FORMULATION AND EVALUATION OF CIPROFLOXACIN HYDROCHLORIDE EMULGEL USING DIFFERENT NATURAL OILS

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ABSTRACT

The study aimed to develop and assess Ciprofloxacin Emulgel formulations utilizing various natural oils, focusing on mustard oil's efficacy. Compatibility between Ciprofloxacin and excipients was evaluated via Fourier-transform infrared (FTIR). Emulgel formulations were subjected to comprehensive characterization encompassing physical appearance, pH, spreadability, drug content, microbial assessment, and in vitro diffusion study. FTIR analysis confirmed the compatibility of the drug and excipients, ensuring formulation stability. Notably, drug release from all emulgels adhered to Zero-order kinetics, with Higuchi Plots indicating Diffusion kinetics, indicating controlled and predictable release profiles. Mustard oil-based emulgel demonstrated enhanced drug release compared to counterparts formulated with other oils, suggesting its suitability for effective topical Ciprofloxacin delivery. This research underscores mustard oil's potential as a preferred component in formulating Ciprofloxacin emulgels, potentially enhancing their therapeutic efficacy in topical applications.

Key-Words: Ciprofloxacin, Emulgel, FTIR, Higuchi Plots, Topical Drug Delivery

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INTRODUCTION

Emulgels are the topical medication delivery systems that are created by blending gels and emulsions in the proper proportions. In order to turn an emulsion into an Emulgel.[1] Gelling agents are employed. While hydrophilic pharmaceuticals are encapsulated in water-in-oil systems, lipophilic medications are solubilized in oil-in-water systems. Emulsions can become more stable by being transformed into emulgel since they are thermodynamically instable.[2] Emulgels offer a number of benefits including a pleasing appearance, greaselessness, ease of spreading, washability, thixotropy, emollient action, non-staining, and a predicted shelf life.[3] Ciprofloxacin is fluoroquinolone with broad-spectrum antibacterial activity. ciprofloxacin is active on both actively dividing as well as dormant bacteria. The mechanism is by inhibition of bacterial DNA gyrase. ciprofloxacin has a wide range of antibacterial activity for the treatment of systemicas well as a local infection.[4] The half-life of ciprofloxacin is 3-5 hrs. ciprofloxacin is slightly soluble in water and methanol. It belongs to BCS class II drug with low solubility and high permeability. The objective of the present study is to formulate and evaluate ciprofloxacin emulgel using different oils.

MATERIALS AND METHODS

A free sample of ciprofloxacin was provided by PVS Labs in Vijayawada. Chemicals such as carbopol 940, different natural oils, span 80, tween 80, and propylene glycol 400 were bought from commercial sources.

Drug – Excipient Compatibility Study:

FTIR Spectrophotometer (BrukerATR Alpha -e, Germany) in KBr disc was used to determine the drug-excipient compatibility tests of ciprofloxacin and created emulgels.

Preparation of Emulgel:

The formula shown in Table 1 was used to create ciprofloxacin emulgels. A magnetic stirrer was used to stir ciprofloxacin (1%) in various oils for 10 minutes at 400–500 rpm. On a magnetic stirrer operating at 400–500 rpm, Span 80 was added while stirring. Tween 80 and propylene glycol were dissolved in water while being stirred with a magnetic stirrer at 400–500 rpm to create the aqueous phase. Then, while swirling continuously, the oil phase was combined with an aqueous phase. Carbopol 940 was dissolved in purified water with steady, moderately-speed swirling to create carbopol gel. By neutralizing the dispersion with triethanolamine and adjusting the pH to 5- 7, the gel was produced. The emulsion produced was combined in 1: 2 and 1: 1.5 ratios.[5]

Table.1: Formulation of Ciprofloxacin Gel and Emulsion

Ingredients(%)	CF 1	CF 2	CF 3	CF 4	CF 5	CF 6	CF 7	CF 8
Formulation of Emulsion								
Ciprofloxacin	1	1	1	1	1	1	1	1
Span 80	6	6	6	6	6	6	6	6
Oil	10	10	10	10	10	10	10	10
Tween 80	6	6	6	6	6	6	6	6
PropyleneGlycol	10	10	10	10	10	10	10	10
Methyl Paraben	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Propyl Paraben	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
Water	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.
Ethanol	2	2	2	2	2	2	2	2
Formulation of Gel								
Carbopol940	1.5	1.5	1.5	1.5	2	2	2	2
DistilledWater	100	100	100	100	100	100	100	100

