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DESIGN EXPERT SOFTWARE ASSISTED DEVELOPMENT AND EVALUATION OF CEFPODOXIME PROXETIL MATRIX TABLET

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Keywords:

Design Expert Software, Cefpodoxime Proxetil, Sustained release, Matrix tablets, Direct compression

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ABSTRACT: Cefpodoxime Proxetil is third generation, broad-spectrum Cephalosporin Antibiotic & it has an oral bioavailability of only 50% and biological half life 2 h so to improve it's bioavailability sustain release matrix formulation was designed. Sustained release matrix tablets of Cefpodoxime Proxetil prepared by direct compression method based on combination of natural Acacia gum & Karaya gum polymers. 3^2 full factorial designs optimization study was carried out by using Design Expert Software to find the effect of independent variables, *i.e.,* Acacia gum (X1) and Karaya gum (X2) concentration on dependent variables *i.e.,* Hardness & % CDR. The drug excipient mixtures were subjected to preformulation studies. The tablets were subjected to physicochemical studies, *in-vitro* drug release, kinetic studies and stability studies. FTIR and DSC studies shown there was no interaction between drug and polymers. Matrix tablet of Cefpodoxime Proxetil were formulated well in term of hardness 5.07 ± 0. 5.93 ± 0.03 kg/cm^2, thickness 2.25 ± 0.1 mm to 3.33 ± 0.3 mm, weight variation were within limits. *In-vitro* release studies show that almost 90 % of drug was release from all the formulation were within 12 h. Formulation F5 selected as a optimized one since it showed optimum hardness & sustained drug release within 12 h in comparison to other formulation. The F5 optimized formulations were subjected to stability studies and shown there were no significant changes in drug content, physicochemical parameters and release pattern. 3^2 full factorial design optimization technique was successfully used in this research work. Developed matrix tablets of Cefpodoxime Proxetil produced a sustained and effective drug release over a prolonged time frame that led to greater therapeutic efficacy.

INTRODUCTION: The oral route is the oldest and convenient route for the administration of therapeutic agents because of the low cost of therapy and ease of administration leads to a higher level of patient compliance [1].

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Approximately 50% of the drug products available in the market are administered orally, and historically, oral drug administration has been the predominant route for drug delivery [2].

The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body to achieve promptly and then maintain the desired drug concentration, *i.e.,* the drug-delivery system should deliver the drug at a rate dictated by the needs of the body over a specified period of treatment [3, 4]. Introduction of matrix tablet as sustained-release has given a new breakthrough for

novel drug delivery systems in the field of Pharmaceutical technology [5, 6]. Matrix systems are widely used for the purpose of sustained release. It is the release system that prolongs and controls the release of the drug that is dissolved or dispersed. By the sustained release method, therapeutically effective concentration can be achieved in the systemic circulation over an extended period of time, thus achieving better compliance of patients [7, 8].

Khandesh is a geographic area in Central India, which forms the northwestern portion of Maharashtra state. Khandesh District is a former governmental division of British India, which included the present-day Jalgaon, Dhule and Nandurbar districts, and a portion of Nasik District in Maharashtra.

Cefpodoxime Proxetil is a third-generation, broad-spectrum cephalosporin antibiotic mainly used in the treatment of respiratory, urinary, skin, and soft tissue infections caused by gram-positive and gram-negative bacteria. It is incompletely absorbed from the gastrointestinal tract and has an oral bioavailability of only 50% and biological half-life 2 h. Matrix tablet is able to prolong the release of drugs and thereby possibly improve oral bioavailability of Cefpodoxime Proxetil [9,10]. Hence, in the present study, an attempt has been made to formulate the sustained release matrix tablets of Cefpodoxime Proxetil using natural polymers like karaya gum and acacia gum in various proportions as release controlling factor by direct compression which will improve its absorption.

MATERIALS AND METHODS:

Materials: Cefpodoxime Proxetil was procured as a gift sample from Shree Swami Samarth Ayurvedic Pharmacy Allopathic division, Jalgaon, Karaya gum procured from the local market Akkalkuwa in Khandesh region. Acacia gum, Magnesium stearate procured from SD Fine Chem. Ltd, Mumbai. Lactose & Talc from Research Lab Fine Chem Industries, Mumbai.

Method:

Formulation of Sustained Release Matrix Tablets: All the matrix tablets containing 100 mg of Cefpodoxime Proxetil, were prepared by direct compression method. Accurately weighed amounts of drug, polymer, and diluent were mixed geometrically in a mortar. This mixture was passed through no. 40 sieve and thoroughly mixed in a polythene bag for 15 min. The powder blend was then lubricated with magnesium stearate and talc for 2 min and compressed into tablets on a 9-station rotary tableting machine using 9-mm round, flat-faced punches. The total weight of the matrix tablets was 280 mg **Table 3,** with different drug-polymer ratios.

Drug - Excipient Compatibility Study: FTIR & DSC studies were conducted to know the compatibility between drug and excipients.

FT-IR Studies: FT-IR spectra for pure Cefpodoxime Proxetil and Different polymers acquired at room temperature using FT-IR spectrophotometer (FTIR-8400S, Shimadzu, Japan) in transmittance mode. The samples were ground in a mortar, mixed with Nujol and placed between two plates of KBr and compressed to form a thin film. The sandwiched plates were placed in the infrared spectrometer and the spectra were obtained. Scanning was performed between wave numbers 4000-400 cm^{-1}. [11]

DSC Analysis: Method for estimating the physical interaction between drug and polymers used for the formulation of different dosage forms is a thermal analysis by DSC. In the present studies, the DSC analysis of drug, and Polymers were carried out using a Shimadzu DSC 60, Japan; to evaluate any possible polymer drug thermal interaction. Exactly weighed 5 to 6 mg samples were hermetically sealed in aluminium crucible and heated at constant rate of 10 °C/min over a temperature range of 40 to 300 °C. Inert atmosphere was maintained by purging nitrogen gas at a flow rate of 50 ml/min.[12]

Evaluation of Sustained Release Matrix Tablets:

Pre-Compression Studies of Powder Blends: A preformulation study is the first step of insane drug development. All studies which are performed prior to the development of dosage form to reduce error and provide remunerative data to carry out dosage form development for the treatment of various diseases.

Angle of Repose: It is defined as the angle of heap to the horizontal plane. Angle of repose was determined by using fixed funnel method. Specified amount of powder drug was transferred to the funnel keeping the orifice of the funnel

blocked by thumb. When the powder was cleared from funnel, then measured its angle of repose.

$$\text{Angle of repose } (\theta) = \tan^{-1} h/r$$

Bulk Density: It is the ratio of the bulk mass of powder to the bulk volume. It is calculated by this formula.

Bulk density = Weight of powder bulk / Bulk volume

Tapped Density: It is the ratio of the weight of blend to the minimum volume occupied in measuring cylinder by powder. The measuring cylinder containing the porous mass of powder was tapped using tapped density apparatus [13].

Tapped density = Weight of powder blend / Tapped volume of packing

Compressibility Indices:

Carr's Index: Based on the apparent bulk density and the tapped density, the percentage compressibility of the powder mixture was determined by the following formula [14].

