Original Article

Preparation, characterization, and stability studies of piroxicam-loaded microemulsions in topical formulations

Fathy I. Abd-Allah*, Hamdy M. Dawaba, Ahmed M. S. Ahmed

Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Al-Azhar University, Nasr City, Cairo, Egypt.

ABSTRACT: The main purpose of this work was to determine the *in vitro* release of piroxicam in microemulsion formulations from different pharmaceutical topical preparations including different gel bases, such as, methyl cellulose (MC), carboxy methyl cellulose (CMC), hydroxypropyl methyl cellulose (HPMC), Carbopol 934, Carbopol 940, and Pluronic F-127 bases. The effect of the employed gel bases on the *in vitro* release profiles of piroxicam was examined to choose the base which gave the highest *in vitro* release. The kinetic treatments and parameters derived from *in vitro* release of piroxicam formulations were calculated according to different kinetic orders or systems. These gel formulations were selected for rheological and stability studies. Stability studies were conducted to investigate the change in drug content, viscosity, and pH of the semisolid formulations. The results showed that, the incorporation of piroxicam in microemulsion formulas could lead to enhancement of piroxicam release profiles by allowing constant and regular *in vitro* release. Three percent MC gel base showed the highest release of piroxicam-microemulsion after 180 min (97.70%) followed by 3% HPMC (94.0%) when compared to bases containing piroxicam alone. All the medicated gel bases containing piroxicam exhibit pseudoplastic flow with thixotropic behavior. The degradation of piroxicam from its topical formulations was found to be a zero-order reaction based on the mean value of correlation coefficients. All formulations were quite stable. The shelf life of the gel containing HPMC base was about 2.85 years. Considering the *in vitro* release, rheological properties and shelf life, HPMC gel base containing 0.5% piroxicam in a microemulsion formula was the best among the studied formulations.

**Address correspondence to:*
Dr. Fathy Ibrahim Abd-Allah, Pharmaceutics Department, Faculty of Pharmacy (Boys), Al-Azhar University, Cairo, Egypt.
e-mail: Fathy_fet@hotmail.com

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1. Introduction

Piroxicam is a non steroidal anti-inflammatory drug (NSAID) that exhibits anti-inflammatory, anti-rheumatoid arthritis (*1*), analgesic (*2*), and antipyretic activities in animal models. Piroxicam like other non steroidal anti-inflammatory drugs causes side-effects on the gastro-intestinal system and other systems of the body. Piroxicam has a number of undesirable physicochemical properties including its poor solubility in water (*3*). Various strategies have been used to overcome the problems arising from its poor aqueous solubility and to improve bioavailability. Among these strategies were the use of penetration enhancers and a prodrug approach (*4*). Thus for this reason, topical administration of piroxicam have been studied as a way to minimize these side effects.

Microemulsions which are optically isotropic and thermodynamically stable systems of water, oil, surfactant and cosurfactant, have been studied as drug delivery systems because of their solubilization capacity for poorly water soluble drugs as well as their enhancement effects on topical and systemic availability. For example, oral microemulsion formulations have been successfully developed for cyclosporine, a highly lipophilic and poorly aqueous soluble drug for improving oral absorption and reducing absorption variation (*5,6*).

It is considered that the improved absorption from microemulsions is due to incorporation of drug into microemulsion droplets, the smaller size of microemulsion droplets, the increased specific surface area, and the increased membrane permeability towards the drug *via* solubilization of certain membrane components and pore formation. All these factors resulted in enhancing contact with the gastro-intestinal tract. Another important factor is the inner polarity of droplets governed by the hydrophilic lipophilic balance of surfactant used. The change in droplet polarity

affects the arrangement of drug and surfactant on the droplet interface and alters drug transdermal (*9*), and parenteral drug delivery systems (*10*). A very few studies have reported the use of microemulsions as nasal drug delivery systems (*11*).

There are different types of topical administration including ointments, creams, and gel preparations. Gels are semisolid preparations containing large proportions of water. They are used pharmaceutically as lubricants and also used as carriers for many drugs because of their local effects and percutaneous absorption (*12*). Gels are particularly suitable for water soluble medicaments and are less satisfactory for insoluble substances which are often difficult to be incorporated uniformly. They are easy to be applied and the evaporation of the water content produces a pleasant sensation. The residual film usually adheres well and gives protection but it is easily removed by washing when the treatment is complete (*13*).

