

DEVELOPMENT OF CONTROLLED RELEASE TRANSDERMAL FILMS CONTAINING ANTHRALIN**Pritam Adak^{1*}, Prateek Jain², Hemant Agrawal³, Naveen Gupta⁴**¹Student- Madhyanchal Professional University (MPU), Bhopal (M.P).^{2,3}Associate Professor- Madhyanchal Professional University (MPU), Bhopal (M.P).⁴Dean- Madhyanchal Professional University (MPU), Bhopal (M.P).

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ABSTRACT

Anthralin is an effective antipsoriatic agent widely used in the treatment of chronic skin disorders such as psoriasis; however, its therapeutic application is limited due to poor patient compliance, skin irritation, and the need for frequent administration. The present study was undertaken to develop and evaluate controlled release transdermal films containing Anthralin in order to enhance drug release control, improve therapeutic efficacy, and prolong drug delivery through the skin. Pre-formulation studies of Anthralin were carried out to determine its physicochemical properties, including organoleptic characteristics, solubility, melting point, λ max determination, calibration curve analysis, and FTIR spectroscopy. Anthralin exhibited maximum absorbance and showed compatibility with the selected excipients used in the

transdermal patch formulation. The transdermal films were prepared by the solvent casting method using combinations of Eudragit L, polyvinylpyrrolidone (PVP), hydroxypropyl methylcellulose (HPMC), polyethylene glycol 400, Tween 20, methanol, and glycerin. Six formulations (TPF1–TPF6) were prepared by varying the polymer composition. The prepared transdermal films were evaluated for folding endurance, tensile strength, percentage elongation, thickness uniformity, drug content, and *in vitro* drug release studies. Among all formulations, TPF5 exhibited the most desirable physicochemical characteristics; including excellent flexibility, tensile strength (25 kg/cm²), percentage elongation (42%), and maximum drug content (95.78%). The optimized formulation also demonstrated a sustained

and controlled drug release profile with 95.06% cumulative drug release over 11 hours. Drug release kinetics of the optimized formulation was analyzed using zero-order, first-order, Higuchi, and Korsmeyer–Peppas kinetic models. The release profile showed the highest correlation with the zero-order kinetic model ($R^2 = 0.976$), indicating concentration-independent and controlled drug release. The Higuchi model also demonstrated good linearity, suggesting diffusion-controlled release behavior from the polymeric matrix. The overall findings of the study indicate that the developed Anthralin transdermal films possess satisfactory physicochemical properties, controlled drug release characteristics, and excellent formulation stability. Therefore, the optimized transdermal patch formulation can be considered a promising alternative drug delivery system for the effective management of psoriasis and related dermatological conditions.

KEYWORDS: Anthralin; Transdermal film; Controlled drug release; HPMC; Drug release kinetics; Psoriasis therapy.

INTRODUCTION

Psoriasis is a chronic autoimmune and inflammatory skin disorder characterized by hyperproliferation and abnormal differentiation of epidermal keratinocytes, resulting in erythematous, scaly, and thickened plaques on the skin (**Lowes et al., 2014; Nestle et al., 2009**). The disease affects approximately 2–3% of the global population and is associated with considerable physical discomfort, emotional stress, and impaired quality of life (**Parisi et al., 2013**). Conventional topical therapies for psoriasis often suffer from poor skin permeation, inadequate drug retention at the site of action, frequent dosing, and reduced patient adherence, thereby limiting their therapeutic effectiveness (**Boehncke and Schön, 2015**).

Anthralin (Dithranol) is one of the oldest and most effective topical antipsoriatic agents used in the treatment of chronic plaque psoriasis. It exhibits antiproliferative, anti-inflammatory, and keratolytic activity by inhibiting DNA synthesis and suppressing excessive keratinocyte proliferation (**Menter et al., 2009**). Despite its clinical effectiveness, the therapeutic use of Anthralin is restricted because of several disadvantages such as skin irritation, burning sensation, instability in the presence of oxygen and light, poor penetration through the skin, and staining of skin and clothing (**Rathi et al., 2011**). Therefore, the development of a novel drug delivery system capable of improving stability, enhancing permeation, and reducing side effects is highly desirable.

