Int. J. Pharm. Investigation, 2026; 16(4):1434-1444.
https://www.jpionline.org

Original Article

# Design, Optimization, and Evaluation of Lincomycin Hydrochloride Transdermal Patches for Sustained Drug Release and Improved Antimicrobial Efficacy

**Pratiksha Akki[1,*], M Mahesh Yadav[1], Fatima S Dasankoppa[1], Agadi Hiremath Viswanatha Swamy[2], M Pradeep Kumar[3], C. Manjula[3], Muneendra[4], Rohan Latwade[5], Shreya A. Prabhu[1], Reshma Vibhuti[1]**

[1]Department of Pharmaceutics, KLE College of Pharmacy (A Constituent Unit of KLE Academy of Higher Education and Research, Belagavi), Hubballi, Karnataka, INDIA.
[2]Department of Pharmacy Practice, KLE College of Pharmacy, (A Constituent Unit of KLE Academy of Higher Education and Research, Belagavi), Hubballi, Karnataka, INDIA.
[3]Department of Pharmaceutics, Vasavi Institute of Pharmaceutical Sciences, Vasavi Nagar, Peddapalli Vi, Sidhout Mandal, Kadapa, Andhra Pradesh, INDIA.
[4]ScieGen Pharmaceuticals 89 Arkay Drive, Hauppauge, New York 11788, USA.
[5]Dr. J. J. Magdum Pharmacy College, Jaysingpur, (Affiliated to Dr. Babasaheb Ambedkar Techological University), Lonere, Maharastra, INDIA.

## ABSTRACT

**Background:** Antimicrobial Resistance (AMR) presents a major global health concern, necessitating the development of novel antimicrobial agents and effective drug delivery systems. Lincomycin hydrochloride, a lincosamide antibiotic active against Gram-positive bacteria, exhibits poor oral bioavailability and causes systemic side effects, limiting its therapeutic potential. Objectives: This study aimed to formulate and evaluate lincomycin hydrochloride-loaded transdermal patches to enhance localized antimicrobial efficacy, improve patient compliance, and minimize systemic toxicity. **Materials and Methods:** Transdermal patches were prepared by the solvent casting method using Hydroxypropyl Methylcellulose (HPMC) K100M and Polyvinyl Alcohol (PVA) as film-forming polymers, propylene glycol as a permeation enhancer, and glycerine as a plasticizer. A $2^2$ full factorial design was employed to optimize polymer concentrations for maximum drug release. The prepared patches were evaluated for physicochemical characteristics, *in vitro* drug release, and antimicrobial activity against Staphylococcus aureus. FTIR analysis was conducted to assess drug-excipient compatibility. **Results:** The patches exhibited uniform thickness, flexibility, suitable surface pH, and stable drug content, confirming formulation stability and skin compatibility. *In vitro* release studies showed that higher polymer concentrations decreased drug release. The optimized formulation containing 1032 mg HPMC K100M and 663 mg PVA achieved 75.87% cumulative drug release over 6 hr. Antimicrobial studies revealed significant inhibition zones, demonstrating superior antibacterial activity compared to pure drug discs. FTIR spectra confirmed no significant drug-excipient interactions. **Conclusion:** Lincomycin hydrochloride transdermal patches demonstrated promising physicochemical stability, controlled release, and potent antibacterial activity. The optimized formulation provides an effective, patient-friendly approach for localized treatment of bacterial infections and may serve as a potential strategy to mitigate antimicrobial resistance.

**Keywords:** Antimicrobial resistance, Factorial design, HPMC K100M, *In vitro* release, Lincomycin hydrochloride, Solvent casting, Transdermal patches.

**Correspondence:**
**Mrs. Pratiksha Akki**
Assistant Professor, Department of Pharmaceutics, KLE College of Pharmacy (A Constituent Unit of KLE Academy of Higher Education and Research, Belagavi), Hubballi, Karnataka, INDIA.
Email: pratiksha.akki8@gmail.com
ORCID: 0000-0002-6513-1517

**Received:** 06-02-2026;
**Revised:** 26-03-2026;
**Accepted:** 12-05-2026.

## INTRODUCTION

Antimicrobial Resistance (AMR) has emerged as one of the most critical global health challenges of the 21st century. The World Health Organization (WHO) warns that AMR threatens to reverse decades of progress in the treatment of infectious diseases by rendering existing antibiotics less effective (World Health Organization, 2020). The increasing resistance of microbial pathogens to conventional antibiotics has intensified the need for innovative therapeutic approaches and advanced drug delivery systems to enhance the efficacy of existing antimicrobial agents.

Among available antibiotics, lincomycin hydrochloride, a member of the lincosamide class, exhibits potent activity against Gram-positive bacteria and certain anaerobes (Rusu *et al.*, 2023). However, its therapeutic potential is limited by poor oral bioavailability, degradation within the gastrointestinal tract,

OPEN ACCESS
Manuscript TECHNOMEDIA

**DOI:** 10.5530/ijpi.20260139

and systemic side effects such as gastrointestinal irritation and diarrhea. Moreover, variable absorption and frequent dosing reduce patient adherence, thereby contributing to the risk of resistance development (Obana *et al.*, 2023). These limitations necessitate the exploration of alternative delivery routes that can maintain therapeutic concentrations at the site of infection while minimizing systemic exposure.

Transdermal Drug Delivery Systems (TDDS) represent a promising strategy to overcome the drawbacks associated with conventional antibiotic delivery. TDDS can bypass gastrointestinal degradation and first-pass hepatic metabolism, offering sustained and controlled drug release with improved patient compliance (Ghaferi *et al.*, 2024). Additionally, localized transdermal delivery can maintain adequate drug levels at the infection site, enhancing antimicrobial efficacy and reducing the probability of systemic toxicity and resistance development (Akombaetwa *et al.*, 2023). Nevertheless, the major challenge of transdermal delivery lies in overcoming the skin's outermost barrier the stratum corneum which restricts the permeation of many hydrophilic drugs. This challenge can be addressed by optimizing polymer composition, incorporating permeation enhancers, or employing formulation design strategies such as factorial optimization (Alkilani *et al.*, 2024).

In this context, the present study focuses on the formulation and evaluation of lincomycin hydrochloride-loaded transdermal patches using a combination of Hydroxypropyl Methylcellulose (HPMC K100M) and Polyvinyl Alcohol (PVA) as film-forming polymers. Propylene glycol was used as a permeation enhancer, while glycerine acted as a plasticizer to improve flexibility and film integrity. A $2^2$ full factorial design was employed to optimize the polymer ratios for maximum drug release and mechanical stability. The developed patches were subjected to comprehensive physicochemical evaluation, *in vitro* drug release studies, antimicrobial activity testing against *Staphylococcus aureus*, and compatibility analysis through Fourier-Transform Infrared (FTIR) spectroscopy.

This study aims to develop a stable, biocompatible, and effective transdermal system for lincomycin hydrochloride that offers sustained drug release, enhanced local antimicrobial action, and reduced systemic toxicity, thus presenting a potential strategy to combat antimicrobial resistance.

## MATERIALS AND METHODS

### Materials

Lincomycin Hydrochloride was obtained as a gift sample, while HPMC K100M, PVA, propylene glycol, and glycerine were procured from standard analytical-grade suppliers. All chemicals used were of analytical grade, and distilled water was employed throughout the study. Materials were stored at controlled room temperature (25±2°C) and protected from light and moisture until use.

