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# Formulation and *In Vitro* characterization of transdermal patches of Etodolac

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## ABSTRACT

1. Formulation of Etodolac patches using different polymers like HPMC, EC alone and their combinations.
2. Characterization of patches.
3. In-vitro evaluation of patches for the release kinetics and related characteristic's

**Methods**

In these study Etodolac transdermal patches was prepared by solvent casting method using polymer HPMC E5 and DMSO, used as a penetration enhancer. The prepared patches were evaluated for thickness, folding endurance, tensile strength, flatness, drug content uniformity, in-vitro permeation studies, kinetic study and calibrated using FT-IR. In vitro release study was performed by using Franz-diffusion cell.

**Results**

Among all prepared batches of TDD'S, batch F7containing HPMC E5 and EC (5:5) showed maximum rate of drug release of 87.825 ± 0.264 within 24 hr.

**Conclusion**

Etodolac transdermal delivery patches can be successfully formulated by using various ratios of EC and HPMC E5 alone and in combination. The appearances of the patches were transparent without air bubbles

**Keywords:** Etodolac, TDDS, Moulding technique, Franz diffusion cell, Zero order kinetics

## INTRODUCTION

Transdermal drug delivery systems are defined as self-contained, discrete dosage forms which, when applied to the intact skin, deliver the drug, through the skin, at a controlled rate to the systemic circulation. The first transdermal patch was approved by the FDA in 1979 for treatment of motion sickness [1].

### Advantages [2]

- Avoids first-pass effect
- They are non-invasive, avoiding the inconvenience of parenteral therapy.
- They are used for drugs with narrow therapeutic window.
- They provide improved bioavailability and uniform plasma levels.

### Disadvantages [3]

- Drugs with very low or high partition co efficient fail to reach system circulation.
- High Melting Drugs, due to their low solubility both in water in fat.
- Ionic Drugs cannot be delivered.
- Drugs with Hydrophilic Structure permeate the skin too slowly to be of therapeutic benefit.

### Factors effecting permeation and penetration [4]

### Biological factors

The biological factors like thickness of the skin, regional site, age, blood flow rate and skin condition

can influence the penetration and permeation. Skin permeability is altered by physical (ultraviolet, infrared or ionizing radiation), chemical (solvents, detergent)

### Physical factor

The molecular weight, size, structure, partition coefficient, pH of the drug solution in the vehicle, and the concentration of the drug on the surface of the skin [5].

### Basic components of transdermal drug delivery system

- Polymer matrix or matrices
- The drug
- Penetration enhancer.
- Release liner and other excipients

### Polymer matrix

The polymer controls the release of the drug from the device and should satisfy the following criteria such as molecular weight, glass transition temperature and chemical functionality of the polymer should be such that the specific drug diffuses properly and gets released through it. It should be stable, non-reactive with drug and easily manufactured [6].

Natural polymers: eg. Cellulose derivatives, gelatin, protein, waxes, starch

Synthetic polymers: eg. Polyvinyl alcohol, polyvinylchloride

Polyethylene synthetic elastomers: eg. Polybutadiene, polysiloxane, acrylonitrile, neoprene etc.

### Drug [7]

### Physicochemical properties

- It should have a molecular weight less than approximately 1000 daltons.
- It should have affinity for both lipophillic and hydrophilic phases.
- It should have a low melting point.

### Biological properties [8]

- It should be potent with a daily dose of order of a few mg/day.
- The half-life ($t_{1/2}$) of drug should be short.
- It must not induce a cutaneous irritant or allergic response.

**Penetration Enhancers:** classified into three main categories:

### Lipophillic solvents [9]

Increases the permeation of lipophillic drugs. Dimethyl sulphoxide increase permeation of lipophillic drugs, hydrophobic enhancer regarding permeability flux, permeation coefficient, epidermal partition coefficient and diffusion coefficient.

### Surface active agents

These enhance the skin permeation especially of hydrophilic drugs. Their use is limited due to their skin irritation properties. Sodium lauryl sulphate and dioctyl sulphosuccinate are few examples.

### Two component systems

Two component systems is reported to be very effective permeation promoters. They are mainly composed of oleic acid and polyethylene glycol.

