

**IN VITRO BUOYANCY AND VITRO DISSOLUTION STUDIES OF
FAMOTIDINE FLOATING TABLETS**

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ABSTRACT

Famotidine is a histamine H₂-receptor antagonist. It is widely prescribed in active duodenal ulcers, gastric ulcers, Zollinger-Ellison syndrome, gastroesophageal reflux disease, and erosive esophagitis. The recommended adult oral dosage of famotidine is 20 mg twice daily or 40 mg once daily. The effective treatment of erosive esophagitis requires administration of 20 mg of Famotidine 4 times a day. a conventional dose of 20 mg can inhibit gastric acid secretion up to 5 hours but not up to 10 hours. An alternative dose of 40 mg leads to plasma fluctuations; thus a sustained release dosage form of famotidine is desirable. The short biological half-life of drug (~2.5-4 hours) also favors development of a sustained release formulation. The present work enumerate to study in vitro buoyancy and dissolution studies of famotidine floating system.

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INTRODUCTION

Floating systems are one of the important categories of drug delivery systems with gastric retentive behavior. Drugs that could take advantage of gastric retention include: furosemide, cyclosporine, allopurinol ciprofloxacin and metformin. Drugs whose solubility is less in the higher pH of the small intestine than the stomach (e.g. chlorthalidone and cinnarizine, the drugs prone for degradation in the intestinal pH (e.g. captopril), and the drugs for local action in the stomach (e.g. misoprostol) can be delivered in the form of dosage forms with gastric retention. Antibiotics, catecholamines, sedative, analgesics, anticonvulsants, muscle relaxants, antihypertensive and vitamins can be administered in HBS dosage form

METHODOLOGY

In vitro buoyancy studies

The in vitro buoyancy was determined by floating lag time method described by Dave B.S.⁶⁰The tablets were placed in 250 ml beaker containing 0.1 N HCl. The time required for the tablets to rise to the surface and float was determined as floating lag time. The time between introduction of dosage form and its buoyancy in 0.1 N HCl and the time during which the dosage form remain buoyant were measured. The time taken for dosage form to emerge on surface of medium called Floating Lag Time (FLT) or Buoyancy Lag Time (BLT) and total duration of time by which dosage form remain buoyant is called Total Floating Time (TFT).

In Vitro dissolution studies

The release rate of famotidine from floating tablets was determined using *The United States Pharmacopoeia* (USP) XXIV dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of 0.1 N HCl, at $37 \pm 0.5^\circ\text{C}$ and 75 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus hourly for 8 hours, and the samples were replaced with fresh dissolution medium. The samples diluted to a suitable concentration with 0.1N HCl. Absorbance of these solutions was measured at

266.2 nm using a Shimadzu UV-1601 UV/Vis double beam spectrophotometer. Cumulative percentage of drug release was calculated using the equation obtained from a standard curve.

RESULTS

In vitro Buoyancy Study:-

On immersion in 0.1N HCl solution pH (1.2) at 37°C, the tablets floated, and remained buoyant without disintegration. Table 9 shows the results of Buoyancy study and Fig shows Buoyancy character of prepared tablet. From the results it can be concluded that the batch containing only HPMC polymer showed good Buoyancy lag time (BLT) and Total floating time (TFT). Formulation containing HPMC K4M, HPMC K100M and Xanthan gum showed good BLT of 45 sec, while the formulation containing Xanthan gum(alone) did not float more than 1.5 hrs. This may be due to the nature of polymer and gas generating agent, which were kept constant in the present study. The gas generated cannot be entrapped inside the gelatinous layer, and it escapes leading to variation in BLT and TFT.

In-vitro Dissolution Study and Kinetic modeling of drug release

All the ten formulation of prepared floating tablets of Famotidine were subjected to invitro release studies these studies were carried out using dissolution apparatus, 0.1N HCL (PH 1.2)

The results obtaining in vitro release studies were plotted in different model of data treatment as follows:

1. Cumulative percent drug released vs. time (zero order rate kinetics)
2. Log cumulative percent drug retained vs. time (First Order rate Kinetics)
3. Log cumulative percent drug released vs. square root of time (Higuchi's Classical Diffusion Equation)
4. Log of cumulative % release Vs log time (Peppas Exponential Equation)
5. (Percentage retained)^{1/3} Vs time (Hixson –Crowell Erosion Equation)

