International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 31, Issue 4, April 2025 **ijppr.humanjournals.com** ISSN: 2349-7203

Transdermal Delivery System for Cefixime Trihydrate: Formulation and Evaluation of a Topical Gel for Wound Infections

J. Gomathi[1]*, S. Fathima Zeenath[2], N. Lavanya[2], S. Sharmila[2], M.Vijayalakshmi[2], S.P.Muralidharan[3]

1* Associate Professor, Department of Pharmaceutics, C. L. Baid Metha College of Pharmacy, Affiliated to The Tamil Nadu, Dr.M.G.R. Medical University, Chennai-600097, Tamil Nadu, India.

2 UG students, Department of Pharmaceutics, C. L. Baid Metha College of Pharmacy, Affiliated to The Tamil Nadu, Dr.M.G.R. Medical University, Chennai-600097, Tamil Nadu, India.

3 Assistant Professor, Department of Pharmacognosy, C. L. Baid Metha College of Pharmacy, Affiliated to The Tamil Nadu, Dr.M.G.R. Medical University, Chennai-600097, Tamil Nadu, India

Received: 2025-4-01 Revised: 2025-4-12 Accepted: 2025-4-20

ABSTRACT

Objective: This study aimed to develop and evaluate a novel transdermal gel formulation of cefixime trihydrate, a third-generation cephalosporin, for treating bacterial wound infections like diabetic foot ulcers. The formulation uses a polymer-based hydrogel system to enhance drug permeability, ensure controlled release, and improve patient compliance compared to conventional therapies. **Methods:** A combination of HPMC K100M and Sodium CMC was used as gelling agents to improve drug stability and bioavailability. Three formulations (F1, F2, F3) were characterized for color, syneresis, spreadability, pH, drug content, and rheological properties. In-vitro drug release and antibacterial efficacy tests were conducted. **Results:** F3 showed the best results, with an optimized pH of 6.4, high drug content (99.4%), superior spreadability (22.5 cm), and prolonged drug release (98.27% over 8 hours). It demonstrated enhanced antibacterial activity against Staphylococcus aureus, Propionibacterium acne, and Pseudomonas aeruginosa. The formulation maintained stability over 90 days with minimal variations, ensuring its suitability for extended use. **Conclusion:** The novel cefixime trihydrate gel exhibits superior physicochemical properties, controlled release, and enhanced antibacterial efficacy, making it a promising candidate for wound infection management. Further in-vivo studies are recommended to validate its clinical use in transdermal antibiotic therapy.

Keywords: Cefixime trihydrate, Novel antibiotic gel, Transdermal drug delivery, Wound infection, antibacterial activity, Controlled drug release.

INTRODUCTION

The skin, the largest organ of the human body, covers approximately 2 square meters and has a thickness ranging between 2.69 ± 0.28 mm. It performs vital functions such as thermoregulation, acting as a barrier against pollutants and ultraviolet radiation, and preventing water loss. The skin consists of two main layers: the epidermis and dermis. The epidermis includes strata like the stratum lucidum, stratum granulosum, stratum spinosum, and stratum basale, while the dermis contains blood vessels, lymphatic vessels, and nerve endings that support skin function. Skin permeability allows drug delivery through the transepidermal and transfollicular routes [1,2].

Wound healing is a complex process that restores skin integrity following injury, involving four overlapping stages: hemostasis, inflammation, proliferation, and remodeling. Hemostasis includes vascular constriction, platelet aggregation, and fibrin clot formation to develop a protective scab. Growth factors such as transforming growth factor-β and epidermal growth factor promote tissue repair and immune cell migration. The inflammatory phase supports capillary growth, collagen synthesis, and extracellular matrix remodeling [3,4].

Chronic wounds, such as venous ulcers and ischemic wounds, disrupt normal tissue regeneration and are prone to bacterial colonization, delaying healing. These conditions increase medical costs due to advanced wound care, including tissue-engineered

skin substitutes and medicated dressings. Despite advancements in wound management, effective treatments for chronic wounds are still limited. Recent research is exploring alternative and traditional therapies to enhance healing [5,6].

