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Development And Characterization Of Transdermal Patch Of Etodolac .

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Abstract: Transdermal patches are a non-invasive drug delivery system designed to deliver medications through the skin directly into the bloodstream, offering an alternative to oral and injectable routes. This method provides sustained and controlled release of drugs, potentially enhancing therapeutic efficacy and patient compliance. This paper reviews the mechanisms of transdermal delivery, the types of drugs suitable for this route, the design and development of transdermal patches, and the advantages and challenges associated with their use. Current advancements in technology and materials, as well as future directions for research and development, are also discussed**.**

Purpose: Transdermal patches deliver medication more directly to the bloodstream by by passing processing in the liver. Transdermal patches deliver medication over a longer period of time than traditional systems, which can be easier on patients who experience extreme side effects.

Method: The process of solvent casting can be utilized for manufacturing Transdermal patch utilizing polymers such as HPMC , PVPK-30 and Eudragit L-100. The ratio of chloroform to mthanol employed as a solvent was 5:5. The mechanical stirrer's speed was 500 rpm.

Result: Among the various formulations evaluated, batch F4 emerged as the most suitable choice for preparing Etodolac Transdermal patch. This particular formulation contains 50% (w/w) Pvpk-30 and 17% (w/w) PEG 400, which have proven to be effective in achieving the desired outcomes. The F-4 formulation exhibited good organoleptic properties and a folding endurance of 5, indicating its durability during handling. In-vitro dissolution studies demonstrated a rapid drug release rate of 97.66% within 8 hr, while the patch disintegrated in just 8 hr. These findings highlight the significant potential of utilizing polymers like Hpmc, Pvpk-30 and Eudragit L-100 for the development of highly effective and patient-friendly Transdermal drug delivery systems**.**

Conclusion: The research indicates that utilizing the solvent casting process with HPMC , PVPK-30 and Eudragit L-100 to create Transdermal patch containing Etodolac is an acceptable method.

Keywords: Transdermal patch , Transdermal drug delivery system , Skin, Matrix, Reservoir, Systemic circulation, routes of penetration.

Introduction:

A transdermal patch is a medicated adhesive patch that is placed on the skin to deliver a specific dose of medication through the skin and into the blood stream [1]. An benefits of a transdermal patch over other types of medication delivery such as oral, topical, intravenous, intramuscular, etc. is that the patch provides a controlled release of the medication into the patient, usually through either a porous membrane covering a reservoir of. medication or through body heat melting thin layers of medication embedded in the adhesive.[2]

Transdermal drug delivery system, the delivery of drugs through the skin has been always a challenging area for researchers, due to barrier properties exhibit by the outermost layer of skin stratum cornum. Specially in last twenty years, the transdermal drug delivery system has become a more focusing technology that offers significant clinical benefits over other dosage forms, because transdermal drug delivery offers controlled as well as state blood concentration.[3]

It lessens the weight that taking medication orally frequently places on the skin. The idea of a regulated drug delivery system or therapeutic system was developed as a result of these factors, as well as additional factors including recurrent dosing and unexpected absorption.

It is practical, particularly for patches that only need to be applied once each week. Such a simple dosing regimen aids in patient adherence to drug therapy[4]

Materials and Methods:

Materials:

Etodolac purchased from Century Pharmaceutical LTD. HPMC, PVPK-30 and Etodolac L-100 Ethyl , Polyethylene glycol- 400 , Propylene Glycol, Chloroform, Ethanol was purchased from Balaji Industries.

Methods:

Method of preparation:

The patches were made by solvent casting technique. The casting solution was formulated by dissolving different polymers (HPMC, PVP K30, and Eudragit L100) in suitable solvents (i.e., methanol and chloroform) using a magnetic stirrer (Remi, India) for 15 minutes to get a uniform dispersion. The drug was added at a slow rate to the solution and then the plasticizer (PEG 400) 36% and permeation enhancer (propylene glycol) 12% were added to the polymeric solution and then dissolved by continuous stirring for a period of 30 minutes, initially at a lower speed and then subsequently at a greater speed. The drug polymeric solution was introduced into a petridish and dried for 12 hours at 40–50°C with air circulation.

Table 1. Formulation table of Transdermal patch of Etodolac .

