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FORMULATION AND EVALUATION OF QUINAPRIL HCL FLOATING TABLET

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ABSTRACT
Quinapril is an angiotensin-converting enzyme inhibitor (ACE inhibitor) used in the treatment of hypertension and congestive heart failure. A prodrug, it is converted to its active metabolite, quinaprilat, in the liver. Quinapril HCl is classified in the Biopharmaceutics Classification Scheme as a class I drug, it has a high solubility and high permeability but the rate limiting step is gastric emptying time. The main objective of this study is to formulate the quinapril floating tablets to float in stomach over the drug release. The present study concludes that gastro retentive floating tablets of Quinapril prepared using HPMC K 4 M, HPMC K 15 M and HPMC K 100 M as retarding polymers. Among all the formulations, F5 formulation has shown optimised results. Present study concludes that gastro retentive floating system may be a suitable method for Quinapril.

KEYWORDS: Quinapril, Prodrug, Floating system, HPMC.

INTRODUCTION

Oral delivery of drugs is the most preferable route of drug delivery. Oral route is considered most natural, uncomplicated, convenient and safe due to its ease of administration, patient compliance and flexibility in formulation and cost effective manufacturing process 1. Many of the drug delivery systems, available in the market are oral drug delivery type systems Pharmaceutical products designed for oral delivery are mainly immediate release type or conventional drug delivery systems, which are designed for immediate release of drug for rapid absorption. These immediate release dosage forms have some limitations such as:

1. Drugs with short half-life require frequent administration, which increases chances of missing dose of drug leading to poor patient compliance.
2. A typical peak-valley plasma concentration-time profile is obtained which makes attainment of steady state condition difficult.
3. The unavoidable fluctuations in the drug concentration may lead to under medication or overmedication as the Css values fall or rise beyond the therapeutic range.
4. The fluctuating drug levels may lead to precipitation of adverse effects especially of a drug with small therapeutic index, whenever overmedication occurs.[2]

In order to overcome the drawbacks of conventional drug delivery systems, several technical advancements have led to the development of controlled drug delivery system that could revolutionize method of medication and provide a number of therapeutic benefits.[3]

Controlled drug delivery systems have been developed which are capable of controlling the rate of drug delivery, sustaining the duration of therapeutic activity and/or targeting the delivery of drug to a tissue.[4]

A controlled drug delivery system is usually designed to deliver the drug at particular rate. Safe and effective blood levels are maintained for a period as long as the system continues to deliver the drug.[6]

Oral drug delivery systems have progressed from immediate release to site-specific delivery over a period of time. Every patient would always like to have a ideal drug delivery system possessing the two main properties that are single dose or less frequent dosing for the whole duration of treatment and the dosage form must release active drug directly at the site of action.[7]

Controlled release or Extended-release dosage forms with prolonged residence times in the stomach are highly desirable for drugs.[8]

Floating drug Delivery Systems or Hydrodynamically Balanced Systems (HBS)

These systems have a bulk density lower than gastric fluids and thus remain buoyant in the stomach without

affecting the gastric emptying rate for a prolonged period of time. While the systems are floating in 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 the gastric retention time and a better control of fluctuations in plasma drug concentration. HBS system contains a homogeneous mixture of drug and the hydrocolloid in a capsule, which upon contact with gastric fluid acquires a bulk density of less than 1 thereby being buoyant on the gastric contents of stomach until all the drug was released.

Quinapril is an angiotensin-converting enzyme inhibitor (ACE inhibitor) used in the treatment of hypertension and congestive heart failure. A prodrug, it is converted to its active metabolite, quinaprilat, in the liver.

Quinapril HCl is classified in the Biopharmaceutics Classification Scheme as a class I drug, it has a high solubility and high permeability but the rate limiting step is gastric emptying time. The main objective of this study is to formulate the quinapril floating tablets to float in stomach over the drug release. There by bio availability may increase.

MATERIALS AND METHODS

Analytical method development

Determination of absorption maximum

10 mg of pure drug was dissolved in 10 ml methanol (primary stock solution - 1000 µg/ml). From this primary stock solution 1 ml was pipette out into 10 ml volumetric flask and made it up to 10 ml with the media (Secondary stock solution – 100 µg/ml). From secondary stock solution again 1ml was taken it in to another volumetric flask and made it up to 10 ml with media (working solution – 10 µg/ml). The working solution was taken for determining the wavelength.

Determination of Calibration Curve

10mg of pure drug was dissolved in 10ml methanol (primary stock solution - 1000 µg/ml). From this primary stock solution 1 ml was pipette out into 10 ml volumetric flask and made it up to 10ml with the media (Secondary stock solution – 100µg/ml). From secondary stock solution required concentrations were prepared (shown in Table 7.1) and those concentrations absorbance were found out at required wavelength.

Drug – Excipients compatibility studies

Fourier Transform Infrared (FTIR) spectroscopy

The compatibility between the pure drug and excipients was detected by FTIR spectra obtained on Bruker FTIR Germany(Alpha T). The solid powder sample directly place on yellow crystal which was made up of ZnSe. The spectra were recorded over the wave number of 4000 to 400cm^{-1}.

Formulation development of Tablets

All the formulations were prepared by direct compression. The compressions of different formulations are given in Table 6.1 & 6.2. The tablets were prepared as per the procedure given below and aim is to prolong the release of Quinapril HCl. Total weight of the tablet was considered as 200mg.

Procedure

1) Quinapril HCl and all other ingredients were individually passed through sieve no ≠ 60.
2) All the ingredients were mixed thoroughly by triturating up to 15 min.
3) The powder mixture was lubricated with talc.
4) The tablets were prepared by using direct compression method.

Optimization of Sodium bicarbonate concentration

Sodium bicarbonate was employed as effervescent gas generating agent. It helps the formulation to float. Various concentrations of sodium bicarbonate were employed; floating lag time and floating duration were observed. Based on floating sodium bicarbonate concentration was finalized and proceeded for further formulations.

Table No. 1: Optimization sodium bicarbonate concentration.

Sl. No	Excipients Name (mg)	EF1	EF2	EF3
1	Quinapril HCl	20	20	20
2	HPMC K100	60	60	60
4	$NaHCO_3$	20	40	60
5	Magnesium Stearate	4	4	4
6	Talc	4	4	4
7	MCC pH 102	Q.S	Q.S	Q.S
8	Total weight	500	500	500

Based on the floating lag time and floating duration the concentration of sodium bicarbonate was optimized.

Table No. 2: Formulation composition for floating tablets.