Carr's index = Tapped density - Bulk density × 100/Tapped Density

Hausner's Ratio:

Hausner's ratio = Tapped density /Bulk density

Post-Compressional Studies of Prepared Matrix Tablets: The matrix tablets were evaluated for appearance, thickness, weight variation, hardness, and friability. All the evaluation parameters of all formulations are given in **Table 2**.

Thickness: The tablet thickness was calculated by Vernier calipers. Tablet was put in between two jaws vertically and measured thickness. It is expressed in mm.

Weight Variation: The weight of 20 tablets was measured, and the average weight was calculated. The individual weight of each tablet was measured to determine its variation. Weight variation was determined by comparison of individual tablet weight with average weight [15].

Hardness: The tablet hardness was determined by Monsanto hardness tester. The tablet was fitted lengthwise between plunger and force applied. Noted down the pressure at which the tablet was crushed. It is measured in kg/cm^2. 6 tablets were used for this study [16].

Friability: It is calculated by the Roche friability apparatus. Preweighed six tablets were subjected to the device, which provided the combined effect of shock and abrasion from a height of six inches with each rotation, at 25 rpm speed, and operated for 100 revolutions. Tablets were dusted and re-weighed [9, 10]. Compressed tablets that lose less than 0.5-1.0% of their weight were generally considered acceptable. It is expressed in percentage (%) and calculated by the following formula:

Friability (%) = Initial weight – Final weight/Initial weight × 100

Drug Content (Assay): Ten tablets were weighed and taken into a mortar and crushed into a fine powder. An accurately weighed portion of the powder equivalent to about 100 mg of Cefpodoxime Proxitil was transferred to a 100 mL volumetric flask containing 70 mL of 0.1N HCl. It was shaken by mechanical means for 1 h. Then it was filtered through a Whatman filter paper (no. 1) and diluted to 100 mL with 0.1N HCl. From this resulted solution, 1 mL was taken, diluted to 50 ml with 0.1N HCl, and absorbance was measured against blank at 258 nm.

***In-vitro* Drug Release Characteristics:** Drug release was assessed by dissolution test under the following conditions: n = 3, USP type II dissolution apparatus (paddle method) at 100 rpm in 900 mL of 0.1N HCl for first 2 h and the phosphate buffer pH 6.8 from 3 to 12 h, maintained at 37 °C ± 0.5 °C. An aliquot (5mL) was withdrawn at specific time intervals and replaced with the same volume of prewarmed (37 °C ± 0.5 °C) fresh dissolution medium. The samples withdrawn were filtered through Whatman filter paper (no. 1), and drug content in each sample was analyzed by UV-visible spectrophotometer at 258 nm [17, 18].

Details of Dissolution Test:

Dissolution test apparatus	:	USPII
Speed	:	100 ± 0.1 rpm
Stirrer	:	paddle type
Volume of medium	:	900 ml
Time interval	:	1, 2, 3, 4, 6, 8, 10 & 12 h
Medium used	:	0.1N HCl for first 2 h and the phosphate buffer pH 6.8 from 3 to 12 h
Temperature	:	37 ± 0.5 °C

Kinetic Analysis of Dissolution Data: To analyze the *in vitro* release data, various kinetic models were used to describe the release kinetics.

Zero Order Rate Equation: Describes the systems where the drug release rate is independent of its concentration.

$$C = K_0 t \ldots\ldots 1$$

Where, K_0 is zero-order rate constant expressed in units of concentration/time and t is the time.

First Order Equation: Describes the release from system where the release rate is concentration-dependent.

$$\text{Log } C = \text{Log} C_0 - K_1 t/2.303 \ldots\ldots 2$$

Where, C_0 is the initial concentration of drug, and K_1 is first-order constant.

Higuchi Equation: Describe the release of drugs from the insoluble matrix as a square root of time dependent process based on Fickian diffusion Eq. (3).

$$Q = K_H t^{1/2} \ldots\ldots 3$$

Where, K_H is the constant reflecting the design variables of the system.

Hixson-Crowell cube root law Equation: Describes the release from systems where there is a change in surface area and diameter of particles or tablets.

$$Q0^{1/3} - Qt^{1/3} = KHC\ t \ldots\ldots 4$$

Where, Q_t is the amount of drug remained in time t, Q_0 is the initial amount of the drug in tablet, and K_{HC} is the rate constant for the Hixson-Crowell rate equation.

Mechanism of Drug Release: Korsmeyer *et al.*, (1983) derived a simple relationship which described drug release from a polymeric system Eq. (5). To find out the mechanism of drug release, first, 60% drug release data was fitted in

Korsmeyer–Peppas Model:

$$M_t / M_\infty = Kt^n \ldots\ldots 5$$

Where $M_t / M\infty$ is a fraction of drug released at time t, K is the release rate constant incorporating structural and geometric characteristics of the tablet, and n is the release exponent. The n value is used to characterize different release mechanisms[19, 20].

Stability Studies of the Optimized Formulation: In the present study, stability studies were carried out at room temperature 40 ± 20 °C and 75 ± 5% RH for a specific time period up to 3 Months for selected F5 formulations. For stability study, the tablets were sealed in aluminum packaging coated inside with polyethylene & studied for various parameters [21].

Optimization by using Full Factorial Design: [22] In the present study, a 3^2 full factorial design was employed to study the effect of independent variables, *i.e.*, amount of Acacia gum (X1) and Karaya gum (X2) on dependent variables, i.e., Hardness,% CDR.

TABLE 1: LAYOUT OF 3^2 FULL FACTORIAL DESIGN BATCHES OF MATRIX TABLETS F1-F9

Batch no.	X1	X2
F1	-1	-1
F2	-1	0
F3	-1	1
F4	0	-1
F5	0	0
F6	0	1
F7	1	-1
F8	1	0
F9	1	1

TABLE 2: TRANSITION OF CODED VALUE IN AN ACTUAL UNIT

Coded value	Acacia gum (X1)	Karaya gum (X2)
-1	30	30
0	40	60
1	50	90

TABLE 3: COMPOSITION OF MATRIX TABLETS CONTAINING KARAYA GUM AND ACACIA GUM

Ingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)	F9 (mg)
Cefpodoxim Proxetil	100	100	100	100	100	100	100	100	100
Karaya gum	30	30	30	60	60	60	90	90	90
Acacia gum	30	40	50	30	40	50	30	40	50
Magnesium Stearate	10	10	10	10	10	10	10	10	10
Talc	10	10	10	10	10	10	10	10	10
Lactose	100	90	80	70	60	50	40	30	20
Total weight	280	280	280	280	280	280	280	280	280

RESULTS:

FTIR:

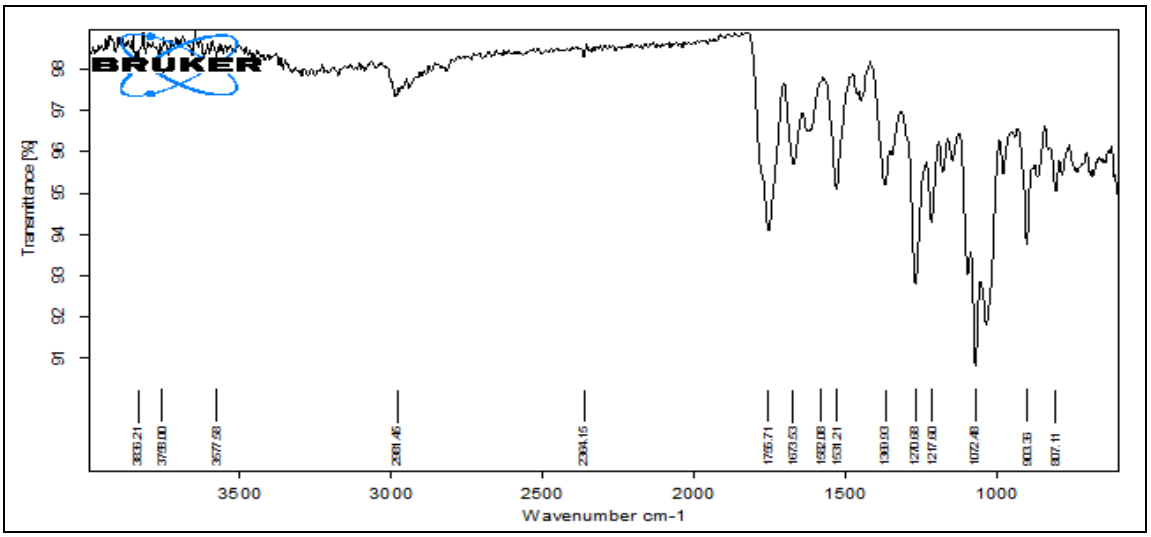

FIG. 1: FTIR SPECTRUM OF CEFPODOXIME PROXETIL (PURE DRUG)

