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# PREPARATION AND CHARACTERIZATION OF DERMAL FILMS CONTAINING AN ANTI-INFLAMMATORY DRUG

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## ABSTRACT

Piroxicam is a potent nonsteroidal anti-inflammatory drug associated with many side effects when taken orally. An attention was paid in this work to formulate and characterize piroxicam containing polymer films for dermal use. The used polymers were cellulose types namely ethylcellulos (EC) and hydroxypropyl methylcellulos (HPMC). In this study, medicated films consisting of drug and carrier were prepared. The carrier consisted of one or two polymers. The physicochemical characterization was done by IR spectroscopy, DSC and X-Ray diffractometry for both piroxicam polymeric films and their corresponding physical mixtures as well as the untreated drug and polymer powders to investigate the drug polymer interaction. The results showed absence of molecular interactions between piroxicam and both EC and HPMC. In-vitro drug release from these polymer films was studied. It is found that when the ratio of HPMC increased the drug release from the film become faster.

## INTRODUCTION

Piroxicam, an oxime derivative, is a nonsteroidal anti-inflammatory drug. It is used in musculoskeletal and joint disorders such as ankylosing spondylitis, osteoarthritis, rheumatoid arthritis including juvenile chronic arthritis, in soft- tissue disorder, and in acute gout.[1] The drug is highly potent, has a long half-life of over 50 hours which makes it suitable for once daily dosage.[2] Piroxicam exists in two different interconvertible crystal polymorphs with melting points of 196-198 °C for the needle form and 199-201 °C for the cubic form and there are no data about a possible different activity of the particular forms.[3] There are two possible tautomeric forms for piroxicam, namely enol and ketone forms.[4]

Application of medicated substances to the skin is a concept as old as humanity. For treatment of skin infections, wide assortments of topical dosage forms are available. It comprises powders, lotions, emulsions, ointments, pastes. aerosols, soaps, plasters, shampoos and other preparations. Today, among these preparations, ointment - like preparations, covers about 80 %.

The application of some ointments to the skin produces systemic actions, which means, certain degree of absorption occurs. Afterwards, systemic drug administration by the transdermal route was achieved with some cream and ointment preparations for protection and treatment from certain diseases. None of these preparations was satisfactory due to variable systemic drug absorption resulted from the absence of specific directions like the area to be covered and the duration of systemic action which controlled by the thickness of the layer of ointment or cream, which varies with repeated application by the patient.

For such reasons medicated topical polymeric films are designed to deliver the drug to the skin surface at a controlled rate. The main advantages of such solid dosage forms [5] are: 1) elimination of variables, which influence G. I. T absorption, 2)avoidance of first pass effect, 3)allows administration of drug with small therapeutic index, 4) permits display of only one pharmacological effect from a drug that in another dosage form may show several effects, 5)an alternative route when oral route is not practicable, 6)elimination of nuisance associated with daily repetitive applications of messy ointments and creams (patient compliance is better), 7)flexibility of the dose used, it has a definite area. (i.e increase area leads to increase in dose and 8)easy to terminate therapy by removing the system. These advantages confirm that

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drug-containing polymer films are very promising medicinal preparations.

The aim of this study is to formulate and Physicochemical characterize a dermatological preparation as a film for piroxicam which is widely used but associated with many side effects when taken orally. Such film could be applied conveniently to the skin, releasing the drug in an effective concentration; so that continuous effect would be achieved for a reasonable time. [5] In this study, medicated films consisting of drug and cellulose polymers were prepared. The physicochemical characterization was done by IR spectroscopy, DSC and X-Ray diffractometry for piroxicam polymeric films and the corresponding physical mixtures as well as the untreated drug and polymer powders to investigate the drug polymer interaction. In-vitro release of the drug from polymer films was also studied.

## MATERIAL AND METHODS

### Materials

Piroxicam (kindly provided by Sedico company for pharmaceutical industries, Cairo, Egypt). Ethylcellulose, type N-22 NF ehoxyl, 48.9 % viscosity 24 CPs (Heircules incorporation U.S.A). Hydroxypropylmethylcellulose, viscosity of 2% aqueous solution (25 $^0$C) approximately 50 CPs (Sigma Chemical Co. Germany). Methylene chloride, acetone and isopropanol (El-Nasr company, Abu-Zaabal, Cairo, Egypt). Other materials and solvents are of reagent and analytical grade, and they were used without further purification.

### Methods

*Preparation of the medicatd Films*

EC, HPMC or mixture of the two polymers (2.1 gm of polymer + 100 mg of piroxicam ) was dissolved in a mixture of methylene chloride: isopropanol in a ratio of 6:4 for EC and methylene chloride:isopropanol: methanol in ratio 4:3:3 for HPMC or its mixture with EC. Ratios used for EC and HPMC polymers are (10:0, 8:2 , 6:4 , 4:6 , 2:8 and 0:10) respectively.