Transdermal drug delivery allows non-invasive therapy through passive diffusion of therapeutic agents across the skin barrier. Gels, which are water-based semi-solid systems, serve as effective carriers for topical drug delivery [7,8]. They are non-greasy, easy to apply, and widely used for ophthalmic, rectal, vaginal, and dermatological conditions, including wound care. Cefixime trihydrate, a third-generation cephalosporin, exhibits broad-spectrum antibacterial activity and is being investigated for its potential in topical gel formulations for wound healing [9,10].

MATERIALS AND METHODS

MATERIALS

Cefixime trihydrate was procured as a gifted sample from Logus Laboratories Pvt. Ltd. All other chemicals were purchased from SD Fine-Chem Limited. The reagents used complied with laboratory specifications.

METHODS

Pre-Formulation Studies

Organoleptic characters

The organoleptic properties of Cefixime trihydrate were evaluated and documented [11].

Solubility studies

Excess cefixime trihydrate was added to 10 mL of each solvent (ethanol, DMSO, propylene glycol, and glycerin) and stirred at room temperature for 24 hours. The solutions were filtered, and drug concentration was determined using UV-visible spectroscopy [12].

Calibration curve of cefixime trihydrate

Preparation of standard curve for cefixime trihydrate

A standard stock solution of cefixime trihydrate (100 µg/ml) was prepared by dissolving 10 mg in 20 ml methanol and diluting to 100 ml with phosphate buffer pH 7.4. Serial dilutions (2, 4, 6, 8, and 10 µg/ml) were made using phosphate buffer pH 7.4, and absorbance was measured at 283 nm using a UV-visible spectrophotometer (phosphate buffer pH 7.4 as blank). Averages of 3 sets of values were used to plot the standard curve [13].

FTIR Study:

The FTIR imaging in the present investigation was carried out using a (Bruker, Alpha). KBr pellet method was used for sample preparation for FTIR study. All samples were subjected to FTIR spectroscopic studies to determine the functional groups of the samples. The scanning range was 400-4000 cm-1 for and the resolution was 4cm-1 [14].

Formulation of Cefixime Trihydrate Gel :

HPMC K100 and Sodium CMC, as per Table 1, are gradually added to warm distilled water (60°C) with continuous stirring to form a uniform polymer mixture. Simultaneously, Cefixime Trihydrate (3% w/v) is dissolved in propylene glycol (5% w/v) and glycerin (5% w/v), followed by ethanol (1.5% w/v) with stirring. This drug solution is slowly incorporated into the polymer dispersion under continuous stirring for 1 hour. Tween 80 (0.5% w/v) is added as a surfactant, while methyl paraben (0.07% w/v) and propyl paraben (0.04% w/v) serve as preservatives. The pH is adjusted to 5.5-6.5 using triethanolamine (0.5% w/v). Gel formation occurs at 4°C, followed by vacuum treatment for 2 hours to remove air bubbles. The final gel is inspected for homogeneity, clarity, color, and pH before storage.

International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 31, Issue 4, April 2025 ijppr.humanjournals.com ISSN: 2349-7203

Table 1 : Formulation of Cefixime trihydrate gel

Ingredients	F1	F2	F3
Cefixime trihydrate (g)	3	3	3
HPMC K100 (g)	0.5	1	1.5
Sodium CMC (g)	0 .5	0.5	0.5
Propylene glycol (g)	5	5	5
Ethanol (g)	1.5	1.5	1.5
Methyl paraben (g)	0.07	0.07	0.07
Propyl paraben (g)	0.04	0.04	0.04
Tween 80 (g)	0.5	.5	.5
Glycerin (g)	5	5	5
Triethanolamine (g)	0.5	0.5	0.5
Water (ml)	83.4	82.9	82.4
Total (gm)	100	100	100

POST EVALUATION STUDIES OF TRANSDERMAL GELS

Clarity test:

Clarity of various formulations was determined by visual inspection under black and white background and it was graded as follows: turbid +; clear ++; very clear (glassy) +++ [16].

Homogeneity test:

All developed gels were tested for homogeneity by visual inspection after the gels have been set in the container. They were tested for their appearance and presence of any aggregates [17].

pH :

2.5 gm of gel was accurately weighed and dispersed in 25ml of distilled water. The pH of the dispersion was determined by using digital pH meter [18].

