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Formulation and *in vitro* Evaluation of Piroxicam Emulgel

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ABSTRACT

The present work is concerned with the formulation and evaluation of Piroxicam emulgel employing carbopol 934 and xanthan gum as polymers. The emulgel is prepared by combining the gel and emulsion. The gel in formulations were prepared by dispersing Carbopol 934 and xanthan gum separately in purified water with constant stirring at a moderate speed and then the pH was adjusted to 4 to 5.4 using Tri-ethanol amine (TEA). The oil phase in the emulsion consists of oleic acid and span-80. The aqueous phase in the emulsion was prepared using Tween-80, propylene glycol and distilled water. The prepared emulgel formulations were subjected to evaluation studies like Physical appearance, rheological studies, estimation of drug content and *in-vitro* drug release. The appearance of prepared emulgel was white. The pH of the emulgel was found to be 5.4. The *in vitro* drug release studies revealed that formulation F1 showed 85.20% and formulation F2 showed 79.23% of drug release at the end of 8 hrs. The drug release of F1 formulation follows zero order kinetics.

Keywords: Piroxicam, Emulgel, Carbopol, Xanthan gum.

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INTRODUCTION

Emulgel as the name suggests they are the combination of gel and emulsion. In order to deliver the drugs to the skin, both oil-in-water and water-in-oil type of emulsions are used as vehicles. They additionally have a high capacity to infiltrate the skin. The nearness of gelling agent in water stage changes over an established emulsion into an emulgel. Emulgel for

dermatological utilize have a few great properties, for example, being thixotropic, greaseless, effortlessly spreadable, effectively removable, emollient, non-recoloring, water dissolvable, longer shelflife of realistic usability, bio agreeable, and satisfying appearance. ^[1] Piroxicam is an NSAID with pain relieving and antipyretic impacts, utilized for the treatment of rheumatoid joint inflammation, osteoarthritis and

horrendous wounds. It is very much retained after oral absorption anyway its utilization has been related with various bothersome reactions on the stomach and kidneys. [2] Dermal conveyance is an elective route however requires a suitable dosage form which guarantees profound skin penetration, permitting helpful impact at particular site. Despite the fact that piroxicam is not effortlessly consumed after topical application, a few investigations have been completed to foresee the percutaneous retention of piroxicam utilizing distinctive substances as penetration enhancers. Numerous broadly utilized topical preparations like ointments, creams, have various disadvantages. [3] Semisolid preparations like ointments are normally sticky, making uneasiness to the patient when used topically. Additionally they likewise have less spreading coefficient and need to apply with rubbing. They additionally display the issue of stability. Because of every one of these variables, inside the real gathering of semisolid dosage forms, the utilization of transparent gels has expanded both in beauty care products and in pharmaceutical products. A gel is colloid that is normally 99% by weight fluid, which is immobilized by surface tension amongst it and a macromolecular system of strands worked from a little measure of a gelating substance. Despite numerous favourable circumstances of gels a noteworthy constraint is the incapability of transporting hydrophobic medications. To defeat this restriction an emulsion based approach is being utilized so a hydrophobic moiety can be effectively fused and conveyed through gels. Whenever gels and emulsions are consolidated together the dosage forms are specified as emulgels. [3-4]

MATERIALS AND METHODS

Materials

Piroxicam was received as a gift sample from HETERO Drugs limited Hyderabad. Carbopol 934 and Xanthan gum were purchased from Loba chemicals. Tween 80, Span 80, Oleic acid, Propylene glycol, Cetostearyl alcohol, Propyl paraben, Xanthan gum, Tri-ethanol amine (TEA) and Distilled water purchased from Himedia. All chemicals used were of analytical grade.

Methodology

Pre formulation study includes API characterization, Standard graph, Compatibility studies.

API characterization

Organoleptic properties

Organoleptic properties the drug such as description, color, odor, taste of the drug were studied.

Fourier-Transform Infrared Spectroscopy (FTIR)

KBr pellet method

Infrared spectra of pure drug and mixture of drug and excipients were recorded by KBr method by using Fourier transform infrared spectrophotometer. In the present study, the potassium bromide disc method was employed. The powdered sample was intimately mixed with dry powdered potassium bromide. This mixture

was then compressed in to transparent disc under high pressure using special dies. This disc was placed in IR spectrometer and spectrums were recorded. The scanning range was 400-4000 cm^{-1} and the resolution was 1 cm^{-1} .