When the solution of drug was prepared, it was left for about 30 minutes to remove any entrapped air bubbles. 20 ml of this solution was poured into a dust free petri dish previously cleaned and dried. The petri-dish was covered with an inverted glass funnel of stem orifice 0.6 cm in diameter. Clearance was provided for the escape of solvent vapors by raising the base of the funnel (2 cm) just above the resting surface. The funnel was an aid in controlling the rate of evaporation of the solvent and reducing the blistering of the surface of the deposited film.[6] The solvent was allowed to evaporate for 24 hours, the film was then removed from the petri-dish, wrapped in an aluminum foil and stored in a dry place at ambient room temperature. The intact complete film was adhered on back of cover of petri dish (8 cm in diameter) to be used for the release study. The films were subjected to evaluation within one week of their preparation.

*Physicochemical characterization*

Infrared spectra of certain medicated films and the corresponding physical mixtures as well as the untreated drug were done at a range of 4000-400 cm$^{-1}$ using KBr disk method. The samples were ground, mixed thoroughly with KBr and compressed at a pressure of 6 ton/cm$^2$ using Shimadzu SSp-10A IR compression machine. Differential scanning calorimetry was recorded using T.A. 501 Differential scanning calorimeter DSC. (Shimadzu Co., Japan). Samples of about 5 mg were accurately weighed and encapsulated into flat-bottomed aluminum pans with crimped-on lids. The scanning speed of 10 °C/min from 0 °C to 250 °C was used in presence of nitrogen at flow rate of 40 ml/min. The X-ray diffraction patterns of the powder samples were obtained using a Phillips 1700 series diffractometer which is equipped with curved graphite crystal monochromater, automatic divergence slit and automatic controller PW/1710. The target used was CuKα radiation operating at 40KV and 30 mA (λka = 1.5418 A). The system was calibrated using silicon disc and/or powder d111 = 3.1355 A) as

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an external standard. The diffraction patterns were achieved using continuous scan mode with 20° ranging from 4° to 60°. The output data achieved represented by 20, d A, intensities are determined via the microprocessor of the PW/1710.

*In-vitro drug release experiments*

The previously prepared film was removed from the plate, weighed on an analytical balance, and the thickness was measured at both the four corners and the center with a micrometer. A thin coating of silicone adhesive was applied to back of petri dish (7cm in diameter) which was used as a glass support. The film was carefully pressed on to the glass support, making sure that all edges are adhered and no silicon adhesive touched the exposed surface.

The temperature of the dissolution medium (250 ml) of citrate buffer (pH=5) was adjusted to 32 ± 0.5°C, the temperature of the skin surface is 32 ± 0.5 °C. The pH of the intact skin lies between 4.5 to 5.5 under occlusive condition, the pH of the skin is more likely to be close to the higher value rather than to the lower value. Condition of release studies at (pH=5) simulates the condition upon which the drug is exposed when applied to the intact skin. The glass support containing the film was placed in the bottom of the vessel, then the paddles of the dissolution tester were allowed to rotate at 60 rpm which was the optimum speed to prevent film rupture.

It was taken into consideration that the used buffer volume affords sink conditions. To avoid water evaporation, the vessels were covered with an aluminum foil during the experiments.

Samples (5 ml each) were obtained while the film remained completely immersed throughout the release study. The removed sample (5 ml) from the release medium was replaced by an equal volume of the buffer. The run was continued for at least 6 hours. All samples were analyzed spectrophotometrically at 360 nm. Blank samples were obtained from the release experiments films containing the same components except the drug.

## RESULTS AND DISCUSSION

**IR studies**

There are two possible tautomeric forms for piroxicam, but in this study the 1724 $cm^{-1}$ band was not observed in the IR spectrum of piroxicam (Figures 1-2 curve A), suggesting that piroxicam was present as an enol form.[7,8] It has also been reported that piroxicam has two interconvertible crystalline forms, namely the needle and cubic forms.[1] The IR absorption peaks at 1634 $cm^{-1}$ and 1629 $cm^{-1}$ are assigned to the stretching of the amide carbonyl groups of the needle form and the cubic form of piroxicam respectively, the peak at 1529 $cm^{-1}$ is due to the stretching of the second amide band for both crystalline forms of piroxicam. The peak at 1629 $cm^{-1}$ was found in the IR spectrum of piroxicam, suggesting that the cubic form of piroxicam was used in the present study.

In addition, Figure 1 curve D, showed the IR spectra of piroxicam: EC: HPMC (2:25:25 weight ratio) physical mixture. The physical mixture showed shifting of carbonyl peak of piroxicam from 1629 $cm^{-1}$ to 1623 $cm^{-1}$. Figure 2 showed peaks at 1616 $cm^{-1}$, 1618 $cm^{-1}$ and 1627 $cm^{-1}$ which were corresponding to cast films of piroxicam: EC (2:50 weight ratio), piroxicam: HPMC (2:50 weight ratio) and piroxicam: EC: HPMC (2:25:25 weight ratio) respectively, were shifted from 1629 $cm^{-1}$ which corresponding to the carbonyl group of the drug, but this shift is not significant.[9] These findings agree with Adibkia *et al.*[10] those investigated the physico-chemical characterizations of nanoparticles of piroxicam and eudragit RS100. They found that there is no chemical interaction between piroxicam and the used polymer.

