RESEARCH PAPER

Development and evaluation of Rufinamide transdermal patches for effective management of epilepsy.

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ABSTRACT

Background: Rufinamide is an antiepileptic drug used in the management of partial seizures and Lennox-Gastaut syndrome. Its oral administration is associated with variable bioavailability and frequent dosing, which may compromise therapeutic efficacy and patient compliance. Transdermal drug delivery systems (TDDS) provide an alternative route to achieve sustained plasma levels and improved adherence.

Methods: Matrix-type transdermal patches of rufinamide were prepared by solvent casting using HPMC E15 LV polymer, with PEG-600 as plasticizer and Tween-40 as permeation enhancer. Patches were evaluated for physicochemical and mechanical properties, drug content, in-vitro drug release, ex-vivo permeation using egg membrane, and stability under varied humidity conditions. Analytical characterization included FTIR for drug–excipient compatibility and UV spectrophotometry for quantification.

Results: All patches were uniform, flexible, and exhibited acceptable thickness, weight variation, surface pH, moisture balance, and mechanical strength. HPMC-based patches provided sustained release of rufinamide (up to 93.8% over 12 h) with controlled permeation, Ex-vivo permeation confirmed higher flux for HPMC-based formulations. Stability studies demonstrated no significant changes in appearance, drug content, or mechanical integrity under accelerated and long-term storage conditions. **Conclusion:** Rufinamide transdermal patches demonstrated robust physicochemical and mechanical properties, controlled or rapid release profiles depending on polymer composition, and acceptable stability. These findings suggest that TDDS can provide a promising alternative to oral administration, with the potential to improve therapeutic outcomes and adherence in epilepsy management.

Keywords Transdermal patches, polymers, rufinamide, sustained release, drug

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INTRODUCTION: Epilepsy is a chronic neurological disorder affecting approximately 1% of the global population and is characterized by recurrent seizures due to abnormal neuronal discharges [1]. Despite the availability of several antiepileptic drugs (AEDs), many patients continue to experience suboptimal seizure control, poor adherence, or adverse systemic effects associated with oral dosing regimens [2]. To address these limitations, advanced drug delivery platforms such as transdermal therapeutic systems have been widely explored [3,4].

Transdermal drug delivery systems (TDDS) offer controlled and sustained release of therapeutic agents through the skin into systemic circulation, thereby circumventing hepatic first-pass metabolism, minimizing gastrointestinal degradation, and providing more consistent plasma concentrations [5,6]. Such systems can significantly

enhance patient compliance, particularly in chronic conditions requiring long-term therapy, by reducing dosing frequency and maintaining steady-state levels [7,8]. Over the past three decades, TDDS have evolved with the use of novel polymers, penetration enhancers, and matrix designs to improve flux across the stratum corneum [9-11].

Rufinamide, a triazole derivative approved for adjunctive treatment of seizures associated with Lennox–Gastaut syndrome and partial-onset seizures, presents itself as a promising candidate for transdermal delivery. The drug exerts its effect by prolonging the inactivated state of voltage-gated sodium channels, thereby stabilizing neuronal membranes and suppressing seizure propagation [12]. However, the oral bioavailability of rufinamide is variable and dose-dependent, with absorption influenced by food intake and subject to considerable inter-patient variability [13,14]. Such pharmacokinetic challenges may compromise therapeutic outcomes and justify the investigation of alternative delivery routes.

Matrix-type patches composed of polymers such as hydroxypropyl methylcellulose (HPMC) has been successfully employed in the development of transdermal films for therapeutic effect, including antiepileptics [15–18]. The physicochemical properties of these polymers allow modulation of drug release profiles, mechanical strength, and skin permeability, particularly when combined with plasticizers and permeation enhancers [19,20]. Prior studies have demonstrated that incorporation of hydrophilic polymers increases matrix hydration and drug diffusion, while penetration enhancers improve partitioning into the skin, thereby optimizing flux [21,22].

Within this context, the present work focuses on the **development and evaluation of rufinamide-loaded matrix-type transdermal patches** using HPMC E 15 LV polymer. The study investigates the physicomechanical characteristics, in-vitro release kinetics, ex-vivo permeation behaviour, and stability profile of these formulations, aiming to establish a viable platform for sustained antiepileptic therapy through the transdermal route.

2. Material and Methods: -

2.1 Materials

Rufinamide (API) was purchased from BL Chemicals, Yuka Enterprises. Hydroxypropyl methylcellulose (HPMC E15 LV), were obtained from Jubilant Life Science Ltd. (Formulation R&D). Polyethylene glycol 600 (PEG-600) was used as a plasticizer, and Tween-40 as a permeation enhancer (Loba Chemie Pvt. Ltd., India). Methanol (analytical grade) was procured from Sai Pvt. Ltd. Distilled water was prepared in laboratory [23–27].

2.2 Methods

2.2.1 Pre-formulation studies

2.2.1.1 Characterization of rufinamide

The drug was characterized for visual appearance (colour, odour), melting point (capillary method), pH of saturated solution, and solubility in different solvents including water, ethanol, methanol, acetone, DMSO, DMF, and acetonitrile [23–27].

2.2.1.2 Preparation of calibration solutions

A stock solution of rufinamide was prepared in phosphate buffer (pH 7.4) and serially diluted to 5–25 µg/mL. Absorbance was measured at 212 nm using a UV–visible spectrophotometer. A calibration curve was constructed (absorbance vs. concentration) to confirm linearity ($r^2 \geq 0.98$ [30,31].

2.2. Dose calculation for patch formulation

Transdermal Dose = (Oral dose × Bioavailability) / 100

Transdermal Dose = (10 × 70) / 100 = 7 mg rufinamide

Area of Petri dish (A) = πr^2 = 3.14 × 3.9 × 3.9 = 47.75 cm^2

(Diameter = 7.9 cm; Radius = Diameter / 2 = 3.9 cm)

Now, if a 2 × 2 cm^2 patch (4 cm^2) contains 7 mg of drug, then the full casting area of 47.75 cm^2 corresponds to:

47.75 × 7 = 334.31 mg rufinamide per batch [28,29].

2.3 Preparation of rufinamide-loaded films (solvent casting)

Transdermal patches were prepared using the solvent casting process with film-forming polymers such as polyvinylpyrrolidone (PVP), and polyvinyl alcohol (PVA), which were accurately weighed and dissolved in the required solvent [23,24]. The polymer solution was left to stand for approximately 10 minutes to allow the polymers to swell [25]. Additional solvent was then added as needed, followed by incorporation of PEG-600 as a plasticizer [26].

Rufinamide was precisely weighed in quantities corresponding to either 2×2 cm² areas, based on the dose calculation, drug was dissolved separately in the required volume of methanol in another beaker [27]. The drug solution was gradually added to the polymer solution under magnetic stirring to ensure homogeneity. Stirring was continued until a clear solution was obtained [28]. The mixture was kept overnight to clarify and remove entrapped air bubbles [29]. The degassed solution was then cast into clean, Petri plates and dried at room temperature for 24-48 hours. To prevent rapid solvent evaporation, an inverted funnel was placed over the Petri plates during drying [30]. The dried films were carefully removed, trimmed to the desired size, and stored in airtight aluminium-foil-lined containers until further evaluation [31,32].

2.4. Evaluation parameters for optimized transdermal patches

2.4.1. Physical evaluation

Physical appearance: The color, transparency, clarity, flexibility, and smoothness of each patch were examined visually. [33].

Weight variation: The weight variation of each finished film was determined using a digital scale. Ten individual pieces from each batch were weighed separately, and the variation of each from the average weight was calculated [33].

