Advances in Bioresearch
Adv. Biores., Vol 17 (2) February 2026: 277-285
©2026 Society of Education, India
Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.17.2.277285

Advances in Bioresearch

ORIGINAL ARTICLE

Formulation, Development and Evaluation of Butenafine Hydrochloride Nanoemulgel

Khanderao R. Jadhav[1], Pranjal K. Aher*[2], Rishikesh S.Bachhav[3]

[1]Department of Pharmaceutics, KCT's RG Sapkal College of Pharmacy, Anjeneri Nashik Savitribai Phule Pune University,

[2]Department of Pharmaceutics, KCT's RG Sapkal College of Pharmacy, Anjeneri Nashik Savitribai Phule Pune University

[3]Department of Pharmacology, KCT's RG Sapkal College of Pharmacy, Anjeneri Nashik Savitribai Phule Pune University

Corresponding Author: Pranjal K. Aher
Email : aherpranj2000@gmail.com

ABSTRACT

Since topical medication delivery techniques can produce site-specific activity, treating skin infections locally has various advantages over systemic side effects. The antifungal agent butenafine hydrochloride belongs to the BCS Class II and is not very soluble in water. The therapeutic potential of butenafine hydrochloride is limited by its poor water solubility in traditional topical preparations. For better topical antifungal activity, the current study set out to create, refine, and assess a nanoemulgel formulation of butenafine hydrochloride. Span 80 and Tween 20 were used as emulsifying agents in the current study to prepare Tea Tee Oil as an oil phase in order to create a Butenafine hydrochloride nanoemulsion using high-energy ultrasonication. The process of creating a nanoemulgel involved combining the optimised nanoemulsion with a Carbopol 934 gel base. Accelerated Stability Testing, zeta potential, in-vitro drug diffusion (% Cumulative Drug Release), antifungal activity by disc diffusion assay study, pH, viscosity, spreadability, uniformity of drug content, particle size, and polydispersity studies were among the tests performed on the formulation. Use of a Box-Behnken Design was used for the optimisation. The optimised formulation demonstrated ethical stability with the maximum percentage drug release (92.56% after 8 hours), a mean particle size of 189.3 nm, a PDI of 0.287, and a zeta potential of -29.4 mV. Comparing in vitro diffusion experiments to traditional gel formulations, the results showed improved drug release. Because tea tree oil (TTO) and butenafine work synergistically in this study, the nanoemulgel also showed enhanced antifungal efficacy against Candida albicans. A set of stability investigations proved the product's physical and chemical stability for three months. The new butenafine nanoemulgel has the potential to be a successful, patient-compliant topical antifungal therapy for skin infections since it offers low minimum inhibitory and fungicidal concentrations in comparison to free butenafine. Improved skin penetration is necessary for traditional formulations to be effective.

***Keywords*:** *Topical Drug Delivery, Nanoemulgel, Antifungal Activity, Tea Tree Oil, Butenafine HCl*

Received 24.09.2025 Revised 21.10.2025 Accepted 30.01.2026

How to cite this article:
Khanderao R. Jadhav, Pranjal K. Aher, Rishikesh S.Bachhav. Formulation, Development and Evaluation of Butenafine Hydrochloride Nanoemulgel. Adv. Biores., Vol 17(2) February 2026: 277-285.

INTRODUCTION

Topical antifungal medications should be used when appropriate to provide the medication directly to the infection site in order to minimise systemic exposure and maximise patient compliance. The treatment of dermatophytosis, candidiasis, and tinea infections—all of which are extremely prevalent superficial fungal infections with greater prevalence rates globally, particularly in tropical and subtropical regions— contains this crucial element. India and several South Asian countries have some of the highest prevalence rates in the world, with 20–25% of the world's population afflicted at any given moment. This is one of the issues associated with superficial fungal infections. Since topical delivery techniques are recurring and patient-friendly, they continue to be the most popular treatment option for these infections globally [1, 2, 3].

