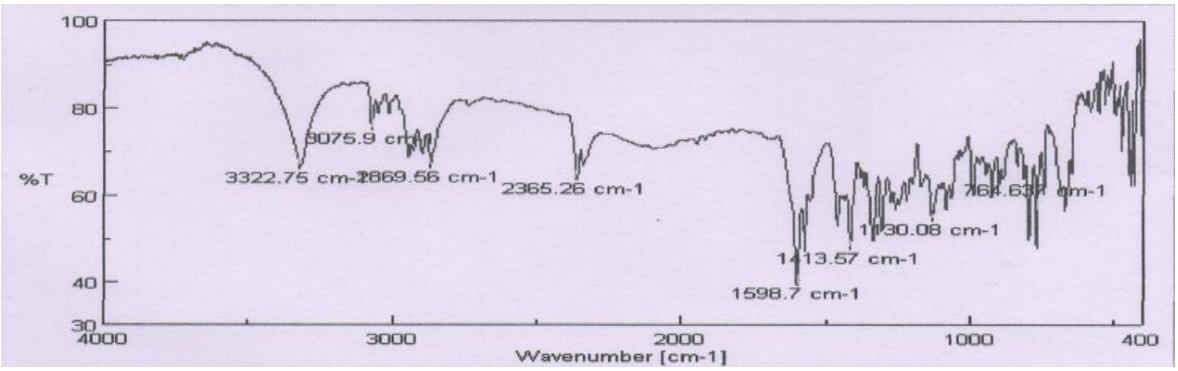


Fig 6: FTIR Spectrum of Quetiapine Fumarate

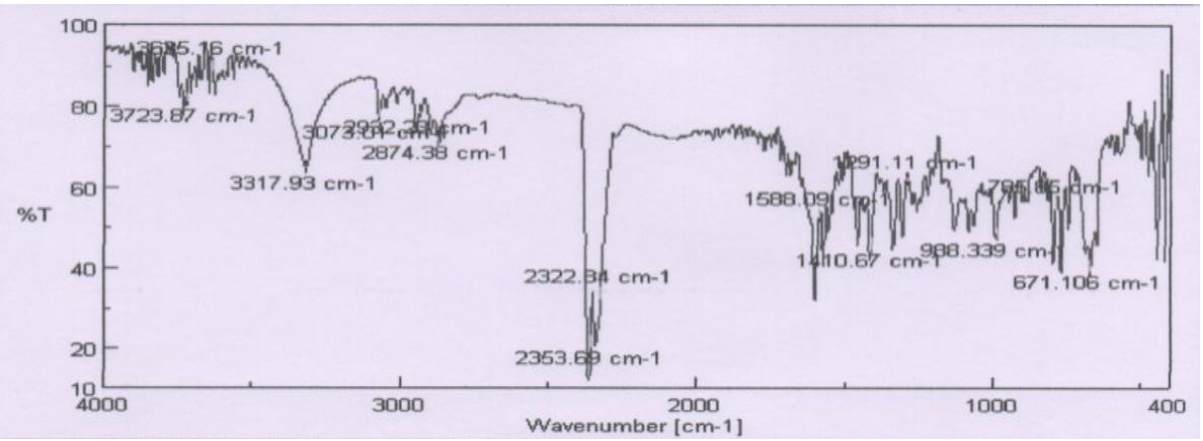


Fig 7: FTIR Spectra of Optimized Formulation

Results of Characterization of Polymer:

i)Viscosity of Polymer

For characterization of polymer used in the present study the viscosities were determined and compared with the reported value and spectra by FTIR of the polymer were taken. The evaluating parameters agreed with reported parameters.

a)Viscosity of Polymer

Table 7: Viscosity of Polymer

S.No.	**Polymer Viscosity Obtained (mPa.s)**	**Viscosity Reported (mPa.s)**
1	HPMC K4M 3000 – 4000	2308 – 3755

ii) Infrared Spectra of Polymers:

a) Infrared spectrum of Hydroxy propyl methyl cellulose K4M

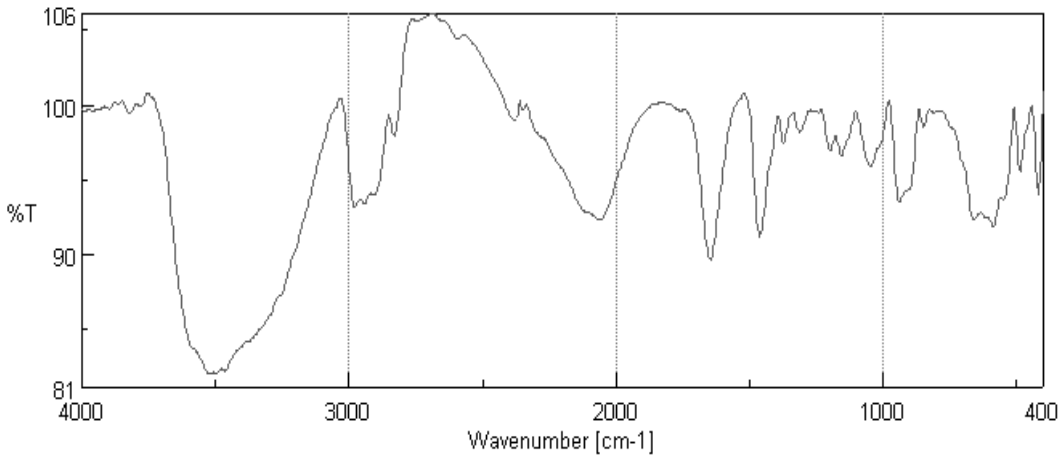


Fig 8: FTIR Spectra of HPMC K4M

DSC Study

Figure 9 and 10 shows the DSC thermographs of pure drug (Quetiapine fumerate) and formulation F9. Thermographs obtained from DSC studies, revealed that the melting point of pure drug is 234°C and that of the drug in the formulation is 233°C as there is no much difference in the melting point of the drug in the thermographs of the drug and that of in the formulation. It may be concluded that, the drug is in the same pure state, even in the formulation without interacting with the polymers.

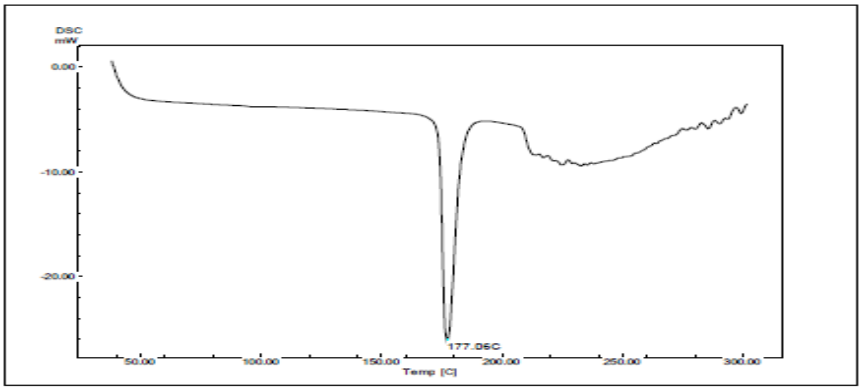


Fig 9: DSC Thermograph of Pure Drug Quetiapine Fumarate

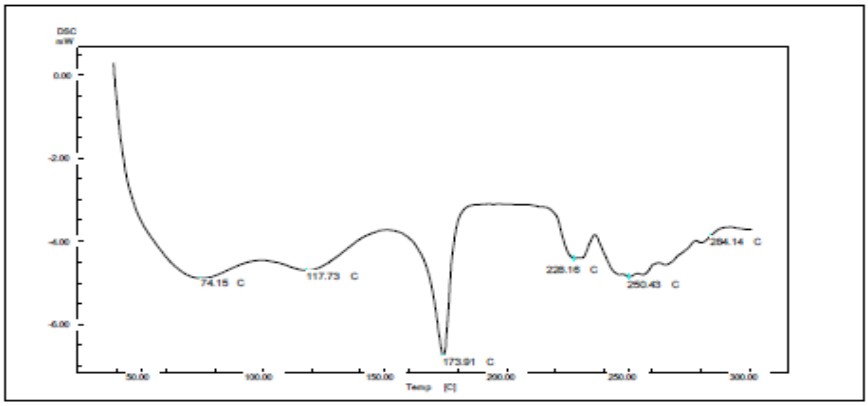


Fig 10: DSC Thermograph of Optimized Formulation

CONCLUSION:

The formulations from F1 to F9 prepared with HPMC K4M polymer in different ratios with three different methods such as Effervescent, Non Effervescent and Sublimation methods. Among this Sublimation method which having Camphor as sublimation material. The Formulation F9 shows 95 % of drug release in 10hrs. As Camphor was sublimed, which causes holes and remained in the tablets, giving the tablets a low density and porous structure and increase in tablet thickness after camphor sublimation due to swelling of tablet caused by phase transition of camphor from solid to gas. The tablets have no lag time and floated over >24hrs. The formulation F7- F9 hardness decreased after camphor sublimation. The formulation F9 could retard the drug release up to desired time period. The tablets containing pores and polymers of HPMC K4M and MCC retard the drug release because both are swellable materials. From the release study it is observed that as increase the concentration of HPMC K4M, the release of drug is decreased. This is possibly due to slower erosion of

HPMC K4M due to the increased viscosity of MCC might have the hydrated gel intact thus releasing the drug for 10 hrs. From Formulation, Kinetic, FTIR, and DSC studies indicated that the drug was stable in the tablets. HPMC K4M can be used as a rate controlling polymer by appropriate selection in different ratios. The release of the drug from a matrix tablet was highly dependent on the polymer concentrations.

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