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Research Article

FORMULATION AND EVALUATION OF FLOATING TABLETS OF CIMETIDINE EMPLOYING ALBIZIA GUM

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ABSTRACT

Cimetidine is histamine H2-receptor antagonist which is used to reduce the treatment of stomach ulcers. The drug has less bioavailability (60%) and lesser half life of 2 hours. The present work is concerned with the formulation and evaluation of floating tablets of Cimetidine using albizia gum in different proportions to enhance its bioavailability and prolonged residence time in stomach. Precompression parameters such as bulk density, tapped density, angle of repose, Hausner's ratio were performed to all the formulations and were found to be in the acceptable limits which ensures the good flow properties. Post compression parameters such as weight variation, hardness, drug content, buoyancy studies and dissolution were performed to all the prepared formulations. The drug release kinetics revealed that the optimized formulation FCDA4 follows zero order kinetics and the mechanism was nonfickian.

INTRODUCTION

Among the various approaches, preparation of drug-embedded floating tablets is one of the major approaches for obtaining the controlled release systems. In the present study Albizia gum was evaluated as rate controlling material for controlled release[1-7]. Floating tablets of Cimetidine was formulated employing Albizia gum in different proportions of drug and polymers and the tablets were evaluated for drug release kinetics and mechanism.

MATERIALS AND METHODS

Cimetidine was obtained as gift sample from Dr. Reddy's lab, India Albizia gum obtained from Girijan stores,Vishakapatnam, Sodium bicarbonate, Lactose, Di Calcium Phosphate, Magnesium Stearate were obtained from Signet chemicals, Mumbai, India. All other materials used were of Pharmacopoeial grade.

Development of calibration curve of Cimetidine

Standard solution

Accurately weighed 50 mg of Cimetidine was dissolved in 50 ml of pH 1.2 hydrochloric acid buffer to get a solution containing 1000 µg/ml of drug.

Scanning

From the standard solution, a solution was prepared to give a concentration of 10 µg/ml in pH 1.2 hydrochloric acid buffer and UV scan was taken between the wavelengths of 200-400 nm. The spectrum was reported in the figure 1. The absorption maxima of 274 nm was selected and utilized for further studies.

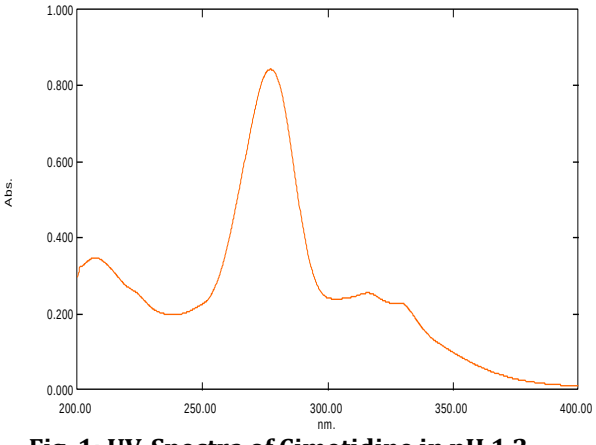


Fig. 1: UV-Spectra of Cimetidine in pH 1.2 hydrochloric acid buffer

Standard Plot

From the standard solution, a stock solution was prepared to give a concentration of 10 µg/ml in pH 1.2 Hydrochloric acid buffers. Concentrations of 1, 2, 3, 4 and 5 µg/ml of Cimetidine was prepared and the absorbance of prepared solutions of Cimetidine in pH 1.2 hydrochloric acid buffer were measured at 274 nm spectrophotometrically against pH 1.2 Hydrochloric acid buffer as blank. Standard plot data of Cimetidine in pH 1.2 Hydrochloric acid buffer is reported in table 1 and graph in figure 2.

Table 1: Standard plot data for cimetidine in pH 1.2 hydrochloric acid buffer

Concentration (µg/ml)	Absorbance at 274 nm (Mean ± S.D*)
1	0.247 ± 0.21
2	0.477 ± 0.36
3	0.682 ± 0.20
4	0.844± 0. 30
5	0.995 ± 0.35

