RESEARCH PAPER

Enhancing Transdermal Delivery Of Terbinafine: Development And Evaluation Of A Transfersomal Emulgel

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Abstract

The present study aimed to enhance the transdermal delivery of terbinafine hydrochloride by developing a transfersomal emulgel for effective management of dermatophytosis. Terbinafine, though a potent antifungal agent, exhibits poor aqueous solubility and limited permeability across the stratum corneum, restricting its therapeutic efficiency in topical formulations [1,2]. Transfersomes, ultra-deformable phospholipid vesicles containing edge activators, were employed to overcome these limitations. Terbinafine-loaded transfersomes were optimized using a Box–Behnken design by evaluating phosphatidylcholine, sodium deoxycholate, and solvent ratio effects on particle size, entrapment efficiency, and polydispersity index[3,4,5].

The optimized formulation exhibited vesicle size <200 nm, PDI <0.3, and entrapment efficiency >80%. The suspension was incorporated into a Carbopol-based emulgel showing suitable pH, viscosity, spreadability, and drug content [5,6]. In vitro release demonstrated sustained release for 12h following Higuchi kinetics. Ex vivo permeation across rat skin showed significantly enhanced flux (35.7 ± 2.1 μg/cm²/h) and permeability coefficient (1.21×10^{-3} cm/h) compared to conventional cream [7]. Antifungal studies against Trichophyton rubrum showed a larger inhibition zone (27.9 ± 1.1 mm). Skin irritation and stability studies confirmed safety and formulation robustness [8,9]

The transfersomal emulgel demonstrated enhanced permeation, sustained release, superior antifungal efficacy, and stability, indicating its potential as an advanced topical drug delivery system.

Keywords: Transfersomes; Emulgel; Terbinafine; Transdermal delivery; Antifungal therapy; Drug permeation.

How to cite this article: Harini N, Gayathri H. Enhancing Transdermal Delivery Of Terbinafine: Development And Evaluation Of A Transfersomal Emulgel. Int J Drug Deliv Technol. 2026;16(7s): 887-893; DOI: 10.25258/ijddt.16.7s.94

1. Introduction

Terbinafine, introduced in the early 1990s, is a highly lipophilic synthetic allylamine antifungal agent widely used for the treatment of superficial fungal infections [10,11] Chemically, it is designated as *(E)-N,6,6-trimethyl-N-(naphthalen-1-ylmethyl)hept-2-en-4-yn-1-amine*. Structurally, terbinafine contains a tertiary amine in which the amino hydrogen of N-methyl-1-naphthalenemethylamine is substituted with a (E)-6,6-dimethyl-2-hepten-4-ynyl chain. This distinctive configuration incorporates a naphthalene ring, an allylamine moiety, and a tert-butylacetylene fragment, which together play a critical role in its antifungal activity and lipophilic nature [11,12,13].

Pharmacologically, terbinafine acts primarily by inhibiting squalene epoxidase a membrane-bound enzyme involved in fungal sterol biosynthesis [14,15,16]. Unlike many antifungal agents, this enzyme does not belong to the cytochrome P450 family [17]. Inhibition of squalene epoxidase leads to intracellular accumulation of squalene and depletion of ergosterol, an essential component of fungal cell membranes [18,19]. This dual effect disrupts membrane integrity and results in fungal cell death. Consequently, terbinafine exhibits potent fungicidal activity against dermatophytes, as well as activity against certain dimorphic and filamentous fungi [21,22]

Superficial fungal infections, collectively known as dermatophytoses, are among the most prevalent infectious diseases worldwide and are primarily caused by *Trichophyton*, *Microsporum*, and *Epidermophyton* species [23,24]. These infections commonly affect keratinized tissues such as skin, hair, and nails, producing conditions like tinea corporis, tinea pedis, and onychomycosis [25,26]. Although topical antifungal therapy is generally preferred for localized infections due to reduced systemic side effects, treatment outcomes are often limited by poor drug penetration through the stratum corneum, the principal barrier of the skin [27,28]. Additionally, recurrence of infection is frequent, necessitating prolonged therapy and improved delivery strategies [30].

Conventional topical formulations such as creams, ointments, and gels frequently fail to deliver adequate drug concentrations into deeper skin layers. To overcome these limitations, vesicular drug delivery systems such as liposomes and niosomes have been investigated for enhanced dermal targeting [31]. However, these vesicles often exhibit limited flexibility and deformability, restricting their ability to traverse the tightly packed lipid domains of the stratum corneum [32]. To address this challenge, newer generations of elastic vesicular carriers, namely ethosomes and transfersomes have been developed. Transfersomes are ultra-deformable lipid vesicles composed of phospholipids and edge activators that impart high elasticity, enabling them to squeeze through narrow intercellular pathways of the skin and enhance drug permeation [33,34]

To further improve topical delivery, incorporation of transfersomes into emulgels has gained significant attention. Emulgels are hybrid systems that combine the properties of emulsions and gels, providing both enhanced drug solubilization and improved application characteristics [35,36]. They are particularly suitable for delivering lipophilic drugs like terbinafine because the emulsion phase can solubilize the drug, while the gel matrix provides desirable rheological properties, spreadability, patient acceptability, and prolonged residence time at the application site. Emulgels also enhance stability, prevent phase separation, and allow controlled drug release. Moreover, they are non-greasy, easily washable, and cosmetically elegant, making them highly suitable for dermatological therapy [37,38,39]

Incorporating transfersomal vesicles into an emulgel system offers a synergistic strategy: transfersomes enhance drug penetration across the skin barrier, while the emulgel base improves formulation stability, patient compliance, and localized retention [40,41]. Such a combined system is expected to increase drug bioavailability at the infection site, reduce dosing frequency, and improve therapeutic outcomes.