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Quinapril HCl (mg)	20	20	20	20	20	20	20	20	20
HPMC K 4 M	20	40	60	-	-	-	-	-	-
HPMC K 15 M	-	-	-	20	40	60	-	-	-
HPMC K 100 M	-	-	-	-	-	-	20	40	60
$NaHCO_3$	40	40	40	40	40	40	40	40	40
Mag. Stearate	4	4	4	4	4	4	4	4	4
Talc	4	4	4	4	4	4	4	4	4
MCC pH102	QS	QS	QS	QS	QS	QS	QS	QS	QS
Total weight	200	200	200	200	200	200	200	200	200

Evaluation parameters

Pre Compression parameters

Bulk density (D_B)

Bulk density is the ratio between a given mass of the powder and its bulk volume.

Bulk density = Mass of Powder / Bulk volume of the powder

Bulk density (D_B) = W /V_0

Procedure: An accurately weighed quantity of granules (w) (which was previously passed through sieve No: 40) was carefully transferred into 250 ml measuring cylinder and measure the bulk volume.

Tapped Density (D_T): Tapped density is the ratio between a given mass of powder (or) granules and the constant (or) fixed volume of powder or granules after tapping.[69]

Tapped density = mass of the powder/ tapped volume

Procedure: An accurately weighed quantity of granules (w) (which was previously passed through sieve No: 40) was carefully transferred into 250 ml measuring cylinder and the cylinder was tapped on a wooden surface from the height of 2.5 cm at two second intervals. The tapping was continued until no further change in volume (until a constant volume) was obtained (V_f). The tapped density was calculated by using the formula,

Tapped density (D_T) =W/V_f

Hausner's ratio

Hausner's ratio is an indirect index of ease of powder flow and was calculated by the formula.[71]

Hausner'sratio = D_T/D_B

Where, D_T is the tapped density

D_B is the bulk density

Compressibility index

Compressibility index (CI) was determined by measuring the initial volume (V_o) and final volume (V_f) after hundred tapping's of a sample in a measuring cylinder. It indicates the powder flow properties and expressed in terms of percentage and given in table no. 14 and calculated by using the formula.[70]

% Compressibility index = V_o - V/V_o x 100

Table No. 3: Carr's index value (as per USP).

Carr's index	Properties
5 – 15	Excellent
12 – 16	Good
18 – 21	Fair to Passable
2 – 35	Poor
33 – 38	Very Poor
>40	Very Very Poor

Angle of repose

Angle of repose[71] was measured by fixed funnel method. It determines flow property of the powder. It is defined as maximum angle formed between the surface of the pile of powder and the horizontal plane.

The powder was allowed to flow through the funnel fixed to a stand at definite height (h). By measuring the height and radius of the heap of powder formed (r), angle of repose was calculated by using formula given below and the calculated values obtained was shown in table no. 14.

$\theta = \tan^{-1}$ (h / r)

Where, θ is the angle of repose

h is the height in cm

r is the radius in cm

Table No. 4: Angle of Repose values (as per USP).

Angle of Repose	Nature of Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Evaluation of post compression parameters for prepared Tablets

The designed formulation floating tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content.

Weight variation test

Twenty tablets were randomly selected and weighed, to estimate the average weight and that were compared with individual tablet weight. The percentage weight variation was calculated as per Indian Pharmacopoeial Specification. Tablets with an average weight 250 mg so the % deviation was ±5%.67.

Table No. 5: IP standards of uniformity of weight.

Sl. No.	Average weight of tablet	% of deviation
1	≤ 80 mg	10
2	> 80 mg to <250 mg	7.5
3	≥ 250 mg	5

Friability test

Twenty tablets were weighed and subjected to drum of friability test apparatus. The drum rotated at a speed of 25 rpm. The friabilator was operated for 4 minutes and reweighed the tablets. % loss (F) was calculated by the following formula.[68]

F =100 (W0-W)/W0

Where W0 = Initial weight, W = Final weight.

Hardness test

The hardness of tablets was measured by using Monsanto hardness tester. The results were complies with IP specification.

Thickness test

The rule of physical dimension of the tablets such as sizes and thickness is necessary for consumer acceptance and maintain tablet uniformity. The dimensional specifications were measured by using screw gauge. The thickness of the tablet is mostly related to the tablet hardness can be used as initial control parameter.[68]

Drug content

The amount of drug in tablet was important for to monitor from tablet to tablet and batch to batch is to evaluate for efficacy of tablets. For this test, take ten tablets from each batch were weighed and powdered. Weighed equivalent to the average weight of the tablet powder and transferred into a 100 ml of volumetric flask and dissolved in a suitable quantity of media. The solution was made up to the mark and mixed well. Then filter the solution. A portion of the filtrate sample was analyzed by UV spectrophotometer.[68]

***In vitro* Buoyancy studies**

The *in vitro* buoyancy was determined by floating lag time and total floating time. The tablets were placed in a 900 ml dissolution beaker containing 0.1N HCL. The time required for the tablet to rise to the surface and float was determined as floating lag time (FLT) and duration of time the tablet constantly floats on the dissolution medium was noted as Total Floating Time respectively (TFT).

***In vitro* drug release studies**

Dissolution parameters

Apparatus -- USP-II, Paddle Method
Dissolution Medium -- 0.1 N HCl
RPM -- 50
Sampling intervals (hrs) -- 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12
Temperature -- 37° C ± 0.5°C

As the preparation was for floating drug release given through oral route of administration, different receptors fluids are used for evaluation the dissolution profile.

Procedure

900 ml of 0.1 HCl was placed in vessel and the USP apparatus –II (Paddle Method) was assembled. The medium was allowed to equilibrate to temp of 37°C ± 0.5°C. Tablet was placed in the vessel and the vessel was covered the apparatus was operated for 12 hours and then the medium 0.1 N HCl was taken and process was continued from 0 to 12 hrs at 50 rpm. At definite time intervals of 5 ml of the receptors fluid was withdrawn, filtered and again 5ml receptor fluid was replaced. Suitable dilutions were done with receptor fluid and analyzed by spectrophotometrically at respective wavelength using UV-spectrophotometer.

Application of Release Rate Kinetics to Dissolution Data

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi and Korsmeyer-Peppas release model.[69]

Zero order release rate kinetics: To study the zero–order release kinetics the release rate data are fitted to the following equation.

$$\mathbf{F = K_o t}$$

Where, 'F' is the drug release at time't', and 'K_o' is the zero order release rate constant. The plot of % drug release versus time is linear.

First order release rate kinetics: The release rate data are fitted to the following equation.

Log (100-F) = kt

A plot of log cumulative percent of drug remaining to be released vs. time is plotted then it gives first order release.

Higuchi release model: To study the Higuchi release kinetics, the release rate data were fitted to the following equation.

F = k t1/2

Where, 'k' is the Higuchi constant. In higuchi model, a plot of % drug release versus square root of time is linear.