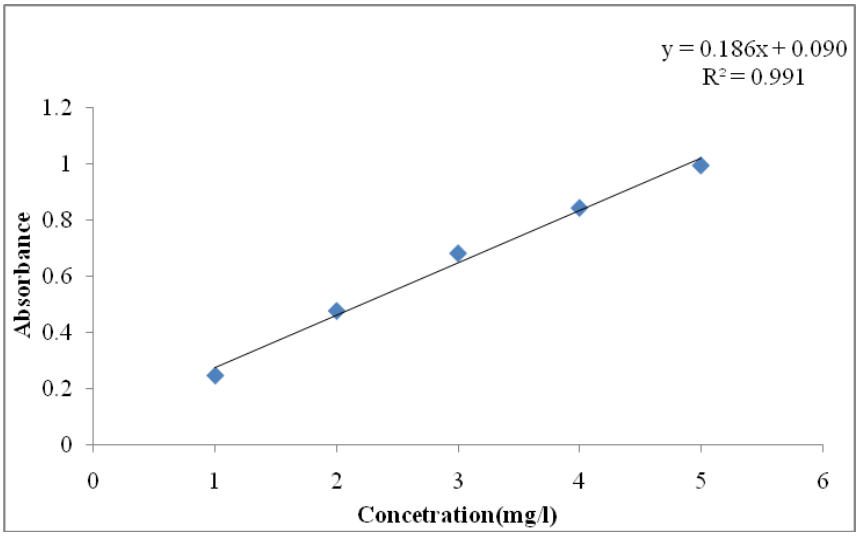


Fig. 2: Standard plot of Cimetidine

Table 2: Preformulation studies for the raw materials

Contents	Bulk density[a] (gm/ml)	Tapped density[a] (gm/ml)	Compressibility index (%)	Hausner's ratio	Angle of repose[a] (θ)
Cimetidine	0.426	0.524	17.84	1.23	27.46
Lactose	0.74	0.888	13.22	1.14	16.32
Albizia gum	0.632	0.702	15.31	1.11	28.45
Magnesium stearate	0.456	0.651	15.23	1.17	26.21
Dicalcium phosphate	0.435	0.458	14.55	1.05	26.56

a= (n=3)

Fourier transform infrared spectroscopy (FT-IR)

CD and optimized Floating tablet formulation FCDA4 were subjected to FT-IR spectroscopic analysis, to ascertain whether there is any interaction between the drug and other excipients used. The obtained spectra are given in figure 3. Characteristic peaks of CD were compared with the peaks obtained for its Floating tablet formulation FCDA4. The data for the same is given in table 3.

Table 3: FT-IR spectral data of Cimetidine and Floating tablet formulation

Functional groups	Frequency of pure drug (cm-1)	Frequency of formulation FCDA4 (cm-1)
CN Stretching	2204	2253
C-S	690	693
N-H Stretching (2⁰ Amine)	3350	3408
N-H Stretching	3200	3250
C=N Stretching	1580	1550
C=C Stretching	1450	1438