Spreadability:

It was determined by wooden block and glass slide apparatus. For the determination of spreadability, excess of sample was applied in between two glass slides and then was compressed to uniform thickness. The weight (50gm) was added to pan. The time required to separate the two slides i.e., the time in which upper glass slide moves over the lower plates was taken as a measure of spreadability (S) [19].

$$S = M . L / T$$

Where M = wt. tied to upper slide

L = length of glass slides

T = time taken to separate the slides

Drug Content

1 gm of prepared gel was dissolved in a 100 ml of phosphate buffer pH 7.4 and taken in a volumetric flask. It was shaken for 2 h on a mechanical shaker to get complete solubility of the drug. The solution was then filtered using Millipore filter (0.45 µm). After suitable dilution of the filtrate, the absorbance was recorded using UV-visible spectrophotometer at the λ max at about 283 nm using phosphate buffer pH 7.4 as blank [20].

Rheological Study

Viscosity was determined by using Brookfield viscometer. Viscosity measurements were carried out at room temperature (25- 27°C) using a Brookfield viscometer (Model RVTDV II, Brookfield Engineering Laboratories, Inc, Stoughton, MA) [21].

***In-Vitro* Permeation Study**

The in vitro release study was performed using a Franz diffusion cell with a cellophane membrane (sac). The phosphate buffer (pH 7.4) serves as the receptor medium. The gel sample is applied onto the membrane and fixed between the donor and receptor compartments of a quality diffusion cell. The receptor compartment contains 100 mL of phosphate buffer (pH 7.4). The temperature of the diffusion medium is thermostatically maintained at 37º ± 0.5ºC using a surrounding water jacket. The medium is continuously stirred at 600 rpm using a magnetic stirrer. At predetermined intervals, samples are withdrawn and replaced with an equal volume of freshly prepared fluid. The withdrawn samples are analyzed spectrophotometrically at 283 nm against their blank [22].

Determination of antibacterial activity

i) Preparation of Inoculum: Fresh bacterial cultures of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Propionibacterium acnes* were suspended in sterile water for 24 hours to obtain a uniform microbial suspension.

ii) Preparation of Nutrient Agar: Beef extract (3.0 g), peptone (5.0 g), and agar (15.0 g) were dissolved in distilled water, stirred for 2 minutes at boiling, and sterilized at 121°C for 15 minutes in an autoclave.

iii) Zone of Inhibition Determination: The agar well diffusion method was used. Liquefied nutrient agar (15–20 ml) was cooled to 42–45°C, inoculated with bacterial culture, and poured into sterile petri plates to solidify. Gel formulations were applied to the agar wells, and plates were incubated at 37°C ± 1°C for 24 hours to assess antibacterial activity [23].

Stability Study

The stability study was carried out for the most satisfactory formulation as per the ICH guidelines. The selected formulation subjected to a stability testing for the period of three months as per ICH norms at a temperature of 25˚±2°C with relative humidity RH= 60±5% and 40º ± 2°C with relative humidity RH= 75±5%. The best formulation was analyzed for the changes in appearance, pH, percentage of drug content and in-vitro diffusion study [24].

RESULTS AND DISCUSSION

Preformulation Studies

Organoleptic characters

The organoleptic evaluation confirmed cefixime trihydrate's authenticity and purity as a pale yellow powder with a bitter taste and unpleasant odor. Its solubility in ethanol, DMSO, propylene glycol, and glycerin aligns with standard properties, ensuring pharmaceutical suitability (Table 2).

TABLE 2: Test for pure cefixime trihydrate drug

Tests	Results of Analysis	Inference
Colour	Pale yellow powder	Complies with data
Odour	Unpleasant odour	Complies with data
Taste	Bitter taste	Complies with data
Solubility	Freely soluble in ethanol, DMSO,propylene glycol and glycerin	Complies with data

Solubility studies

Cefixime trihydrate showed the highest solubility in DMSO (30 mg/mL), followed by propylene glycol, while ethanol and glycerin had lower solubility. These results as shown table 3.

