

Formulation and Evaluation of Sustained Release Transdermal Patch of *Tabernaemontana Divaricata* Flower Extract for the Treatment of Migraine

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ABSTRACT

Background: Migraine is a highly prevalent and disabling neurological disorder, and long-term use of oral anti-migraine agents is frequently limited by first-pass metabolism, gastrointestinal intolerance, and erratic bioavailability. Transdermal delivery bypasses these limitations and, combined with a herbal active, may offer a gentler, sustained-release alternative for migraine care.

Objective: This study aimed to develop and evaluate a sustained-release transdermal patch containing ethanolic extract of *Tabernaemontana divaricata* flowers using the solvent-casting technique.

Methods: Fresh flowers of *Tabernaemontana divaricata* were authenticated, shade-dried, and extracted by Soxhlet extraction. The extract was screened for phytochemical constituents and characterized by thin-layer chromatography (TLC), UV-visible spectroscopy, and Fourier-transform infrared (FTIR) spectroscopy. Three patch formulations (TDF1–TDF3) were prepared with increasing concentrations of hydroxypropyl methylcellulose (HPMC) as the film-forming polymer and polyethylene glycol (PEG) as plasticizer, and were evaluated for physicochemical and mechanical parameters and for *In-vitro* drug release using a Franz diffusion cell.

Discussion: TDF1 exhibited favorable physicochemical and mechanical properties with controlled 12-hour drug release, supporting the feasibility of *T. divaricata* flower extract as a sustained-release transdermal system for further investigation in migraine management.

Results: The extract yield was 8% w/w, and preliminary screening confirmed the presence of alkaloids, flavonoids, and terpenoids. All three patches were smooth, flexible, and free of visible defects. Surface pH (7.0–7.4) remained within the physiological skin range, folding endurance exceeded 297 folds, and tensile strength ranged from 2.21–2.25 kg/cm². TDF1, containing the lowest HPMC concentration, showed the lowest moisture content (7.53 ± 0.15%), moisture uptake (8.29 ± 0.04%), and swelling index (12.03 ± 0.20%), together with a controlled 12-hour cumulative drug release of 96.15%.

Conclusion: An HPMC-based sustained-release transdermal patch of *Tabernaemontana divaricata* flower extract was successfully formulated, with TDF1 emerging as the optimized formulation. The findings support further pharmacological and clinical evaluation of this herbal transdermal system as a patient-friendly option for migraine treatment.

Keywords: *Tabernaemontana divaricata*; transdermal patch; migraine; sustained release; solvent casting; herbal drug delivery.

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1. Introduction

Migraine is a chronic, cyclical neurological disorder characterised by recurrent attacks of moderate-to-severe headache accompanied by nausea, photophobia, and phonophobia, and it progresses through

premonitory, aura, headache, and postdrome phases [1]. It is one of the leading causes of disability worldwide: the Global Burden of Disease 2019 analysis ranked migraine second among all causes of years lived with disability, and first among young women [2], and its

prevalence has continued to rise over the past three decades [3]. Beyond the headache itself, migraine imposes a substantial economic and psychosocial burden on patients, their families, and health systems, affecting work productivity, family life, and quality of life [4]. Current pathophysiological models implicate trigeminovascular activation, cortical spreading depression, and neuropeptides such as calcitonin gene-related peptide (CGRP) in the generation of migraine pain [5].

Pharmacological treatment of migraine relies on acute (abortive) and prophylactic therapy, most commonly delivered as oral triptans, non-steroidal anti-inflammatory drugs, and preventive agents [6]. Oral therapy, however, is compromised by hepatic first-pass metabolism, delayed and variable absorption during migraine-associated gastric stasis, and gastrointestinal adverse effects, all of which can blunt clinical response and reduce adherence [7,8]. Transdermal drug delivery offers a rational alternative: by delivering the active agent directly across the skin into systemic circulation, it avoids first-pass hepatic metabolism, minimises gastrointestinal exposure, permits sustained and controlled plasma levels from a single application, and improves compliance in patients who find oral dosing during an attack difficult [9]. The success of the sumatriptan iontophoretic transdermal system in clinical use illustrates the feasibility of this route specifically for migraine therapy [10].

In parallel, there is growing scientific and regulatory interest in plant-derived therapeutics as safer, better-tolerated alternatives or adjuncts to synthetic drugs, reflecting both a long history of traditional use and their continuing contribution as leads for modern drug discovery [10]. *Tabernaemontana divaricata* (L.) R.Br. ex Roem. & Schult. (Apocynaceae), commonly known as crape jasmine, is a widely distributed ornamental and medicinal shrub whose various parts have been investigated for antioxidant, anti-inflammatory, antinociceptive, antimicrobial, and antihypercholesterolemic activity [11]. of particular relevance to the present work, the flower extract of *Tabernaemontana divaricata* has been reported to contain indole alkaloids with demonstrable antinociceptive activity in experimental models [12]. Providing a pharmacological rationale for exploring this botanical drug as a candidate for pain-related indications such as migraine. Despite this promising phytochemical and pharmacological profile, no published study, to the best of our knowledge, has formulated *Tabernaemontana divaricata* flower extract into a transdermal delivery system [13].

Among the available polymer systems for transdermal film formation, hydroxypropyl methylcellulose (HPMC) is a hydrophilic, biocompatible, and widely used film-forming polymer that, together with polyethylene glycol (PEG) as a plasticiser, is well suited to the solvent-casting method for laboratory-scale patch fabrication [14]. Solvent-cast HPMC matrices have been used successfully to formulate

sustained-release transdermal systems for a range of synthetic and herbal actives [15,16]. Building on this rationale, the present study was undertaken to authenticate and extract *Tabernaemontana divaricata* flowers, characterise the resulting extract phytochemically and spectroscopically, and formulate and evaluate HPMC-based sustained-release transdermal patches (TDF1–TDF3) with respect to their physicochemical, mechanical, and in-vitro drug release behaviour, with the broader aim of laying the groundwork for a herbal transdermal option for migraine treatment [17].