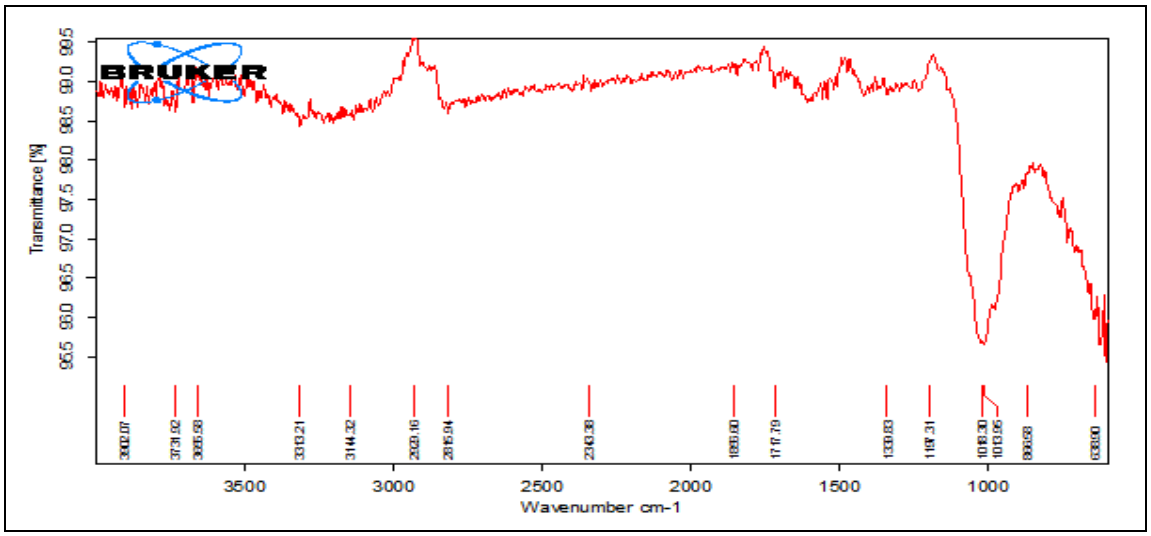

FIG. 2: FTIR SPECTRUM OF KARAYA GUM

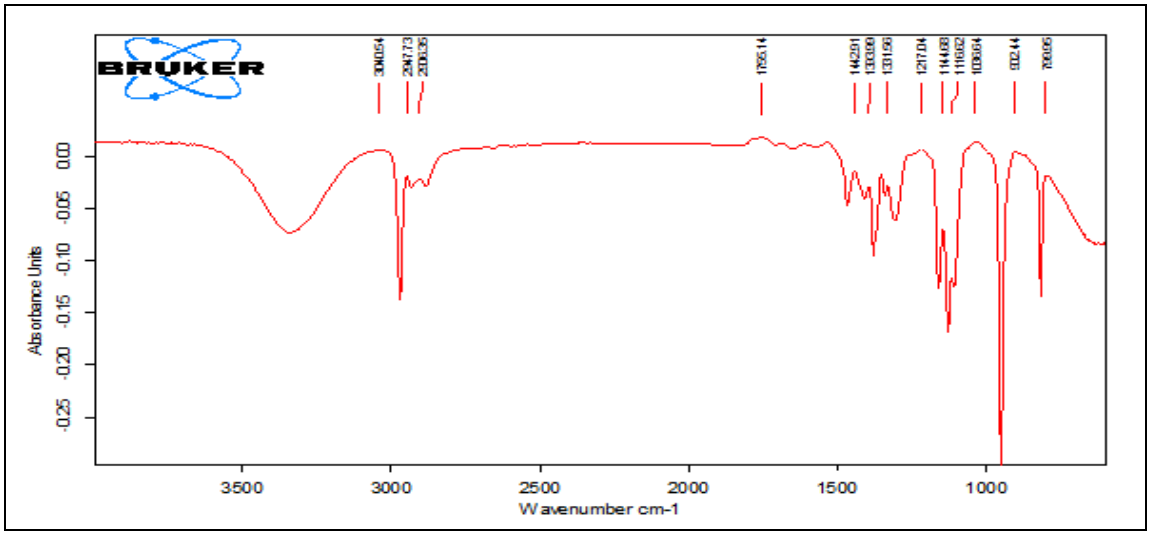

FIG. 3: FTIR SPECTRUM OF CEFPODOXIME PROXETIL WITH KARAYA GUM

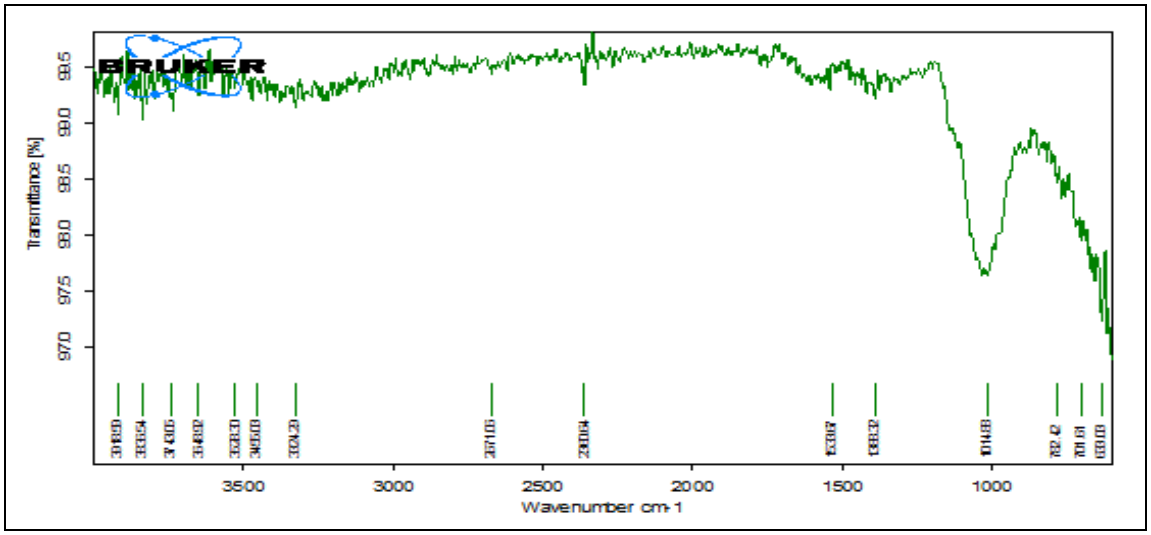

FIG. 4: FTIR SPECTRUM OF ACACIA GUM

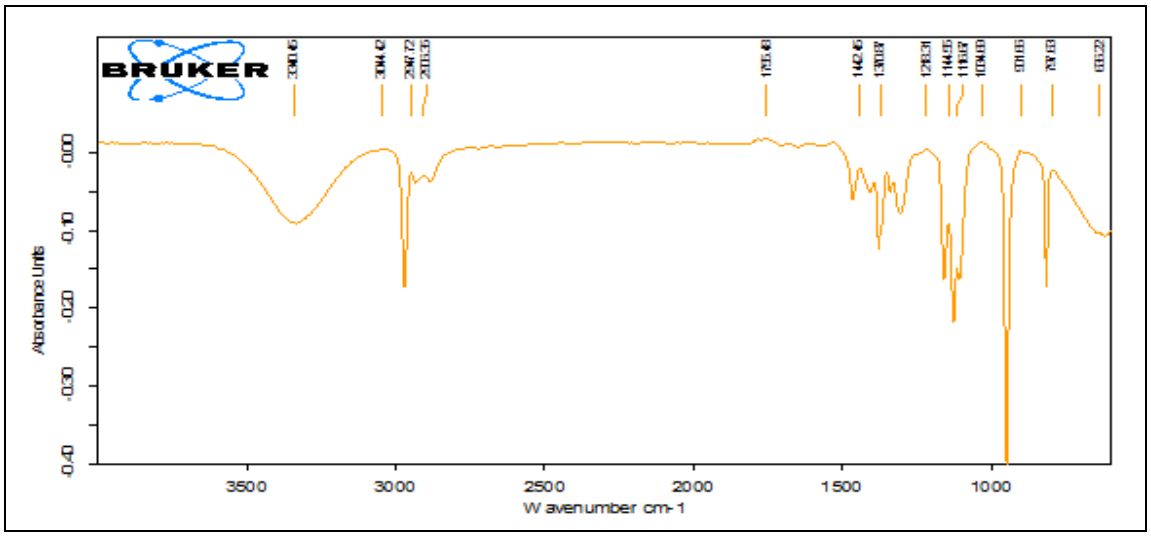

FIG. 5: FTIR SPECTRUM OF CEFPODOXIME PROXETIL WITH ACACIA GUM

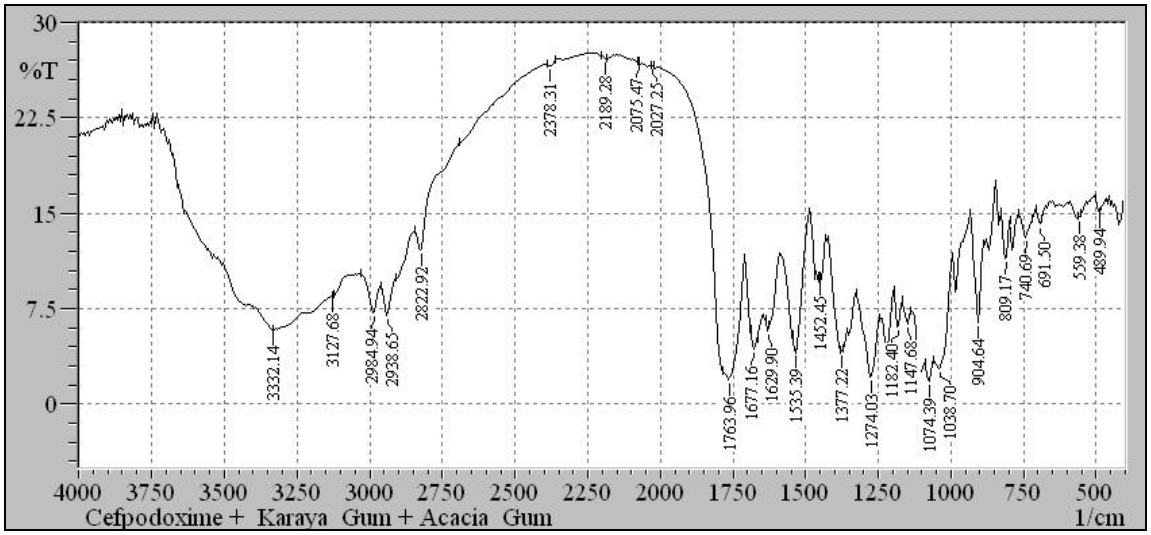

FIG. 6: FTIR SPECTRUM OF BLEND (CEFPODOXIME PROXETIL + KARAYAGUM + ACACIA GUM)

All the characteristic peaks of Cefpodoxime Proxetil were present in spectra, thus indicating compatibility between drug. It shows that there was no significant change in the chemical integrity of the drug.

DSC:

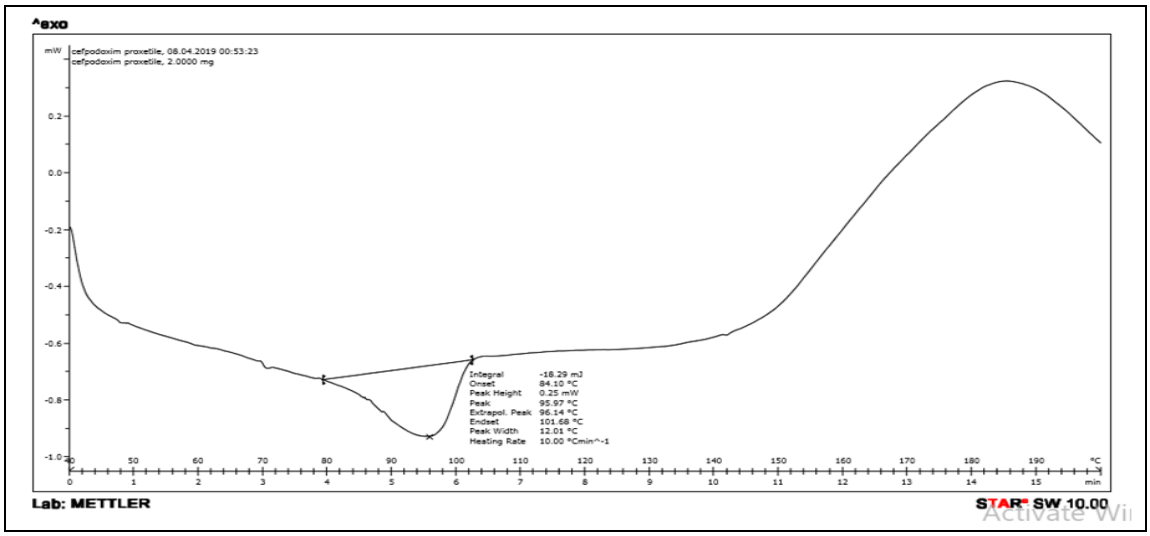

FIG. 7: DSC ANALYSIS OF CEFPODOXIME PROXETIL (PURE DRUG)