International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 31, Issue 4, April 2025 ijppr.humanjournals.com ISSN: 2349-7203

TABLE 3: Solubility studies of pure drug

S.NO	SOLVENT	SOLUBILITY
1.	Ethanol	5mg/mL
2.	DMSO	30mg/mL
3.	Propylene glycol	10mg/mL
4.	Glycerin	5mg/Ml

Calibration curve

A calibration curve for cefixime trihydrate at 283 nm showed a strong linear relationship ($y = 0.070x + 0.003$, $R^2 = 0.999$), confirming adherence to Beer-Lambert's law. The minimal intercept indicates negligible systematic error, while the slope reflects good sensitivity. The method is reliable for quantitative analysis, with accuracy supported by data consistency, though further validation would enhance reliability. Results are shown in Table 4 and Figures 1 and 2.

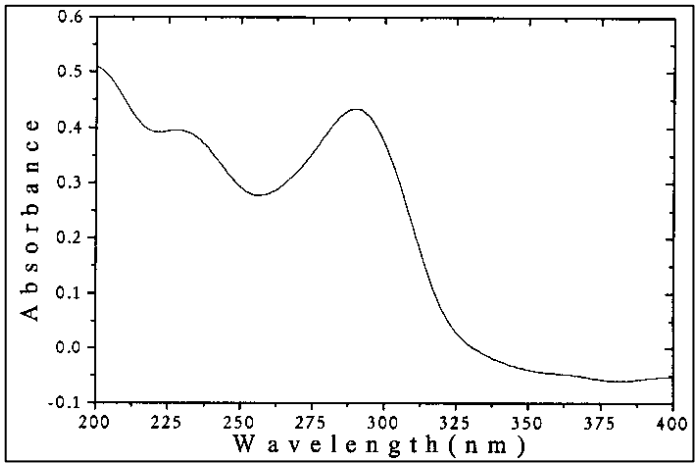

Figure 1: λmax of Cefixime trihydrate

Table 4: Standard curve of cefixime trihydrate

S.NO	Concentration[µg/ml]	Absorbance[nm]
1	2	0.142
2	4	0.284
3	6	0.431
4	8	0.574
5	10	0.702

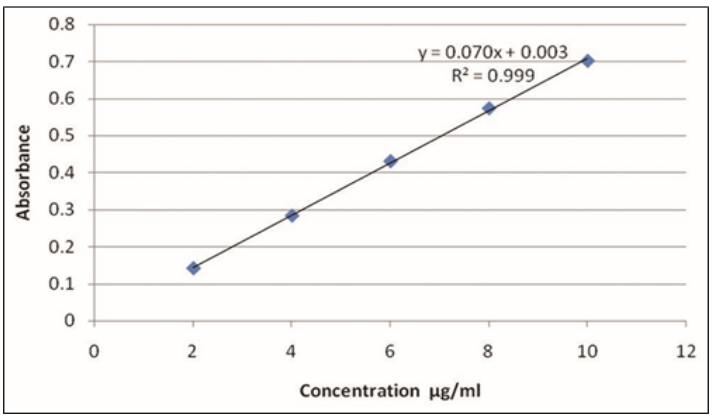

Figure 2 :Calibration curve of cefixime trihydrate

International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 31, Issue 4, April 2025 **ijppr.humanjournals.com** ISSN: 2349-7203

FTIR STUDY

The FTIR analysis of Cefixime Trihydrate (CFX) standard confirmed key functional groups with characteristic peaks. Formulation F3 exhibited similar peaks without significant shifts, indicating no interaction between the drug and excipients as shown in figures 3 and 4. The consistency in absorption bands suggests that the formulation maintains the drug's physicochemical properties, stability, and bioavailability, ensuring its therapeutic efficacy.