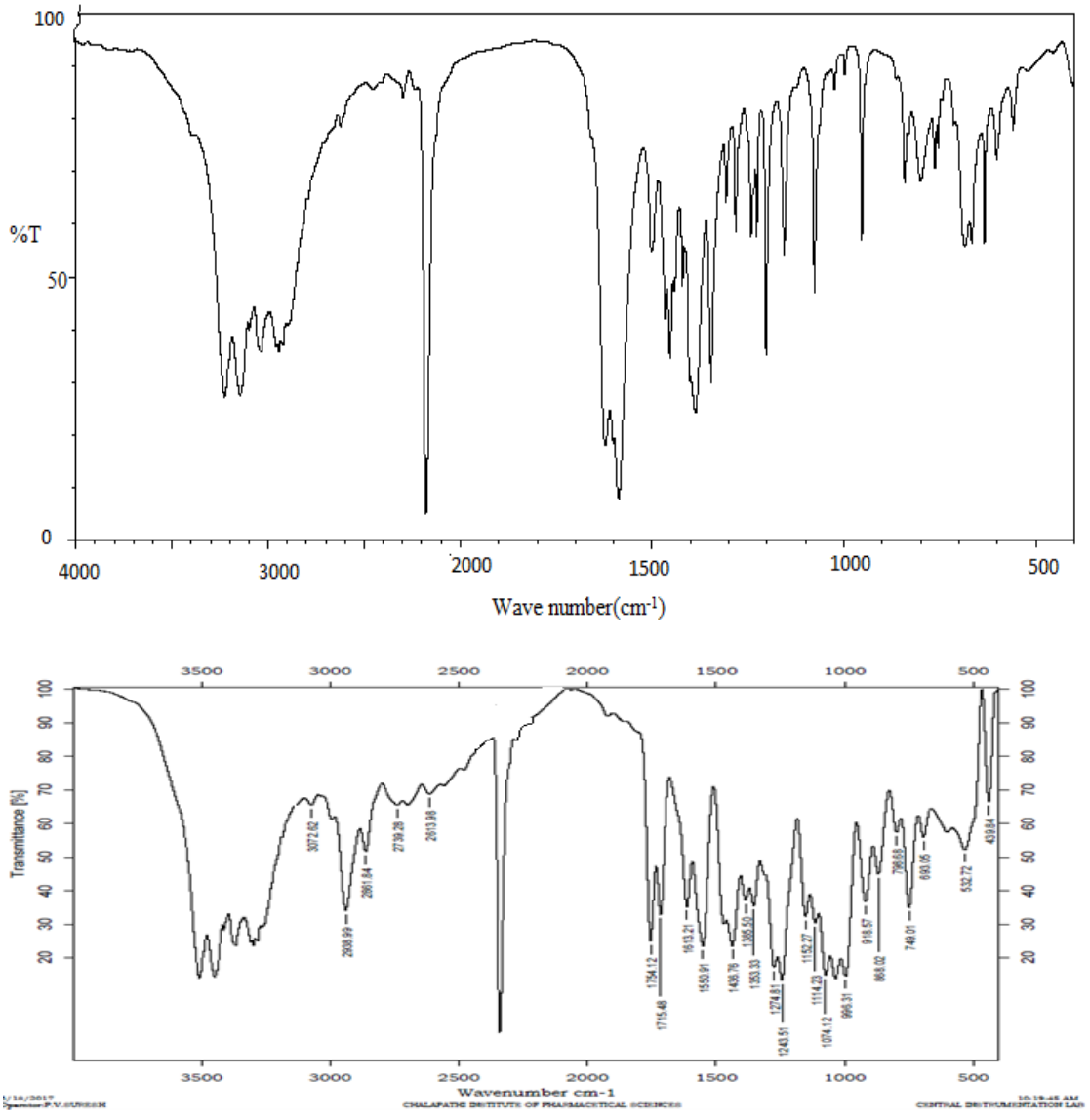


Fig. 3: FTIR of pure drug and optimized formulation (FCDA4)

Differential scanning calorimetry (DSC) DSC studies were carried out for Cimetidine and formulation FCDA4 and the thermograms obtained are presented in figure 4. Thermogram of pure drug showed a sharp endothermic peak at 141°C, which corresponds to its melting point. Floating tablet formulation FCDA4 also showed endothermic peak at 141°C, which corresponds to the melting point of the drug. The evaluation of thermograms revealed no interaction between the drug and the excipients. From the thermograms, it was evident that the melting point of Cimetidine has not changed after it was formulated as a floating tablet.

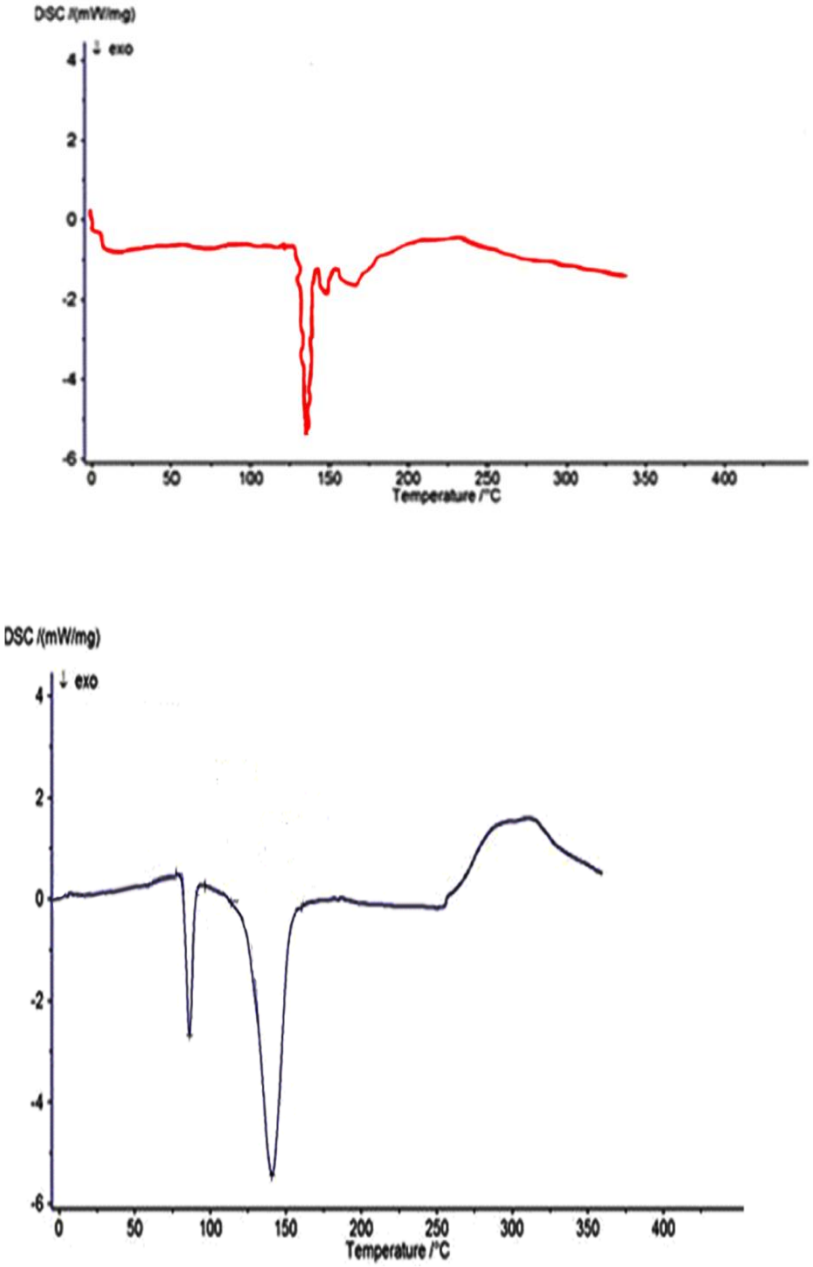


Fig. 4: DSC thermogram of pure drug and optimized formulation (FCDA4)

Method of Preparation

The formulations prepared are shown in tables together with their compositions. The drug, polymer/s, and diluent were screened through # 40 and preblended using a lab scale double cone blender. The lubricant was added and the blend was mixed again prior to compression. The tablet blends were directly compressed by using rimek tablet compression machine. To avoid processing variables all batches of tablets were compressed under identical conditions. All the tablets prepared were further evaluated for physical parameters such as weight uniformity, hardness, friability and uniformity of drug content