Transdermal drug delivery systems (TDDS) have emerged as promising alternatives to conventional topical dosage forms because they can provide sustained and controlled drug release, improve therapeutic efficacy, reduce dosing frequency, and enhance patient compliance **(Prausnitz et al., 2004)**. Matrix-type transdermal patches are particularly advantageous due to their ease of preparation, flexibility, uniform drug distribution, and ability to maintain prolonged drug release over an extended period **(Jain et al., 2013)**. The effectiveness of transdermal patches largely depends upon the proper selection of polymers, plasticizers, and permeation enhancers that influence film characteristics and drug permeation behavior **(Keleb et al., 2010)**.

In the present investigation, Anthralin-loaded matrix-type transdermal patches were developed using the solvent casting technique employing different combinations of Eudragit L and Polyvinylpyrrolidone (PVP) along with Hydroxypropyl Methylcellulose (HPMC) as a film-forming polymer. Polyethylene glycol 400 was used as a plasticizer to improve flexibility, while Tween 20 served as a permeation enhancer to facilitate transdermal drug transport **(Mutalik and Udupa, 2005)**. Prior to formulation development, detailed pre-formulation studies including organoleptic evaluation, solubility analysis, melting point determination, UV spectrophotometric analysis, calibration curve preparation, and Fourier Transform Infrared (FTIR) spectroscopy were performed to assess the physicochemical properties and compatibility of Anthralin with excipients **(Lachman et al., 2013)**.

The prepared transdermal patches were evaluated for various physicochemical and mechanical properties such as folding endurance, tensile strength, percentage elongation, thickness uniformity, drug content, and in-vitro drug release behavior. In addition, different kinetic models including zero-order, first-order, Higuchi, and Korsmeyer–Peppas models were applied to determine the mechanism and kinetics of drug release from the optimized formulation **(Dash et al., 2010)**.

The main objective of the present study was to formulate and evaluate a stable and effective Anthralin transdermal patch capable of delivering the drug in a sustained manner for improved management of psoriasis. The developed formulation is expected to enhance therapeutic efficacy, minimize adverse effects, improve patient compliance, and provide an alternative approach for long-term antipsoriatic therapy.

2. MATERIALS AND METHODS

2.1 Materials

Anthralin was obtained as a gift sample from a reputed pharmaceutical company. Hydroxypropyl methylcellulose (HPMC), Eudragit L, Polyvinylpyrrolidone (PVP), Polyethylene glycol 400 (PEG 400), Tween 20, methanol, ethanol, dimethyl sulfoxide (DMSO), potassium bromide (KBr), glycerin, phosphate buffer pH 6.8, and all other chemicals and reagents used in the study were of analytical grade.

2.2 Pre-formulation Studies

Pre-formulation studies were carried out to evaluate the physicochemical properties of Anthralin and its suitability for transdermal formulation development. These studies included organoleptic evaluation, solubility analysis, melting point determination, UV spectrophotometric analysis, calibration curve preparation, and Fourier Transform Infrared (FTIR) spectroscopy (Patel et al., 2014).

2.3 Organoleptic Properties

The organoleptic properties of Anthralin were evaluated by visual inspection to determine its color, odor, appearance, and physical state. These parameters are important for preliminary identification, quality assessment, and ensuring consistency of the drug sample before formulation development (Aulton and Taylor, 2018).

2.4 Solubility Study

The solubility behavior of Anthralin was studied qualitatively in various solvents according to USP-NF guidelines. Approximately 1 mg of Anthralin was transferred into separate test tubes containing 1 mL of methanol, ethanol, distilled water, and dimethyl sulfoxide (DMSO). The mixtures were shaken thoroughly, and the solubility of the drug in each solvent was visually observed and recorded (USP-NF, 2007; Sodeifian et al., 2025).