Thickness: Thickness was measured at five different points of each film using a vernier caliper, and the mean value was calculated [33,34]. Additionally, the thickness of three different 2 × 2 cm² sections of each batch was determined using the glass slide method:

- First, the thickness of two overlapping glass slides was measured (T1).
- Next, the patch was placed between the slides and the thickness recorded (T2).
- Patch thickness was calculated as: $\mathbf{Thickness\ (mm) = T2 - T1}$ [35].

Folding endurance: Folding endurance was evaluated by manually folding the patch repeatedly at the same point until it broke. The number of folds required to cause breakage was recorded as the folding endurance. The experiment was repeated three times, and the mean value was reported [35,36].

Surface pH:

Three patches from each formulation were placed on agar plates and allowed to swell for 2 h. The surface pH was then measured using pre-calibrated pH paper applied to the swollen surface. The average of three readings was noted [37].

Swelling index:

Swelling behavior was evaluated by placing patches in PBS (pH 7.4) at 37 ± 0.5 °C. Patches were cut into 2 × 2 cm² sections and weighed (W1). At intervals of 5, 10, 15, 20, 25, and 30 minutes, patches were removed, gently blotted, and reweighed (W2). The swelling index was calculated as:

$$\%\ \text{Swelling Index} = \frac{W2 - W1}{W1} \times 100$$

The test was performed in triplicate [37,38,34].

Percent moisture loss:

Patches were accurately weighed and kept in desiccators containing anhydrous calcium chloride for 3 days. They were then reweighed, and moisture loss was calculated as:

$$\%\ \text{Moisture Loss} = \frac{W_0 - W_t}{W_0} \times 100$$

where W_0 = initial weight and W_t = weight after storage [39].

Percent moisture absorption:

Patches were weighed and then placed in a closed chamber above a beaker containing water, covered with pierced aluminium foil to maintain humidity. After 24 h, patches were reweighed and moisture absorption was calculated as:

$$\%\ \text{Moisture Absorption} = \frac{W_f - W_i}{W_i} \times 100$$

where W_i = initial weight and W_f = final weight after 24 h [40].

Disintegration time:

Disintegration time was determined using a locally modified USP disintegration apparatus. Patches (5 cm²) were placed in 900 mL of phosphate buffer (pH 7.4, simulating skin pH maintained at 37 °C. The basket was moved up and down at a rate equivalent to 30 strokes/min. The time required for no visible patch material to remain above the gauze was recorded [40,37].

2.4.2. Chemical evaluation

Drug content estimation:

Three films of 2 × 2 cm² were cut, dissolved in 5 mL methanol, and diluted to 100 mL with phosphate buffer (pH 7.4). From this, 10 mL was pipetted and further diluted to 100 mL to obtain a 10 µg/mL solution. The drug content was determined spectrophotometrically at 212 nm λmax. [45,46]. Percentage drug content was calculated as:

$$\% \text{ Drug Content} = \frac{\text{Test Absorbance}}{\text{Standard Absorbance}} \times 100$$

In-vitro drug release: Dissolution rate studies to assess the drug release from the transdermal patches were carried out in paddle type USP dissolution apparatus II. 900 ml of phosphate buffer 7.4 pH was taken as dissolution medium because of mean pH of skin and the release study was performed at 37 ± 0.50 °C and speed at 50 rpm. The transdermal patch is attached to the glass disk. The disk is allocated to the bottom of the dissolution vessel. and samples of 1 ml were withdrawn from the dissolution medium at specified time intervals of 1, 2, 3, 4, 5, 6, 8, 9, 10 hours until drug was completely released from formulation and that amount was replaced with fresh medium to maintain the constant volume. The samples were filtered using Whattman filter paper. and diluted to a suitable concentration with 7.4 phosphate buffer. The absorbance of the diluted samples was measured at 212 nm by using UV Visible spectrophotometer. Percentage drug release was calculated using an equation obtained from standard curve.

2.4.3. Mechanical evaluation

Tensile strength:

Tensile strength was determined to evaluate the mechanical strength of the transdermal films. Film strips were placed between two clamps spaced $3-5$ cm apart. The clamps were designed to secure the patch without crushing it, with the lower clamp fixed and the upper clamp allowed to move. During testing, the upper clamp pulled the strip at a constant rate of 100 mm/min until the film broke [47].

In some cases, a modified physical balance was also employed to assess tensile strength by recording the weight required to break the strip [48]. At the breaking point, both the applied force and the extension of the strip were noted. Tensile strength was calculated using the following formula [49]:

$$\text{Tensile Strength} = \frac{\text{Weight required to break the patch}}{a \times b(1 + \Delta l/l)}$$

where $a =$ thickness of the film, $b =$ width of the film, $l =$ initial length of the film, and $\Delta l =$ change in length at break.

Percent elongation:

The percentage elongation at break was calculated as the maximum deformation a film could withstand before splitting. It was calculated using the formula [50]:

$$\% \text{ Elongatin at break} = \frac{\text{Increase in length at break}}{\text{Initial film length}} \times 100$$

2.4.4. Biological evaluation

***Ex-vivo* permeation studies:**

Ex-vivo diffusion studies of rufinamide patches were performed using Franz diffusion cells, with Cellulose nitrate membrane employed as the diffusion barrier [51]. The receptor chamber was filled with phosphate buffer (pH 7.4), maintained at 37°C, and magnetically stirred at 50-100 rpm throughout the experiment. [52]

Samples were withdrawn at 30-minute intervals over the required study period and immediately replaced with fresh buffer to maintain sink conditions. Drug permeation was quantified spectrophotometrically at 212 nm. [52]

The cumulative percentage of drug permeated was plotted against time, were calculated using the following equations [53]:

$$J = \frac{M}{A \times t}$$

$$P = \frac{J}{C_{\text{donor}}}$$

where $M =$ amount of drug permeated, $A =$ diffusion area, $t =$ time, and Cdonor = concentration in the donor compartment. Drug permeation profiles were compared with cumulative in-vitro release results to assess correlation.

2.4.5. Stability studies

For stability testing, rufinamide patches were placed in a humidity chamber under different relative humidity (RH) conditions (45±5% & 75±5%). Accordingly, ICH Guide line Samples were removed weekly and analysed for drug content by UV spectrophotometry [54]. Accelerated stability studies were also conducted at 40±5°C and 37 ± 5 °C for three months [55].

At each interval, patches were examined for organoleptic properties (color, odour, texture, surface pH) and drug content. Mechanical properties were also re-evaluated to detect changes in flexibility or plasticization during storage [56,57]. Minor loss of drug, if any, was noted and correlated with the duration of storage.

3. Results

3.1 Preformulation study of rufinamide

The melting point of rufinamide, determined by the capillary method using a melting point apparatus, was found to be **239 °C**. Solubility studies were carried out by dissolving 10 mg of the active pharmaceutical ingredient in 100 mL of different solvents. The solvents tested were distilled water, ethanol, methanol, DMSO, DMF, acetone, and acetonitrile. Rufinamide exhibited the **lowest solubility in water**, while the highest solubility was observed in **DMSO, DMF, and methanol**, with intermediate solubility in ethanol and acetone.