### Release liners

During storage the patch is covered by a protective liner that is removed and discharged immediately before the application of the patch to skin. As the liner is intimate contact with the delivery system, it should comply with specific requirements regarding chemical inertness and permeation to the drug, penetration enhancer and water.

### Other excipients

### Adhesives

Adhesive systems should possess the following characteristics

- Should not irritate or sensitize the skin or cause an imbalance in the normal skin flora during its contact time with skin.
- Should not leave an unwashable residue on the skin.

Rubber based adhesives: eg. Natural gum (Karaya gum), olylisoprene, polybutene, polyisobutelene.

Polyacrylic based: eg. Ethylacrylate,2-ethylhexylacrylate, iso-octyl acrylate.

Polysiloxane based: eg. Polydimethyl siloxane, polysilicate resins, sulfoxaneblends.

### Backing Membrane [10]

Backing membranes are flexible and they provide a good bond to the drug reservoir, prevent drug from leaving the dosage form through

the top and accept printing. It is impermeable substance that protects the product dosing use on the skin, eg. Metallic plastic laminate, plastic backing with absorbent pad and occlusive base plate (aluminum foil) etc.

## MATERIALS AND METHODOLOGY

### Materials

**Table 1 : List of chemicals and reagents**

| Materials | Source |
|---|---|
| Etodolac | Spectrum labs, Hyderabad |
| Hydroxypropyl methylcellulose E 5 | Shreeji Chemicals, Mumbai |
| Ethylcellulose | Rolex Chemical Industries, Mumbai |
| Octanol | S.D. Fine chem. Ltd, Mumbai |
| Chloroform | Qualigens fine chemicals, Mumbai |

**Table 2: List of equipments and instruments**

| Equipment | Model/Company |
|---|---|
| UV Visible spectrophotometer | UV-1800, Shimadzu, Tokyo |
| Digital pH meter | 335, Systronics |
| Franz diffusion cell | Fabricated in laboratory |
| Electronic weighing scale | DS-852J series, Essae teroka Ltd |
| FT-IR Spectophotometer | IR Affinity-1,Shimadzu,Tokyo |

## METHODOLOGY

### Preformulation studies

### Determination of pH

The pH of the Etodolac was determined using potentiometer for freshly prepared 1% aqueous solution of Etodolac.

### Determination of melting point

Melting point of the Etodolac was determined by using open capillary tube method in digital melting point apparatus

### Determination of solubility

The solubility of Etodolac was determined using a 0.45-micron whattsmann filter paper, to separate the undissolved drug particles and diluted suitably at concentration of Etodolac in the filtrate was determined spectrophotometrically at 274nm

### Determination of partition coefficient

The partition coefficient of the drug was determined by taking equal volumes of 1-octanol and aqueous solution in a separating funne

### Determination of drug-exciepient compatibility

FT-IR spectroscopy was employed to ascertain the compatibility between Etodolac and the selected polymers. The pure drug and drug with exciepient were scanned separately. The FT-IR spectrum of Etodolac was compared with FT-IR spectra of Etodolac with combination of polymers.

### Preparation of transdermal patches

In the present study, drug loaded matrix type transdermal films of Etodolac were prepared by solvent evaporation method. A mould of 4.6cm length and 4.5cm width with a total area of 20.25cm2 was fabricated and used. The bottom of the mould was wrapped with aluminium foil, 300mg. Polymer was accurately weighed and dissolved in 5ml of chloroform: methanol (1:1) and kept aside to form clear solution. Dibutyl phthalate was used as plasticizer and dimethyl sulfoxide was used as permeation enhancer as shown in table 5.3 and mixed thoroughly. 30mg of Etodolac was dissolved in the above solution and mixed for 10min. The resulted uniform solution was cast on the aluminum foil and dried at 40oC in the hot air oven for 24h. An inverted funnel was placed over the mould to prevent fast

evaporation of the solvent. After 24h the dried films were taken out and stored in a dessicator for further studies.