Ingredients	F1	F2	F3	F4	F5	F6
Etodolac	20	20	20	20	20	20
HPMC	300	400	-	-	-	-
PVPK-30	-	-	300	400	-	-
Eudragit L-100	-	-	-	-	300	400
Polyethylene glycol- 400	2	2	2	2	2	2
Propylene glycol	0.5	0.5	0.5	0.5	0.5	0.5
Chloroform: Methanol	5:5	5:5	5:5	5:5	5:5	5:5

Evaluation parameters:

Calibration curve of Etodolc

A UV-visible spectrophotometer was used to get the UV spectra of Etodolac 10 mg of the drug precisely measured and added to 100 ml of the volumetric flask. Using 0.1 N HCl a volume of up to 100 ml was made. This mixture served as a standard solution. To obtain the concentration of 10 micrograms/ml, 1 ml of aliquots from the stock solution were taken, and the quantity was increased up to 10 ml. To determine maximum wavelength in O.1 N HCl the sample was scanned from 200 to 400 nm .

Compatibility Studies:

Prior to developing Transdermal patch , the drug-excipient compatibility was examined using an FT-IR spectrophotometer.

1. **Drug content determination**: After breaking the transdermal patch, it is dissolved in solvent to evaluate the drug content. A particular analytical technique is then used to measure the amount of drug present in the filtrate.
2. **Weight Uniformity :** Before testing, the created patches must be dried for four hours at 60°C. A particular patch section needs to be divided into several sections and weighed using a digital balance. From the individual weights, the average weight and standard deviation values must be determined
3. **Patch Thickness :** The goal of this patch is to keep transdermal compositions consistent. It is ascertained by using a micrometer to measure the patch's thickness three times.[38]
4. **Folding Endurance** : Assessing the folding durability of films that are frequently folded under harsh conditions entails figuring out their folding capacity. The film is folded at the same spot repeatedly until it breaks to assess the folding endurance. The quantity of The folding endurance value () is the number of times the films could be folded in the same direction without breaking.
5. **Moisture Content :** The transdermal patch's moisture loss after being stored in a desiccator can be used to compute this value. Weighed and stored in desiccators, the patch Calcium chloride for 24 hours, after which the ultimate The transdermal patch's weight is established. It is stated as a percentage:% (Initial Mass - Final Mass) / Initial Moisture Content mass times 100
6. **Moisture Uptake** : The weighing films must be stored in desiccators with saturated potassium chloride solutions that allow you to maintain a RH of 84% for 24 hours at room temperature. The films must be reweighed after 24 hours in order to calculate the percentage of moisture uptake

using the formula below. [Final Weight-Initial Weight/Initial Weight] × 100 = percent moisture uptake.

7. **Flatness:** A transdermal patch should not tighten over time and have a smooth surface. The study of flatness can be used to illustrate this. Two strips are cut from each side of the patches and one from the center to determine the flatness of the patches. Every strip's length is measured and the % constriction is used to measure the variance in length. One hundred percent flatness is equal to zero percent constriction.
8. **Tensile Strength:** The film's tensile strength was ascertained using a typical strength testing The upper is moveable and the lower is fixed. A 4-by-1-centimeter test film is placed between these cell grips, and pressure is exerted gradually until the film breaks. (30) The dial reading in kg is immediately used to determine the film's tensile power. This is how tensile strength is expressed. Tensile strength is equal to cross sectional area / tensile load at break.
9. **Water vapour transmission studies (WVT):** One gram of calcium chloride is placed into previously dried, empty vials with similar diameters to estimate WVT. Using an adhesive such as silicon adhesive grease, the polymer films are adhered to the brim and then Let it sit for five minutes.

   The vials are weighed precisely and put in a humidity chamber with a 68% relative humidity. Subsequently, the vials undergo repeated weighing for a period of seven days, with an increase in weight being interpreted as a quantitative indicator of the amount of moisture transferred via the patch.
10. **Stability Studies:** The patch is kept at 40 ± 0.5 °C and 75 ± 5% relative humidity to ensure stability. Drug analysis is performed on samples throughout storage at intervals of 0, 30, 60 days.material to provide insight into the stability of the product.

In-vitro drug release:

The in vitro drug dissolution from the patch was assessed using a modified USP XXIV dissolving equipment type I (basket). In separate runs, the test was conducted in 900 milliliters of distilled water containing 0.1 HCl (pH 1.2) as the dissolving media. Every run was done at a speed of 100 rpm. The samples (5 ml each) were taken out and periodically subjected to spectrophotometric analysis at 430 nm. To maintain a steady sink condition, the release medium was supplemented with a fresh medium of the same volume. The majority of the tests were conducted in two different instances. A standard curve was used to calculate the cumulative drug release (%)

Result:

Preformulation Studies:

Properties of Organoleptic Systems:

1. Colour: Off White
2. Odour: Sulphide
3. Melting Point: 140ºC-145 ºC

   The purity of the medicine samples is ensured by the fact that all of the pharmaceuticals' physical attributes fell inside the provided parameters.