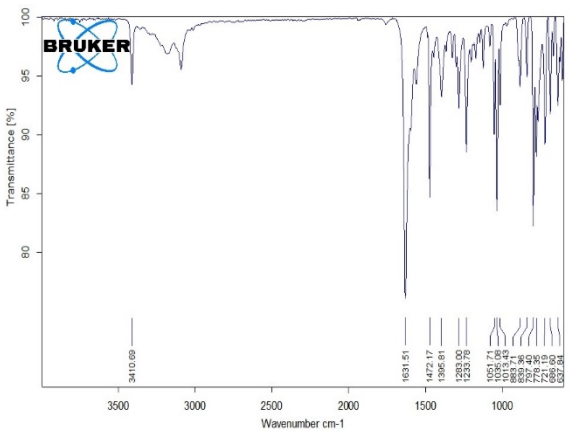
3.2 Quantitative analysis

A calibration curve was prepared using standard rufinamide solutions in phosphate buffer (pH 7.4) at concentrations ranging from **5–25 µg/mL**. The calibration plot of absorbance (y) versus concentration (x) was linear and described by the equation:

$$y=0.0007x+0.3292$$

with a correlation coefficient ($r^2 = 0.9863$). The determined λmax was **212 nm**, confirming the suitability of UV spectrophotometry for routine quantification of rufinamide.

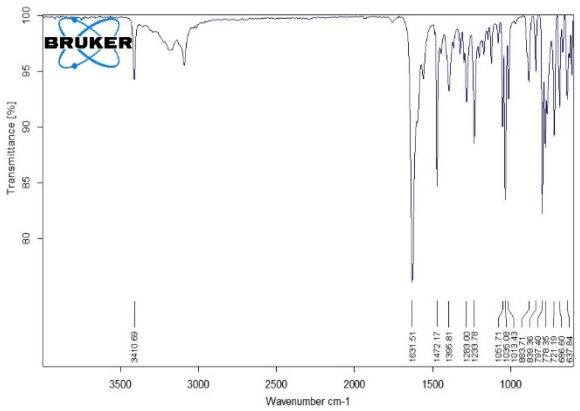
3.3 Drug polymer interaction and compatibility study by FTIR



Fourier-transform infrared (FTIR) spectroscopy was performed to detect any possible interactions between rufinamide and the selected polymers. Evidence of incompatibility would be indicated by shifts, disappearance, or significant changes in the positions of characteristic absorption bands.

Spectra were recorded in the wavelength range of **3500–1000 cm⁻¹**. The FTIR spectra of pure rufinamide showed all the characteristic absorption bands corresponding to its functional groups. Pure drug Rufinamide recorded in the wavelength **3410.69 cm⁻¹.** In the spectra of the physical mixtures of rufinamide with HPMCE 15 LV & drug loaded transdermal patches these characteristic bands were retained without any notable shifts or disappearance. This indicates that **no significant chemical interaction occurred between rufinamide and the polymers**, confirming compatibility of the drug with the chosen excipients.

A



Spectral Analysis of Pure drug Rufinamide, mixture of Rufinamide & polymer and drug loaded patch by FTIR

C

B

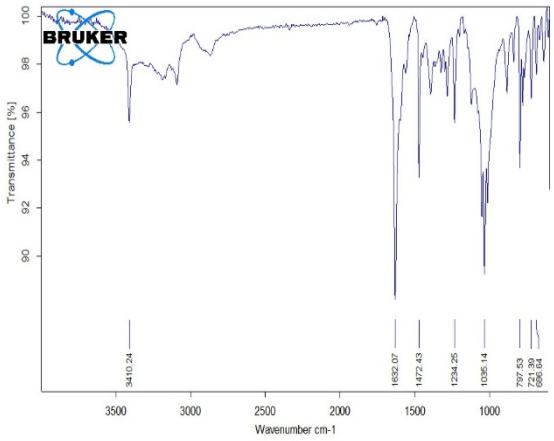
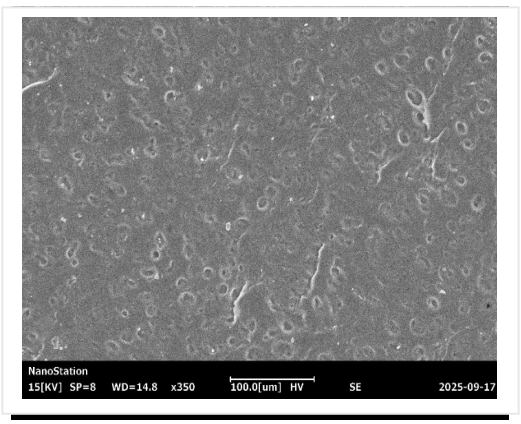


Figure no. 1. A. FT-IR spectra of Pure drug rufinamide. B. FTIR spectrum of rufinamide-polymer physical mixture. C.FTIR spectra of Drug loaded transdermal patches

Fig. no. 2. Representative SEM Images of A blank patch, B is a Drug loaded patch polymer containg HPMC E 15 LV.

A

B



3.5. Thermal Analysis of optimized formulation transdermal patches of Rufinamide-

Thermogram obtained from DSC (Differential scanning colorimetry) analysis of pure drug rufinamide, Drug with HPMC E15 LV & Drug with mixture of polymer and Drug loaded transdermal patches Figure no. 3 Pure drug represents the peak at 239.75°C corresponds to melting endotherm of Rufinamide. Drug and mixture of polymer HPMC E15 LV showed two endothermic peaks, one at 68.40° C corresponding to the melting of HPMC E 15 LV and the other at 239.37°C for Rufinamide. The thermogram for drug loaded transdermal patch contain different excipient showed two peaks at 109.61°C, and 239.75C corresponding to melting transitions of HPMC E 15 LV and Rufinamide respectively.

3.4. Scanning electron microscope (SEM)- High-resolution images of the surface and cross-section of blank and drug loaded patches were captured using SEM (Scanning electron microscope) (fig no. 3). SEM analysis deciph
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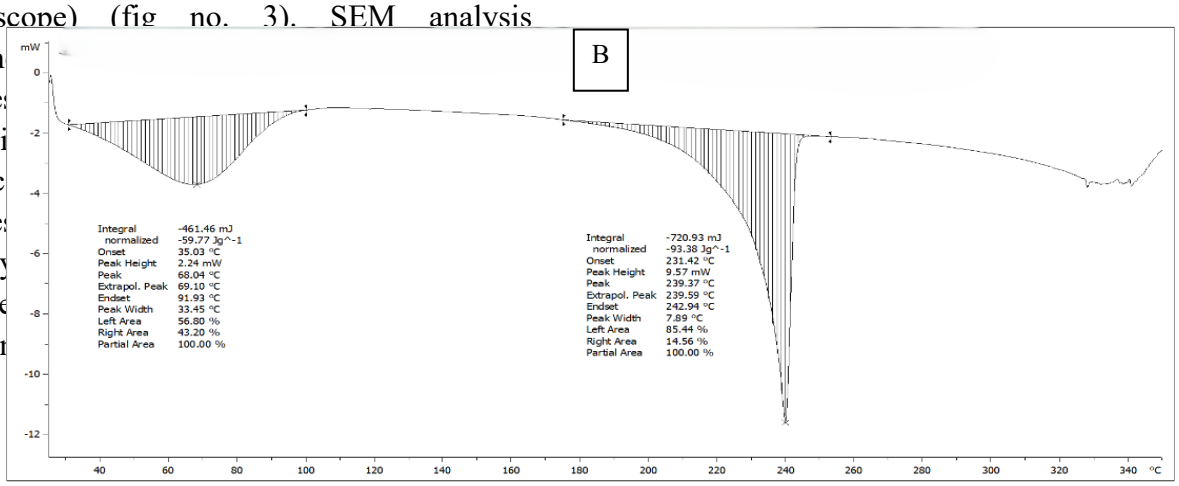
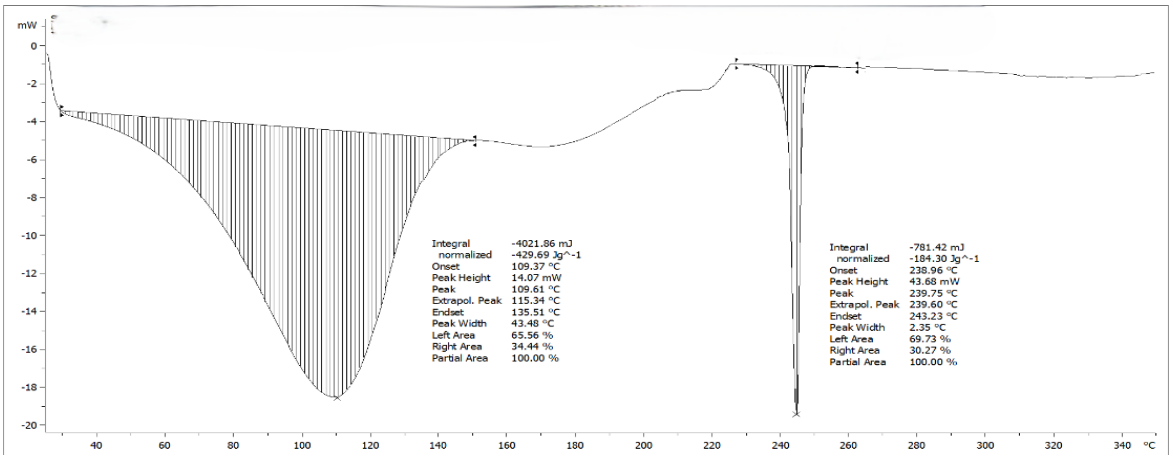
B