Preparation of Standard graph

An accurately weighed amount of 100 mg of drug was transferred separately into 100 ml volumetric flask and then the volume was made up to the mark with buffer. From the stock solution, several drug concentrations were prepared using phosphate buffer (pH 7.4) and were analyzed at 240 nm and calibration curve was plotted taking concentration on x-axis and absorbance units on y-axis [5] as per the method reported by Sindhuri *et al.*, (2017). The graph was shown in the Figure 2.

Methods

Preparation of gel base F1 by using Carbopol

Carbopol is dissolved in distilled water using mechanical stirrer at optimum rpm and TEA is added to adjust the pH. Carbopol is pH sensitive polymer forms gel in particular pH.

Preparation of emulsion

Oil phase

Span 80 was dissolved in oleic acid and piroxicam was added to the above phase.

Aqueous phase

Tween 80 is dissolved in distilled water, Propyl paraben is dissolved in propylene glycol separately and both are mixed. Heat both the phases separately to 70-80°C. Mix both phases slowly at the constant stirring until cooled to room temperature, which results in formulation of o/w emulsion.

Preparation of emulgel

Emulsion and Gel base are mixed in 1:1 proportion with constant stirring, which results in piroxicam emulgel.

Preparation of gel base F2 by using Xanthan gum

Xanthan gum is dissolved in distilled water using mechanical stirrer at optimum rpm, TEA is added to adjust the pH. Carbopol is pH sensitive polymer forms gel in the pH range of 4-6.

Preparation of emulsion

Oil phase: Span 80 was dissolved in oleic acid and piroxicam was added to the above phase.

Aqueous phase: Tween 80 was dissolved in distilled water and propyl paraben was dissolved in propylene glycol separately as per the composition in the formulation and both are mixed.

Both the phases are heated separately to 70-80°C and then mixed slowly with constant stirring until cooled down to room temperature, which results in formulation of o/w emulsion.

Preparation of emulgel

Emulsion and Gel base are mixed in 1:1 proportion with constant stirring, results in piroxicam emulgel as per the method reported by Mohamed M (2004). [6] The flow charts of emulgel were shown in Figure 1.

Evaluation Parameters

Physical appearance

The prepared emulgel formulations were inspected visually for their color, homogeneity, consistency and pH. The pH values of 1% aqueous solutions of the prepared gellified emulsions were measured by pH meter (Digital pH meter).^[7]

Rheological Study

The viscosity of the different emulgel formulations was determined at 25°C using a cone and plate viscometer with spindle 52 (Brookfield Engineering Laboratories,) which is connected to a thermostatically controlled circulating water bath.^[8]

Drug Content Determination

Drug content in gellified emulsion was measured by spectrophotometer by dissolving known quantity of gellified emulsion in methanol with the aid of sonication. Absorbance was measured after suitable dilution in UV/VIS spectrophotometer.^[8-9]