2. Materials and Methods

2.1 Plant material, chemicals, and instruments

Fresh, healthy flowers of *Tabernaemontana divaricata* were collected from Stadium Road, Residency Garden, Bareilly, Uttar Pradesh, India, in August 2025, and were authenticated (RUPS/DT/204) by a botanist at M.J.P. Rohilkhand University, Bareilly, Uttar Pradesh. The collected flowers were cleaned to remove soil and dust, shade-dried at room temperature, and reduced to a fine powder using a mechanical grinder. Analytical-grade chemicals and reagents (toluene, ethyl acetate, formic acid, hydrochloric acid, potassium bismuth iodide, potassium mercuric iodide, sodium hydroxide, sulphuric acid, lead acetate, chloroform, methanol, ethanol, acetone, hydroxypropyl methylcellulose, and polyethylene glycol) were procured from standard commercial suppliers (Avantor Performance Materials India Pvt. Ltd.; Central Drug House (P) Ltd.; Sisco Research Laboratories). Instrumentation included a magnetic stirrer with hot plate, hot-air oven, muffle furnace, digital analytical balance, Franz diffusion cell, UV–visible spectrophotometer, and a Fourier-transform infrared spectrophotometer [18].

2.2 Physicochemical evaluation and extraction

Total ash and acid-insoluble ash values were determined by incinerating a known quantity of powdered flower material in a silica crucible in a muffle furnace, and treating the resulting ash with 2N hydrochloric acid, in accordance with standard pharmacognostic procedure [17]. Solubility was assessed qualitatively in water, hot water, ethanol, hot ethanol, methanol, and acetone [19]. The powdered flowers were extracted by Soxhlet extraction: the material was first defatted with petroleum ether (40–50 °C, 8 h) and then successively extracted with ethanol (40–50 °C, 8 h). The ethanolic extract was filtered and concentrated on a water bath (60–80 °C) to yield a solvent-free crude hydroalcoholic extract, and the percentage yield was calculated relative to the starting powder weight [20].

2.3 Phytochemical screening and TLC profiling

The extract was subjected to standard qualitative tests for alkaloids (Mayer's, Dragendorff's, Hager's, and Wagner's tests), flavonoids (Shinoda test, alkaline reagent test, sulphuric acid test, lead acetate test), and

terpenoids (Salkowski test, Noller's test), following established phytochemical screening protocols (Harborne, 1998). Thin-layer chromatography was performed on pre-coated silica gel plates using toluene:ethyl acetate:formic acid (10:8:2) as the mobile phase, and retardation factor (Rf) values were calculated for the resolved spots [21].

2.4 Spectroscopic characterisation

For UV–visible spectroscopy, standard stock solutions of the extract were serially diluted, scanned across the UV–visible range to determine λ_{max} , and the resulting absorbance values were used to construct a calibration curve of absorbance against concentration. FTIR spectral analysis (IR Spirit X, Shimadzu) was performed to identify the principal functional groups present in the extract, in accordance with standard vibrational spectroscopic interpretation [22].

2.5 Formulation of transdermal patches by solvent casting

Transdermal patches were prepared by the solvent-casting technique. HPMC was dispersed gradually in distilled water under continuous magnetic stirring for 30 min. Separately, the *Tabernaemontana divaricata* extract was dissolved in ethanol, and this drug solution was incorporated into the polymer dispersion with continued stirring for 30 min. Polyethylene glycol was added as a plasticiser, and the mixture was stirred to homogeneity and then sonicated for 1–2 h to eliminate entrapped air. The casting solution was poured into a glycerin-coated Teflon mould and dried in a hot-air oven at 35–40 °C until film formation was complete. The dried film was cut into 2 cm × 2 cm patches and stored in a desiccator prior to evaluation. Three formulations (TDF1, TDF2, TDF3) were prepared with a fixed extract concentration (0.50 g) and increasing HPMC and PEG concentrations (Table 1). Two preliminary trial formulations using chitosan as the film-forming polymer were also attempted but were discontinued because the resulting films adhered to the mould and developed cracks on drying; these are not reported further [23].

Table 1: Composition of *Tabernaemontana divaricata* Transdermal Patch Formulations (TDF1–TDF3)

Ingredient	TDF1	TDF2	TDF3
<i>Tabernaemontana divaricata</i> extract	0.50 g	0.50 g	0.50 g
Hydroxypropyl methylcellulose (HPMC)	2 g	3 g	4 g
Polyethylene glycol (PEG)	0.3 mL	0.4 mL	0.5 mL
Distilled water	q.s.	q.s.	q.s.

2.6 Evaluation of transdermal patches

Prepared patches were evaluated for the following parameters, each performed in triplicate (n = 3) unless stated otherwise, with results expressed as mean ± SD:

2.6.1 Determination of Surface pH

The prepared transdermal patch was placed in distilled water and allowed to remain for 15 minutes at room temperature. A pH paper was gently brought into contact with the surface of the patch. The pH paper was kept in contact with the patch for approximately 1 minute. The colour change observed on the pH paper was carefully noted. The corresponding pH value was determined by comparing the colour with the standard pH scale and recorded as the surface pH of the patch [24].

2.6.2 Percentage Moisture Content

After each manufactured film was weighed, it was stored for 24 hours at room temperature in a desiccator filled with fused calcium chloride. The films were reweighed after a 24-hour period, and the percentage moisture content was calculated using the procedure below [25].

Formula:

$$\% \text{ Moisture content} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

2.6.3 Moisture Uptake

The moisture uptake study was performed to evaluate the hygroscopic nature and stability of the prepared films under controlled humidity conditions. Initially, the films were accurately weighed and kept in a desiccator at room temperature for 24 hours to remove any residual moisture. The dried films were then exposed to an environment of 84% relative humidity maintained using a saturated potassium chloride (KCl) solution. After a specified period of exposure, the films were reweighed to determine the amount of moisture absorbed

Formula:

$$\text{Percentage moisture uptake (\%)} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

2.6.4 Weight Uniformity and Percentage Deviation

The weight uniformity of the prepared transdermal patches was evaluated by randomly selecting five patches from each formulation batch. Each patch was individually weighed using an analytical balance, and the average weight was calculated. The patches were then dried in a hot air oven at 45°C for 4 hours to remove residual moisture and allowed to cool at room temperature. After drying, the patches were reweighed, and weight uniformity was determined by comparing the individual patch weights with the mean weight of the respective formulation. The percentage deviation of

each patch from the average weight was calculated to assess the consistency and uniform distribution of formulation components within the prepared transdermal patches [26].