C

A



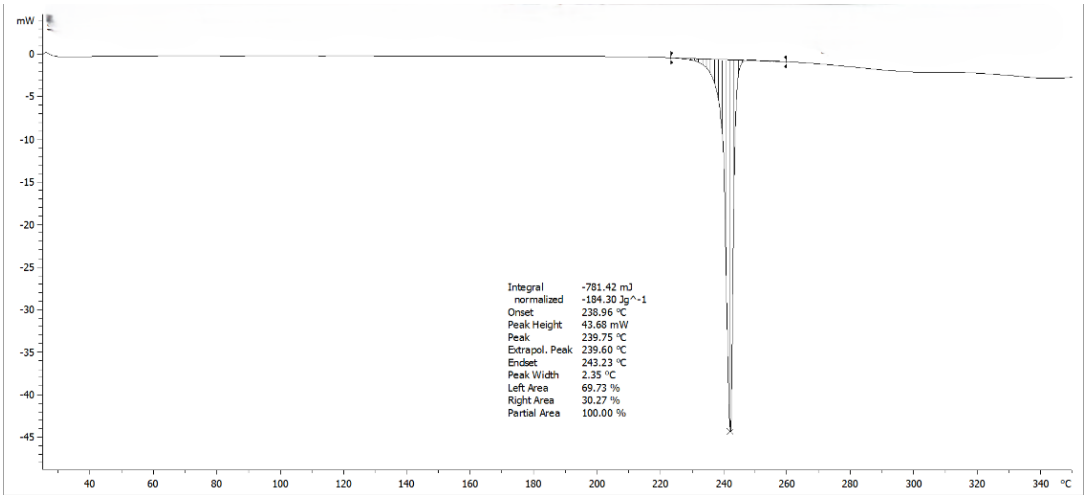
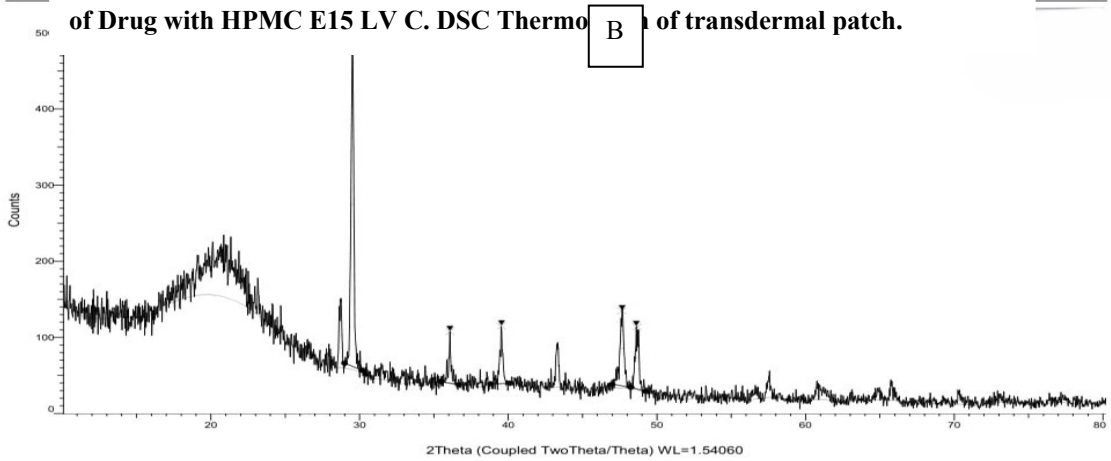


Figure no. 3. A DSC Thermogram of pure drug rufinamide. B. DSC Thermogram of Drug with HPMC E15 LV C. DSC Thermo[illegible] of transdermal patch.

B

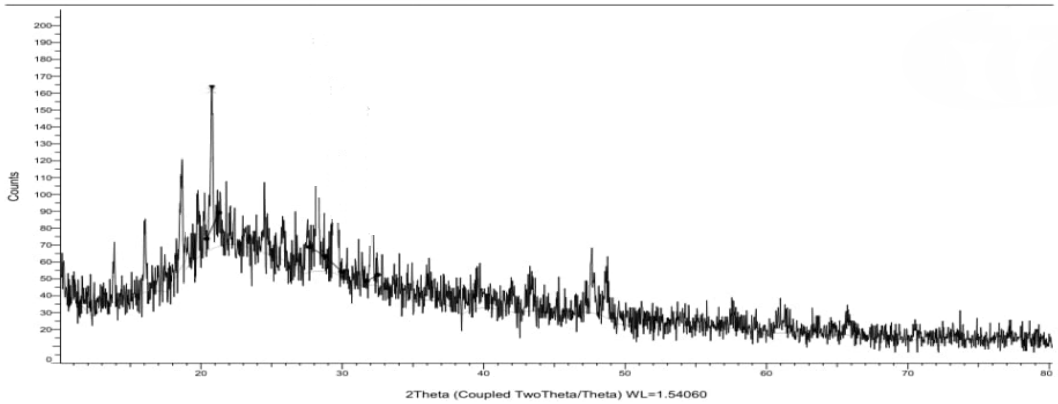


XRD Analysis of Drug, Drug & Polymer, Drug loaded formulation of transdermal patches:

The XRD pattern of Pure Drug, blank and blended patches are depicted in Fig.3 The XRD technique was utilized to investigate the compatibility of the polymer combination with the drug and identify and characterize the crystalline and amorphous forms of the sample . The XRD Pattern of the Pure drug showed a peak around 23°C indicating semi-crystalline characters,

The XRD Pattern of the Pure drug showed a peak around 23°C indicating semi-crystalline characters, The XRD patterns of blank patches developed from HPMC E 15 LV showed a peak around 30°C, whereas the Drug loaded transdermal patches showed a two peak around a 23°C &around 29°C. The appearance of Pure Drug Rufinamide & HPMC E 15 LV peaks in

A



drug loaded transdermal patches might have resulted indicating the compatibility of developed patches.