Martix type transdermal patches of Etodoac were prepared by moulding method total 7 patches as shown in the dose of the etodoac is 150mg daily divided base .calculation for transdermal formulation:

a) surface area for the final circular patch $=\prod r^2 = 3.14\times2\times2 = 12.56$ cm2
b) Surface area of the mould $= 4.6\times4.5 = 20.25$ cm2
c) 150mg of the drug should be present in a $\rightarrow$12.56 cm2

$\rightarrow$20.25 cm2$=\frac{20.25\times150}{12.56}= 250$mg

**Table 3: Composition of different formulations containing Etodolac**

| Formulation | $F_1$ | $F_2$ | $F_3$ | $F_4$ | $F_5$ | $F_6$ | $F_7$ |
|---|---|---|---|---|---|---|---|
| Etodolac, mg | 250 | 250 | 250 | 250 | 250 | 250 | 250 |
| HPMC E(5cps), mg | 150 | - | 30 | 40 | 50 | 60 | 75 |
| Ethylcellulose, mg | - | 150 | 120 | 110 | 100 | 90 | 75 |
| Dibutyl phthalate | 0.12 | 0.12 | 0.12 | 0.12 | 0.12 | 0.12 | 0.12 |
| DMSO, ml | 0.06 | 0.06 | 0.06 | 0.06 | 0.06 | 0.06 | 0.06 |
| Chloroform: Methanol (1:1), ml | 5 | 5 | 5 | 5 | 5 | 5 | 5 |

* No ingredients was used; HPMC = Hydroxypropyl methylcellulose; DMSO = Dimethyl sulfoxide

## Evaluation of TDD'S

### Physical appearance

The prepared patches visually tested for color, clarity, flexibility and smoothness.

### Thickness uniformity

The thickness of the film was measured at 3 different points using a digital caliper

### Weight uniformity

For weight variation test, 3 films from each batch were weighed individually and the average weight was calculated.

### Folding endurance

A strip of film (5 x 5 cm) was cut and repeatedly folded at the same place till it broke.

### Percentage moisture absorption

$$\frac{\text{Final wt-Initial wt}*100}{\text{Initial wt}}$$

### Tensile strength

The test film of size ($4*1$ cm$^2$) was fixed between these cell grips and force was gradually applied till the film broke.

### In-vitro-Drug release

Done by a modified Franz diffusion cell with a receptor compartment capacity of 20ml.The synthetic cellophane membrane was mounted between the donor and receptor compartment of the diffusion cell. The formulated patches were cut into size of 1cm2 and placed over the drug release membrane and the receptor compartment of the diffusion cell was filled with phosphate buffer pH 7.4. The whole assembly was fixed on a magnetic stirrer, and the solution in the receptor compartment was constantly and continuously stirred using magnetic beads at 50 rpm; the temperature was maintained at 37 ± 0.50C. The samples of 1ml were withdrawn at time interval of 1, 2…12, for 24 h, analysed for drug content spectrophotometric ally at 274nm against blank. The receptor phase was replenished with an equal volume of phosphate buffer at each time of sample withdrawal.

### Kinetic modelling of drug release

### Zero order release model

$Q=K_0T$, Q=Amount of drug release at time t
$K_0$=zero order release rate constant
plot of % drug release versus time is linear.

### First order release model

$\ln(100-Q) = \ln100 - k_1t$,
Q=percent drug release at time t
$K_1$=first order release rate constant

plot of log % drug release versus time is linear.

### Higuchi's release model

$Q=K_Ht^{1/2}$ Q= percent drug release at time t

$K_H$= Higuchi's (diffusion) rate constant

plot of %drug release versus square root of time is linear.

### Korsmeyer-peppas release model

$F= (M_t/M) =K_mt^n$, $M_t$=drug release at time t

M=total amount of drug in dosage for

F=fraction of drug release at time t

$K_m$=constant dependent on geometry of dosage form

n=diffusion exponent indicating the mechanism of drug release.

In this model, a plot of log ($M_t$/M) versus log (time) is linear

## RESULTS AND DISCUSSION

### Preformulation studies: Physicochemicalparameters of Etodolac

**Table 1: Data of parameters**

| Sl.No. | Drug | pH | Melting point | Solubility |
|---|---|---|---|---|
| 1. | Etodolac | 7.4 | 145–148 °C | 3.92e-02 mg/ml |

### Determination of partition coefficient

The partition coefficient value was experimentally 3.7.