2.5 Melting Point Determination

The melting point of Anthralin was determined by the open capillary method using a Thiele's tube apparatus. A small amount of the drug was filled into a capillary tube sealed at one end. The capillary tube was attached to a thermometer and immersed in liquid paraffin oil. The temperature was gradually increased until the drug started melting, and the melting temperature was recorded. This study was performed to assess the purity and thermal stability of the drug (Patel et al., 2014).

2.6 Determination of λ_{max}

A stock solution of Anthralin was prepared by dissolving the drug in methanol to obtain a concentration of 1 mg/mL. Further dilution was made to prepare a working solution of 100 $\mu\text{g/mL}$. The solution was scanned between 200–400 nm using a Shimadzu UV-Visible spectrophotometer (Model 1700), and the wavelength corresponding to maximum absorbance was recorded as λ_{max} (Ali *et al.*, 2022).

2.7 Preparation of Calibration Curve

The stock solution of Anthralin was diluted appropriately with methanol to prepare standard solutions of varying concentrations. The absorbance of each solution was measured at the determined λ_{max} using methanol as blank. A calibration curve was plotted between concentration and absorbance to establish Beer-Lambert's law and for quantitative estimation of the drug during further studies (Kaur *et al.*, 2017).

2.8 Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectroscopy was carried out using the KBr pellet method to identify the characteristic functional groups of Anthralin and evaluate possible drug-excipient interactions. The drug sample was mixed with dried potassium bromide and compressed into a transparent pellet using hydraulic pressure. The pellet was scanned over the range of 4000–400 cm^{-1} using an FTIR spectrophotometer, and the spectrum obtained was analyzed for characteristic peaks (Menon *et al.*, 2012).

2.9 Formulation of Anthralin Transdermal patch

Drug-loaded matrix-type Transdermal patches of Anthralin were prepared by using solvent casting method. A petri dish with a total area of 44.15 cm^2 was used. Polymers were accurately weighed and dissolved in 10 mL of methanol solution and kept aside to form clear solution. Drug was dissolved in the above solution and mixed until clear solution was obtained. Polyethylene glycol 400 (30% w/w of total polymer) was used as plasticizer, HPMC (200mg) and propylene glycol (15% w/w of total polymer) and Tween 20 (0.1% common permeation enhancer) was used as permeation enhancer. The resulted uniform solution was cast on the Petri dish, which was lubricated with glycerin and dried at room temperature for 24 h. An inverted funnel was placed over the Petri dish to prevent fast evaporation of the solvent. After 24 h, the dried patches were taken out and stored in a desiccator for further studies (El-Nabarawi *et al.*, 2013, Singh and Bali 2016, Prajapati *et al.*, 2011).

2.9.1 Composition of Formulation

Table 1: Composition of Transdermal patch.

Ingredients	Formulation batches					
	TPF 1	TPF 2	TPF 3	TPF 4	TPF 5	TPF 6
Anthralin (mg)	100	100	100	100	100	100
Polyethylene glycol (ml)	0.5	0.5	0.5	0.5	0.5	0.5
Polyvinylpyrrolidone (mg)	-	-	-	150	200	250
Eudragit L (mg)	150	200	250	-	-	-
Tween 20	0.1	0.1	0.1	0.1	0.1	0.1
HPMC (mg)	200	200	200	200	200	200
Methanol	10	10	10	10	10	10
Glycerin	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.

2.10 Evaluation of Anthralin Transdermal Patches

2.10.1 Folding Endurance

Folding endurance was determined by repeatedly folding a strip of transdermal patch (2 × 2 cm) at the same place until it broke. The number of folds required to break the film was recorded as the folding endurance value, indicating the flexibility and mechanical strength of the patch (Shivalingam et al., 2021).

2.10.2 Tensile Strength

Tensile strength was evaluated using a tensiometer. Film strips of dimensions 2 × 2 cm were fixed between two grips, and force was gradually applied until the film broke. The tensile strength was recorded directly from the instrument in kg/cm² (Jacob et al., 2022).