Table 4: Composition of Cimetidine (200mg) Floating Tablets Formulated Using Albizia gum

Ingredients [mg/tablet]	FORMULATIONS					
	FCDA1	FCDA2	FCDA3	FCDA4	FCDA5	FCDA6
Cimetidine	200	200	200	200	200	200
Albizia gum	50	75	100	50	75	100
DCP	75	50	25	----	---	---
Lactose	----	---	---	75	50	25
Sodium bicarbonate	30	30	30	30	30	30
Magnesium stearate	2.5	2.5	2.5	2.5	2.5	2.5
Talc	2.5	2.5	2.5	2.5	2.5	2.5
Total wt of tablet (mg)	360	360	360	360	360	360

Table 5: Pre compression parameters of the prepared formulations

Formulation	Bulk density[a] (gm/ml)	Tapped density[a] (gm/ml)	Compressibility index (%)	Hausner's ratio	Angle of repose[a] (θ)
FCDA1	0.54	0.62	11.33	1.10	23.20
FCDA2	0.58	0.67	10.88	1.12	22.12
FCDA3	0.50	0.61	12.25	1.14	27.15
FCDA4	0.47	0.51	11.22	1.05	24.22
FCDA5	0.48	0.54	13.25	1.12	21.36
FCDA6	0.44	0.52	12.44	1.13	21.32

Table 6: Weight Variation, Hardness, Friability, Thickness and Drug Content of Cimetidine Floating Tablets

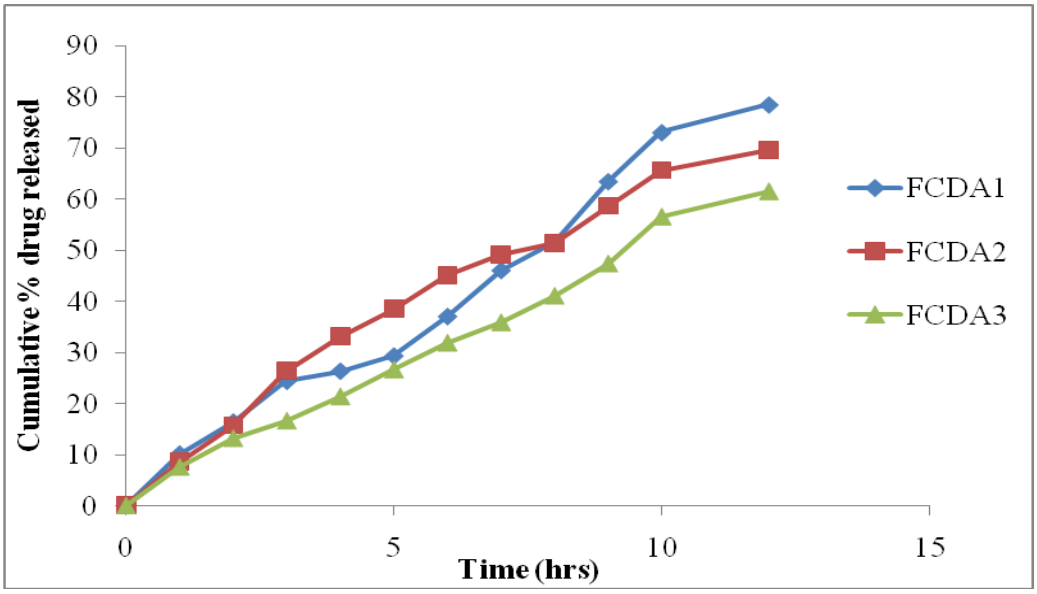
Formulation Code	Weight Variation	Friability (%)	Hardness (Kg/Cm^2)	Thickness (mm)	Cimetidine (%)
FCDA1	360.0± 1.42	0.32 ± 0.02	4.50 ± 0.14	3.5-3.6	97.85 ± 0.09
FCDA2	359.0± 0.68	0.48± 0.36	5.2 ± 0.30	3.4-3.5	96.53 ± 0.07
FCDA3	360.0± 1.02	0.22 ± 0.29	4.9. ± 0.19	3.4-3.6	96.12 ± 0.15
FCDA4	358.0± 1.18	0.47 ± 0.61	5.00 ± 0.33	3.5-3.6	97.02 ± 0.06
FCDA5	359.0± 0.79	0.39 ± 0.22	4.50 ± 0.21	3.4-3.5	97.53 ± 0.12
FCDA6	361.0± 0.63	0.49 ± 0.27	5.10 ± 0.15	3.5-3.6	96.98 ± 0.11

Table 7: Floating characteristics of Cimetidine tablets using Albizia gum

Formulation Code	Floating lag time (Sec)	Duration of floating (hrs)	Swelling Index at end of 12hr
FCDA1	140	12	67.2±0.46
FCDA2	129	12	70.21±0.14
FCDA3	127	12	72.22±0.46
FCDA4	122	12	73.2±0.33
FCDA5	118	12	75.0±0.19
FCDA6	116	12	79.23±0.22