Solubility:

Solubility of Etodolac of soluble in ethanol, methanol, Chloroform.

Determination of λ max in 0.1 N HCl and calibration curve

Sr. No	Concentration (µg/ml)	Absorbance
1.	5	0.064
2.	10	0.098
3.	15	0.124
4.	20	0.152
5.	25	0.176

By measuring the absorbance of Etodolac in 0.1N HCL at concentrations ranging from 5 to 25 µg/ml at 280 nm, the standard calibration curve for Etodolac was developed. The resulting curve was then plotted with its absorbance on the y-axis and Etodolac level on the x-axis.
Slope of Y = 0.0054(x) + 0.041.

$R^2 = 0.994$

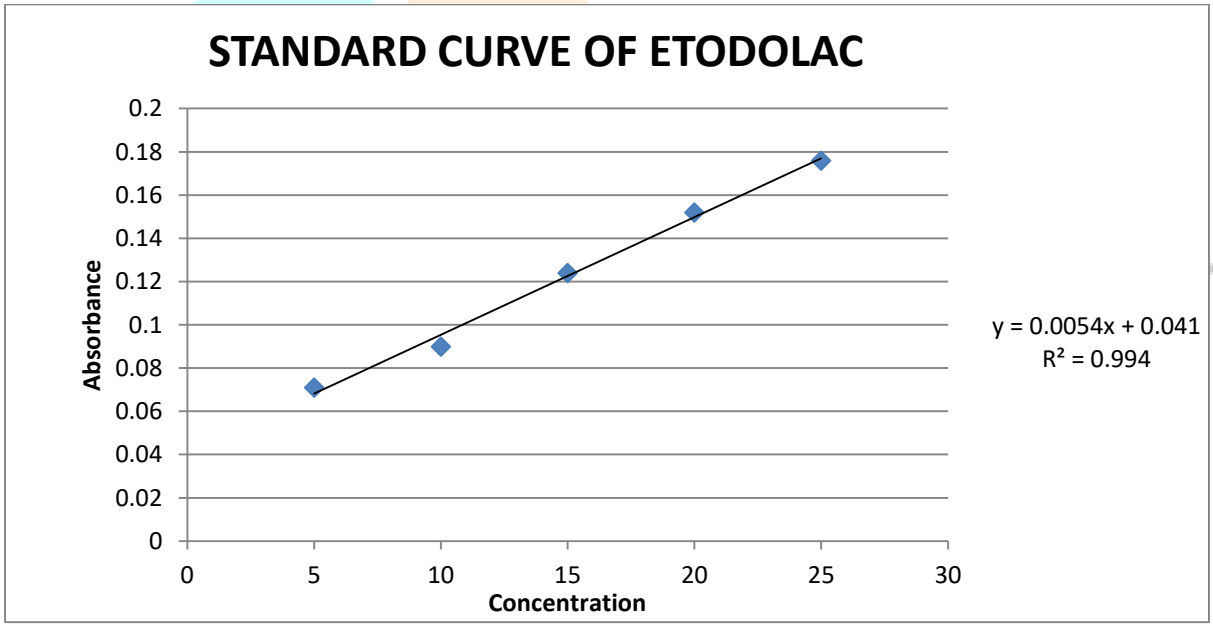

Figure 1. Standard Curve of Etodolac Phosphate in 0.1 N HCL

Evaluation :

Formulation Code	Thickness (mm)	Folding Endurance	Weight Variation (mg)	Surface pH
F1	0.67± 0.020	40.77 ± 5.57	42.84 ± 3.57	6.1 ± 0.31
F2	0.37 ± 0.012	51.33 ± 4.04	52.87 ± 4.36	6.7 ± 0.21
F3	0.77± 0.026	62.33 ± 5.51	38.71 ± 5.51	6.1 ± 0.2
F4	1.17 ± 0.006	91.33 ± 4.73	41.7± 4.04	6.2 ± 0.15
F5	0.92 ± 0.012	103 ± 5.57	38.87 ± 2.08	6.3 ± 0.21
F6	1.09 ± 0.015	117 ± 4.51	41.4 ± 4.51	6.3 ± 0.31

Table No.2 The results for the thickness, folding endurance, weight variation, surface pH:

- Thickness: The thickness of the patch ranges from 0.230 mm to 0.326 mm.
- Folding Endurance: The folding endurance of the patch ranges from 5 to 6 folds.
- Weight Variation: The weight variation of the patch ranges from 160.7± 2.31 mg to 245.9± 2.45 mg.
- Surface pH: The surface pH of the patch ranges from 6.1 to 6.6.