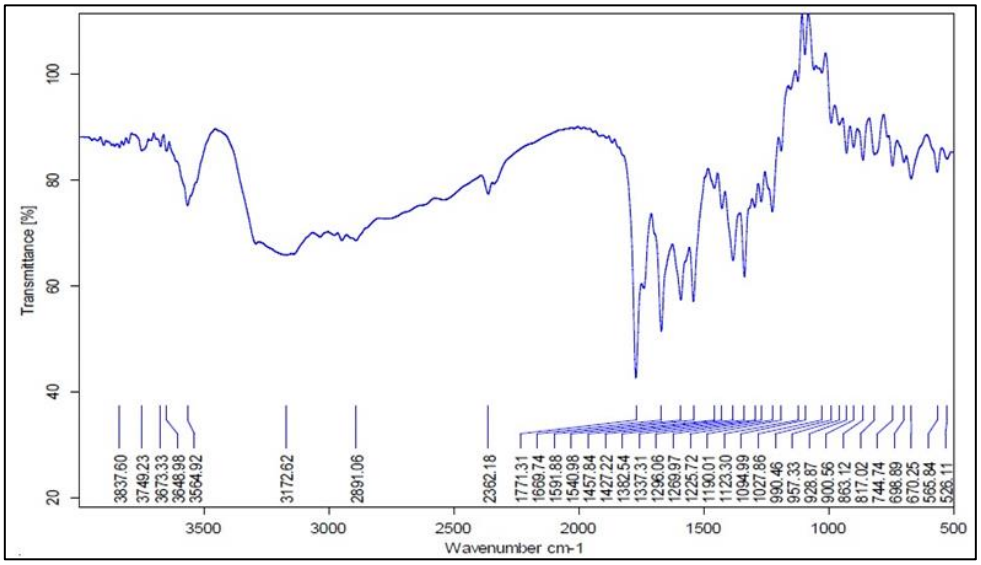

Figure 3: FTIR Spectrum of pure drug of cefixime Trihydrate

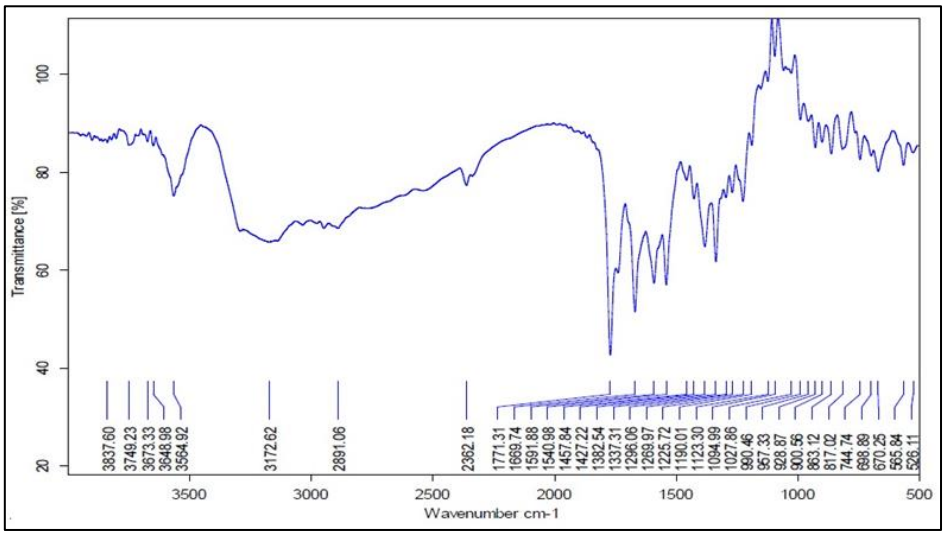

Figure 4: FTIR Spectrum of Formulated Cefixime Trihydrate Gel (F3)

Formulation of Cefixime Trihydrate Gel

The prepared Cefixime Trihydrate gel was successfully formulated using a polymeric base composed of HPMC K100 and Sodium CMC**,** which provided the required viscosity and consistency. The incorporation of the drug solution into the polymer matrix was facilitated by continuous stirring, ensuring a homogeneous dispersion of active ingredients.

International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 31, Issue 4, April 2025 ijppr.humanjournals.com ISSN: 2349-7203

POST EVALUATION STUDIES OF CEFIXIME TRIHYDRATE GELS

Clarity test

All formulations were free from visible particles**,** confirming proper dispersion. Among the formulations, F1 and F2 were clear, while F3 appeared very clear**.** The results are shown in Table 5.