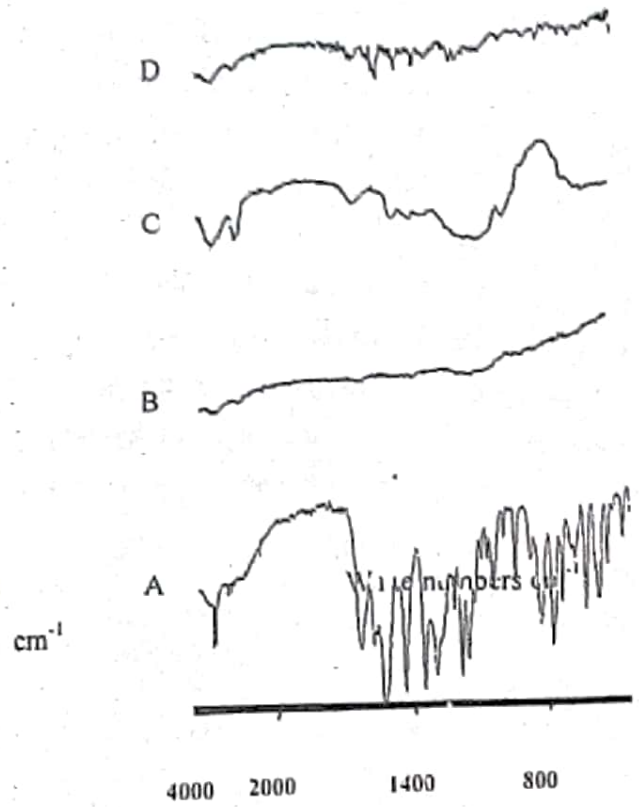


Fig. (1): The IR spectra of : (A) Untreated pirc xicam powder (B)ethylcellulose (EC) (C) hydroxy ɔropyl methylcellulose (HPMC) (D) piroxicam: EC: HPMC (2:25:25) physical mixt.ure

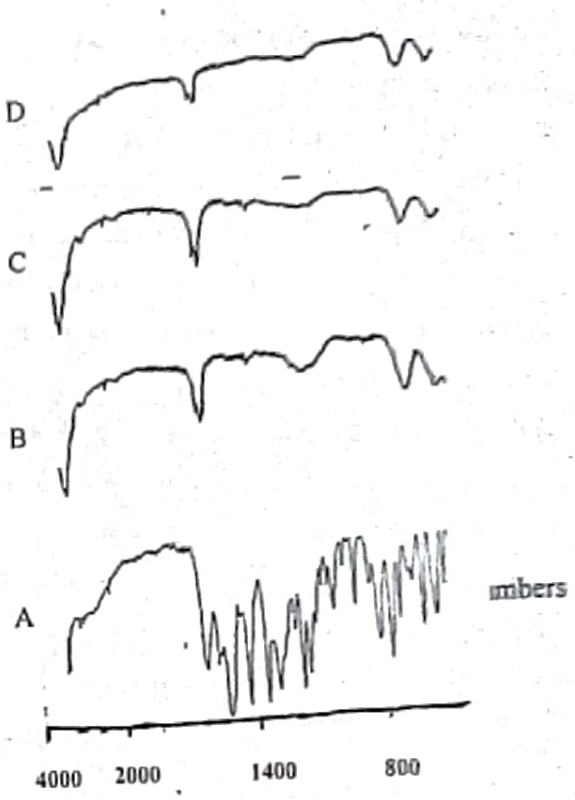


Fig. (2): The IR spectra of: (A) untreated piroxicam powder (B) piroxicam: EC (2:50 w/w) film (C) piroxicam: HPMC (2:50 w/w) film (D) piroxicam: EC: HPMC (2:25:25 w/w) cast film.

**Differential scanning calorimetery (DSC)**

In order to shed a light on the possibility of solid state changes of piroxicam with different used polymers, DSC was performed on drug: polymer cast films (2:50 weight ratio of drug: polymer) and their physical mixtures as well as the individual components.

The DSC curves of untreated piroxicam (Figures 3-4 curve A) show an endothermic peak at 201.3°C at a scanning rate of 10 °C/min.

Figures 3 and 4, showed disappearance of melting endothermic peaks of piroxicam crystal with physical mixture of piroxicam: EC: HPMC (2:25:25) respectively, and cast films of piroxicam: EC (2:50), piroxicam: HPMC (2:50) and piroxicam: EC: HPMC (2:25:25) respectively. These results suggest that piroxicam exists as an amorphous form.

As mentioned above, the characteristic endothermic peak of piroxicam in its polymer almost disappeared or reduced in intensity, shifted to lower temperatures and lost its sharpened distinct appearance. This observation confirms the presence of piroxicam in an amorphous form in these physical mixtures or cast films.

Similar DSC results were obtained by Kohoda et al.[11] who noticed the disappearance of the endothermic peak of lidocaine hydrochloride in the solid dispersion films containing hydroyprpbylcellulose. They explained this phenomenon on the basis that solid dispersion resulted in an amorphous form of the drug. Also, Ismail et al.[12] showed that salicylic acid endothermic peak disappeared in both physical mixtures and coevaporate. They stated that this phenomenon could be correlated to an amorphous state of the drug present in the casting

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film due to incorporation of salicylic acid in Eudragit polymer.