Korsmeyer and Peppas release model

The mechanism of drug release was evaluated by plotting the log percentage of drug released versus log time according to Korsmeyer- Peppas equation. The exponent 'n' indicates the mechanism of drug release calculated through the slope of the straight Line.

$$\mathbf{M_t / M_\infty = K t^n}$$

Where, M_t/ M_∞ is fraction of drug released at time 't', k represents a constant and 'n' is the diffusional exponent, which characterizes the type of release mechanism during the dissolution process. For non-Fickian release, the value of n falls between 0.5 and 1.0; while in case of Fickian diffusion, n = 0.5; for zero-order release (case I I transport), n=1; and for supercase II transport, n > 1. In this model, a plot of log (M_t/ M_∞) versus log (time) is linear.

RESULTS AND DISCUSSION

The present study was aimed to developing gastro retentive floating tablets of Quinapril HCl using natural polymers. All the formulations were evaluated for physicochemical properties and *in vitro* drug release studies.

Graph of Quinapril HCl was taken in Simulated Gastric fluid at 242 nm.

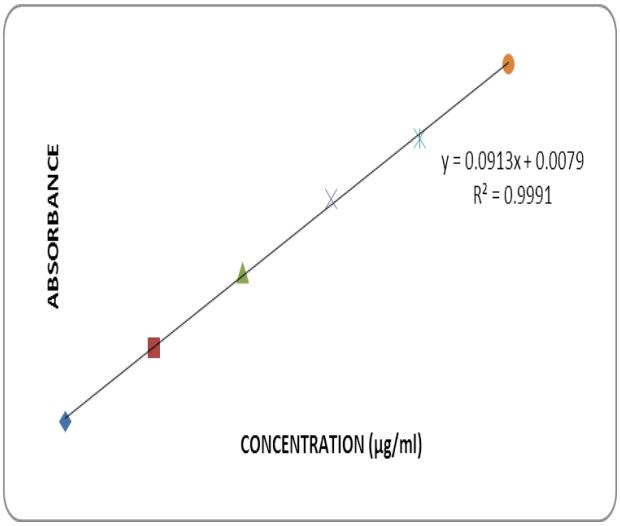

Figure 1: Standard graph of Quinapril HCl in 0.1N HCl.

Table No. 6: Observations for graph of Quinapril HCl in 0.1N HCl (242 nm).

Sl. No	Concentration (µg/ml)	Absorbence at 242nm
1	0	0
2	2	0.189
3	4	0.382
4	6	0.571
5	8	0.726
6	10	0.918

Drug – Excipients compatibility studies

Fourier Transform-Infrared Spectroscopy

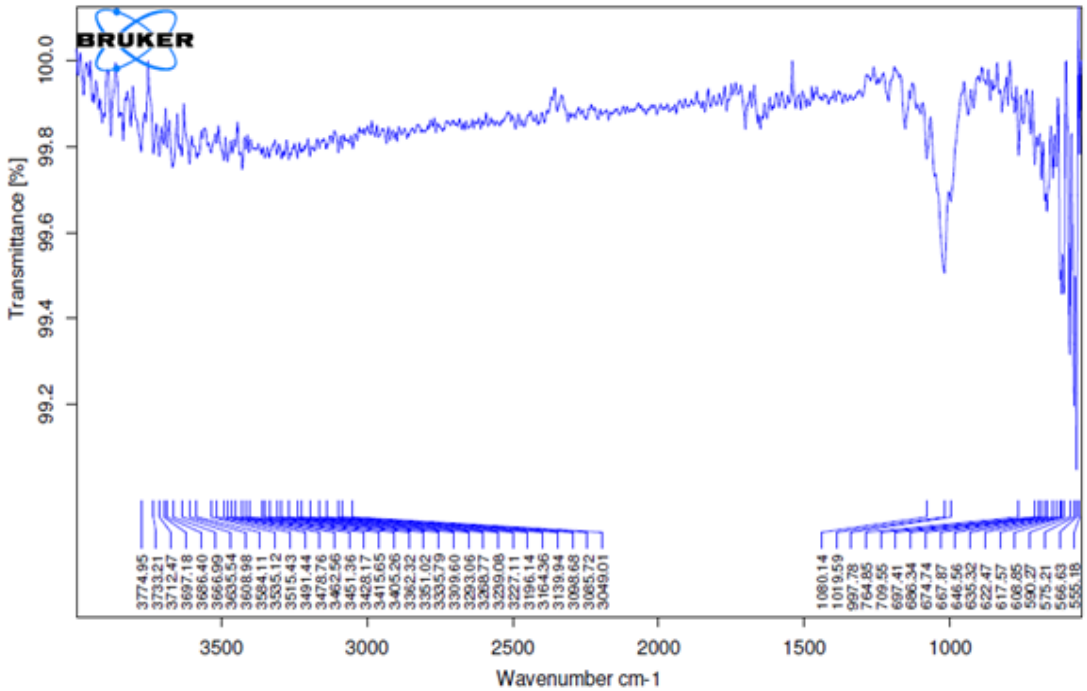

Figure 2: FT-TR Spectrum of Quinapril HCl pure drug.

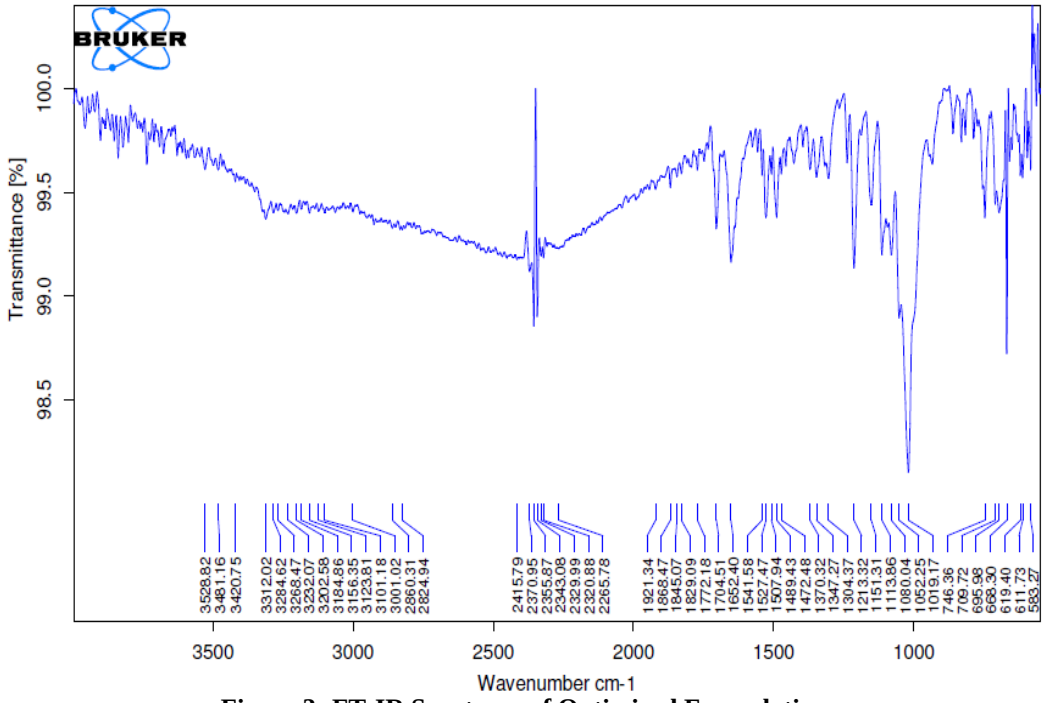

Figure 3: FT-IR Spectrum of Optimized Formulation.

