

# Formulation Development and *In Vitro* Evaluation of Transdermal Patches of Etodolac

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## ABSTRACT

The objective of the present study transdermal drug delivery of Etodolac was developed to overcome the first pass metabolism and to reduce frequency of dosing compared to oral route. Matrix type of transdermal patches was developed by using polymers Eudragit-L100, HPMCK<sub>4</sub>M and HPMCK<sub>15</sub>M. The formulation blend was evaluated for various physicochemical properties and all the parameters were found to be within limits. The formulations F1-F12 were formulated and evaluated for various quality control parameters. All the formulations were passed the tests and the results were within limits. Among all the 12 formulations F6 formulation which contain HPMC K4M 200mg had shown 96.5% cumulative drug release with in 12 hours.

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Keywords: Etodolac , HPMC K15M, HPMC K4M,Eudragit-L100 & Transdermal patch

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## 1. Introduction

The purpose of writing this review on transdermal drug delivery systems(TDDS). The main purpose of developing alternative drug delivery technologies is to increase efficiency and safety of drug delivery and provide more convenience for the patient. Substantial research conducted during the past several years has lead to the development of technologies that meet the requisite criteria for delivering the drug through a non-invasive route. One of such technologies is transdermal drug delivery These systems are useful to several problems encountered during the development of a pharmaceutical dosage form.

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## 2. Materials and Methods

Etodolac,Eudragit L-100, HPMCK<sub>15</sub>M , HPMCK<sub>4</sub>M , Dibutyl Phthalate , Laurocapran , Tween-80, DMSOall the chemicals used were laboratory grade.

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## 3. Formulation of Etodolac Transdermal Patch

**Development of Transdermal patches:** Transdermal drug delivery patches were prepared by solvent casting method.

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# **Method of Preparation:**

**Solvent casting method:** Transdermal patches were prepared according to the formula shown in Table 3.3. Eudragit L100, HPMCK<sub>4</sub>M and HPMCK15M were weighed in requisite ratios and they were then dissolved in DMSO as solvent using magnetic stirrer. Etodolac (300 mg), Laurocapran and Tween 80 were added to the above dispersion under continuous stirring. The uniform dispersion was poured in the petri plate. The rate of evaporation of solvent was controlled by inverting cut funnel over the patches. After 24h, the dried films weretaken out and stored in desiccators.

# **Evaluation of Transdermal patch by physical methods :**

The designed formulation patch were studied for their physicochemical properties like weight variation, thickness, physical appearance, flatness, folding endurance, moisture uptake, moisture content, swelling study, drug content determination.

# **Evaluation of Trandermal patch by permeation studies:**

The designed formulation patch were studied for their permeation studies like diffusion cell, In vitro permeation studies using dialysis membrane.

# **Kinetic modeling of drug release**

Mechanism of drug release, Zero order release model, First order release mode, Higuchi's Release Model, Korsmeyer - peppas release model, Drug excipients interaction studies : FT-IR spectrum interpretation.

Table 1: Formulations of Etodolac Transdermal Patch

S.No	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	Drug (mg)	300	300	300	300	300	300	300	300	300	300	300	300
2	Eudragit-L100 (mg)	100	150	200	--	--	--	--	--	--	100	100	--
3	HPMCK <sub>4</sub> M (mg)	--	--	--	100	150	200	--	--	--	100	--	100
4	HPMCK <sub>15</sub> M (mg)	--	--	--	--	--	--	100	150	200	--	100	100
5	DMSO (ml)	8	8	8	8	8	8	8	8	8	8	8	8
6	Laurocapran (ml)	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2
7	Tween-80 (ml)	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2