CF1 and CF5: Neem Oil, CF2 and CF6: Ground nut Oil, CF3 and CF7: Sesame Oil, CF4 and CF8: Mustard Oil

Evaluation of Emulgel:

a) Spreadability:

An instrument recommended by Mutimer et al. was used to measure spreadability. The device, which is made of a wooden block with a pulley at one end, was modified. The block had a rectangular ground glass plate attached to it. Gel (approximately 2 g) was added to the lower plate and sandwiched between the lower and upper glass plates, which were both equipped with hooks and the same dimensions. To remove air and create a homogenous gel film, 500 mg of weight was placed on the tops of the two plates for five minutes. The extra gel was removed with a scraper. A 50 g pull was applied to the upper plate. The upper plate needed 10 seconds to travel the distance of 10 cm.

S = M x L/ T; Where, S= Spreadability , M=Weight tied to the upper slide, L=Length of the glass slide, T = time taken for plates to slide the entire length (sec).

b) *In-vitro* Diffusion Study:

The egg membrane was used in an in-vitro diffusion experiment in a Franz diffusion cell. In the space between the donor and receptor compartments, there was an egg membrane. The donor compartment received 1g of the gel. The receptor compartment, which held 25 ml of pH 6.8 phosphate buffer, was in touch with the membrane's whole surface. A magnetic stirrer operating at 50 revolutions per minute stirred the donor cell's contents while maintaining a 37-1°C temperature. 2 ml were taken out and replaced with an equivalent volume of fresh, pH 6.8 phosphate buffer at intervals of 15, 30, 60, 120, 180, 240, 300, 360, 420, and 480 minutes. Samples were assessed using a 276 nm absorbance measurement.[6]

c) Release Experiment / Model dependent method:

Drug release from emulgels was examined using Higuchi's kinetic, zero order, and first order models.[7]

d) Zone of Inhibition:

Utilizing this method, one can investigate the compound's bacteriostatic properties. Eight agar plates containing the Escherichia coli and Bacillus subtilis strains were used to assess the Zone of Inhibition caused by Ciprofloxacin emulgels. In this investigation, agar medium and cup plate technique were employed. Bacillus subtilis and Escherichia coli were injected into the clean agar media plates after growing in culture overnight. The production of the single-cup and the filling of the cups with gels in each agar plate. Distilled water was applied consistently. A total of 24 hours were spent incubating the eight agar plates. The zone of inhibition was measured after 24 hours of watching the plates.[8]

RESULTS AND DISCUSSION

FTIR spectra are used to assess the drug excipient compatibility of ciprofloxacin with excipients. The spectra are displayed in Figures 1 and 2.[9] Ciprofloxacin exhibited the characteristic peaks listed in Table 2.

Table. 2: Peaks observed in FTIR spectra of Ciprofloxacin.

PROMINENT PEAK (cm^{-1})	REASON
3050 & 3000	Due to stretching vibrations of hydroxyl group and inter molecular hydrogen bonding: presence of –NH stretching vibrations.
2700	Presence of –CH3 of methyl group.
1750-1700	Presence of acidic carbonyl C=O stretching
1650-1600	Due to N-H bending vibration of quinolones.
1550-1500	Corresponds to CH2 of aromatic ring.
1450-1400	Due to stretching vibrations of CH2; Presence of methylene group in benzoxazine
1400-1350	Due to bending vibration of hydroxyl group.
1250-1200	Due to stretching vibrations of oxo group.
1050-1000	This strong absorbance peak is due to C-F group.
900-800	Due to plane bending vibrations of double bond ‘enes’ or =CH group.

Drug peaks did not significantly change in the drug and excipient mixture's spectra. It can be inferred from this that there was no discernible interaction between the study's excipients and the medicine.