Preformulation parameters of powder blend

Table No. 7: Pre-formulation parameters of blend.

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
F1	24.12 ± 0.86	0.36 ± 0.01	0.43 ± 0.07	16.27±0.09	1.19±0.04
F2	21.63 ± 0.27	0.34 ± 0.01	0.41 ± 0.01	17.07±0.07	1.20±0.08
F3	25.54 ± 0.91	0.32 ± 0.02	0.40 ± 0.06	20.00±0.06	1.25±0.02
F4	22.36 ± 0.54	0.35 ± 0.06	0.42 ± 0.08	16.66±0.06	1.20±0.07
F5	28.63 ± 0.23	0.37 ± 0.04	0.46 ± 0.01	19.56±0.05	1.24±0.03
F6	24.17 ± 0.14	0.36 ± 0.06	0.45 ± 0.02	20.01±0.07	1.25±0.06
F7	23.69 ± 0.39	0.39 ± 0.05	0.48 ± 0.04	18.75±0.04	1.23±0.07
F8	26.18 ± 0.61	0.37 ± 0.03	0.46 ± 0.03	19.56±0.02	1.24±0.03
F9	25.05 ± 0.81	0.31 ± 0.02	0.39 ± 0.01	20.51±0.08	1.25±0.06

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.31 ± 0.02 to 0.39 ± 0.05 (gm/cm3) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.39 ± 0.01 to 0.48 ± 0.04 showing the powder has good flow properties. The compressibility index of all the formulations was found to be ranging from 16.27±0.09 to 20.51±0.08 which show that the powder has good flow properties. All the formulations have shown the hausner's ratio ranging from 1.19±0.04 to 1.25±0.06 indicating the powder has good flow properties.

Optimization of sodium bicarbonate concentration

Three formulations were prepared with varying concentrations of sodium bicarbonate. The formulation containing sodium bicarbonate in 40 mg concentration showed less floating lag time of 1 min and the tablet was in floating condition for more than 12 hours.

Post compression Parameters for tablets

Tablet quality control tests such as weight variation, hardness and friability, thickness and drug release studies in different media were performed on the tablets.

All the parameters such as weight variation, friability, hardness, thickness and drug content were found to be within limits.

Table No. 8: *In vitro* quality control parameters for tablets.

Formulation code	Weight variation(mg)	Hardness (kg/cm^2)	Friability (% loss)	Thickness (mm)	Drug content (%)	Flaoting lag time(min)	Duration of floating time
F1	202.6 ± 0.86	5.6 ± 0.01	0.61 ± 0.05	4.5 ± 0.02	95.14 ± 0.14	0.50 ±0.01	<5 hr
F2	200.3 ± 0.91	5.1 ± 0.02	0.39 ± 0.08	4.5 ± 0.01	97.12 ± 0.16	1.10±0.02	8 hr
F3	199.4 ± 0.63	5.3 ± 0.03	0.51 ± 0.12	4.4 ± 0.03	96.93 ± 0.19	1.40 ±0.05	> 7 hr
F4	202.5 ± 0.48	5.0 ± 0.02	0.48 ± 0.09	4.5 ± 0.02	98.14 ± 0.24	0.30 ±0.04	9 hr
F5	197.8 ± 0.37	5.6 ± 0.01	0.43 ± 0.10	4.4 ± 0.02	97.24 ± 0.23	0.45±0.06	12 hr
F6	200.1 ± 1.01	5.8 ± 0.02	0.71 ± 0.15	4.5 ± 0.01	98.36 ± 0.48	0.56± 0.07	> 12 hr
F7	197.6 ± 0.94	5.8 ± 0.03	0.29 ± 0.09	4.4 ± 0.01	98.28 ± 0.36	0.37±0.06	12 hr
F8	196.3 ± 0.77	5.6 ± 0.01	0.66 ± 0.12	4.4 ± 0.02	98.56 ± 0.21	0.39±0.01	> 12 hr
F9	201.8 ± 1.91	5.7 ± 0.02	0.74 ± 0.13	4.5 ± 0.01	97.21 ± 0.72	0.34±0.07	> 12 hr

Weight variation and thickness

All the formulations were evaluated for uniformity of weight using electronic weighing balance and the results are shown in table 7.3. The average tablet weight of all the formulations was found to be between 196.3 ± 0.77 to202.6 ± 0.86**.** The maximum allowed percentage weight variation for tablets weighing <250 mg is 7.5% and no formulations are not exceeding this limit. Thus all the formulations were found to comply with the standards given in I.P. And thickness of all the formulations was also complying with the standards that were found to be between 4.4 ± 0.01 to 4.5 ± 0.02.

Hardness and friability

All the formulations were evaluated for their hardness, using monsanto hardness tester and the results are shown in table 7.3. The average hardness for all the formulations was found to be from 5.0 ± 0.02 to 5.8 ± 0.03 Kg/cm^2 which were found to be acceptable.

Friability was determined to estimate the ability of the tablets to withstand the abrasion during packing, handling and transporting. All the formulations were evaluated for their percentage friability using rochefriabilator and the results were shown in table 7.3. The average percentage friability for all the formulations was between 0.29 ± 0.09 and0.74 ± 0.13, which was found to be within the limit.

Drug content

All the formulations were evaluated for drug content according to the procedure described in methodology section and the results were shown in table 7.3. The drug content Values for all the formulations were found to be in the range of **(**95.14 ± 0.14 to98.56 ± 0.21**).** According to IP standards the tablets must contain not less than 95% and not more than 105% of the stated amount of the drug. Thus, all the formulations comply with the standards given in IP.

***In vitro* buoyancy studies**

All formulations were examined for buoyancy studies, in that to determine the floating lag time and duration of floating time. The floating lag time of most of the formulations were showed within 1minute only. But duration of floating time was difference, it dependence on the concentration of polymer and type of polymer. Among all the formulation F5 to F9 were showed 12 hours or more than 12 hours.

***In-Vitro* Drug Release Studies**

Table No. 9: Dissolution Data of Quinapril HCl Tablets Prepared With HPMC K 4 M.