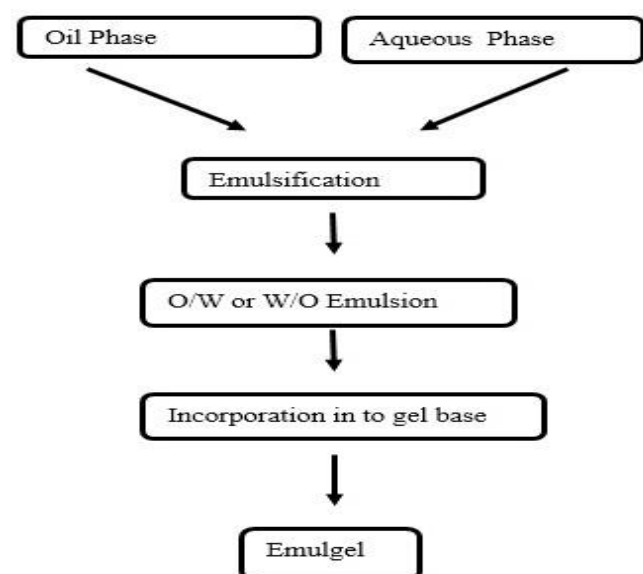


Fig. 1: Flow chart of emulgel preparation

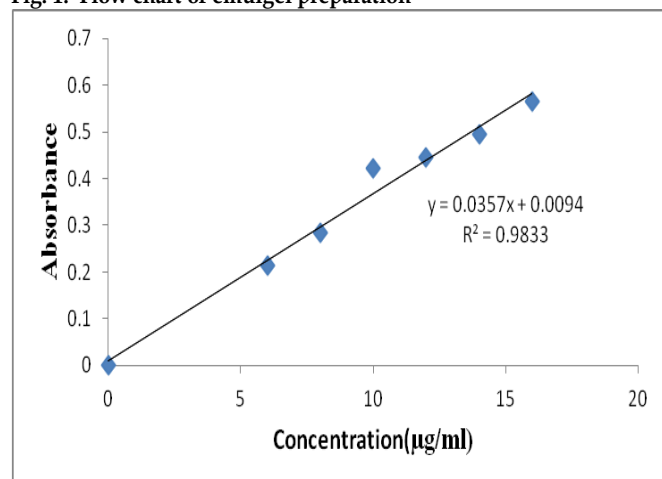


Fig. 2: Standard graph of piroxicam

In vitro drug Release Study

Franz diffusion cell (with effective diffusion area 3.14 cm² and 15.5 ml cell volume) was used for the drug release studies. Gellified Emulsion (500 mg) was applied evenly to the surface of egg membrane which

was clamped between the donor and the receptor chamber of diffusion cell. The receptor chamber was filled with freshly prepared PBS (pH 7.4) solution to solubilize the drug. The receptor chamber was stirred by magnetic stirrer. The samples (1.0 ml aliquots) were collected at suitable time intervals. Samples were analyzed for drug content by UV/VIS visible spectrophotometer after appropriate dilutions. The cumulative amount of drug released across the egg membrane was determined as a function of time.^[10-11]

Table 1: Composition of emulgel formulation F1 & F2 (by using carbopol & xanthan gum)

S. No	Ingredients	% w/w (F1)	% w/w (F2)
1	Piroxicam	0.5	0.5
2	Oleic acid	20	20
3	Propylene glycol	5	5
4	Cetostearyl alcohol	4	4
5	Span 80	2.8	2.8
6	Tween 80	1.1	1.1
7	Carbopol 934	0.5	-
8	Xanthan gum	-	0.5
9	Propyl paraben	0.02	0.02
10	Triethanolamine	Qs	Qs
11	Water	76	76

Table 2: *In vitro* drug release profile

S. No	Time (hours)	<i>In vitro</i> drug release $\pm$ SD	
		F1 $\pm$ SD	F2 $\pm$ SD
1	1	7.02 $\pm$ 0.1	6.20 $\pm$ 0.01
2	2	17.64 $\pm$ 0.7	15.32 $\pm$ 0.1
3	3	23.54 $\pm$ 0.8	26.40 $\pm$ 0.2
4	4	41.43 $\pm$ 0.9	30.90 $\pm$ 0.25
5	5	50.26 $\pm$ 0.99	42.61 $\pm$ 0.35
6	6	57.49 $\pm$ 0.42	50.31 $\pm$ 0.42
7	7	72.81 $\pm$ 0.35	60 $\pm$ 0.59
8	8	85.20 $\pm$ 0.38	79.23 $\pm$ 0.66

Table 3: Drug release kinetics of F1 & F2 formulations

Formulation	R ² value					
	Zero order	First order	Higuchi	Hixon crowell	Korsemeyer peppas n value	
F1	0.9908	0.9105	0.966	0.9777	0.9786	0.3068
F2	0.9828	0.8711	0.945	0.978	0.938	0.2903

RESULTS

Evaluation parameters

Physical examination

Color-White

Odour- mentholic

Phase separation-No

Rheological study

The preparation is stable and free from grittiness. The viscosity of the emulgel formulation F1 was found to be 28790cp and F2 formulation was found to be 25681cp.

Measurement of pH

pH of the emulgel preparation was found to be 5.4, which is in the normal pH range (4 - 5.5) of skin and would not produce any skin irritation.