Table 8: Drug Release Profiles of Cimetidine Floating Tablets Prepared Employing Albizia Gum Using DCP and Lactose as Diluent

Time (hrs)	Cumulative % drug released					
	FCDA1	FCDA2	FCDA3	FCDA4	FCDA5	FCDA6
	DCP			Lactose		
1	10.11±0.41	8.62±0.17	7.56±0.23	10.47±0.61	12.47±0.51	14.62±0.22
2	16.39±0.61	15.67±0.31	13.21±0.11	18.45±0.11	16.50±0.47	20.79±0.77
3	24.36±0.87	26.32±0.71	16.63±0.23	37.14±0.18	25.26±0.33	25.33±0.74
4	26.34±0.32	33.12±0.49	21.40±0.28	51.40±0.17	32.10±0.11	27.27±0.18
5	29.33±0.18	38.47±0.41	26.66±0.35	65.23±.0.25	39.26±0.23	30.33±0.81
6	37.06±0.63	45.11±0.26	31.91±0.35	70.19±0.19	45.13±0.58	38.60±0.36
7	46.10±0.33	49.13±0.96	35.91±0.43	78.26±0.54	49.31±0.69	47.01±0.63
8	51.58±0.46	51.41±0.48	41.12±0.15	82.66±0.19	52.14±0.84	52.85±0.34
9	63.51±0.45	58.68±0.76	47.43±0.43	88.19±0.37	63.86±0.67	64.52±0.55
10	73.13±0.24	65.64±0.57	56.63±0.47	93.15±0.85	79.46±0.75	77.31±0.42
12	78.57±0.63	69.63±0.56	61.61±0.37	99.31±0.64	90.36±0.65	83.58±0.36



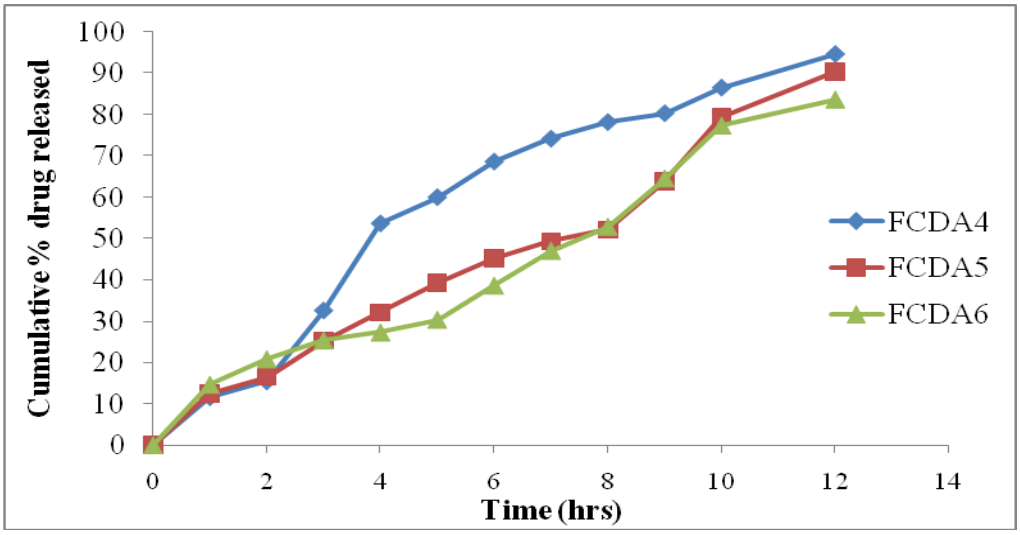
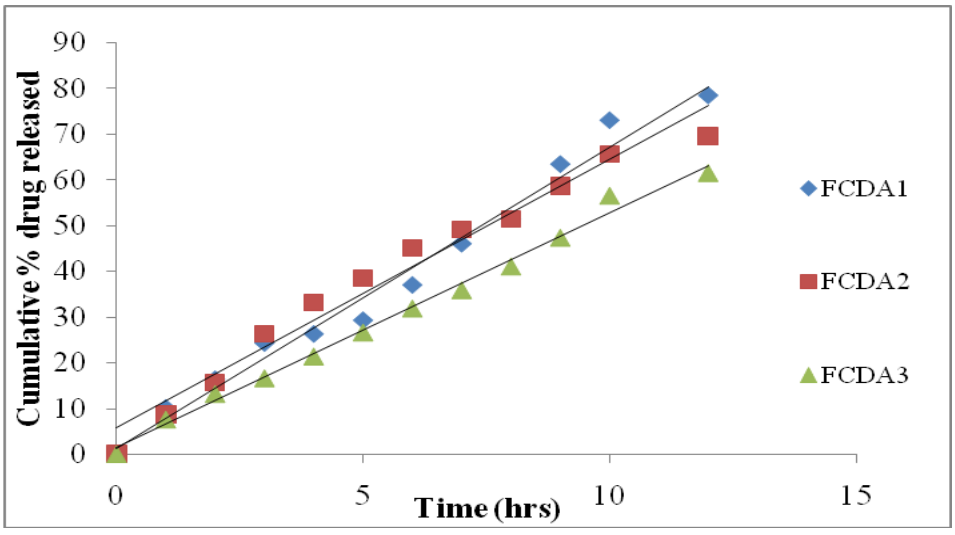