Some of the gelling agents are available in different grades with a different viscosity at a definite concentration (*14*). According to the nature of the colloidal properties, gel bases are classified into: inorganic gel bases, *e.g.* Bentonite magma; organic gel bases which were further subdivided according to the nature of the dispersed organic molecule (*15*), polypeptides, *e.g.* gelatin; synthetic block copolymers, *e.g.* poloxamers (*16*), and semi-synthetic polymers, *e.g.* effective cellulose derivatives including sodium carboxy methyl cellulose (CMC), hydroxyl propyl cellulose and hydroxyl propyl methyl cellulose (HPMC) (*17,18*).

The objective of this study was to determine the *in vitro* release of piroxicam in microemulsion formulations from different pharmaceutical topical preparations including different gel bases such as methyl cellulose (MC), CMC, HPMC, Carbopol 934, Carbopol 940, and Pluronic F-127 bases. The effect of the employed gel bases on the *in vitro* release profiles of piroxicam was studied to choose the base which gave the highest *in vitro* release. The kinetic treatments and parameters derived from the *in vitro* release of piroxicam formulations were calculated according to different kinetic orders or systems. These gel formulations were selected for rheological and stability studies. Stability studies were conducted to see the change in drug content, viscosity, and pH of the semisolid formulations. Finally, the composition of the formulation with best overall properties was determined.

2. Materials and Methods

2.1. *Materials*

Piroxicam (Batch No. 20030202) and CMC were purchased from El-Nasr Pharmaceutical Chemicals (Cairo, Egypt). Methyl cellulose, HPMC, triethanolamine (TEA), and Pluronic F-127 were from Sigma-Aldrich (St Louis, MO, USA). Carbopol 934 and 940 were from Goodrich Chemical Co. (London, England). All other materials were of analytical grade and they were used without any further purification.

2.2. *Microemulsion formulation and phase diagram construction*

The selected oil (oleic acid), surfactant (Tween-80) and cosurfactant (propylene glycol) from the solubility studies (*22*) were used in this method. The microemulsion domains were distinguished using the corresponding phase diagrams. The microemulsion phases were identified as the area in the phase diagram where clear and transparent formulations were produced based on visual inspection of many samples.

The domains of existing transparent, isotropic systems were considered to correspond to the microemulsion phases. Phase diagrams were constructed at room temperature, approximately 25°C as outlined by Li *et al*. (*11*) with slight modifications. The ternary phase diagrams of surfactant, cosurfactant, and oil were developed at a constant water percent from 0 to 400% of total initial weight of surfactant, co-surfactant, and oil mixtures, with mixtures containing 0% water referring to premicroemulsion.

For initial determination of microemulsion phase areas within the entire phase diagram, about 36 sample mixtures (based on 10% change in weight) of oil, surfactant, and cosurfactant were carefully weighed, mixed with the aid of a vortex and visually inspected for phase clarity and flowability. For more exact determination of the areas corresponding to premicroemulsions additional mixtures of surfactant, co-surfactant, and oil were prepared with a concentration change rate of 5% for each component at the boundary obtained from the previous step. Samples were then titrated with water in a drop-wise manner and mixed thoroughly by vortexing until clear and transparent microemulsion phase regions could be identified. Once the microemulsion phase was identified additional samples were prepared to determine the boundary regions. No heating was used during the preparation.

The clear areas corresponding to either pre-microemulsions or diluted microemulsions were constructed inside the triangular phase diagram using the Microsoft program AutoCAD 2000.

2.3. *Preparation of microemulsions containing piroxicam*

Piroxicam was accurately weighed and added simply to the selected premicroemulsion bases from the constructed phase diagrams. Vortexing was required to dissolve piroxicam completely in microemulsion

systems. The final piroxicam concentration was adjusted to be 0.5% (w/v).

2.4. *Determination of particle size*

The determination of the particle was done for both premicroemulsion formulas (*i.e.,* piroxicam free formulas) and microemulsions containing piroxicam using a JEOL Transmission Electron Microscope (JTEM) model 1010 (JEOL, Ltd., Tokyo, Japan).

