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# Comparative evaluation of selected vegetable oils and Terpenes on Transdermal permeation of Ketorolac Tromethamine

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**Abstract**

A reservoir type transdermal patch for delivery of ketorolac tromethamine (KT), a potent analgesic agent was studied. Studies were carried out to investigate the effect of permeation enhancers on the in vitro permeation of KT across rat skin. Films were prepared by using hydroxy propyl methyl cellulose (HPMC) and polyvinylalcohol (PVA) polymers by incorporating glycerine as plasticizers using solvent casting method. A total of fourteen formulations were prepared by using same drug polymer ratio of 1:1 and incorporated different terpenes and vegetable oils as permeation enhancers in same concentrations. The prepared systems released the drug in the following order: FP2 > FP3 > FH2 > FP5 > FH3 > FP4 > FH5 > FH4 > FH6 > FP6 > FH7 > FP7 > FH1 > FH1. The various permeation parameters such as enhancement ratio and percent of drug permeated were determined for all the formulations. The maximum percent of drug permeation was observed with PVA monolithic system containing 10% d-limonene. Permeation enhancement of KT with different enhancers followed the order: d-limonene > cineole > olive oil > menthol >linseed oil > sunflower oil. The *in vitro* release studies revealed that terpenes showed better permeation enhancement than vegetable oils and the release was sustained up to 24 h and it follows zero-order kinetics. All the films were found to be stable at 37°C and 45°C with respect to their physical parameters. A reservoir type transdermal patch for delivery of KT thus appears to be feasible of delivering KT across skin.

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***Key words:***
Ketorolac tromethamine (KT), transdermal, HPMC, PVA, terpenes, vegetable oils, permeation

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## Introduction:

Keotrolac (administered as tromethamine salt), a prostaglandin synthetase inhibitor is a non-steroidal anti-inflammatory drug with potent analgesic and moderate anti-inflammatory activities [1].

Administered as oral and injectable formulations, it has shown a high analgesic potency almost equivalent to that of morphine [2]. It is currently administered orally, intramuscularly or intravenously for short-term management of moderate to severe pain, including postoperative and postpartum pain and visceral pain associated with cancer.

Oral bioavailability of ketorolac tromethamine is reported to be 90% with a very low first pass metabolism. However, the drug is reported to cause severe gastrointestinal side effects like gastrointestinal bleeding, perforation and peptic ulceration. Therefore, parenteral administration of ketorolac is the preferred route of administration for moderate to severe pain management. The biological half life of Ketorolac ranges from 4 to 6 hours, because of such a short life, frequent dosing is required to alleviate pain in post operative patients. However, to avoid an invasive drug delivery technique (intra muscular injection) and to eliminate frequent dosing regimens, there is a need for an alternative; non-invasive mode of delivery of Ketorolac tromethamine [3].

There has been increased interest and challenges in the delivery of an active ingredient through the skin. Drug delivery via the percutaneous route potentially has many advantages over intravenous and oral administration [4] but human skin is designed to be a barrier to the passage of molecules either from inside to out or vice versa [5]. The principal barrier to topical drug delivery is the stratum corneum, which poses a formidable barrier to drug penetration, thereby limiting topical and transdermal bioavailability [6]. Many approaches have been employed to mitigate stratum corneum permeability, and the most commonly used approach is that of sorption promoters, also known as penetration enhancers [4, 7]. Since there are several problems associated with synthetic permeation enhancers like dimethyl sulfoxide and dimethyl formamide which cause reversible denaturation of keratin and lead to keratolysis, the skin may take few days to recover during which it may be prone to invasive. The use of ionic surfactants is limited by their irritation potential. Hence there is a quest for permeation enhancers of proven safety. The fixed oils are thick viscous liquids; they cause occlusion of the skin and are likely to increase the permeation of drugs. Since they are food materials, toxicity is of less concern. They are metabolized in the body and are cheap and easily available [8]. Terpenes are a very safe and effective class of penetration enhancers, obtained from natural sources. The FDA classifies them as generally regarded as safe (GRAS) [9]. However, there is a lack of work pertaining to comparative study on efficacy and safety between the terpenes and vegetable oils in the transdermal permeation of drugs.

Hence in the present study, transdermal monolithic films of ketorolac tromethamine will be prepared using various film forming agents and an comparative evaluation between various vegetable oils like sesame oil, castor oil, linseed oil, coconut oil, sunflower oil and terpenes like menthol, cineole, limonene, citral etc will be carried out. No reports are available on the comparative evaluation of different oils on the transdermal permeation enhancement of ketorolac tromethamine. Thus, the present study is aimed at comparing and finding the efficacy and safety of the above said oils in the transdermal permeation of the selected model drug.

**Materials and method:**

**Materials:**

ketorolac tromethamine was obtained as gift sample from centaur Pharmaceuticals Pvt Ltd, Goa. Hydroxypropyl methylcellulose (HPMC K15M) and Ethyl cellulose (EC 20cps) were obtained from Colorcon Ltd, Goa. PVA was obtained from SD fine chemicals, mumbai. All other reagents and solvent used were of analytical grade.

**Method:**

The transdermal films of ketorolac tromethamine were prepared by employing various polymers like HPMC, PVA and EC was used for preparing rate limiting membrane by solvent casting method.