### Drug-exciepients compatibility studies

The peaks can be considered as characteristic peaks of Etodolac, Conforming the purity of drug observed in FT-IR spectra of Etodolac along with polymers.

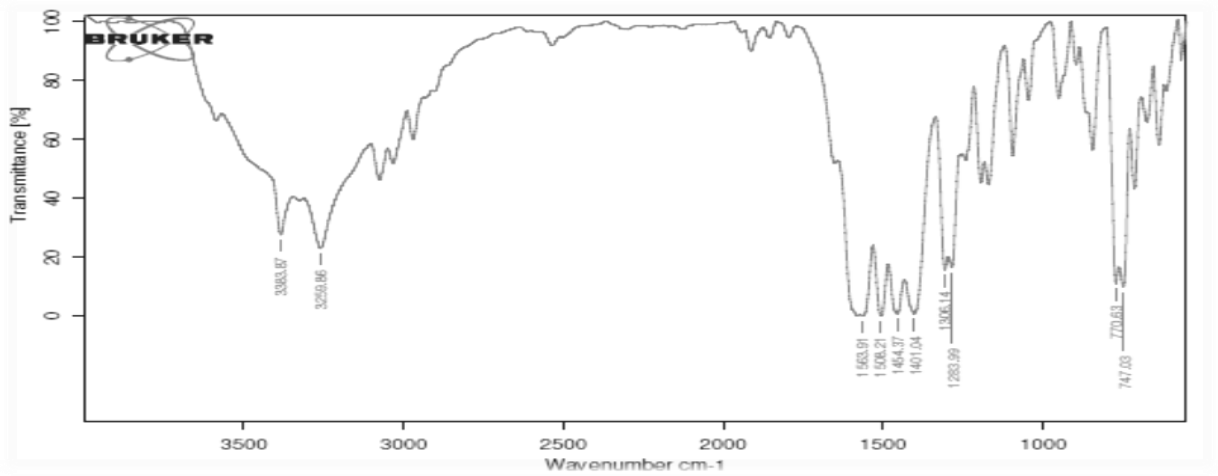


**Figure1: FT-IR pure Etodolac**

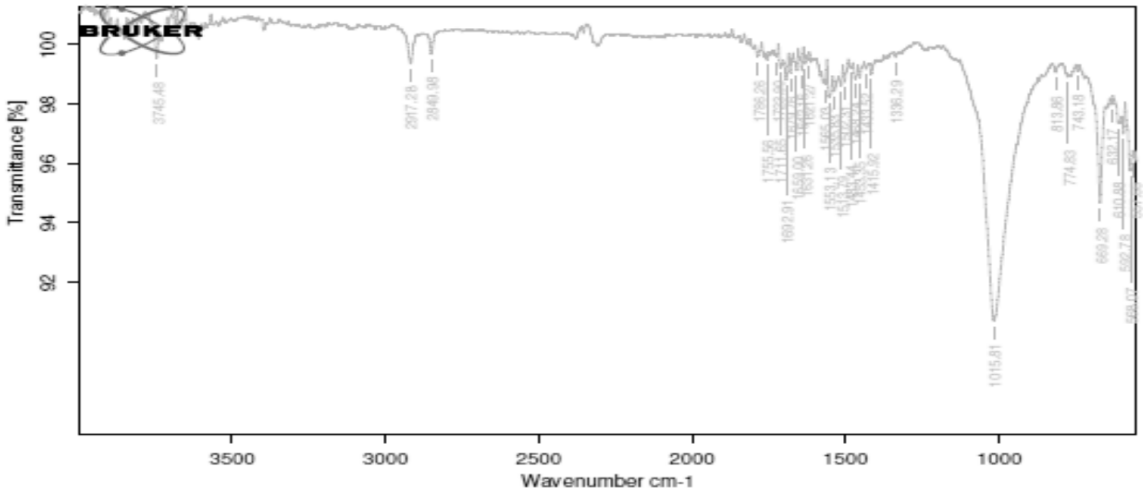


**Figure 2: FT-IR of Etodolac with combination of polymers**

## Analytical methods

## Determination of λ max of Etodolac in pH 7.4 phosphate buffer solution

10µg/ml of test solution was scanned between 200- 400 nm. The $\lambda_{max}$ was found to be 274nm