### Methods

#### *Preparation of Standard Stock Solutions*

A primary stock solution of lincomycin hydrochloride (1 mg/mL) was prepared by dissolving 100 mg of drug in 100 mL of distilled water using a volumetric flask. From this, a secondary stock solution (100 µg/mL) was obtained by diluting 10 mL of the primary stock to 100 mL with distilled water (Naveed *et al.*, 2014).

### Determination of $\lambda_{max}$

An aliquot of 1 mL from the secondary stock solution was diluted to 10 mL to obtain a 10 µg/mL working solution. The solution was scanned in the range of 200-400 nm using a UV-visible spectrophotometer (Shimadzu, Japan) with distilled water as blank. The maximum absorbance ($\lambda_{max}$ was observed at 204 nm, which was used for further analysis.

### Calibration Curve of Lincomycin Hydrochloride

Aliquots of 1-8 mL from the secondary stock solution were separately diluted to 10 mL with distilled water to obtain concentrations ranging from 10-80 µg/mL. The absorbance of each solution was measured at 204 nm against distilled water as blank. A calibration curve was plotted between concentration (µg/mL) and absorbance to determine linearity and regression coefficient (Najim *et al.*, 2014).

### Drug-Excipient Compatibility Study (FTIR)

Compatibility between lincomycin hydrochloride and polymers was evaluated using Fourier Transform Infrared (FTIR) spectroscopy (PerkinElmer, USA). Spectra were recorded for pure drug, individual excipients (HPMC K100M, PVA, propylene glycol, and glycerin), and their physical mixtures in the range of 4000-400 $cm^{-1}$ using the KBr pellet method. Any significant shifts or disappearance of characteristic peaks were noted to assess possible chemical interactions (Ganjoo *et al.*, 2016).

### Preparation of Lincomycin Hydrochloride Transdermal Patches

#### *Preparation of Backing Membrane*

Polyvinyl alcohol (0.8 g) was dissolved in 15 mL of distilled water under constant stirring at 300 rpm with gentle heating. Glycerin (0.3 mL) was added as a plasticizer. The homogeneous solution was poured into a clean glass Petri dish and allowed to dry at ambient temperature for 24 hr to form a flexible backing membrane (Alkilani *et al.*, 2023).

## Preparation of Drug-Loaded Layer

Required quantities of HPMC K100M and PVA (as per factorial design) were dissolved in 15 mL of distilled water with continuous stirring until a clear solution was obtained. Lincomycin hydrochloride, propylene glycol, and glycerin were then added and mixed thoroughly to obtain a uniform viscous dispersion. The prepared mixture was carefully cast over the pre-formed PVA backing membrane and dried at room temperature (25±2°C) for 24 hr. After complete drying, patches were cut into 2 × 2 cm squares and stored in airtight containers until further use (Park *et al.*, 2018) (Table 1).

## Application of Adhesive and Release Liner

A thin layer of hot-melt pressure-sensitive adhesive was applied to one surface of the dried patch. The patch was then covered with a siliconized release liner to protect the adhesive layer. Finished patches were stored in moisture-proof containers to prevent degradation and maintain integrity (Wokovich *et al.*, 2010).

## Experimental Design ($2^2$ Full Factorial Design)

A two-factor, two-level ($2^2$) full factorial design was used to optimize the formulation variables. The independent variables were: $X_1$: Concentration of HPMC K100M (mg), $X_2$: Concentration of PVA (mg). Each variable was studied at two levels (low and high). The dependent response variable was the cumulative percentage drug release at 6 hr. Four experimental batches (F1-F4) were formulated as per the factorial combinations, and evaluated for physicochemical and *in vitro* parameters (Gunst *et al.*, 2009).

## Evaluation of Transdermal Patches

### *Physical Appearance*

The prepared patches were visually examined for color, transparency, surface smoothness, flexibility, and homogeneity (Arora *et al.*, 2002).

## Thickness

The thickness of each patch (2 × 2 cm) was measured at three random positions using a digital micrometer screw gauge. The mean±Standard Deviation (SD) was calculated to assess uniformity.

## Weight Uniformity

Three patches from each batch were individually weighed using an analytical balance. The mean weight and standard deviation were determined to ensure uniform distribution of polymer and drug.

## Folding Endurance

A strip of each patch (2 × 2 cm) was repeatedly folded at the same point until it broke. The number of folds required to break the patch was recorded as the folding endurance value, which indicates flexibility and mechanical strength (Prabhakara *et al.*, 2010).

## Surface pH

Each patch (2 × 2 cm) was placed in contact with 2 mL of distilled water for 1 hr. The surface pH was measured using a digital pH meter by placing the electrode in contact with the surface. This test ensures compatibility with skin pH and minimizes the risk of irritation.

## Moisture Content

Patches were initially weighed and kept in a desiccator containing activated silica gel for 24 hr. They were re-weighed until a constant weight was obtained. The percentage moisture content was calculated from the initial and final weights.

## Adhesive Strength (Tack Test)

Adhesive strength was determined by lightly pressing the patch between thumb and forefinger and assessing its tackiness upon removal. A good patch should exhibit moderate tackiness, ensuring firm adhesion without leaving residue on the skin.

## Drug Content Uniformity

An accurately weighed patch (4 $cm^2$) was dissolved in 100 mL of phosphate buffer (pH 7.4) and stirred overnight. The solution was filtered, suitably diluted, and analyzed spectrophotometrically at 204 nm. Drug content (%) was calculated in relation to the theoretical amount of lincomycin hydrochloride.

**Table 1: Formulation table using $2^2$ full factorial design.**

| Ingredients | F1 | F2 | F3 | F4 |
|---|---|---|---|---|
| Lincomycin HCl (mg) | 1500 | 1500 | 1500 | 1500 |
| HPMC (mg) | 750 | 750 | 500 | 500 |
| PVA (mg) | 800 | 1200 | 800 | 1200 |
| PG (mL) | 01 | 01 | 01 | 01 |
| Glycerine (mL) | 0.4 | 0.4 | 0.4 | 0.4 |
| Water (mL) | 15 mL | 15 mL | 15 mL | 15 mL |

### *In vitro* Drug Release Study

*In vitro* drug release was performed using a Franz diffusion cell equipped with a dialysis membrane (molecular weight cutoff 12,000-14,000 Da). The receptor compartment contained 50 mL of phosphate buffer (pH 7.4) maintained at 37±0.5°C and stirred continuously at 100 rpm. A patch of 4 $cm^2$ was mounted on the donor compartment with the drug-loaded side facing the membrane. At predetermined intervals, 1 mL of the receptor medium was withdrawn and replaced with an equal volume of fresh buffer to maintain sink conditions. Samples were analyzed spectrophotometrically at 204 nm to determine cumulative percentage drug release (Shivalingam *et al.*,2021; Hardainiyan *et al.*, 2017)

## RESULTS

### Determination of Absorption maxima

The Absorption Maximum ($\lambda_{max}$) of Lincomycin Hydrochloride was determined using a UV-visible spectrophotometer with distilled water as solvent. The maximum absorbance was observed at 204 nm as shown in Figure 1, confirming the characteristic absorption peak of the drug.