There is a positive correlation between thickness and folding endurance. This means that the thicker the patch, the more folds it can withstand before breaking. There is also a positive correlation between thickness and weight variation. This means that the thicker the patch, the more weight it will vary by.

A high folding endurance indicates that the patch is strong and durable. Except patch made with Hpmc other patch showed promising results.

The surface pH of the patch is all within the acceptable range for Transdermal patch. The ideal surface pH for Transdermal patch is 5 to 6 so all of the formulations in the chart are within the ideal range**.**

Here are some observations from the chart:

- Formulations F4, F5, and F6 have the highest folding endurance.
- Formulations F3 and F3 have the highest weight variation.
- Formulations F1 have the lowest surface pH**.**

Fourier Transform Infrared Spectroscopy (FTIR)

The FTIR spectrum analysis was used to determine the drug+polymer compatibility research. The same peaks were also seen in the formulation, demonstrating the drug's stable nature.

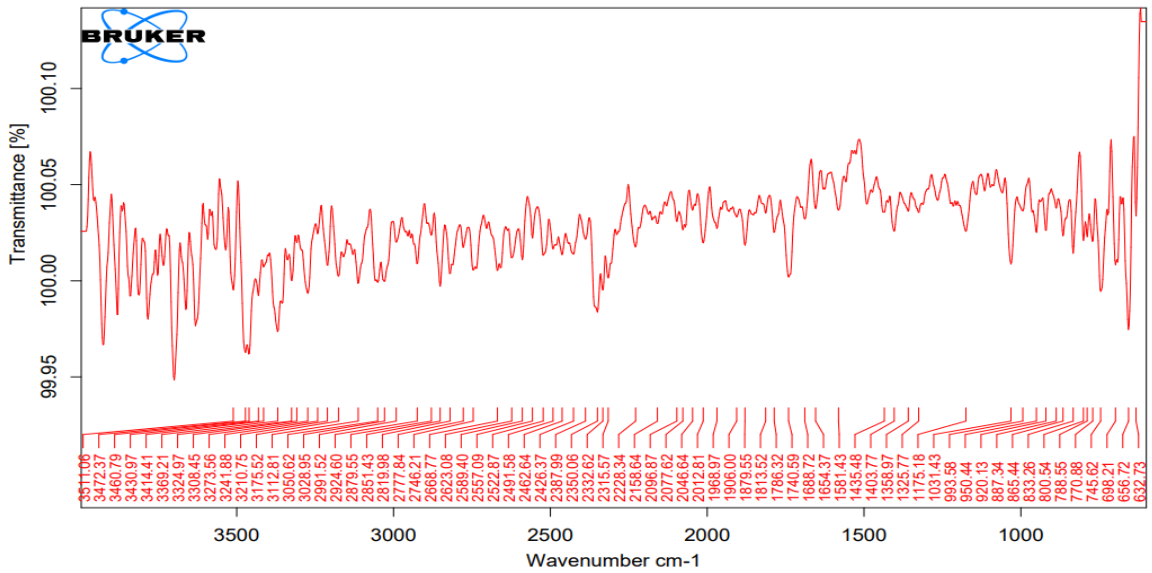

Figure 2. FTIR Spectrum of Etodolac.

Table No 4. Range of functional group present in FTIR.

Sr. No	Functional group	Observed Ranges (cm^{-1})	Standard Ranges (cm^{-1})
1.	Nitro Compounds	1510.19	1550-1475
2.	Alkenes	975.24	1000-650
3.	Aromatics	871.40	900-675
4.	Aliphatic amines	1145.40	1250-1020
5.	Carbonyl	1666.78	1760-1665

