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Formulation, Characterization of Piroxicam Ointment for Topical Drug Delivery with Various Enhancers

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Abstract

The primary objective of the current study was to develop and then assess Piroxicam ointment with penetration enhancers, including castor oil, thymus oil, and clove oil. As per B. P., 4.750 g of hard paraffin melted at sixty degrees Celsius, and then 4.75 g of Cetostearyl alcohol, 4.75 g wool fat was added to create the 0.5% formulations of Piroxicam salt ointment was mix in it. Following the addition of 82.25 g of soft paraffin, and 3 ml of each of the following oils, such as thymol, clove, and castor, were added, first separately and then all at once, while stirring constantly. At last, the room temperature was reached by letting the ointment cool. These formulations were subjected to a comprehensive evaluation of their consistency, homogeneity, spread ability, viscosity, pH, drug content, UV absorbance, FTIR, DSC, and XRD study conducted. In addition to utilizing dialysis cellulose membrane, an in vitro study was carried out using Franz cells. Very well physicochemical properties were demonstrated by every synthesized composition. According to FTIR, SEM and XRD studies, the active ingredient (piroxicam salt) and additives used as drug permeation enhancers (oils) did not exhibit any physicochemical incompatibilities. The maximal release of the F4 thymol enhancer formulation was 69.183%. The current study found that the topical ointment of Piroxicam salt can be more permeable when it contains thymus oil >DNSO>clove oil >and castor oil.

Keywords: Piroxicam, Ointment, Thymus Oil, DMSO, Clove Oil, Castor Oil

Introduction

Piroxicam ointment is a topical non-steroidal anti-inflammatory drug (NSAID) with many benefits, such as avoiding first-pass metabolism, lowering gastrointestinal side effects, and increasing patient compliance. transdermal medication administration has become a viable substitute for traditional oral and injectable methods. Despite being a very effective barrier, the stratum corneum of the skin makes it difficult for therapeutic substances to penetrate, especially for medications with weak permeability or low solubility (1). To get over this restriction, penetration enhancers have been thoroughly researched for their capacity to temporarily break down the epidermal barrier, which makes it easier for drugs to be absorbed (2). Non-steroidal anti-inflammatory drugs (NSAIDs), such as piroxicam salt (2H-1,2-Benzothiazine-3-carboxamide, 4-hydroxy-2-methyl-N-2-pyridinyl-, 1,1-dioxide), are commonly used to treat

inflammatory diseases such as osteoarthritis, arthritis, and musculoskeletal problems. Because it inhibits cyclooxygenase enzymes, oral Piroxicam salt is frequently linked to gastrointestinal issues, such as ulcers and gastritis, despite its effectiveness. Because topical administration of Piroxicam salt localizes the drug's activity and reduces systemic exposure, it provides a workable solution to these problems. To achieve therapeutic efficacy, however, sophisticated formulations and penetration enhancers are required due to the drug's restricted skin permeability and poor solubility. The transdermal distribution of Piroxicam salt is significantly improved by the penetration enhancers. These enhancers improve medication flux across the skin by acting through processes such as lipid extraction, structural disturbance of the stratum corneum, and improved drug solubility. For example, research has shown that by changing the lipid-protein domains of the skin, these penetration enhancers can greatly increase the penetration of Piroxicam salt (3, 4). An important discovery in topical medication distribution is the creation of Piroxicam salt ointments with penetration enhancers. Ointments are perfect for localized therapy because they offer a suitable carrier for prolonged medication release and enhanced skin retention. Additionally, these formulations' long-term safety and acceptance are guaranteed by the inclusion of biocompatible and non-irritating enhancers. With an emphasis on maximizing medication penetration and therapeutic efficacy, this study attempts to design and assess Piroxicam salt ointments utilizing a variety of penetration enhancers (5). The goal of this research is to help create topical formulations of piroxicam salt that are both patient-friendly and efficacious by investigating the mechanisms of action and synergistic effects of various enhancers. By addressing the shortcomings of the present delivery systems and improving patient outcomes, the study's findings may open the door to better treatment choices for inflammatory disorders (6).

