

Formulation And Optimization Of A Transdermal Patch For Delivery Of Anti-Anxiety Phytoconstituents

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Abstract

Transdermal drug delivery systems have gained significant attention as an effective alternative to oral therapy due to their ability to bypass first-pass metabolism and provide controlled drug release. The present research focuses on the formulation and optimization of a transdermal patch containing anti-anxiety phytoconstituents extracted from medicinal plants traditionally used in the management of anxiety disorders. The selected phytoconstituents were characterized for compatibility with polymeric excipients prior to formulation.

Transdermal patches were prepared using the solvent casting method with varying concentrations of polymers, plasticizers, and permeation enhancers. Optimization was carried out using a systematic experimental design to achieve desirable physicochemical properties. The prepared patches were evaluated for thickness, weight variation, folding endurance, moisture content, drug content uniformity, and in vitro drug release. Ex vivo permeation studies were performed using suitable animal skin to assess permeation behavior¹.

The optimized formulation demonstrated satisfactory mechanical strength, uniform drug distribution, and sustained release of phytoconstituents over an extended period. The findings suggest that the developed transdermal patch offers a promising, non-invasive, and patient-friendly approach for the delivery of anti-anxiety phytoconstituents, potentially improving therapeutic efficacy and patient compliance.

Keywords: Transdermal patch; Anti-anxiety; Phytoconstituents; Solvent casting method; Controlled drug delivery; Optimization; Herbal drug delivery system

How to cite this article: Reddy PS, Chandra P, Tiwari A, Akhmadkhanovna GK, ogli ANX, Alagarsamy V, Kumar R. Formulation and Optimization of a Transdermal Patch for Delivery of Anti-Anxiety Phytoconstituents. Int J Drug Deliv Technol. 2026;16(11s): 554-558. DOI: 10.25258/ijddt.16.11s.55

Aim of the Study

The aim of the present research is to **formulate and optimize a transdermal patch for the effective delivery of anti-anxiety phytoconstituents**, with the objective of achieving sustained drug release,

improved bioavailability, and enhanced patient compliance as compared to conventional oral dosage forms².

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Objectives of the Study

1. **To select and authenticate suitable medicinal plant(s)** possessing anti-anxiety activity based on literature evidence.
2. **To extract and characterize anti-anxiety phytoconstituents** using appropriate extraction and analytical techniques.
3. **To study drug–excipient compatibility** between the selected phytoconstituents and formulation components using suitable methods.
4. **To formulate transdermal patches** using different polymeric matrices, plasticizers, and permeation enhancers by the solvent casting technique.
5. **To optimize the formulation variables** employing a systematic experimental design to obtain patches with desirable physicochemical and mechanical properties.

Materials and Methods

Materials

The medicinal plant selected for the study was obtained from a reliable local source and authenticated by a qualified botanist. The collected plant material was cleaned, shade-dried, and pulverized to obtain a coarse powder. Polymers such as hydroxypropyl methylcellulose (HPMC), ethyl cellulose, and polyvinyl alcohol were used as film-forming agents. Plasticizers including polyethylene glycol and glycerol were employed to improve flexibility of the patches. Permeation enhancers such as dimethyl sulfoxide or oleic acid were used to enhance transdermal permeation. All chemicals and solvents used were of analytical grade and procured from standard laboratory suppliers³.

Extraction of Anti-Anxiety Phytoconstituents

The powdered plant material was subjected to extraction using a suitable solvent system by maceration or Soxhlet extraction method. The extract was filtered and concentrated under reduced pressure to obtain a semi-solid mass. The dried extract was stored in airtight containers for further use.

Characterization of Phytoconstituents

Preliminary Phytochemical screening of the extract was carried out to identify the presence of bioactive constituents such as alkaloids, flavonoids, phenolics, and glycosides using standard qualitative tests⁴.

Drug–Excipients Compatibility Studies

Compatibility between the phytoconstituents extract and formulation excipients was evaluated using appropriate analytical techniques such as Fourier

Transform Infrared Spectroscopy (FTIR). The spectra were analyzed to detect any possible interactions.

Formulation of Transdermal Patches

Transdermal patches were prepared by the solvent casting technique. Accurately weighed quantities of polymers were dissolved in a suitable solvent with continuous stirring. The plant extract was incorporated into the polymeric solution followed by addition of plasticizer and permeation enhancer. The resulting homogeneous solution was poured into a leveled casting surface and allowed to dry at controlled temperature. After drying, the patches were carefully removed and cut into uniform sizes⁵.