Formula:

$$\text{Average weight} = \frac{\text{Sum of individual patch weight}}{\text{Number of patch}}$$

Formula:

$$\% \text{ Deviation} = \frac{\text{Individual weight} - \text{Average weight}}{\text{Average weight}} \times 100$$

2.6.5 Swelling Index

The swelling characteristics of the prepared transdermal patches were evaluated in phosphate buffer (pH 7.4). Each patch was weighed accurately to obtain its initial weight and then immersed in the buffer solution. After 1 hour of incubation, the patch was carefully removed and the excess surface liquid was gently wiped off using tissue paper. The swollen patch was immediately weighed to determine its final weight. The percentage swelling index was calculated to assess the water absorption capacity of the patch matrix [27].

Formula:

$$\text{Swelling index (\%)} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Final weight}} \times 100$$

2.6.6 Thickness

The thickness of the patch was determined by taking measurements at three different locations using a digital vernier calliper gauge, and then calculating the average value [28].

2.6.7 Tensile strength

A transdermal film of uniform dimensions was cut and its thickness was measured at different points using a micrometer screw gauge, and the average thickness was recorded. The film was then fixed vertically between two clips, with one clip attached to a stationary support and the other connected to a lightweight container using a thread. Care was taken to ensure that the film was held firmly without any folds or wrinkles. Water was gradually added to the suspended container at a constant rate, thereby increasing the load applied to the film. The addition of water was continued until the film ruptured. The total volume of water required to break the film was recorded and converted into weight. The tensile strength of the film was then calculated using the breaking force and the cross-sectional area of the film. The experiment was performed in triplicate, and the average tensile strength value was reported [29].

Formula:

$$\text{Tensile strength} = \frac{\text{Force to break the patch}}{\text{Width of the patch strip} \times \text{Thickness of the patch}}$$

2.6.8 Folding Endurance

Five patches were randomly selected from each formulation batch and weighed individually using an analytical balance. The average weight of the patches was calculated. To remove any residual moisture, the patches were dried in a hot air oven at 45°C for 4 hours and allowed to cool to room temperature. The dried patches were then reweighed, and weight uniformity was determined by comparing the weight of individual patches with the mean weight of the sample set [30].

2.7 In-vitro drug release studies

Drug release from the optimised patches was assessed using a Franz diffusion cell fitted with a hydrated synthetic membrane, with phosphate buffer (pH 7.4, 15 mL) as the receptor medium maintained at $37 \pm 0.5^\circ\text{C}$ under continuous magnetic stirring. A $2\text{ cm} \times 2\text{ cm}$ patch (4 cm^2 surface area) was mounted in the donor compartment with the drug-loaded surface facing the membrane. Aliquots (1 mL) were withdrawn from the receptor compartment at predetermined time points over 12 h and immediately replaced with an equal volume of fresh buffer. Withdrawn samples were analysed spectrophotometrically at 285 nm (λ_{max}), and cumulative percentage drug release was calculated from the previously constructed calibration curve, with correction for sample replacement. Release data were further examined against zero-order, first-order, Higuchi, and Korsmeyer–Peppas models to characterise the release kinetics and mechanism [31].

3. Results

3.1 Pharmacognostic and physicochemical characterisation

The powdered flowers of *Tabernaemontana divaricata* were yellowish-brown, with a characteristic odour, bitter taste, and fine texture (Table 2). The total ash value was 6%, the acid-soluble ash was 6%, and the acid-insoluble ash was 0%, indicating good purity and negligible siliceous contamination of the crude drug. Solubility testing showed the powdered extract to be soluble in ethanol, hot ethanol, and hot water, sparingly soluble in methanol, and insoluble in water and acetone. Soxhlet extraction of 50 g of powdered flowers yielded 4 g of dried ethanolic extract, corresponding to a percentage yield of 8%. The concentrated extract itself was a dark brown, sticky, semi-solid mass with a characteristic aromatic odour and bitter taste. Microscopic examination of the powdered material revealed calcium oxalate crystals, stomata, and xylem elements, consistent with diagnostic features previously reported for this species.



Figure 1. Fresh flowers of *Tabernaemontana divaricata* collected for extraction.

Table 2 Pharmacognostic and Physicochemical Characteristics of *Tabernaemontana divaricata* Flower Powder

Parameter	Observation
Colour (powder)	Yellowish brown
Odour	Characteristic
Taste	Bitter
Appearance	Fine powder
Total ash value	6%
Acid-soluble ash	6%
Acid-insoluble ash	0%
Extraction yield	8% w/w
Extract appearance	Dark brown, sticky semi-solid mass
Solubility	Soluble in ethanol, hot ethanol, hot water; sparingly soluble in methanol; insoluble in water, acetone

3.2 Phytochemical screening

Preliminary phytochemical screening indicated a strong presence of alkaloids (Mayer's, Hager's, and Wagner's tests) and flavonoids (Shinoda, alkaline, sulphuric acid, and lead acetate tests), a moderate presence of alkaloids by Dragendorff's test and

terpenoids by Salkowski's test, and a negative result for terpenoids by Noller's test (Table 3). These findings are broadly consistent with earlier phytochemical reports on *Tabernaemontana divaricata*, which describe indole alkaloids and flavonoid constituents as major phytoconstituents of this species.

Table 3 Preliminary Phytochemical Screening of *T. divaricata* Flower Extract

Phytoconstituent	Test	Observation	Result
Alkaloids	Mayer's test	Pale yellow precipitate	+++
Alkaloids	Dragendorff's test	Light yellow precipitate	++
Alkaloids	Hager's test	Yellow crystalline precipitate	+++
Alkaloids	Wagner's test	Brown precipitate	+++
Flavonoids	Shinoda test	Crimson red colour	+++
Flavonoids	Alkaline test	Yellow colour	+++
Flavonoids	Sulphuric acid test	Yellow colour	+++
Flavonoids	Lead acetate test	Yellow precipitate	+++
Terpenoids	Salkowski test	Reddish-brown colour	++
Terpenoids	Noller's test	Light purple colour	–

Note. +++ = strongly present; ++ = moderately present; + = weakly present; – = absent.