Materials and Methods

Chemicals

Piroxicam salt was obtained from Martin-Dow marker limited, Quetta, Balochistan. DMSO, Clove oil, castor oil, thymus oil, ethanol, Cetostearyl alcohol, Soft and hard paraffin, wool fat, and DI-water were provided by the Pharmaceutics department UOB. The cellulose membrane given by the Islamia university Bwalpure. All other chemical were used of standard grade.

Preparation of Piroxicam ointment:

4.75g of hard paraffin melts at sixty degrees Celsius to create a general B.P. ointment.
Adding 4.75g of cetostearyl alcohol adding 4.75g of wool fat and mix it, then adding 82.25g of soft paraffin, and finally and thoroughly mixing it with three milliliters of adding each one in various formulations (DMSO, Ethanol, castor oil, thymus oil, and clove oil). The resulting ointment was subsequently permitted to cool to room temperature. Given in Table 1. (7)

Table 1: Formulations of Piroxicam ointment with various enhancers

Ingredients	F1	F2	F3	F4	F5
Piroxicam	0.5	0.5	0.5	0.5	0.5
hard paraffin	4.75	4.75	4.75	4.75	4.75
Cetostearyl alcohol	4.75	4.75	4.75	4.75	4.75
Wool fat	4.75	4.75	4.75	4.75	4.75
DMSO	3	-	-	-	-
Ethanol	-	3	-	-	-
Castor oil	-	-	3	-	-
Thymus oil	-	-	-	3	-
Clove oil	-	-	-	-	3
soft paraffin	82.25	82.25	82.25	82.25	82.25

Calibration Curve

To prepare the piroxicam standard curve, a stock solution was prepared. Accurately weigh 100 mg in 100 ml V.flask and dissolve in 0.01N methanolic Hcl make the volume up to the mark. Diluted 1 ml of this solution in to 100 ml V.flak and make the volume up to mark with methanolic Hcl . From this stock, serial dilutions were prepared at concentrations of 0.01, 0.015, 0.02, 0.025, 0.03, 0.035 and mg/mL. Take absorbance at 333 nm against 0.01 N methanolic HCl as a blank. Linearity graph shown in Figure1.

Pharmaceutical evaluation of Piroxicam ointment:

The physicochemical characteristics of Piroxicam ointment were clarified as follows to assess the product's suitability for topical use.

pH: A titrated pH scale was used to calculate the pH scale for Piroxicam ointment (8).

Viscosity

To measure the viscosity of the preparation, the Brookfield RVDV ultra programmable rheometer (Brookfield Engineering Labs, Middleboro, MA) was used by rotating the spindle at 10 cpm at 25 °C. The spindle CP-41 was selected to evaluate the viscosity of multiple preparations in triplicate,(9).

Spreadability

The diameter of the 0.5 g creation that was produced when two 10 g glass slices were compressed was used to measure the spread of each preparation (10).

Consistency

The conical protrusion method was used to evaluate the consistency of Piroxicam ointment. To determine the consistency of the ointment, a funnel is attached to a 10-cm attaching bar that is placed in the middle of the cup occupied with oint; the distance travelled over 50 seconds is noted (11,12).

Homogeneity
Ointment homogeneity was checked for any lumpy objects, ointment was placed inside narrow, transparent glass tubes and examined under a light source (13)

Fourier Transform Infrared Spectroscopy (FTIR)
FTIR analysis was performed to evaluate the compatibility between the drugs and excipients in the formulation.. FTIR spectra were measured in the range of 4000–400 cm^{-1} using a FTIR (Perkin-Elmer, USA). The samples were prepared by mixing the components and analyzed under the same conditions as the pure drug and excipient formulations (14).