2.4.1. *Preparation of plain cellulosic gel bases*

The weighed amounts of the cellulosic polymer powder was sprinkled gently on a vortex in a 100 mL beaker containing distilled water, and magnetically stirred at high speed. Stirring was continued until a thin hazy dispersion, without lumps, was formed. For complete gel dispersion it was necessary to leave samples overnight in the refrigerator (*19,20*). The same method was used for all cellulosic substances except boiling distilled water was used for the MC gel, and a portion of hot distilled water at 80°C was used for the HPMC gel preparation while the remaining amount of cold water was added and mixing was continued until a smooth homogenous HPMC gel was formed (*21*).

2.4.2. *Preparation of cellulosic gel bases containing piroxicam*

The formulas for cellulosic gel bases were prepared by addition of piroxicam in microemulsion form (*22*), or piroxicam alone was added during the stirring process and the steps were completed as mentioned above for plain cellulosic gel bases.

2.4.3. *Preparation of plain Carbopols (934 and 940) gel bases*

Carbopol 934 or 940 gel bases were prepared by homogenizing 0.5% (w/v) Carbopol dispersion in sufficient water using a magnetic stirrer for 30 min and leaving it to equilibrate for 24 h. After that, pH was adjusted to 5-7 with triethanolamine (*23*).

2.4.4. *Preparation of Carbopols (934 and 940) gel bases containing piroxicam*

Formulas of both Carbopol 934 and 940 gel bases were prepared by addition of piroxicam in microemulsion form or piroxicam alone during the stirring process and the steps were completed as mentioned for Carbopol plain gel bases.

2.4.5. *Preparation of plain Pluronic F-127 gel base*

The required amount of Pluronic F-127 powder was slowly added to cold distilled water (5-10°C) while maintaining constant agitation with a magnetic stirrer. The dispersion was left overnight in a refrigerator to form a clear viscous solution (*19,20*).

2.4.6. *Preparation of Pluronic F-127 gel bases containing piroxicam*

The formulas of Pluronic F-127 gel bases were prepared by addition of piroxicam in microemulsion form or piroxicam alone to the gel and mixing is done while the gel is liquid. The poloxamer gels exhibit thermal behavior and therefore are fluid at lower temperatures (*19,20*).

2.5. *In vitro release of piroxicam from different gel bases*

The release pattern of the drug from the gel bases was examined using a cell diffusion model as described elsewhere (*24*), holding the temperature of the water bath at 37 ± 2°C. The dissolution apparatus (USP dissolution test apparatus II, version DT 600, Heusenstamm, Germany) adapted for semi-solid formulations was set up, containing 300 mL phosphate buffer pH 7.4, at a speed of 120 rpm: the diffusion system had a static cell. A synthetic cellulose acetate membrane (7.54 cm) previously treated with distilled water at 100°C for 5 min and maintained at 4°C was fixed at the end of the glass tube of the diffusion cell. The experimental procedure was carried out using 2 g of gel base. The analysis was performed with 2 mL samples withdrawn from the dissolution medium at 15 min intervals. The removed samples were replaced with equal volumes of phosphate buffer at the same pH to maintain a constant volume for the receiving medium.

Control samples with the same composition of oil, surfactant, and cosurfactant in gel bases were treated as before in order to eliminate the effect of microemulsion components on the UV absorption of piroxicam. The amount of the drug released from the bases was determined spectrophotometrically at 350 nm by measuring the test samples against blank samples. Experiments were done in triplicate and mean results were reported (*25*).

2.6. *Kinetic analysis of drug release data*

The kinetic data for the *in vitro* release of piroxicam was estimated using different kinetic orders (zero-, first-, and second-order) or systems such as Higuchi's diffusion model (*26*), the Hixson-Crowel cup root law (*27*), and the Baker-Lonsdale equation (*28*). A special computer program was used to calculate the kinetic treatments, kinetic parameters and kinetic data for the *in vitro* release from piroxicam microemulsions.

2.7. *Rheological properties of semisolid preparations*

A Brookfield LVT DV-II Programmable Viscometer of Engineering Laboratories, Inc. (Middleboro, MA, USA) was connected to a thermostatic water bath adjusted to 25°C. The viscosity of the plain gel bases and the medicated bases containing piroxicam which gave the highest *in vitro* release was determined. Measurements were carried out to determine the most suitable gel bases.

Viscosity was measured on each base by using spindle 40. A defined amount (0.5 g) of each gel base was placed inside the plate and carefully closed. The measurement was started by operating the viscometer at 0.6 rpm, the speed was gradually increased and the measurement was recorded when the torque reached 10%. The speed was gradually increased at a constant rate for all tested samples until the torque reached 90%, with 30 sec between each successive speed. The rheological parameters, including viscosity, shear rate, shear stress, and yield value, were directly obtained from the monitor. The speed was then reduced gradually, using the same order as the increasing speeds, until reaching the starting rpm.