Synthetic benzylamine antifungal butenafine hydrochloride inhibits the squalene epoxidase, which is involved in the fungal cell membrane's ergosterol production. Certain yeasts make it effective for treating candidal infections, tinea pedis, and tinea corporis, and its derivatives have demonstrated strong antidermatophyte activity [4]. Actually, the oily or occlusive bases of creams and gels that need frequent dosage limit their bioactivity in conventional formulations due to their limited water solubility, low skin penetration, and poor patient compliance. Nanoemulsions have become a significant advancement in the field of medication delivery systems based on nanotechnology in order to address all of these issues. Because of their enormous surface area, nanoemulsions—a thermodynamically stable dispersion of tiny droplets (20–200 nm)—display improved medication solubilisation, epidermal penetration, and bioavailability. Despite their benefits, ionic liquids' low viscosity hinders their use in topical delivery systems where precise dosage, patient compliance, and simplicity of application are crucial. [5] A promising method to get over this limitation is the use of nanoemulgel, a hybrid system that combines the benefits of gels and nanoemulsion. The formulation known as nanoemulgel, which increases medication delivery and, consequently, patient compliance with improved spreadability and less oily feel, is created by incorporating the nanoemulsion phase into a gel basis. The gels are a more desirable option for dermatological treatments since they also provide a cooling sensation and improved adherence at the application site.[5] An essential oil that occurs naturally and has well-known antibacterial, antifungal, and anti-inflammatory qualities is tea tree oil, which is the oil phase employed here. [6] It was anticipated that it would be used not only as a solvent for the lipophilic medication but also possibly in concert with it to increase antifungal action. The gelling agent, Carbopol 934, was chosen because to its high viscosity, stability, and ability to provide a smooth texture and spreadability in topical applications. Stable droplets were formed by stabilising the nanoemulsion and reducing interfacial tension with the help of the surfactants Span 80 and Tween 20.In this case, a Carbopol 934 gel base was stabilised by a mixture of Span 80 and Tween 20, and a nanoemulgel loaded with Butenafine was created based on the oil phase of tea tree oil. The composition's physicochemical properties, in vitro drug release, antifungal efficacy, and storage stability were all carefully evaluated after it was statistically optimised using Box-Behnken Design.

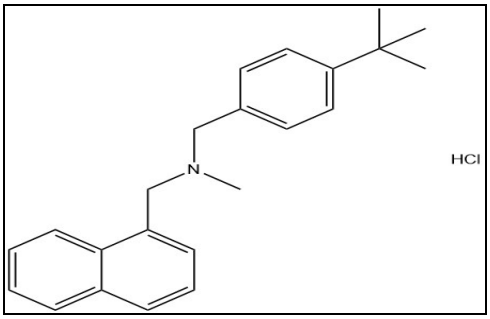

Figure 1: Structure Of Butenafine Hydrochloride.

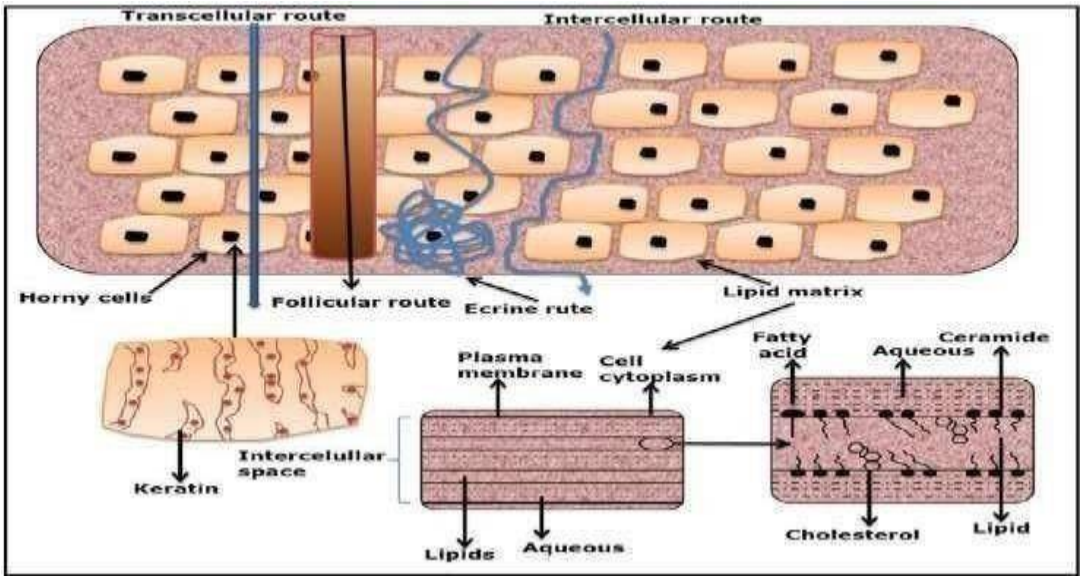

Figure 2 : Possible drug penetration routes across human skin [7]