**Drug reservoir:**

The polymeric solution was prepared by dissolving the required quantity of polymer in distilled water (2.5 ml) and glycerine (30% w/w of polymer) was added as plasticizer to this solution under stirring. The weighed amount of ketorolac tromethamine was added to the above solution. To the above solution the calculated amount of permeation enhancers were added. After proper mixing the casting solution (5 ml) was poured in a clean glass bangle (an area of 9.61 cm2) which is placed on the mercury surface. The films were dried at room temperature for 24 h. The dried films thus obtained were cut by cork borer into circular discs of definite size of 14 mm diameter (an area of 1.539 cm2) containing 40 mg of drug.

**Preparation of rate limiting membrane:**

The rate controlling membrane was prepared by dissolving required quantity of ethyl cellulose in chloroform. Dibutyl phthalate (30% w/w of polymer) was added as plasticizer. The polymeric solution was poured on a clean glass petridish and dried at room temperature for 12 hrs. Circular discs of 10mm diameter were cut using cork borer.

**Preparation of transdermal films:**

The reservoir films containing the drug were sandwiched in between the rate controlling membranes. They were fixed by applying chloroform on the edges of the rate controlling membrane.

**Evaluation of Transdermal Patches [10]**

The transdermal membranes prepared were evaluated for the following parameters:

**Physical appearance:** All the prepared patches were visually inspected for color, clarity, flexibility and smoothness.

**Film Thickness uniformity:** The thickness of the formulated film was measured at 3 different points using a digital caliper and average thickness of three reading was calculated.

**Film Weight variation:** For each formulation, three randomly selected patches were used. For weight variation test, 3 films from each batch were weighed individually and the average weight was calculated.

**Folding endurance:** The folding endurance was measured manually for the prepared films. A strip of film (5 x 5 cm) was cut and repeatedly folded at the same place till it broke. The number of times the film could be folded at the same place without breaking/cracking gave the value of folding endurance.

**Percentage moisture absorption:** The films were weighed accurately and placed in the desiccators containing 100 ml of saturated solution of potassium chloride, which maintains 80-90% RH. After 3 days, the films were taken out and weighed. The study was performed at room temperature. The percentage moisture absorption was calculated using the formula:

$$\text{Percentage moisture absorption} = \frac{\text{Final Weight} - \text{Initial Weight}}{\text{Initial Weight}} \times 100$$

**Percentage moisture loss:** The films were weighed accurately and kept in a desiccators containing anhydrous calcium chloride. After 3 days, the films were taken out and weighed. The moisture loss was calculated using the formula:

$$\text{Percentage moisture loss} = \frac{\text{Final Weight} - \text{Initial Weight}}{\text{Initial Weight}} \times 100$$

**Tensile strength:** Tensile strength of the film was determined with Universal strength testing machine (Hounsfield, Slinfold, Horsham, U.K.). The test film of size (4 × 1 cm2) was fixed between these cell grips and force was gradually applied till the film broke. The tensile strength of the film was taken directly from the dial reading in kg. Tensile strength is expressed as follows:

$$\text{Tensile strength} = \frac{\text{Tensile load at break}}{\text{Cross section area}}$$

**Drug Content Uniformity of Films:** The patches (1cm2) were cut and added to a beaker containing 100 ml of phosphate buffer saline of pH 7.4. The medium was stirred with magnetic bead. The contents were filtered using whatman filter paper and the filtrate was examined for the drug content against the reference solution consisting of placebo films (contains no drug) at 322 nm spectrophotometrically.

**FTIR studies:**

Pure drug and optimized formulation were subjected for FTIR analysis using Fourier transformer infrared spectrophotometer (8600, Shimadzu Corporation, Japan).The samples were prepared on KBr-press (Spectra Lab, India) and scanned over wave number range of 4000 to 400 $cm^{-1}$. Spectra were analyzed for drug polymer interactions and functional groups

**DSC studies:**

The optimized formulation were subjected to differential scanning calorimeter (DSC Q20 V24.4 Build 116, Japan.) at a heating rate of 10 $^{o}$C/min over a temperature range of 0-300 $^{o}$C. The sample (pure drug and optimized formulation) was hermetically sealed in an aluminum crucible. Nitrogen gas was purged at the rate of 10 ml/min for maintaining inert atmosphere.

**In vitro permeation across the rat abdominal skin**

**Preparation of the rat skin** [11]

The experiment was conducted according to the protocol approved by the institutional animal ethics committee (IAEC NO: 576/2002/bc/IAEC/CPCSEA). The experiment was conducted according to the guidelines of CPCSEA (Committee for the purpose of control and supervision of experiment on animal). The male abdominal rats were sacrificed by decapitation. The fresh abdominal skin was excised from male albino rat weighing 170-190 g. The abdominal skin of excised hairless rat skin was separated along the epidermal junction. The hair of skin was removed using depilatories. The process of the removal of hair did not alter the skin properties and delivery of the drug. It was kept in water bath which was maintained at 60˚C for exactly 50 seconds. The heat treated skin was cleared of it subcutaneous fatty substance an immediately kept in refrigerator at 10˚C. This step maintained integrity and viability of the skin

**Permeation studies** [12]

A vertically assembled Franz diffusion cell having downstream volume of 75 ml was used. The above skin was mounted on the diffusion cell and receiver compartment was filled with 75 ml phosphate buffer of pH 7.4 and the temperature was maintained at 37$^{o}$C. The samples were withdrawn every hour (replaced with 5 ml fresh buffer to maintain sink condition) and their concentrations were measured in UV- spectrophotometer at 322.5 nm.