2.10.3 Percentage Elongation Break Test

The percentage elongation at break was calculated by measuring the increase in length of the film before breaking using the following equation

$$\% \text{ Elongation} = \frac{L_f - L_i}{L_i} \times 100$$

Where:

- L_f = Final length of the strip
- L_i = Initial length of the strip

2.10.4 Thickness Measurement

The thickness of the prepared patches was measured using a digital micrometer screw gauge at three different positions, and the average value was calculated (Aulton and Taylor, 2018).

2.10.5 Drug Content Uniformity

A patch of specified area (2×2 cm) was dissolved in 100 mL methanol and shaken continuously for 24 h. The solution was ultrasonicated for 15 min and filtered. The drug content was estimated spectrophotometrically at 318 nm using a UV-visible spectrophotometer (Kaur *et al.*, 2017).

2.10.6 In-vitro Drug Release Study

In-vitro drug release studies were performed using a Franz diffusion cell having a receptor compartment capacity of 60 mL. A cellulose acetate membrane (0.45 μ m pore size) was mounted between the donor and receptor compartments. The transdermal patch was placed over the membrane, and the receptor compartment was filled with phosphate buffer pH 6.8. The system was maintained at $32 \pm 0.5^\circ\text{C}$ with continuous stirring using a magnetic stirrer. Samples were withdrawn at predetermined time intervals and analyzed spectrophotometrically for drug content. An equal volume of fresh phosphate buffer was added after each withdrawal to maintain sink conditions (Jacob *et al.*, 2022).

2.10.6.1 Drug Release Kinetic Studies

The in-vitro drug release data were fitted into different kinetic models including zero-order, first-order, Higuchi, and Korsmeyer–Peppas models to determine the mechanism of drug release from the transdermal patches (Higuchi, 1963).

Zero-order Kinetics

$$A_t = A_0 + K_0 t$$

First-order Kinetics

$$\log C = \log C_0 - \frac{Kt}{2.303}$$

Higuchi Model

$$Q = K_H \sqrt{t}$$

The correlation coefficient (R^2) values obtained from each model were used to identify the best-fit kinetic model governing drug release behavior.

3. RESULT AND DISCUSSION

3.1 pre-formulation Studies

3.1.1 Organoleptic Evaluation

Table 2: Organoleptic evaluation of Anthralin.

S. No.	Physical parameter	Observation
1	Color	Yellow
2	Odor	Odorless
3	State	Solid
4	Appearance	Yellow to orange crystalline powder

3.1.2 Melting Point determination

Table 3: Melting point of Anthralin.

S. No.	Drug	Specification	Inference
1.	Anthralin	216-220°C	219°C

3.1.3 Solubility Studies of Anthralin

Table 4: Solubility study of Anthralin.

S. No.	Solvents	Category
1	Methanol	Freely soluble
2	Ethanol	Sparingly soluble
3	DMSO	Freely soluble
4	Water	Soluble
5	PBS 6.8	Freely soluble

3.1.4 Determination of λ max

Solution was scanned under UV-Vis Spectrophotometer and λ max was determined. It was found to be as per the monograph.

3.1.5 Calibration Curve of Anthralin.

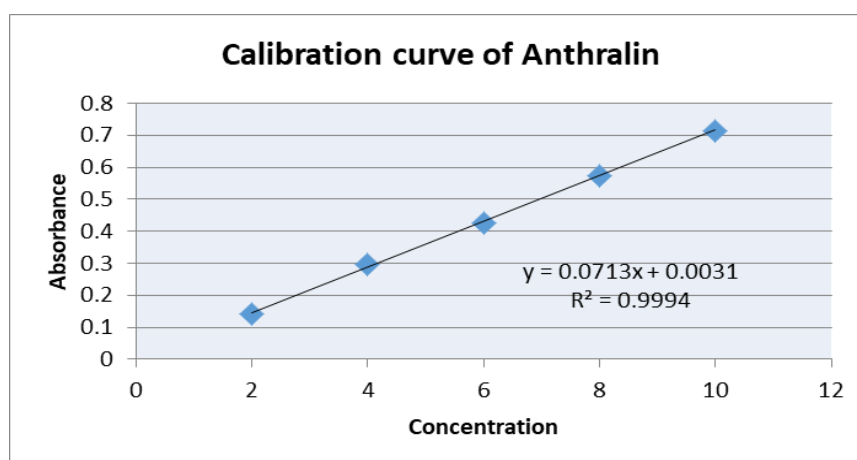


Figure 1: Calibration curve of Anthralin in Methanol at 318 nm.