3.3 Thin-layer chromatography *Tabernaemontana divaricata* flowers Extract

TLC analysis of the extract using toluene:ethyl acetate:formic acid (10:8:2) as the mobile phase

resolved distinct, well-defined spots across six replicate plates, with R_f values ranging narrowly from 0.66 to 0.76, indicating a stable and reproducible chromatographic profile over the study period.

Table 4 R_f Values of the *Tabernaemontana divaricata* flowers Extract

S NO	TLC Sample Code	R_f Values
1	A1	0.66
2	A2	0.68
3	A3	0.69
4	A4	0.70
5	A5	0.73
6	A6	0.76

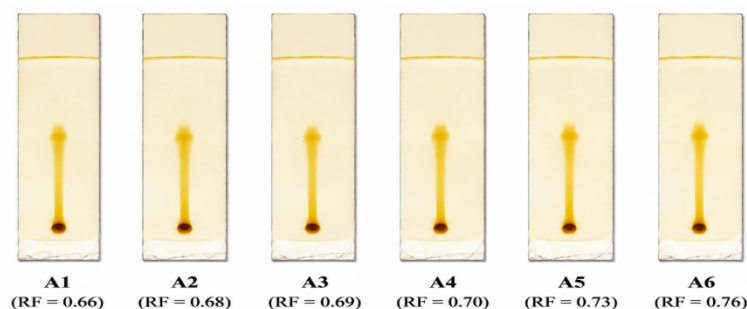


Figure 2. Thin Layer Chromatography Profile of *Tabernaemontana divaricata* Flowers Extract

3.4 UV–visible spectroscopic

UV–visible spectroscopic analysis produced a linear calibration curve of absorbance against concentration over the 2–12 $\mu\text{g/mL}$ range (mean absorbance

increasing from 0.156 to 1.093), confirming the suitability of the method for quantitative estimation of the extract during release studies.

Table 5 Standard Calibration Curve Data of *Tabernaemontana divaricata*

Concentration ($\mu\text{g/mL}$)	Absorbance 1	Absorbance 2	Absorbance 3	Mean Absorbance
0	0	0	0	0
2	0.154	0.157	0.157	0.156
4	0.350	0.353	0.353	0.352
6	0.452	0.454	0.456	0.454
8	0.658	0.660	0.662	0.660
10	0.842	0.844	0.846	0.844
12	1.091	1.093	1.095	1.093

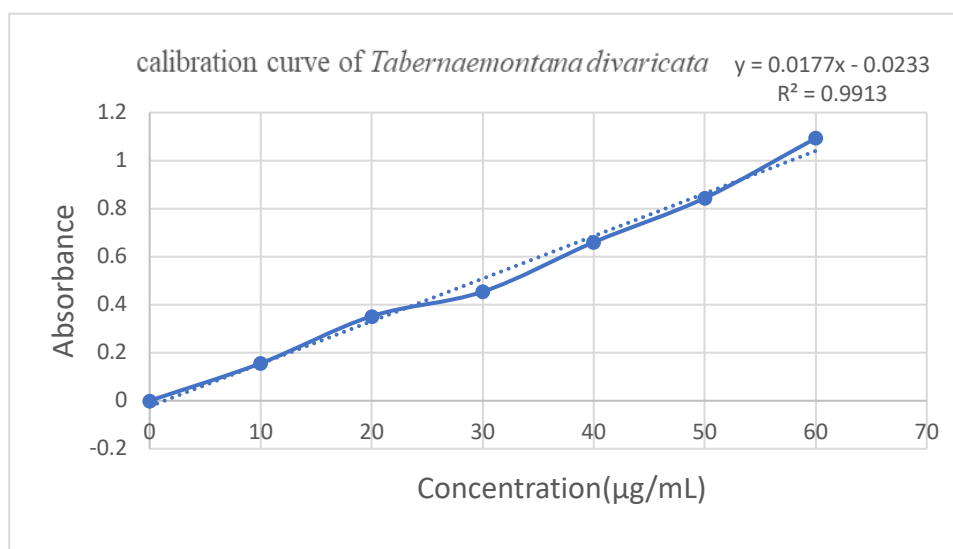


Figure 3 Calibration curve of *Tabernaemontana divaricata*

3.5 Fourier Transform Infrared (FTIR) of *Tabernaemontana divaricata* Flowers Powder Extract

FTIR was used to identify the main functional groups in B1 and HPMC and to check whether the two interact. *Tabernaemontana divaricata* B1 (Figure 4a) showed bands at 2920.32, 2849.93, 1665.57, 1659.11, 1529.83, 1452.98, 1381.15, 1244.69, 1075.91, 927.23, 815.19, and 717.51 cm^{-1} . HPMC (Figure 4b) had bands at 2931.09, 1644.74, 1459.44, 1378.28, and 945.91 cm^{-1} , with additional peaks at lower wavenumbers. In the

HPMC + *Tabernaemontana divaricata* (B1) physical mixture (Figure 4c), the main bands from both components were still present. The peaks shifted slightly and some intensities changed, but no major bands disappeared and no new strong bands appeared. Bands near 2921.32 and 2848.83 cm^{-1} , along with those in the 1668–1648, 1455, 1383, 1246, and 1079 cm^{-1} regions, were visible in the mixture. These small shifts are likely due to intermolecular interactions, such as hydrogen bonding, between *Tabernaemontana divaricata* (B1) and HPMC. Overall, the spectra show

no obvious chemical incompatibility between supports their use together in formulation development. *Tabernaemontana divaricata* (B1) and HPMC, which