### Standard Calibration Curve of Lincomycin Hydrochloride

A standard calibration curve was constructed for Lincomycin Hydrochloride in the concentration range of 10-60 µg/mL. The absorbance values were recorded at 204 nm, and the mean of triplicate readings was analyzed using a linear regression model:

$$(y=mx + c)$$

The calibration curve exhibited excellent linearity (Figure 2), indicating compliance with Beer-Lambert's law.

### Drug-Excipient Compatibility Study (FTIR Analysis)

Fourier Transform Infrared (FTIR) spectroscopy was employed to assess potential interactions between Lincomycin Hydrochloride and excipients (HPMC K100M, PVA, propylene glycol, and glycerin). The spectra were recorded over the 4000-400 $cm^{-1}$ range.

The FTIR spectrum of pure Lincomycin Hydrochloride (Figure 3) showed characteristic peaks corresponding to functional groups such as O-H, N-H, and C-H stretching. The mixture of drug and excipients (Figure 4, Table 2) exhibited all the prominent peaks of the pure drug with no significant shifts, indicating absence of chemical interactions and excellent compatibility. These characteristic peaks confirmed the structural integrity of the drug and its compatibility with selected excipients.

### Formulation of Lincomycin Hydrochloride Transdermal Patches

Transdermal patches (F1-F4) were successfully prepared using the solvent casting technique based on a $2^2$ full factorial design. The patches were smooth, flexible, and transparent, as shown in Figure 5.

### Evaluation Parameters

#### *Physical Appearance*

All patches were smooth, translucent, and flexible, indicating successful film formation and uniform polymer distribution.