## 4. Results and Discussion

### 4.1 Determination of $\lambda$ max of Etodolac in pH 7.4 phosphate buffer solution

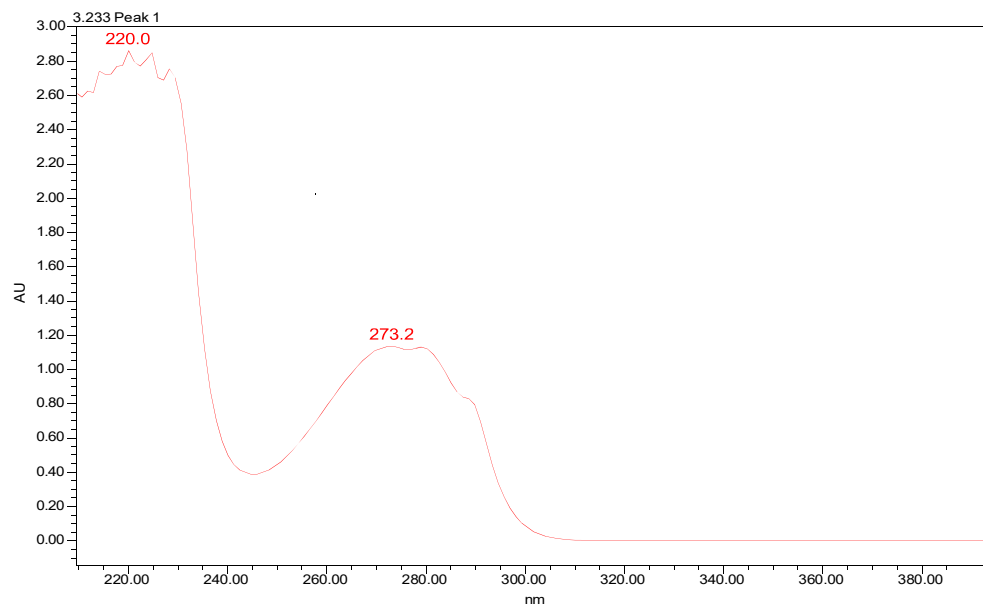


Fig No. 1:  $\lambda$  max of Etodolac in pH 7.4 phosphate buffer solution

### 4.2 Standard graph of Etodolac

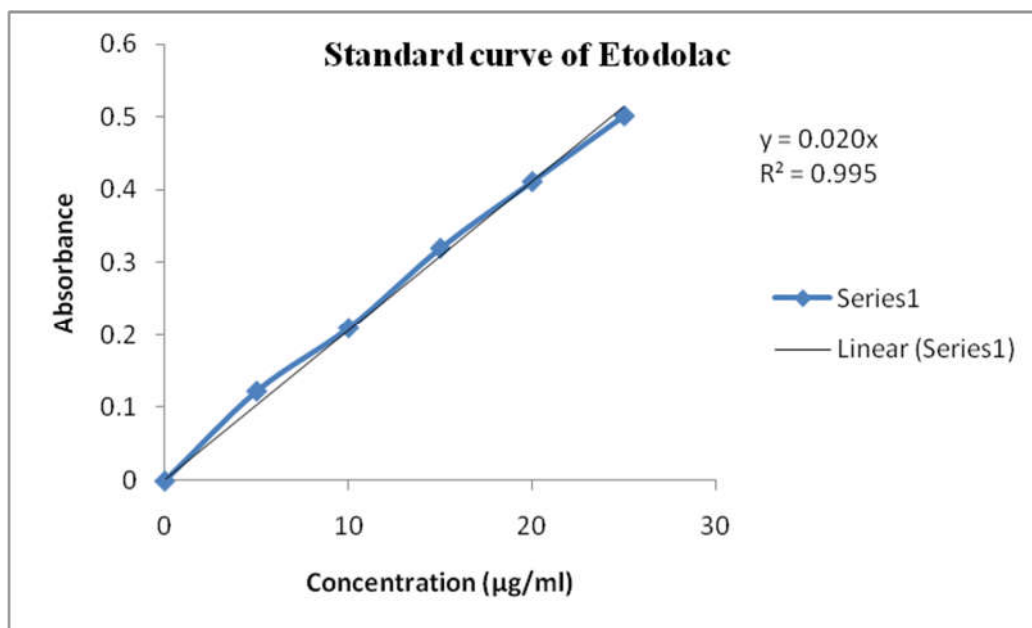


Fig 2. Standard graph of Etodolac

**Table No:2 Standard graph of Etodolac**

Concentration (µg/ml)	Absorbance
5	0.123
10	0.210
15	0.320
20	0.411
25	0.501

#### 4.3 Evaluation of Etodolac Transdermal patches:

1. **Physical appearance:** All the Transdermal patches were visually inspected for color, clarity, flexibility.
2. **Flatness:** All the Transdermal patches was found to be flat without any foams.