Also, Similar DSC results were obtained by Najib and Suleiman [13] who noticed the disappearance of the endothermic peak of PEG 4000 solid dispersions with diflunisal. They explained this phenomenon on the basis that solid dispersion resulted in an amorphous form of the drug. In addition, Al-Angary et al.[14] showed that lorazepam endothermic peak disappeared when incorporated in PEG 10000 solid dispersions. They stated that this phenomenon can be correlated to an amorphous state of the drug present in the solid dispersion. Other investigators supported this explanation.[15,6]

However, the disappearance of the endothermic peak corresponds to the melting of piroxicam in the drug: polymer physical mixture may be due to its solubility in the melted polymer. This finding agrees with Simonelli et al.[17] who showed the disappearance of the endothermic peak of hydrochlorothiazide in both physical mixture and solid dispersion with PEG 6000, which might indicate the solubility of the drug in the molten polymer during running the thermograms. Moreover, Khidr [18] found the same behavior when he studied the solid dispersion of nifedipine with pluronic F: 127.

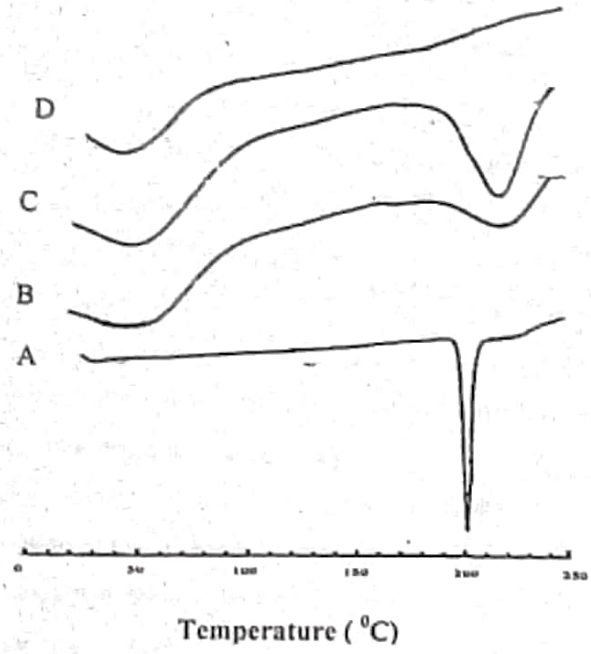


Fig. (3): Differential scanning calorimetery (D.S.C.) curves of (A) Untreated piroxicam powder (B) E.C (C) HPMC (D) piroxicam: E.C: HPMC (2:25:25 w/w) physical mixture.

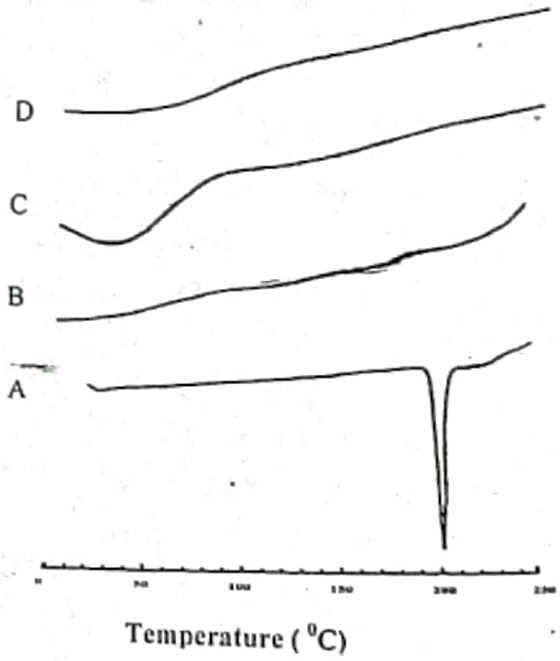


Fig. (4): Differential scanning calorimetery (D.S.C.) curves of (A) Untreated piroxicam powder (B) Piroxicam: E.C (2:50 w/w) film (C) Piroxicam: HPMC (2:50 w/w) film (D) Piroxicam: E.C: HPMC (2:25:25 w/w) film.

### 3.3. X-Ray diffraction properties

To get further evidence on the solid state change, X-ray diffraction pattern was carried out on untreated drug, medicated films formed of EC, HPMC or of both polymrs (drug: polymr = 2:50) and their physical mixtures as well as the individual components. The presence of numerous distinct peaks in the X-ray diffraction spectrum of piroxicam indicates that piroxicam is present as a crystalline material with characteristic diffraction peaks appeared at diffraction angels of 2θ at 8.69A°, 14.57A°, 15.21A°, 15.83A°, 17.75A°, 25.91A°, 26.82A°, 27.45A° and 34.37A° with relative intensities of 50, 48, 54, 57, 68, 100, 65, 67 and 22, respectively.

EC and HPMC polymers are amorphous in nature due to the absence of complete stereo regularity and

presence of bulky side groups. Representative X-ray diffraction pattern for these polymers Figure 5 shows no sharp peaks. However, the physical mixture or the cast films of the same composition did not contain sharp peaks associated with drug molecules Figures 5-6. These diffraction patterns are identical to those of the pure polymer. The results strongly suggest the transformation of the drug from crystalline state to amorphous one in EC and HPMC polymers. These results are in agreement with other authors [19] who found that drugs-PVP co-precipitates show disappearance of the X-ray diffraction peaks of the drug crystals.