Drug content

The drug content of the formulated emulgel was estimated spectrophotometrically at 240 nm. The results for F1 were found to be 99.5% in 1.0 g gel.

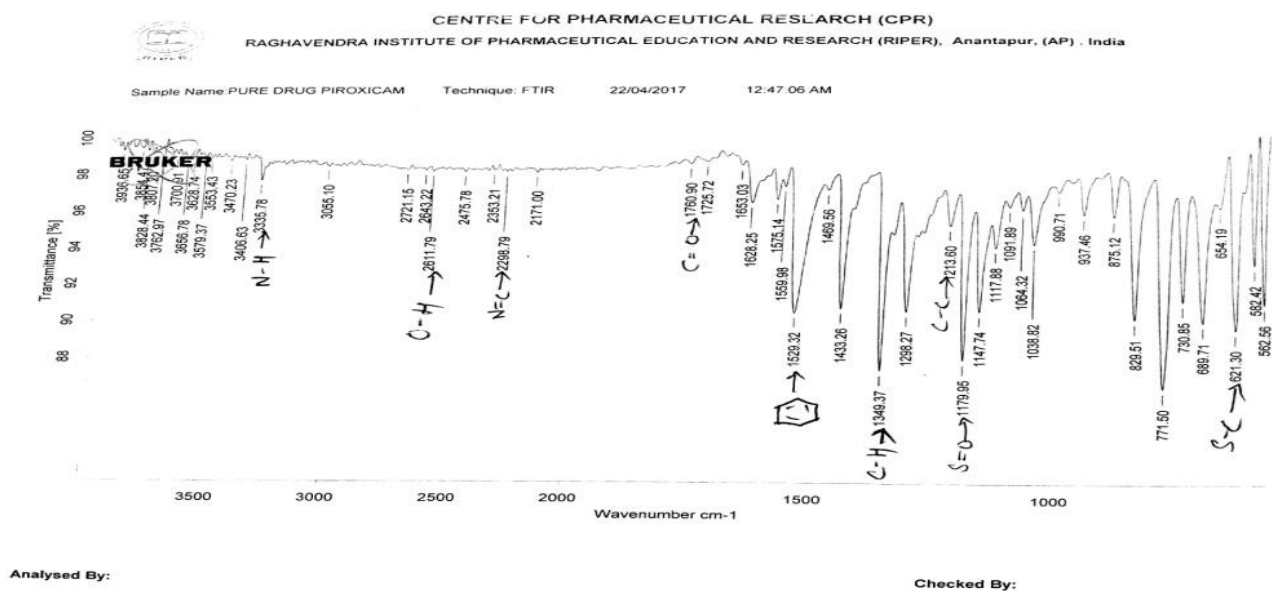


