Formulation and Evaluation of Gastroretentive Floating Tablets of Famotidine Using Natural Polymers

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ABSTRACT:
In the present research work gastro retentive floating matrix formulation of Famotidine by using Natural polymers were developed. Initially analytical method development was done for the drug molecule. Absorption maxima was determined based on that calibration curve was developed by using different concentrations. Gas generating agent sodium bicarbonate concentration was optimised. Then the formulation was developed by using different concentrations of polymers Xanthan gum, guar gum and Karaya Gum as polymeric substances. The formulation blend was subjected to various preformualation studies, flow properties and all the formulations were found to be good indicating that the powder blend has good flow properties. Among all the formulations the formulations Karaya Gumas polymer were retarded the drug release more than12 hours. Whereas in low concentrations the polymer was unable to produce the desired action. The formulations prepared with guar gum were also retarded the drug release up to 12 hours (F6=96.32). The optimised formulation dissolution data was subjected to release kinetics, from the release kinetics data it was evident that the formulation followed zero order mechanism of drug release.
KEYWORDS:Floating Tablets Famotidine, Xanthan Gum, Guargum,Karayagum

I. 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] Floating systems or dynamically controlled systems are low density systems that have sufficiently buoyancy to flow over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time.[2] This result is an increased gastric retention time and a better control of the fluctuations in plasma drug concentration. Floating drug delivery systems (FDDS) 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.[3]while the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach.[4]The objective of present investigation was to design and formulate gastric-floating controlled release tablets of famotidine containing polymers, floating assistant agent and effervescent substance based on swelling and floating mechanism. By using single-factor test and orthogonal test, preparation technology was optimized. Furthermore, the drug release kinetic model and its release mechanism were used for fitting. *In vitro* buoyancy study and *in vivo* gamma scintigraphy method were conducted to validate gastric residence characteristic of the optimized formulation.

II. MATERIALS

Famotidine was obtained from Dr. Reddy's Laboratories, HYD. Xanthan Gum, Guar gum and Karayagumwere procured from Vijaya chemicals, Hyderabad, and other chemicals, and the reagents used were of analytical grade.

METHODOLOGY

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 4000cm^{-1} to 550cm^{-1}. [6]

Formulation of tablets:

Table-1: Formulation composition for Floating tablets

Formulation Code	F1	F2	F3	F4	F5	F6	F7	F8	F9
Famotidine	20	20	20	20	20	20	20	20	20

Xanthan Gum	20	40	60	-	-	-	-	-	-
Guar Gum	-	-	-	20	40	60	-	-	-
Karaya Gum	-	-	-	-	-		20	40	60
PVP K30	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
$NaHCO_3$	15	15	15	15	15	15	15	15	15
Citric Acid	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Mg. Stearate	3	3	3	3	3	3	3	3	3
Talc	3	3	3	3	3	3	3	3	3
MCC PH 102	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Total weight	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**

Evaluation of post compression parameters for prepared Tablets

Weight variation test:

To study the 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. The weight variation test would be a satisfactory method of deter mining the drug content uniformity. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in the following table and none deviate by more than twice the percentage.[7] The mean and deviation were determined.The percent deviation was calculated using the following formula.

% Deviation = (Individual weight – Average weight / Average weight) × 100

Hardness:

Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. For each formulation, the hardness of three tablets was determined using Monsanto hardness tester and the average is calculated and presented with deviation.[8]

Thickness:

Tablet thickness is an important characteristic in reproducing appearance. Tablet thickness is an important characteristic in reproducing appearance. Average thickness for core and coated tablets is calculated and presented with deviation.[9]

Friability:

It is measured of mechanical strength of tablets. Roche friabilator was used to determine the friability by following procedure. Preweighed tablets were placed in the friabilator. The tablets were rotated at 25 rpm for 4 minutes (100 rotations).[10]at the end of test, the tablets were re- weighed, and loss in the weight of tablet is the measure of friability and is expressed in percentage as

$$\% \text{ Friability} = [(W1-W2) / W1] \times 100$$

Where, W1 = Initial weight of tablets

W2 = Weight of the tablets after testing

Determination of drug content:

Both compression-coated tablets of were tested for their drug content. Ten tablets were finely powdered quantities of the powder equivalent to one tablet weight of drug were accurately weighed, transferred to a 100 ml volumetric flask containing 50 ml water and were allowed to stand to ensure complete solubility of the drug. The mixture was made up to volume with water. The solution was suitably diluted and the absorption was determined by UV –Visible spectrophotometer. The drug concentration was calculated from the calibration curve.[11]

In vitro Buoyancy studies:

The in vitro buoyancy was determined by floating lag time, and total floating time. (As per the method described *by Rosa et al*) The tablets were placed in a 100ml 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).[12]

In vitro drug release studies

900ml 0f 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 media and analyzedby spectrophotometricallyat272 nm using UV-spectrophotometer. [13]

Application of Release Rate Kinetics to Dissolution Data[14]

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.

Zero order release rate kinetics:

To study the zero–order release kinetics the release rate data ar e fitted to the followingequation.

$$F = K_o t$$

Where, 'F' is the drug release at time't', and 'K_o' is the zero order release rateconstant. 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 plottedthen 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 ofdrug 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.

$$M_t/ M_\infty = K\ t^n$$

Where,M_t/ M_∞ is fraction of drug released at time 't', k represents a constant, and 'n' isthe 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.

III.RESULTS AND DISCUSSION

Drug – Excipient compatability studies
Fourier Transform-Infrared Spectroscopy:

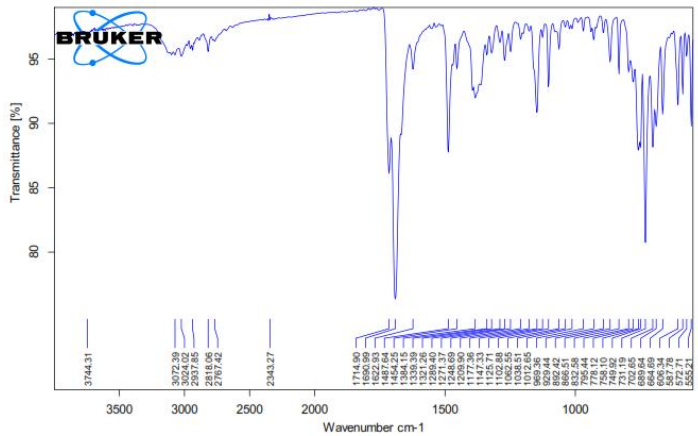

Fig-1: FTIR Spectrum of pure drug

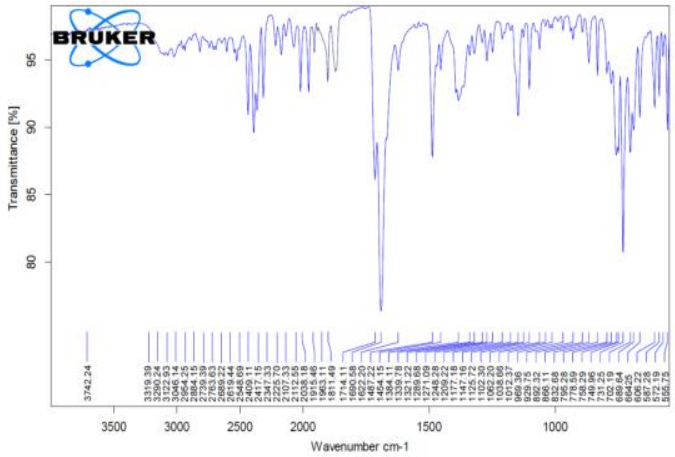

Fig-2: FTIR Spectrum of optimised formulation

There was no disappearance of any characteristics peak in the FTIR spectrum of drug and the polymers used. This shows that there is no chemical interaction between the drug and the polymers used. The presence of peaks at the expected range confirms that the materials taken for the study are genuine and there were no possible interactions.
Famotidine are also present in the physical mixture, which indicates that there is no interaction between drug and the polymers, which confirms the stability of the drug.