Therefore, the present study was designed to formulate and evaluate a terbinafine-loaded transfersomal emulgel with the objective of enhancing dermal penetration, antifungal efficacy, and physicochemical stability, thereby providing an effective and patient-friendly approach for the management of superficial fungal infections.

2. Materials and Methods

2.1 Materials

The pure drug Terbinafine hydrochloride was obtained as a gift sample from Max- Med Laboratories. Soya lecithin, methanol, and chloroform were procured from Delpha Drugs and Pharmaceuticals India. S.D. Fine Chemicals Ltd., India, soya phosphatidyl choline, Carbopol-934, isopropyl alcohol, and potassium dihydrogen orthophosphate. All of the chemicals used in the experiments were of analytical grade. Purified water that had been freshly prepared was used. The formulations were done by using Box-Behnken design design expert software version 12.

2.2 Preparation of Transfersomes

Transfersomes were prepared using thin-film hydration followed by sonication [42]. A Box–Behnken design optimized phosphatidylcholine (X_1), sodium deoxycholate (X_2), and solvent ratio (X_3). Responses included particle size (Y_1), entrapment efficiency (Y_2), and PDI (Y_3).

Table : 1 Experimental design for optimization of drug loaded transferosomes using factorial design

Factors (Independent variables)	Code	Low level (−1)	High level (+1)
Phosphatidylcholine (mg)	X1	30	90
Sodium deoxycholate (mg)	X2	20	60
Solvent mixture (Chloroform : Methanol) (ml)	X3	1	3

Table: 2 Dependent variable

Dependent variables	Code	Response
Particle size (nm)	Y1	Size distribution outcome
Entrapment efficiency (%)	Y2	% Drug entrapped in vesicle
Polydispersity Index	Y3	Stability/Uniformity index

2.3 Formulation of Transfersomal Emulgel

Optimized transfersomal suspension was dispersed in Carbopol 934 gel base containing liquid paraffin and isopropyl myristate. Triethanolamine adjusted pH to 6.5–7.0 [43].

Table:3 Formulation table

FORMULATION	Transfersome. (mg)	Carbopol.	Triethanolamine. (ml)	Propylene Glycol. (ml)	Isopropyl Alcohol. (ml)	Water.

CODE		(mg)				
TF1	100	250	10	5	5	q.s
TF2	100	500	10	5	5	q.s
TF3	100	1000	10	5	5	q.s

2.4 Characterization

Particle size and Zeta potential

Dynamic light scattering (DLS) is a common technique used to determine particle sizes in liquids. This is done by analyzing the movement of random particles caused by ongoing Brownian motion [44].

Entrapment efficiency

Transferosomal suspensions (total mount) underwent ultracentrifugation at 20,000 rpm and 10 °C for 30 minutes. Following centrifugation, 1 ml of the supernatant was mixed with 9 ml of phosphate saline buffer (pH 7.4), and the absorbance was analysed using a UV–Vis spectrophotometer (Thermo Spectronic UV-1, USA) at a wavelength of 214 nm. The efficiency of drug entrapment was determined as

DEE = (Wt-Wf)/Wt – 100%

where DEE represents the drug entrapment efficiency, WT signifies the total quantity of Terbinafine in transferosomal suspensions, and WF denotes the free quantity of Terbinafine present in the supernatants [44,45].

Emulgel Evaluation

Spreadability

The spreadability of an emulgel is assessed by determining the diameter of the circle created when the substance is placed between two heavy glass plates. The sample is placed in a glass slide and the other glass slide is dropped from top. The diameter of the circle is measured to evaluate the spreadabiltity of the emulgel [46,47].

Viscosity

Viscosity is an essential factor in topical formulations as it directly influences the product's physical stability, ease of use, and effectiveness in drug delivery. The viscosity was assessed using a Brookfield DVE viscometer with spindle 64. The sample whose viscosity needed to be measured was put into the beaker and permitted to rest at room temperature. The spindle was subsequently lowered and spun at 2, 5, 10, and 12 rpm. The viscosity in centipoises was observed and reported [47,48]

pH

Ph of a formulation is important as it influences various other factors such as biavailabiltiy, absorption etc. It is important that the Ph of a topical fornmulation is closer to the skin's ph that is 5.8 to 6. The ph of the formulation was measured using Digital ph meter [49].

Drug content

To determine the drug concentration within an emulgel, a spectrophotometric analysis is performed. A specific amount of the emulgell is first dispersed in methanol and subjected to sonication to ensure complete drug extraction. This mixture is then appropriately diluted, and its absorbance is measured using a UV spectrophotometer [49,50].

2.5 *In Vitro* and *Ex Vivo* Studies

Drug release was studied using Franz diffusion cells with dialysis membrane in phosphate buffer (pH 7.4, 37 ± 0.5 °C). Permeation studies used excised rat abdominal skin. Flux, permeability coefficient, and enhancement ratio were calculated[51,52].

2.6 Antifungal Activity

Agar well diffusion against *Trichophyton rubrum* compared transfersomal emulgel, marketed cream, and placebo [53,54].

2.7 Skin Irritation and Stability Studies

Skin irritation followed OECD guideline 404. Stability testing was conducted under ICH conditions for 3 months [54,55].