A complete rheogram was obtained by either plotting the shear rate as a function of the shear stress or plotting the viscosity as a function of shear rate.

The flow properties of microemulsion formulas can be determined by using the equation for non-Newtonian systems as follows. For plastic flow, plastic viscosity (η) was described in the following equation.

$$\eta = (F - f)/G \qquad \text{----- Ex. 1}$$

Where, f is the yield value or intercept, on the shear stress axis is dyne cm^{-2}, F is the shear stress and G is the rate of shear. For pseudoplastic flow, several approaches have been used to obtain meaningful parameters that will allow different pseudoplastic materials to be compared (*29*). Of those, the exponential formula has been used most frequently.

$$\eta' = (F^N)/G \qquad \text{----- Ex. 2}$$

The exponent N (Farrow's constant) rises as the flow becomes increasingly non-Newtonian. The term η' represents viscosity coefficient. By arrangement of the above equation,

$$\log G = N \log F - \log \eta' \qquad \text{----- Ex. 3}$$

An equation for a straight line is obtained. Many pseudoplastic systems fit this equation when log G is plotted as a function of log F.

2.8. *Measurement of thixotropy*

Measurement of thixotropic behavior of both plain and medicated gel bases was determined using the cut and weight method (*30*) in order to calculate the hysteresis loop between the upward curve and downward curve of each plain and medicated gel base using calc paper (70 g, 21 × 29.7 cm).

2.9. *Stability studies of semisolid preparations*

The prepared plain and medicated gel bases were stored in well stoppered polyvinyl chloride (PVC) plastic containers in the dark for 6 months at room temperature. They were checked for drug content, viscosity, and pH change bimonthly throughout the period. The method used by Tas *et al*. (*31*) to investigate the stability of chlorpheniramine maleate in gels prepared using different cellulose derivatives were followed in the present studies.

2.9.1. *Piroxicam content study*

An accurately weighted quantity of each gel base (about 100 mg) was dissolved in about 50 mL of phosphate buffer (pH 7.4). These solutions were quantitatively transferred to volumetric flasks and appropriate dilutions were made with the same buffer solution. The resulting solutions were then filtered through 0.45 μm membrane filters before subjecting the solution to spectrophotometric analysis for piroxicam at 350 nm (*20*,*32*).

2.9.2. *Viscosity measurements*

A Brookfield Viscometer was used to measure the viscosity of the prepared gel bases. The spindle was rotated at 10 rpm. Samples of the bases were allowed to settle over 30 min at room temperature before the measurements were taken (*20*,*32*).

2.9.3. *pH measurements*

The pH was measured in each base using a pH meter that was calibrated before each use with buffered solutions at pH 4, 7, and 10. A defined amount of each tested base was taken and diluted with calibrated distilled water and mixed well. The electrode of the pH meter was immersed in the prepared base solution for pH determination (*33*).

3. Results and Discussion

3.1. *Preparation of topical formulations*

Preliminary screening using different concentration of polymers in the gel formulations (3% methyl cellulose, 2% carboxy methylcellulose, 3% hydroxypropyl methylcellulose, 0.5% Carbopols (934 and 940), and 20% Pluronic F-127) was performed before the present

study. The lowest concentration of each polymer needed to form gels was used to prepare the formulations for dissolution, rheological, and stability studies. It was found that drug release decreased with higher polymer concentration. One obvious reason for this would be the increase in viscosity due to the increase in polymer concentration. It is also possible that at higher polymer concentrations the active substance was trapped by the polymer molecules and by its close proximity to polymer molecules. This increased the resistance to diffusion more than expected. Additionally the density of chain structures which has been observed in gels microstructure increased at higher polymer concentrations and this limits the active substance movement area (*34-37*).

3.2. *In vitro release of piroxicam from gel bases*

The previously mentioned concentrations of gel bases were selected since they gave the best release with most previously studied drugs and it is apparent that drug release rate decreases as the concentration of the gel increases (*38-41*).