#### 4.4 Evaluation of Transdermal patch by physical methods

**Table No. 3: Evaluation of Transdermal patch by physical methods**

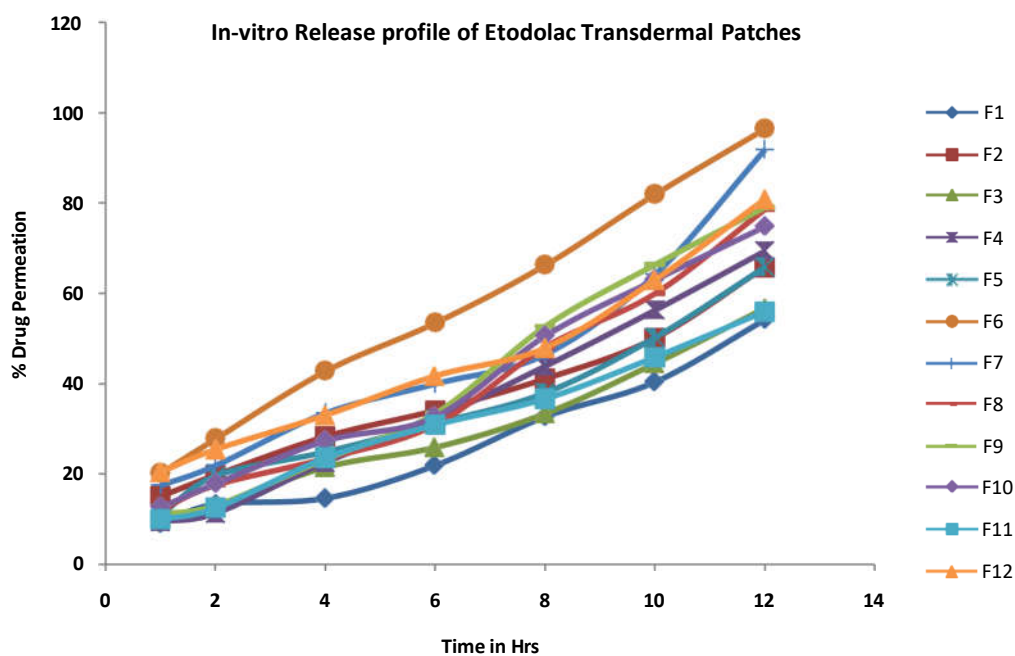
Formulation	Thickness (mm)	Folding endurance	Drug content (%)	Moisture uptake (%)	Moisture content (%)
F1	0.3569	20	45	7.98	3.77
F2	0.3520	25	65	25.05	9.2
F3	0.3470	27	57.5	13.09	5.16
F4	0.3496	24	60	15.63	5.66
F5	0.3460	30	67.5	11.73	4.87
F6	0.3517	32	92.5	19.65	12.67
F7	0.3478	40	101.7	9.42	3.43
F8	0.3437	37	85	10.87	4.72
F9	0.3503	34	55	16.44	6.62
F10	0.3532	29	62.5	13.08	6.17
F11	0.3546	26	85	20.63	7.94
F12	0.3503	31	82.5	15.73	6.55

The prepared Etodolac Transdermal patches were evaluated by physical methods such as Physical appearance, Flatness, Weight variation, Thickness, Folding endurance, Drug content, Moisture uptake and Moisture content and all the results were found to be within the pharmacopoeial limits.