Fig. 5: Cumulative % drug released Vs Time



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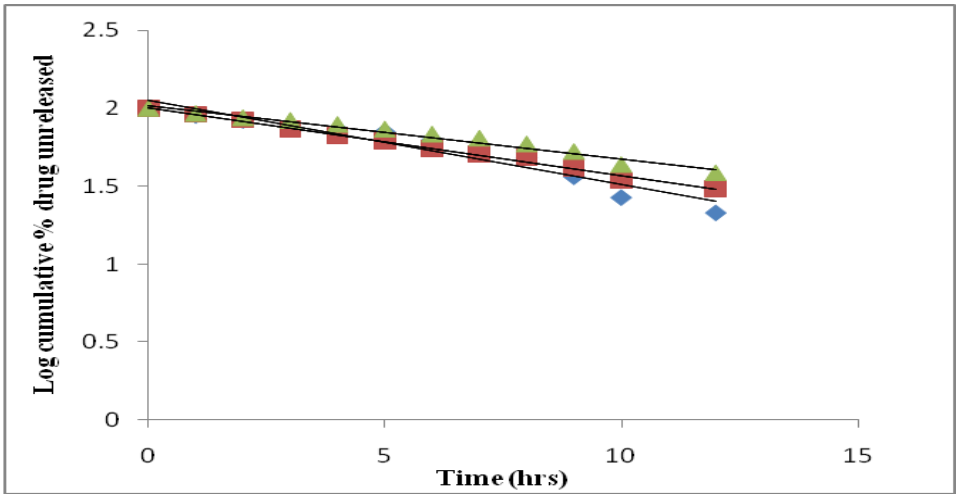

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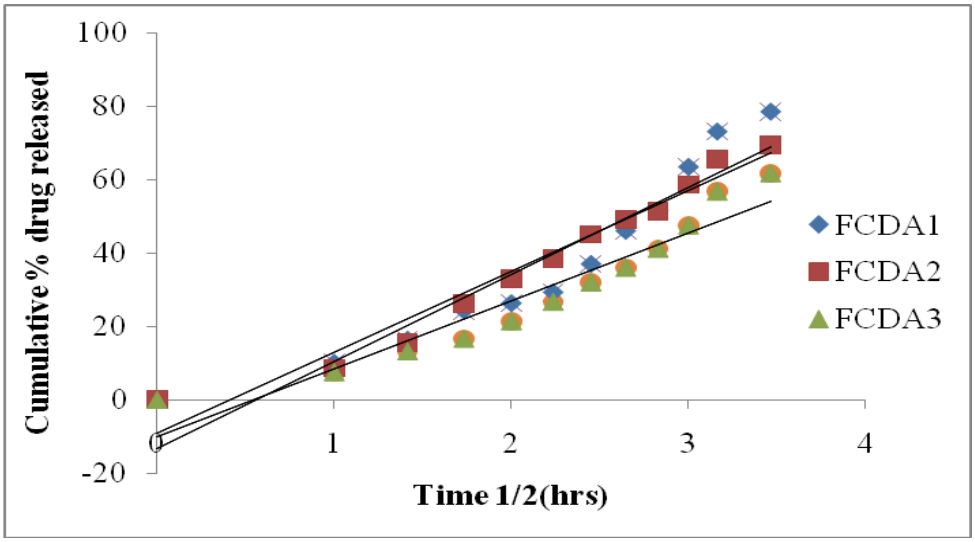