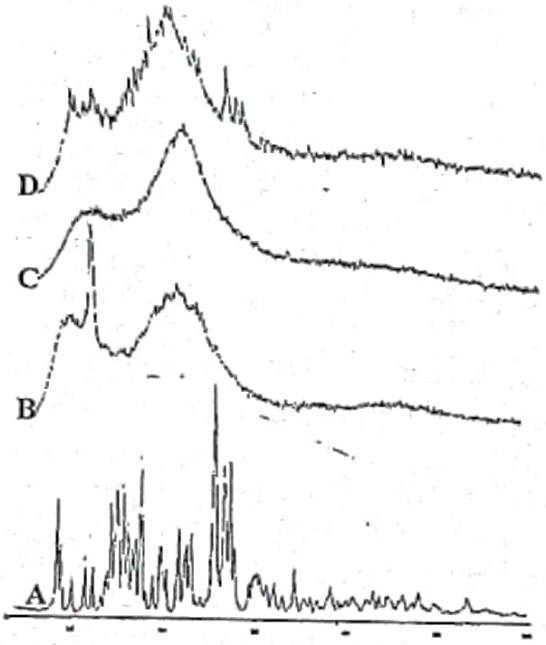


**Fig. (5):** X-ray diffraction pattern of **(A)** Untreated piroxicam powder (B) E.C (C) HPMC (D) piroxicam: E.C: HPMC (2:25:25 w/w) physical mixture.

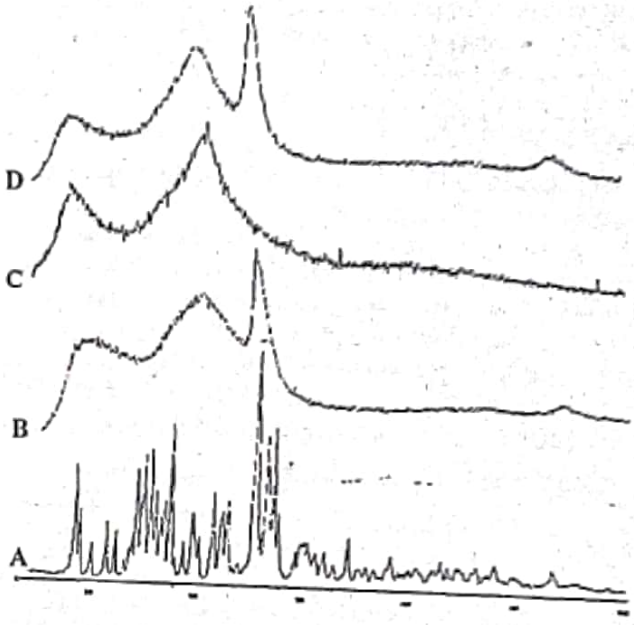


**Figure (6):** X-ray diffraction pattern of (A) Untreated piroxicam powder (B) Piroxicam: E.C (2:50 w/w) film (C)Piroxicam: HPMC (2:50 w/w) film(D) Piroxicam: E.C: HPMC (2:25:25 w/w) film.

**Evaluation of piroxicam release from cellulosic films**

To study the release profile of piroxicam, medicated films were stuck to the glass plate using thin layer of amir adhesive. Thus, the release of drug from the film was from one planar surface. The release of piroxicam from ethylcellulose films was found to be very slow and only about 3.34 % of drug content in the film was released after six hours. This may be due to the hydrophobic nature of piroxicam, which prefers to remain in ethylcellulose film having the same nature. The release of piroxicam was found to follow the first order kinetics as shown in Table 2. Hydroxypropylmethylcellulose (HPMC) being water soluble, therefore the release of piroxicam from its films was rapid (complete drug release within two hours). The release of piroxicam from HPMC film was found to follow zero order kinetics and thereby the release of drug from this polymer is largely controlled by dissolution rate of polymer and solvent penetrability. It was obvious that the film forming polymer exerted its influence on the type and the rate of release of drug which agreed with Ebrahim investigations [20].

As a result of the previous work, modified bases for preparing the films were carried out, by using mixtures of ethylcellulose and HPMC in different ratios (10:0, 8:2, 6:4 ,4:6, 2:8 , and 0:10) respectively. The solvent system used to prepare the films was a mixture of methylene chloride: methanol: isopropanol in ratio 4:3:3 instead of methylene chloride: isopropanol solvent system (in ethylcellulose films), from the point of drug release from these films, a variety of different drug release rates were developed. The rate of drug release was found to increase as the ratio of HPMC increased; as shown in Table 1 and illustrated in Figure 7. This can be explained on the basis, that the film was a matrix of ethylcellulose with hydroxypropyl methylcellulose, piroxicam transport would be expected to occur through channels formed due to the presence of dispersed HPMC as channeling agent.

It can be suggested that two factors might be operating in these films, resulting in the formation of two types of channels that permit transport; one was due to hydration and dissolution of the HPMC leaving pores in the film; the other was due to the hydrated HPMC retained in the film acting as a barrier for drug. This would require diffusion of the drug through the hydrated film for transport to occur, thus considerably reducing the transport rate. While the formation of the

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hydrated film would be the first step in formation of a transport channel, the retention time of the hydrated HPMC as a barrier film would be a function of the thickness of the film and the concentration of HPMC in the film. In our case, the effect of thickness was ignored to all films because they were prepared to have nearly the same thickness. Consequently, when there was low concentration of HPMC in the film, a comparatively longer retention time might be expected due to the support provided by the hydrophobic ethylcellulose matrix. The observed rate of transport would then be a function of the balance of the two operating factors previously stated.