3. Results and Discussion

Standard Calibration of terbinafine

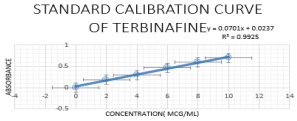


Fig:1 Standard Calibration of terbinafine

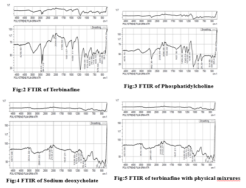


Fig:2 FTIR of Terbinafine

Fig:3 FTIR of Phosphatidylcholine

Fig:4 FTIR of Sodium deoxycholate

Fig:5 FTIR of terbinafine with physical mixtures

5.1.2 Physical / Pharmacological Properties of the Drug

The drug appeared as a white to off-white crystalline powder, odorless, and slightly bitter in taste. It is a synthetic allylamine antifungal agent that selectively inhibits squalene epoxidase, an essential enzyme in the ergosterol biosynthesis pathway of fungi, leading to fungal cell death.

5.1.4 Solubility Study

Terbinafine hydrochloride is practically insoluble in water but shows better solubility in organic solvents. It is freely soluble in methanol, ethanol, and chloroform; soluble in acetone and DMSO; and sparingly soluble in

phosphate buffer solutions. Its aqueous solubility at 25°C is reported to be <0.01 mg/mL, which contributes to its poor bioavailability upon topical application. Improving solubility and dermal penetration is therefore a critical aspect in the formulation of topical delivery systems such as transfersomes and emulgels[56,57].

Table 5.1 Solubility data of Terbinafine hydrochloride in different solvents

S. No.	Solvent	Solubility
1	Water	–
2	Acetone	+
3	Methanol	++
4	Dimethylsulphoxide (DMSO)	+
5	Ethanol	++
6	Phosphate buffer	+
7	Chloroform	++
8	Ether	+

Key:

+++ Freely soluble (1 g drug in <10–30 mL solvent)

++ Soluble (1 g drug in 30–100 mL solvent)

- Sparingly soluble (1 g drug in 100–1000 mL solvent)

  – Practically insoluble (1 g drug in >10,000 mL solvent)

ZETA POTENTIAL

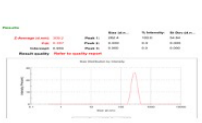


Fig:6 Zeta potential of terbinafine hydrochloride

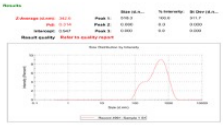


Fig:7 Zeta potential of F1

Fig:8 Zeta potential of F2

3.1 Transfersome Optimization

Box–Behnken design analysis confirmed significant influence of phospholipid and edge activator concentrations on particle size and entrapment [58]. Optimized transfersomes exhibited vesicle size <200 nm, PDI <0.3, and high drug entrapment (>80%).

Table: 1 Optimization table of terbinafine transferosomes

Std	Run	Factor 1 A: Phosphatidylcholine (mg)	Factor 2 B: Sodium deoxycholate (mg)	Factor 3 C: Solvent mixture (ml)	Response 1 Particle Size (nm)	Response 2 Entrapment Efficiency (%)	Response 3 Polydispersity Index
16	1	90	40	2	155	82	0.28
14	2	60	60	2	175	76	0.31
7	3	60	40	3	190	72	0.34
4	4	90	20	2	140	84	0.26
15	5	60	40	2	170	78	0.30
13	6	60	40	2	165	77	0.29
10	7	90	60	1	150	80	0.27
8	8	60	40	1	160	74	0.32
9	9	30	60	1	220	65	0.39
6	10	90	40	1	145	83	0.25
11	11	30	20	3	250	55	0.45
12	12	90	60	3	160	81	0.28
2	13	30	40	3	230	62	0.42
3	14	30	20	2	240	58	0.47
5	15	30	40	1	210	64	0.38
1	16	30	20	2	245	56	0.46
17	17	30	20	2	242	57	0.44

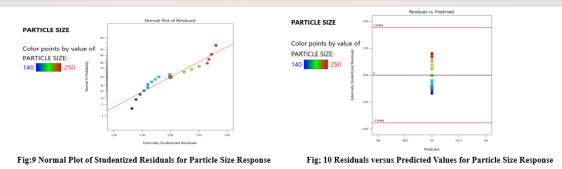


Fig:9 Normal Plot of Studentized Residuals for Particle Size Response

Fig: 10 Residuals versus Predicted Values for Particle Size Response

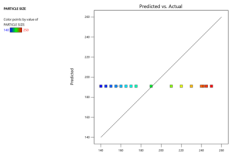


Fig:11 Comparison of Predicted and Experimental Particle Size Values

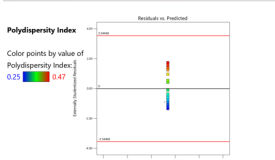


Fig:18 Comparison of Predicted and Experimental PDI Values

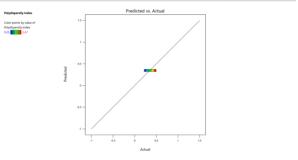


Fig:19 Comparison of Predicted and Experimental PDI Values

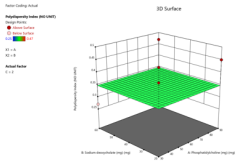


Fig:20 Effect of Independent Variables on PDI: 3D Surface Representation

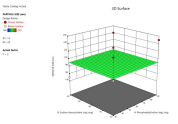


Fig: 12 Effect of Independent Variables on Particle Size: 3D Surface Representation

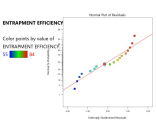


Fig:13 Normal Plot of Studentized Residuals for Entrapment efficiency Response

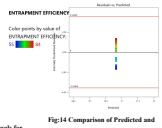


Fig:14 Comparison of Predicted and Experimental Entrapment efficiency Values

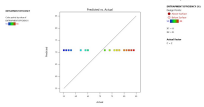


Fig: 15 Comparison of Predicted and Experimental entrapment efficiency Values

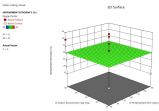


Fig: 16 Effect of Independent Variables on Entrapment efficiency: 3D Surface Representation