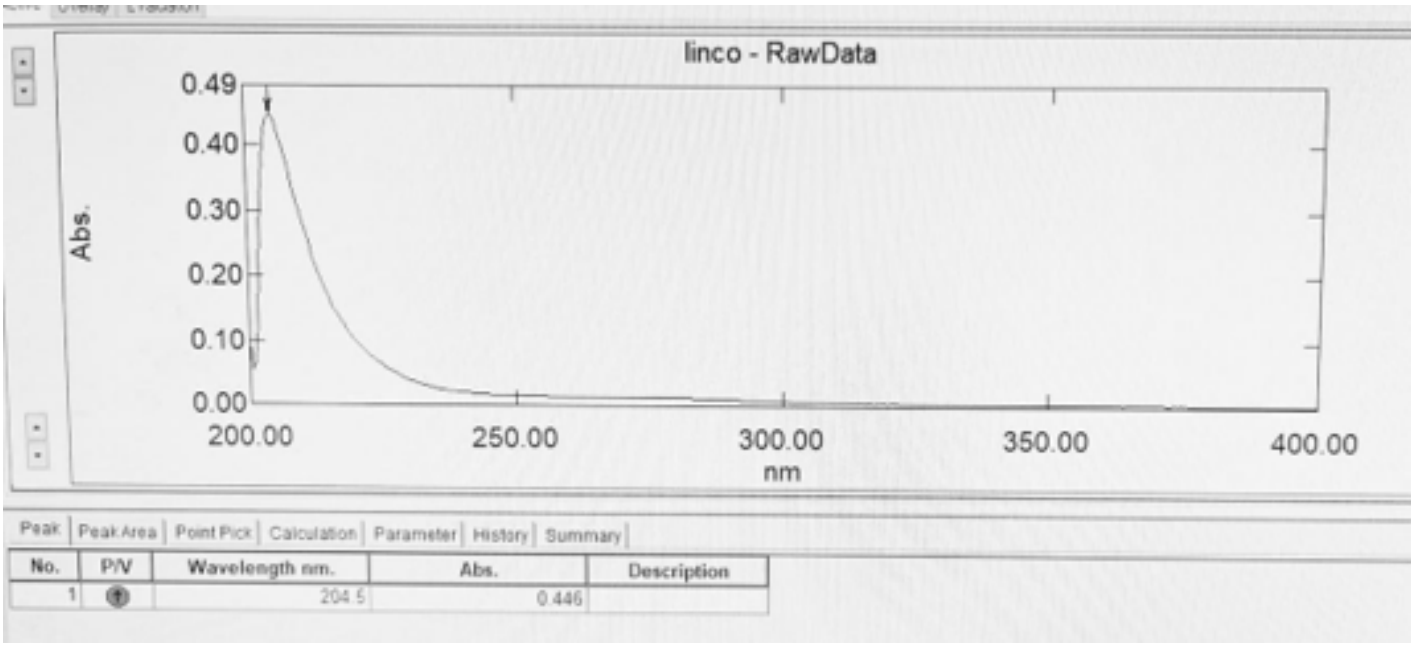



**Figure 1:** UV Absorption Spectrum of Lincomycin Hydrochloride.

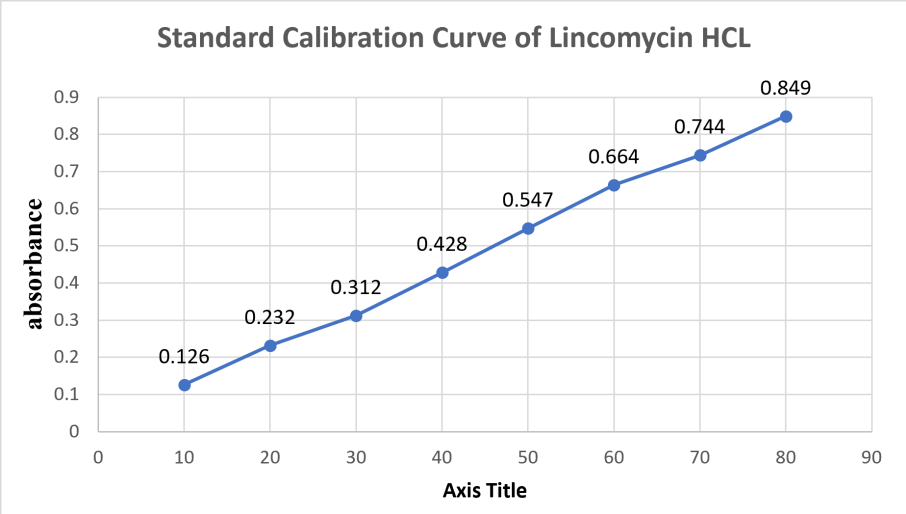



**Figure 2:** Standard Calibration Curve of Lincomycin Hydrochloride.

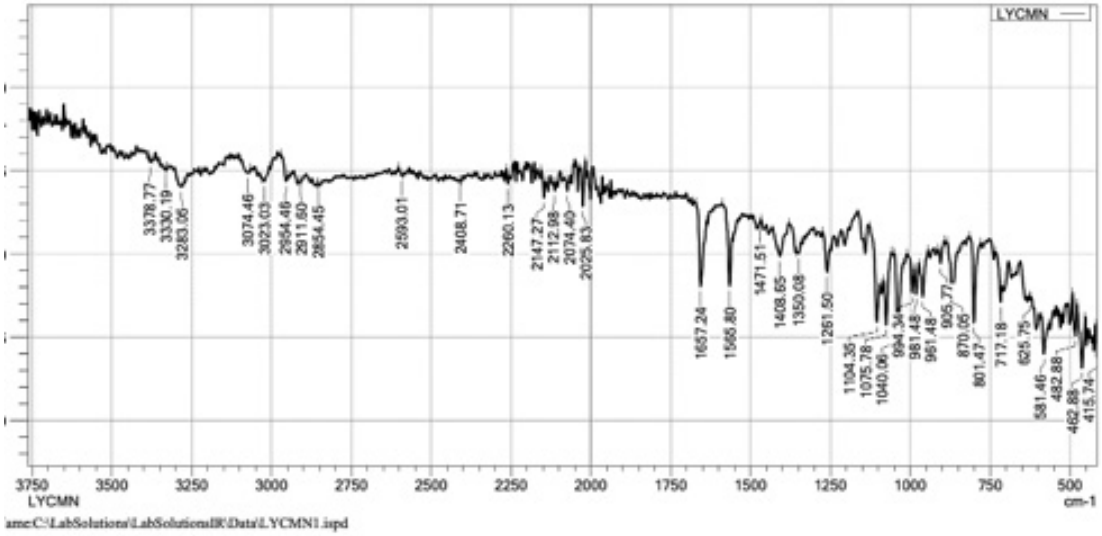



**Figure 3:** FTIR spectra of pure Lincomycin Hydrochloride.

KLE College of Pharmacy, Hubballi

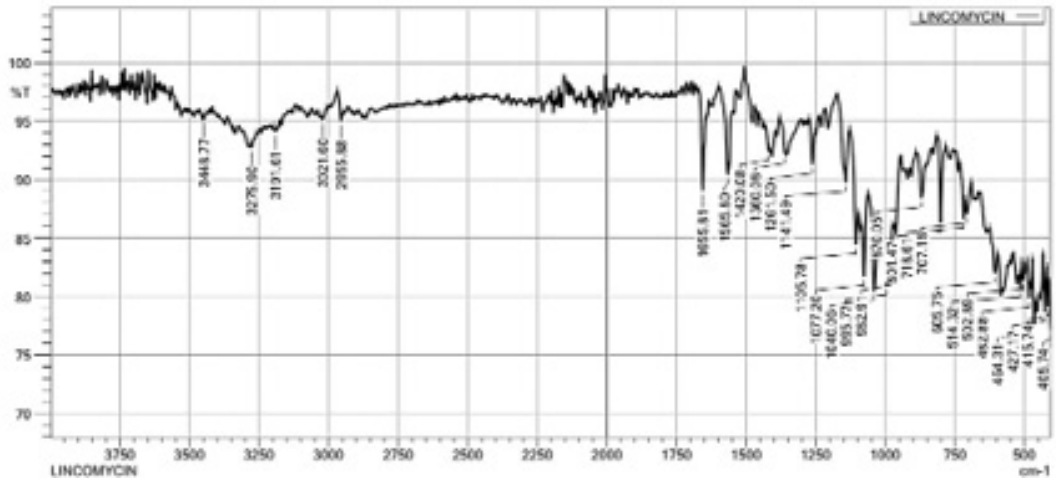



**Figure 4:** FTIR spectra of drug-excipient mixture.

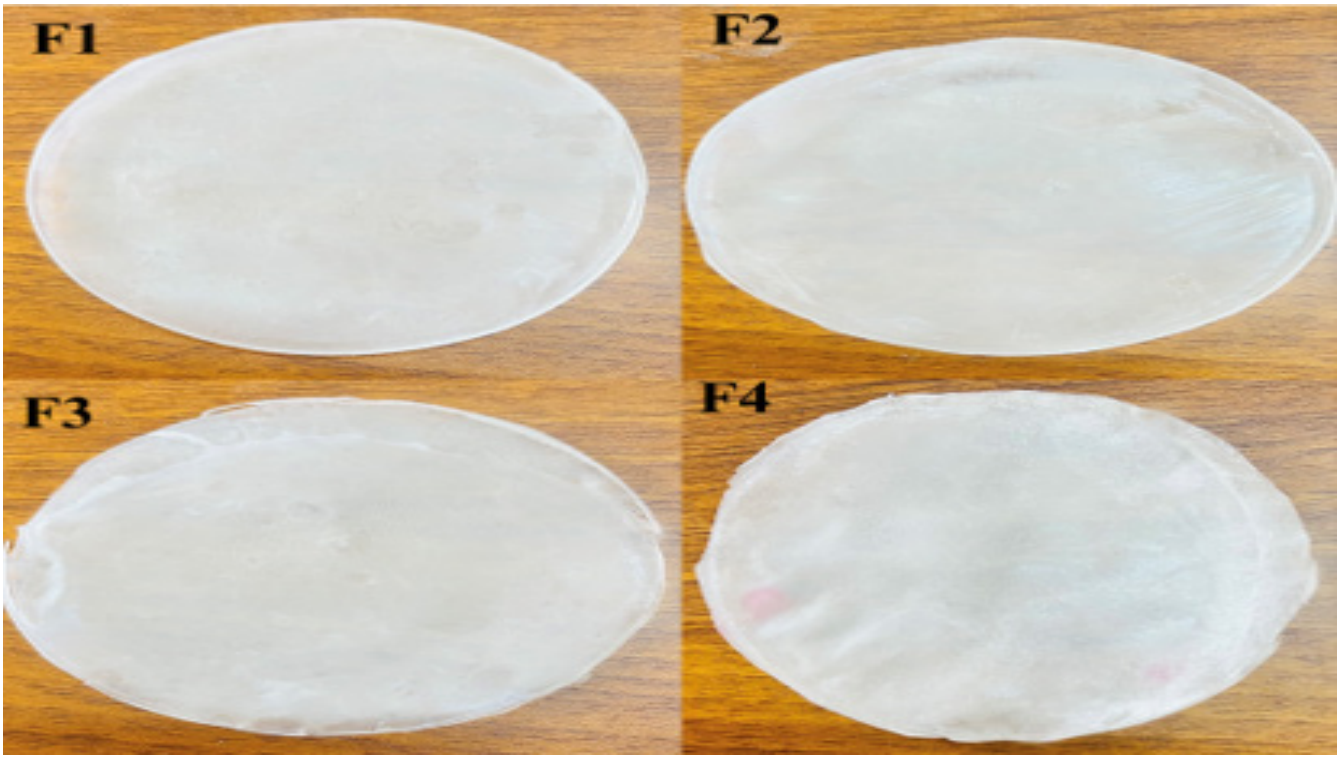



**Figure 5:** Drug-loaded transdermal patch formulations (F1-F4).

**Table 2: FTIR spectral data of Lincomycin Hydrochloride.**

| Observed Peak ($cm^{-1}$) | Reported Range ($cm^{-1}$) | Functional Group |
|---|---|---|
| 3448.77 | 3400-3500 | O-H / N-H stretching (hydroxyl or amine) |
| 3275.90 | 3200-3300 | N-H stretching (secondary amine) |
| 3291.61 | 3200-3500 | O-H stretching (alcohol) |
| 3021.60 | 3000-3100 | =C-H stretching (aromatic/ aliphatic) |
| 2955.88 | 2850-2960 | C-H stretching (alkane) |

## Folding Endurance

The folding endurance values of the patches ranged between 217±1.23 to 291±1.52, suggesting excellent flexibility and mechanical strength required for application on skin. Evaluation parameters of formulated patches are shown in Table 3.