X-ray diffraction (XRD)
X-ray diffraction examinations of standard drug (Piroxicam) and ointment preparations were conducted via a software PAN analysis tool (*Netherlands) to confirm the pureness of the drug and prepared ointment (i.e., to determine whether amorphous or crystalline). The measurements were determined using a Cu-Ka anode with a voltage of 30 kV and an electric current of 15 mA. After that, the temperature was maintained at normal while the diffractograms were obtained at a pace of two minutes. For this purpose, a step width of 0.02° and 2X between the 2° and the 60° was used (14).

Scanning electron microscopy (SEM)
For the purpose stated above, an electron microscope [Maker FEI software (Hillsboro, Oregon, USA) was utilized.(14).

Drug content
To determine the amount of Piroxicam in the prepared ointments, 100 mg of each sample was liquefied, agitated in 100 ml dissolve in 0.01N methanolic Hcl make the volume up to the mark. Diluted 1 ml of this solution in to 100 ml V.flak and make the volume up to mark with methanolic Hcl filtered via a 0.2 μm filtering membrane, while observed by UV-Vis Spectrophotometer (15).

In vitro diffusion study
In laboratory propagation investigations, nylon membranes, dialysis cellulose membranes, and Franz diffusion cell equipment made by the well-known Perm Gear USA were chosen. The future and the owner of the donor's equipment for the Franz operation cells were given the membranes (16). The receptor chamber/compartment was filled with 5 millilitres of phosphate buffer with a pH of 7.3. Piroxicam ointment was made and applied to the chamber at 37 degrees Celsius. The prepared ointment contains 1, 2, and 3 percent clove oil. On and off at 0.5, 1 and 1.5, 2, 3, 4, 8, 12, 16, 20, and 24 hours. 2 ml samples were taken from the cells, which were then immediately packed with buffer at 37 ℃. The samples were filtered using a type of Millipore filter sieve. Whatman, Germany, 150 millimeters of filter paper, and the "UV visible spectrophotometry process" was used to estimate the content of piroxicam ointment (17).

Piroxicam release kinetic analysis in vitro
The amount of Piroxicam ointment released was evaluated by in vitro diffusion tests. To determine whether specific kinematic models matched the drug release through dialysis cellulose membrane, the release of drug aspects and linear regression were investigated. (18).

Stability study
For three months, in compliance with ICH recommendations, samples of ointment formulations were tested for stability in terms of pH, spreadability, viscosity, and medicine content (16)

Statistical analysis

The SPSS software's ANOVA test was used to analyze the data. For the drug release kinetics of transdermal Piroxicam ointment, various kinetic modes were employed with DD solver (19).

Results and Discussions

Physical characteristic: Physical character of piroxicam ointment Formulations Table 1 discusses the organoleptic characteristics of the ointment preparations, such as their homogeneity and appearance, and texture. The ointments were described as having a smooth texture, a white and yellowish-white colour, and good homogeneity. All formulations' pH values fell between 5.42±0.143 and 6.30±0.263, which is within the recommended range and falls within the typical skin pH range listed in Table 1. As presented in Table 2, the viscosity of each formulation was measured and determined to be between 2112±5.13 and 2602±7.03 CPS at 10 r.p.m. As indicated in Table 2, the ointment dispersion capability of formulated ointment is explained by measuring the diameter of the 0.5-gram preparation after pressing b/w 02 glass slices 10g. Table 2 shows that the Peroxicam ointment medication concentration ranged from 96.34to 98.11%. Dialysis cellulose membrane was used in this investigation; statistically, the membranes were seen to have been well freed. The formulation with the highest release (69.19%) was F4. These findings are consistent with previous research by (20), that provided a thorough verbal description of the release of piroxicam in semi-solubilized dosage forms. Figure 2 shows the release of Peroxicam ointment from the topical formulation and its passage via the dialysis cellulose membrane. Stability analysis of According to ICH criteria, samples of ointment formulations were examined for stability; the results are shown in Table 3. The findings demonstrated that, over three months, there was no discernible variation in the ointment's pH, spreadability, viscosity, or medication content [11].