**In vivo studies**

**Anti-inflammatory activity:**[ 13]

The animals, wistar rats were divided into two groups. Acute inflammation was reduced by sub planter injection 0.1ml of 1% solution of carrageenan in normal saline, in the right hind paw of the rats; one hour after application of patch .The paw volume was measured by using plethysmometer at regular periods of time interval after the injection of carrageenan.

**Analgesic activity** [14, 15, 16]

**Procedure:** Twelve albino mice were selected and divided into two groups each having six mice. The ventral surface of the animals were depilated and divided into group-I (control) and group-II (test). The selected test film containing the dose of

ketorolac tromethamine equivalent to body weight was stuck on the animal and a backing laminate of aluminum foil was placed over the film and it was kept intact with the help of an adhesive tape. Acetic acid 0.6% v/v injected intraperitonially (1ml/ 100 gram of body weight of animal) was induced to both the groups and the number of writhes was noted. The activity of the formulation was statistically analyzed by "student t' test".

**Skin irritation studies:** [13]

The skin irritation test was performed on six healthy albino rabbits weighing between 2.0 to 3.5 kg. Aqueous solution of formalin 0.8% was used as standard irritant. Drug free polymeric patches of 20 $cm^2$ were used as test patches. 0.8% of formalin is applied on the left dorsal surface of each rabbit, where as the test patches were placed on identical site, on the right dorsal surface of the rabbit. The patches were removed after a period of 24hours with the help of alcohol swab. The skin was examined for erythma /edema.

**Results and discussion:**

The thickness of the prepared transdermal films was determined by micrometer screw gauge. The thickness of the transdermal films was found to be directly proportional to the polymeric concentration. The thickness of the transdermal films varied between 0.173±0.008 to 0.230±0.004 mm. The weights of transdermal films were determined by electronic balance. The weights were found to be in between 17.6±0.156 to 34±0.065 mg. The folding endurance of a film is frequently used to estimate the ability of the film to withstand repeated bending, folding and creasing and may be encountered as a measure of the quality of the films. The folding endurance for transdermal films were found to be in the range of 88.0±5.12 to 125.24±7.30. The percentage moisture absorption test was carried out to check physical stability or integrity of the film at humid condition. Among all, the formulations containing PVA showed maximum moisture absorption (15.98±0.67) when compared to the formulations containing HPMC+EC (13.41±0.12).The percentage moisture loss study was carried out to check the integrity of the transdermal films at dry condition. Among all, the formulations containing HPMC+EC showed maximum moisture loss (20.69±0.8) when compared to the formulations containing PVA (15.81±042). Tensile strength of the film was determined to measure the ability of a patch to withstand rupture with Universal strength testing machine. As the concentration of hydrophilic polymer was increased there is increase in tensile strength. The tensile strength for transdermal films were found to be in the range of 3.54 ±0.057 to 7.05± 0.056 kg/$mm^2$. The studies were carried out in triplicate and the results are shown in Table 4.

**Drug content uniformity:**

The drug content uniformity of the transdermal films was determined according to procedure described in methodology. The drug content in all the formulations was found to be in between 0.934±0.054 to 0.987±0.063 mg. The results showed that, the drug content was uniform and reproducible in each batch of different transdermal film formulations. The results of the drug content are shown in Table 4.

**FTIR Studies:**

The IR spectrum of formulations KT, KT+HPMC, KT+PVA containing the pure drug and polymer is taken as the representative formulations and characterized. The spectra's clearly indicate that there is no interaction of the drug with the polymer and excipients used in the present study as shown in figure 6- 8.

**DSC studies:**

The observations of the nature of the endothermic peaks and their corresponding values indicating the melting points, suggest that the melting point of the drug and its formulations KT, KT+HPMC, KT+PVA similar to the reported

literature. These values indicate that there is no interaction of the drug with the polymer and various excipients used for the study as shown in figure 9-11. Thus like IR spectra DSC thermograms also support the fact that no interaction of the drug with the polymers in the formulations prepared.

**In- vitro release study:**

The *in vitro* release of drug across rat kin from HPMC and PVA Transdermal films showed only 55.22% (FH1) and 61.25% (FP1) at the end of 24hr respectively (fig 3, fig 4 and fig 5) the poor drug release which might be attributed to tough barrier, the stratum corneum of skin which contributes to low diffusivity. It was evident from the above result that, the release of drug was less. Hence, there is a need to incorporate permeation enhancer in the system.

Transdermal films of HPMC and PVA were prepared using permeation enhancers like d-limonene, cineole, menthol, olive oil, linseed oil and sunflower oil at 10 % concentration.

The release from PVA transdermal patches using permeation enhancers were. FP2 (10% d- limonene) 93.19%, FP3 (10% cineole) 88.63%, FP4 (10% menthol) 83.10%, FP5 (10%olive oil) 85.68%, FP6 (10%linseed oil) 79.40%, FP7 (10% sunflower oil) 75.28%.

The release from HPMC transdermal patches using permeation enhancers and EC as rate controlling membrane were.