Time (hr)	Cumulative Percent Drug Released (n=3 ± sd)		
	f1	f2	f3
0	0	0	0
0.5	14.66	12.34	11.42
1	26.38	20.08	18.67
2	39.61	36.92	32.41
3	51.63	43.76	40.06
4	69.07	58.16	49.77
5	82.63	67.44	58.46
6	96.55	74.28	70.16
7	-	87.09	83.855
8	-	98.57	94.55
9	-	-	94.55
10	-	-	-
11	-	-	-
12	-	-	-

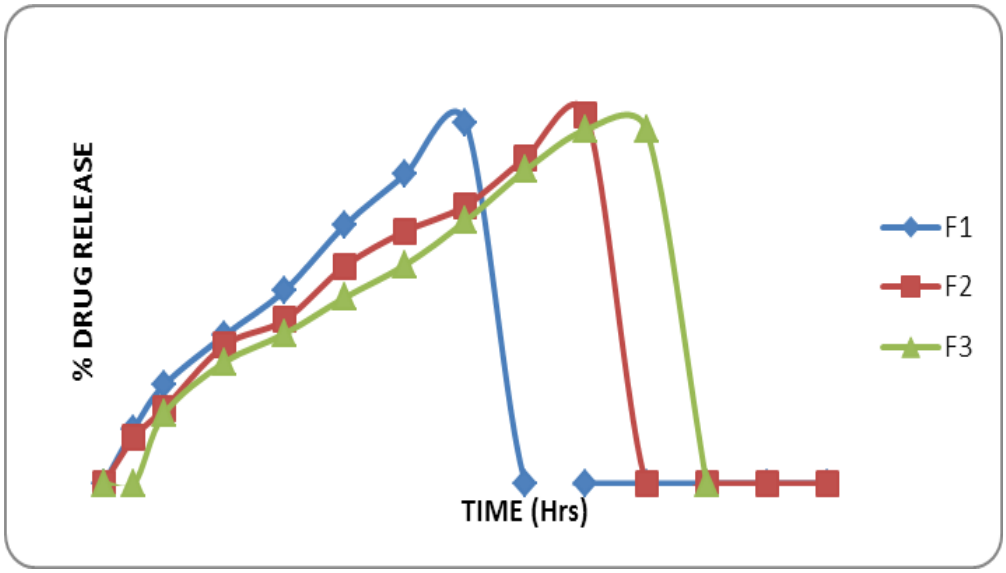

Fig: 3: Dissolution profile of Quinapril HCl floating tablets (F1, F2, F3 formulations).

Table No. 10: Dissolution Data of Quinapril HCl Tablets Prepared With HPMC K 15 M.

Time (hr)	Cumulative Percent Drug Released(n=3±sd)		
	f4	f5	f6
0	0	0	0
0.5	8.45	6.32	3.61
1	13.21	10.24	8.14
2	21.56	16.43	12.87
3	36.57	21.67	20.74
4	49.36	29.18	26.39
5	62.25	38.69	32.98
6	73.96	45.71	39.74
7	84.26	52.33	46.19
8	99.734	60.09	51.38
9	-	70.18	58.16
10	-	79.67	65.73
11	-	84.13	71.58
12	-	96.73	76.32

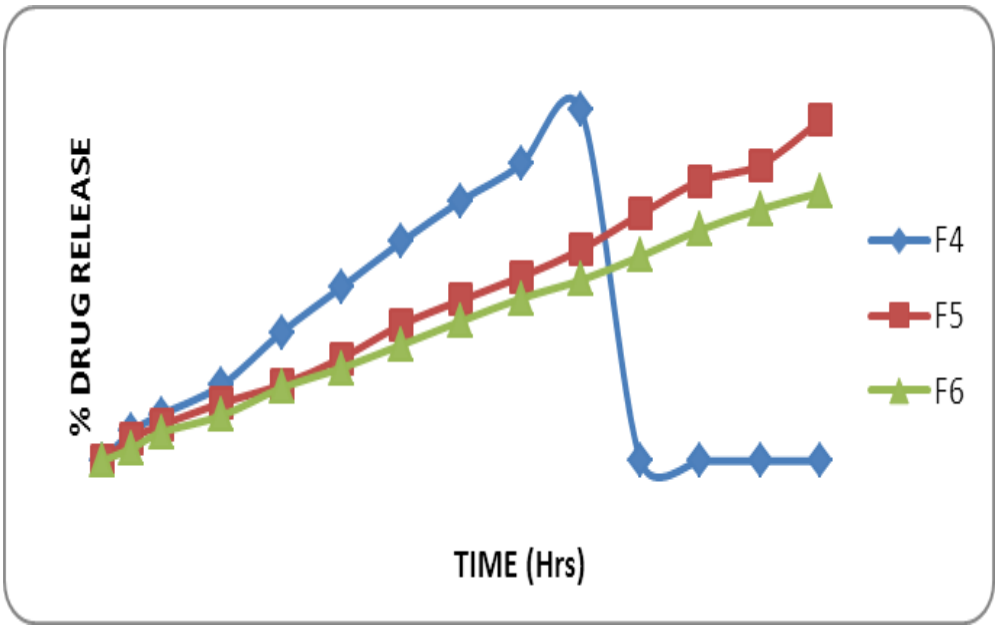

Fig: 4 Dissolution profile of Quinapril HCl floating tablets (F4, F5, F6 formulations).

Table No. 11: Dissolution Data of Quinapril HCl tablets prepared with HPMC K 100 M.

Time (hr)	Cumulative Percent Drug Reieased (n=3±sd)		
	f7	f8	f9
0	0	0	0
0.5	2.85	2.01	1.16
1	8.26	6.59	3.54
2	10.35	11.34	8.63
3	17.58	15.94	13.54
4	21.41	20.18	19.22
5	29.07	26.34	25.31
6	36.73	32.98	30.57
7	40.56	41.36	38.46
8	48.22	50.83	43.12
9	65.59	59.61	48.34
10	71.63	66.14	55.69
11	79.37	74.31	62.17
12	90.14	86.19	69.13

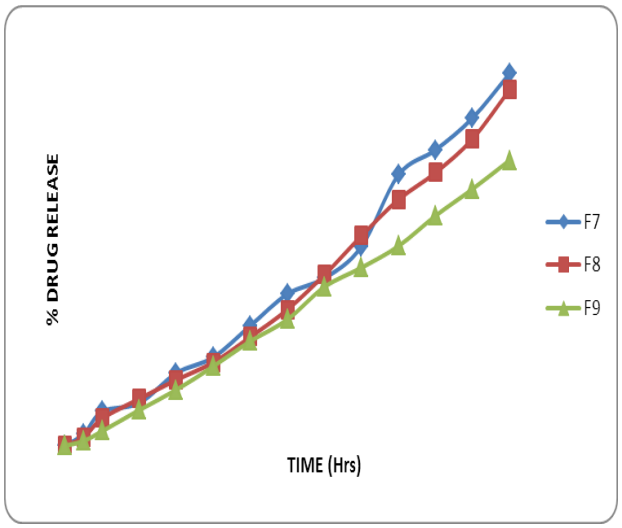

Fig: 5. Dissolution profile of Quinapril HCl floating tablets (F7, F8, F9 formulations).