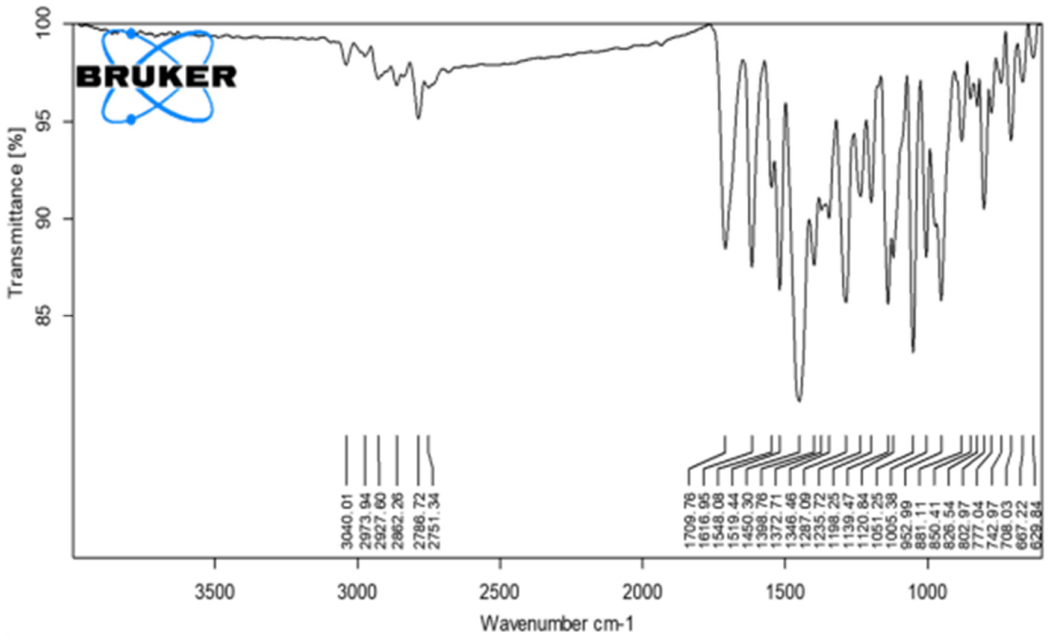


Fig. 1: FTIR spectra of Ciprofloxacin HCl

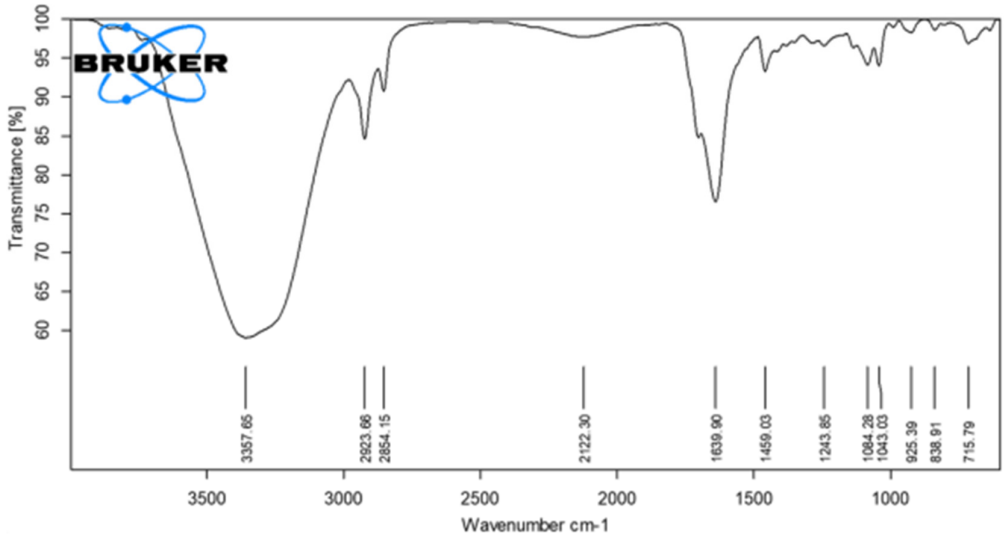


Fig. 2: FTIR Spectra of Ciprofloxacin Emulgel Containing 2% of Carbopol 940

Evaluation of emulgel

Emulgels were discovered to be yellowish, white, thick, creamy formulations with a smooth, uniform texture, and glossy appearance without grittiness or phase separation. There was no physical separation of the emulsion from the emulgel, and the prepared emulgels were discovered to be stable. Table 3 presented the outcomes. The prepared emulgels were tested for pH, spreadability, and drug content. The results are shown in Table 4 and Fig.3, and the pH of the prepared emulgel formulation was found to be in the acceptable range for topical medicines, which is between 5.5 and 6.8. The formulation's spreadability was determined to be in the range of 23.87-75.55 g.cm/s. The spreadability investigations showed that spreadability reduces as the gelling agent concentration rises. When compared to Bacillus subtilis (gram +ve bacteria) ciprofloxacin emulgels were found to be more efficient