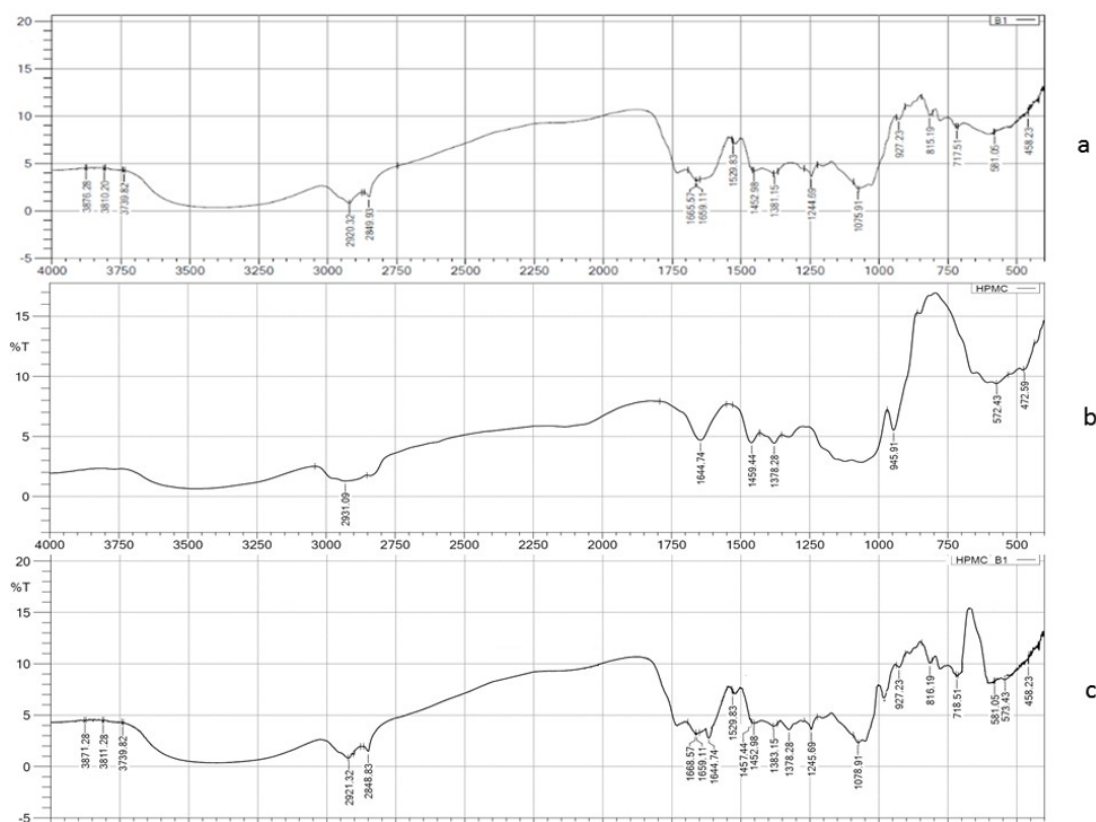


Figure 4. FTIR spectrum of a) the ethanolic extract of *Tabernaemontana divaricata* flowers, b) FTIR of the HPMC & c) FTIR of Physical Mixture.

3.4 Preparation of Transdermal patch of *Tabernaemontana divaricata* by solvent casting method:

The transdermal patch formulations (TDF1, TDF2, and TDF3) were successfully prepared by the solvent casting method using different concentrations of *Tabernaemontana divaricata* extract, HPMC, and PEG. TDF1, TDF2, and TDF3 individually produced smooth, flexible, uniform, and crack-free films without visible

air bubbles as shown in figure 5. The films were further evaluated for surface pH, thickness, weight uniformity, percentage deviation, folding endurance, moisture content, moisture uptake, swelling index, tensile strength, and in vitro drug release using a Franz diffusion cell. The composition of each individual formulation is presented in Table 6.



Figure 5. Transdermal patch of *Tabernaemontana divaricata*

3.5 Evaluation parameters of Transdermal Patch

3.5.1 Determination of surface pH:

The surface pH of TDF1, TDF2, and TDF3 was found to be 7.0 ± 0.1 , 7.2 ± 0.35 , and 7.4 ± 0.68 , respectively.

The values were within a suitable range for skin application, indicating acceptable surface compatibility of the developed patches.

Table 6 Determination of surface pH

S NO	Formulation code	pH
1.	TDF1	7.0 ± 0.1
2.	TDF2	7.2 ± 0.35
3.	TDF3	7.4 ± 0.68

Values are expressed as Mean ± SD (n = 3)

3.5.2 Percentage Moisture Content:

The moisture content of TDF1, TDF2, and TDF3 was 7.53 ± 0.15%, 28.51 ± 0.06%, and 12.48 ± 0.03%, respectively. TDF1 showed the lowest moisture

content, whereas TDF2 exhibited the highest value, indicating differences in moisture retention among the formulations.

Table 7 Percentage Moisture Content

S. No.	Formulation code	Initial Weight (gm)	Final Weight (gm)	Moisture Content (%)
1	TDF1	0.13	0.12	7.53 ± 0.15
2	TDF2	0.14	0.10	28.51 ± 0.06
3	TDF3	0.08	0.07	12.48 ± 0.03

Values are expressed as Mean ± SD (n = 3)

3.5.3 Moisture Uptake:

The moisture uptake values for TDF1, TDF2, and TDF3 were 8.29 ± 0.04%, 20.02 ± 0.03%, and 25.02 ± 0.03%, respectively. TDF1 demonstrated the lowest

moisture uptake, while TDF3 showed the highest value, suggesting greater moisture absorption with increasing polymer concentration.

Table 8 Moisture Uptake

S NO	Formulation code	Initial Weight (gm)	Final Weight (gm)	Moisture Uptake (%)
1.	TDF1	0.12	0.13	8.29 ± 0.04
2.	TDF2	0.10	0.12	20.02 ± 0.03
3.	TDF3	0.08	0.10	25.02 ± 0.03

Values are expressed as Mean ± SD (n = 3)

3.5.4 Weight Uniformity and Percentage Deviation:

The mean weights of TDF1, TDF2, and TDF3 were 0.108 ± 0.025 g, 0.094 ± 0.024 g, and 0.098 ± 0.035 g, respectively. The corresponding percentage deviations

were 20.00 ± 8.63%, 20.42 ± 11.62%, and 26.94 ± 19.06%. The results indicated reasonably consistent weight distribution among the prepared patches.

Table 9 Weight Uniformity and Percentage Deviation

S NO	Formulation code	Weight Uniformity (gm)	Percentage Deviation (%)
1.	TDF1	0.108 ± 0.025	20.00 ± 8.63
2.	TDF2	0.094 ± 0.024	20.42 ± 11.62
3.	TDF3	0.098 ± 0.035	26.94 ± 19.06

Values are expressed as Mean ± SD (n = 3)

3.5.5 Swelling Index:

The swelling indices of TDF1, TDF2, and TDF3 were 12.03 ± 0.20%, 16.66 ± 0.15%, and 17.00 ± 0.15%,

respectively. The progressive increase in swelling was associated with the increasing concentration of the hydrophilic polymer in the formulations.