Figure 1: Calibration Curve of Piroxicam

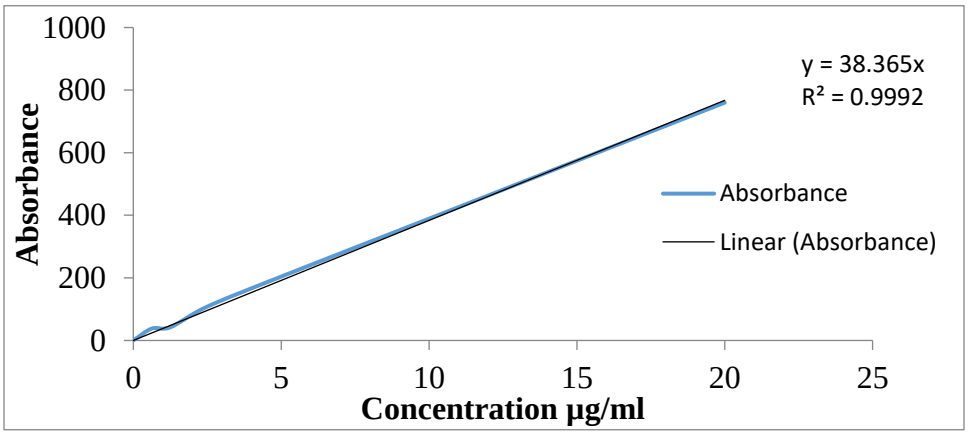


Table 1: Physical Characteristics for the formulation of piroxicam ointment

S. No	coded formulation	Percentage of API in formulation	pH	Consistency	Texture and color
1	F_1	0.5%	5.45	Good homogeneity	Milky-white
2	F_2	0.5%	6.28	Good homogeneity	Milky-white
3	F_3	0.5%	6.30	Good homogeneity	Milk-white
4	F4	0.5%	5.41	Good homogeneity	Milk-white
5	F5	0.5%	5.41	Good homogeneity	Light yellow

Table 2: Pharmaceutical characteristics of piroxicam oint. Formulation

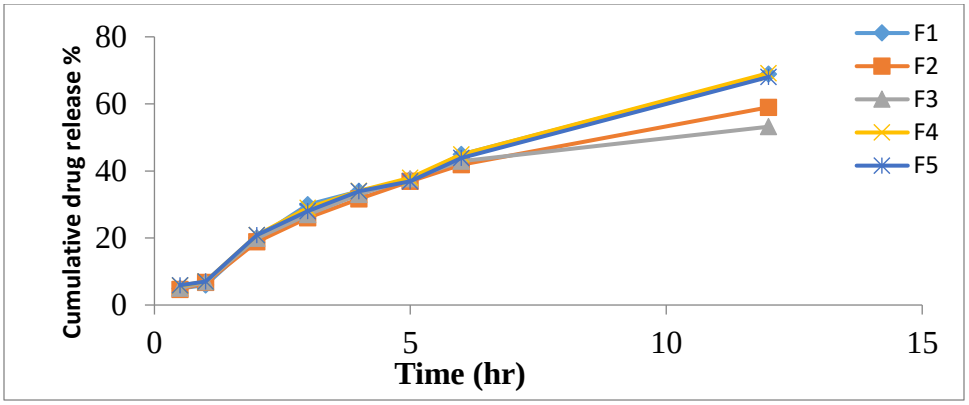
S. No	coded formulation	Percentage of API in formulation	Viscosity (centipoise (cP))	Spread ability(g.cm/s)	Drug content	Skin displeasure
1	F_1	0.5%	2312	5.12	98.01	Nill
2	F_2	0.5%	2423	5.33	97.22	Nill
3	F_3	0.5%	2602	5.40	96.34	Nill
4	F4	0.5%	2312	5.40	97.12	Nill
5	F5	0.5%	2112	5.20	98.11	Nill