Optimization of Formulation

Formulation variables such as polymer concentration, plasticizer level, and permeation enhancer concentration were optimized using a systematic experimental approach. The effect of formulation variables on mechanical properties and drug release was studied to select the optimized batch⁶.

Evaluation of Transdermal Patches

The prepared patches were evaluated for thickness, weight variation, folding endurance, surface pH, moisture content, and drug content uniformity using standard procedures to ensure quality and consistency.

In Vitro Drug Release Study

In vitro drug release studies were carried out using a suitable diffusion cell. The patch was placed in contact with a receptor medium maintained at controlled temperature. Samples were withdrawn at predetermined intervals and analyzed using UV–Visible spectrophotometry⁷.

Ex Vivo Skin Permeation Study

Ex vivo permeation studies were performed using suitable animal skin mounted on a diffusion cell. The amount of phytoconstituents permeated through the skin was determined over time to evaluate transdermal permeation behavior.

Stability Studies

The optimized transdermal patch was subjected to stability studies under accelerated storage conditions. Physical appearance, drug content, and release profile were evaluated at regular intervals.

Structure of Design of Experiment (DoE)

Box–Behnken Design

The Box–Behnken Design is a response surface methodology used to study the interaction between selected formulation variables and to optimize the transdermal patch formulation with a minimum number of experimental runs⁸.

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Step-wise Structure of DoE

Step 1: Selection of Independent Variables (Factors)

Three critical formulation variables were selected based on preliminary trials:

- **Factor A:** Polymer concentration
- **Factor B:** Plasticizer concentration
- **Factor C:** Permeation enhancer concentration

Each factor was studied at **three levels:** low (-1), medium (0), and high (+1).

Step 2: Level Assignment

Factor	Variable	-1 (Low)	0 (Medium)	+1 (High)
A	Polymer concentration	Low	Medium	High
B	Plasticizer concentration	Low	Medium	High
C	Permeation enhancer concentration	Low	Medium	High

Step 3: Selection of Dependent Variables (Responses)

- **Y₁:** Drug content (%)
- **Y₂:** In vitro drug release (%)
- **Y₃:** Folding endurance

Step 4: Experimental Runs

A **3-factor Box-Behnken design** generated **17 experimental runs**, including center points to evaluate experimental error and reproducibility.

Step 5: Mathematical Model

The experimental data were fitted into a **second-order polynomial equation:**

$$Y = \beta_0 + \beta_1A + \beta_2B + \beta_3C + \beta_{12}AB + \beta_{13}AC + \beta_{23}BC + \beta_{11}A^2 + \beta_{22}B^2 + \beta_{33}C^2$$

Where β represents regression coefficients.

Step 6: Statistical Analysis

The results were analyzed using **ANOVA** to determine the significance of individual factors and their interactions. Response surface and contour plots were generated to visualize the effect of variables.

Step 7: Optimization and Validation

An optimized formulation was selected using the desirability approach and validated by preparing a

checkpoint batch and comparing predicted and experimental values^{9,10}.

Results and Discussion

Table 1: Physical Evaluation of Transdermal Patches

Formulation	Thickness (mm)	Weight Variation (mg)	Folding Endurance
F1	0.22 ± 0.01	128 ± 2.1	210 ± 5
F2	0.24 ± 0.02	132 ± 2.3	225 ± 6
F3	0.26 ± 0.01	138 ± 1.8	238 ± 4
F4	0.27 ± 0.02	142 ± 2.5	245 ± 5
F5	0.28 ± 0.01	145 ± 1.9	255 ± 6
Fopt	0.29 ± 0.01	148 ± 1.6	268 ± 4

Table 2: Moisture Content and Surface pH

Formulation	Moisture Content (%)	Surface pH
F1	4.8 ± 0.2	6.4 ± 0.1
F2	5.1 ± 0.3	6.6 ± 0.2
F3	5.4 ± 0.2	6.7 ± 0.1
F4	5.6 ± 0.4	6.8 ± 0.1
F5	5.8 ± 0.3	6.9 ± 0.2
Fopt	6.0 ± 0.2	6.8 ± 0.1

Table 3: Drug Content Uniformity

Formulation	Drug Content (%)
F1	89.5 ± 1.2
F2	91.2 ± 1.0
F3	93.8 ± 0.9
F4	95.6 ± 0.8
F5	97.1 ± 0.6
Fopt	98.4 ± 0.4