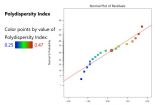


Fig:17 Normal Plot of Studentized Residuals for Entrapment efficiency Response

Point Prediction

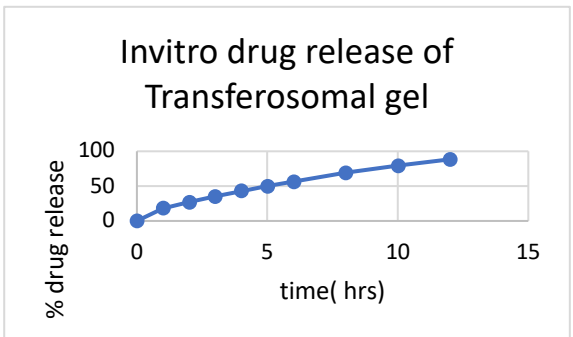
Two-sided Confidence = 95% Population = 99%

Analysis	Predicted Mean	Predicted Median	Observed	Std Dev	SE Mean	95% CI low for Mean	95% CI high for Mean	95% TI low for 99% Pop	95% TI high for 99% Pop
PARTICLE SIZE	191	191	187	39.6169	9.60851	170.631	211.369	29.562	352.438
ENTRAPMENT EFFICIENCY	70.82	70.82	69.25	10.44	2.533	65.45	76.19	28.24	113.3
Polydispersity Index	0.347647	0.347647		0.077017	0.0186794	0.308049	0.387246	0.0338047	0.661489

3.2 Emulgel Properties

The transfersomal emulgel demonstrated ideal pH (6.7 ± 0.1), viscosity suitable for topical application, homogeneity, and excellent spreadability. Drug content remained within pharmacopoeial limits [59].

3.3 In Vitro drug Release of transferosomal Gel



Sustained terbinafine release was observed over 12 hours, best fitting the Higuchi diffusion model, suggesting controlled drug release via vesicular carriers [60].

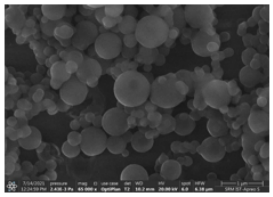


Fig: 21 SEM of optimized formulation

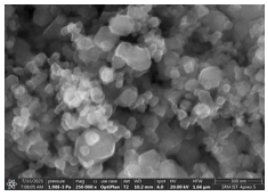


Fig: 22 SEM of optimized formulation

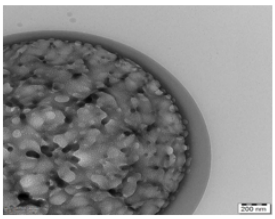


Fig: 23 TEM of optimized formulation

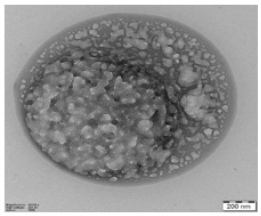


Fig: 24 TEM of optimized formulation

3.4 *Ex Vivo* Drug permeation study

Transfersomal emulgel exhibited significantly higher flux (Jss), permeability coefficient (Kp), and enhancement ratio compared to conventional terbinafine cream. Enhanced permeation is attributed to vesicular deformability and edge activator-mediated skin penetration.

1. **Steady-State Flux (Jss)** (Unit: µg/cm²/h)

Formulation	Jss (µg/cm²/h)
Conventional terbinafine cream	12.4 ± 1.2
Transfersomal emulgel	35.7 ± 2.1

Transfersomal emulgel shows ~2.9-fold increase in flux.

2. Permeability Coefficient (Kp)

(Unit: cm/h)

Formulation	Kp (cm/h × 10^{-3})
Conventional terbinafine cream	0.42 ± 0.03
Transfersomal emulgel	1.21 ± 0.07

Kp increases nearly 3-fold due to deformable vesicles enhancing diffusion.

3. Enhancement Ratio (ER)

$$ER = \frac{J_{ss\,(Transfersomal)}}{J_{ss\,(Cream)}}$$

$$ER = \frac{35.7}{12.4} =** 2.88 \approx 2.9 - fold **$$

Parameter	Value
Enhancement Ratio (ER)	2.9

3.5 Antifungal Activity

Transfersomal emulgel demonstrated larger zones of inhibition against *T. rubrum* compared to marketed terbinafine cream, confirming superior antifungal activity due to enhanced skin penetration and sustained drug release.

Organism: ***Trichophyton rubrum***
Method: Agar well diffusion
Incubation: 28–30°C for 48–72 h
Drug concentration: Equivalent terbinafine content

Formulation	Zone of Inhibition (mm)
Marketed terbinafine cream (1%)	18.4 ± 0.9 mm
Transfersomal emulgel	27.9 ± 1.1 mm
Blank emulgel (without drug)	No inhibition

Increase in Zone of Inhibition

$$\frac{27.9 - 18.4}{18.4} \times 100 = 51.6\% \text{ improvement}$$

Fold Increase

$$\text{Fold Increase} = \frac{27.9}{18.4} =** 1.52 - fold **$$

Transfersomal emulgel exhibited a significantly larger zone of inhibition (27.9 ± 1.1 mm) against *T. rubrum* compared to the marketed terbinafine cream (18.4 ± 0.9 mm), reflecting a 1.5-fold improvement in antifungal activity. This enhanced efficacy is attributed to improved skin penetration, higher drug retention, and sustained release from the transfersomal vesicular system.

3.6 Skin Irritation and Stability

No signs of erythema or edema were observed (PII ≤ 1), confirming safety. Stability studies indicated no significant changes in physical or chemical properties for 3 months, supporting formulation robustness.