An explanation for this behavior is the increased number of micelles at higher gel concentration as in the case of Pluronic F-127, resulting in a more entangled system and a more rigid gel (*40*). Also, decreased drug release by an increase in the concentration of the gel may be attributed to the differences in the viscosity of the polymers (*38,41*). As shown in Figures 1 and 2, piroxicam in its microemulsion form clearly exhibited a higher *in vitro* release as compared with plain piroxicam.

3.2.1. *Release of piroxicam from cellulose derivative gel bases*

The direct addition of MC and HPMC into water causes coagulation and subsequent dissolution is slow and difficult. Both MC and HPMC are soluble in hot water, consequently the initial uniform dispersion can be done in hot water followed by cooling (*42*). As shown in Figure 1, it was clear that the release of piroxicam from 3% MC gel bases was higher than that from other tested cellulose derivative gel bases (CMC and HPMC). The *in vitro* release of piroxicam-microemulsion formulas from different cellulose derivative gel bases could be arranged in a descending manner as follows: 3% MC > 3% HPMC and finally 3% CMC. By combining the two previous arrangements, the *in vitro* release of piroxicam from plain drug and drug-microemulsion cellulose derivative gel bases could be arranged in a descending manner as follows: 3% MC-ME > 3% HPMC-ME > 3% MC > 3% HPMC > 3% CMC-ME and finally 3% CMC gel base.

3.2.2. *Release of piroxicam from Carbopols and Pluronic F-127 gel bases*

The least concentration of both Carbopols 934 and 940 and Pluronic F-127 was used since the decreased release encountered by increasing the concentration of the gel may be attributed to the difference in the viscosity of the polymers (*40,41,43*). As shown in Figure 2, Carbopol 934 gels showed a higher release than Carbopol 940 gels. These results were attributed to the fact that Carbopol 934 gel base exhibited a lower viscosity than the Carbopol 940 gel base (*44*).

The *in vitro* release of piroxicam from different Carbopols and Pluronic F-127 gel bases can be arranged in a descending manner as follows: 0.5% Carbopol 934 > 0.5% Carbopol 940 and Pluronic F-127. The *in vitro* release of the piroxicam-microemulsion formula from different Carbopols and Pluronic F-127 gel bases could be arranged in a descending manner as follows:

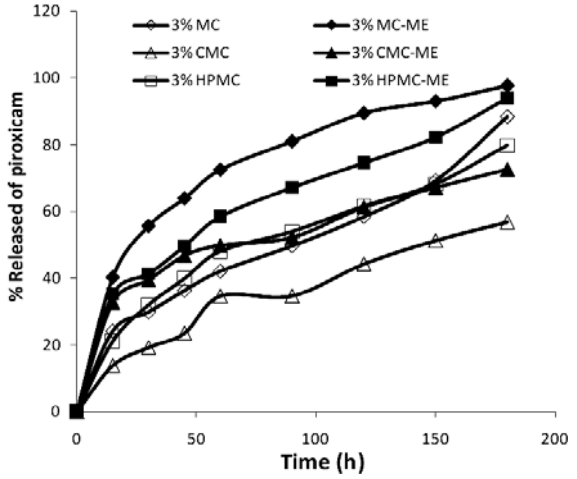

Figure 1. Percentage of piroxicam released from plain and microemulsion gel base. Open circle, 3% MC; Closed circle, 3% MC-ME; Open triangle, 3% CMC; Closed triangle, 3% CMC-ME; Open square, 3% HPMC; Closed square, 3% HPMC-ME.

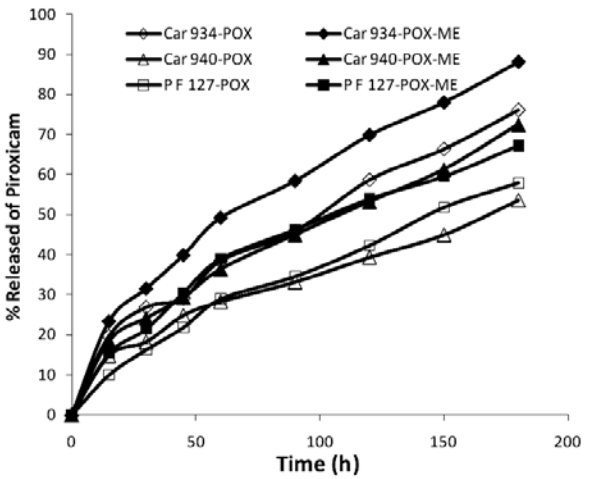

Figure 2. Percentage of piroxicam released from Carbapol and Pluronic F-127 from plain and microemulsion gel base. Open circle, Carbapol 934; Closed circle, Carbapol 934-ME; Open triangle, Carbapol 940; Closed triangle, Carbapol 940-ME; Open square, Pluronic F-127; Closed square, Pluronic F-127-ME.