From the dissolution data it was evident that the formulations prepared with HPMC K 4 M was unable to retard the drug release up to desired time period.

The formulations prepared with HPMC K 15 M also unable to retard the drug release at lower concentration of polymer whenever increase the concentration of HPMC K 15 M in the formulation (F5) it was showed maximum drug release at 12 hours.

The drug release of formulations prepared with HPMC K 100 M at retarded the drug release more than 12 hours.

Among all the formulation, F5 formulation was considered as optimized formulation.

Application of Release Rate Kinetics to Dissolution Data

Ted for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi and Korsmeyer-Peppas release model.

Table No: 12: Release kinetics data for optimised formulation.

Cumulative (%) Reiease (Q)	Time (T)	Root (T)	Log(%) Reiease	Log (T)	Log (%) Remain
0	0	0			2.000
6.32	0.5	0.707	0.801	-0.301	1.972
10.24	1	1.000	1.010	0.000	1.953
16.43	2	1.414	1.216	0.301	1.922
21.67	3	1.732	1.336	0.477	1.894
29.18	4	2.000	1.465	0.602	1.850
38.69	5	2.236	1.588	0.699	1.788
45.71	6	2.449	1.660	0.778	1.735
52.33	7	2.646	1.719	0.845	1.678
60.09	8	2.828	1.779	0.903	1.601
70.18	9	3.000	1.846	0.954	1.475
79.67	10	3.162	1.901	1.000	1.308
84.13	11	3.317	1.925	1.041	1.201
96.73	12	3.464	1.986	1.079	0.515

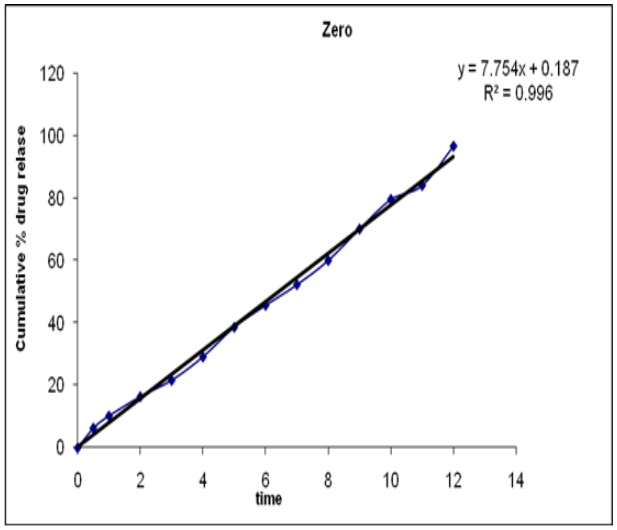

Fig: 6 Zero order release kinetics graph.

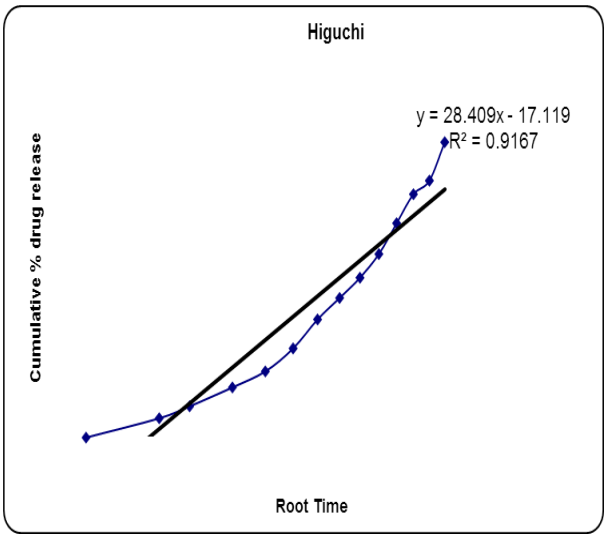

Fig: 7 Higuchi release kinetics graph.

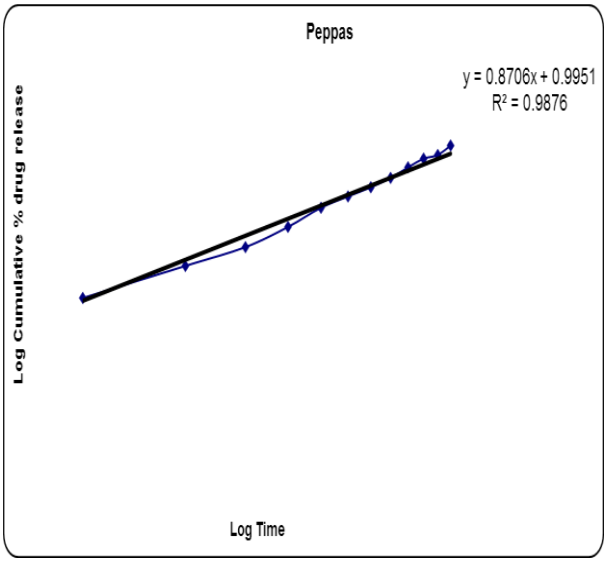

Fig: 8 Kars mayerpeppas graph.

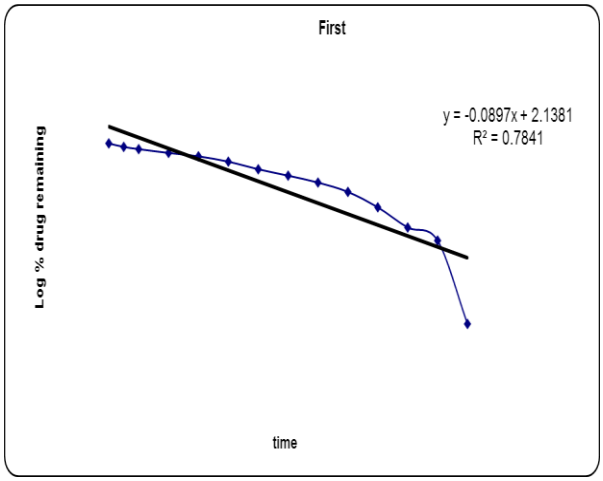

Fig: 9 First order release kinetics graph.

CONCLUSION

Development of Gastro retentive floating drug delivery of Quinapril tablets is to provide the drug action up to 12 hours. Gastro retentive floating tablets were prepared by direct compression method using hydrophilic polymers HPMC K 4 M, HPMC K 15 M and HPMC K 100 M. The formulated gastro retentive floating tablets were evaluated for different parameters such as drug excipients compatibility studies, weight variation, thickness, hardness, content uniformity, *In vitro* Buoyancy studies, *In vitro* drug release. *In vitro* drug release studies performed in 0.1N HCL for 12 hrs and the data was subjected to zero order, first order, Higuchi release kinetics and korsmayerpeppas graph.