3.1.6 Functional group identification by FTIR.

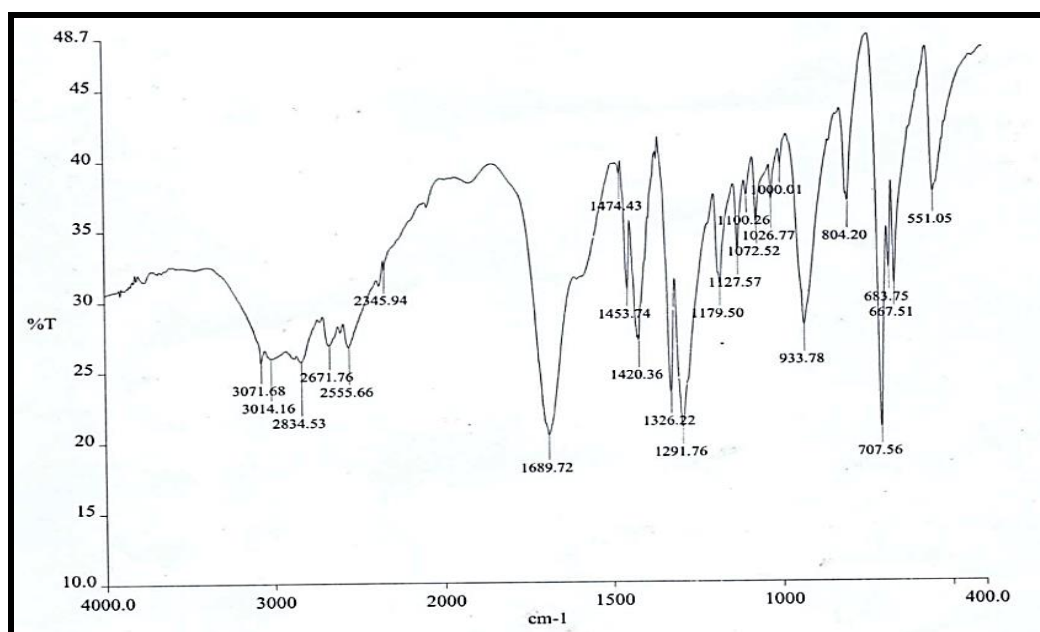


Figure 2: FTIR graph of Anthralin.

Table 5: Interpretation of IR spectrum of Anthralin.

S. No.	Peak obtained	Reference peak	Functional group	Name of functional group
1	3071.68	3100-3000	C-H stretching	alkene
2	2834.53	3000-2800	N-H stretching	amine salt
3	2555.66	2600-2550	S-H stretching	thiol
4	1689.72	1710-1685	C=O stretching	conjugated aldehyde
5	1326.22	1342-1266	C-N stretching	aromatic amine
6	1179.50	1210-1163	C-O stretching	ester
7	1072.52	1085-1050	C-O stretching	primary alcohol

3.2 Evaluation of Dermal film

Table 6: Evaluation of Transdermal Film.

S. No.	Evaluation parameters	Formulation batches					
		TPF 1	TPF 2	TPF 3	TPF 4	TPF 5	TPF 6
	Texture	Flexible	Flexible	Flexible	Flexible	Flexible	Flexible
1	Folding endurance	76	79	82	79	82	81
2	Tensile strength kg/cm ²	18	20	23	24	25	24
3	% elongation break test	38	35	37	37	42	41
4	Thickness (mm)	0.31	0.37	0.31	0.33	0.35	0.36
5	Drug content %	78.67	93.47	90.31	79.03	95.78	89.19

3.2.1 Release of all formulation

Table 7: In- vitro Drug Release Study of Patches Formulation (11 hrs).