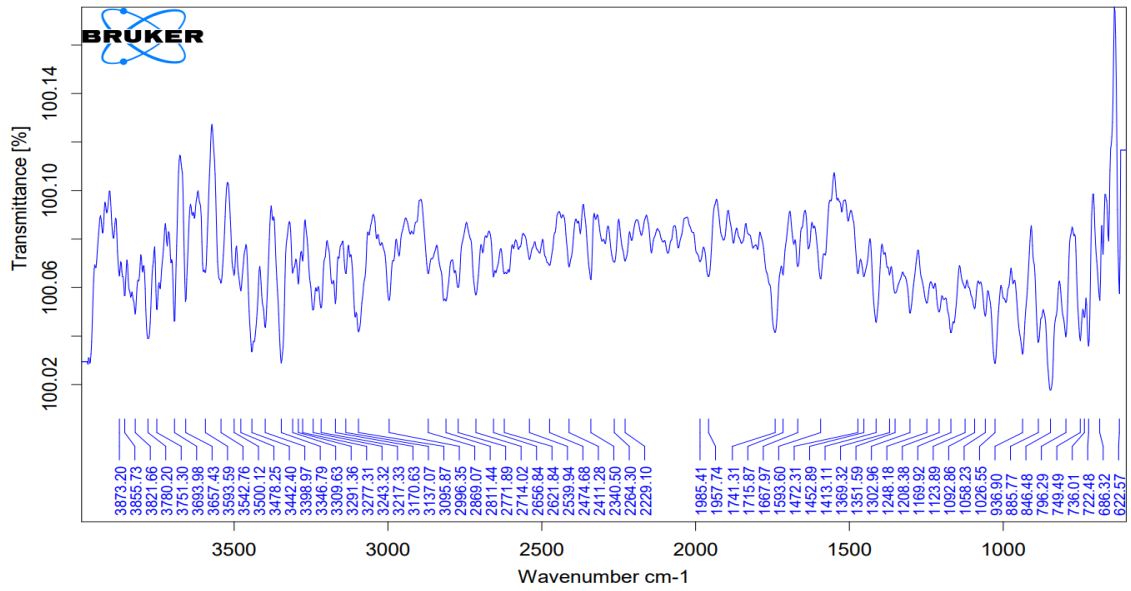

Figure 3. FTIR Spectrum of Etodolac + HPMC.

Table No 5. Range of functional group present in FTIR.

Sr. No	Functional group	Observed Ranges (cm^{-1})	Standard Ranges (cm^{-1})
1.	Aromatics	845.66	900-675
2.	Carbonyl	1669.55	1760-1665
3.	Aliphatic amines	1208.01	1250-1020

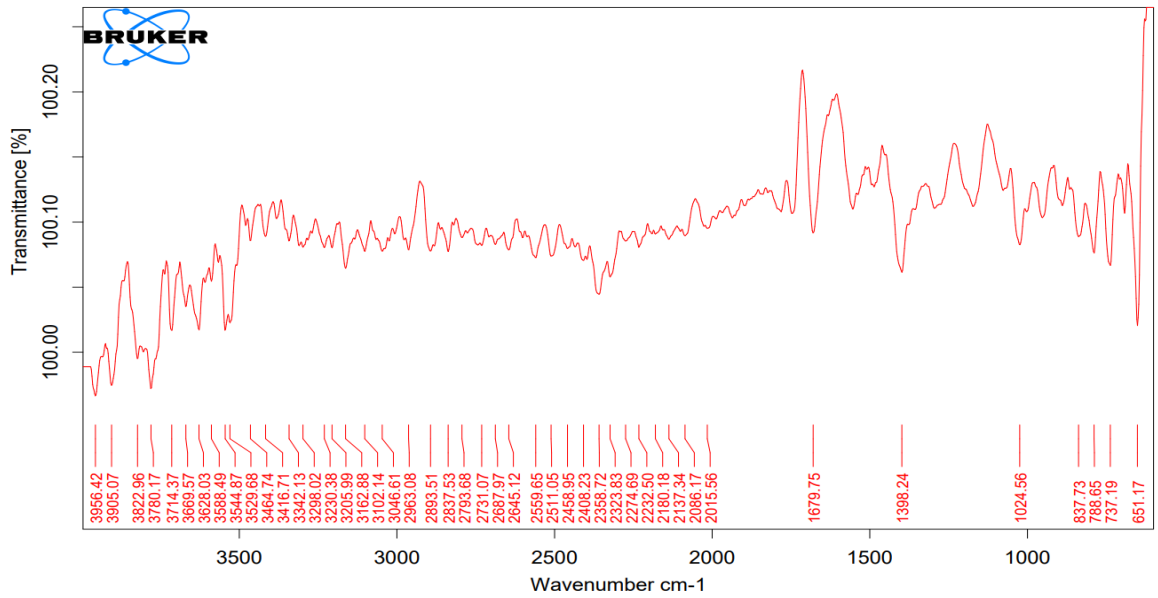

Figure 4FTIR Spectrum of Etodolac + Pvpk -30.

Table No 6. Range of functional group present in FTIR.