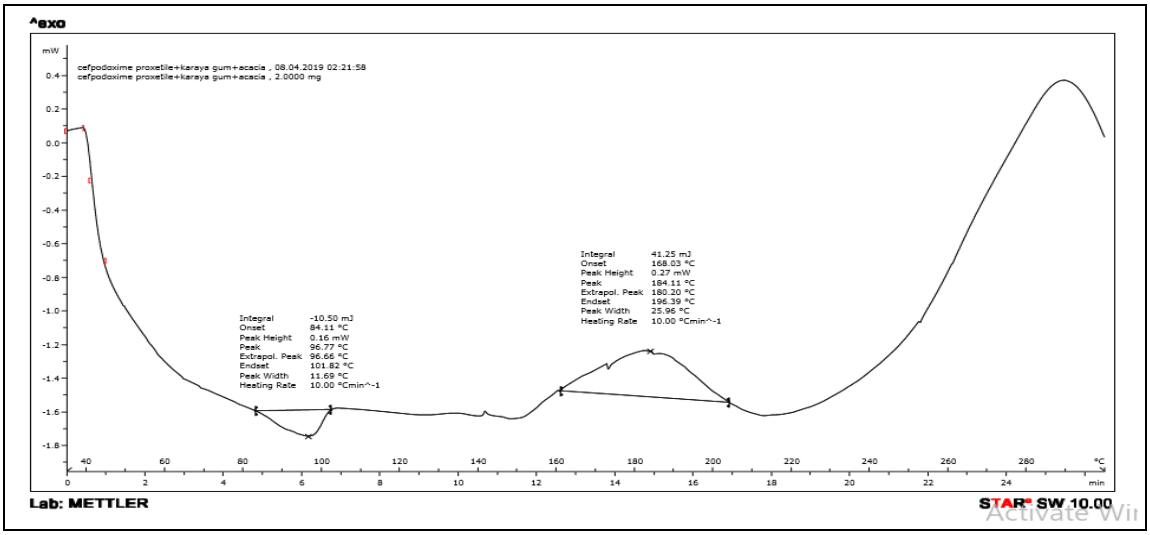

FIG. 8: DSC ANALYSIS OF BLEND (CEFPODOXIME PROXETIL + KARAYA GUM + ACACIA GUM)

DSC study shows an endothermic peak at 96.77 °C correspond to the melting point of Cefpodoxime Proxetil in formulation blend no significant changes in characteristic endothermic peak of Cefpodoxime Proxetil that indicate there is compatibility of drug within formulation blend.

Pre-compression Parameters: The prepared formulations were evaluated for precompression parameters, and their results were given in **Table 4**. The powder blend was evaluated for various parameters like angle of repose, tapped density, bulk density, Carr's index, and Hausner's ratio, respectively. The value of the angle of repose of all formulations ranges between 25.64 ± 0.11 to 28.75 ± 0.22 (θ), which shows very good powder flow property. The result of bulk density and tapped density ranges from 0.21 ± 0.1 to 0.51 ± 0.04 g/ml and 0.25 ± 0.03 to 0.59 ± 0.06 g/ml respectively. The values of compressibility indices and Hausner's ratio ranged from 7.18 ± 0.04 to 15.90 ± 0.09 and 1.07 ± 0.09 to 1.18 ± 0.09, respectively.

Post-compression Parameters: The weight of Cefpodoxime proxetile matrix tablets was found to be in the range of 289 ± 0.2 ± 0.004 to 297 ± 0.3 ± 0.002 gm. Thickness was observed as 2.25 ± 0.1mm to 3.33 ± 0.3 mm and % friability of various formulations was found to be in between 0.25 ± 0.009 to 0.64 ± 0.011. The hardness of the tablet was found to be 5.07 ± 0. 5.93 ± 0.03 kg/cm^2. The *in-vitro* drug release that was performed for karaya and acacia gum containing formulations.

The % *in-vitro* drug release from formulations F1, F2, F3, F4, F5, F6, F7, F8 and F9 at the end of 12 h was found to be 97.20 ± 0.032%, 96.30 ± 0.01%, 95.40 ± 0.056%, 94.50 ± 0.013%, 98.10 ± 0.067%, 93.60 ± 0.045%, 92.70, 91.80, & 90.09% respectively. Drug release kinetics parameters with n, R^2 value are provided in **Table 8**. The regression coefficient value of zero order was observed R^2 value 0.9814 so, the drug release was found to be zero order kinetics.

TABLE 4: PRE-COMPRESSION PARAMETER OF BLEND

Parameter Batches	Bulk Density (gm/cm^3) (mean ± SD)	Tapped Density (gm/cm^3) (mean ± SD)	Compressibility Index (%)	Hausner's Ratio	Angle of Repose (^{0})
F1	0.29 ± 0.04	0.31 ± 0.02	7.91	1.08	25.64
F2	0.29 ± 0.09	0.31 ± 0.01	7.52	1.08	26.56
F3	0.29 ± 0.02	0.32 ± 0.04	7.18	1.07	27.47
F4	0.21 ± 0.1	0.25 ± 0.03	14.74	1.17	27.02
F5	0.48 ± 0.03	0.53 ± 0.03	9.12	1.10	26.38
F6	0.52 ± 0.01	0.59 ± 0.06	12.53	1.14	28.75
F7	0.48 ± 0.06	0.57 ± 0.08	15.90	1.18	27.33
F8	0.41 ± 0.04	0.48 ± 0.01	14.69	1.17	26.43
F9	0.51 ± 0.04	0.59 ± 0.01	13.70	1.15	27.34

TABLE 5: POST-COMPRESSION PARAMETER OF FORMULATION F1-F9

Formulation	Thickness (n=3) (mm) (SD)	Hardness (kg/cm^2) (n=3) (SD)	Friability (%) (n=10)	Weight Variation (n=20) (mg) (SD)	Drug content (%)
F1	2.25 ± 0.1	5.93 ± 0.03	0.33	293 ± 0.4	98.50 ± 0.2
F2	2.35 ± 0.3	5.07 ± 0.04	0.30	297 ± 0.3	96.50 ± 0.4
F3	3.20 ± 0.3	5.08 ± 0.06	0.20	295 ± 0.7	93.51 ± 0.6
F4	3.14 ± 0.2	5.50 ± 0.10	0.33	291 ± 0.1	92.55 ± 0.2
F5	3.33 ± 0.3	5.66 ± 0.06	0.25	289 ± 0.2	99.48 ± 0.8
F6	3. 11 ± 0.4	5.41 ± 0.07	0.15	294 ± 0.5	95.39 ± 0.7
F7	3.20 ± 0.3	5.16 ± 0.02	0.64	296 ± 0.2	94.03 ± 0.2
F8	2.98 ± 0.3	5.08 ± 0.02	0.48	297 ± 0.1	91.99 ± 0.2
F9	3.15 ± 0.2	5.25 ± 0.05	0.42	294 ± 0.4	90.51 ± 0.4

The hardness of the tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The hardness of the formulations F1-F9 was observed within the range of 2.25 ± 0.1 to 3.11 ± 0.4 kg/cm^2 as shown in **Table 5**.