Quality Control Parameters For tablets:

Table 2 quality control tests such as weight variation, hardness, and friability, thickness, Drug content and drug release studies were performed for floating tablets.

Table-2: *Invitro* quality control parameters

Formulation codes	Weight variation(mg)	Hardness(kg/cm2)	Friability (%loss)	Thickness (mm)	Drug content (%)	Floating lag time	Total Floating Time(hrs)
F1	148.4	5.1	0.61	3.3	98.42	5.5	4
F2	149.2	5.2	0.58	3.2	99.65	4.2	6
F3	151.3	5.5	0.45	3.4	99.12	5	12
F4	146.3	5.1	0.61	3.3	98.42	5.1	6
F5	148.6	5.3	0.59	3.5	99.65	4	8
F6	152.4	5.5	0.65	3.4	99.12	3.2	12
F7	150.6	5.3	0.62	3.6	98.16	4.5	5
F8	151.2	5.2	0.59	3.4	98.11	3.6	12
F9	147.5	5.4	0.6	3.3	98.25	4.7	12

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

***In Vitro* Drug Release Studies**

Table-3: Dissolution data of Floating Tablets

Time (hr)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	35.32	30.04	24.63	19.17	14.90	10.49	23.56	16.76	10.15
1	54.53	47.56	30.63	24.12	20.45	17.63	46.45	21.89	15.41

2	69.90	54.35	42.52	38.64	32.02	26.55	51.23	28.24	20.98
3	74.96	63.52	50.31	50.20	39.31	32.84	70.54	33.32	25.09
4	86.14	74.75	58.25	69.56	47.82	39.39	79.73	37.75	29.54
5	92.85	82.54	65.78	75.43	53.47	44.71	86.46	42.09	33.36
6		89.26	70.17	83.01	59.74	53.05	98.12	49.16	39.67
7		95.95	75.79	95.57	64.05	60.87		53.36	44.36
8			82.27		79.93	67.02		59.12	50.77
9			89.64		84.26	74.15		63.78	56.42
10			94.87		95.45	79.24		67.79	60.02
11						87.54		76.31	64.46
12						96.32		84.45	69.39