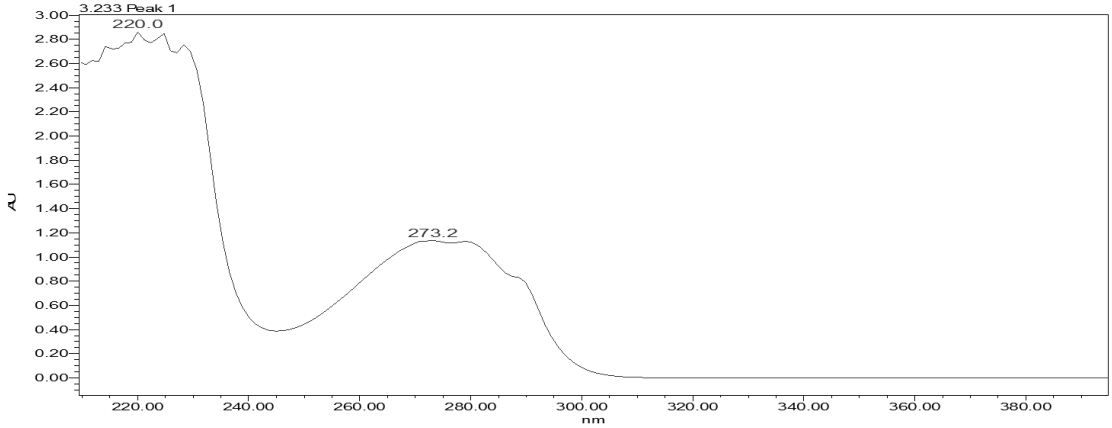


**Figure 3: UV spectrum of Etodolac in 274nm**

**Table 3: Data for calibration curve of Etodolac in pH 7.4 buffer solution**

| Sl. No. | Concentration µg/ ml | Absorbance at 274 nm, Mean ± SD* |
|---|---|---|
| 2 | 2.0 | 0.072 ± 0.008 |
| 3 | 4.0 | 0.138 ± 0.007 |
| 4 | 6.0 | 0.196 ± 0.012 |
| 5 | 8.0 | 0.261 ± 0.008 |
| 6 | 10.0 | 0.324 ± 0.008 |
| 7 | 12.0 | 0.399 ± 0.004 |
| 8 | 14.0 | 0.456 ± 0.011 |
| 9 | 16.0 | 0.519 ± 0.006 |
| 10 | 18.0 | 0.571 ± 0.004 |
| 11 | 20.0 | 0.640 ± 0.006 |

## Evaluation of transdermal patches

### Physical appearance

The prepared patches were visually inspected for colour,clarity, flexibility and smoothness.

### Thickness uniformity

Thickness uniformity of F1 to F7 patch formulations

**Table 4: Data for thickness uniformity**

| Sl. No. | Formulation code | Average thickness (mm) | | | |
|---|---|---|---|---|---|
| | | Trial 1 | Trial 2 | Trial 3 | Average |
| 1 | $F_1$ | 0.17 | 0.19 | 0.19 | 0.18 |
| 2 | $F_2$ | 0.19 | 0.28 | 0.36 | 0.27 |
| 3 | $F_3$ | 0.38 | 0.45 | 0.53 | 0.45 |
| 4 | $F_4$ | 0.14 | 0.14 | 0.17 | 0.15 |
| 5 | $F_5$ | 0.27 | 0.29 | 0.30 | 0.28 |
| 6 | $F_6$ | 0.38 | 0.38 | 0.39 | 0.38 |
| 7 | $F_7$ | 0.17 | 0.18 | 0.20 | 0.19 |