All the polynomial equations for hardness variable were found to be statistically significant as determined using ANOVA, as per the provision of Design-Expert software.

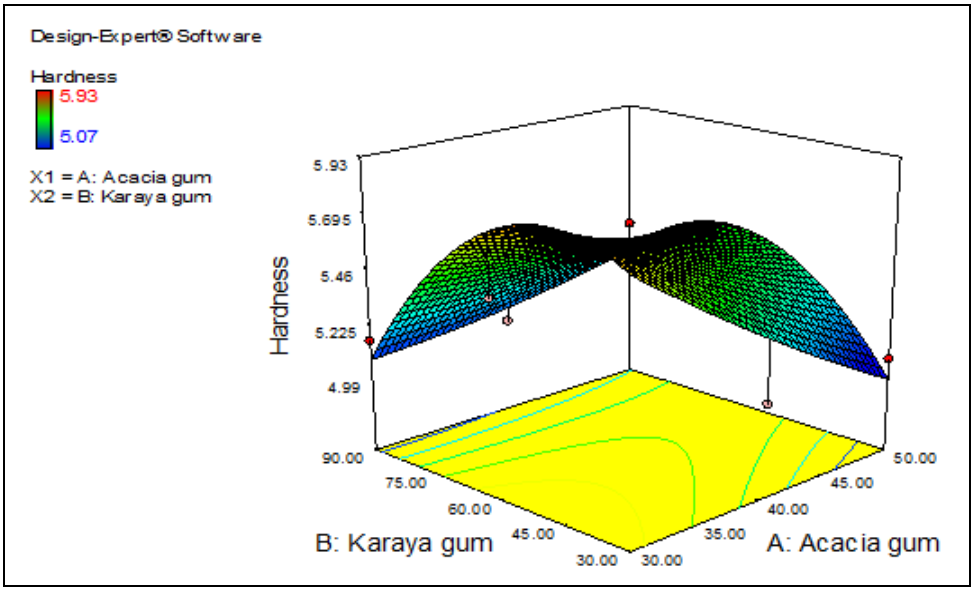

FIG. 9: RESPONSE SURFACE PLOTS PRESENTING THE EFFECTS OF ACACIA GUM (X1) AND KARAYA GUM AMOUNT (X2) ON HARDNESS

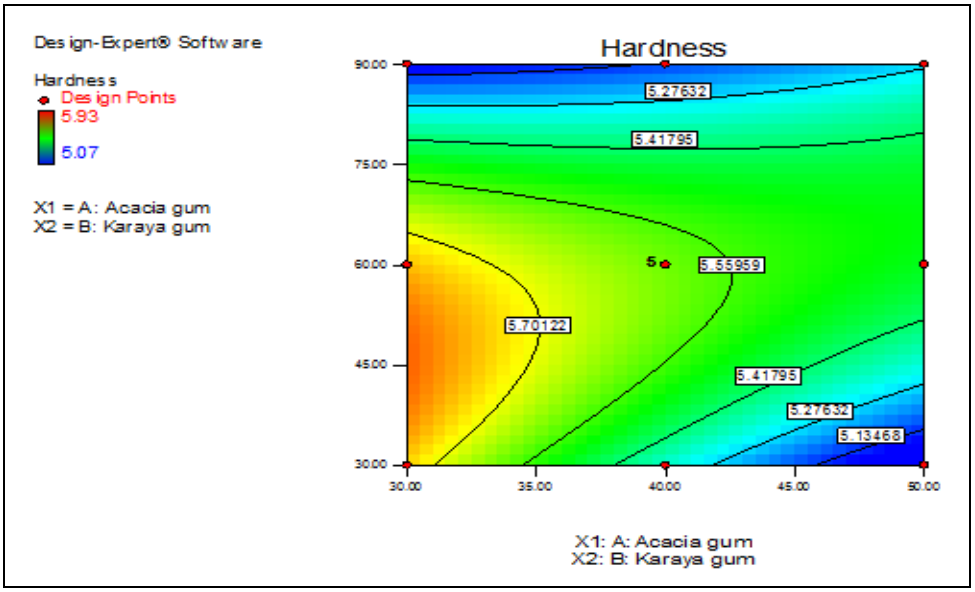

FIG. 10: CONTOUR PLOTS PRESENTING THE EFFECTS OF *ACACIA GUM* (X1) AND *KARAYA GUM* AMOUNT (X2) ON HARDNESS

TABLE 6: *IN-VITRO* DRUG RELEASE STUDY OF FORMULATION F1-F9

Time (hrs)	Cumulative % Drug Release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1	1.35	11.70	15.30	8.10	9.90	10.80	7.20	8.10	13.50
2	13.50	19.35	20.70	18.90	22.50	17.10	17.10	18.90	17.10
3	19.80	27.00	24.30	25.20	26.10	23.40	22.50	24.30	24.30
4	38.70	37.80	34.20	36.90	34.20	33.30	31.50	32.40	31.50
5	44.10	43.20	40.50	43.20	40.50	36.90	39.60	37.80	40.50
6	45.90	45.00	48.60	45.00	44.10	46.80	44.10	43.20	45.90
7	61.20	51.30	53.10	49.50	50.40	52.20	47.70	48.60	50.40
8	68.40	62.10	55.80	62.10	61.20	54.00	61.20	59.40	62.10
9	76.50	65.70	71.10	71.10	70.20	67.50	66.60	67.50	66.60
10	84.60	77.40	75.60	79.20	76.50	72.90	77.40	74.70	80.10
11	89.82	89.10	87.30	84.60	88.20	83.70	82.80	85.50	85.50
12	97.20	96.30	95.40	97.23	98.10	96.60	92.70	93.80	90.09