FH2 (10% d- limonene) 87.47%, FH3 (10% cineole) 85.39%, FH4 (10% menthol) 81.04%, FH5 (10%olive oil) 82.38%, FH6 (10%linseed oil) 80.45%, FH7 (10% sunflower oil) 76.48%.

From the results it indicates that the release profile of PVA Transdermal films using permeation enhancers showing highest release profile when compared to the HPMC Transdermal films prepared with permeation enhancers of same concentration. Further it was observed that transdermal patches using terpenes as permeation enhancers showed highest release profile FP2 (10% d- limonene) 93.19%. When compared to formulations prepared with vegetable oils as permeation enhancers (fig 5). Enhancement ratios of vegetable oils and terpenes on formulated transdermal films of ketorolac tromethamine are shown in fig 1.

Terpenes probably modify the solvent nature of the stratum corneum, improving drug portioning into the tissue. Terpenes permeate the skin well. The results permeate that terpenes may also modify drug diffusivity through the membrane and bring about a reduction of the lag time for permeation, indicating an increase in the diffusivity of the drug through the membrane following terpenes treatment [17].

***In vivo* studies:**

The formulation (FP2) with better *in vitro* release profile was selected for *in vivo* studies.

**Anti-inflammatory activity**

To find out the efficacy of drug in controlling inflammation, anti-inflammatory activity for the formulation FP2 was evaluated using formalin induced rat paw oedema method [18]. The percentage of oedema reduction for the system FP2 was found to 64% at the end of 12 hrs. The data was analyzed by using P-STAT package. Formulation FP2 showed a significant anti-inflammatory activity at $p < 0.001$, 0.05 and 0.01.

**Analgesic activity**

The analgesic activity for the formulation FP2 was carried out by acetic acid induced writhing [16]. The formulation showed good analgesic activity up to 12hrs. The data was analyzed by using P-STAT package and showed significant analgesic activity at $p < 0.05$ and 0.001. A bar graph of mean of number of writhes per 15 minutes versus time was plotted as shown in fig 2.

**Skin irritation studies [14]**

The skin irritation study was performed by applying the sterile optimized transdermal patch FP2 on the skin of Swiss albino rabbits. After administration of the formulation FP2 no signs of

redness or erythma observed for 24 hrs after application of the patch. Thus it was concluded that the formulation remained non irritant to rabbit skin.

**Conclusion:**

Various batches of ketorolac tromethamine transdermal films were prepared using solvent casting method and evaluated. Reservoir type transdermal films (formulation FP2) consisting of 10% d-limonene satisfied all the pharmaceutical parameters of transdermal films and showed the highest percent of drug release in controlled manner over the period of 24 hrs. The said promising formulation would be able to offer benefits such as increase permeation of drug, prolonged drug release, reduction in frequency of administration and thereby may help to improve the patient compliance with the limitation that formulation is non-erodible. Further work may be carried out to establish the therapeutic utility of this system by pharmacokinetic and pharmacodynamic studies in human beings.

**Acknowledgement:**

The authors are grateful to centaur Pharmaceuticals Pvt Ltd, Goa for providing gift sample of ketorolac tromethamine. The authors would like to acknowledge the management, N.E.T Pharmacy College, Raichur, India for providing necessary facilities during research.

**Table No. 1:** Composition of transdermal films of ketorolac tromethamine using HPMC

| Formulation Code | Drug Reservoir | | Permeation Enhancers | | | | | | Plasticizer (30% of Polymer) | Rate Limiting Membrane |
|---|---|---|---|---|---|---|---|---|---|---|
| | Ketorolac Tromethamine (mg) | HPMC (mg) | Terpenes (ml) | | | Vegetable Oils (ml) | | | Glycerine (ml) | Ethyl Cellulose (%) |
| | | | d-limonene | menthol | eucalyptol | Olive oil | Linseed oil | Sunflower oil | | |
| FH1 | 250 | 250 | - | - | - | - | - | - | 0.0597 | 2 |
| FH2 | 250 | 250 | 0.029** | - | - | - | - | - | 0.0597 | 2 |
| FH3 | 250 | 250 | - | 0.0280** | - | - | - | - | 0.0597 | 2 |
| FH4 | 250 | 250 | - | - | 0.0271** | - | - | - | 0.0597 | 2 |
| FH5 | 250 | 250 | - | - | - | 0.0277** | - | - | 0.0597 | 2 |
| FH6 | 250 | 250 | - | - | - | - | 0.0271** | - | 0.0597 | 2 |
| FH7 | 250 | 250 | - | - | - | - | - | 0.0272** | 0.0597 | 2 |
| Casting Solvent | Water (2.5 ml) | | | | | | | | | Chloroform |

**Table No. 2:** Composition of transdermal films of ketorolac tromethamine using PVA

| Formulation Code | Drug Reservoir | | Permeation Enhancers | | | | | | Plasticizer (30% of Polymer) |
|---|---|---|---|---|---|---|---|---|---|
| | Ketorolac Tromethamine (mg) | PVA (mg) | Terpenes (ml) | | | Vegetable Oils (ml) | | | Glycerine (ml) |
| | | | d-limonene | menthol | eucalyptol | Olive oil | Linseed oil | Sunflower oil | |
| FP1 | 250 | 250 | - | - | - | - | - | - | 0.0597 |
| FP2 | 250 | 250 | 0.029** | - | - | - | - | - | 0.0597 |
| FP3 | 250 | 250 | - | 0.0280** | - | - | - | - | 0.0597 |
| FP4 | 250 | 250 | - | - | 0.0271** | - | - | - | 0.0597 |
| FP5 | 250 | 250 | - | - | - | 0.0277** | - | - | 0.0597 |
| FP6 | 250 | 250 | - | - | - | - | 0.0271** | - | 0.0597 |
| FP7 | 250 | 250 | - | - | - | - | - | 0.0272** | 0.0597 |
| Casting Solvent | Water (2.5 ml) | | | | | | | | |