## Thickness

The patch thickness ranged from 0.312±0.08 mm to 0.398±0.09 mm, demonstrating uniformity across formulations. Increased polymer concentration resulted in slightly thicker patches.

## Uniformity of Weight

Patch weights were consistent, ranging between 0.28±0.05 g and 0.37±0.07 g, ensuring reproducibility.

## Moisture Content

All formulations exhibited acceptable moisture content values between 0.481±0.01% and 2.312±0.01%, which help maintain patch flexibility and prevent brittleness.

## Surface pH

The surface pH of all formulations ranged from 5.6 to 6.4, which is within the skin's physiological range (4.5-6.5). This ensures that the patches are non-irritant and skin-compatible.

## Drug Content Uniformity

Drug content among all formulations ranged between 78.98±0.03% and 86.65±0.08%, indicating uniform drug distribution throughout the matrix and compliance with pharmacopeial limits.

## Antibacterial Activity (Zone of Inhibition)

Antibacterial activity was evaluated using the disc diffusion method against *Staphylococcus aureus* (ATCC 25923). The inhibition zone increased proportionally with drug concentration, indicating dose-dependent efficacy (Figure 6).

**1 mg disc:** 26±0.4 mm.

**3 mg disc:** 29±0.5 mm.

**5 mg disc:** 32±0.6 mm.

The Lincomycin HCl transdermal patch (50 mg) exhibited a significantly larger zone of inhibition (39±0.5 mm), confirming

sustained and potent antibacterial activity due to prolonged drug release.

## *In vitro* Drug Release Study

*In vitro* release studies were performed in phosphate buffer (pH 7.4) using the Franz diffusion cell method. The results demonstrated that drug release was inversely proportional to polymer concentration. Formulation F3 exhibited the highest cumulative drug release (78.44%), whereas F1 showed the lowest (67.92%) after 6 hr (Figure 7).

## Statistical Analysis and Design of Experiment (DOE)

A $2^2$ full factorial design was employed to evaluate the influence of polymer concentrations on the cumulative drug release of Lincomycin HCl transdermal patches. The independent factors were HPMC K100M ($X_1$) and PVA ($X_2$), each studied at two levels (low and high), while the dependent variable was the percentage cumulative drug release (Y) after 6 hr. Four formulations (F1-F4) were prepared to cover all combinations of the factor levels.

The cumulative drug release values demonstrated that drug diffusion decreases with increasing polymer concentrations, consistent with the expected behavior of hydrophilic polymer matrices, where higher polymer content forms a denser network that slows drug release.

## ANOVA Analysis

The factorial model was statistically analyzed using ANOVA to determine the significance of the factors. The model exhibited a high F-value (518.44) and a *p*-value of 0.0310, indicating statistical significance ($p<0.05$). Among the individual factors, PVA (A) showed a stronger effect on drug release than HPMC K100M (B) (Table 4).

## Model Summary Statistics

The model exhibited excellent predictability with $R^2=0.9990$, Adjusted $R^2=0.9971$, and Predicted $R^2=0.9846$, while the adequate precision (48.49) indicated a strong signal-to-noise ratio, confirming the suitability of the model for optimization.

## Regression Equation

The regression equation in terms of coded factors is:

$$Y=73.03-3.73A-1.53BY = 73.03 - 3.73A - 1.53BY=73.03-3.73A-1.53B$$

Where:

**Y** = % cumulative drug release.

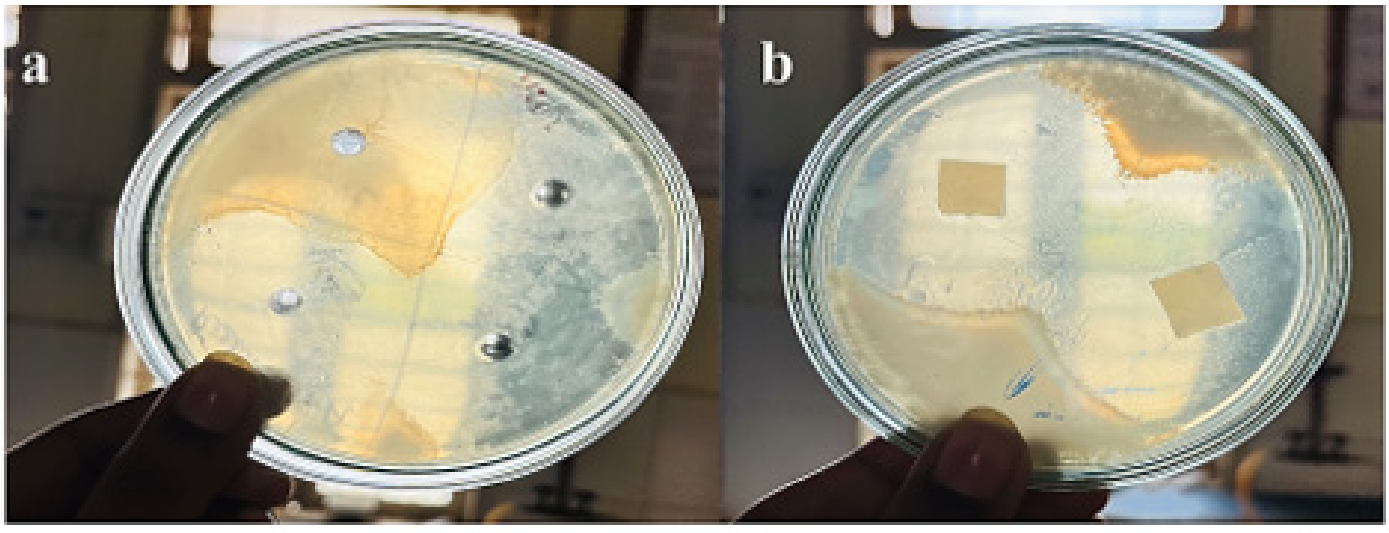
**A** = PVA concentration.

**B** = HPMC K100M concentration.

**Table 3: Evaluation of Lincomycin Hydrochloride Transdermal Patches.**

| Formulation Code | Folding Endurance | Thickness (mm) | Weight uniformity (g) | % Moisture Content | Surface pH | % Drug Content |
|---|---|---|---|---|---|---|
| F1 | 217±1.23 | 0.345±0.03 | 0.28±0.05 | 0.481±0.01 | 5.6 | 80.62±0.01 |
| F2 | 245±0.09 | 0.398±0.09 | 0.34±0.07 | 1.334±0.04 | 6.2 | 78.98±0.03 |
| F3 | 291±1.52 | 0.312±0.08 | 0.37±0.07 | 2.312±0.01 | 6.4 | 82.87±0.01 |
| F4 | 234±1.32 | 0.361±0.04 | 0.32±0.03 | 0.830±0.01 | 5.8 | 86.65±0.08 |

Mean±SD, *n*=3.