Disintegration times, though not a standard TDDS parameter, were measured as an additional quality attribute. HPMC E 15 LV patches disintegrated in **30±0.001, 42±0.003, and 57±0.002 min,** for formulation F1, F2 & F3 Respectively swelling indices were **15±0.005%, 19±0.001%, and 27±0.005%** for formulation F1, F2 & F3 Respectively for HPMC E 15 LV formulations, while indicating lower water uptake due to the hydrophilic nature of HPMC E 15 LV.

C

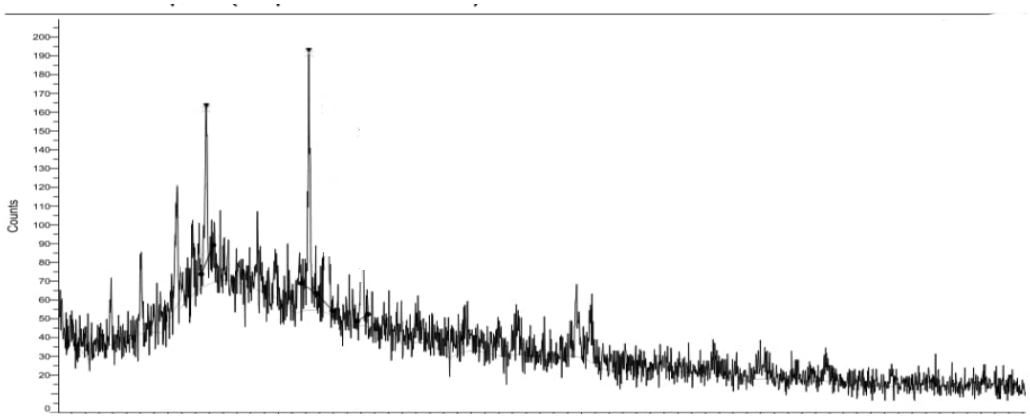


Figure no. 4. A. XRD of Pure Rufinamide, B. XRD of Blank Patch, C. XRD of Drug Loaded transdermal patches.

3.5 Physicochemical evaluation of transdermal patches

The physicochemical characteristics of rufinamide patches are presented in **Table 1**. Formulations containing **HPMC E15 LV** showed mean weight variation of **0.052±0.25, 0.054±0.29, and 0.057±0,15 g** for formulation F1, F2 & F3 Respectively**.** The mean thickness of HPMC-based films was **0.1±0.01, 0.1±0.01, and 0.2±0.02 mm**, for formulation F1, F2 & F3. The uniformity of weight and thickness with low standard deviation values confirms reproducibility of the casting method. Folding endurance values for formulation F1, F2 & F3 patches were **350**±5**, 510**±5**, and 550**±5, HPMC E 15 LV containing patches indicates superior flexibility and resistance to mechanical stress, while all batches showed satisfactory strength without brittleness. Moisture content was consistently **5±0.003, 4±0.001 & 4±0.002 %** for formulation F1, F2 & F3 Respectively. across all formulations, and moisture absorption values were **6±0.001%, 5±0.01% & 6±0.003%** for formulation F1, F2 & F3 Respectively. Low moisture absorption minimizes microbial risk and prevents excess bulk, while limited moisture content helps maintain patch stability and reduces brittleness. The surface pH was **6.4±0.04, 6.4±0.01 & 6.3±0.03** for formulation F1, F2 & F3 Respectively for HPMC E 15 LV films these values lie within the normal skin pH range, suggesting the formulations are unlikely to cause irritation or discomfort.

Table 1. Physicochemical evaluation of rufinamide transdermal patch.

3.6 Estimation of drug content, tensile strength, and elongation

The results for drug content, tensile strength, and percentage elongation are summarized in **Table 2**. The mean drug content of HPMC E15 LV-based patches was **95±0.15%,**

S. NO	Parameters	F1	F2	F3
1	Weight variation	0.052±0.25	0.054±0.29	0.057±0.15
2	Folding endurance	350±5	510±5	550±5
3	Thickness	0.1±0.01	0.1±0.01	0.2±0.02
4	pH	6.4±0.04	6.4±0.01	6.3±0.03
5	% Moisture content	5 ±0.003	4±0.001	4±0.002
6	% Moisture absorbs	6±0.001	5±0.01	6±0.003
7	Disintegration time (min)	30±0.001	42±0.003	57±0.002
8	Swelling index	15±0.005%	19±0.001%	27±0.003%

90±0.28%, and 85±0.25% for formulation F1, F2 & F3 Respectively**,** these findings indicate consistent drug loading with minimal variation across formulations, confirming uniform drug distribution within the polymeric matrices.

Table 2. Estimation of percentage drug content, tensile strength, and elongation of rufinamide patches.

S. No	Parameters	F1	F2	F3
1	% Drug content	95±0.15	90±0.28	85±0.25
2	Tensile strength (kg/cm²)	2.134±0.12	2.532±0.01	3.165±0.05
3	% Elongation at break	10±0.01	20±0.05	30±0.15

3.7 *In-vitro* drug release study

The determination of drug release rates is a vital tool for evaluating transdermal delivery systems. In this study, the *in-vitro* release profile of rufinamide was evaluated using paddle type dissolution apparatus, and the cumulative percentage release was calculated at predetermined intervals.

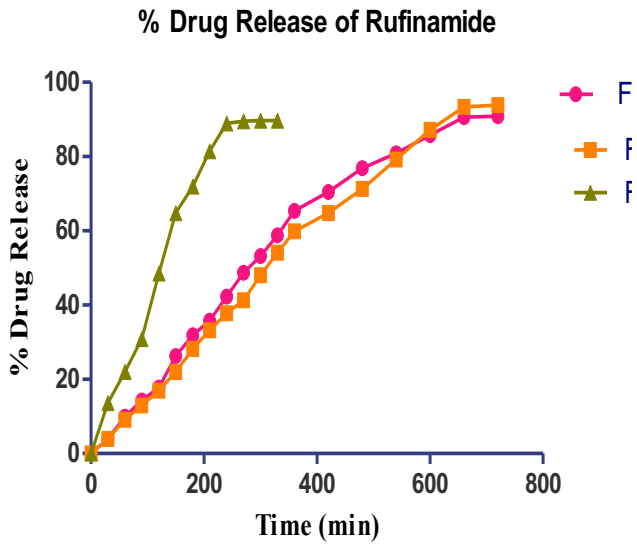
For **HPMC E15 LV-based patches**, the release order was **F2 > F1 > F3**. Formulation F2 released **93.80%** of drug over 12 hours, F1 released **90.59%**, and F3 released **89.66%** within 6 hours. Among these, F2 and F3 demonstrated extended release up to 12 hours, confirming the **sustained-release property** of HPMC matrices.

Overall, the release profiles clearly demonstrate that **polymer concentration and polymer type strongly influenced the release pattern** of rufinamide patches, with HPMC E 15 LV favouring sustained delivery.

Tensile strength values for HPMC-based films were **2.134±0.12, 2.532±0.01, and 3.165±0.05 kg/cm** for formulation F1, F2 & F3 Respectively (as obtained using a modified balance method). These results suggest that HPMC patches had adequate strength, measured values under the applied test conditions.

The percentage elongation of HPMC patches was **10±0.01%, 20±0.05%, and 30±0.15%,** for formulation F1, F2 & F3 Respectively it shows greater flexibility, which is advantageous for conforming to skin movements during application.