However, with time the retained HPMC would tend to dissolve to permit an increase in the transport rate (i.e release rate). Such a mechanism would be consistent with the observation of increased permeability with time. The exact effect of the dispersed HPMC becomes more significant when comparing two film mixture matrix one has high ratio of HPMC and the other has low ratio as shown in Table 1 and Figure 7.

Hence, the release rate was enhanced by the addition of hydrophilic polymer (HPMC) to ethylcellulose matrix as shown in Figure 7. These results were in a good agreement with Shah et al.[21] At 2:8 ratio of EC and HPMC, 100% drug release occurred after six hours, which fulfills our aim.

Upon analysis of data, it was surprising that the order of drug release from films of ethylcellulose and Hydroxypropyl methylcellulose was not the same as shown in Table 2. As shown in the Figures 8-10, ratios of ethylcellulose and Hydroxypropyl methylcellulose as (10:0, 6:4 and 4:6) respectively showed first-order kinetics. However, ratios (2:8 and 8:2) showed diffusion controlled mechanism and ratio (0:10) were zero order kinetics. From the obtained data, the preferred formula would be a mixture film composed of ethylcellulose and Hydroxypropylmethylcellulose of ratio (2:8).

**Table (1):** Percentage of drug released from ethylcellulose films each containing 20 mg of piroxicam at different EC: HPMC ratios.

| EC: HPMC ratios | % Drug released | | | | | |
|---|---|---|---|---|---|---|
| | Time (min.) | | | | | |
| | 60 | 120 | 180 | 240 | 300 | 360 |
| 10:0 | 1.25 | 1.65 | 2.06 | 2.48 | 2.90 | 3.34 |
| 8:2 | 5.91 | 7.95 | 9.34 | 10.63 | 11.65 | 12.56 |
| 6:4 | 11.18 | 14.24 | 18.64 | 23.27 | 26.47 | 29.86 |
| 4:6 | 32.17 | 45.60 | 62.45 | 73.71 | 81.31 | 86.84 |
| 2:8 | 51.83 | 60.98 | 77.86 | 95.04 | 98.38 | 100 |
| 0:10 | 77.72 | 100 | - | - | - | - |

**Table (2):** Kinetic data of percentage of drug release from polymeric films each containing 20 mg of piroxicam at different EC: HPMC ratios.

| Mechanism of Release | | EC: HPMC ratios % w/w of polymer | | | | | |
|---|---|---|---|---|---|---|---|
| | | 10:0 | 8:2 | 6:4 | 4:6 | 2:8 | 0:10 |
| First order | R | 0.999 | 0.978 | 0.998 | 0.999 | 0.961 | 0.977 |
| | $K_1$ ($min^{-1}$) | 0.0004 | 0.0005 | 0.0008 | 0.0029 | 0.0068 | 0.0088 |
| Zero order | R | 0.998 | 0.989 | 0.997 | 0.979 | 0.960 | 0.999 |
| | $K_0$ (% released/min) | 0.007 | 0.0217 | 0.0642 | 0.193 | 0.1763 | 0.360 |
| Higuchi's diffusion | R | 0.998 | 0.999 | 0.990 | 0.996 | 0.975 | 0.992 |
| | $K_h$ (%released/$min^{1/2}$) | 1.85 | 0.591 | 1.717 | 5.294 | 4.822 | 5.885 |
| Log Q vs log t | R | 0.996 | 0.999 | 0.990 | 0.996 | 0.978 | 0.985 |
| | Slope | 0.647 | 0.425 | 0.670 | 0.637 | 0.408 | 0.276 |
| Best fitted model | | First order | Diffusion model | First order | First order | Diffusion model | Zero order |

R : Correlation coefficient
$K_1$ : First order release rate constant
$K_0$ : Zero order rate constant
$K_h$ : Diffusion rate constant