#### 4.5 In-vitro permeation studies using dialysis membrane

**Table No. 4: Evaluation of Transdermal patch by In-vitro permeation studies using dialysis membrane**

Time (hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	9.05	15.1	10.1	9.49	10.9	20.2	17.5	12.0	11.1	12.7	10.0	20.4
2	13.3	19.8	12.8	11.3	19.6	27.8	21.9	17.5	13.0	17.9	12.5	25.4
4	14.6	28.3	21.5	22.6	24.9	42.8	33.5	23.4	23.3	27.4	23.6	33.0
6	21.9	34.1	25.9	32.3	31.2	53.5	40.0	30.9	33.4	32.7	30.9	41.7
8	32.7	41.1	33.4	43.9	38.0	66.3	46.5	48.1	52.7	50.6	36.7	47.9
10	40.4	50.1	44.5	56.3	50.3	82.0	64.2	60.0	66.4	63.0	45.9	63.0
12	54.2	65.8	56.7	69.4	65.9	96.5	91.9	78.7	79.1	74.8	56	80.9



**Fig. 3: Release profile of In-vitro permeation studies using dialysis membrane**

The prepared Etodolac Transdermal patches were evaluated for In-vitro permeation studies using dialysis membrane, Among all the 12 formulations F6 formulation which contain HPMC K4M 200mg had shown 94% cumulative drug release with in 12 hours. And compared to HPMC K15M, HPMC K4M showed better drug release profile.

#### 4.6 Release Kinetics

Table No 5: kinetics of In-vitro permeation studies using dialysis membrane

Cumulative (%) Release Q	Time ( T )	Root ( T )	Log (%) Release	Log ( T )	Log (%) Remain
0	0	0	--	--	2.000
20.2	0.5	0.707	1.305	-0.301	1.902
27.8	1	1.000	1.444	0.000	1.859
42.8	2	1.414	1.631	0.301	1.757
53.5	3	1.732	1.728	0.477	1.667
66.3	4	2.000	1.822	0.602	1.528
82.0	5	2.236	1.914	0.699	1.255
96.5	6	2.449	1.985	0.778	0.544