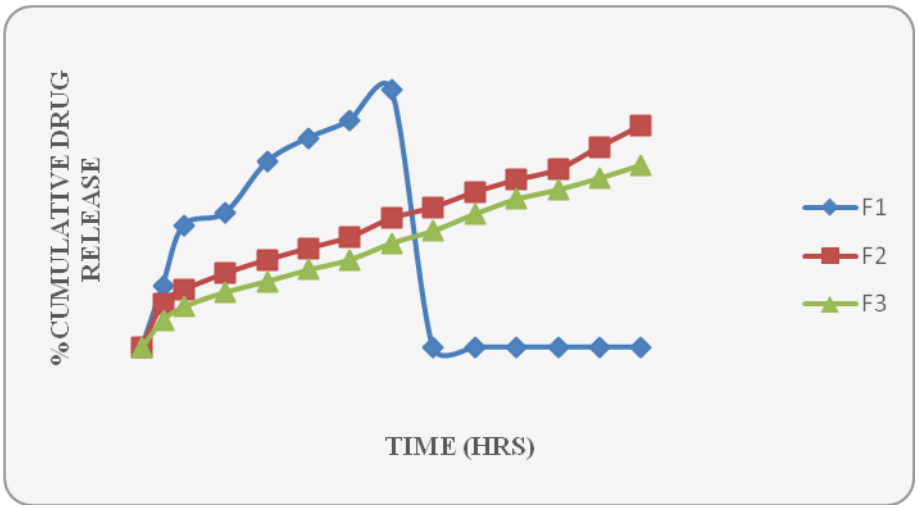

Fig-3: Dissolution Graph of Famotidine Floating tablets containing Xanthan Gum

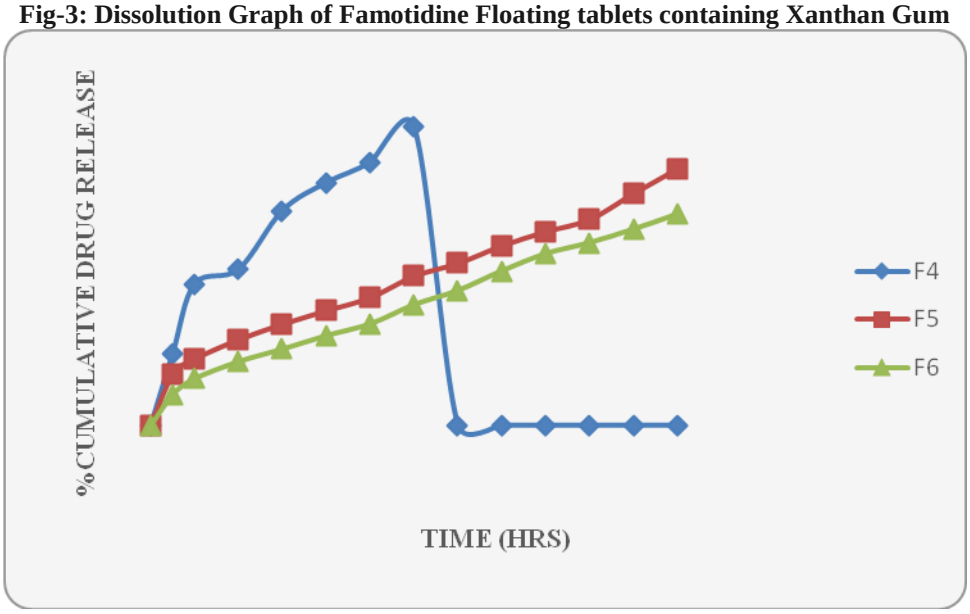

Fig-4: Dissolution Graph of Famotidine Floating tablets containing Guar Gum

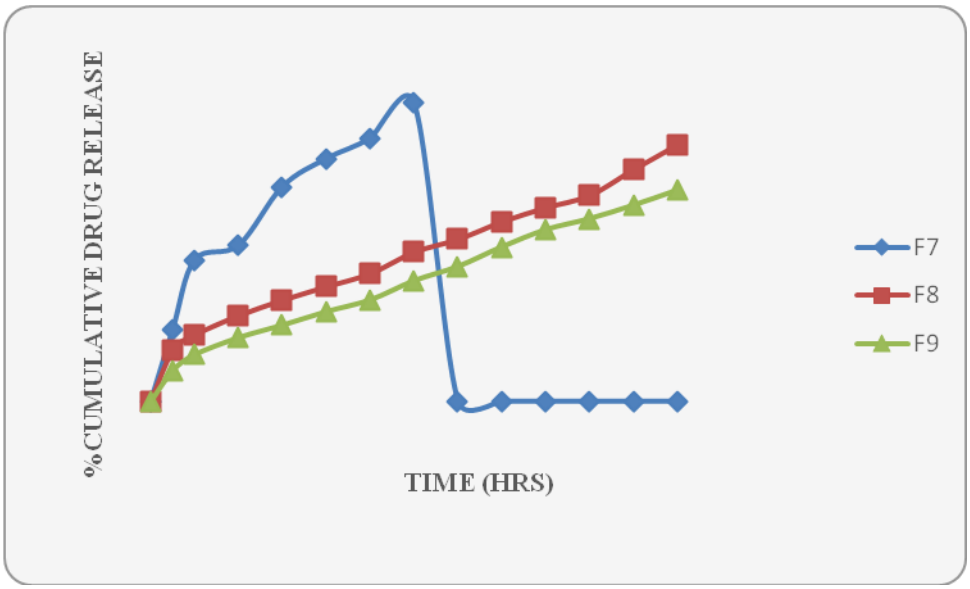

Fig-5: Dissolution graph of Famotidine Floating tablets containing Karaya Gum

From the dissolution data it was evident that the formulations prepared with Karaya Gum as polymer were retarded the drug release more than 12 hours.Whereas the formulations prepared with higher concentration of guar gum retarded the drug release up to 12 hours in the concentration 60 mg. In lower concentrations the polymer was unable to retard the drug release.The formulations prepared with xanthan gum showed very less retardation capacity hence they were not considered.Hence from the above dissolution data it was concluded that F6 formulation was considered as optimised formulation because good drug release (96.32%) in 12 hours.