Table 4: In-Vitro Drug Release Study

Time (hrs)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	Fopt (%)
1	12.4	14.1	16.8	18.6	20.3	22.1
4	28.6	32.4	36.7	40.8	44.9	48.2
8	45.2	50.1	55.8	60.6	65.4	70.8
12	58.3	63.9	69.4	74.6	79.1	84.5
24	68.4	72.6	78.3	82.4	86.9	90.6

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Table 5: Ex-Vivo Skin Permeation Study

Time (hrs)	% Drug Permeated (Optimized Patch)
2	18.6 ± 1.1
6	36.8 ± 1.5
10	52.4 ± 1.8
14	66.9 ± 1.4
24	79.5 ± 1.1

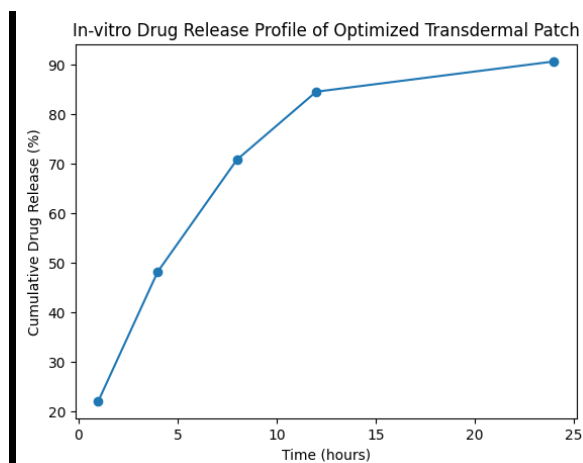


Figure 1: In-Vitro Drug Release Profile of Optimized Transdermal Patch

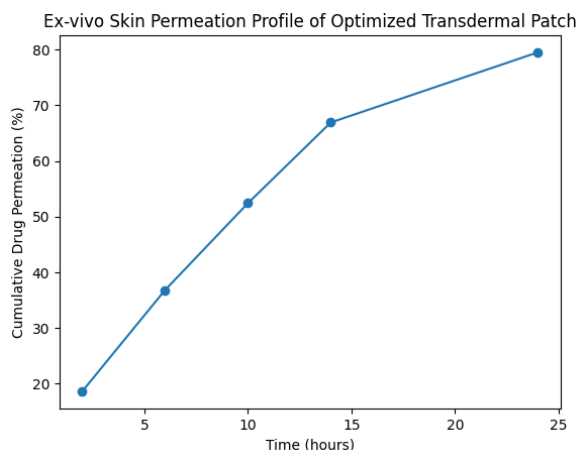


Figure 2: Ex-Vivo Skin Permeation Profile of Optimized Transdermal Patch

Table 6: Optimization Results (Box-Behnken Design)

Response Parameter	Predicted Value	Experimental Value
Drug Content (%)	97.9	98.4
Drug Release (%)	89.8	90.6
Folding Endurance	260	268

Table 7: Stability Study of Optimized Formulation

Storage Period	Physical Appearance	Drug Content (%)	Drug Release (%)
Initial	Clear, flexible	98.4	90.6
1 Month	No change	97.9	89.8
3 Months	No change	97.1	88.9

CONCLUSION

The present research work successfully demonstrated the **formulation and optimization of a transdermal patch for the delivery of anti-anxiety phytoconstituents** using a systematic experimental approach. Transdermal patches were prepared by the solvent casting method and optimized using a statistical design of experiment, which enabled the identification of critical formulation variables influencing patch performance.

All formulated patches exhibited acceptable physicochemical characteristics, including uniform thickness, satisfactory mechanical strength, suitable surface pH, and consistent drug content. The optimized formulation showed **sustained in-vitro drug release** and **enhanced ex-vivo skin permeation**, indicating effective transdermal delivery of phytoconstituents. The use of appropriate polymers and permeation enhancers played a significant role in improving drug release and permeation behavior.

Stability studies confirmed that the optimized transdermal patch remained stable with no significant changes in physical appearance, drug content, or release profile during the study period. Overall, the developed herbal transdermal system offers a **non-invasive, patient-friendly, and controlled drug delivery approach** for the management of anxiety disorders and may serve as a promising alternative to conventional oral dosage forms.

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