**Table No. 3:** Kinetic analysis of release data based on best curve-fitting method for optimized transdermal films of Ketorolac tromethamine

| Formulation code | Zero order | | First order | | Highuchi | | Korsmeyer-peppas | |
|---|---|---|---|---|---|---|---|---|
| | n | $r^2$ | n | $r^2$ | N | $r^2$ | n | $r^2$ |
| **FP2** | 4.018 | 0.996 | -0.043 | 0.903 | 20.41 | 0.911 | 1.001 | 0.996 |
| **FP5** | 3.630 | 0.998 | -0.029 | 0.952 | 18.47 | 0.916 | 1.265 | 0.957 |
| **FH2** | 3.820 | 0.994 | -0.035 | 0.957 | 19.56 | 0.924 | 1.088 | 0.997 |
| **FH5** | 3.515 | 0.999 | -0.032 | 0.942 | 17.89 | 0.917 | 1.076 | 0.998 |

Average of three determinations ± SD

**Fig 1:** Enhancement ratio of ketorolac tromethamine with different enhancers

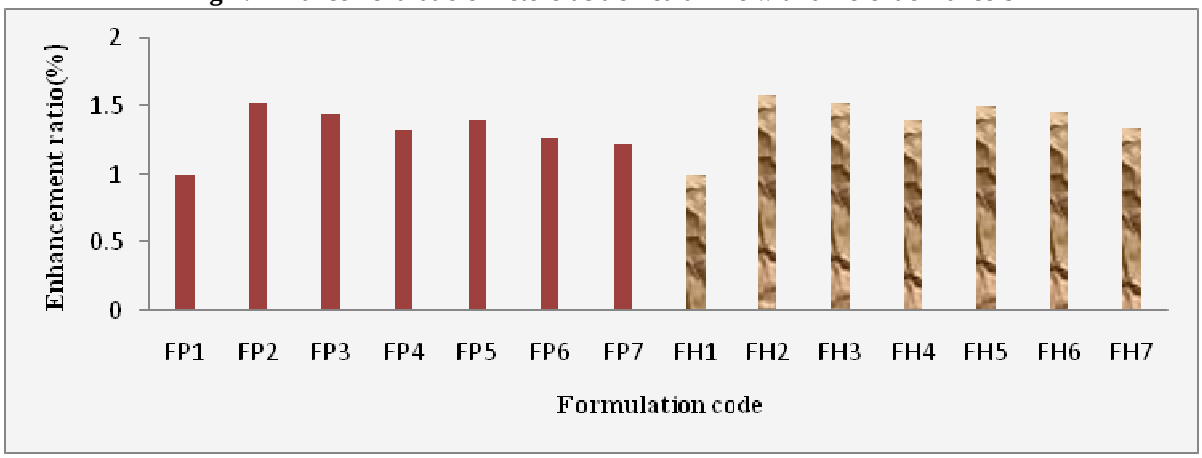


**Fig 2:** Analgesic activity of control and FP2 formulation

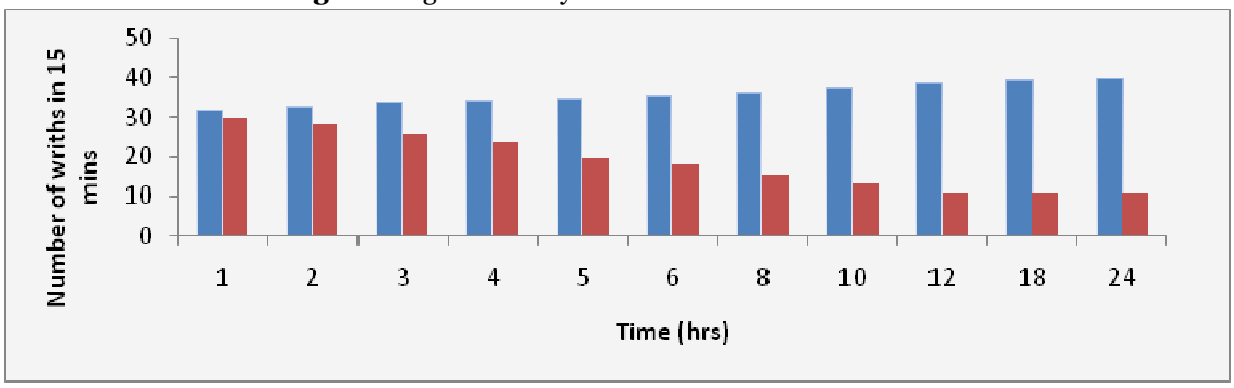


**Fig 3:** Effect of permeation enhancers on *in-vitro* permeation of Ketorolac tromethamine from PVA transdermal films in PSB of pH 7.4