against E. coli (gram -ve bacteria),Table 5 and Figs. 4 and 5 contain the results. The viscosity of the emulgel increases and the zone of inhibition decreases with increase in carbopol content.[10-12]

Table:3: Physical Characteristics of Ciprofloxacin Emulgel

Formulation	Colour	Phase separation	Grittiness
CF1	Yellowish White	No	None
CF2	Yellowish	No	None
CF3	White	No	None
CF4	Yellowish	No	None
CF5	White	No	None
CF6	Yellowish	No	None
CF7	White	No	None
CF8	Yellowish	No	None

Table 4: Evaluation Parameters of Emulgel Preparations

Batch	CF1	CF2	CF3	CF4	CF1	CF2	CF3	CF4
pH	6.8	5.8	6.4	6.2	5.5	6.0	5.6	5.8
Spreadability (g.cm/s)	33.30	55.55	23.87	65.55	45.23	60.08	30.83	75.55
Drug content (%)	97.64	98.22	98.57	98.80	97.64	94.31	96.31	95.28

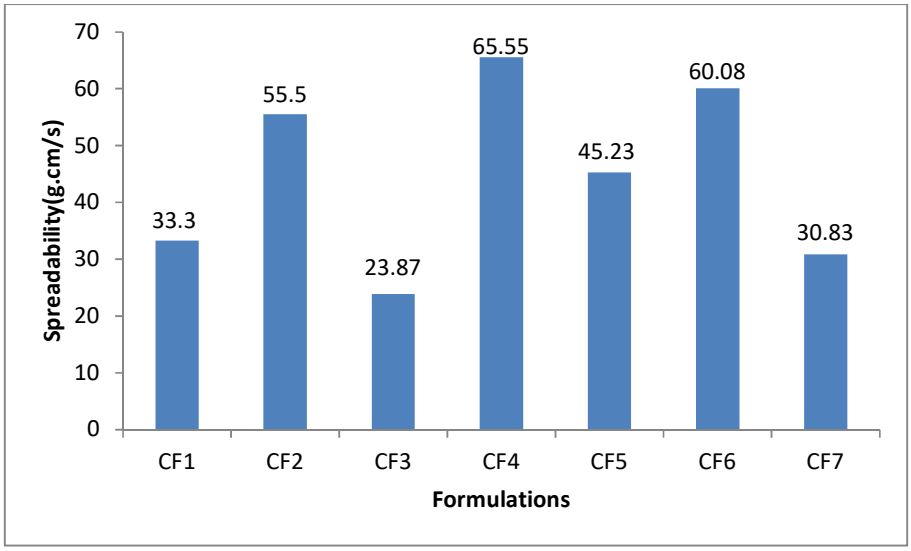


Fig. 3: Spreadability of Ciprofloxacin Emulgel Preparations

Table 5: Zone of Inhibition Obtained from Ciprofloxacin Emulgel Formulations

Zone of inhibition of emulgel formulation		
Formulation	**Bacillus subtilis (cm)**	***E. coli* (cm)**
CF1	5.2	5.6
CF2	4.3	4.8
CF3	4.1	4.7
CF4	3.9	4.4
CF5	5.0	5.4
CF6	4.0	4.9
CF7	4.2	4.7
CF8	3.8	5.0