Sr. No	Functional group	Observed Ranges (cm^{-1})	Standard Ranges (cm^{-1})
1.	Alkenes	971.88	1000-650
2.	Aromatics	837.58	900-675
3.	Aliphatic amine	1052.10	1250-1020

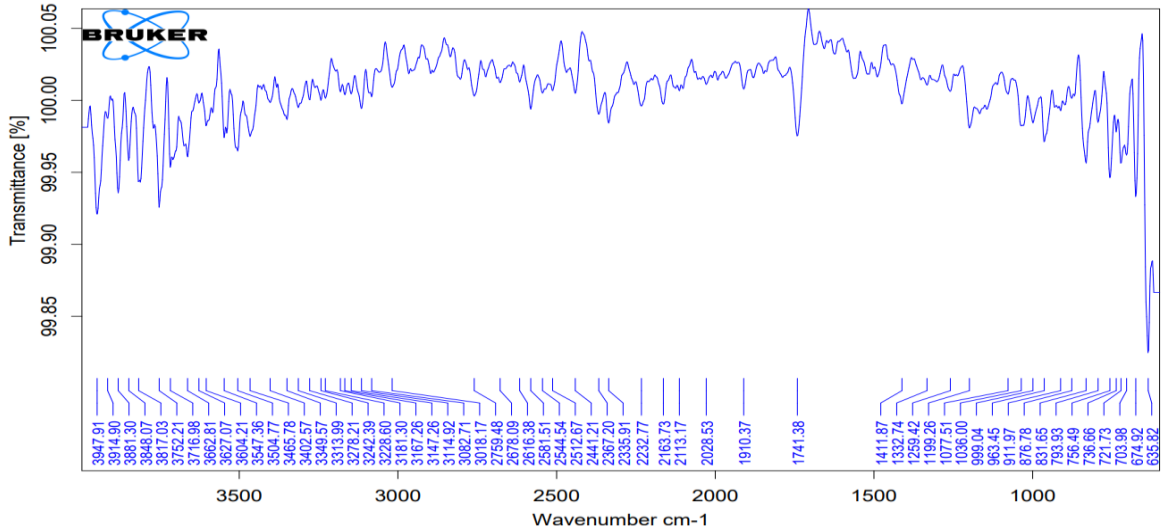

Figure 5. FTIR Spectrum of Etodolac + Eudragit L-100.

Table No 7. Range of functional group present in FTIR.

Sr. No	Functional group	Observed Ranges (cm^{-1})	Standard Ranges (cm^{-1})
1.	Aromatics	884.81	900-675
2.	Carbonyl	1668.25	1760-1665
3.	Alkenes	976.89	1000-650

DSC Study of Etodolac:

Differential Scanning Colourimetry (DSC) was used to evaluate the melting point,crystalinity,Decomposition and drug-excipient interaction by studing the thermal behavior of the Preparation .The DSC curve of Etodolac shown a shows a sharp endothermic peak at 153.17 ºC at 10.7 min.