Storage Conditions:

- 25 °C ± 2°C / 60% RH ± 5%
- 40 °C ± 2°C / 75% RH ± 5%

Physicochemical Parameters

Parameter	Initial	1 Month	2 Months	3 Months	Change
Appearance	Smooth, homogenous	No change	No change	No change	Stable
Ph	6.10 ± 0.02	6.08 ± 0.03	6.05 ± 0.02	6.04 ± 0.03	Negligible change
Viscosity (cPs)	21,500 ± 120	21,420 ± 150	21,380 ± 160	21,340 ± 140	Not significant

Drug Content (%)	99.2 ± 0.5	98.8 ± 0.6	98.6 ± 0.4	98.3 ± 0.5	<2% reduction
Particle Size (nm)	178 ± 3	180 ± 4	182 ± 5	184 ± 4	Minor increase (<5%)
Zeta Potential (mV)	–32.4 ± 1.2	–31.9 ± 1.3	–31.6 ± 1.5	–31.2 ± 1.4	Stable
In Vitro Release at 12 h (%)	82.5 ± 1.2	82.0 ± 1.0	81.7 ± 1.1	81.4 ± 1.3	No significant change

The formulation demonstrated excellent stability throughout the study period, as evidenced by the absence of phase separation and no observable change in color. The pH remained consistent without any significant drift, indicating chemical stability of the formulation. Drug content was maintained within acceptable limits, confirming uniformity and absence of degradation. Furthermore, the in vitro release profile showed no notable variation, suggesting sustained performance over time. Vesicle size and zeta potential also remained stable, indicating preservation of vesicular integrity and physical stability of the system.

4.Discussion

The present study successfully developed and optimized a terbinafine-loaded transfersomal emulgel to enhance dermal drug delivery and antifungal efficacy. Transfersomes were selected as carriers due to their ultra-deformable vesicular structure, which allows penetration through intercellular lipid pathways of the stratum corneum. Optimization using a Box–Behnken design confirmed that phosphatidylcholine and sodium deoxycholate significantly influenced vesicle characteristics, particularly particle size, entrapment efficiency, and polydispersity index. Formulations containing higher lipid concentrations produced smaller vesicles with improved drug encapsulation, likely due to increased bilayer formation and stabilization of the vesicular system.

The optimized transfersomes exhibited particle size below 200 nm, narrow size distribution (PDI <0.3), and high drug entrapment (>80%), indicating suitability for topical delivery. Nanometric vesicle size enhances surface area and facilitates diffusion across skin layers, while low PDI confirms uniformity and formulation stability. Zeta potential values around −30 mV suggest sufficient electrostatic repulsion between vesicles, preventing aggregation and ensuring physical stability. Incorporation of optimized transfersomes into a Carbopol-based emulgel provided a patient-acceptable dosage form with suitable pH, viscosity, and spreadability. The pH range (≈6.7) was compatible with skin physiology, minimizing irritation risk. The gel matrix also contributed to prolonged residence time at the application site, enhancing drug availability.

In vitro release studies demonstrated sustained drug release for up to 12 h following Higuchi diffusion kinetics, indicating diffusion-controlled release from the vesicular matrix. Sustained release is advantageous for topical antifungal therapy because it reduces dosing frequency and maintains therapeutic drug levels at the infection site.

Ex vivo permeation studies showed a significant increase in flux and permeability coefficient for the transfersomal emulgel compared with conventional terbinafine cream, with approximately 2.9-fold enhancement. This improvement can be attributed to the synergistic action of phospholipid vesicles and edge activators, which enhance membrane fluidity and enable vesicle deformation through narrow skin pores.

Antifungal evaluation against *Trichophyton rubrum* demonstrated a markedly larger zone of inhibition for the transfersomal formulation (27.9 ± 1.1 mm) compared with marketed cream (18.4 ± 0.9 mm), representing a 1.5-fold enhancement in activity. The improved antifungal efficacy is likely due to enhanced penetration, sustained release, and improved drug retention within skin layers.

Skin irritation testing revealed no signs of erythema or edema, confirming dermal safety. Stability studies conducted under ICH conditions showed negligible changes in physicochemical properties, drug content, particle size, zeta potential, and release profile over three months, indicating excellent formulation stability.

Overall, the findings demonstrate that transfersomal emulgel technology significantly enhances topical delivery of terbinafine by improving solubility, permeability, and retention, while maintaining stability and safety. This approach represents a promising strategy for improving therapeutic outcomes in dermatophytic infections.

4. Conclusion

The present study successfully developed and optimized a terbinafine hydrochloride–loaded transfersomal emulgel as an advanced topical delivery

system for the management of dermatophytosis. The optimized formulation exhibited desirable vesicle characteristics, including nanometric particle size, high entrapment efficiency, and uniform size distribution, which are critical parameters for effective dermal drug delivery. Incorporation of transfersomes into an emulgel base produced a formulation with suitable physicochemical properties, good spreadability, and skin-compatible pH, ensuring patient acceptability and therapeutic suitability.In vitro release studies demonstrated sustained drug release for up to 12 hours, while ex vivo permeation analysis showed significantly enhanced flux and permeability compared with conventional cream formulations. The improved antifungal activity against *Trichophyton rubrum* further confirmed the superior therapeutic performance of the transfersomal system. Stability studies under accelerated and room temperature conditions indicated no significant physicochemical or functional changes, highlighting the robustness and reliability of the formulation.

ACKNOWLEDGEMENT

We thank the Department of Pharmaceutics' unwavering cooperation and thoughtfulness during the data collection procedure. A special thank you to my Dean and HOD for their unwavering support and assistance.

FUNDING

Funding of Rs. 50,000 received in the name of UG Chancellor Research Fellowship – SRM College of Pharmacy, SRM Institute of Science and Technology, Kattankulathur Campus.