0.5% Carbopol 934 > 0.5% Carbopol 940 and Pluronic F-127. By combining the two previous arrangements, the *in vitro* release of piroxicam from plain drug and drug-microemulsion could be arranged in a descending manner as follows: 0.5% Carbopol 934-ME > 0.5% Carbopol 934 > 0.5% Carbopol 940-ME > Pluronic-ME > Pluronic and finally 0.5% Carbopol 940 gel base.

3.3. *Kinetic data of piroxicam in vitro release*

According to the results obtained from the *in vitro* release data for all gel bases, the bases that gave the best release were chosen to study kinetic behavior. In order to develop an ideal kinetic model to interpret the diffusion data in terms of meaningful parameters, various kinetic models including zero-order, first-order, and the Higuchi diffusion model were applied to obtain the best fit for the results. As shown in Table 1, it was found that *in vitro* release of piroxicam-microemulsion formulas followed zero-order for Carbopol 940, first-order for 3% MC and Pluronic F-127, and Higuchi diffusion order for 3% CMC, 3% HPMC, and 0.5% Carbopol 934. The kinetic data showed that the *in vitro* release of piroxicam followed different kinetic orders and that no single kinetic order could be used to express drug release from specific types of topical formulations.

3.4. *Rheological properties of topical formulations*

The rheological evaluation of pharmaceutical semisolids is useful since it provides a method of quality control during and after the manufacturing process and information about the structure of the phases present in a product and the influence of various agents used in its formulation. All the investigated gel bases (plain or medicated) were subjected to rheological examination. All the studied gel bases exhibited pseudoplastic behavior with thixotropic character. The results are shown in Table 2. Gel formulations containing piroxicam micremulsion in MC and HPMC bases were at the top in terms of thixotropy. Thixotropy is a desirable property in liquid pharmaceutical systems because these systems retain their high consistency in the container yet can be poured from the containers precisely and spread on the skin easily (*45*). Besides, thixotropy improves product stability by decreasing the rate of sedimentation, which may be crucial for parenteral products.

3.5. *Stability studies*

Shelf storage stability tests of semisolid preparations based on storing the preparation at room temperature

Table 1. Kinetic parameters of piroxicam released from cellulosic derivatives, Carbapols and Pluronic F-127 gel bases containing piroxicam-microemulsion formulae

Bases	Kinetic order or model	Intercept (a)	Slope (b)	Correlation (r^2)	Rate constant (k)	$t_{1/2}$ (min)
MC (3%)	Zero	46.66	0.319	0.9497	0.319	156.6
	First	1.92	–0.018	**0.9872**	–0.018	38.2
	Diff.	23.07	5.852	0.9858	5.852	73.0
CMC (3%)	Zero	27.97	0.234	0.9934	0.224	213.7
	First	1.88	–0.021	0.9964	–0.005	143.2
	Diff.	11.89	4.144	**0.9966**	4.143	154.6
HPMC (3%)	Zero	33.42	0.341	0.9908	0.341	146.5
	First	1.96	–0.006	0.9572	–0.013	54.7
	Diff.	9.36	6.056	**0.9958**	6.056	68.2
Carbopol 934 (0.5%)	Zero	21.81	0.383	0.9920	0.383	130.5
	First	1.99	–0.005	–0.9862	–0.011	65.2
	Diff.	4.63	6.809	**0.9985**	6.809	53.9
Carbopol 940 (0.5%)	Zero	15.16	0.318	**0.9978**	0.318	157.4
	First	1.97	–0.003	0.9899	–0.006	111.5
	Diff.	6.20	5.579	0.9929	5.580	80.3
Pluronic F-127 (20%)	Zero	25.34	0.305	0.9813	0.305	163.9
	First	1.91	–0.003	**–0.9997**	–0.007	99.9
	Diff.	3.86	5.466	0.9968	5.466	83.7

Higuchi model was written in the table as diffusion model (Diff.).