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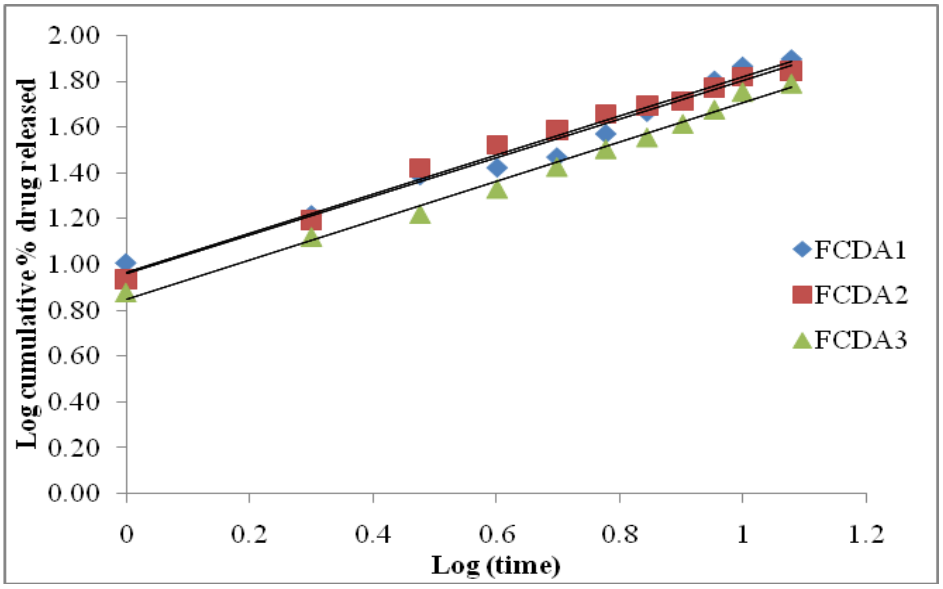
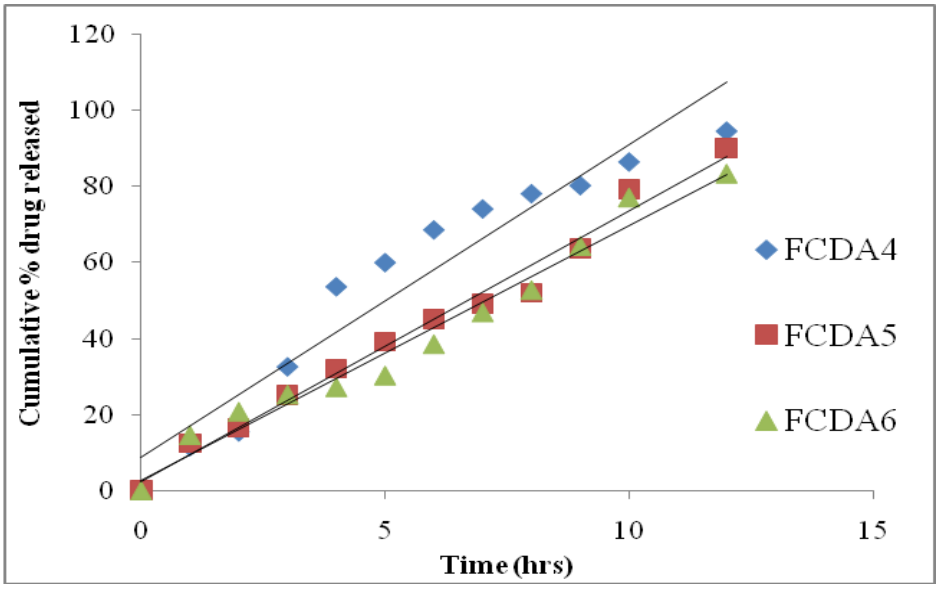


(d)

Fig. 6: Linear regression plots for Cimetidine Floating Tablets Prepared Employing Albizia gum Using DCP as Diluent (a)Zero order plot, (b) First order plot (c) Higuchi plot and (d) Peppas plot

Table 9: Correlation Coefficient (r^2) Values in the Analysis of Release Data of Cimetidine floating Tablets Prepared Employing Albizia gum Using DCP as Diluent as per Various Kinetic Models

Formulation	Correlation Coefficient (r^2) Values				
	Zero order	First order	Higuchi's	Peppas's	
				r^2	n
FCDA1	0.903	0.928	0.897	0.974	0.582
FCDA2	0.972	0.992	0.964	0.988	0.577
FCDA3	0.953	0.971	0.917	0.991	0.531



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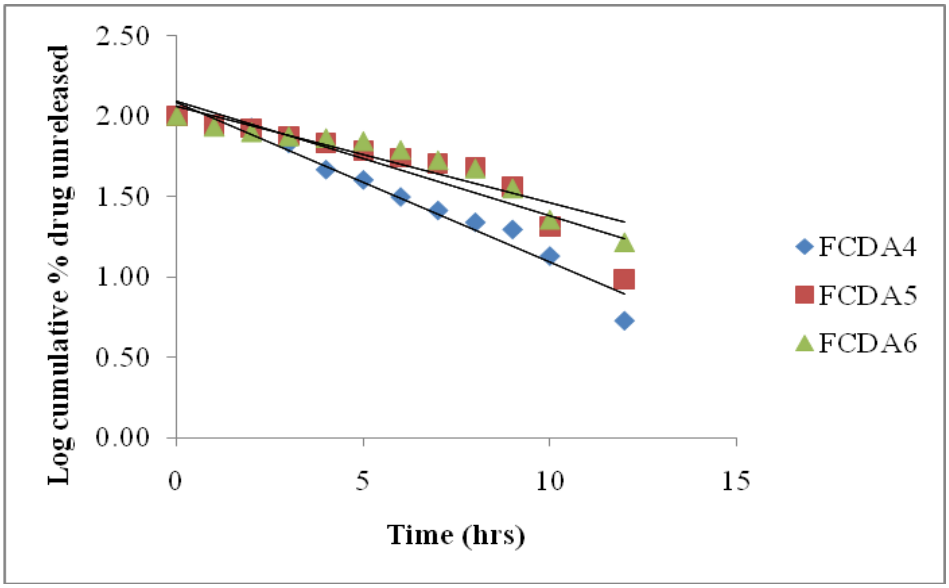