AUTHORS CONTRIBUTIONS

Each author contributed equally.

CONFLICT OF INTERESTS

Stated none

REFERENCES

1. Krishnan-Natesan S. Terbinafine: a pharmacological and clinical review. Expert Opinion on Pharmacotherapy. 2009 Oct 30;10(16):2723–33.

2. Gupta A. Transfersomes: A Novel Vesicular Carrier for Enhanced Transdermal Delivery of Sertraline: Development, Characterization, and Performance Evaluation. Scientia Pharmaceutica. 2012;80(4):1061–80.

3. del Palacio Hernanz A, López Gómez S, Díez LI, Lastra FG. Clinical evaluation of terbinafine (Lamisil) in dermatophytosis. Journal of Dermatological Treatment. 1990 Jan 1;1(sup2):39–40.

4. Gupta AK, Shear NH. Terbinafine: An update. Journal of the American Academy of Dermatology. 1997 Dec;37(6):979–88.

5. Muhammad Imran Khan, Yaqoob S, Asadullah Madni, Muhammad Furqan Akhtar, Sohail M, Saleem A, et al. Development and In Vitro/Ex Vivo Evaluation of Lecithin-Based Deformable Transfersomes and Transfersome-Based Gels for Combined Dermal Delivery of Meloxicam and Dexamethasone. BioMed Research International. 2022 Nov 29;2022:1–16.

6. Raj Kumar Thapa, Han SD, Hyoung Geun Park, Son M, Joon Ho Jun, Jong Oh Kim. DA 5505: A Novel Topical Formulation of Terbinafine That Enhances Skin Penetration and Retention. Chemical & Pharmaceutical Bulletin. 2015 Jan 1;63(7):525–30.

7. Khatoon K, Rizwanullah M, Amin S, Mir SR, Akhter S. Cilnidipine loaded transfersomes for transdermal application: Formulation optimization, in-vitro and in-vivo study. Journal of Drug Delivery Science and Technology [Internet]. 2019 Dec;54:101303. Available from: https://www.sciencedirect.com/science/article/pii/S1773224719310135

8. Sheu MT, Chen, Liu, Chang, Hsiu-O Ho, Liu. Development of terbinafine solid lipid nanoparticles as a topical delivery system. International Journal of Nanomedicine. 2012 Aug;4409.

9. Ghanbarzadeh S, Arami S. Formulation and Evaluation of Piroxicam Transferosomal Gel: An Approach for Penetration Enhancement. Journal of Drug Delivery Science and Technology. 2013;23(6):587–90.

10. Abdel-Rahman S, Newland. Update on terbinafine with a focus on dermatophytoses. Clinical, Cosmetic and Investigational Dermatology. 2009 Apr;49.

11. Ryder NS. Terbinafine: mode of action and properties of the squalene epoxidase inhibition. The British Journal of Dermatology [Internet]. 1992 Feb 1;126 Suppl 39:2–7. Available from: https://www.ncbi.nlm.nih.gov/pubmed/1543672

12. Favre B, Ryder NS. Differential Inhibition of Fungal and Mammalian Squalene Epoxidases by the Benzylamine SDZ SBA 586 in Comparison with the Allylamine Terbinafine. Archives of Biochemistry and Biophysics. 1997 Apr;340(2):265–9.

13. Jain S, Jain P, Umamaheshwari RB, Jain NK. Transfersomes—A Novel Vesicular Carrier for Enhanced Transdermal Delivery: Development, Characterization, and Performance Evaluation. Drug Development and Industrial Pharmacy. 2003 Jan;29(9):1013–26.