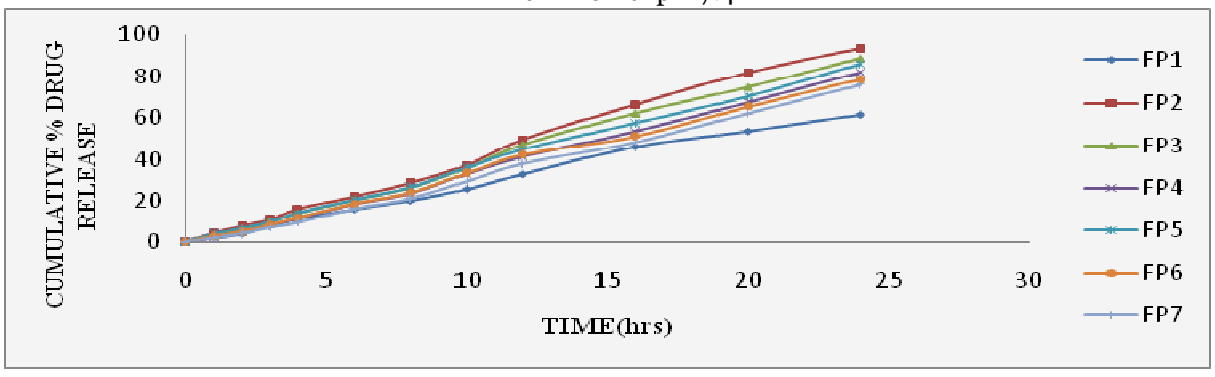

**Fig 4:** Effect of permeation enhancers on *in-vitro* permeation of Ketorolac tromethamine from HPMC transdermal films in PSB of pH 7.4

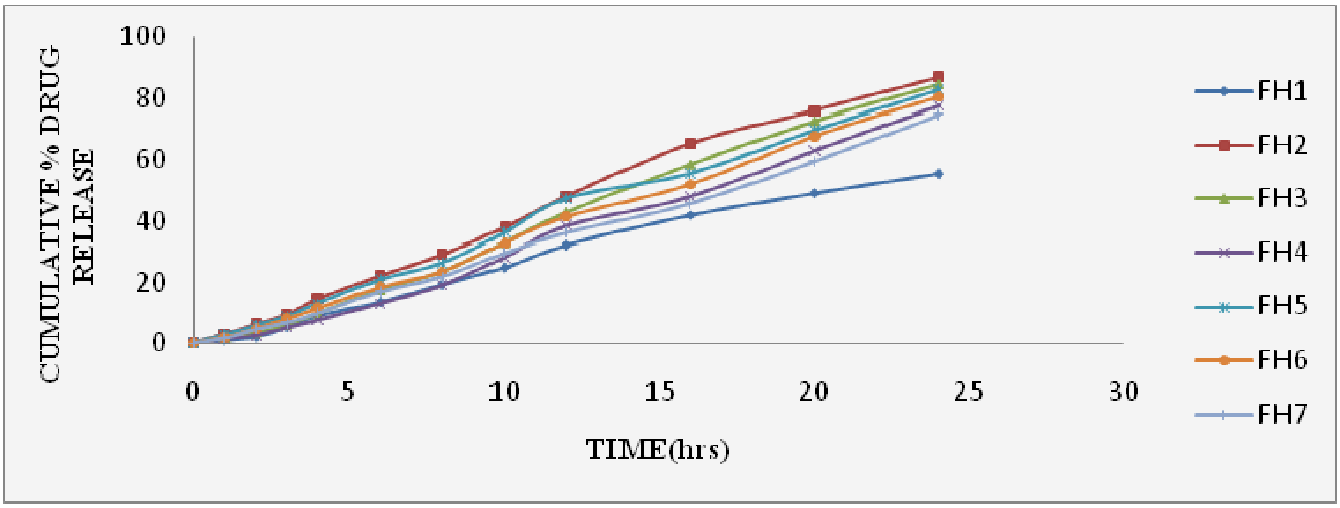


**Fig 5:** Comparision of Terpenes and Vegetable oils on *in-vitro* permeation of Ketorolac tromethamine from transdermal films