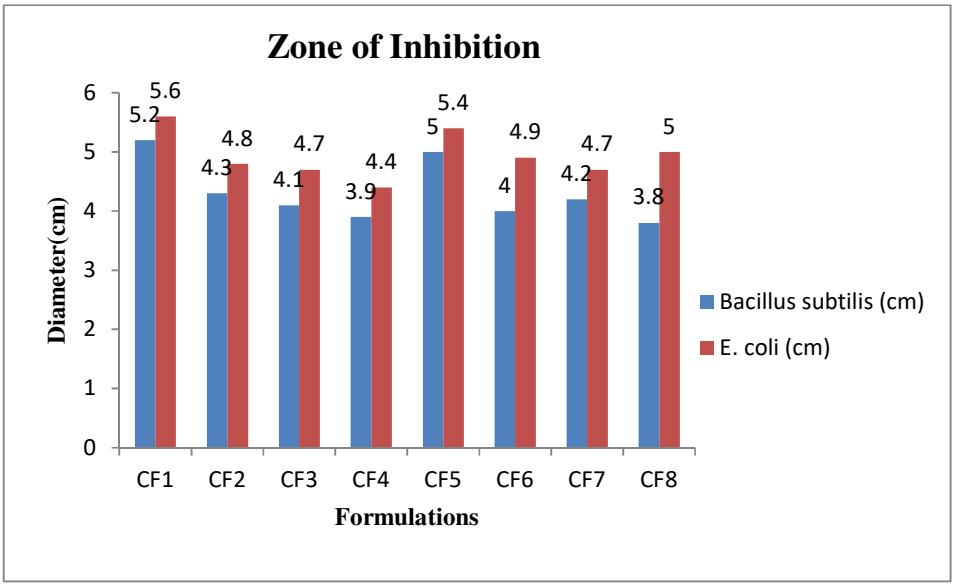
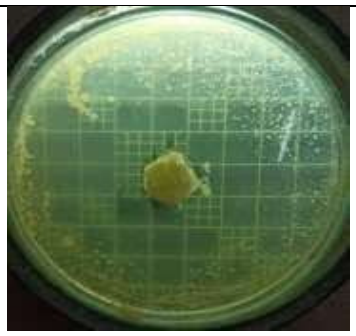
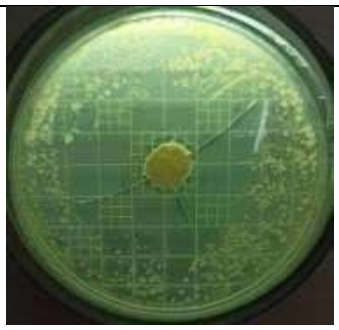
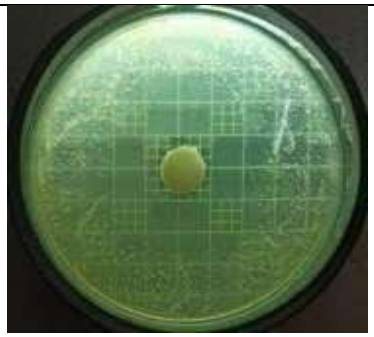
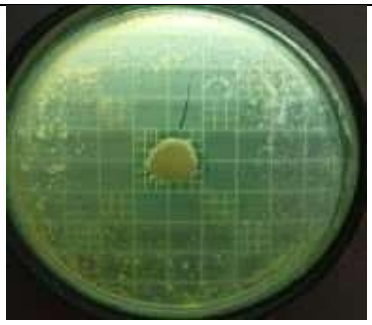
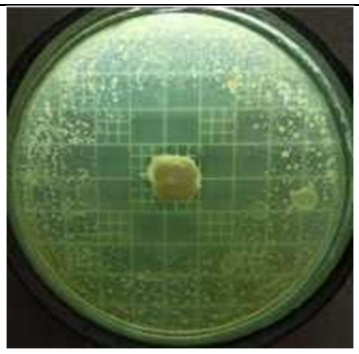
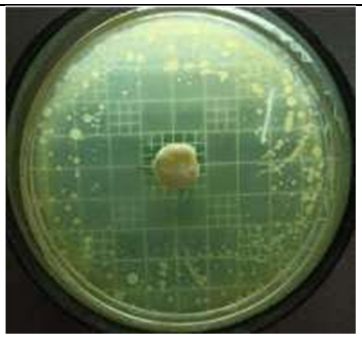
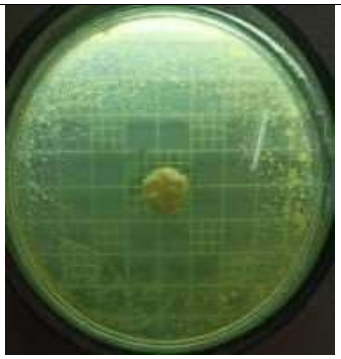
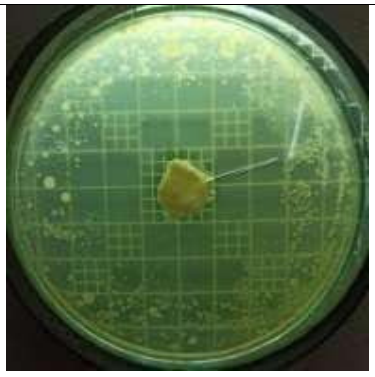