Figure no. 5 percentage drug release of Rufinamide from HPMC E 15LV based patches



3.8 *Ex-vivo* permeation of rufinamide from transdermal patches

Ex-vivo permeation studies were performed using Franz diffusion cells with cellulose nitrate used as the diffusion barrier. Flux (J) and permeability coefficient (P) were calculated to characterize drug transport across the membrane.

Flux was determined using the equation:

$$J = \frac{M}{A \times t}$$

where M is the mass of drug permeated, A is the effective diffusion area, and t is the time. The unit of flux is expressed as $\text{mol} \cdot \text{cm}^{-2} \cdot \text{min}^{-1}$.

Permeability coefficient was calculated using:

$$P = \frac{J}{C_{\text{donor}}}$$

where C_{donor} is the concentration of the donor compartment in the Franz diffusion cell. The cumulative amount of drug permeated ($\mu g/cm^2$) was plotted against time to obtain permeation profiles.

For HPMC E15 LV-based patches (F1, F2, F3), the cumulative amount of permeation after 12 hours was $\mathbf{0.579, 0.569}$, and $\mathbf{0.528 \mu\ g/cm^2}$, respectively. These results indicate that HPMC E 15 LV formulations allowed sustained permeation over 10-12 hours.

The overall order of permeability was:

$$F1 > F2 > F3.$$

Formulations F1 and F2 maintained drug release for 12 hours, whereas F3, achieved complete permeation in under 5 hours.

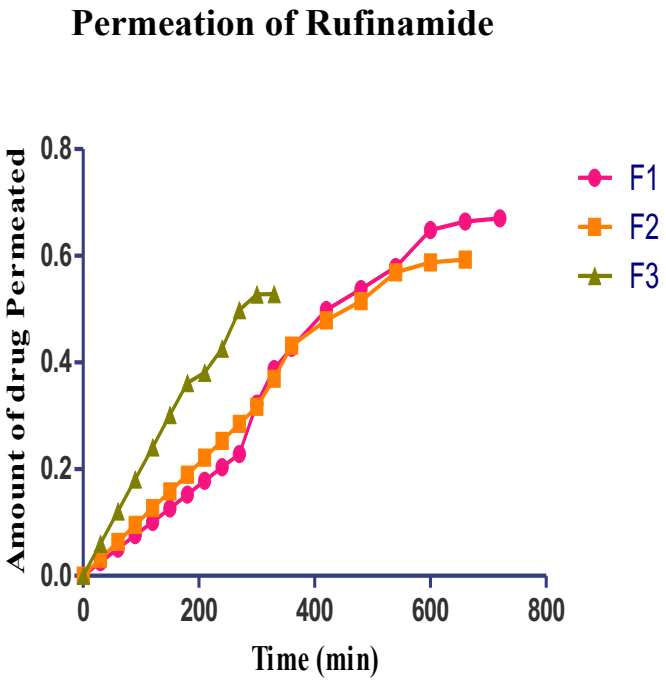


Figure no. 6 *Ex-vivo* permeation profile of rufinamide contain HPMC E15 LV polymer.

3.9 Stability study of transdermal patches

Stability testing of rufinamide-loaded transdermal patches was carried out to assess changes in organoleptic properties, surface pH, and drug content under different relative humidity (RH) conditions (40±5% and 75±5 %).

After **a 1, 2 & 3 months of storage**, patches remained stable, with no visible alterations in appearance, colour, or odour, and surface pH values remained unchanged. Drug content showed slight but acceptable variation across all RH conditions (Table 3).

These findings confirm that the developed formulations exhibited **satisfactory physical and chemical stability** under both intermediate and long-term storage conditions.

measured as an additional property lower for HPMC E15 LV patches, reflecting differences in hydration and matrix

Table 3. Stability study of rufinamide transdermal patches after a 1, 2 & 3 month at room temperature.

S. NO	Parameters	Observation month					
		40±5% RH			75±5 % RH		
		1	2	3	1	2	3
		No change	No change	No change	No change	No change	No change
1	Weight variation	0.052±0.25	0.052±0.25	0.052±0.25	0.052±0.25	0.052±0.25	0.052±0.25
2	% Moisture absorbs	6±0.001	6±0.001	6±0.001	6±0.001	6±0.001	6±0.001
3	Thickness	0.1±0.01	0.1±0.01	0.1±0.01	0.1±0.01	0.1±0.01	0.1±0.01
4	pH	6.4±0.04	6.4±0.01	6.3±0.03	6.4±0.04	6.4±0.01	6.3±0.03
5	% Drug Release	95±0.15	95±0.15	95±0.15	94±0.15	94±0.05	94±0.15

4. Discussion

The preformulation studies confirmed the physicochemical suitability of rufinamide for transdermal delivery. The standard calibration curve constructed in phosphate buffer (pH 7.4) showed excellent linearity (5–25 µg/mL) with r^2 = 0.9863, slope = 0.0007, and intercept = 0.329, validating UV spectrophotometry for routine quantification [59]. Solubility analysis demonstrated lowest solubility in water and greatest solubility in methanol, DMSO, and DMF, findings consistent with the known solubility behavior of rufinamide [60].

Physicomechanical evaluation demonstrated that the patches possessed acceptable uniformity and robustness. Weight variation ranged from 0.052±0.25 g (F2) to 0.057 g (F4), and thickness was 0.1±0.01-0.2±0.02 mm, confirming reproducibility of the casting method [61]. Folding endurance values were highest in formulation F4 (550±5), consistent with reports that synthetic hydrophilic polymers enhance flexibility [62,63]. Surface pH remained within 6.4±**0.04**, 6.4±**0.01** & 6.3±**0.03** indicating suitability for dermal application without irritation [64]. 5% moisture contained obtained in formulation F2, F3 & F4 5±0.003%, 4±0.001 % & 4±0.002 % and % Moisture absorption 6±0.001, 5±0.01 & 6±0.003% obtained in F2 F3& F4 Minimum % moisture contained obtained in F3 were low, contributing to patch stability [65]. Disintegration time was integrity [66].

Drug content analysis (Table 2) revealed uniform distribution across formulations, with values between **95±0.15 – 85±0.25%.** HPMC E 15 LV films showed slightly more consistent loading, while These formulations also remained within acceptable limits. Similar results have been reported for other transdermal polymeric systems [67]. Tensile strength was higher in HPMC E 15 LV films, while elongation at break increased, confirming their greater elasticity and adaptability to skin movements [68].

In-vitro release profiles (Figures no. 5) further highlighted polymer effects. HPMC E 15 LV films followed the order F3 > F2 > F4, with sustained release up to 12 h (93.80% for F3).

Ex-vivo permeation profiles (Figures no. 6) correlated with *in-vitro* release. The order of permeability was F2 > F3 > F4. HPMC E 15 LV-based patches maintained sustained permeation for 10–12 h. [70].

Finally, stability studies (Tables 3) confirmed the robustness of the optimized patches. No changes in appearance, Weight variation, % Moisture absorbs, Thickness, pH were observed under 45±5 % & 75±5 % RH, and only minor variations in drug content occurred during 3 months of storage. These results demonstrate satisfactory physical and chemical stability, supporting the practical applicability of the developed formulations [71].

5. Conclusion

The present study successfully developed and evaluated rufinamide-loaded matrix-type transdermal patches using HPMC E15 LV polymer. Preformulation studies confirmed the physicochemical suitability of rufinamide for transdermal delivery, while UV and FTIR analyses validated drug quantification methods and ensured drug–excipient compatibility. Physicochemical and mechanical evaluations demonstrated that all patches possessed acceptable quality attributes, with HPMC E 15 LV films exhibiting higher flexibility and swelling, and HPMC films also providing greater mechanical strength and stability.