Table 10 Swelling Index

S NO	Formulation code	Swelling index (%)
1.	TDF1	12.03 ± 0.20
2.	TDF2	16.66 ± 0.15
3.	TDF3	17.00 ± 0.15

Values are expressed as Mean ± SD (n = 3)

3.5.6 Thickness:

The thickness of TDF1, TDF2, and TDF3 was 0.053 ± 0.02 mm, 0.073 ± 0.02 mm, and 0.093 ± 0.02 mm, respectively. The increase in thickness corresponded

with the higher HPMC concentration used in the formulations, while the films maintained acceptable thickness uniformity.

Table 11 Thickness

S NO	Formulation code	Thickness (mm)
1.	TDF1	0.053 ± 0.02
2.	TDF2	0.073 ± 0.02
3.	TDF3	0.093 ± 0.02

Values are expressed as Mean $\pm$ SD (n = 30)

3.5.7 Tensile Strength:

TDF1, TDF2, and TDF3 exhibited tensile strength values of 2.25 ± 0.16 , 2.21 ± 0.16 , and 2.24 ± 0.12

kg/cm², respectively. These results indicated adequate mechanical strength of the prepared transdermal films.



Fig 6. Tensile strength

Table 12 Tensile strength

S NO	Formulation code	Tensile strength (kg/cm ²)
1.	TDF1	2.25 ± 0.16
2.	TDF2	2.21 ± 0.16
3.	TDF3	2.24 ± 0.12

Values are expressed as Mean $\pm$ SD (n = 3)

3.5.8 Folding Endurance:

The folding endurance of TDF1, TDF2, and TDF3 was 301 ± 3.6 , 315 ± 2.5 , and 297.3 ± 2.5 folds, respectively.

The high folding endurance values demonstrated good flexibility and resistance of the films to repeated folding.



Fig 7 Folding endurance

Table 13 Folding Endurance

S NO	Formulation code	Folding Endurance (folds)
1.	TDF1	324 ± 3.6
2.	TDF2	315 ± 2.5
3.	TDF3	297.3 ± 2.5

Values are expressed as Mean $\pm$ SD (n = 3)

3.5.9 In-vitro drug release

Cumulative percentage drug release over 12 h is presented in Table 14 and Figure 4. All three formulations exhibited a controlled, sustained release pattern without an appreciable initial burst. At the end of 12 h, cumulative release reached 96.15% for TDF1, 95.13% for TDF2, and 92.47% for TDF3. Although

TDF2 showed a marginally higher release at several intermediate time points, TDF1—formulated with the lowest HPMC concentration—combined a comparable overall release extent with the lowest moisture content, moisture uptake, and swelling index among the three formulations, indicating a more favourable balance of release performance and physical stability.

Table 14 Cumulative Percentage *In-Vitro* Drug Release from TDF1–TDF3 over 12 Hours

Time (h)	TDF1 (%)	TDF2 (%)	TDF3 (%)
0	0	0	0
1	23.20	14.77	14.76
2	25.86	25.53	20.18
3	34.70	36.27	27.09
4	41.83	49.48	38.18
5	47.43	55.46	43.73
6	54.43	60.96	50.51
7	60.62	66.62	57.41
8	67.97	71.51	64.93
9	76.53	81.92	74.44
10	83.91	86.69	81.82
11	91.03	96.82	88.16
12	96.15	95.13	92.47

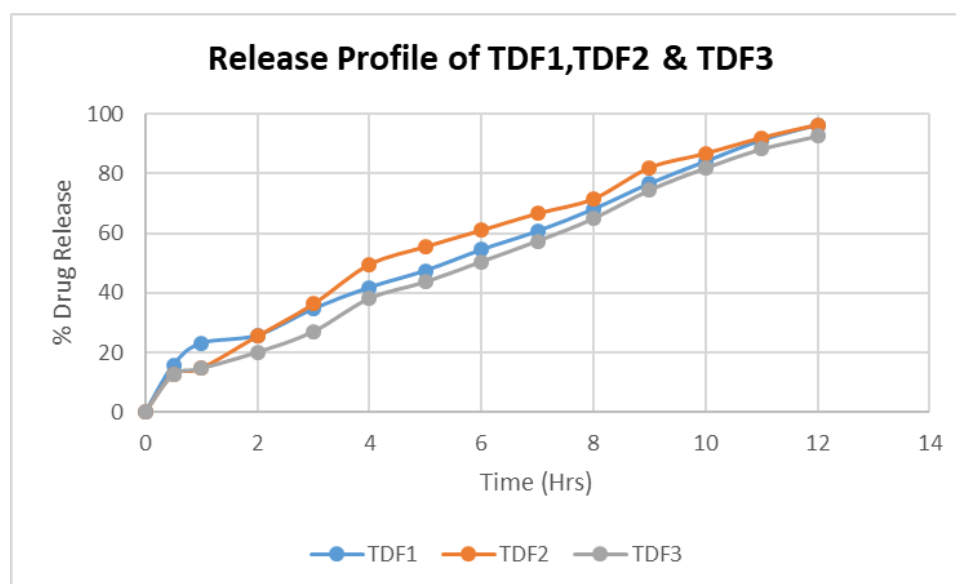


Figure 4. *In-vitro* cumulative drug release profile of TDF1, TDF2, and TDF3 over 12 h (Franz diffusion cell, phosphate buffer pH 7.4, 37 ± 0.5 °C).

4. Discussion

This study set out to formulate and characterise a sustained-release transdermal patch of *Tabernaemontana divaricata* flower extract as a candidate herbal delivery system for migraine treatment motivated by the well-documented limitations of oral anti-migraine therapy—hepatic first-pass metabolism, gastrointestinal intolerance, and erratic absorption during attack-associated gastric stasis and by earlier pharmacological evidence for antinociceptive indole alkaloids in this plant.

The pharmacognostic and phytochemical profile obtained here—low ash values, a semi-solid dark-

brown extract rich in alkaloids and flavonoids, and an FTIR fingerprint consistent with an indole-alkaloid matrix—agrees closely with previous reports on *Tabernaemontana divaricata* supporting the identity and quality of the plant material used. The narrow, reproducible R_f range obtained on TLC (0.66–0.76) further indicated that the extract remained chemically stable under the conditions of this study, a prerequisite for reliable formulation work.