Fig. 4: Zone of Inhibitions of Ciprofloxacin Emulgel preparations

	
CF 1 – Neem Oil	**CF 1 – Neem Oil**
	
CF 2 – Sesame Oil	**CF 2 – Sesame Oil**
	
CF 3 – Groundnut Oil	**CF 3 – Groundnut Oil**
	
CF4 – Mustard Oil	**CF4 – Mustard Oil**

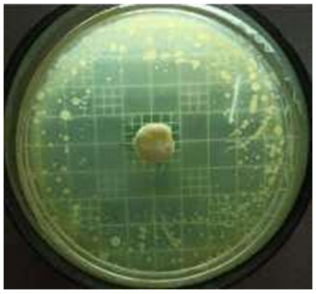
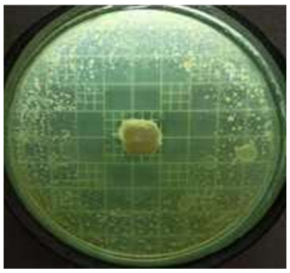
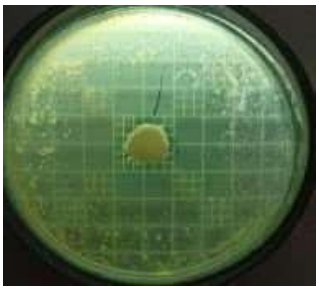
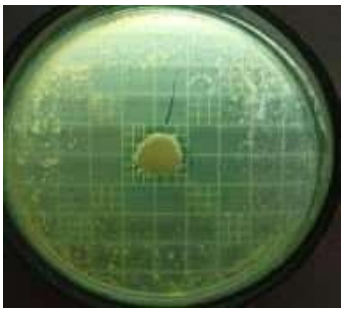
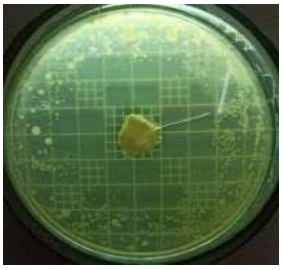
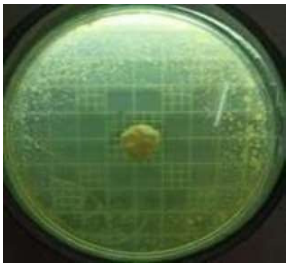
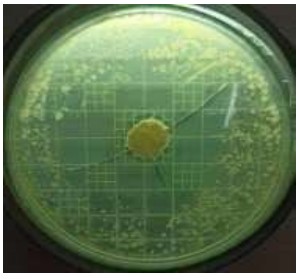
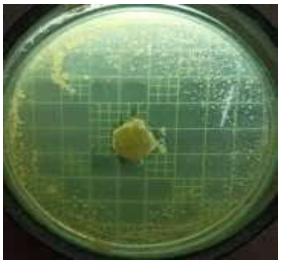
	