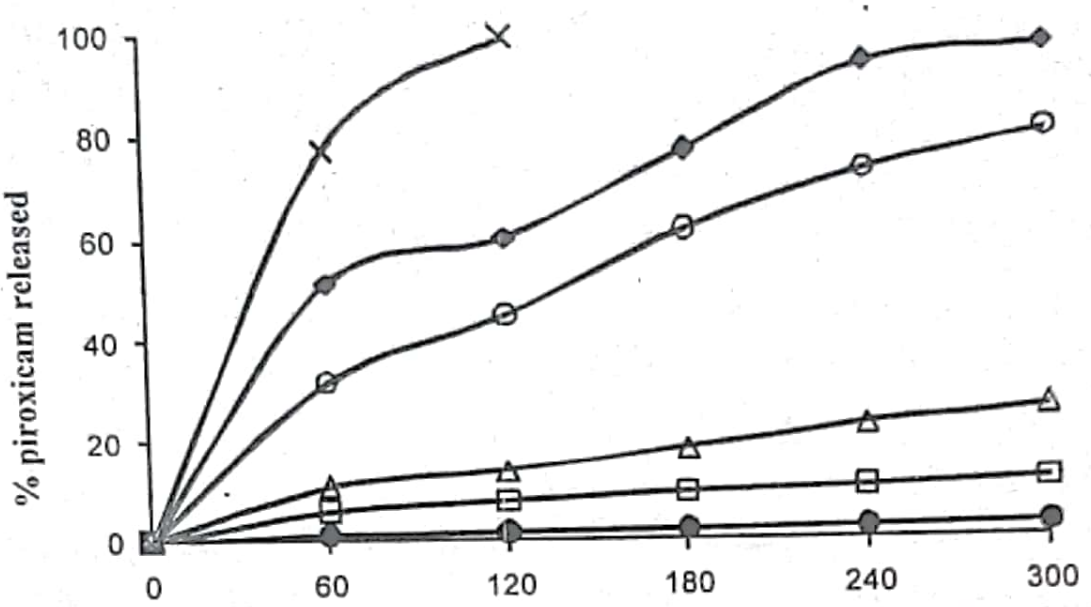


**Figure (7):** Drug release profile from polymeric films containing 20 mg of piroxicam at different EC:HPMC ratios. Key: (•), 10:0; (□),8:2; (Δ), 6:4; (O),4:6; (◆), 2:8; (x), 0:10.

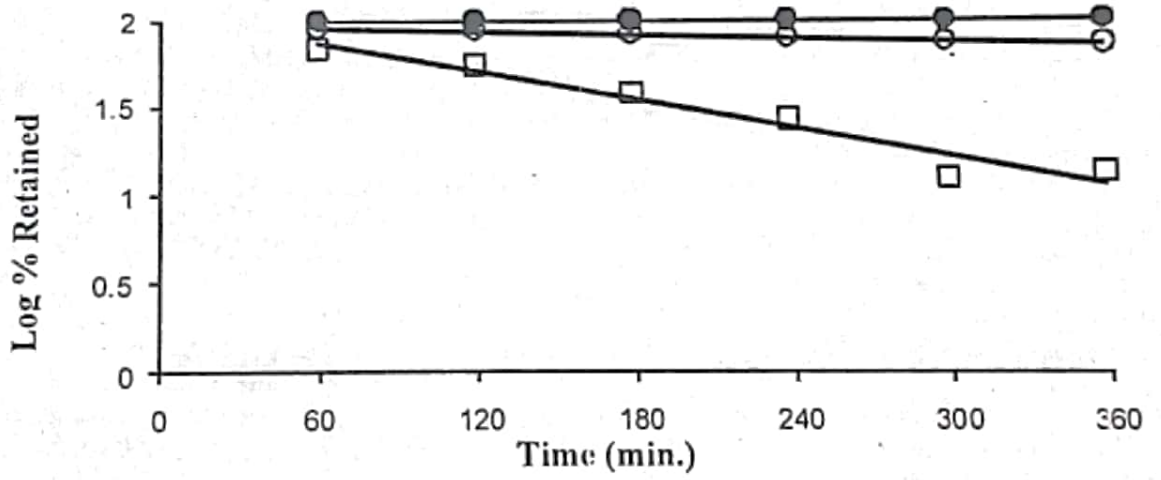


**Figure (8):** Drug release profile from polymeric films containing 20 mg of piroxicam at different EC: HPMC ratios. Key: (•), 10:0; (O),6:4; (□), 4:6. *(first order mechanism)*

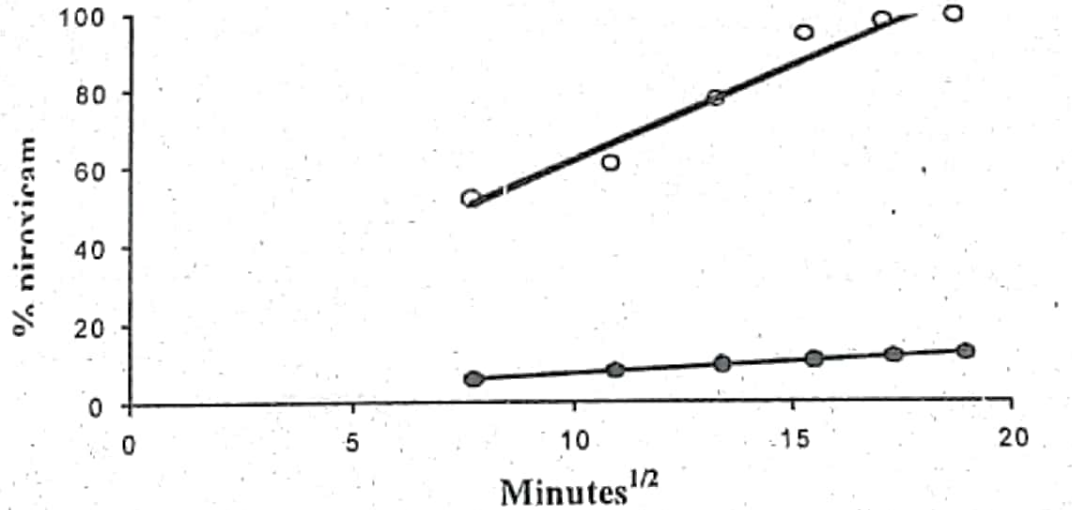


**Figure (9):** Drug release profile from polymeric films containing 20 mg of piroxicam at different EC:HPMC ratios. Key: (•), 8:2; (O), 2:8. *(Higuchi's diffusion model)*