The release data obtained for formulations FT1 to FT10 were tabulated in table 9 and fig no.6 shows the plot of cumulative % drug released as a function of time for different formulations. The invitro release of all ten batches of floating tablets showed the release with an initial effect. In the first hour % drug released were 49.19, 40.30, 37.41, 31.44, 46.66, 34.51, 39.47, 26.66, 30.66 and 27.09 For FT1, FT2, FT3, FT4, FT5, FT6, FT7, FT8, FT9 and FT10 respectively. The kinetic values obtained for formulation FT10 were shown in table 11. The values of invitro release were attempted to fit into various mathematical models. Plots of zero order, first order, Higuchi matrix, Peppas and Hixson-Crowell were depicted in fig no 7, 8, 9, 10, and 11 respectively. The regression coefficients values for formulation FT10 of zero order and first order plots were found to be 0.9942 and 0.9850 respectively. Fig shows the graphical representation of cumulative drug released as a function of square root of time. This Higuchi plot was almost linear with regression coefficient values of 0.9880 for formulation FT10. The linearity suggests that the release of Famotidine from Xanthan gum, HPMC K4M, HPMC K100M was diffusion controlled. The 'n' value for FT10 was found to be 0.6725 which indicates that the release. Approximates non-fickian diffusion mechanism.

Hixson- crowell plot of the formulation were shown in fig. The regression coefficient of formulation FT10 was found to be -0.9936. These results indicated that the release rate was limited by the drug particles dissolution rate and erosion of the polymer matrix. The in-vitro drug release profile of tablet from each batch (FT1 to FT10) was carried out and results shown in Table 9. % cumulative drug release V/s time (hr) was plotted and shown in Fig. From the in-vitro dissolution data it was found that formulation FT1, FT2, FT3, FT4, FT5, FT6, FT7 and FT9 released more than 90% of drug before 8 hr of the study indicating that the polymer amount is not sufficient to control the drug release. While FT8 and FT10 containing Xanthan gum & HPMC K100M released more than 90% of drug with in 8 hr. It concludes F10 had better controlled release than the other formulation. Thus, it may be concluded that the drug release from gastro retentive famotidine tablet is best explained by Zero-order Kinetic model. The values of slope and intercept for Zero-order Kinetic model are 10.120 and 17.177 respectively.

Table → Standard calibration curve of famotidine

Concentration($\mu\text{g/ml}$)	Absorbance
0	0.000
1	0.0251
2	0.0552
3	0.0797
4	0.1031
5	0.1379
6	0.1661
7	0.1921
8	0.2123
9	0.2424
10	0.2681
Slope value(b) =	0.0270
R² Value =	0.999

Table → Composition of Famotidine Floating Tablets										
INGREDIENTS	FT1	FT2	FT3	FT4	FT5	FT6	FT7	FT8	FT9	FT10
Famotidine	40	40	40	40	40	40	40	40	40	40
HPMC K4M	40	-	-	-	80	-	40	-	40	20
HPMC K100M	-	40	-	80	-	-	40	40	-	40
Xanthan gum	-	-	40	-	-	80	-	40	40	20
Sodium bicarbonate	20	20	20	20	20	20	20	20	20	20
Citric acid (anhydrous)	10	10	10	10	10	10	10	10	10	10
PVP-K-30	20	20	20	20	20	20	20	20	20	20
Avicel PH-102	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Magnesium Stearate	1	1	1	1	1	1	1	1	1	1
Talc	2	2	2	2	2	2	2	2	2	2

All quantities were in milligrams.

All the batches contained 1% w/w talc and 0.5% w/w magnesium stearate

Table → Effect of hardness on Buoyancy Lag Time of formulation FT10

Hardness in kg/cm²	Buoyancy Lag Time (sec)
4	47
5	58
6	76
7	89
8	186

Table → Kinetic values obtained from invitro released data of formulation FT10

Kinetic Model	Intercept	Slope	R²
Zero-order plot	17.177	10.120	0.9942
First-order plot	4.7579	-0.4795	0.9850
Higuchi plot	-3.6818	37.99	0.9880
Hixson Crowell	4.7579	-0.4795	-0.9936
Peppas-korsmeyer	1.4767	0.6214	0.9555