Table 3: Stability Assessment of Piroxicam ointment in different concentrations

S. No	Physicochemical Characteristic	Stability test (Mean±SD) 0 M	Stability test (Mean±SD) 1 M	Stability test (Mean±SD) 2 M	Stability test (Mean±SD) 3 M
1	pH	6.12	6.01	6.32	6.02
2	Viscosity (cP)	2301	2113	2234	21.1
3	Drug content (%)	96.00	96.45	92.156	89.11

M stands for Month, SD stands for Standard Deviation

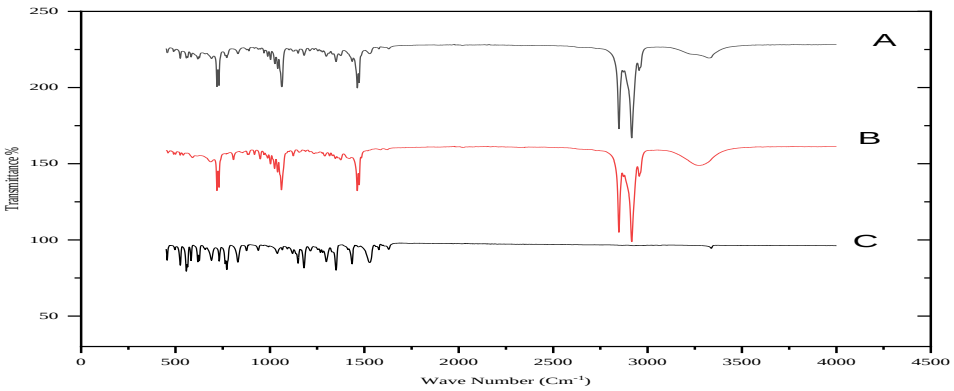
Figure .2 Release OF Piroxicam oint via Cellulose membrane



FTIR Analysis

No expressive interaction between the drug and excipient was noticed by FTIR for Piroxicam ointment formulation. Piroxicam was observed with retention of characteristic peaks at 1000 cm^{-1} to 1500 cm^{-1} corresponding to C=O stretching while at 3000 cm^{-1} with retention of N-H stretching peak in the spectrum for piroxicam; it thus, depicts their stability within the ointment shown in Figure 3.

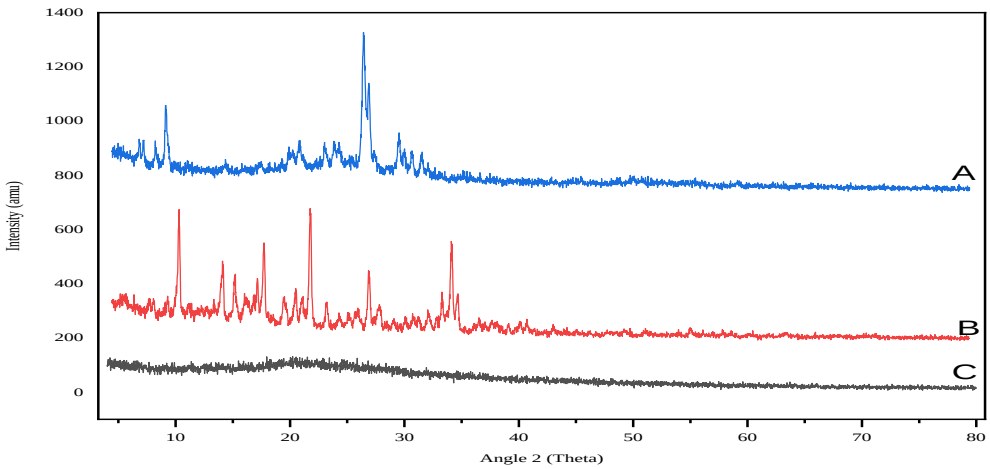
Figure:3 FTIR spectra of Piroxicam drug A, Blank B, Formulation F4 is C