Homogeneity test

All developed gels (F1-F3) showed good homogeneity with absence of lumps. The developed preparations were much clear and transparent. The consistency test confirmed uniform viscosity across the formulations, with F3 showing the excellent. The results are shown in Table 5.

pH : The pH of the formulated gels (F1, F2, and F3) was measured using a digital pH meter (average of three readings). Results (Table 5) showed pH values ranged from 6.0 to 6.4, within the acceptable range for topical formulations (typically 5.5–6.5), ensuring skin compatibility. Slight pH variations may be due to differences in excipient composition and concentration.

Spreadability test : Spreadability evaluation showed a progressive increase across formulations: F1 (19.7±0.57 mm), F2 (20.3±0.57 mm), and F3 (22.5±0.20 mm) (Table 5). The differences were statistically significant ($p < 0.05$), suggesting variations in physical properties. F3's higher spreadability may indicate better gel consistency, potentially from higher polymer concentration.

Drug content

Drug content analysis of gel formulations was conducted using a UV-visible spectrophotometer (283 nm). Results (Table 5) showed high drug content, confirming uniform distribution: F1 (96.3±0.05%), F2 (97.5±0.05%), and F3 (99.4±0.10%). Differences were statistically significant, with F3 showing the highest content.

Table 5: Post Evaluation Parameters of Formulated Cefixime Trihydrate Gel

Formulation code	Colour and appearance	clarity	Homogeneity	Spreadability [cm] *	pH*	Drug content(%) *
F1	Yellow and opaque	++	Good	19.7±0.57	6.2±0.18	96.3±0.05
F2	Yellow and transparent	++	Good	20.3±0.57	6.0±0.15	97.5±0.05
F3	Yellow and transparent	+++	Excellent	22.5±0.20	6.4±0.14	99.4±0.10

***** (mean n ± 3 SD)

Rheological study

The viscosity values of the formulations were 23230 Cp (F1), 20800 Cp (F2), and 15900 Cp (F3)**.** F1 exhibited the highest viscosity**,** indicating stronger intermolecular interactions, while F3 had the lowest, suggesting better spreadability but potentially lower structural integrity. The differences could be due to variations in polymer concentration as shown in table 6.

Table 6: Rheological properties of cefixime trihydrate gels

Formula No.	Viscosity (Cp) (ŋ)
F1	23230
F2	20800
F3	15900

In vitro Diffusion study of cefixime trihydrate gels

The in-vitro diffusion release study of cefixime trihydrate gel formulations (F1, F2, F3) in phosphate buffer (pH 7.4) at 37°C ± 0.5°C showed varying drug release due to different HPMC K100 and Sodium CMC ratios. Increasing HPMC K100 (F1 to F3) enhanced controlled release. F1 (1:1 ratio) showed more controlled release, while F2 (2:1 ratio) displayed moderate improvement.

F3 (3:1 ratio) exhibited the highest drug release, indicating faster diffusion and polymer erosion. The results highlight the significant impact of polymer ratio on drug release kinetics, with F3 achieving the most efficient release (Table 7, Figure 5).

Table 7: *In vitro* diffusion studies data of cefixime trihydrate gels

	% cumulative drug release		
Time in minutes	**F1**	**F2**	**F3**
30	79.10	81.45	84.45
60	81.38	83.29	86.45
90	84.93	86.76	92.13
120	86.48	87.39	94.39
240	88.41	89.10	98.27