S.No	Formulation Code	Cumulative % drug release (11 hrs)
1.	TPF 1	72.23
2.	TPF 2	79.56
3.	TPF 3	88.84
4.	TPF 4	87.82
5.	TPF 5	95.06
6.	TPF 6	94.17

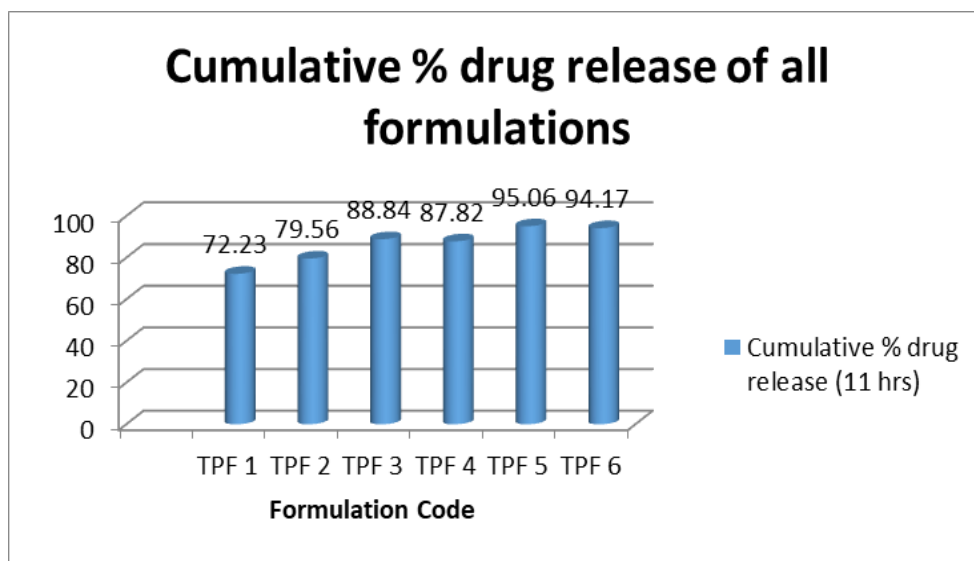


Figure 3: Graphical Representation of Cumulative % Drug Release.

Release kinetics study of TPF 5 formulation

Table 8: Release kinetics study of final formulation (TPF 5).

S. No.	Time (hrs)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remaining	log Cumu % drug released	log time
1.	0	0	100	0.000	2.000	0.000	0.000
2.	2	20.12	79.88	1.414	1.902	1.304	0.301
3.	3	26.01	73.99	1.732	1.869	1.415	0.477
4.	4	38.56	61.44	2.000	1.788	1.586	0.602
5.	5	48.16	51.84	2.236	1.715	1.683	0.699
6.	6	64.31	35.69	2.449	1.553	1.808	0.778
7.	8	79.08	20.92	2.828	1.321	1.898	0.903
8.	10	85.89	14.11	3.162	1.150	1.934	1.000
9.	11	93.06	6.94	3.317	0.841	1.969	1.041