### Weight uniformity

**Table 5: Data for F1-F7patch formulation**

| S. No | Formulation code | Average weight (g) | | | |
|---|---|---|---|---|---|
| | | Trial 1 | Trial 2 | Trial 3 | Average |
| 1 | F1 | 0.40 | 0.43 | 0.42 | 0.416 |
| 2 | F2 | 0.38 | 0.36 | 0.36 | 0.366 |
| 3 | F3 | 0.40 | 0.38 | 0.37 | 0.383 |
| 4 | F4 | 0.41 | 0.39 | 0.38 | 0.393 |
| 5 | F5 | 0.35 | 0.41 | 0.38 | 0.380 |
| 6 | F6 | 0.38 | 0.34 | 0.36 | 0.360 |
| 7 | F7 | 0.43 | 0.40 | 0.41 | 0.413 |

### Tensile strength

**Table 6: Data for F1-F7 formulations**

| S. No | Formulation Code | Tensile strength $Kg/mm^2$ | | | |
|---|---|---|---|---|---|
| | | Trial 1 | Trial 2 | Trial 3 | Average* |
| 1 | $F_1$ | 3.85 | 3.96 | 3.71 | 3.86 |
| 2 | $F_2$ | 2.85 | 2.96 | 3.07 | 2.98 |
| 3 | $F_3$ | 3.05 | 3.14 | 3.13 | 3.13 |
| 4 | $F_4$ | 3.18 | 3.29 | 3.21 | 3.22 |
| 5 | $F_5$ | 3.22 | 3.31 | 3.28 | 3.27 |
| 6 | $F_6$ | 3.27 | 3.39 | 3.36 | 3.34 |
| 7 | F7 | 3.32 | 3.47 | 3.44 | 3.41 |

### Percentage moisture

**Table7: Data of percentage moisture absorption**

| S.No | Formulation code | Percentage moisture absorption | | | |
|---|---|---|---|---|---|
| | | Trial 1 | Trial 2 | Trial 3 | Average* |
| 1 | $F_1$ | 4.651 | 6.97 | 9.3 | 6.973 |
| 2 | $F_2$ | 0 | 2.63 | 2.63 | 1.753 |
| 3 | $F_3$ | 0 | 2.94 | 2.94 | 1.960 |
| 4 | $F_4$ | 2.70 | 2.70 | 5.50 | 3.630 |
| 5 | $F_5$ | 2.43 | 2.43 | 4.87 | 3.243 |

| | | | | | |
|---|---|---|---|---|---|
| 6 | $F_6$ | 2.70 | 5.40 | 5.40 | 4.50 |
| 7 | F7 | 4.761 | 7.142 | 7.142 | 6.348 |

## Drug content

**Table 8: Data of percentage drug content**

| Sl. No. | Formulation code | Concentration Mean ± SD* (mg/cm$^2$) | % Drug content |
|---|---|---|---|
| 1 | $F_1$ | 1.178 ± 0.071 | 98 |
| 2 | $F_2$ | 1.054 ± 0.071 | 87.66 |
| 3 | $F_3$ | 1.083 ± 0.047 | 90.25 |
| 4 | $F_4$ | 1.083 ± 0.053 | 90.25 |
| 5 | $F_5$ | 1.114 ± 0.071 | 92.83 |
| 6 | $F_6$ | 1.114 ± 0.031 | 92.83 |
| 7 | F7 | 1.145 ± 0.035 | 95.41 |