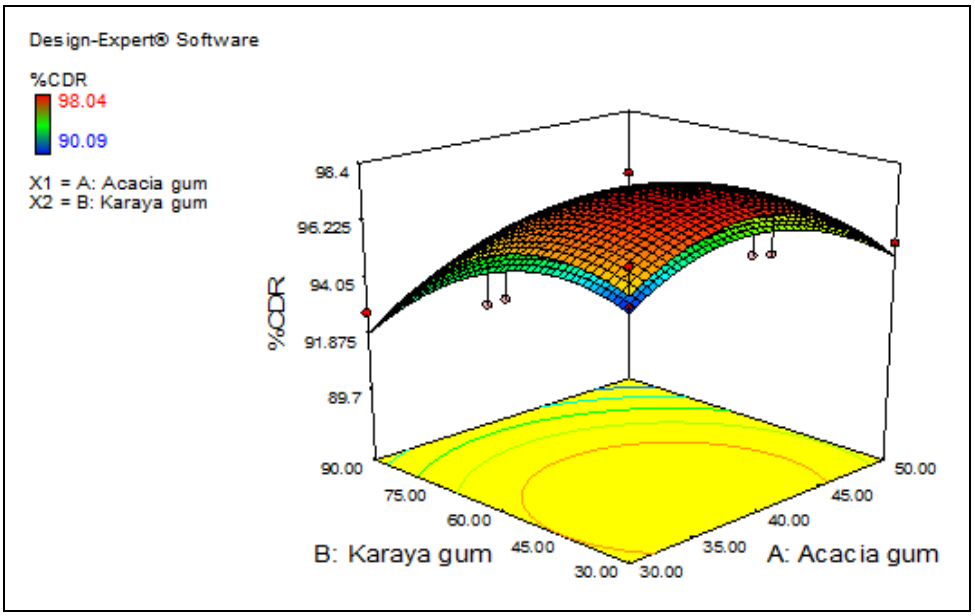

FIG. 11: RESPONSE SURFACE PLOTS PRESENTING THE EFFECTS OF *ACACIA GUM* (X1) AND *KARAYA GUM* AMOUNT (X2) ON %CDR

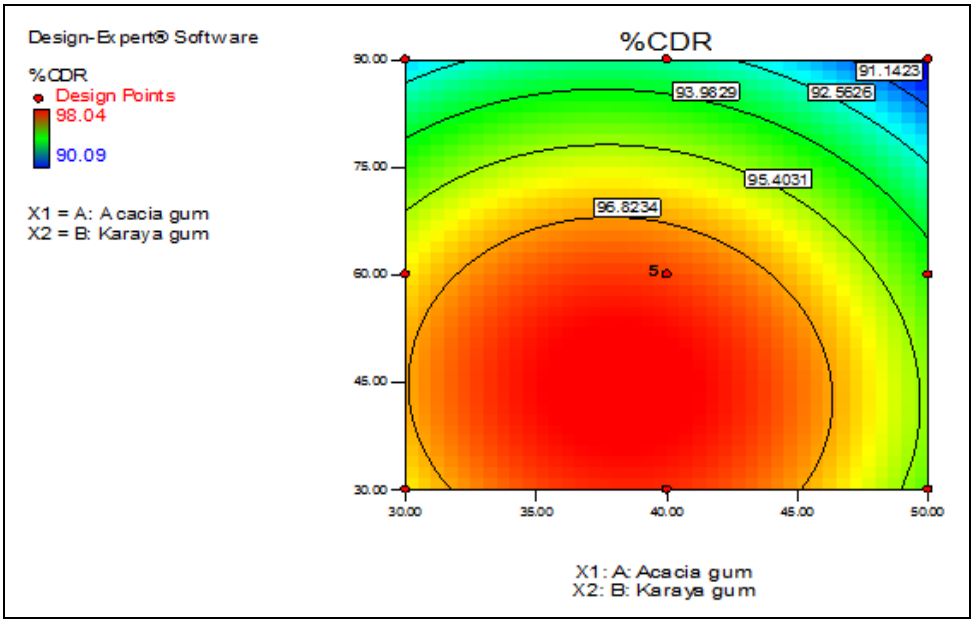

FIG. 12: CONTOUR PLOTS PRESENTING THE EFFECTS OF *ACACIA GUM* (X1) AND *KARAYA GUM* AMOUNT (X2) ON %CDR

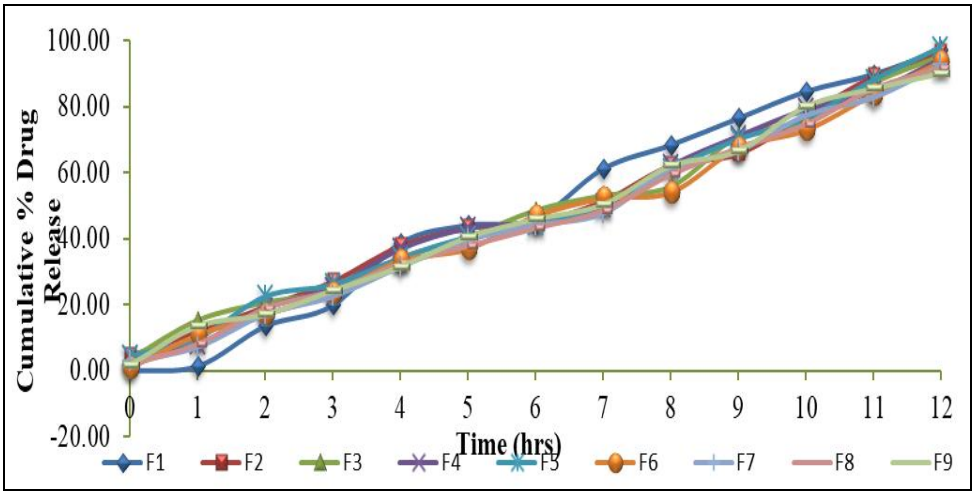

FIG. 13: % DRUG RELEASE OF CEFPODOXIME PROXETIL IN FORMULATION F1-F9

TABLE 7: RESULT OF ANOVA

Response model	Sum of square	Degree of freedom	Mean square	F value	P value	R square	Ade. Precision
Hardness	0.99	5	0.182	4.88	Significant	0.9770	6.36
%CDR	91.20	5	17.64	10.74	Significant	0.8023	9.63

TABLE 8: *IN-VITRO* DRUG RELEASE STUDY OF FORMULATION F5

Batch	Zero order		First order		Higuchi		Hixson- Crowell		Korsmeyer-Peppas		
F5	r^2	$K_0(h^{-1})$	r^2	$K_1(h^{-1})$	r^2	K_H $(h^{-1/2})$	r^2	K_{HC} $(h^{-1/3})$	r^2	n	$K_{KP}(h^{-n})$
	0.9814	7.6770	0.8277	-0.1803	0.8853	21.5000	0.9013	-0.0422	0.9544	1.4900	2.8307

* r^2= Correlation coefficient; K = Kinetic constant; n= Diffusional exponent

TABLE 9: STABILITY STUDY OF OPTIMIZED BATCH (F5)

Parameters	Time (months)	Hardness (kg/cm^2)	Friability (%)	Drug content (%)	% drug Release
Before stability study	0	5.66 ± 0.06	0.26	99.48± 0.8	98.15
After stability study	3	5.14 ± 0.03	0.25	98.87± 0.68	97.10