**Figures 6:** Zones of inhibition for a) Lincomycin Hydrochloride pure drug and b) transdermal patches.

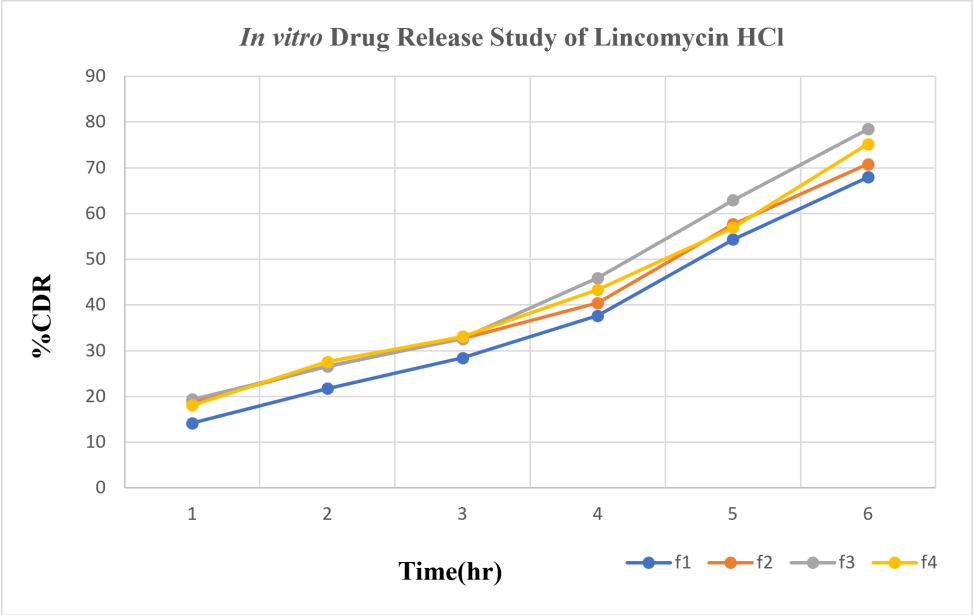



**Figure 7:** Cumulative drug release profile of all formulations over 6 hr.

**Table 4: ANOVA summary.**

| Source | Sum of Squares | $d_f$ | Mean Square | F-value | *p*-value | |
|---|---|---|---|---|---|---|
| Model | 64.80 | 2 | 32.40 | 518.44 | 0.0310 | Significant |
| PVA (A) | 55.50 | 1 | 55.50 | 888.04 | 0.0214 | |
| HPMC K100M (B) | 9.30 | 1 | 9.30 | 148.84 | 0.0521 | |
| Residual | 0.0625 | 1 | 0.0625 | — | — | |
| Total | 64.87 | 3 | — | — | — | |

The negative coefficients indicate that increasing either polymer reduces drug release, confirming the anticipated impact of matrix density on diffusion kinetics.

## Graphical Analysis

Contour plots (Figure 8) and 3D surface plots (Figure 9) illustrate the interaction between HPMC K100M and PVA on drug release. Maximum drug release occurred at lower polymer concentrations, while increasing either factor progressively decreased drug diffusion. These plots effectively demonstrate the combined effect of both polymers on cumulative release.

## Optimization of Formulation

Optimization using the desirability function targeted maximum drug release with minimal polymer content. The overlay plot (Figure 10) indicated the optimal formulation at:

The predicted drug release for this optimized combination was 73.03%, while the experimentally observed value was 75.87%, confirming model reliability.

The factorial design confirmed that both HPMC K100M and PVA significantly influence cumulative drug release. Higher polymer concentrations reduce drug release due to matrix densification, whereas lower concentrations allow faster diffusion. The optimized patch achieved a balance between mechanical integrity and drug release, providing sustained delivery suitable for antimicrobial applications. The DOE approach demonstrated robust predictive capability, ensuring formulation reproducibility and efficiency.

# DISCUSSION

The present study focused on the formulation and evaluation of Lincomycin HCl transdermal patches to improve antimicrobial efficacy and overcome the limitations of oral delivery. Preformulation studies confirmed the $\lambda_{max}$ of Lincomycin HCl at 204 nm, and the calibration curve exhibited linear absorbance in the 10-60 µg/mL range, validating the method for quantitative analysis. FTIR spectroscopy indicated no significant drug-excipient interactions, confirming chemical compatibility of HPMC K100M, PVA, propylene glycol, and glycerine with Lincomycin HCl, consistent with previous reports on polymer-based transdermal systems.

All prepared patches were smooth, flexible, and translucent, with folding endurance ranging from 217±1.23 to 291±1.52 folds, demonstrating excellent mechanical integrity suitable for handling and application. Patch thickness and weight were

uniform across formulations, while moisture content (0.48-2.31%) and surface pH (5.6-6.4) were within acceptable ranges, ensuring skin compatibility and stability. Drug content analysis revealed uniform dispersion (78.98-86.65%), fulfilling pharmacopoeial standards and indicating successful incorporation of Lincomycin HCl into the polymer matrix.

*In vitro* release studies demonstrated that cumulative drug release ranged from 67.92% to 78.44% over 6 hr, with F3 (lower polymer concentration) showing the highest release. This trend correlates with the hydrophilic nature and network density of the polymers, where higher polymer content creates a denser matrix, slowing drug diffusion. The $2^2$ factorial design and DOE analysis confirmed the significant effect of both PVA and HPMC K100M