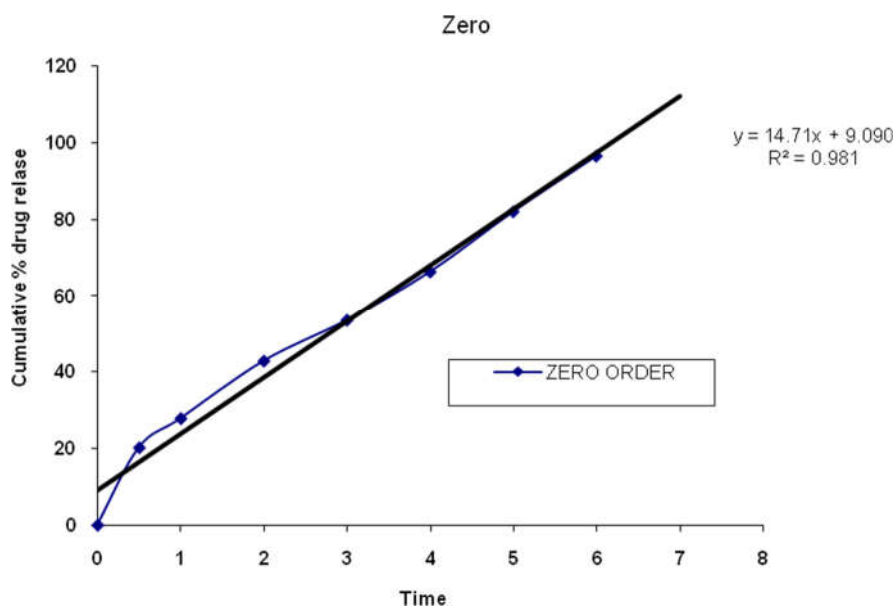


Fig. 4: Zero order kinetics

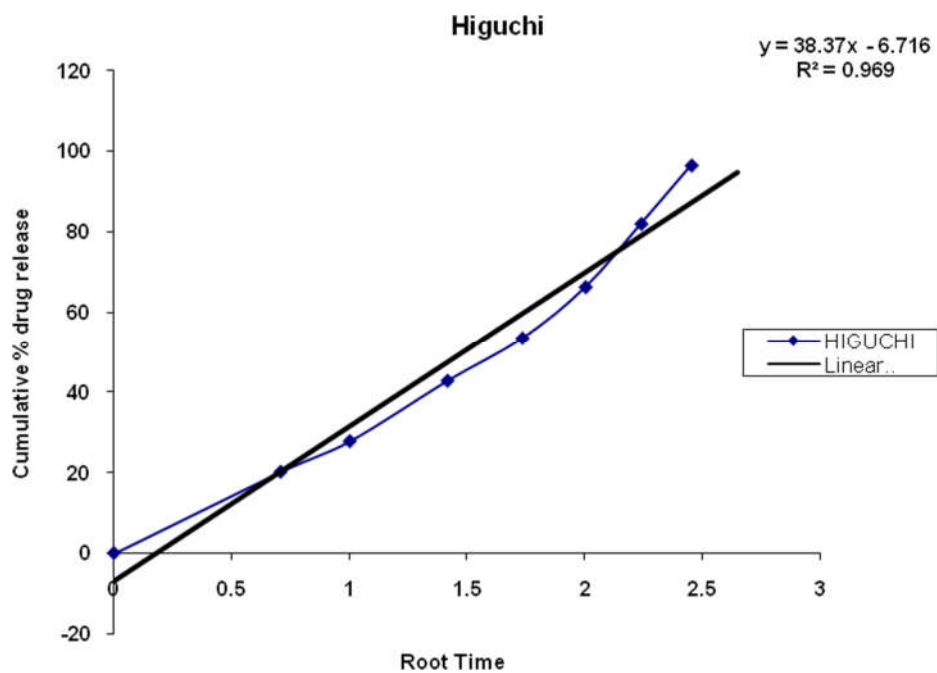


Fig. 5: Higuchi plot

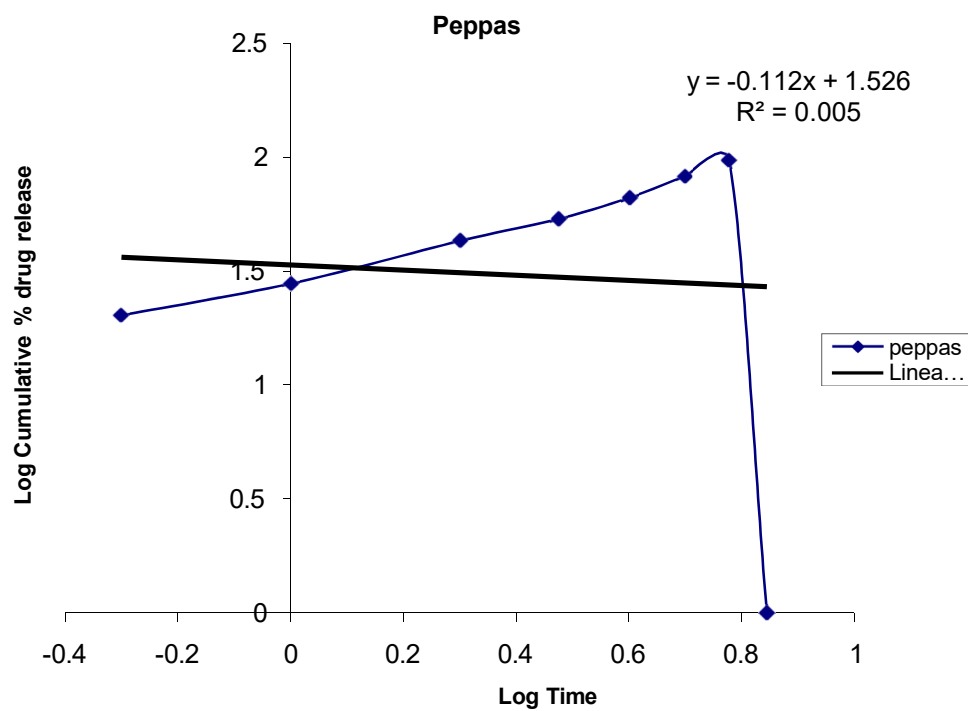


Fig. 6: Peppas plot

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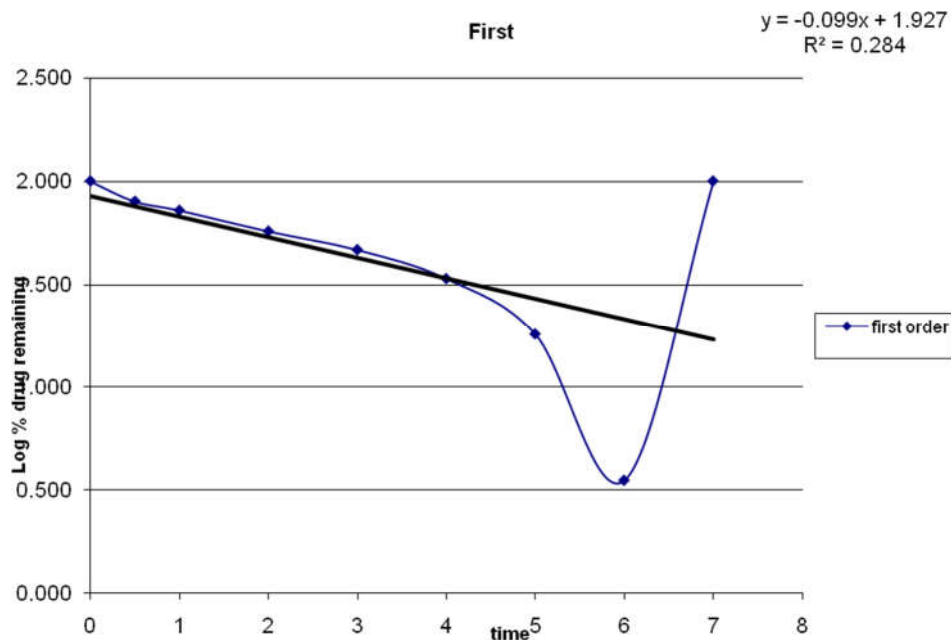


Fig 7: First order kinetics

The kinetics of In-vitro permeation studies using dialysis membrane for F6 formulation was plotted and the Regression coefficient value was found to be high for Korsmeyer-peppas release model i.e., 0.9892. And the n value was found to be 0.6203 which indicates the drug release pattern was found to be non-Fickian diffusion