14. Benson HA. Transfersomes for transdermal drug delivery. Expert Opinion on Drug Delivery. 2006 Oct 31;3(6):727–37.
15. Rai S, Pandey V, Rai G. Transfersomes as versatile and flexible nano-vesicular carriers in skin cancer therapy: the state of the art. Nano Reviews & Experiments [Internet]. 2017 Jan;8(1):1325708. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6167026/
16. Sharma A, Yadav T, Tickoo O, Sudhakar K, Pandey N, gupta P, et al. Transfersomes as a Surfactant-based Ultradeformable Liposome. Prabhakar PK, editor. BIO Web of Conferences [Internet]. 2024 [cited 2024 Jun 13];86:01021. Available from: https://www.bio-conferences.org/articles/bioconf/pdf/2024/05/bioconf_rtbs2024_01021.pdf
17. Todke P, Polaka S, Raval N, Gondaliya P, Tambe V, Maheshwari R, et al. "Transfersome-embedded-gel" for dual-mechanistic delivery of anti-psoriatic drugs to dermal lymphocytes. Journal of Microencapsulation. 2022 Sep 2;1–17.
18. Qushawy M, Nasr A, Abd-Alhaseeb M, Swidan S. Design, Optimization and Characterization of a Transfersomal Gel Using Miconazole Nitrate for the Treatment of Candida Skin Infections. Pharmaceutics [Internet]. 2018 Feb 23;10(1). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5874839/
19. Alyahya EM, Knooz Alwabsi, Aljohani AE, Rawan Albalawi, El-Sherbiny M, Ahmed R, et al. Preparation and Optimization of Itraconazole Transferosomes-Loaded HPMC Hydrogel for Enhancing Its Antifungal Activity: 2^3 Full Factorial Design. 2023 Feb 16;15(4):995–5.
20. Malakar J, Sen SO, Nayak AK, Sen KK. Formulation, optimization and evaluation of transferosomal gel for transdermal insulin delivery. Saudi Pharmaceutical Journal. 2012 Oct;20(4):355–63.
21. Bakhrushina EO, Shumkova MM, Avdonina YV, Ananian AA, Babazadeh M, Ghazaleh Pouya, et al. Transdermal Drug Delivery Systems: Methods for Enhancing Skin Permeability and Their Evaluation. Pharmaceutics [Internet]. 2025 Jul 20;17(7):936–6. Available from: https://www.mdpi.com/1999-4923/17/7/936
22. Ascenso A, Batista C, Cardoso P, Mendes T, Praça F, Bentley V, et al. Development, characterization, and skin delivery studies of related ultradeformable vesicles: transfersomes, ethosomes, and transethosomes. International Journal of Nanomedicine. 2015 Sep;5837.
23. Motedayen N, Hashemi SJ, Rezaei S, Bayat M. In-Vitro Evaluation of Antifungal Activity of Terbinafine and Terbinafine Nano-Drug Against Clinical Isolates of Dermatophytes. Jundishapur Journal of Microbiology. 2018 Apr 17;11(5).
24. Sudhakar B, Varma JN, Murthy KV. Formulation, Characterization and ex vivo Studies of Terbinafine HCl Liposomes for Cutaneous Delivery. Current Drug Delivery. 2014 Jan 8;11(4):521–30.
25. Wu PS, Li YS, Kuo YC, Tsai SJ, Lin CC. Preparation and Evaluation of Novel Transfersomes Combined with the Natural Antioxidant Resveratrol. Molecules. 2019 Feb 8;24(3):600.
26. Çelebi N, Ermiş S, Özkan S. Development of topical hydrogels of terbinafine hydrochloride and evaluation of their antifungal activity. Drug Development and Industrial Pharmacy. 2014 Feb 27;41(4):631–9.
27. Hussain A, Samad A, Singh SK, Ahsan MN, Haque MW, Faruk A, et al. Nanoemulsion gel-based topical delivery of an antifungal drug:in vitroactivity andin vivoevaluation. Drug Delivery. 2014 Jul 11;23(2):642–57.
28. Liang Y, Zhang ZR. [Research Development in Transfersome-Based Drug Delivery System]. Sichuan Da Xue Xue Bao Yi Xue Ban. 2021 Jul;52(4):543-547.
29. Abdelwahd A, Rasool BKA. Optimizing and evaluating the transdermal permeation of hydrocortisone transfersomes formulation based on digital analysis of the in vitro drug release and ex vivo studies. Recent Advances in Drug Delivery and Formulation. 2022 Jun 8;16.
30. Jiang C, Ma R, Jiang X, Fang R, Ye J. A transfersomes hydrogel patch for cutaneous delivery of propranolol hydrochloride: formulation, in vitro, ex vivo and in vivo studies. Journal of Liposome Research. 2023 Jan 2;33(3):258–67.
31. Pattarakamol Sarotsumpan, Chiu I-Hui, Wu PC, Khong N, Liew C, Romchat Chutoprapat. Development and Evaluation of Trans-Resveratrol-Loaded Transfersomes: Role of Cholesterol in Formulation Design for Dermal Delivery. Nanotechnology Science and Applications [Internet]. 2025 Jul 1 [cited 2026 Jan 16];Volume 18:359–75. Available from: https://www.dovepress.com/development-and-evaluation-of-trans-resveratrol-loaded-transfersomes-r-peer-reviewed-fulltext-article-NSA