Fig. 3: (FTIR) Spectrum for Piroxicam

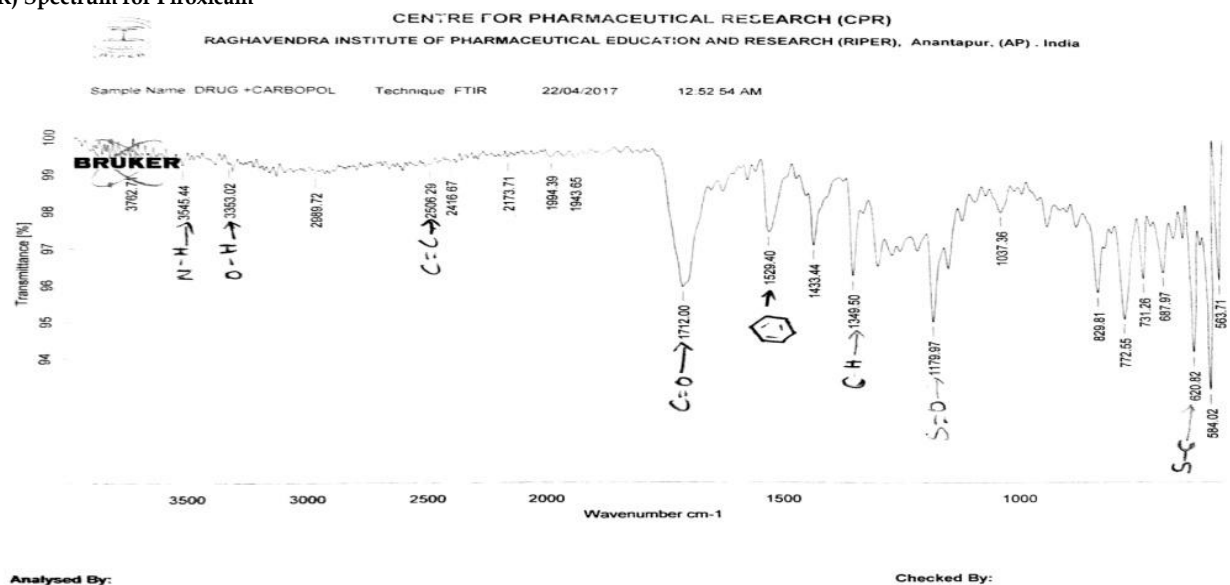


Fig. 4: (FTIR) Spectrum for Piroxicam + Carbopol (F1)

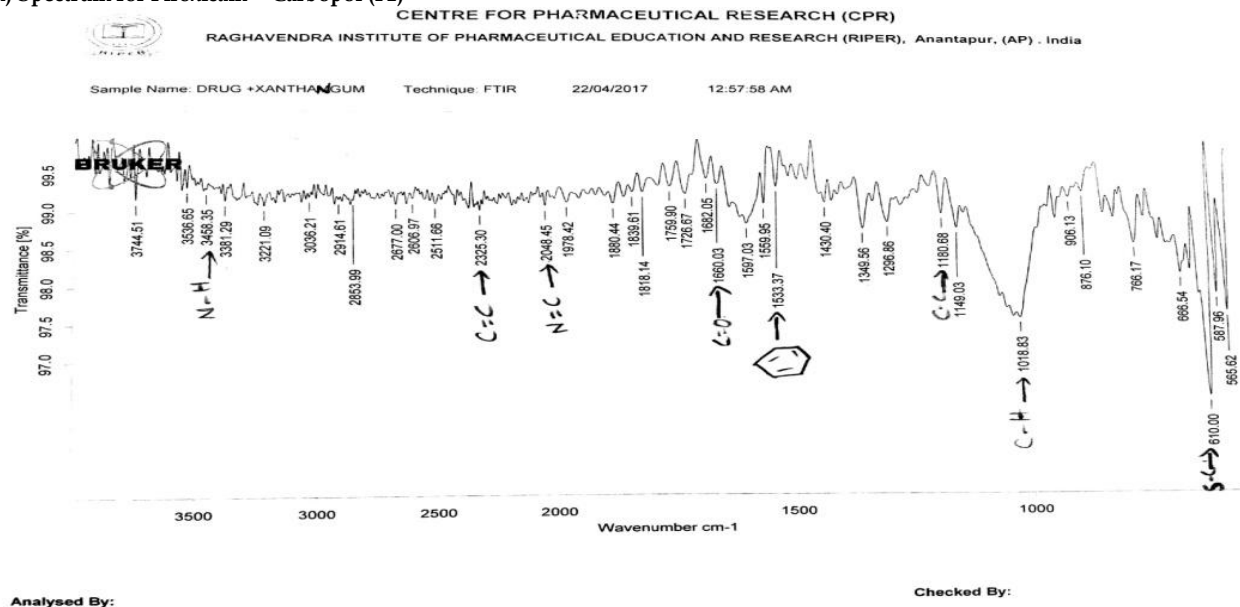


Fig. 5: (FTIR) Spectrum for Piroxicam + Xanthan gum (F2)