∗ Standard deviation n=3; DC vary from1.054 ± 0.071mg to 1.178 ± 0.071mg

## Drug release kinetics of F1

**Table 9: Drug release kinetics of F1**

| Time (h) | T | Log T | %Cumulative drug release Mean ± SD* | Log% Cumulative drug release | % Cumulative drug retained | Log% Cumulative drug retained |
|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 ± 0 | 0 ± 0 | 100 ± 0 | 2 ± 0 |
| 0.5 | 0.707 | - | 14.556±0.330 | 1.162±0.009 | 85.445±0.330 | 1.931±0.001 |
| 1 | 1 | 0 | 18.951±0.461 | 1.277±0.010 | 81.049±0.461 | 1.908±0.002 |
| 2 | 1.414 | 0.301 | 29.285±0.306 | 1.466±0.002 | 70.714±0.306 | 1.849±0.002 |
| 3 | 1.732 | 0.477 | 34.235±0.485 | 1.534±0.006 | 65.765±0.485 | 1.817±0.003 |
| 4 | 2 | 0.602 | 46.842±0.352 | 1.670±0.003 | 53.159±0.352 | 1.725±0.002 |
| 5 | 2.236 | 0.698 | 55.138±0.306 | 1.741±0.002 | 44.862±0.306 | 1.651±0.003 |
| 6 | 2.449 | 0.778 | 59.651±0.315 | 1.775±0.002 | 40.349±0.315 | 1.605±0.003 |
| 7 | 2.645 | 0.845 | 63.580±0.776 | 1.803±0.005 | 36.419±0.776 | 1.561±0.009 |
| 8 | 2.828 | 0.903 | 67.713±0.219 | 1.830±0.001 | 32.286±0.219 | 1.509±0.003 |
| 9 | 3 | 0.954 | 70.043±0.766 | 1.844±0.005 | 29.956±0.766 | 1.475±0.010 |
| 10 | 3.162 | 1 | 72.286±0.568 | 1.858±0.003 | 27.715±0.568 | 1.442±0.009 |
| 11 | 3.316 | 1.041 | 74.672±0.486 | 1.872±0.002 | 25.328±0.486 | 1.403±0.008 |
| 12 | 3.464 | 1.079 | 76.652±0.393 | 1.884±0.002 | 23.348±0.393 | 1.367±0.007 |
| 24 | 4.898 | 1.38 | 87.825±0.264 | 1.938±0.002 | 13.188±0.262 | 1.119±0.008 |

*standard deviation n=3

## Comparative In-Vitro release profile of Etodolac TDDS

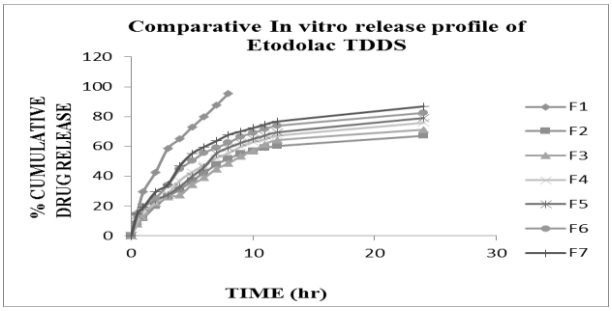


**Fig 1: Comparative In vitro release profile of Etodolac TDDS**

**Fig 5: Comparative in vitro release profile of Etodolac TDD'S done using peppas plot**

**Table10: Regression co-efficient ($R^2$) values of different kinetic models and diffusion exponent (n) of Peppas model for Etodolac TDDS**

| Batch | Zero order | First order | Higuchi | Peppas plot | |
|---|---|---|---|---|---|
| | $R^2$ Mean ± SD* | $R^2$ Mean ± SD* | $R^2$ Mean ± SD* | $R^2$ Mean ± SD* | n values Mean ± SD* |
| $F_1$ | 0.9596±0.004 | 0.9144±0.033 | 0.9957±0.008 | 0.9856±0.002 | 0.6361±0.009 |
| $F_2$ | 0.7411±0.020 | 0.8278±0.030 | 0.5919±0.024 | 0.9697±0.005 | 0.6178±0.017 |
| $F_3$ | 0.7560±0.006 | 0.8596±0.008 | 0.5788±0.006 | 0.9716±0.002 | 0.6225±0.021 |
| $F_4$ | 0.766±0.007 | 0.8837±0.008 | 0.5643±0.009 | 0.9743±0.003 | 0.5749±0.008 |
| $F_5$ | 0.7811±0.003 | 0.8940±0.005 | 0.5298±0.004 | 0.9555±0.001 | 0.5151±0.006 |
| $F_6$ | 0.7451±0.001 | 0.8939±0.005 | 0.5781±0.001 | 0.9711±0.003 | 0.5183±0.006 |
| $F_7$ | 0.7318±0.002 | 0.9132±0.005 | 0.5781±0.004 | 0.9673±0.003 | 0.5227±0.003 |