Application of Release Rate Kinetics to Dissolution Data for optimised formulation:

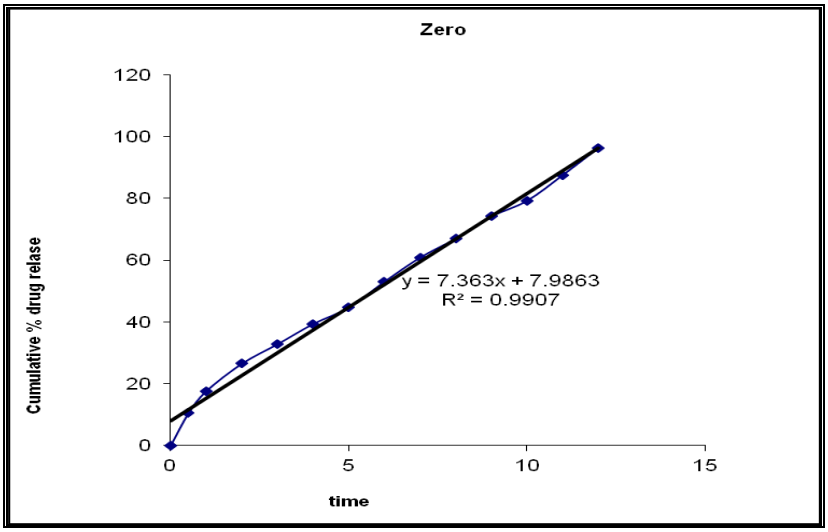

Fig-6: Zero order release kinetics of optimized formulation

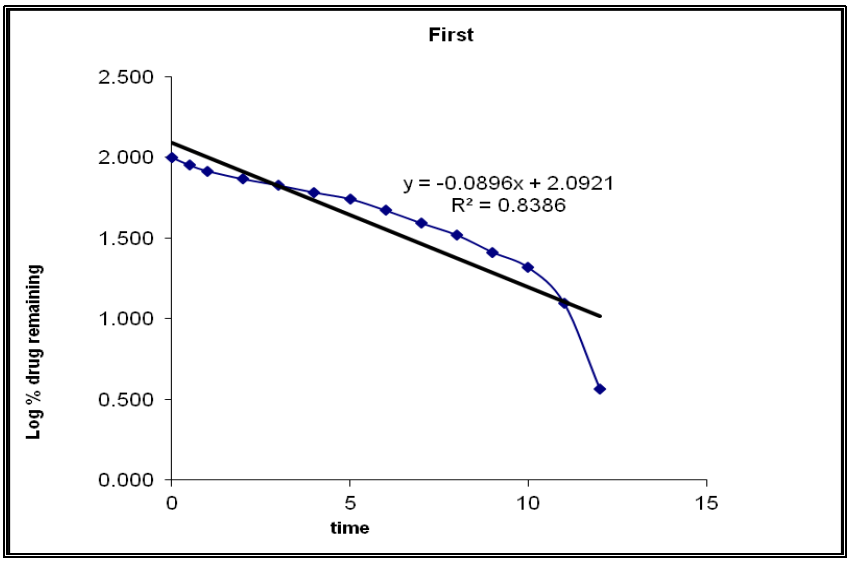

Fig-7: First order release kinetics of optimized formulation

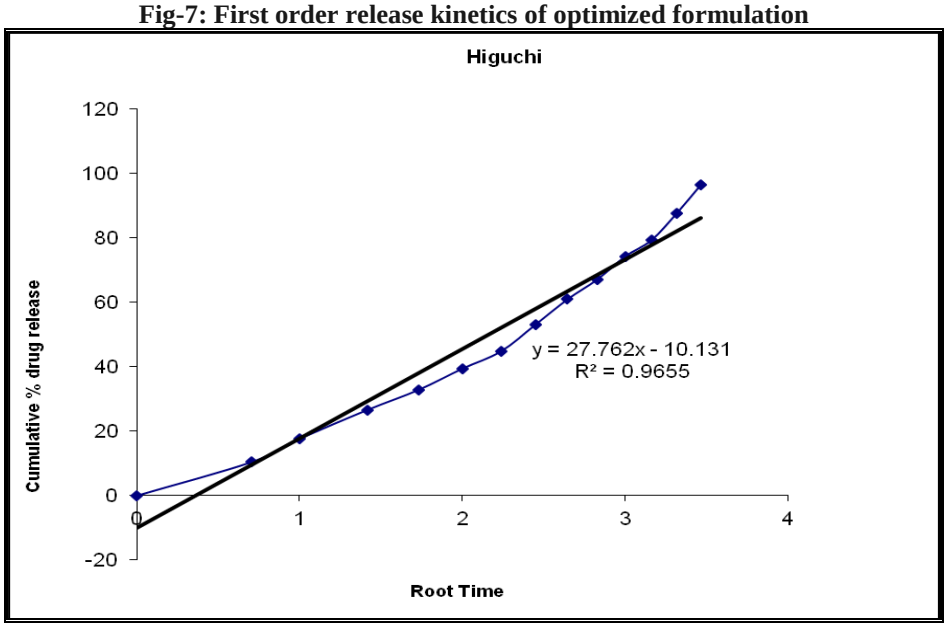

Fig-8: Higuchi release kinetics of optimized formulation

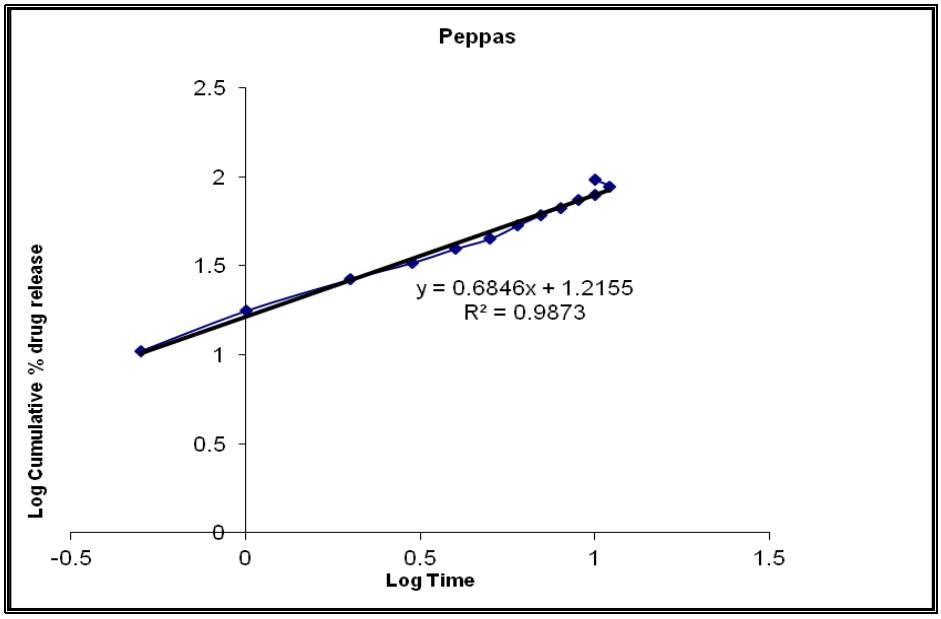

Fig-9: Korsmayer peppas release kinetics of optimized formulation

Optimised formulation F6 was kept for release kinetic studies. From the above graphs it was evident that the formulation F6 was followed Zero order release mechanism.

CONCLUSION

FTIR studies concluded that there was no interaction between drug and excipients.The physico-chemical properties of all the formulations prepared with different polymers Xanthan gum, guar gum and Karaya Gum 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 F6 formulation has shown good results.Finally concluded release kinetics to optimised formulation (F6) has followed Zero order kinetics.Present study concludes that gastro retentive floating system may be a suitable method for Famotidine administration.

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