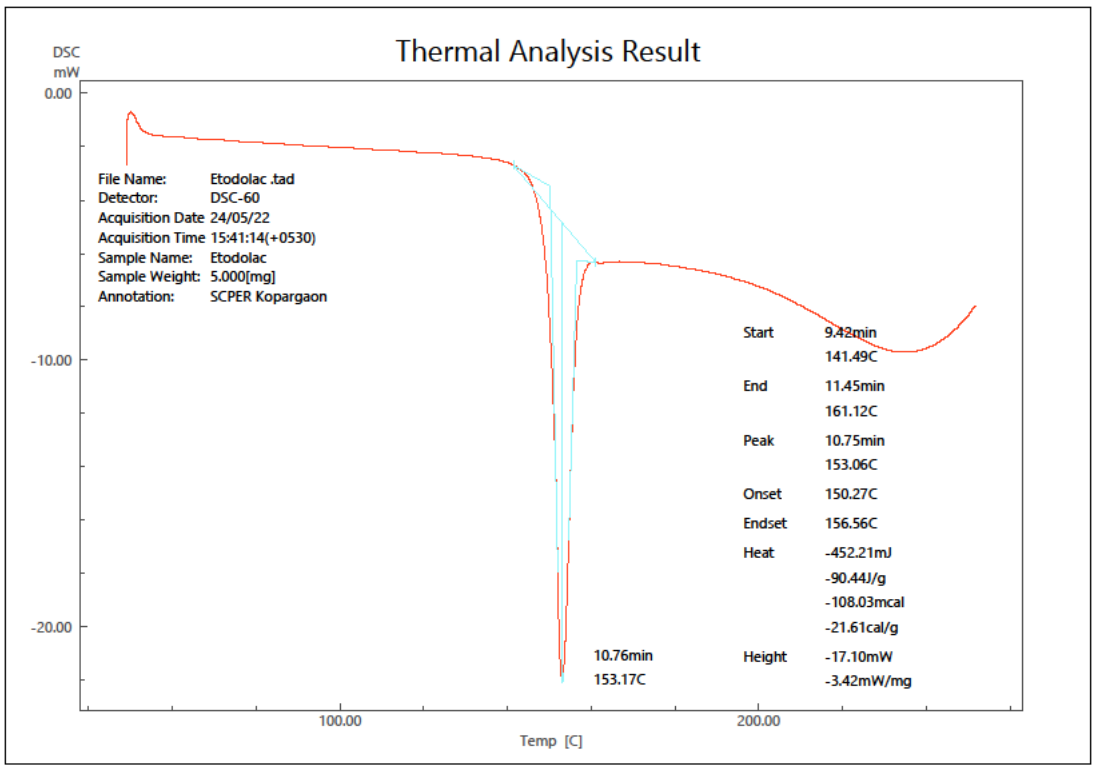

Fig.6 DSC Study of Etodolac

DSC Study of Drug and All Excipient :

The DSC curve of Etodolac shown a shows a sharp endothermic peak at 153.17 ºC at 10.7 min . And DSC thermogram of drug excipient mixture indicate broadening of base peak And slight shifting of melting point to 153.17 ºC.Thus it indicate the absence of chemical Intraction between the drug and excipient mixtyre.The DSC of Etodolac and excipient Show the they are compatible

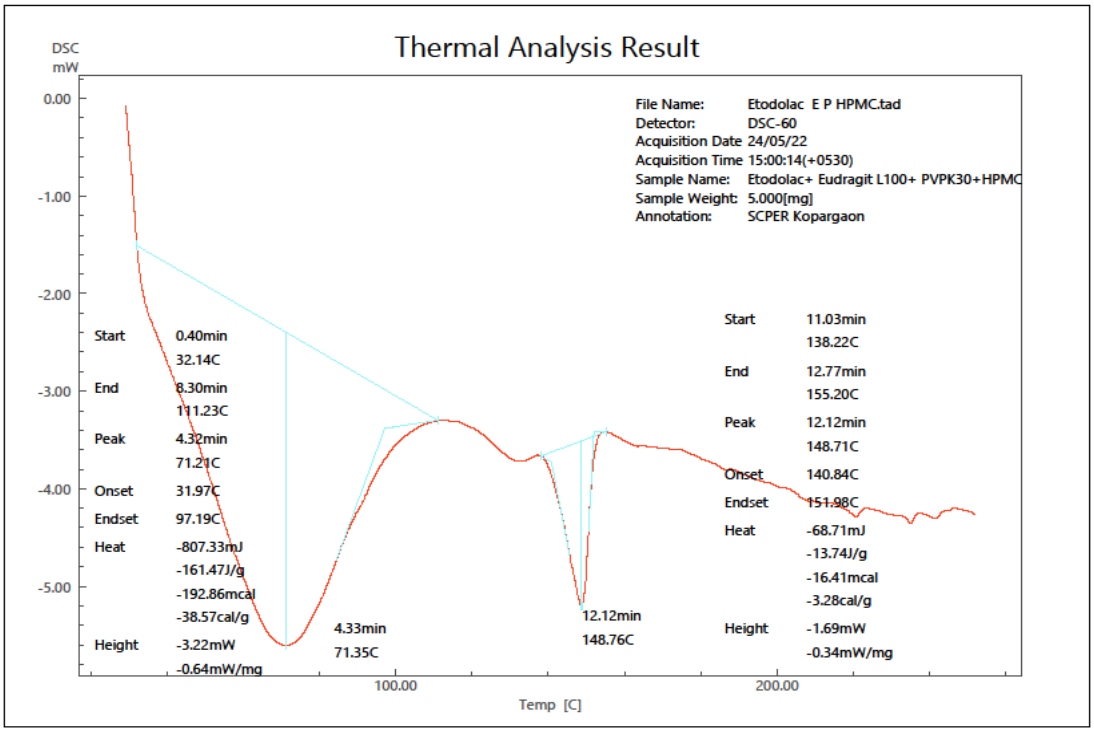

Fig.6 DSC Study of Etodolac and All Excipient

In-vitro Drug Release Study:

Time (hrs)	F1	F2	F3	F4	F5	F6
1	7.03±0.41	4.74±0.32	5.99±0.15	7.03±0.12	8.07±1.12	8.07±0.35
2	20.40±0.3	18.52±2.01	19.15±0.13	20.20±1.25	20.02±2.06	25.62±2.12
3	25.69±15	25.89±0.13	26.93±1.25	25.69±2.58	27.98±1.18	32.17±0.18
4	32,17±2.63	39.05±1.19	41.14±2.03	34.67±1.13	39.48±2.16	39.50±0.63
5	40.54±2.15	48.29±0.36	55.18±2.08	55.35±2.15	60.38±1.18	58.09±2.45
6	51.22±1.12	57.72±2.15	62.32±3.16	62.55±1.18	74.03±2.06	76.94±1.18
7	60.44±2.03	62.98±1.73	68.84±2.94	78.84±2.16	83.28±0.26	85.58±0.35
8	84.03±1.02	92.59±3.15	90.33±0.52	97.62±0.26	88.54±1.13	92.30±1.25