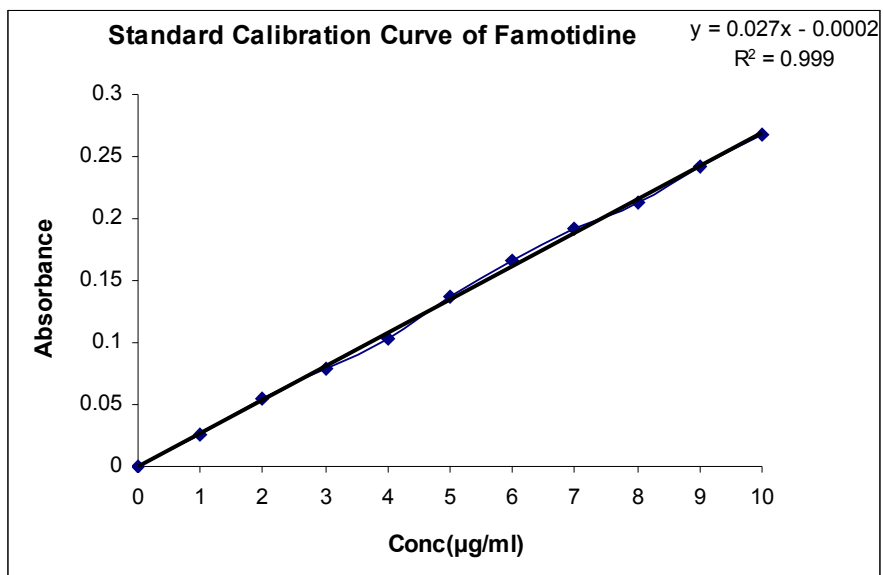


FIG NO: STANDARD CALIBRATION CURVE OF FAMOTIDINE

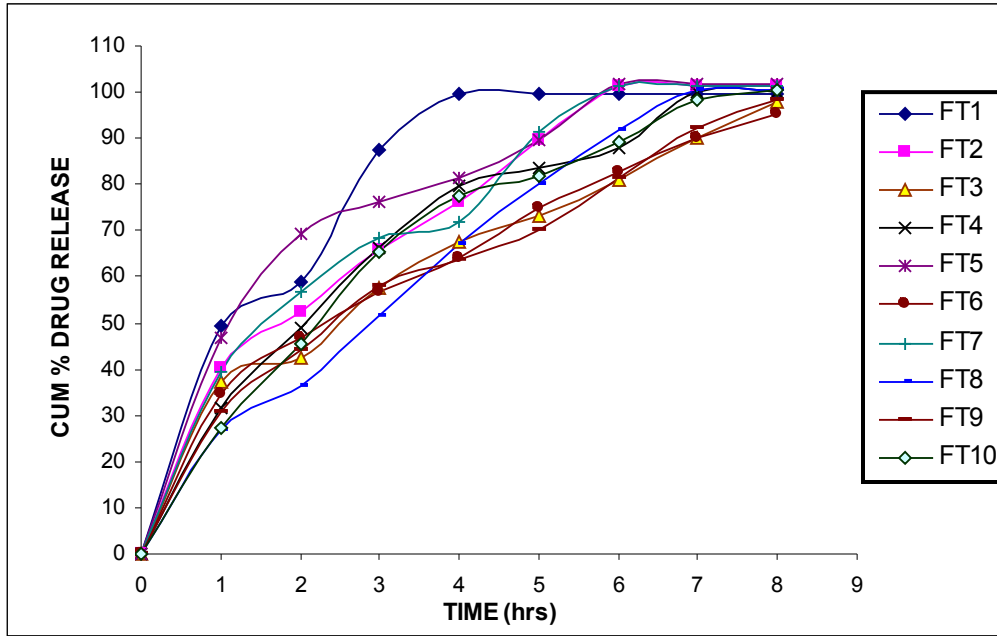


FIG NO : IN VITRO DISSOLUTION PROFILE FOR TABLETS OF BATCHES FT1 TO FT10 (USING DISSOLUTION APPARATUS)