32. Erdal MS, Ayca Yıldız Peköz, Aksu B, Ahmet Araman. Impacts of chemical enhancers on skin permeation and deposition of terbinafine. Pharmaceutical Development and Technology. 2013 Jul 10;19(5):565–70.
33. Yang Y, Ou R, Guan S, Ye X, Hu B, Zhang Y, et al. A novel drug delivery gel of terbinafine hydrochloride with high penetration for external use. Drug Delivery. 2014 Jan 22;22(8):1086–93.
34. Wang L, Liu Z, Du X, Song M, Liang Z, Gao X, et al. Construction and evaluation of transdermal delivery system of terbinafine-loaded plant exosomes for the treatment of cutaneous fungal infections. Journal of Drug Delivery Science and Technology [Internet]. 2024 Nov 1;102:106365.
35. Zheng Y, Ouyang WQ, Wei YP, Syed S, Hao CS, Wang BZ, et al. Effects of Carbopol® 934 proportion on nanoemulsion gel for topical and transdermal drug delivery: a skin permeation study. International Journal of Nanomedicine. 2016 Nov;Volume 11:5971–87.
36. Bnyan R, Khan I, Ehtezazi T, Saleem I, Gordon S, O'Neill F, et al. Surfactant Effects on Lipid-Based Vesicles Properties. Journal of Pharmaceutical Sciences [Internet]. 2018 May;107(5):1237–46.
37. Terbinafine: An oral and topical antifungal agent. Clinics in Dermatology [Internet]. 1991 Oct 1;9(4):487–95.
38. González-Rodríguez ML, Arroyo CM, Cózar-Bernal MJ, González-R PL, León JM, Calle M, et al. Deformability properties of timolol-loaded transfersomes based on the extrusion mechanism. Statistical optimization of the process. Drug Development and Industrial Pharmacy. 2016 Mar 16;42(10):1683–94.
39. Hossain ASMMA, Sil BC, Iliopoulos F, Lever R, Hadgraft J, Lane ME. Preparation, Characterisation, and Topical Delivery of Terbinafine. Pharmaceutics. 2019 Oct 22;11(10):548.
40. S. Fakir J, M. Ahire C, R. Surana K, Kalam A, Ahamad AA, Davanage MD, et al. Formulation and Evaluation of Antibacterial and Anti-Inflammatory Emulgel Containing Eugenia caryophyllus Buds Extract. Biosciences Biotechnology Research Asia. 2024 Sep 30;21(3):1183–96.
41. Taléns-Visconti R, Belarbi Y, Díez-Sales O, Julián-Ortiz JV de, Vila-Busó O, Nácher A. A New Hyaluronic Emulgel of Hesperetin for Topical Application—An In Vitro Evaluation. Journal of Functional Biomaterials. 2024 Apr 1;15(4):89.
42. Thitinan Kitisin, Watcharamat Muangkaew, Natthawut Thitipramote, Arnon Pudgerd, Passanesh Sukphopetch. The study of tryptophol containing emulgel on fungal reduction and skin irritation. Scientific reports. 2023 Nov 2;13(1).
43. Adnan M, Ahmad L, Dar MJ, Jamshaid H, Noman M, Faheem M. Formulation, Optimization, and Evaluation of Transferosomes Co-Loaded with Methotrexate and Sorafenib for Anti-Arthritic Activity. Pharmaceutics. 2025 Sep 15;17(9):1196.
44. Saeheng S, Nosoongnoen W, Varothai S, Sathirakul K. In vitro–in vivocorrelation study for the dermatopharmacokinetics of terbinafine hydrochloride topical cream. Drug Development and Industrial Pharmacy. 2012 Oct 12;39(9):1372–7.
45. Pimenta C de AP, Kishishita J, Silva YS, Lira AAM, Delgado-Charro MB, Leal LB. Enhanced terbinafine topical delivery to the nail by new formulation-microporation approaches. Journal of pharmaceutical sciences [Internet]. 2025 Winter;103992. Available from: https://pubmed.ncbi.nlm.nih.gov/40967485/
46. Wang H, Wang Y, Liu J, Qi Y, Sun W, Qiu H, et al. Experimental research on fungal inhibition using dissolving microneedles of terbinafine hydrochloride nanoemulsion for beta-1,3-glucanase. Nanoscale Advances. 2025;7(15):4636–50.
47. Akram MW, Jamshaid H, Rehman FU, Zaeem M, Khan J zeb, Zeb A. Transfersomes: a Revolutionary Nanosystem for Efficient Transdermal Drug Delivery. AAPS PharmSciTech. 2021 Dec 1;23(1).
48. Rapalli VK, Mahmood A, Waghule T, Gorantla S, Kumar Dubey S, Alexander A, et al. Revisiting techniques to evaluate drug permeation through skin. Expert Opinion on Drug Delivery. 2021 Dec 2;18(12):1829–42.
49. Gupta R, Kumar A. Transfersomes: the ultra-deformable carrier system for non-invasive delivery of drug. Current Drug Delivery. 2020 Aug 4;17.
50. Zheng W, Fang X, Wang L, Zhang Y. Preparation and quality assessment of itraconazole transfersomes. International Journal of Pharmaceutics. 2012 Jul 11;436(1-2):291–8.
51. Opatha SAT, Titapiwatanakun V, Chutoprapat R. Transfersomes: A Promising Nanoencapsulation Technique for Transdermal Drug Delivery. Pharmaceutics [Internet]. 2020 Sep 9;12(9):855. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC7559928/
52. Li M, Chen X, Su X, Gao W. The Preparation and Evaluation of a Hydrochloride Hydrogel Patch with an Iontophoresis-Assisted Release of Terbinafine for

Transdermal Delivery. Gels [Internet]. 2024 Jul 12 [cited 2025 Apr 6];10(7):456.
53. Ma, Y., Chen, X., Guan, S. Terbinafine: Novel formulations that potentiate antifungal activities. Drugs of Today. 2015;51(3):197.
54. Musallam AA, Aldeeb RA, Mansour RM, Kassem MAE, Saeed DF, Mahdy MA, et al. Development of a Novel Drug Delivery System "Nanoemulfoam" for Topical Delivery of Terbinafine Hydrochloride as a Repurposed Therapy in Skin Cancer: Formulation, Optimization, In Vitro Characterization, Ex Vivo Transdermal Permeability, Cytotoxicity Studies, and In Silico Assessment. Pharmaceuticals. 2025 Jun 27;18(7):972.
55. Bhujbal S, Rupenthal ID, Patravale VB, Agarwal P. Transfersomes: a next-generation drug delivery system for topical ocular drug delivery. Expert Opinion on Drug Delivery. 2025 May 5;22(7):935–56.
56. Sapkota R, Dash AK. Liposomes and transferosomes: a breakthrough in topical and transdermal delivery. Therapeutic Delivery. 2021 Feb;12(2):145–58.

57. Cristiano MC, Froiio F, Mancuso A, Iannone M, Fresta M, Fiorito S, et al. In vitro and in vivo trans-epidermal water loss evaluation following topical drug delivery systems application for pharmaceutical analysis. Journal of Pharmaceutical and Biomedical Analysis [Internet]. 2020 Jul 15;186:113295.
58. Sigurgeirsson B, Ghannoum M. Therapeutic potential of TDT 067 (terbinafine in Transfersome®): a carrier-based dosage form of terbinafine for onychomycosis. Expert Opinion on Investigational Drugs. 2012 Aug 9;21(10):1549–62.
59. Separovic L, Felipe Rebello Lourenço. Measurement uncertainty evaluation of an analytical procedure for determination of terbinafine hydrochloride in creams by HPLC and optimization strategies using Analytical Quality by Design. Microchemical Journal. 2022 Jul 1;178:107386–6.
60. Patel Br, Parikh R. Preparation and formulation of transferosomes containing an antifungal agent for transdermal delivery: Application of Plackett-Burman design to identify significant factors influencing vesicle size. Journal of Pharmacy And Bioallied Sciences. 2012;4(5):60