In-vitro and ex-vivo studies highlighted the critical role of polymer composition in drug release and permeation behaviour. HPMC-based formulations offered sustained release for up to 12 hours with controlled permeation, Stability studies confirmed that the optimized formulations maintained their physical integrity, chemical stability, and performance under accelerated and long-term storage conditions.

Overall, the findings demonstrate that rufinamide transdermal patches can provide either sustained or rapid delivery profiles depending on polymer selection, offering flexibility for clinical applications in epilepsy management. The study establishes a strong foundation for further pharmacokinetic and in-vivo investigations, with the potential to enhance therapeutic outcomes, improve patient adherence, and reduce dosing frequency compared to conventional oral administration.

References

1. Ajay Sharma, Seema Saini, A.C. Rana. *Transdermal Drug Delivery System: A Review.* Int J Res Pharm Biomed Sci. ISSN: 2229-3701.
2. Guy R.H. *Current status and future prospects of transdermal drug delivery.* Pharm Res. 1996; 13:1765–1769.
3. Vikas Chander Jhawat, Vipin Saini, Sunil Kamboj, Nancy Maggon. *Transdermal Drug Delivery Systems: Approaches and Advancements in Drug Absorption through Skin.* Int J Pharm Sci Rev Res. 2013;20(1):47–56.
4. Gaur P.K., Mishra S., Purohit S., Dave K. *Transdermal Drug Delivery System: A Review.* Asian J Pharm Clin Res. 2009;2(1):14–20.
5. Darwhekar G., Jain D.K., Patidar V.K. *Formulation and evaluation of transdermal drug delivery system of clopidogrel bisulphate.* Asian J Pharm Life Sci. 2011;1(3):269–278.
6. Panchagnula R. *Transdermal delivery of drugs.* Indian J Pharma col. 1997; 29:140–156.
7. Latheeshjlal L., Phani tejaswini P., Soujanya Y., Swapna U., Sarika V., Moulika G. *Transdermal drug delivery systems: An overview.* Int J PharmTech Res. 2011;3:2140–2148.
8. Lembhe S., Dev A. *Transdermal drug delivery system: An overview.* World J Pharm Pharm Sci. 2016;5:584–610.
9. Kandavilli S., Nair V., Panchagnula R. *Polymers in transdermal drug delivery systems.* Pharm Technol. 2002:62–78.
10. Wokovich A.M., Prodduturi S., Doub W.H., Hussain A.S., Buhse L.F. *Transdermal drug delivery system (TDDS) adhesion as a critical safety, efficacy and quality attribute.* Eur J Pharm Biopharm. 2006;64:1–8.
11. Ahlam Zaid Alkilani, Maelíosa T.C. McCrudden, Ryan F. Donnelly. *Transdermal Drug Delivery: Innovative Pharmaceutical Developments Based on Disruption of the Stratum Corneum.* Pharmaceutics.
12. Priyanka Yadav, Anubhav Dubey. *Formulation and characterization of anti-epileptic drug transdermal patch for enhanced skin permeation.* Eur J Biomed Pharm Sci. 2021;8(9):784–790.
13. Harisudha K., Lavanya G., Eswarudu M.M., Eswaraiah M.C., Spandana B.N., Sunil M. *RP-HPLC method development and validation for estimation of rufinamide.* Int J Res Pharm Chem.
14. Sareesh Kankanala, Santhosh Anasuri, Suhasini Koyyada, Navya Pravala, Sunil Kumar Chaitanya Padavala. *Stability-related impurity studies of rufinamide and zonisamide.* Int J Pharm Pharm Res. 2022;25(4).
15. Deependra Singh, Manoj Kumar Mishra. *Formulation and development of carbamazepine transdermal patches: in vitro and ex vivo.* Ind J Sci Res. 2023;3(1):10–17.
16. Anju Parambil, Seenivasan Palanichamy, Arul Kuttalingam, Vellapandian Chitra. *Preparation and characterization of trifluoperazine-loaded transdermal patches.* Int J Appl Pharm. 2021;13(6):80–87.
17. Long Mo, Guijing Lu, Xiping Ou, Dongsheng Ouyang. *Formulation and development of novel controlled release transdermal patches of carvedilol.* Saudi Pharm J. 2021.

18. Kunal N. Patel et al. *Formulation and characterization of drug-in-adhesive transdermal patches of diclofenac acid.* Int J Pharm Pharm Sci. 2012;4(1).
19. Ifrah Jafri, Muhammad Harris Shoaib, Rabia Ismail Yousuf, Fatima Ramzan Ali. *Effect of permeation enhancers on transdermal delivery of lamotrigine from matrix patches.* Drug Dev Ind Pharm. 2019.
20. Kusum Devi V., Saisivam S., Maria G.R., Depti P.U. *Design and evaluation of matrix diffusion-controlled transdermal patches of verapamil hydrochloride.* Drug Dev Ind Pharm. 2003;29(5):495–503.
21. Rohini Rana, Kamal Saroha, Uditi Handa, Ajay Kumar, Sanju Nanda. *Transdermal patches as a tool for permeation of drug through skin.* J Chem Pharm Res. 2016;8(5):471–481.
22. Sharma N., Parashar B., Sharma S., Mahajan U. *Blooming pharma industry with transdermal drug delivery system.* Indo Glob J Pharm Sci. 2012;2(3):262–278.
23. Mohalkar A.V., Thorat R.R., Muley S.D., Kolhe S.D. *Formulation and evaluation of transdermal patches.* J Res Pharm Sci. 2024;10(4):80–87.
24. Kumar S.R., Jain A., Nayak S. *Development and Evaluation of Transdermal Patches of Colchicine.* Der Pharm Lett. 2012;4(1):330–343.
25. Kusum Devi V., Saisivam S., Maria G.R., Depti P.U. *Design and evaluation of matrix diffusion-controlled transdermal patches of verapamil hydrochloride.* Drug Dev Ind Pharm. 2003;29(5):495–503.
26. Sravanthi K. et al. *Preparation and In-Vitro Evaluation of Transdermal Patch of Aceclofenac.* Am J PharmTech Res. 2020.
27. Patel K.N. et al. *Formulation and characterization of drug-in-adhesive transdermal patches of diclofenac acid.* Int J Pharm Pharm Sci. 2012;4(1).
28. Rohini Rana, Kamal Saroha, Uditi Handa, Ajay Kumar, Sanju Nanda. *Transdermal patches as a tool for permeation of drug through skin.* J Chem Pharm Res. 2016;8(5):471–481.
29. Jalhan S., Kaur K., Kaur P., Jain U.K. *Formulation and in-vitro evaluation of transdermal matrix patches of doxophylline.* Asian J Pharm Clin Res. 2016;9(5):140–145.
30. Gandla Kumaraswamy, Repudi Lalitha, K. Vijayprakash. *Method development and validation for estimation of rufinamide in tablet dosage forms by RP-HPLC.*
31. Mathrusri Annapurna M., Sai Pavan Kumar B., Raj Prakash, Venkatesh B. *Derivative spectrophotometric methods for determination of rufinamide.* Recent Adv Pharm Sci Res. 2012;1(1).
32. Aashli S., Reddy G., Murthy H.C.A., Kumar B.S., Prashanthi K. *Fabricating transdermal films of montelukast sodium with improved stability and extended release.* Int J Appl Pharm.
33. Pokhariyal T., Singh V.K., Tiwari A.K. *Formulation and evaluation of buccal patches of prazosin hydrochloride.* Int J Med Pharm Res. 2013;1(2):206–211.
34. Shaik F., Rao K.V., Sridhar P.G., Rajeswari K., Rafia S., Vardhan R.V. *Formulation and evaluation of pantoprazole mucoadhesive buccal films.* J Global Trends Pharm Sci. 2013;4(1):1044–1052.
35. Sandhya P., Nazera T., Sunitha M., Sirisha M., Sunil R. *Formulation and evaluation of buccal films of ketorolac tromethamine.* JGTPS. 2013;4(3):1184–1192.
36. Zainab E.J., Sulaiman H.T., Jabir S.A.H. *Transdermal drug delivery system.* J Pharm Res. 2018.
37. Vyas S.P., Khar R.K. *Controlled Drug Delivery: Concepts and Advances.* Vallabh Prakashan; 2002.
38. Long Mo, Lu G., Ou X., Ouyang D. *Controlled release carvedilol patches.* Saudi Pharm J. 2021.
39. Anju P., Palanichamy S., Kuttalingam A., Chitra V. *Preparation and characterization of trifluoperazine-loaded transdermal patches for sustained release.* Int J Appl Pharm. 2021;13(6):80–87.
40. Sharma N., Parashar B., Sharma S., Mahajan U. *Blooming pharma industry with transdermal drug delivery system.* Indo Glob J Pharm Sci. 2012;2(3):262–278.
41. Rohini Rana, Kamal Saroha, Uditi Handa, Ajay Kumar, Sanju Nanda. *Transdermal patches as a tool for permeation of drug through skin.* J Chem Pharm Res. 2016;8(5):471–481.
42. Aashli S., Reddy G., Murthy H.C.A., Kumar B.S., Prashanthi K. *Fabricating transdermal film formulations of montelukast sodium.* Int J Appl Pharm.
43. Suhel Khan, Nayyar Parvez, Pramod Kumar Sharma, Md Aftab Alam, Musarrat Husain Warsi. *Novel approaches – Mucoadhesive buccal drug delivery systems.* Int J Res Dev Pharm Life Sci. 2016;5(4):2201–2208.