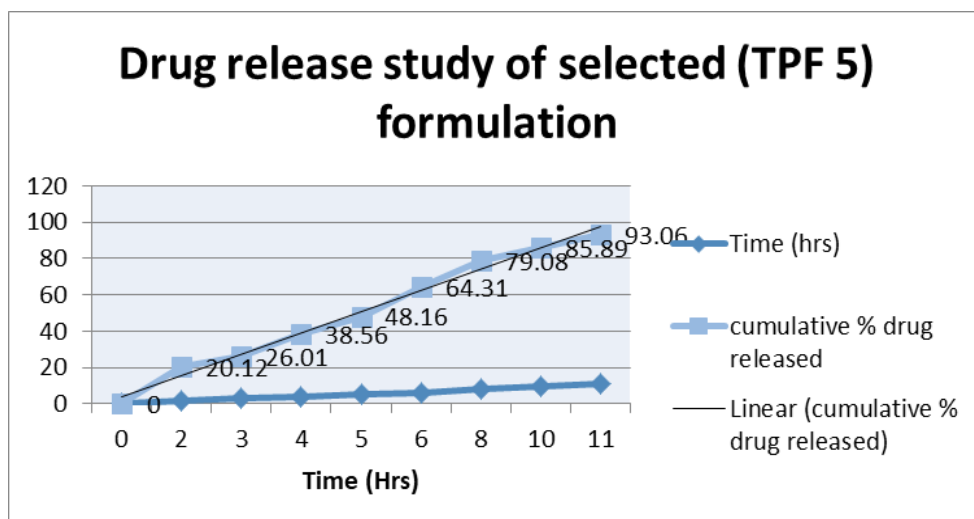


Figure 4:- Graphically Representation of Drug Release.

Correlation value (R^2 value)

Table 9: Correlation value (R^2 value).

Formulation	Model	Kinetic parameter values
Patches	Zero Order	$R^2 = 0.976$
	First Order	$R^2 = 0.921$
	Higuchi	$R^2 = 0.921$
	Korsmeyerpeppas	$R^2 = 0.845$

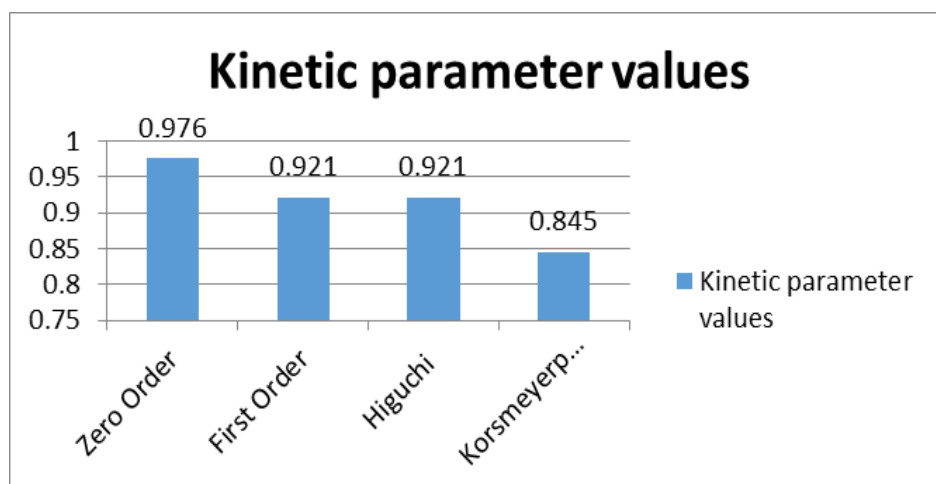


Figure 5: Graphically Representation of Kinetic Parameter.

DISCUSSION

The present study successfully formulated and evaluated Anthralin-loaded matrix-type transdermal patches using the solvent casting method. Pre-formulation studies confirmed the purity, stability, and compatibility of Anthralin with selected excipients. The drug showed satisfactory solubility in methanol, DMSO, and phosphate buffer, while the melting point and

FTIR studies confirmed its identity and purity.

All prepared transdermal patches exhibited good flexibility, uniform thickness, acceptable tensile strength, and satisfactory drug content. Among all formulations, TPF5 showed the best performance with maximum drug content (95.78%), highest tensile strength, and sustained drug release of 95.06% within 11 hours. The release kinetic analysis revealed that the optimized formulation followed zero-order kinetics, indicating controlled and constant drug release behavior.

Overall, the study demonstrated that Anthralin transdermal patches can serve as an effective and sustained drug delivery system for psoriasis treatment.

4. CONCLUSION

Anthralin-loaded matrix-type transdermal patches were successfully prepared and evaluated. The optimized formulation (TPF5) showed satisfactory physicochemical properties, good mechanical strength, and sustained drug release. The release profile followed zero-order kinetics, indicating controlled drug delivery. The developed transdermal patch may improve therapeutic efficacy, reduce dosing frequency, and enhance patient compliance in psoriasis management. Further in-vivo and stability studies are recommended to confirm its clinical potential.

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