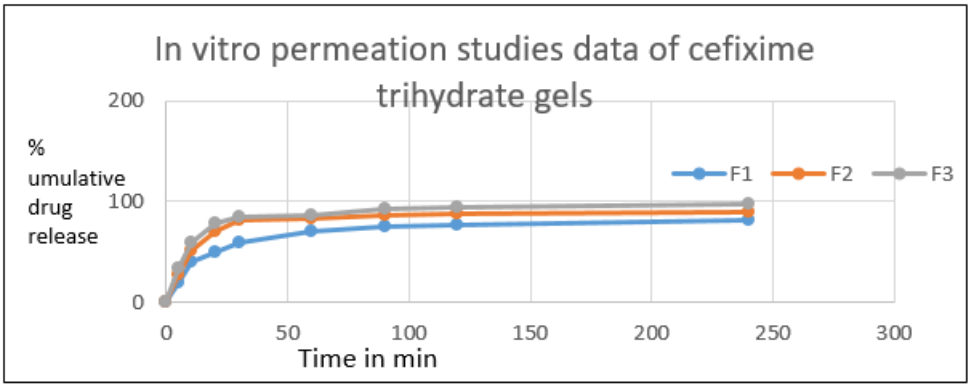

Figure 5: *In vitro* diffusion studies data of cefixime trihydrate gels

Determination of antibacterial activity of cefixime trihydrate gels

Three formulations (F1, F2, F3) with varying HPMC K100 and sodium CMC concentrations were tested for antimicrobial activity. F3 showed the highest activity: 32.00 ± 1.63 mm (S. aureus), 12.33 ± 0.94 mm (P. aeruginosa), and 33.33 ± 1.24 mm (P. acne). Gram-negative bacteria showed lower sensitivity due to membrane resistance. F3 demonstrated the best antibacterial efficacy, making it suitable for dermatological applications (Table 8).

Table 8: Evaluation of of cefixime trihydrate gels for Antibacterial activity.

Zone of Inhibition (mm)	Staphylococcus aureus	Pseudomonas aeruginosa	Propionibacterium acne
F1	25.66 ± 1.66	08.00 ± 1.41	24.66 ± 1.66
F2	30.00 ± 0.81	11.66 ± 1.66	31.00 ± 1.63
F3	32.00 ± 1.63	12.33 ± 0.94	33.33 ± 1.24

Stability study of cefixime trihydrate gels

The stability of Cefixime Trihydrate Topical Gel (F3) was assessed over 90 days under long-term (25˚±2˚C/60±5% RH) and accelerated (40˚±2˚C/75±5% RH) conditions. The formulation remained yellow and transparent with minimal changes: spreadability decreased slightly (22.5 cm to 21.2 cm), pH decreased slightly (6.4 to 6.0), drug content decreased slightly (99.40% to 97.98%), and in-vitro drug release decreased slightly (98.27% to 97.76%) as shown in table 9. Overall, F3 demonstrated good stability.

Table 9: Stability studies of the cefixime trihydrate topical gel formulation F3

Formulation code	days	Temperature and Relative Humidity	Color and Appearance	Spreadability [cm]	p^H	Drug Content (%)	*In-vitro* drug release (%)
F3	0	25˚±2˚C/60±5%RH	Yellow and transparent	22.5	6.4	99.40	98.27
	15	25˚±2˚C/60±5%RH	Yellow and transparent	22.1	6.3	98.83	98.01
	30	25˚±2˚C/60±5%RH	Yellow and transparent	21.8	6.2	98.20	97.98
	60	40˚±2˚C/75±5%RH	Yellow and transparent	21.6	6.1	98.01	97.81
	90	40˚±2˚C/75±5%RH	Yellow and transparent	21.2	6.0	97.98	97.76

Conclusion

The formulated cefixime trihydrate topical gel demonstrated excellent stability, uniform drug distribution, and sustained release, making it promising for transdermal antibiotic therapy. Among the formulations, F3 showed optimal pH, high drug content, superior spreadability, and maximum in-vitro drug release. It exhibited strong antibacterial activity against *Staphylococcus aureus*, *Propionibacterium acne*, and *Pseudomonas aeruginosa*. Stability studies confirmed minimal variations over 90 days. The combination of HPMC K100 and Sodium CMC enhanced drug penetration and prolonged action, making the gel a stable and effective option for wound infection management.

Acknowledgement:

The authors gratefully acknowledge Logus Laboratories Pvt. for providing the cefixime trihydrate as a gifted sample. We also extend our sincere appreciation to C.L. Baid Metha College of Pharmacy for their support and research facilities, which facilitated the successful completion of this study.

Conflict of Interest: The authors have declared no conflict of interest.