44. Vyas S.P., Khar R.K. *Controlled Drug Delivery: Concepts and Advances.* Vallabh Prakashan; 2002.
45. Gandla Kumaraswamy, Repudi Lalitha, K. Vijayprakash. *Method development and validation for estimation of rufinamide in tablet dosage forms by RP-HPLC.*
46. Mathrusri Annapurna M., Sai Pavan Kumar B., Raj Prakash, Venkatesh B. *Derivative spectrophotometric methods for determination of rufinamide.* Recent Adv Pharm Sci Res. 2012;1(1).
47. Kurz A., Farlow M., Lefevre G. *Pharmacokinetics of a novel transdermal rivastigmine patch for the treatment of Alzheimer's disease.* Int J Clin Pract. 2009;63(5):799–805.
48. Kumar S.R., Jain A., Nayak S. *Development and Evaluation of Transdermal Patches of Colchicine.* Der Pharm Lett. 2012;4(1):330–343.
49. Kusum Devi V., Saisivam S., Maria G.R., Depti P.U. *Design and evaluation of matrix diffusion-controlled transdermal patches of verapamil hydrochloride.* Drug Dev Ind Pharm. 2003;29(5):495–503.
50. Patel K.N., Patel H.K., Patel V.A., Patel N.A., Patel H.R. *Formulation and characterization of drug-in-adhesive transdermal patches of diclofenac acid.* Int J Pharm Pharm Sci. 2012;4(1):296–302.
51. Rana R., Saroha K., Handa U., Kumar A., Nanda S. *Transdermal patches as a tool for permeation of drug through skin.* J Chem Pharm Res. 2016;8(5):471–481.
52. Mathrusri Annapurna M., Sai Pavan Kumar B., Raj Prakash, Venkatesh B. *New derivative spectrophotometric methods for the determination of rufinamide in pharmaceutical dosage forms.* Recent Adv Pharm Sci Res. 2012;1(1).
53. Sravanthi K. et al. *Preparation and in-vitro evaluation of transdermal patch of aceclofenac.* Am J PharmTech Res. 2020.
54. Anju P., Palanichamy S., Kuttalingam A., Chitra V. *Preparation and characterization of trifluoperazine-loaded transdermal patches for sustained release.* Int J Appl Pharm. 2021;13(6):80–87.
55. Zainab E.J., Sulaiman H.T., Jabir S.A.H. *Transdermal drug delivery system.* J Pharm Res. 2018.
56. Vyas S.P., Khar R.K. *Controlled Drug Delivery: Concepts and Advances.* Vallabh Prakashan; 2002.
57. Sharma N., Parashar B., Sharma S., Mahajan U. *Blooming pharma industry with transdermal drug delivery system.* Indo Glob J Pharm Sci. 2012;2(3):262–278.
58. Rana R., Saroha K., Handa U., Kumar A., Nanda S. *Transdermal patches as a tool for permeation of drug through skin.* J Chem Pharm Res. 2016;8(5):471–481.
59. Harisudha K., Lavanya G., Eswarudu M.M., Eswaraiah M.C., Spandana B.N., Sunil M. *RP-HPLC method development and validation for estimation of rufinamide.* Int J Res Pharm Chem.
60. Kankanala S., Anasuri S., Koyyada S., Pravala N., Padavala S.K.C. *Stability-related impurity studies of rufinamide and zonisamide.* Int J Pharm Pharm Res. 2022;25(4).
61. Mohalkar A.V., Thorat R.R., Muley S.D., Kolhe S.D. *Formulation and evaluation of transdermal patches.* J Res Pharm Sci. 2024;10(4):80–87.
62. Kumar S.R., Jain A., Nayak S. *Development and evaluation of transdermal patches of colchicine.* Der Pharm Lett. 2012;4(1):330–343.
63. Kusum Devi V., Saisivam S., Maria G.R., Depti P.U. *Design and evaluation of matrix diffusion-controlled transdermal patches of verapamil hydrochloride.* Drug Dev Ind Pharm. 2003;29(5):495–503.
64. Lembhe S., Dev A. *Transdermal drug delivery system: An overview.* World J Pharm Pharm Sci. 2016;5:584–610.
65. Patel D., Chaudhary S.A., Parmar B., Bhura N. *Transdermal drug delivery system: A review.* Pharma Innov. 2012;1:78–87.
66. Premjeet S., Bilandi A., Sahil K., Akanksha M. *Transdermal drug delivery system (patches), applications in present scenario.* Int J Res Pharm Chem. 2011;1:1139–1151.
67. Priyanka Y., Dubey A. *Formulation and characterization of anti-epileptic drug transdermal patch for enhanced skin permeation.* Eur J Biomed Pharm Sci. 2021;8(9):784–790.
68. Patel K.N., Patel H.K., Patel V.A., Patel N.A., Patel H.R. *Formulation and characterization of drug-in-adhesive transdermal patches of diclofenac acid.* Int J Pharm Pharm Sci. 2012;4(1):296–302.
69. Mo L., Lu G., Ou X., Ouyang D. *Formulation and development of novel controlled release transdermal patches of carvedilol.* Saudi Pharm J. 2021;29(3):193–201.
70. Rana R., Saroha K., Handa U., Kumar A., Nanda S. *Transdermal patches as a tool for permeation of*

drug through skin. J Chem Pharm Res. 2016;8(5):471–481.

71. Sharma N., Parashar B., Sharma S., Mahajan U. *Blooming pharma industry with transdermal drug delivery system.* Indo Glob J Pharm Sci. 2012;2(3):262–278.