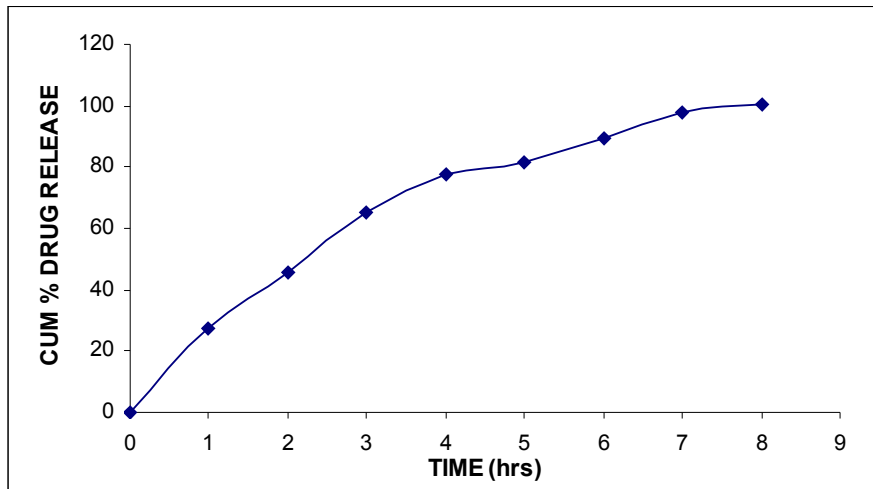


FIG NO: INVITRO CUMULATIVE % DRUG RELEASD V/S TIME FOR FORMULATION (FT10) OF FAMOTIDINE [ZERO ORDER RATE]

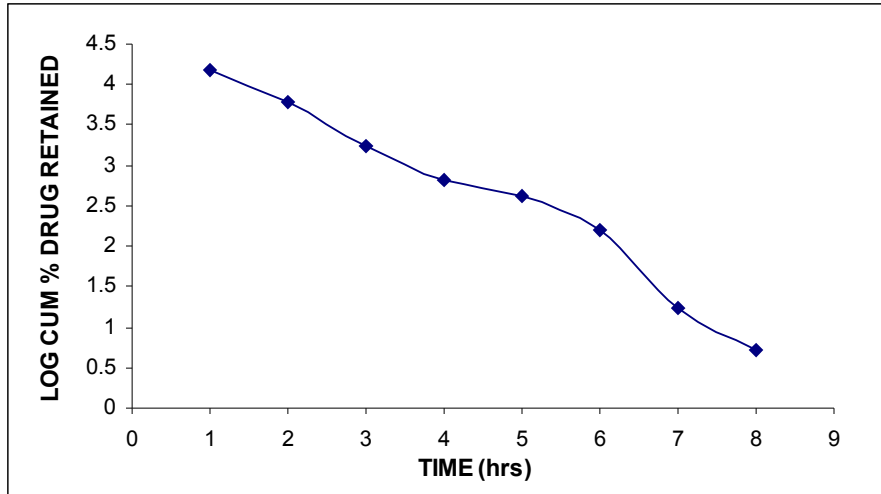


FIG NO: LOG CUMULATIVE % DRUG RETAINED V/S TIME FOR FORMULATION (FT10) OF FAMOTIDINE [FIRST ORDER PLOT]

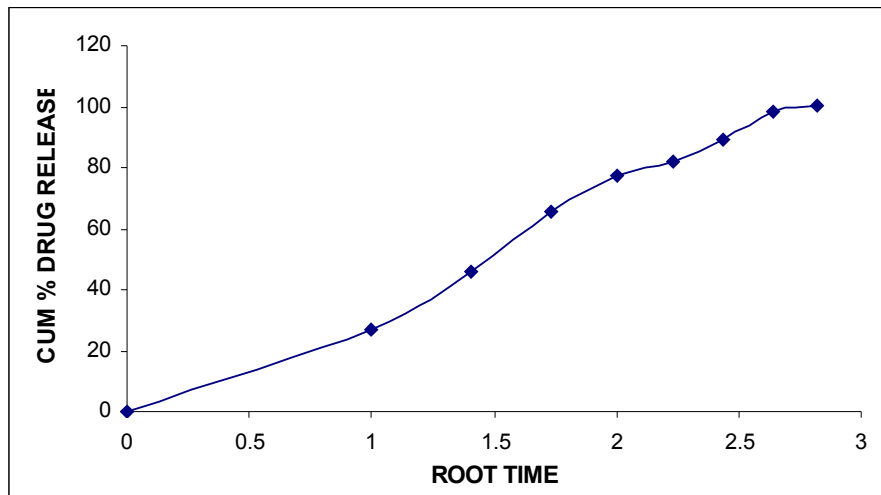


FIG NO: CUMULATIVE % DRUG RELEASED V/S ROOT TIME FOR FORMULATION (FT10) OF FAMOTIDINE [HIGUCHI MATRIX]