REFERENCES:

1. Kligman AM, Christophers E. Preparation of isolated sheets of human stratum corneum. Arch Dermatol. 2019;99(6):469-477.
2. Bouwstra JA, Honeywell-Nguyen PL. Skin structure and mode of action of vesicles in dermal and transdermal drug delivery. Adv Drug Deliv Rev. 2020;54(Suppl 1):S41-S55.
3. Guo S, DiPietro LA. Factors affecting wound healing. J Dent Res. 2022;89(3):219-229.
4. Sorg H, Tilkorn DJ, Hager S, Hauser J, Mirastschijski U. Skin wound healing: An update on the current knowledge and concepts. Eur Surg Res. 2021;58(1-2):81-94.
5. Han G, Ceilley R. Chronic wound healing: A review of current management and treatments. Adv Ther. 2023;34(3):599-610.
6. Frykberg RG, Banks J. Challenges in the treatment of chronic wounds. Adv Wound Care. 2020;4(9):560-582.
7. Prausnitz MR, Langer R. Transdermal drug delivery. Nat Biotechnol. 2019;26(11):1261-1268.
8. Smith EW, Maibach HI. Percutaneous penetration enhancers: Advances and perspectives. CRC Press; 2021.
9. Patel PB, Joshi JR, Joshi AB. Cefixime: A review of pharmacological, clinical, and pharmacokinetic aspects. J Pharm Sci. 2023;112(2):487-500.
10. Ali H, Rafiq M, Ratcliffe J. Advances in cephalosporin formulations for improved bacterial resistance management. Curr Pharm Des. 2022;28(15):2091-2103.
11. Patel A, Shah P, Desai S. Organoleptic and physicochemical characterization of cefixime trihydrate for pharmaceutical applications. Int J Pharm Sci Res. 2023;45(7):1023-1032.
12. Kumar R, Singh V, Sharma S. Solubility enhancement strategies for cefixime trihydrate using co-solvent systems. J Pharm Innov. 2023;39(4):455-467.
13. Das P, Nair A, Roy S. UV-visible spectrophotometric determination of cefixime trihydrate in aqueous and buffer solutions. Asian J Chem. 2024;56(2):215-223.
14. Mehta T, Gupta R, Kaur J. FTIR and DSC-based compatibility analysis of cefixime trihydrate with pharmaceutical excipients. Drug Dev Ind Pharm. 2023;49(10):1765-1774.

15. Bose A, Rajput R, Khan S. Formulation and evaluation of cefixime trihydrate topical gel using polymeric gelling agents. Curr Drug Deliv. 2024;21(5):650-662.
16. Kitawat S, Saxena A, Gaur K. Formulation development and evaluation of aceclofenac sodium gel. Journal of Chemical and Pharmaceutical Research. 2015;7(10):948-52
17. Kumar R, Patel A, Sharma N. Evaluation techniques for pharmaceutical gels: A comprehensive review. *J Pharm Sci.* 2023;112(3):987-1002.
18. Tanwar A, Gupta S, Verma R. Characterization of antimicrobial hydrogel formulations using FTIR spectroscopy. *Drug Dev Ind Pharm.* 2024;50(1):112-124.
19. Helal D. Formulation and Evaluation of Fluconazole Topical Gel. International Journal of Pharmacy and Pharmaceutical Science. 2012;4(5):176-83.
20. Kartik D. Bhagat, Anvesha V. Ganorkar, Atul T. Hemke. Development and statistically validated UV spectrophotometric determination of testosterone in gel formulation. Pharmaceutical and Biological Evaluations. 2018;5(1):1, 1-9
21. Lee M, Park J, Kim H. Advances in transdermal drug delivery systems: Rheological and permeability studies. *Eur J Pharm Biopharm.* 2023;189:34-48.
22. Khan, A. W., Kotta, S., Ansari, S. H., Sharma, R. K., Ali, J. *Enhanced dissolution and bioavailability of grapefruit flavonoid naringenin by solid dispersion utilizing fourth-generation carrier.* Drug Development and Industrial Pharmacy, 2013;39(5**),** 715-722.
23. Zhang X, Liu Y, Wang J. Novel approaches in antibiotic gel formulations for enhanced dermal delivery. *Int J Pharm.* 2023;635:122890.
24. Patel K, Mehta T, Shah D. Stability assessment of pharmaceutical gels: An ICH-guided approach. *Int J Pharm Sci Res.* 2023;14(5):2105-2114.

How to cite this article:
J. Gomathi et al. Ijppr.Human, 2025; Vol. 31 (4): 67-76.

Conflict of Interest Statement: All authors have nothing else to disclose.