The following conclusions could be drawn from the results of various experiments

- FTIR studies concluded that there was no interaction between drug and excipients.
- The physico-chemical properties of all the formulations were shown to be within limits.
- Quality control parameters for tablets such as weight variation, Hardness, Friability, thickness, drug content and floating lag time were found to be within limits. *In-vitro* drug release studies were carried out for all prepared formulation and from that concluded F5 formulation has shown good results.
- Finally Applied release kinetics to optimised formulation (F5) has followed zero order release kinetics.

8. REFERENCES

1. Leon lachman, herbert a. Liberman, the theory and practice of industrial pharmacy: p.293-302.
2. Robinson jr, lee v.h.l, controlled drug delivery: fundamentals and applications, 2nd edn. Marcel dekker, new york, 1978; p.24-36.
3. Brahmankard.m, jaiswals.b, biopharmaceutics and pharmacokinetics a treatise, 1st ed. Vallabhprakashan; new delhi, 1995; 64-70.
4. Cheiny.w, novel drug delivery systems, 2nd ed.: marcel dekker; new york, 1992; 4-56.

5. Ansel, pharmaceutical dosage form and drug delivery system, lipincott, 7th edition: p. 553.
6. Gennaror.a.Remington, the science and practice of pharmacy., 20th ed. New york: lippincottwilliams, 2000; 1045.
7. Banker g.s, rhodes c.t, modern pharmaceutics. 3rd ed. Marcel dekker, new york, 1996; 678-721.
8. Vyass.p, kharr.k, controlled drug delivery: concepts and advances, 1st ed. Vallabhprakashan, new delhi, 2002; 345-376.
9. Shwetaarora, floating drug delivery: a review, aapspharmscitech., 2005; 47(11): 268-272.
10. Libo yang, a new intragastric delivery system for the treatment of h.pylori associated with gastric ulcers, elsevier j. Of controlled release., apr. 1999; 34(5): 215-222.
11. Ross and wilson, anatomy physiology and health education. 9th ed. Churchillivingston, p. 295-311.
12. Wilson k.r.w, waugh a. Anatomy and physiology in health and illness, 9th ed. Churchill livingstone: London, 1996; 342-345.
13. Garimachawla- a means to address regional variability in intestinal drug absorption: pharmtech., 2003; 234-238.
14. Chawla g, gupta p, koradia v, bansal a, gastroretention: a means to address regional variability in intestinal drug absorption, pharm. Tech., 2003; 50-68.
15. Desai s, bolton s. A floating controlled release system: *in-vitro* and *in-vivo* evaluation, *Journal of Pharma Research.*, 1993; 10: 1321-1325.
16. Garg s, sharma s. Gastroretentive drug delivery systems, pharmatech, 2003; 160-164.
17. Dr.jose, khalid shah, gastroretentive drug delivery system, business brief, pharmtech., 2003; 165-173.
18. Deshpande AA, shah NH, rhodes CT, development of a novel controlled release system for gastric retention, *Journal of Pharma Research.*, 1997; 14(6): 815-819.
19. Garimachawla- a means to address regional variability in intestinal drug absorption: pharmtech., 2003; 234-238.
20. David SS. The effect of density on the gastric emptying on single and multiple unit dosage forms. *Journal of Pharma research.*, 1986; 3: 208-213.
21. H.g. Sivakumar, floating drug delivery system for prolonged gastric residence time: a review, ind. J. Pharm. Edu., oct-dec-2004; 311-316.
22. B.n.singh, h.kim, floating drug delivery system an approach to control drug delivery via gastric retention, *Journal of Controlled release.*, 2000; 63(7): 235-259.
23. B.y.choi, h.j.park, preparation of alginate beads for floating drug delivery system: effect of co_2 gas forming agent. *Journal of Contolledrelease.*, 2000; 25(6): 488-491.
24. Ingani HM, timmermans J, moes AJ, concept and *in-vivo* investigation of peroral sustained release floating dosage forms with enhanced gastrointestinal transit, int. *Journal of Pharma*., 1987; (35): 157-164.
25. Bhavana V, khopade AJ, jain WD, shelly and jain NK, targeted oral drug delivery, indiandrugs., 1996; (33): 365-373.
26. Roop K. Khar, controlled drug delivery, gastroretentive system 4th edn. P. 202-203.
27. Hradman JG, limbrid, goodmangilman's, the pharmacological basis of therapeutics, 10th edn, newyork: (2001); p. 1765.
28. Ichikawa M, watanabe S, miyake Y, a new multiple-unit oral floating dosage system: preparation and *in-vitro* evaluation of floating and sustained-release characteristics, *journal of Pharma Science*., 1991; (80): 1062-1066.
29. Abubakr O. Nur and jun S. Zhang, captopril floating and/or bioadhesive tablets: design and release kinetics, taylor & francis: 2000; 26(9): 965 – 969.
30. Menon A, wolfgang AR, saks A. Development and evaluation of a monolithic floating dosage form for furosemide, *Journal of Pharma Science*., 1994; (83): 239-245.
31. Ozdemir N, ordu S, ozkan Y. Studies of floating dosage forms of furosemide: *in-vitro* and *in vivo* evaluations of bilayer tablet formulations, drug. Dev. Ind. Pharm., 2000; 857-866.
32. Xu X, sun M, floating matrix dosage form for phenaporlaminehcl based on gas forming agent, int. *Journal of Pharma.* 2006; 25(4): 324-332.
33. Srivastava AK, wadwa S. Oral sustain delivery of atenolol from floating matrix tablets and *invitro*evaluation, drug. Dev. Ind. Pharm., 2005; 31(45): 367-374.
34. Wie JP, huang, preparation of the 5-fluoro uracil floating sustain release tablets for gastric retention, beijing, da xuexuebao, 2004; 36(4): 493-442.
35. Streubel A, siepmann J, bodmeier R, floating matrix tablets based on low density foam powder: effects of formulation and processing parameters on drug release, eur.*Journal of Pharma Science*., 2003; (18): 37-45.
36. Nur OA, zhang JS, captopril floating and/or bioadhesive tablets: design and release kinetics, drug dev. Ind. Pharm., 2000; 26(9): 965-969.
37. Dao Y, development and pharmacokinetic study of miocamycin sustain release tablet remaining floating in stomach, drug. Dis. Delivery., 1998; 165-75.
38. Dr.shenoy, hand book pharmaceutical chemicals, multitech publication, 2000; 204.
39. Kibbe, americanpharmaceticalassosiation and pharmaceutical society of great britain. Hand book of pharmaceutical excipients, 3rd end. (1986).
40. Mendhan J, denney RC, barnes DJ, thomas M. Vogel's textbook of quantitative chemical analysis, 6th ed. Pearson education ltd: new delhi, 2000; 367-384.
41. Himasankar K, design and biopharmaceutical evaluation of gastric floating drug delivery system of metformin hcl, ind. *Journal of Pharmaeducation*., jan-mar 2006; 40(1): 369-382.
42. M. Sravanthi*, dr. K. Abbulu and aasthasaxena "formulation and evaluation of bilayer floating