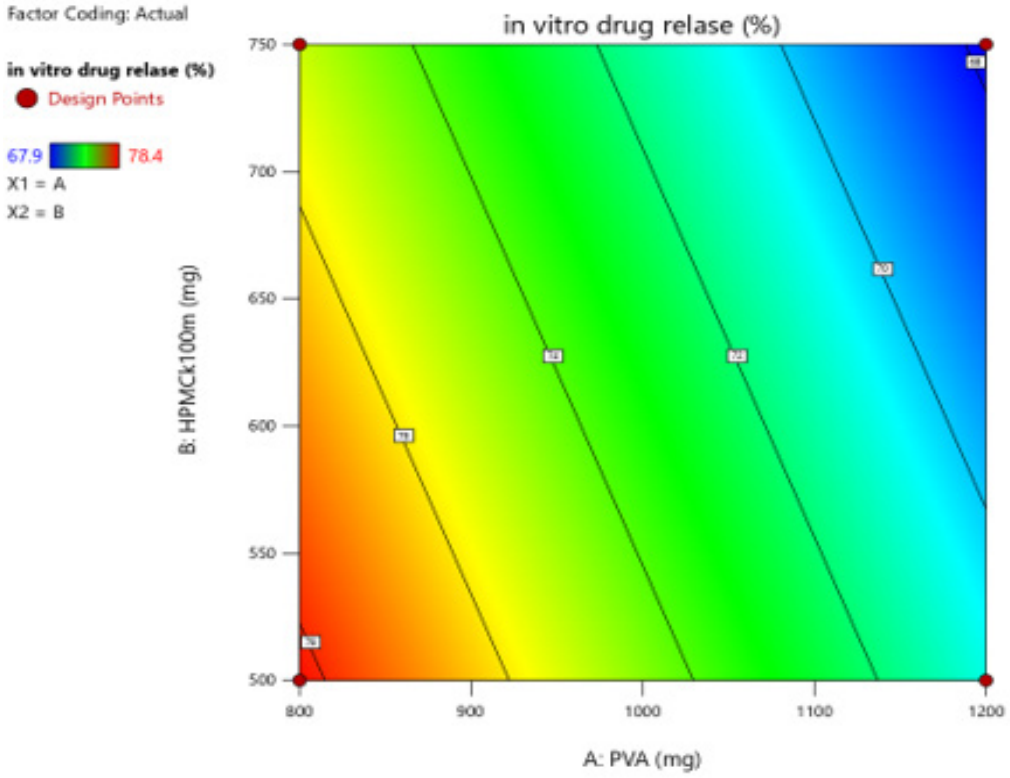



**Figure 8:** Contour plot showing the effect of HPMC K100M and PVA on % cumulative drug release.

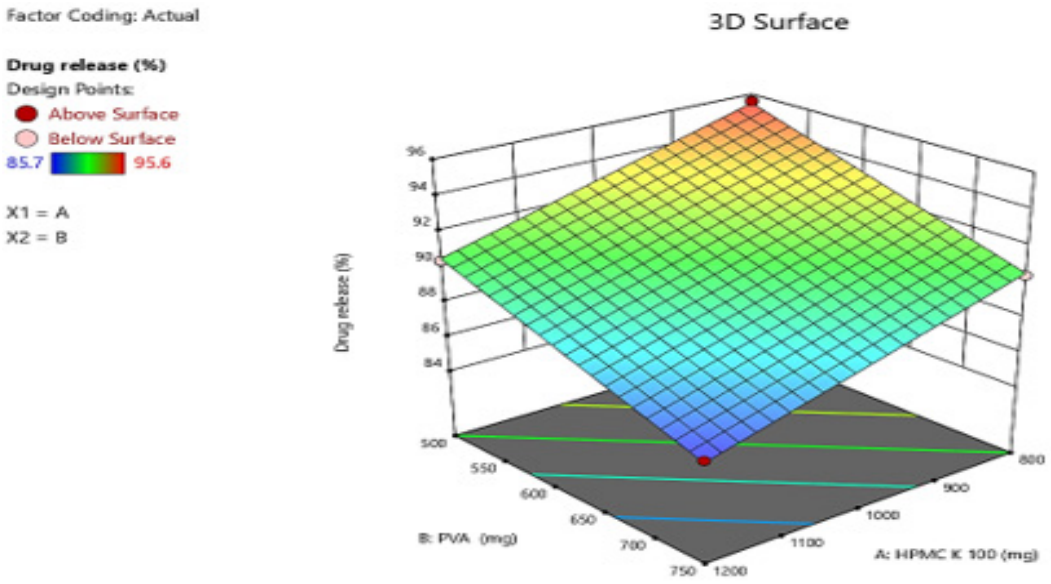



**Figure 9:** 3D response surface plot showing % cumulative drug release as a function of HPMC K100M and PVA concentrations.

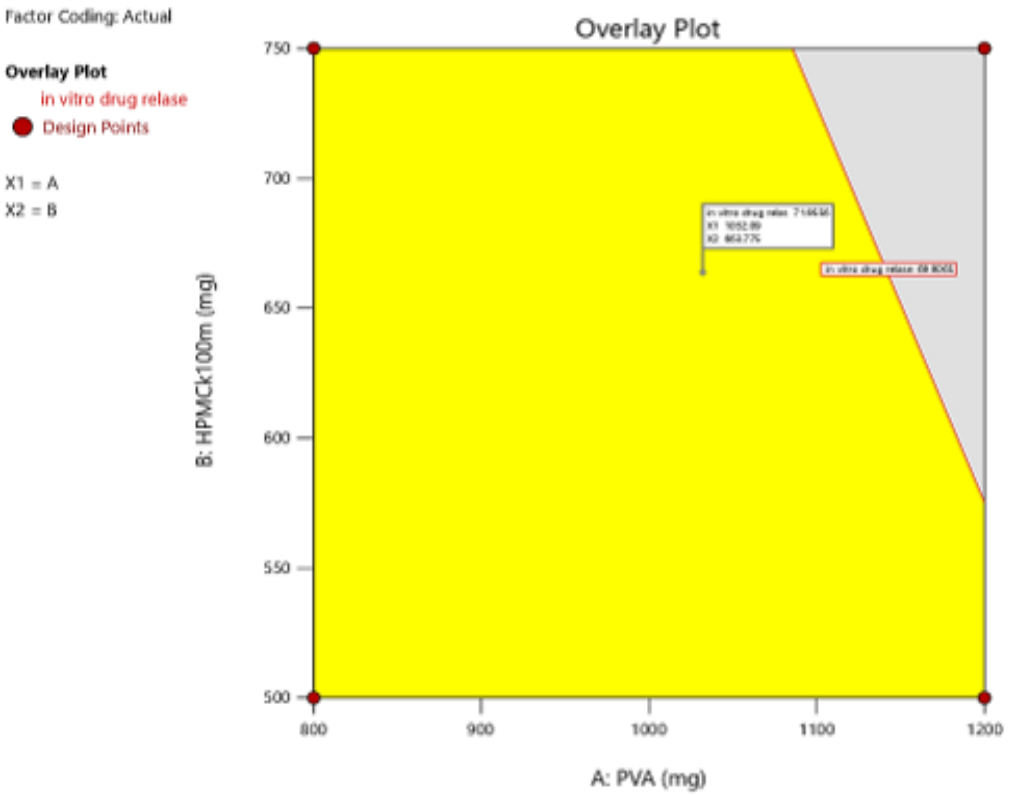



**Figure 10:** Overlay plot for optimized formulation indicating the ideal polymer range.

on drug release, with PVA exerting a more prominent influence. The regression equation:

$$(Y=73.03 - 3.73A - 1.53B)$$

3D response plots illustrated that drug release decreases as polymer concentrations increase, in agreement with similar studies on HPMC and PVA-based transdermal systems.

Antimicrobial evaluation against *Staphylococcus aureus* demonstrated a clear dose-dependent zone of inhibition. The optimized transdermal patch (50 mg drug loading) produced a zone of 39±0.5 mm, exceeding the inhibition observed with equivalent drug-loaded discs, indicating enhanced localized antibacterial efficacy. This improvement is likely due to sustained release from the polymeric matrix, ensuring prolonged exposure of bacteria to the drug while reducing systemic absorption and side effects.

The optimization process identified the ideal formulation (HPMC K100M 1032 mg, PVA 663 mg) that balanced mechanical stability with maximal drug release. The observed cumulative release (75.87%) closely matched the predicted value (73.03%), validating the factorial model and demonstrating the reliability of DOE for transdermal formulation development. Overall, these results suggest that Lincomycin HCl transdermal patches provide a viable alternative to oral therapy, offering sustained local delivery, reduced systemic toxicity, and potential to mitigate antimicrobial resistance.

In summary, the study highlights the successful formulation of stable, effective transdermal patches with desirable physicochemical properties, optimized drug release, and significant antibacterial activity. The integration of DOE allowed systematic optimization, providing a reproducible and efficient platform for antimicrobial patch development.