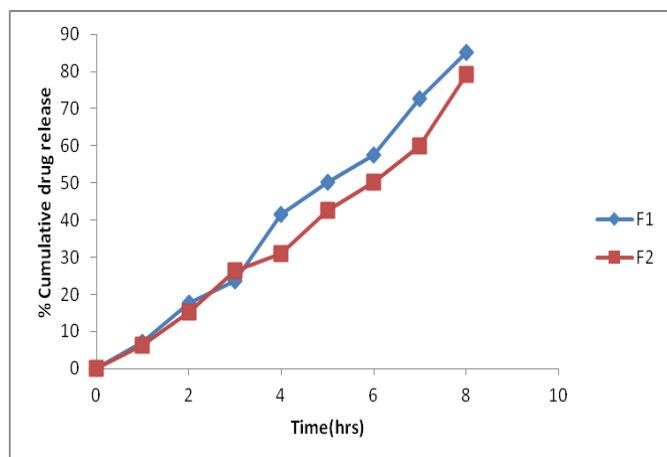
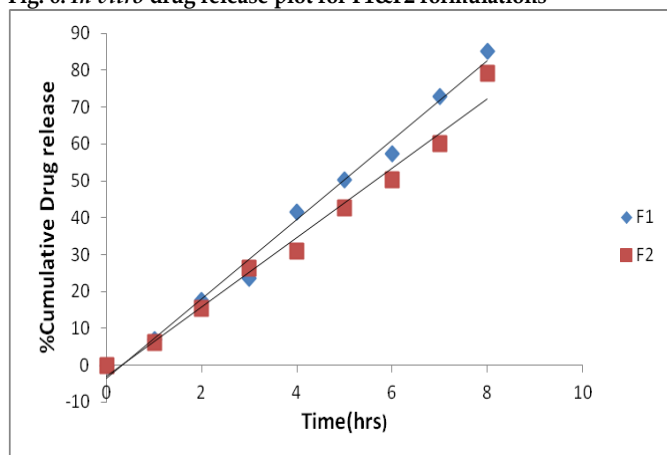
Fig. 6: *In vitro* drug release plot for F1&F2 formulations