XRD Studies

Examine the Piroxicam ointment's chemical and physical characteristics. The polymeric matrix of the ointment formulation displayed prominent peaks of spreading at an angle of 2θ value of 20.15 degrees, 25.23 degrees, and 28.10 degrees, among others, according to X-ray diffraction studies (21). The crystalline nature of piroxicam is demonstrated by the X-ray diffractograms in Fig. 4, A. However, the medication formulation in Figure. 4(C) revealed no peaks or peaks of lower intensity, whereas the ointment's diffractograms showed fused peaks. In polymeric pharmaceuticals with a molecularly discrete character, the drug transformed into an amorphous type, as shown by the irregular peaks of the blank Figure 4, B.

Figure:4 X-ray diffractogram of Piroxicam drug A, Blank B, Formulation F4 is C

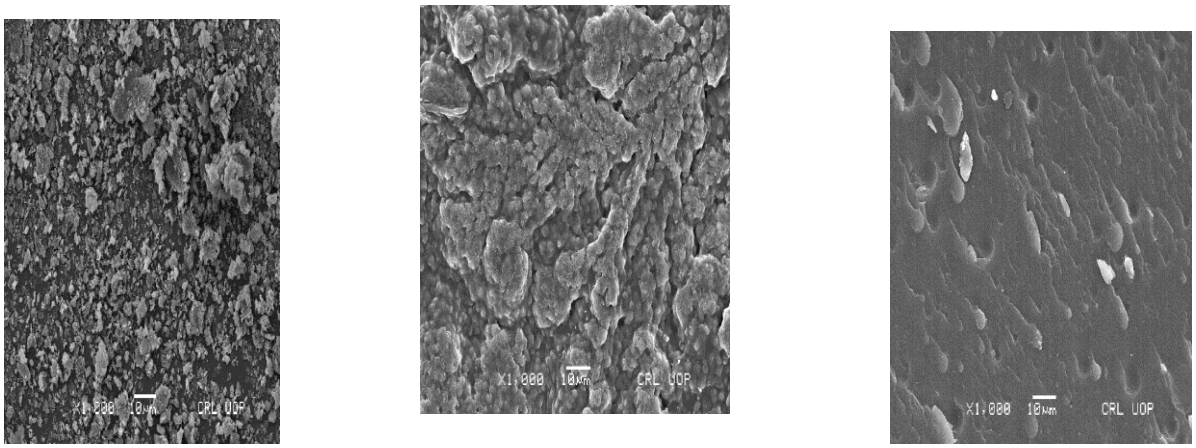


Scanning electron microscopy (SEM)

Using scanning electron microscopy, the size and morphology of the produced piroxicam ointment were ascertained. SEM pictures of various preparations were captured. ointment containing piroxicam. was visible in SEM pictures (Fig. 5(A)). Most pure drugs had an ointment with a large, crystal-like form, while fig. 5(B) blank shows tiny white spots, indicating of the excipients formulation (Fig. 5(C) indicating the drug dispersed throughout the ointment preparations

Figure:5 scanning electron microscopy of Piroxicam drug A, Blank B, Formulation F4 is C

A B C



Conclusion

The formulation and assessment of piroxicam ointments using various penetration enhancers demonstrated that the choice of enhancer significantly influences the drug's release and skin permeation profile. Among the formulations evaluated those containing enhancers such as, thymus oils, DMSO castor oil, ethanol and clove showed improved in this order thymus oil >DMSO>clove oil >and castor oil physicochemical characteristics, better spreadability, and enhanced drug diffusion through the skin barrier. These findings suggest that optimizing penetration enhancers in topical piroxicam formulations can significantly enhance therapeutic efficacy while minimizing systemic exposure. Overall, this study underscores the importance of formulation strategy in developing effective and patient-friendly topical drug delivery of Piroxicam.

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Conflict of Interests

We guarantee that there are no conflicts of interest in this article.

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