Among the excipients evaluated, HPMC concentration was the principal determinant of patch behaviour. As HPMC increased from TDF1 to TDF3, thickness, moisture uptake, and swelling index increased in

parallel, consistent with the greater hydrophilicity and gel-forming capacity of HPMC at higher polymer loading. This trade-off is a familiar one in hydrophilic matrix systems: higher polymer content improves film-forming ability and mechanical cohesion up to a point, but excessive hydration can compromise dimensional and physical stability during storage. In the present formulations, TDF1—despite carrying the lowest HPMC concentration—achieved the highest folding endurance and the lowest moisture content and swelling index, while still sustaining a comparable or even marginally superior cumulative drug release (96.15% at 12 h) relative to TDF2 and TDF3. This combination of favourable mechanical integrity, low residual moisture, and consistent extended release identifies TDF1 as the most balanced formulation among those tested.

The release profiles of all three patches showed a gradual, sustained rise over 12 h without a pronounced initial burst, indicating that drug release was governed primarily by diffusion through the hydrated polymer matrix rather than by rapid surface dissolution. This is consistent with the behaviour typically reported for HPMC-based solvent-cast transdermal systems loaded with both synthetic and herbal actives and supports the suitability of HPMC as a matrix former for sustained delivery of *Tabernaemontana divaricata* extract.

To the best of our knowledge, this is the first report describing a transdermal patch loaded with *Tabernaemontana divaricata* flower extract, and it therefore extends the pharmaceutical exploration of this plant beyond its previously reported antioxidant, anti-inflammatory, and antinociceptive applications into a delivery-system context. Nonetheless, the present investigation was limited to physicochemical, mechanical, and *In-vitro* release characterisation, and did not include *ex-vivo* skin permeation, formal release-kinetic modelling, pharmacological efficacy testing, or stability studies under accelerated storage conditions. These represent logical and necessary next steps before the translational potential of this formulation can be fully assessed.

5. Conclusion

A sustained-release transdermal patch containing *Tabernaemontana divaricata* flower extract was successfully developed by the solvent-casting method using HPMC as the film-forming polymer and PEG as plasticiser. All three formulations were physicochemically and mechanically acceptable, but TDF1 offered the most favourable overall profile, combining low moisture content and swelling index, high folding endurance, and a controlled 12-hour release of 96.15%. These findings establish feasibility for an HPMC-based herbal transdermal system incorporating *Tabernaemontana divaricata* extract and provide a foundation for further pharmacological, permeation, and clinical studies directed at migraine treatment.

6. Future Scope

Future work should focus on isolating and characterising the specific bioactive constituents of *Tabernaemontana divaricata* responsible for antinociceptive activity, using techniques such as HPLC, GC-MS, and LC-MS for phytochemical profiling and standardisation. Combination transdermal systems incorporating *Tabernaemontana divaricata* extract alongside other antimigraine botanicals could be explored for potential synergism. *Ex-vivo/In-vivo* permeation studies, pharmacokinetic and toxicological evaluation, formal release-kinetic modelling, accelerated stability testing, and ultimately well-designed clinical studies will be required to establish the safety, efficacy, and translational potential of this delivery system.

Declarations

Ethics approval and consent to participate: Not applicable. This study involved only plant material, *In-vitro* phytochemical analysis, and formulation/evaluation of a transdermal patch; no human participants, human data, or animal subjects were involved.

Consent for publication: Not applicable.

Availability of data and materials: The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

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Authors' contributions: Navjot Kaur: conceptualisation, methodology, investigation, formal analysis, writing—original draft.

Shailendra Kumar Verma: supervision, validation, writing—review and editing.