Fig. 7: Zero order plot for F1&F2 formulations

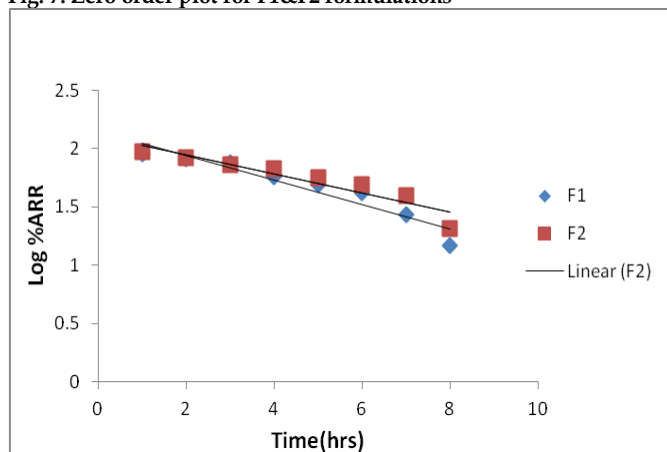


Fig. 8: First order plot for F1&F2 formulations

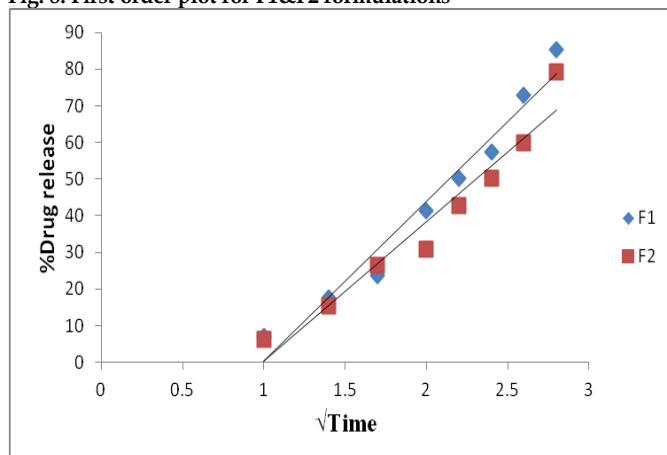


Fig. 9: Higuchi plot for F1&F2 formulations

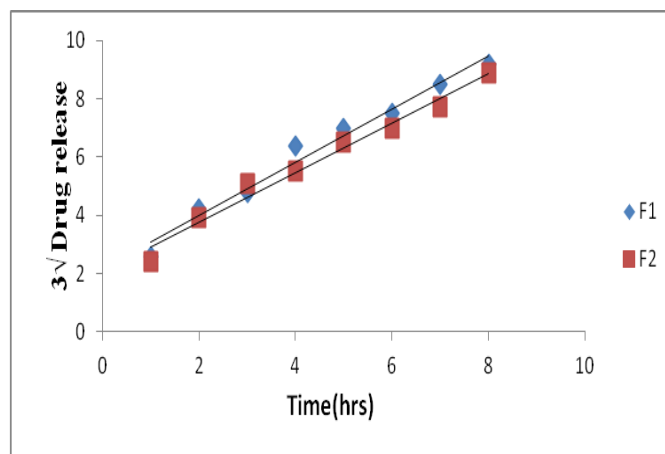


Fig. 10: Hixon crowell plot for F1&F2 formulations

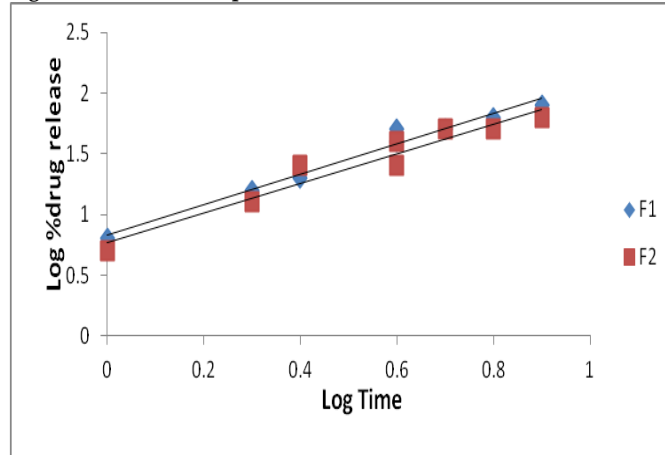


Fig. 11: Korsemeyer peppas plots for F1&F2 formulations

In vitro drug Release Study

The *in-vitro* drug release for the prepared emulgels was evaluated using phosphate buffer pH 7.4 for 8 hrs as per the method reported by Preeti *et al.* [11] and results were tabulated in Table 2 and Figure 6 and 7.

The drug release data of all the formulations was fitted to various kinetic models like Zero order, first order, Higuchi, Hixoncrowell and Korsemeyer peppas were shown in Figure 7-11 respectively, the data was obtained linear for Zero order kinetics. The correlation coefficient values (R^2) of different kinetic models are given in the Table 3.

DISCUSSION

From the literature survey Piroxicam belongs to BCS class-II. [12] From the pre-formulation studies the drug was identified as pure drug. The calibration curve of Piroxicam was constructed by using UV/VIS spectrophotometer in phosphate buffer pH 7.4. The curve was shown in the Figure 2 and there is an increase in the absorbance with an increase in the concentration range of 6-16 $\mu\text{g/ml}$ with the R^2 value is 0.9833.

The results of Drug-Excipients interaction revealed that addition of excipients does not affect the stability of drug. The FTIR Spectrum of drug and combination of excipients were showed in Figures 3, 4, 5 which are compatible with respect to the formulation. The IR spectrum showed that extra peaks were not observed

and functional groups were not shifted when drug mixed with the excipients, which supports that drug is stable in all formulations indicating that there is no interaction between drug and excipients. The prepared formulations were stable in terms of stability and free from grittiness i.e., without any particulate matter. The viscosity of the emulgel F1 formulation was found to be 28790cp and for F2 formulation was found to be 25681cp.

The drug content of the formulated emulgel was estimated spectrophotometrically at 240 nm. The results of F1 formulation were found to be 99.5% and F2 formulation was found to be 95.5% in 1.0 g gel. From the r^2 values, the diffusion of the drug from the emulgel through the membrane follows zero order kinetics. Formulation F1 showed maximum drug release i.e., 85.20% at the end of 8 hours and followed zero order kinetics.

The topical emulgel of piroxicam was prepared successfully by using Carbopol934 and Xanthan gum as polymers. The prepared emulgel was subjected to physicochemical studies. The *in vitro* studies revealed that formulation F1 showed 85.20% and formulation F2 showed 79.23% of drug release at the end of 8 hrs. The drug release of F1 formulation follows zero order kinetics as the R^2 value of zero order kinetics of F1 formulation is more than the R^2 value of first order kinetics and also the release rate is independent of the concentration of the drug. Hence it can be concluded that piroxicam was a suitable drug candidate for formulating emulgel as topical delivery to achieve better patient compliance.

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