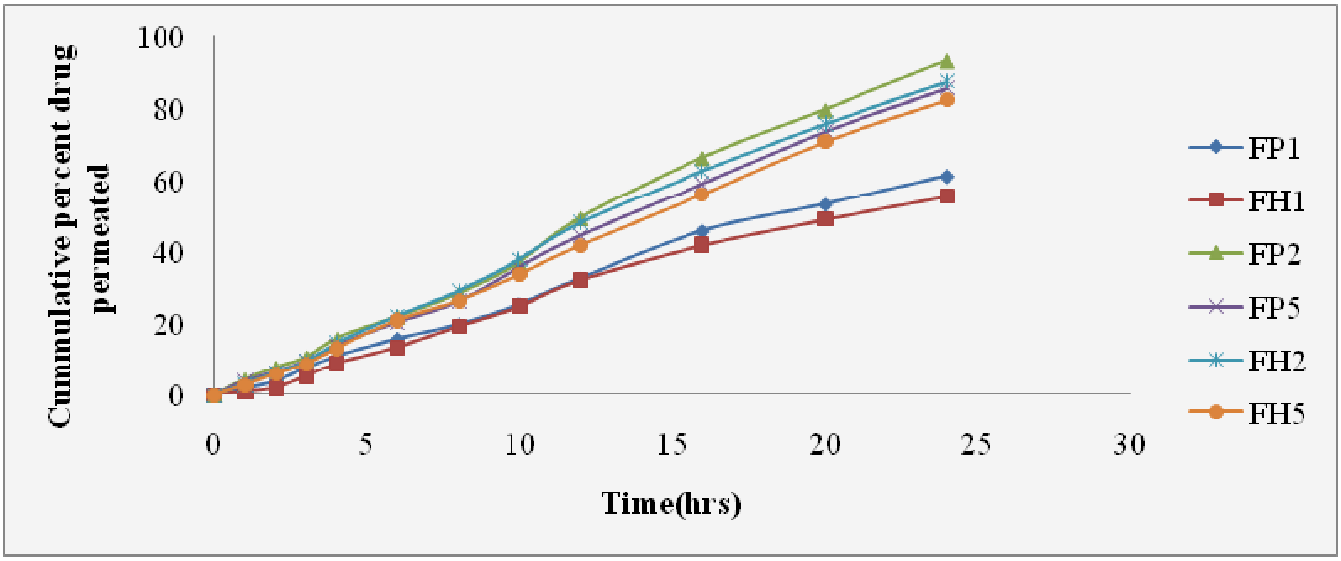


**Fig 6:** IR spectra of pure ketorolac tromethamine

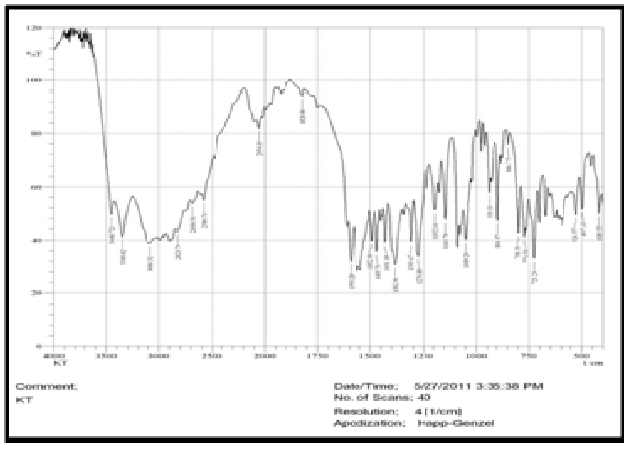

**Fig 7:** IR spectra of optimized PVA reservoir film of Ketorolac tromethamine

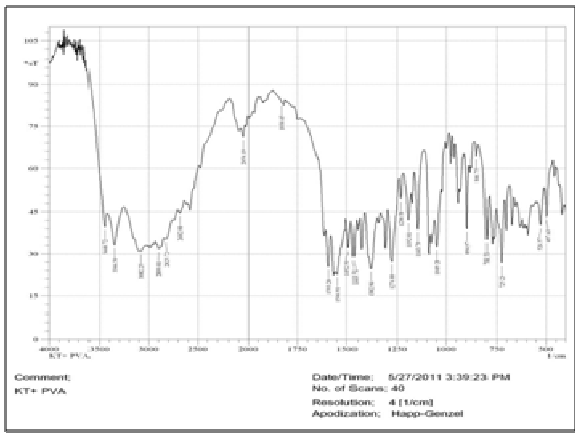

**Fig 8:** IR spectra of optimized HPMC reservoir film of Ketorolac tromethamine

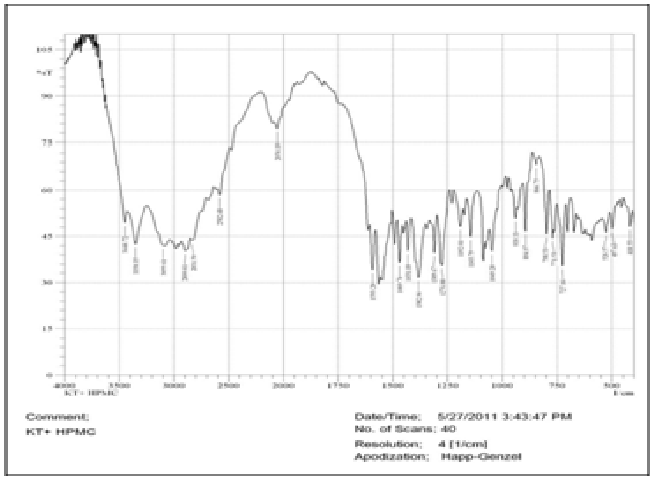

**Fig 9:** DSC of KTM pure drug:

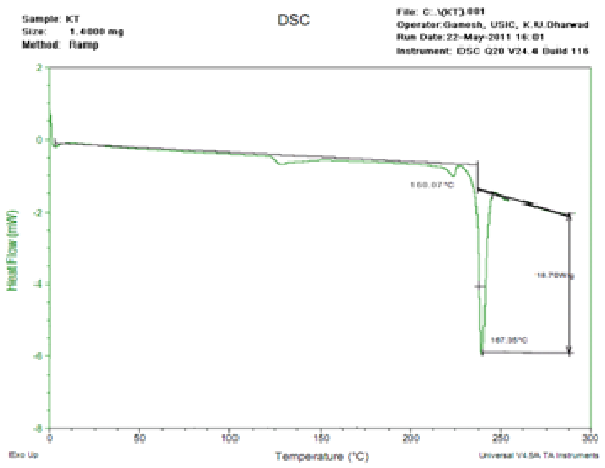


**Fig 10:** DSC of KTM + PVA

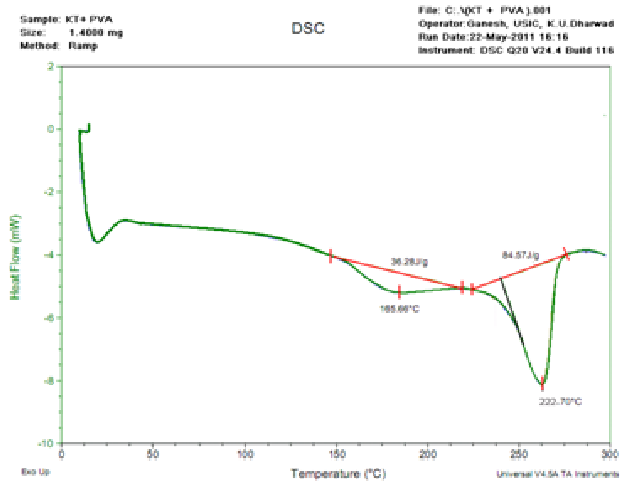


**Fig 11:** DSC of KTM + HPMC

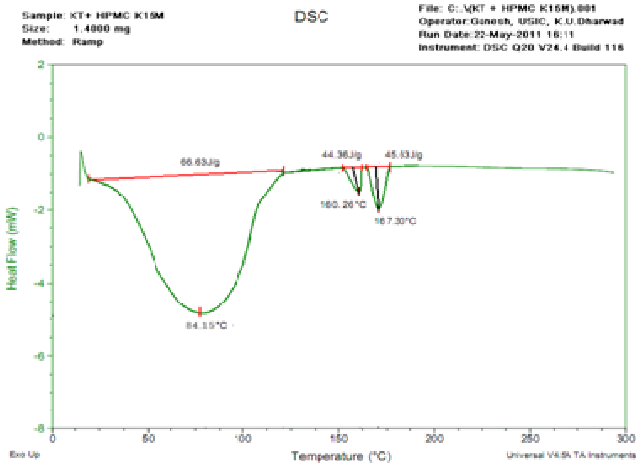


**Table No. 4:** Physicochemical evaluation of ketorolac tromethamine transdermal films using HPMC and PVA

| Formulation code | Weight variation (mg) | Thickness (mm) | % Moisture Loss | % Moisture Absorption | Folding endurance | Drug content (mg) | Tensile strength (Kg/mm²) |
|---|---|---|---|---|---|---|---|
| FH1 | 16.6±0.156 | 0.230±0.008 | 16.56±0.64 | 13.41±0.12 | 88.0±5.12 | 0.934±0.054 | 4.73±0.054 |
| FH2 | 22.3±0.201 | 0.227±0.006 | 14.67±0.26 | 12.93±0.89 | 97.0±4.71 | 0.964±0.082 | 5.05±0.015 |
| FH3 | 24±0.215 | 0.224±0.0019 | 17.81±0.42 | 14.04±0.15 | 107.33±3.56 | 0.955±0.064 | 3.54±0.057 |