## CONCLUSION

The present study successfully developed and evaluated Lincomycin HCl transdermal patches using HPMC K100M and PVA as polymeric matrices, with propylene glycol as a permeation enhancer and glycerine as a plasticizer. Preformulation studies confirmed drug stability and compatibility with excipients, while physicochemical evaluation demonstrated uniformity in thickness, weight, folding endurance, moisture content, surface pH, and drug content, ensuring mechanical integrity and skin compatibility. *In vitro* drug release studies revealed that polymer concentration significantly influenced cumulative drug release, with lower polymer levels promoting faster diffusion. Factorial design and statistical optimization identified an optimized formulation (HPMC K100M 1032 mg, PVA 663 mg), achieving a cumulative release of 75.87%, closely matching predicted values, confirming model reliability. Antimicrobial studies showed that the patches exhibited significant dose-dependent antibacterial

activity against *Staphylococcus aureus*, demonstrating their potential for localized, sustained antimicrobial therapy. Overall, Lincomycin HCl transdermal patches represent a promising alternative to conventional oral therapy, offering improved patient compliance, sustained drug release, reduced systemic side effects, and potential to mitigate antimicrobial resistance. This study provides a robust formulation and evaluation strategy that can be applied to other antibiotics and therapeutic agents for enhanced transdermal delivery.

## ACKNOWLEDGEMENT

The author would like to thank all the faculty members of KLE College of Pharmacy, Hubballi for providing necessary support.

## ABBREVIATIONS

**HPMC:** Hydroxypropyl Methylcellulose; **PVA:** Polyvinyl Alcohol; **HCl:** Hydrochloride; **FTIR:** Fourier Transform Infrared Spectroscopy; **$\lambda_{max}$:** Wavelength of Maximum Absorbance; **UV:** Ultraviolet; **SD:** Standard Deviation; **%CDR:** Percent Cumulative Drug Release; **DOE:** Design of Experiment; **ANOVA:** Analysis of Variance; **rpm:** Revolutions per Minute; **ºC:** Degree Celsius; **nm:** Nanometer; **µg/mL:** Microgram per Milliliter; **PBS:** Phosphate Buffered Saline; **IP:** Indian Pharmacopoeia; **API:** Active Pharmaceutical Ingredient; **$R^2$:** Coefficient of Determination; **CI:** Confidence Interval; **PI:** Prediction Interval; **ATCC:** American Type Culture Collection; **PDA:** Polymeric Drug Adhesive; **%MC:** Percentage Moisture Content.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## REFERENCES

Akombaetwa, N., Ilangala, A. B., Thom, L., Memvanga, P. B., Witika, B. A., & Buya, A. B. (2023). Current advances in lipid nanosystems intended for topical and transdermal drug delivery applications. Pharmaceutics, 15(2), 656. https://doi.org/10.3390/pharmaceutics15020656

Alkilani, A. Z., McCrudden, M. T., & Donnelly, R. F. (2024). Transdermal drug delivery: Innovative strategies and recent developments. Pharmaceuticals, 17(10), 1346. https://doi.org/10.3390/ph17101346

Arora, P., & Mukherjee, B. (2002). Design, development, physicochemical, and *in vitro* and *in vivo* evaluation of transdermal patches containing diclofenac diethylammonium salt. Journal of Pharmaceutical Sciences, 91(9), 2076-2089. https://doi.org/10.1002/jps.10190

Ganjoo, R., Soni, S., Ram, V., & Verma, A. (2016). Medium molecular weight chitosan as a carrier for delivery of lincomycin hydrochloride from intra-pocket dental film: Design, development, *in vitro* and *ex vivo* characterization. Journal of Applied Pharmaceutical Science, 6(10), 8-19. https://doi.org/10.7324/JAPS.2016.601002

Ghaferi, M., Alavi, S. E., Phan, K., Maibach, H., & Mohammed, Y. (2024). Transdermal Drug Delivery Systems (TDDS): Recent advances and failure modes. Molecular Pharmaceutics, 21(11), 5373-5391. https://doi.org/10.1021/acs.molpharmaceut.4c00423

Gunst, R. F., & Mason, R. L. (2009). Fractional factorial design. Wiley Interdisciplinary Reviews: Computational Statistics, 1(2), 234-244. https://doi.org/10.1002/wics.19

Hardainiyan, S. W., Kumar, K. R., Nandy, B. C., & Saxena, R. I. (2017). Design, formulation and *in vitro* drug release from transdermal patches containing imipramine hydrochloride as model drug. International Journal of Pharmacy and Pharmaceutical Sciences, 9(6), 220-225.

Najim, S. S. (n.d.). Spectrophotometric determination of lincomycin in pharmaceutical medication.

Naveed, S., Shah, S. N., Qamar, F., Waheed, N., & Nazeer, S. (2014). Simple UV spectrophotometric assay of lincomycin. International Journal of Pharmaceutical Research and Drug Development, 1(2), 10-12.

Obana, N., Takada, H., Crowe-McAuliffe, C., Iwamoto, M., Egorov, A. A., Wu, K. J., Chiba, S., Murina, V., Paternoga, H., Tresco, B. I., & Nomura, N. (2023). Genome-encoded ABCF factors implicated in intrinsic antibiotic resistance in Gram-positive bacteria: VmlR2, Ard1 and CplR. Nucleic Acids Research, 51(9), 4536-4554. https://doi.org/10.1093/nar/gkad288

Park, S., Han, U., Choi, D., & Hong, J. (2018). Layer-by-layer assembled polymeric thin films as prospective drug delivery carriers: Design and applications. Biomaterials Research, 22(1), 29. https://doi.org/10.1186/s40824-018-0135-2

Prabhakara, P., Koland, M., Vijaynarayana, K., Harish, N. M., Shankar, G., Ahmed, M. G., Narayana, C., & Satyanarayana, D. (2010). Preparation and evaluation of transdermal patches of papaverine hydrochloride. International Journal of Research in Pharmaceutical Sciences, 1(3), 259-266.

Rusu, A., Moga, I. M., Uncu, L., & Hancu, G. (2023). The role of five-membered heterocycles in the molecular structure of antibacterial drugs used in therapy. Pharmaceutics, 15(11), 2554. https://doi.org/10.3390/pharmaceutics15112554

Shivalingam, M. R., Balasubramanian, A. R., & Ramalingam, K. O. (2021). Formulation and evaluation of transdermal patches of pantoprazole sodium. International Journal of Applied Pharmaceutics, 13(5), 287-291.

Wokovich, A. M., Shen, M., Doub, W. H., Machado, S. G., & Buhse, L. F. (2010). Release liner removal method for transdermal drug delivery systems (TDDS). Journal of Pharmaceutical Sciences, 99(7), 3177-3187. https://doi.org/10.1002/jps.22057

World Health Organization. (2020). Antimicrobial resistance: Global report on surveillance. Geneva: World Health Organization.

Zaid Alkilani, A., Musleh, B., Hamed, R., Swellmeen, L., & Basheer, H. A. (2023). Preparation and characterization of patch loaded with clarithromycin nanovesicles for transdermal drug delivery. Journal of Functional Biomaterials, 14(2), 57. https://doi.org/10.3390/jfb14020057

**Cite this article:** Akki P, Yadav MM, Dasankoppa FS, Swamy AHV, Kumar MP, *et al*. Design, Optimization, and Evaluation of Lincomycin Hydrochloride Transdermal Patches for Sustained Drug Release and Improved Antimicrobial Efficacy. Int. J. Pharm. Investigation. 2026;16(4):1434-44.