*Standard deviation, n=3

## DISCUSSION

TDD'S is a most suitable system for a long term treatment or for a multi dose treatment. TDDS also increases the bioavailability of drug by avoiding the first pass metabolism and increases the therapeutic efficacy of drug by reaching into the systemic circulation. Among the class of NSAIDs, Etodolac is indicated for relief of signs and symptoms of rheumatoid arthritis and osteo arthritis. Polymers HPMC E5 and EC were selected on basis of their adhering property and non-toxicity. It is concluded that ETD in combination with HPMC E5, EC and with incorporation of DBT and DMSO produced smooth, flexible and transparent film. FT-IR studies showed characteristic peaks of ETD, obtaining the purity of the drug. FT-IR spectral studies indicated there was no interaction between ETD and polymers used.TD patches were evaluated it for physical parameters such as thickness, drug content, weight variation, moisture absorption. The percentage of drug release at each time interval was calculated and plotted against time .Drug release from (F1) and (F2) was found to be as 95.526 ± 0.982 % With-in 8hrs and 67.078 ± 1.875 % within 24h, respectively. Among the formulations F3 to F7 which has varying proportion of HPMC and EC showed release of 71.224 ± 0.925 % to 86.812 ± 0.262 %, F7 showed maximum rate of drug release of 87.825 ± 0.264 % for 24 h due to presence of higher portions of HPMC which is more permeable than EC. Hence, formulation F7 fulfils the requirements of prolonged drug release. The study of drug release kinetics showed that majority of the formulations were governed by Peppas model by diffusion, by swelling or by erosion mechanism, the data was plotted according to Higuchi's equation. The co-efficient of determination indicated that the release data for formulation F1 followed zero order release kinetics with diffusion mechanism, while formulation F2 to F7 followed first order release kinetics with diffusion mechanism Higuchi equation explains the diffusion release mechanism. The diffusion exponent 'n' values were found to be in the range of 0.5 to 1 indicating Non-Fickian mechanism. Hence, Concentration of hydrophilic polymer (HPMC), increases the thermodynamic activity of the drug, which results in increased drug release during in vitro studies

## CONCLUSION

A suitable UV Spectroscopy method for the analysis of Etodolac was developed. Etodolac showed maximum absorption at wave length 274 nm in isotonic phosphate buffer (pH 7.4) solutions. The R2 value for the standard curve was found to be 0.999, The pre-formulation studies involving description, solubility, melting point, partition coefficient. Drug-polymer compatibility studies by FT-IR gave confirmation about their purity and showed no interaction between the drug and selected polymers. Various formulations were developed by using hydrophilic and hydrophobic polymers like HPMC E5 and EC respectively in single and combinations by solvent evaporation technique with incorporation of penetration enhancer such as dimethylsulfoxide and dibutyl phthalate as plasticizer. Developed transdermal patches possessed the required physicochemical properties such as drug content uniformity, folding endurance, weight uniformity,

thickness uniformity, tensile strength and water vapour transmission rate (WVTR). Patches exhibited higher tensile strength as the concentration of HPMC was increased. Most of the batches shows high folding endurance values (more than 50). In vitro studies concluded that HPMC E5 patches has better release than that of EC patches, which may attributed to high water vapour permeability of HPMC patches and hydrophobic nature of EC. Formulation F7 containing equal ratio of HPMC E5: EC (5:5) showed maximum and sustained release of 87.825 ± 0.264 with-in 24 h. Kinetic models were used to confirm release mechanism of the formulation Etodolac release from the patches F1 to F7 followed the non Fickian diffusion rate controlled mechanism. In-vitro diffusion studies were carried out using diffusion cell and pH 7.4 phosphate buffers as receptor medium. The absorption kinetics was studied by regression analysis. The drug release pattern of F1 followed zero order with non Fickian diffusion mechanism, whereas the release pattern of F2 to F7 followed first order with non Fickian diffusion mechanism. On the basis of the in-vitro characterization it was concluded that Etodolac could be administered transdermally through matrix type TDDS. Transdermal patches consisting of the hydrophilic HPMC E5 and hydrophobic EC with DMSO as permeation enhancer demonstrated significant in vitro diffusion studies, the possibility of sustained release of the drug for 24 hr.

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