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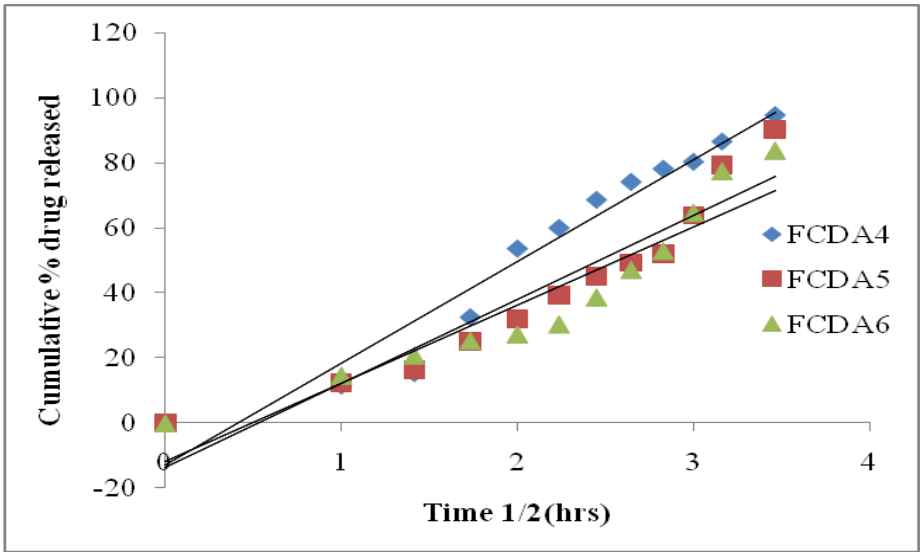

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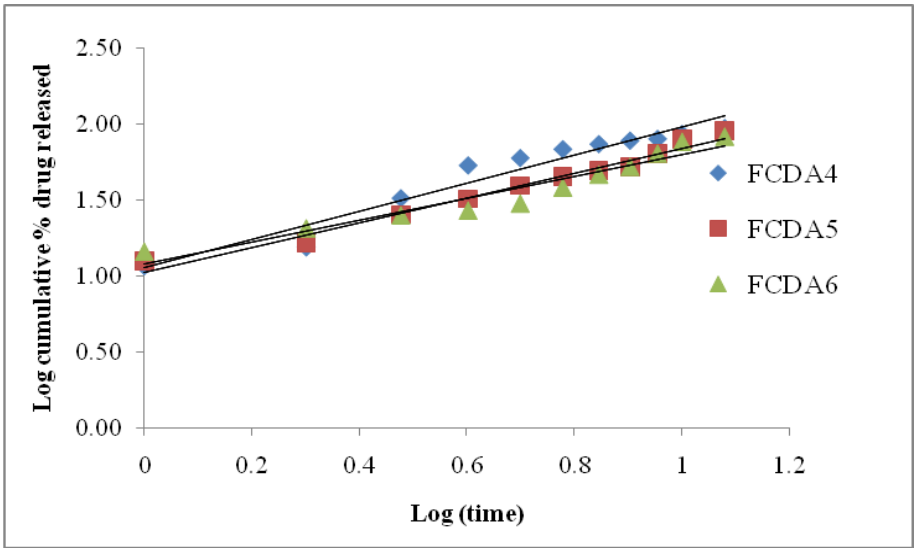

(d)

Fig. 8: Linear regression plots for Cimetidine Floating Tablets Prepared Employing Albizia gum Using Lactose as Diluent (a)Zero order plot, (b) First order plot (c) Higuchi plot and (d) Peppas plot

Table 10: Correlation Coefficient (r^2) Values in the Analysis of Release Data of Cimetidine floating Tablets Prepared Employing Albizia gum Using Lactose as Diluent as per Various Kinetic Models

Formulation	Correlation Coefficient (r^2) Values				
	Zero order	First order	Higuchi's	Peppas's	
				r^2	n
FCDA4	0.997	0.965	0.943	0.945	0.880
FCDA5	0.984	0.849	0.905	0.917	0.816
FCDA6	0.972	0.890	0.885	0.929	0.718

RESULTS AND DISCUSSION

The Floating tablets of cimetidine were prepared by direct compression technique using Albizia gum, as polymer for controlling the drug release. Pure drug and optimized formulation FCDA4 were subjected to the drug excipient compatibility studies using FTIR and DSC. The studies revealed that there is no interaction between the drug and excipients. The increase in the polymer content with the constant amount of drug (higher polymer-drug ratio) resulted in decreased release rate of drug due to the formation of low porosity and high tortuosity. In order increase the drug release channeling agents were introduced namely Lactose and DCP. Lactose is water soluble diluent and DCP is water insoluble diluent. Precompression parameters such as bulk density, tapped density, angle of repose, hausners ratio were performed to all the formulations and were found to be in the acceptable limits which ensures the good flow properties. Formulation FCDA4 containing albizia gum and lactose as channeling agent showed good results when compared with other formulations. The floating lag time of optimized formulation FCDA4 was found to be 122sec and the percentage of drug release at the end of 12 hours was found to be 99.31%. The drug release kinetics revealed that formulation FCDA4 follows zero order kinetics and the mechanism was nonfickian.

CONCLUSION

Cimetidine floating tablets were successfully prepared using albizia gum in various ratios by direct compression method. Among all the formulations, FCDA4 was considered suitable for controlled release of Cimetidine up to 12 hours when compared with other formulations.

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