tablets of amlodipine besylate and metoprolol succinate", ipp, 2014; 2(1): 328-339.
43. Martindale: thirty first edition, the complete drug reference. P.102.1.
44. Lakshmaiah AS., akki R., & reddy DN, Formulation and evaluation of hydrodynamically balanced floating tablets of antidiabeticagent. *actachim. Pharm. Indica*, 2014; *4*(1): 7-19.
45. Alam, p., mkanwer and ma ghanie. "Development and evaluation of gastroretentive floating tablets of ginger extract: antiulcer activity", 2014; 3(11): 2455-2465.
46. Rao, MS., Madhuri, KSN., & Kumar, GV. Formulation and evaluation of controlled release floating tablets of lamivudine employing HPMC K4M and sodium alginate. *International Journal Pharma Science & Research*. 2014; *4*(1): 396-400.
47. Chavan Bhagyashri and AbhaDoshi. "Formulation and evaluation of floating tablets of losartan potassium.", 2013; 048-059.
48. CH Swarna Kamala, K. Srinivas Reddy Kota, M. Hadassah, E. Hepsibha Metilda and S.Sridevi. "Formulation and evaluation of gastroretentive floating tablets of gabapentin using effervescent technology."*Int J Pharm*. 2012; 3(4): 202-208.
49. Margret Chandira, R., Arafath, A. M. Y., Bhowmik, D., Jayakar, B., & Kumar, K. S. Formulation and Evaluation of Bilayered Floating Tablets of Metformin Hydrochloride, 2012; 1(5): 23-34.
50. Sivabalan, M., Vani, T., Phaneendhar Reddy, V., & Anup Jose, N. G. Formulation and evaluation of gastroretentive Glipizide floating tablets. *International Journal of Comprehensive Pharmacy*. 2011; *2*(1): 1-4.
51. Kumar M. Vinoth, D. Krishnarajan, R. Manivannan, and K G. Parthiban. "Formulation and evaluation of bi-layer domperidone floating tablets." *International journal of Pharmaceutical sciences and Research*, 2011; 2: 2217-2225.
52. Tadros, M. I. Controlled-release effervescent floating matrix tablets of ciprofloxacin hydrochloride: Development, optimization and< i>*in vitro–in vivo*</i> evaluation in healthy human volunteers. *European journal of pharmaceutics and biopharmaceutics*, 2010; *74*(2): 332-339.
53. Bomma, R., Swamy Naidu, R., Yamsani, M., & Veerabrahma, K. Development and evaluation of gastroretentivenorfloxacin floating tablets. *Actapharmaceutica*. 2009; *59*(2): 211-221.
54. Sungthongjeen, S., Sriamornsak, P., & Puttipipatkhachorn, S. Design and evaluation of floating multi-layer coated tablets based on gas formation. *European journal of pharmaceutics and biopharmaceutics*, 2008; *69*(1): 255-263.
55. Jaimini, M., Rana, AC., & Tanwar, YS. Formulation and evaluation of famotidine floating tablets. *Current drug delivery*. 2007; *4*(1): 51-55.
56. Dhumal, RS., Rajmane, ST., Dhumal, ST., & Pawar, AP. Design and evaluation of bilayer floating tablets of cefuroxime axetil for bimodal release. *Journal of scientific and industrial research*. 2006; *65*(10): 812.
57. Patel, VF., Patel, NM., & Yeole, PG. Studies on formulation and evaluation of ranitidine floating tablets. *Indian journal of pharmaceutical sciences*. 2005; *67*(6): 703-709.
58. Streubel, A., Siepmann, J., & Bodmeier, R. Floating matrix tablets based on low density foam powder: effects of formulation and processing parameters on drug release. *European journal of pharmaceutical sciences*, 2003; 1*8*(1): 37-45.
59. Xu, G., & Groves, MJ. (2001). Effect of FITC-dextran molecular weight on its release from floating cetyl alcohol and HPMC tablets. *Journal of pharmacy and pharmacology*, 2001; *53*(1): 49-56.
60. Baumgartner.S., Kristl, J., Vrečer, F., Vodopivec, P., & Zorko, B. (2000). Optimisation of floating matrix tablets and evaluation of their gastric residence time. *International journal of pharmaceutics*. 2000; *195*(1): 125-135.
61. http://en.wikipedia.org.
62. http://www.drugbank.ca.
63. http://www.rxlist.com.
64. Handbook of Pharmaceutical Excipients, sixth edition, edited by Raymond C Rowe, Paul J Sheskey and Marian E Quinn, 622-624.
65. Handbook of Pharmaceutical Excipients, sixth edition, edited by Raymond C Rowe, Paul J Sheskey and Marian E Quinn, 110-114.
66. Handbook of Pharmaceutical Excipients, sixth edition, edited by Raymond C Rowe, Paul J Sheskey and Marian E Quinn, 326-329.
67. Chethan M and Vijay R, Patil, "Formulation and evaluation of sustained release matrix tablets of Metformin hydrochloride", World Journal of Pharmacy and Pharmaceutical Sciences, 2012; 1(2): 717-730.
68. Kamlesh J, Wadhar and Rajendra B, Kakde, "Formulation of Sustained Release Metformin Hydrochloride Matrix Tablets: Influence of Hydrophilic Polymers on the Release Rate and *In Vitro* Evaluation", International Journal of Research in Controlled Release, 2001; 1(1): 9-16.
69. Korsmeyer. RW; Gurny. R; Doelker, EM and Buri. P "Mechanism of solute release from porous hydrophilic polymers", International Journal of Pharmaceutics, 1983; 15: 25-35.
70. Seetha Sunkara, Deekonda Sravanthi, Karna Male Maheswari, Shaik Salma and Buchi N. Nalluri, Development of modified release tablet dosage forms of capecitabine for better therapeutic efficacy, Journal of Chemical and Pharmaceutical Research, 2013; 5(1): 320-328.
71. Pramod Patil, Suresh V Kulkarni, Someshwara Rao B, Anand Ammanage, Chetan Surpur, Formulation And In Vitro Evaluation Of Mucoadhesive Tablets Of Ofloxacin Using Natural Gums, International Journal of Current Pharmaceutical Research, 2011; 3(2): 93-98.