Prashant Kumar Sharma: investigation, formal analysis, conceptualisation

Sanjeev Kumar: investigation, formal analysis

Pushpendra Kannoja : investigation

Sanskar Singh : Methodology

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References

1. Ali Khan, M. S., Misbah, Ahmed, N., Arifuddin, M., Rehman, A., & Ling, M. P. (2018). Indole alkaloids and anti-nociceptive mechanisms of *Tabernaemontana divaricata* (L.) R. Br. flower methanolic extract. *Food and Chemical Toxicology*, 118, 953–962. <https://doi.org/10.1016/j.fct.2018.06.007>
2. Anbukkarasi, M., Sundararajan, M., Venkadeswaran, K., Ruban, V. V., Anand, T., & Geraldine, P. (2019). Antihypercholesterolemic, antioxidative and anti-inflammatory potential of an extract of the plant *Tabernaemontana divaricata* in experimental rats fed an atherogenic diet. *Biocatalysis and Agricultural Biotechnology*, 22, 101115. <https://doi.org/10.1016/j.bcab.2019.101115>
3. Arulmozhi, S., Mazumder, P. M., Lohidasan, S., & Thakurdesai, P. A. (2007). Antioxidant and free radical scavenging activity of *Tabernaemontana divaricata*. *Pharmaceutical Biology*, 45(7), 534–540. <https://doi.org/10.1080/13880200701498983>
4. Azwanida, N. N. (2015). A review on the extraction methods used in medicinal plants: Principles, strength and limitation. *Medicinal & Aromatic Plants*, 4(3), 196. <https://doi.org/10.4172/2167-0412.1000196>
5. Bácskay, I., Hosszú, Z., Budai, I., Ujhelyi, Z., Fehér, P., Kósa, D., et al. (2024). Formulation and evaluation of transdermal patches containing BGP-15. *Pharmaceutics*, 16(1), 36. <https://doi.org/10.3390/pharmaceutics16010036>
6. Bijeshmon, P. P., & George, S. (2014). Antimicrobial activity and powder microscopy of the flowers of *Tabernaemontana divaricata* R. Br. *Indo American Journal of Pharmaceutical Research*, 4(3), 1601–1605. <https://doi.org/10.51847/a4HyCO9Yt7>
7. Bolay, H., Reuter, U., Dunn, A. K., Huang, Z., Boas, D. A., & Moskowitz, M. A. (2002). Intrinsic brain activity triggers trigeminal meningeal afferents in a migraine model. *Nature Medicine*, 8(2), 136–142. <https://doi.org/10.1038/nm0202-136>
8. Burch, R. C., Buse, D. C., & Lipton, R. B. (2019). Migraine: Epidemiology, burden, and comorbidity. *Neurologic Clinics*, 37(4), 631–649. <https://doi.org/10.1016/j.ncl.2019.06.001>
9. Charles, A. (2018). The pathophysiology of migraine: Implications for clinical management. *The Lancet Neurology*, 17(2), 174–182. [https://doi.org/10.1016/S1474-4422\(17\)30435-0](https://doi.org/10.1016/S1474-4422(17)30435-0)
10. Choudhury, S., Das, R., Sharma, P., Mohanty, J. P., Ghosh, A., Banik, B., et al. (2025). Comprehensive disquisition on the phytochemical spectrum and pharmacodynamic nuances of *Tabernaemontana divaricata*. *International Journal of Advanced Biochemistry Research*, 6(2), 115–120. <https://doi.org/10.33545/27072827.2025.v6.i2a.153>
11. Cragg, G. M., & Newman, D. J. (2013). Natural products: A continuing source of novel drug leads. *Nature Reviews Cancer*, 13(6), 371–384. <https://doi.org/10.1038/nrc3465>
12. Devi, P., Singh, U. P., & Kumar, A. (2024). Phytochemistry, pharmacognosy and pharmacological properties of *Tabernaemontana divaricata*: A review. *International Journal of Pharmaceutical Sciences and Medicine*, 9(5), 119–125. <https://doi.org/10.47760/ijpsm.2024.v09i05.012>
13. Dias, M., Hadgraft, J., & Lane, M. E. (2007). Influence of membrane characteristics in Franz diffusion cell studies. *International Journal of Pharmaceutics*, 336(1), 108–114. <https://doi.org/10.1016/j.ijpharm.2006.11.018>
14. Dodick, D. W. (2018). Migraine. *The Lancet*, 391(10127), 1315–1330. [https://doi.org/10.1016/S0140-6736\(18\)30478-1](https://doi.org/10.1016/S0140-6736(18)30478-1)
15. Edvinsson, L. (2019). The trigeminovascular pathway: Role of CGRP and CGRP receptors in migraine. *Headache*, 59(Suppl 2), 33–45. <https://doi.org/10.1111/head.13581>
16. Ekor, M. (2014). The growing use of herbal medicines: Issues relating to adverse reactions and challenges in monitoring safety. *Saudi Pharmaceutical Journal*, 22(5), 391–406. <https://doi.org/10.1016/j.jsps.2013.07.006>
17. Franz, T. J. (1975). Percutaneous absorption: On the relevance of in vitro data. *Journal of Investigative Dermatology*, 64(3), 190–195. <https://doi.org/10.1111/1523-1747.ep12533356>
18. Ghosh, P., Poddar, S., & Chatterjee, S. (2021). Morphological features, phytochemical and ethnopharmacological attributes of *Tabernaemontana divaricata* Linn.: A comprehensive review. *Journal of Pharmacognosy and Phytochemistry*, 10(6), 31–36. <https://doi.org/10.22271/phyto.2021.v10.i6a.14253>
19. Goadsby, P. J., Holland, P. R., Martins-Oliveira, M., Hoffmann, J., Schankin, C., & Akerman, S. (2017). Pathophysiology of migraine: A disorder of sensory processing. *Physiological Reviews*, 97(2), 553–622. <https://doi.org/10.1152/physrev.00034.2015>
20. Gurib-Fakim, A. (2006). Medicinal plants: Traditions of yesterday and drugs of tomorrow. *Molecular Aspects of Medicine*, 27(1), 1–93. <https://doi.org/10.1016/j.mam.2005.07.008>
21. Harborne, J. B. (1998). *Phytochemical methods: A guide to modern techniques of plant analysis* (3rd ed.). Springer. <https://doi.org/10.1007/978-94-009-5570-7>
22. Headache Classification Committee of the

- International Headache Society (IHS). (2018). The International Classification of Headache Disorders, 3rd edition (ICHD-3). *Cephalalgia*, 38(1), 1–211.
<https://doi.org/10.1177/0333102417738202>
23. Iyengar, S., Ossipov, M. H., & Johnson, K. W. (2019). The role of calcitonin gene-related peptide in peripheral and central pain mechanisms including migraine. *Pain*, 160(3), 543–559.
<https://doi.org/10.1097/j.pain.0000000000001426>
24. Jamaludin, W. B., Muthia, R., Kartini, K., Setiawan, F., Juhrah, S., & Yulida, N. (2024). Formulation and evaluation of transdermal patches from *Eleutherine bulbosa* Urb. bulb extract with plasticizer variations. *International Journal of Applied Pharmaceutics*, 16(1), 202–208.
<https://doi.org/10.22159/ijap.2024v16i1.46421>
25. Kola, M., Veeraganti, S., & Sravani, V. (2022). Formulation and in vitro evaluation of ketoconazole patches for transdermal drug delivery system. *International Journal of Creative Research Thoughts*.
<https://doi.org/10.5281/zenodo.7311156>
26. Leonardi, M., & Raggi, A. (2019). A narrative review on the burden of migraine: When the burden is the impact on people's life. *The Journal of Headache and Pain*, 20(1), 41.
<https://doi.org/10.1186/s10194-019-0993-0>
27. Pandey, A., & Tripathi, S. (2014). Pharmacognostic and physicochemical evaluation of medicinal plants: A review. *Journal of Pharmacognosy and Phytochemistry*, 2(5), 55–61.
28. Parhi, R., & Padilam, S. (2018). In vitro permeation and stability studies on developed drug-in-adhesive transdermal patch of simvastatin. *Biomedicine & Pharmacotherapy Open Access*, 1, 1–8.
<https://doi.org/10.1016/j.bfopcu.2018.04.001>
29. Petrovska, B. B. (2012). Historical review of medicinal plants' usage. *Pharmacognosy Reviews*, 6(11), 1–5.
<https://doi.org/10.4103/0973-7847.99948>
30. Prausnitz, M. R., & Langer, R. (2008). Transdermal drug delivery. *Nature Biotechnology*, 26(11), 1261–1268.
<https://doi.org/10.1038/nbt.1504>
31. Prausnitz, M. R., Mitragotri, S., & Langer, R. (2004). Current status and future potential of transdermal drug delivery. *Nature Reviews Drug Discovery*, 3(2), 115–124.
<https://doi.org/10.1038/nrd1304>