CF 5 – Neem Oil	**CF 5 – Neem Oil**
	
CF 6 – Sesame Oil	**CF 6 – Sesame Oil**
	
CF 7 – Groundnut Oil	**CF 7 – Groundnut Oil**
	
CF 8 – Mustard Oil	**CF 8 – Mustard Oil**

Fig. 5: Zone of Inhibitions of Ciprofloxacin Emulgel Preparations

In vitro drug release study

The in vitro release characteristics of ciprofloxacin from its various emulgel formulations are shown in figure. 6. The better drug release from all emulgel formulations, as can be seen from the figures, is a common trend. Depending on the amount of Carbopol, the rate of drug release varied. When the formulations CF1 through CF4 were made using 1.5% carbopol, the drug was released quickly. CF5 to CF8 formulations had sluggish drug release since they used 2% carbopol in their formulation. The Franz diffusion cell in vitro diffusion assays showed that CF4 released the medication more effectively than the other formulations. The in vitro ciprofloxacin release data were fitted to the Korsmeyer-Peppa release model, and the interpretation of release exponent values (n) enlightens us in comprehending the complex mechanism of drug release from the emulgel. The values of the release exponents thus found ranged from 0.585 to 0.754. The equation showed non-fickian transport based on these parameters. Since the plot of Higuchi's model was found to be linear (R2>0.943), the drug release was diffusion-controlled. The formulations had greater R2 values for the zero-order plot, as shown in Table 6, which suggested that zero order kinetics applied to drug release. When compared to emulgels made with other oils, those made with mustard oil (CF4) showed a larger release.

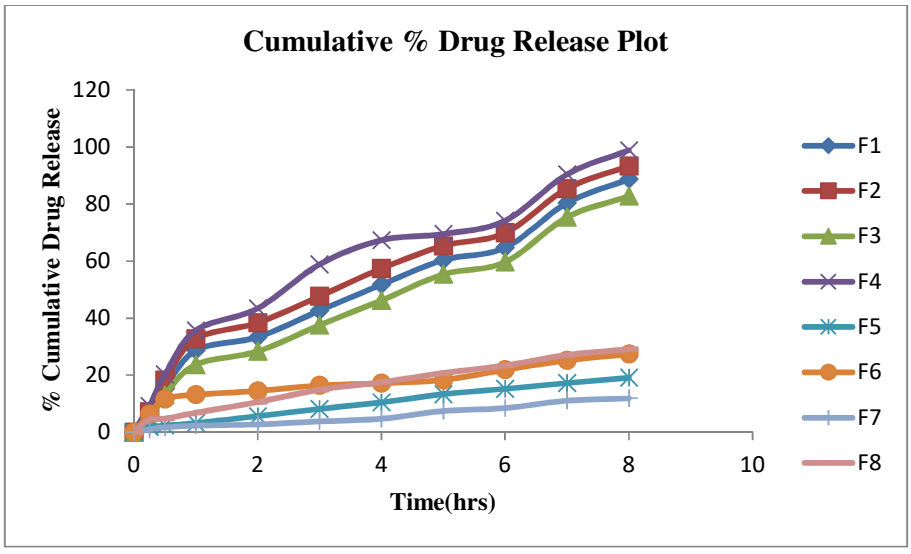


Fig. 6: Percentage release plot of ciprofloxacin HCl Emulgel

Table 6: Co-efficient of Determination(r^2) Values as per zero order , first order, higuchi and peppas plots

Formula	Zero order	First order	Higuchi Plot	Peppas Plot
F1	0.984	0.963	0.986	0.976
F2	0.979	0.949	0.990	0.979
F3	0.989	0.972	0.982	0.978
F4	0.967	0.885	0.992	0.983
F5	0.998	0.997	0.977	0.990
F6	0.943	0.933	0.970	0.958
F7	0.987	0.986	0.943	0.971
F8	0.996	0.992	0.988	0.985

CONCLUSION

Carbopol 940 and mustard oil were used to create a ciprofloxacin emulgel that is stable, attractive, and efficient. In-vitro drug release and viscosity results for Ciprofloxacin Emulgel were favorable. Emulgel functions as a drug repository that gradually releases the medicine at the applied spot. Therefore, it is advised to use mustard oil and carbopol 940 for creating ciprofloxacin emulgels for effective topical drug delivery.

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