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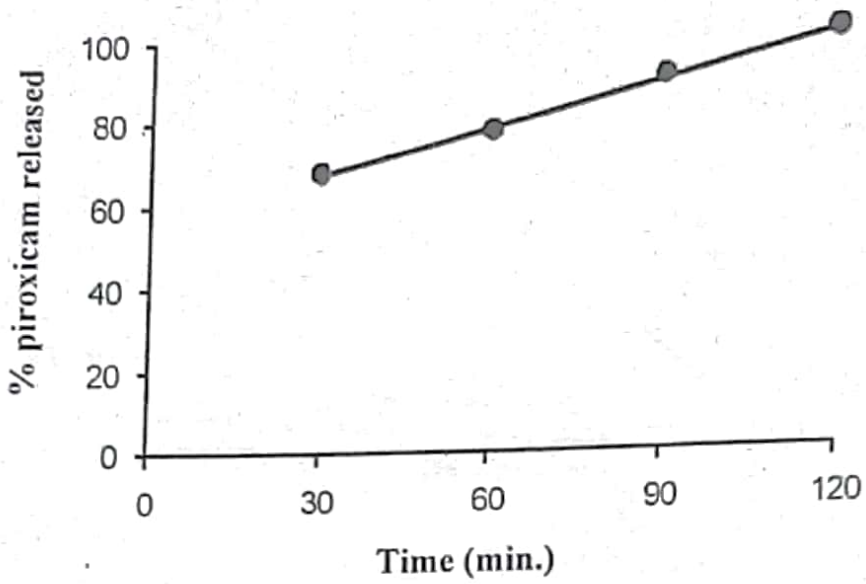


**Figure (10):** Drug release profile from HPMC film containing 20 mg of piroxicam. *(Zero order model)*

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# تحضير ووصف الأغشية البوليمرية للاستعمال الموضعي والمحتوية علي عقار مضاد للالتهابات

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يهدف هذا العمل إلي دراسة إمكانية تحضير وصياغة تركيبات مناسبة لأغشية بوليمرية موضعية دوائية محتوية علي عقار البيروكسيكام والذي يعد واحدا من الأدوية الفعالة ذات التأثير المضاد للإلتهاب ، ويعتبر عقار البيروكسيكام من مضادات الإلتهاب الغير ستيرودية، فهو يستخدم في علاج كثير من الأمراض الروماتزمية والتهابات المفاصل وغيرهما. وعقار البيروكسيكام متاح فى العديد من الصيغ الموضعية والتى لها فترة تأثير قصيرة (لا تتعدي أربعا وعشرين ساعة) مما يتطلب استخدامها باستمرار وعلى فترات قصيرة.وعلى هذا الأساس فإنه قد تم التفكير فى صياغة عقار البيروكسيكام فى أغشية بوليمرية والتى عن طريقها يمكن التحكم فى معدل انطلاق الدواء وكذلك إطالة فترة تأثير العقار لذلك كان الهدف من هذا العمل هو صياغة وتقييم أغشية بوليمرية تحتوى على البيروكسيكام وذلك باستخدام اثنين من بوليمرات السليلوز وهي الإيثيل سليلوز والهيدروكسي بروبايل ميثيل سليلوز. وقد تم تحضير العديد من هذه الأغشية البوليمرية والمحتوية على عقار البيروكسيكام ومن ثم تم تقييم انطلاق العقار منها وتقييمها فيزيائيا وكيميائيا باستخدام الأشعة تحت الحمراء والمسح الحراري وحيود الأشعة السينية.

أوضح استخدام الأشعة تحت الحمراء غياب الإزاحة العددية للمجموعات المميزة لعقار البيروكسيكام فى كل من الأغشية البوليمرية والمخاليط الطبيعية لكلا البوليمرين المستعملين مما يدل على عدم وجود تفاعل بينها وبين عقار البيروكسيكام. من ناحية أخري بين استخدام المسح الحراري التفاضلى اختفاء القيمة المعبرة عن انصهار العقار فى الأغشية البوليمرية وكذلك فى المخاليط الطبيعية. وقد أعزى اختفاء القمة المعبرة عن انصهار العقار فى الأغشية البوليمرية إلى وجود العقار فى هذه الأغشية فى الصورة الغير بللورية والتى يصعب ظهور القيمة المعبرة عن درجة انصهارها باستخدام المسح الحراري التفاضلى. من ناحية أخري أوضحت دراسات حيود الأشعة السينية تحول العقار من الشكل البللورى إلي الشكل الغير بللورى نتيجة لتكوين الأغشية البوليمرية. إضافة إلي ما تقدم، تم دراسة انطلاق الدواء من الأغشية البوليمرية وتبين أن انطلاقه من الأغشية يزداد بزيادة نسبة البوليمر المحب للماء وانطلاقه منها اسرع من انطلاقه من تلك المحتوية علي البوليمر الكاره للماء.