## 5. Compatibility Studies

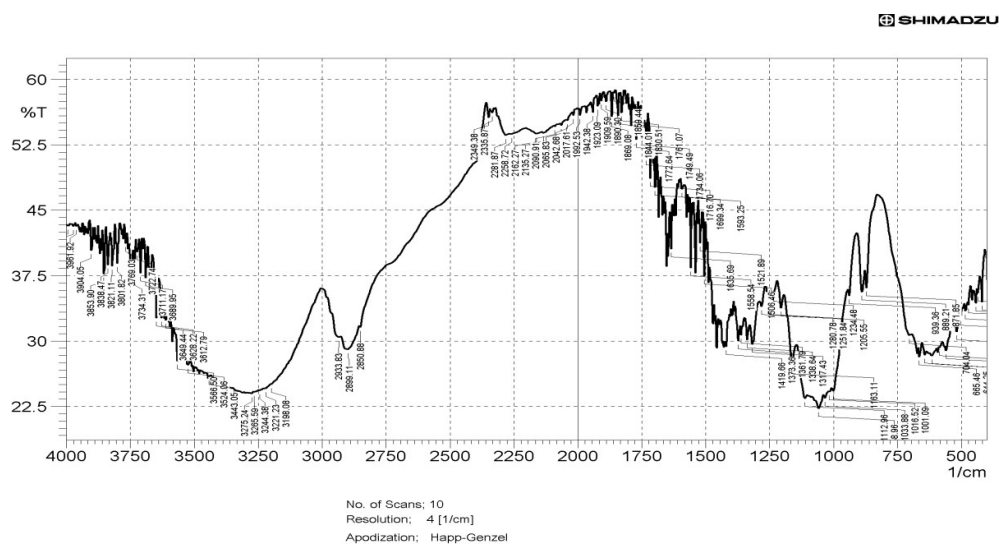


Fig 8: FTIR spectrum of pure drug



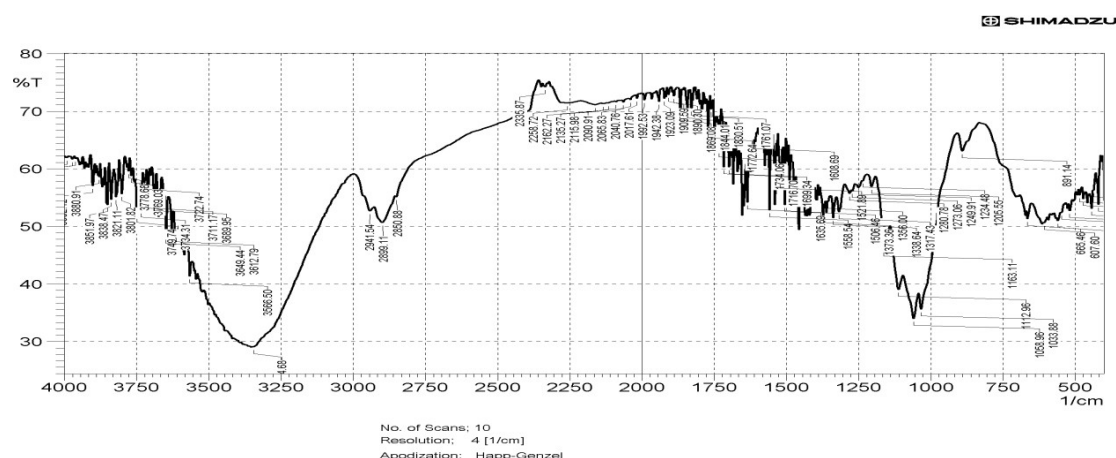


Fig 9: FTIR optimized formulation

The above figure is the FT- IR spectrum of the optimized formula by which the compatability of the drug to all other excipients can be known by the wave numbers which are present. It is observed that there is no interaction between drug and other excipients.

## 6. Conclusion

The objective of the present study transdermal drug delivery of Etodolac was developed to overcome the first pass metabolism and to reduce frequency of dosing compared to oral route. Matrix type of transdermal patches was developed by using polymers Eudragit-L100, HPMCK<sub>4</sub>M and HPMCK<sub>15</sub>M. Transdermal patches were prepared by employing solvent casting method. Propylene glycol and Tween80 were selected as permeation enhancer and plasticizer. Drug excipient compatibility studies were carried out by using FTIR, and it was observed that there were no interactions. Formulations were prepared with the varying concentrations polymers ranging from F1 -F12, and all the formulations were evaluated for various physical parameters Physical appearance, Flatness, Weight variation, Thickness, Folding endurance, Drug content, Moisture uptake, Moisture content and Swelling study and all the results were found to be with in the pharmacopeial limits, invitro drug release studies by using dialysis membrane. Among all the 12 formulations F6 formulation which contain HPMC K4M 200mg had shown 96.5% cumulative drug release with in 12 hours. And compared to HPMC K15M, HPMC K4M showed better drug release profile. For F6 formulation release kinetics were plotted and the Regression coefficient value was found to be high for Korsmeyer-peppas release model i.e., 0.9892. The n value was found to be 0.6203 which indicates the drug release pattern was found to be non-Fickian diffusion.

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