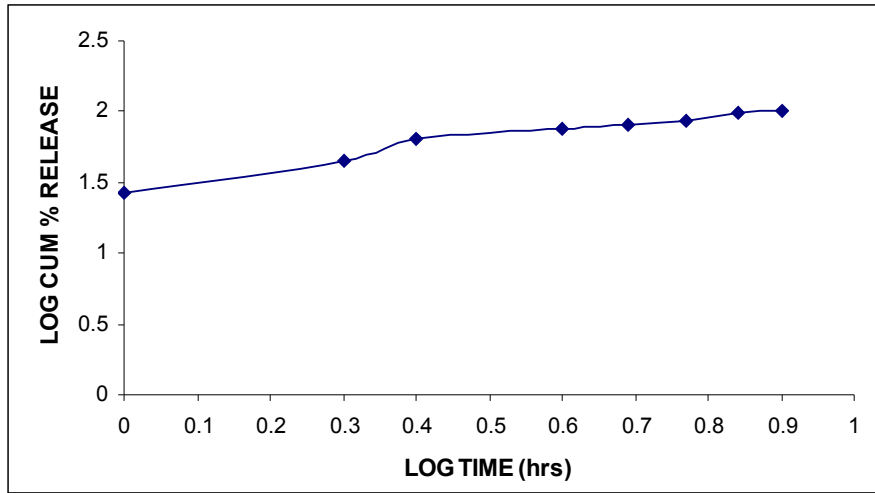
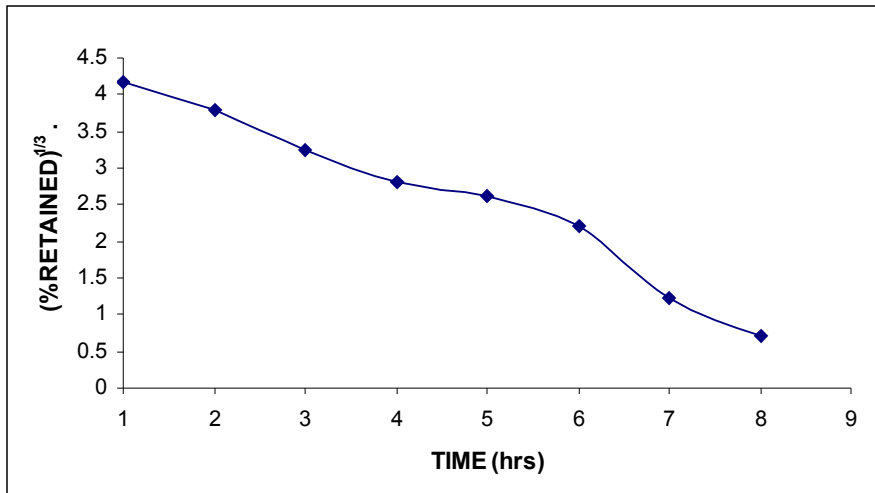


FIG NO: LOG CUMULATIVE % DRUG RELEASED V/S LOG TIME FOR FORMULATION (FT10) OF FAMOTIDINE [PEPPAS]

**FIG NO:
CUBE
ROOT
OF %
DRUG**



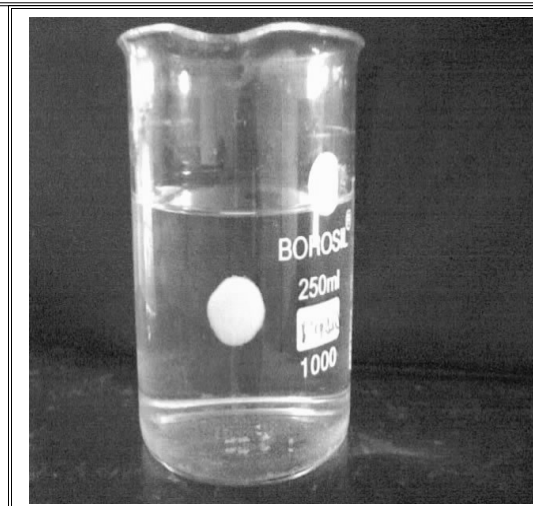
RETAINED V/S TIME FOR FORMULATION (FT10) OF FAMOTIDINE [HIXSON-CROWELL]

FIG NO: INVITRO BUOYANCY STUDY OF FORMULATION FT10

INVITRO BUOYANCY STUDY OF FORMULATION FT10



At initial time



After 25 Seconds



After 45 Seconds



After 8 Hours

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