Table 2. Viscosity and thixotropic behavior of piroxicam prepared from microemulsion in different gel bases

Formulae	Viscosity (cp)		Thixotropic behavior (cm^2)	Farrow's constant
	Max	Min		
3% MC	289	63	2.36	1.74
3% CMC	9,310	1,210	5.34	1.42
3% HPMC	74	35	2.16	1.92
0.5% Carbopol 934	6,630	784	1.63	1.42
0.5% Carbopol 940	9,550	337	2.10	1.31

were carried out to detect any changes in drug content, viscosity, and pH of the preparations through 6 months. The results are summarized in Table 3. All of the gel samples showed excellent results in these studies. Drug degradation was found to be in the range 3.3-7.9% after 6 months. Viscosity values after 6 months compared to the initial viscosity were in the range 2-52%, while pH changed 0.08-0.23 units only. In all cases, MC and HPMC showed the smallest changes in these parameters (Table 3).

According to the results obtained from the kinetic analysis of the stability tests, it was obvious that the degradation of piroxicam was found to obey a zero-order reaction for all the tested gel bases, based on the values of the correlation coefficient (*r*) (Table 4). After knowing the half-life ($t_{1/2}$) of all the investigated gel bases, it was possible to calculate the time after which the gel bases lose 10% of their initial content (t_{90}). This is a direct calculation of the length of time through which the gel bases would remain and complies with the official requirement of drug content. From these results, it was obvious that 3% HPMC and 3% MC gave the longest t_{90} in years of 2.85 and 2.08, respectively.

4. Conclusion

The incorporation of piroxicam in microemulsion formulas could lead to enhancement of piroxicam release profiles by allowing constant and regular *in vitro* release as well as reduction in piroxicam microemulsion particle size. Thus usage of the microemulsion technique led to improvement in piroxicam availability which can offer many promising features for its use as a topical vehicle for piroxicam delivery. Various gel bases containing piroxicam-microemulsion were studied for drug release, rheologic behavior, and stability of the topical formulations. Three percent MC gel base showed the highest release of piroxicam-microemulsion after 180 min (97.7%) followed by 3% HPMC (94.0%) when compared to bases containing piroxicam alone. All the medicated gel bases containing piroxicam exhibited pseudoplastic flow with thixotropic behavior. The degradation of piroxicam from its topical formulations was found to be a zero-order reaction based on the mean values of correlation coefficients. All formulations were quite stable. The shelf life of the gel containing HPMC base were about 2.85 years. Considering *in vitro* release, rheological properties and shelf life, the HPMC gel base containing 0.5% piroxicam in microemulsion formula was the best among the studied formulations.

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Table 3. Various parameters for shelf storage stability tests for up to 6 months

Parameters	Storage periods (Months)						
	0	1	2	3	4	5	6
Piroxicam content (%)							
3% MC	100	99.6	99.2	98.3	97.5	96.5	95.8
3% CMC	100	99.4	98.7	97.4	96.1	94.5	92.1
3% HPMC	100	99.5	99.0	98.5	97.9	97.1	96.7
Viscosity (dyne/cm)							
3% MC	265	266	268	268	269	269	270
3% CMC	2,914	2,907	2,898	2,895	2,887	2,879	2,862
3% HPMC	69	67	67	66	66	65	65
pH values							
3% MC	7.28	7.28	7.25	7.25	7.22	7.19	7.19
3% CMC	7.80	7.84	7.88	7.92	7.96	7.98	8.03
3% HPMC	7.71	7.77	7.77	7.68	7.66	7.63	7.63

Table 4. Kinetic parameters for shelf stability testing of piroxicam released from different gel bases

Formulae	Kinetic order	Intercept (a)	Slope (b)	Correlation (r^2)	Rate constant (*k*)	$t_{1/2}$ (min)
3% MC	Zero	–0.593	0.401	0.9957	0.401	124.6
	First	2.003	–0.002	–0.9954	–0.004	–168.6
	Second	0.009	0.001	0.9951	< 0.001	237.8
3% CMC	Zero	–1.350	0.714	0.9833	0.714	70.0
	First	2.006	–0.003	–0.9812	–0.008	–93.0
	Second	0.009	< 0.001	0.9791	< 0.001	128.8
3% HPMC	Zero	–0.154	0.293	0.9968	0.293	170.9
	First	2.001	–0.001	–0.9966	–0.003	–232.1
	Second	0.009	< 0.001	0.9964	< 0.001	328.5

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