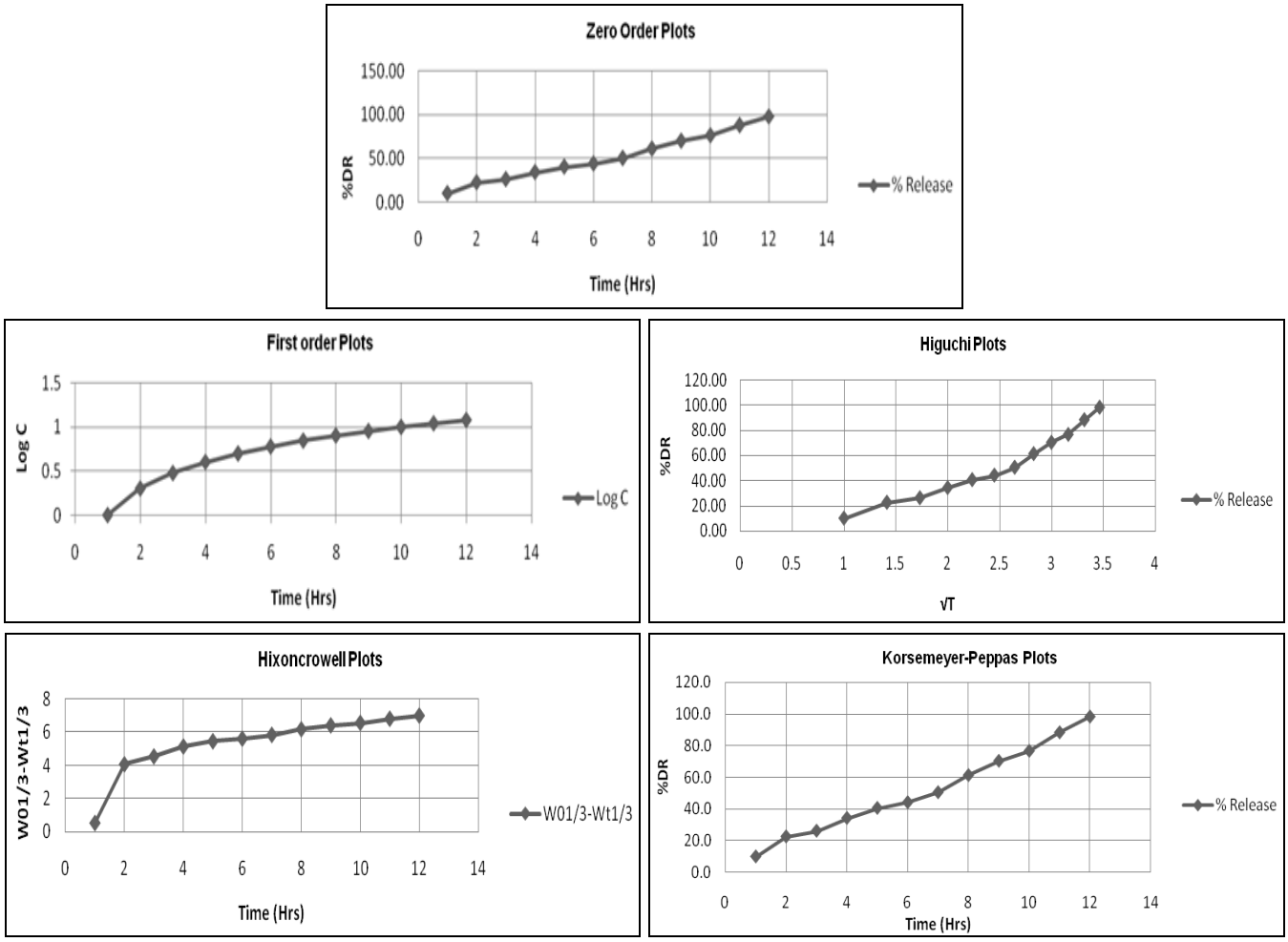

FIG. 14: KINETIC ANALYSIS OF DISSOLUTION DATA OPTIMIZED BATCH (F5)

DISCUSSION:

Pre-compression Study of Powder Blend: The powder blend was evaluated for various parameters as shown in **Table 4**. This showed that powder blend from all the formulations showing good flow property according to standard values [23].

Post-compression Studies of Prepared Matrix Tablets: The results of post-compression evaluation parameters are given in **Table 5**, and its description is given below.

Thickness: The determined thickness, according to the die and punches size of all formulation, was found to be 2.25 ± 0.1 mm to 3.33 ± 0.3 mm. It was upon the die and punched size during compression of tablets and their total weight.

Weight Variation: The determined weight variation of formulating tablets was found to be in the range of 289 ± 0.2 ± 0.004 to 297 ± 0.3 ± 0.002 gm. It was found to be within pharmacopeias limit of ± 5% as per I.P [24].

Hardness: The hardness of tablet (n=3) of formulation code F1, F2, F3, F4, F5, F9, which was given satisfactory result as per standard. On increasing the concentration of polymer hardness was also increases gradually. Since a high concentration of natural polymer enhances more hardness than natural polymer.

% Friability: The result of friability was found to be 0.25 ± 0.009 to 0.64 ± 0.011, which was less than 1% as per the pharmacopeias limit. The highest concentrations of polymers in the matrix tablet also affect the friability. It showed that tablets have sufficient strength to tolerate transportation stress [25].

***In-vitro* Drug Release Study:** The *in-vitro* drug release was carried out in 0.1 n HCl for 2 h and phosphate buffer of pH 6.8. The formulations F1 to F9 were given sustained drug release profile for 12 h study as 97.20 ± 0.032%, 96.30 ± 0.01%, 95.40 ± 0.056%, 94.50 ± 0.013%, 98.10 ± 0.067%, 93.60 ±

0.045%, 92.70, 91.80, & 90.09% respectively. The optimized formulation profile was given by F5.

***In-vitro* Drug Release Kinetics:** The release kinetics model was used for the goodness of fit by linear regression analysis with the help of zero order, first order, Higuchi's, and Korsmeyer Peppas equation in order to determine release and mechanism of drug action. The regression coefficient value of zero-order was observed R^2 value 0.9814. So, the drug release was found to be zero-order kinetics. The first order equation depends upon the Noyes Whitney equation. Higuchi describes the release of drugs from the insoluble matrix as the square root t dependent release, and R^2 value was found to be 0.8853. Korsmeyer Peppas describe the mechanism of drug release was found to be non-fickian super case II [26].

Stability Studies: In the present study, stability studies were carried out at room temperature 40 ± 20 °C and 75 ± 5% RH for a specific time period up to 3 months for selected F5 formulations. For stability study, the tablets were sealed in aluminum packaging coated inside with polyethylene & studied for various parameters. The outcome of stability studies is no significant change in all parameters after stability study, so the formulation is stable [27].

CONCLUSION: The Matrix tablet of Cefpodoxime Proxetil was prepared by a direct compression method using different natural polymers such as karaya gum and acacia gum in different concentrations. From FTIR, DSC, and physical observation it can be concluded that there is no significant drug excipient interaction, so drug and other excipient are compatible with each other. Matrix tablet of Cefpodoxime Proxetil were formulated well in term of hardness 5.07 ± 0. 5.93 ± 0.03 kg/cm^2, thickness 2.25 ± 0.1 mm to 3.33 ± 0.3 mm, weight variation 289 ± 0.2 ± 0.004 to were within 12 h. Formulation F5 showed sustained drug release within 12 h in comparison to other formulation.

Stability studies were conducted for the F5 formulation at 40 °C/75% RH for 3 months. Various parameters like hardness, thickness, drug content, and dissolution rate were analyzed at a time interval of 1 month till the period of 3 months. Not much variation or change was observed in any parameters throughout the study period. Best formulation batch F5 drug content is 98% found to be stable.

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CONFLICTS OF INTEREST: Nil

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