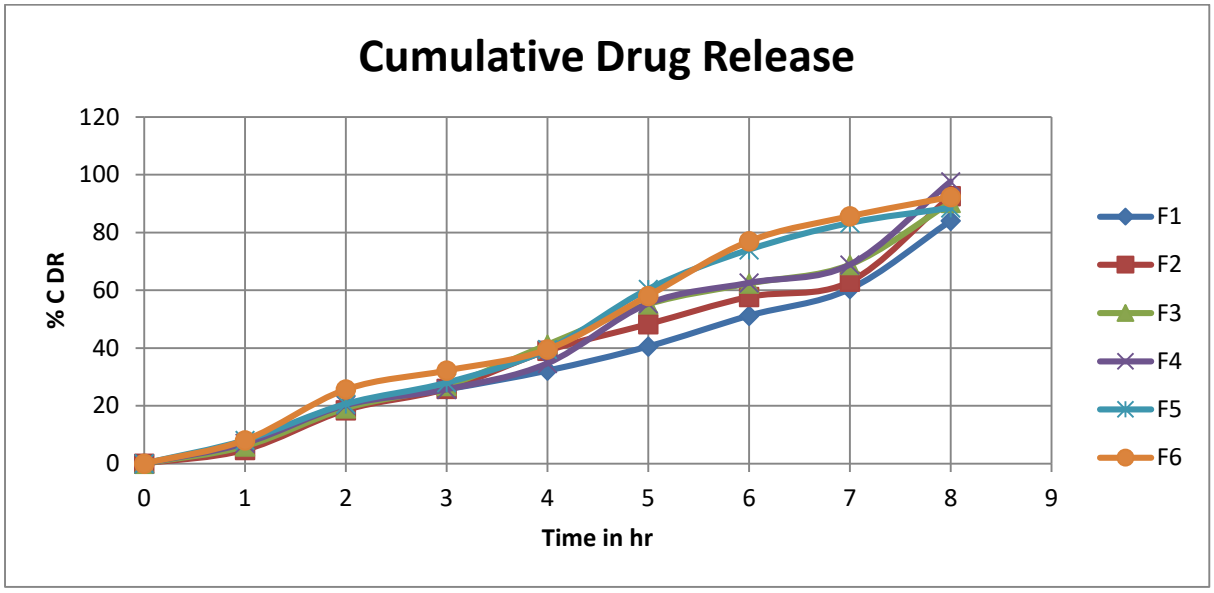

Fig 7. In-Vitro Drug Release of Batch F1 to F8

Figure 6. In-Vitro drug release Formulation F1 to F8

Sr. No	Time (hrs)	%CDR
1	1	84.03±1.12
2	2	92.59±0.22
3	3	90.33±0.96
4	4	97.62±2.03
5	5	89.54±0.36
6	6	79.67±1.14
7	7	88.54±1.18
8	8	92.30±1.03

Discussion:

We conducted all of the Transdermal Patch assessment parameters. This yields findings that are acceptable and fall within the expected range.

Conclusion:

Drug delivery via TDDS devices has proven to be painless, efficient, non-toxic, and patient-compliant. The creation of a reliable method for NSAID transdermal delivery could high local soft tissue and joint concentrations, as well as lessens the adverse effects of oral administration. A range of NSAID medications can be used to treat different types of skin conditions, however not can be administered in this way due to their physicochemical characteristics, which are crucial for transdermal drug delivery. The aim of the present study was to develop a Transdermal patch of Etodolac for quick onset action by analgesic,anti-inflammatory ,antipyretic properties

Among the various formulations evaluated, batch F4 emerged as the most suitable choice for preparing Etodolac Transdermal patch. This particular formulation contains 50% (w/w) Pvpk-30 and 17% (w/w) PEG 400, which have proven to be effective in achieving the desired outcomes. The F-4 formulation exhibited good organoleptic properties and a folding endurance of 5, indicating its durability during handling. In-vitro dissolution studies demonstrated a rapid drug release rate of 97.66% within 8 hr, while the patch disintegrated in just 8 hr. These findings highlight the significant potential of utilizing polymers

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