| FH4 | 25±0.143 | 0.226±0.02 | 16.21±0.32 | 11.33±0.18 | 114.4±6.47 | 0.973±0.067 | 3.87±0.087 |
| FH5 | 30.3±0.175 | 0.218±0.015 | 16.85±0.21 | 15.98±0.67 | 104.4±6.14 | 0.987±0.046 | 6.74±0.031 |
| FH6 | 32.3±0.123 | 0.225±0.016 | 18.23±0.38 | 13.26±0.28 | 113.0±6.54 | 0.970±0.063 | 5.59±0.048 |
| FH7 | 33±0.065 | 0.224±0.018 | 20.69±0.8 | 10.81±0.57 | 118.24±7.30 | 0.979±0.021 | 6.93±0.087 |
| FP1 | 17.6±0.156 | 0.173±0.008 | 10.78±0.92 | 13.41±0.12 | 118.0±5.12 | 0.949±0.054 | 6.73±0.066 |
| FP2 | 22.3±0.201 | 0.185±0.006 | 13.56±0.57 | 10.93±0.89 | 117.0±4.71 | 0.927±0.082 | 7.05±0.056 |
| FP3 | 24±0.215 | 0.205±0.0019 | 12.57±0.54 | 10.04±0.15 | 117.33±3.56 | 0.985±0.064 | 6.54±0.011 |
| FP4 | 24±0.143 | 0.216±0.02 | 13.56±0.64 | 8.33±0.18 | 114.4±6.47 | 0.964±0.067 | 5.87±0.085 |
| FP5 | 29.3±0.175 | 0.212±0.015 | 11.67±0.26 | 8.98±0.67 | 114.4±6.14 | 0.979±0.046 | 6.74±0.055 |
| FP6 | 31.3±0.123 | 0.218±0.016 | 15.81±0.42 | 9.26±0.28 | 121.0±6.54 | 0.987±0.063 | 6.59±0.062 |
| FP7 | 34±0.065 | 0.215±0.018 | 13.21±0.32 | 11.81±0.57 | 125.24±7.30 | 0.967±0.021 | 6.93±0.041 |

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