PROBLEM STATEMENT

Due to conventional butenafine hydrochloride (BTF) creams' inadequate skin penetration and inferior residence length, superficial fungal infections continue to occur frequently. BTF, a BCS class II medication, has inconsistent cutaneous absorption and low water solubility, which results in insufficient drug levels at the infection site and frequent re-dosing. A topical method that concurrently improves transstratum-corneum administration, prolongs release, and increases BTF solubility without sacrificing safety or spreadability is required. In order to close that gap, a 33 factorial design was used to construct and optimise a BTF nanoemulgel. The key formulation variables were Span 80 + Tween 20 (Smix), Carbopol 934 (gelling agent), and Tea Tree Oil (oil phase/adjunct antibacterial). In comparison to a commercially available BTF cream, the goal is to create a stable nanoemulgel with a narrow PDI, tiny droplet size, appropriate viscosity/pH, improved in-vitro release, and higher antifungal activity while preserving acceptable cytotoxicity and storage stability. This project intends to build and optimise a BTF nanoemulgel that overcomes the stratum-corneum barrier, sustains release, and enhances antifungal outcomes without sacrificing safety. Conventional BTF creams function poorly because of their poor solubility and skin penetration. Consequently, Through the development and optimisation of a BTF nanoemulgel, this project aims to address the butenafine hydrochloride (BTF) in conventional creams' poor solubility, limited skin penetration, and uneven therapeutic levels. The optimised nanoemulgel's antifungal activity, tolerable cytotoxicity, and storage stability will be evaluated by comparing it to a commercially available BTF cream. This method should result in a scalable, patient-friendly topical system that enhances drug deposition at the site of infection, maintains release, lowers the frequency of dosage, and decreases the recurrence of superficial fungal infections.

MATERIAL AND METHODS

Materials: Gift samples of butenafine hydrochloride were acquired . Tea Tree Oil, Carbopol 934, Span 80, Tween 20, Propylene Glycol, Glycerine, and Triethanolamine were procured from standard sources.

Method of preparation:

Smix (Surfactant Mixture) preparation: A surfactant mixture (Smix) was prepared in a 1:1 ratio using Span 80 as the surfactant and Tween 20 as the co-surfactant. The required quantities of both components were accurately measured and mixed thoroughly until a clear and homogeneous mixture was obtained. This Smix was subsequently used to stabilize the nanoemulsion formulation by reducing interfacial tension and improving system stability [8].

***Preparation of Nanoemulsion** [9,10] :*

The nanoemulsion was prepared using high-energy ultrasonication. Butenafine hydrochloride was dissolved in tea tree oil as the oil phase, followed by addition of Smix with continuous stirring. The aqueous phase was prepared by dissolving propylene glycol and glycerine in distilled water. Both phases were heated to 70–80 °C, and the oil phase was gradually added to the aqueous phase under magnetic stirring (1000–1500 rpm) for 10 minutes to obtain a coarse emulsion. The coarse emulsion was then subjected to probe ultrasonication at 20 kHz and 100 W for 10 minutes (with intermittent cooling) to produce a stable nanoemulsion.

Figure 3 : O/W Type Nanoemulsion of Butenafine HCl

Preparation of Nanoemulgel:

Carbopol 934 was dissolved in distilled water and allowed to swell for three to four hours in order to form the base gel. Triethanolamine was then added to the basic gel to bring its pH down to 6.5–6.8. A homogeneous nanoemulgel formulation was achieved by gradually adding the produced nanoemulsion in a 1:1 ratio to the gel base while gently mixing.

Experimental Design: *[11,12,13]*
Using Design-Expert software, a 3-factor, 3-level Box-Behnken Design (BBD) was used to optimise the formulation. Smix ratio (X3), Tea Tree Oil concentration (X2), and Carbopol concentration (X1) were the independent variables. The reactions that were investigated included drug release, viscosity, and particle size. Twelve different formulas were created and evaluated.

Table 1: Composition of nanoemulsion

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Butenafine HCl (1%)	0.15 g	0.15 g	0.15 g	0.15 g	0.15 g	0.15 g	0.15 g	0.15 g	0.15g	0.15 g	0.15 g	0.15 g
Tea Tree Oil (%)	3% (0.45 ml)	3% (0.45 ml)	2% (0.30 ml)	1% (0.15 ml)	3% (0.45 ml)	1% (0.15 ml)	2% (0.30 ml)	2% (0.30 ml)	3% (0.45 ml)	2% (0.30 ml)	1% (0.15 ml)	1% (0.15)
Smix (Span80 + Tween 20) (%)	2% (0.30 ml)	2% (0.30 ml)	3% (0.45 ml)	1% (0.15 ml)	3 % (0.45 ml)	2% (0.30 ml)	1 (0.15 ml)	1% (0.15 ml)	1% (0.15 ml)	3% (0.45 ml)	2% (0.30 ml)	3% (0.45 ml)
Propylene Glycol (10%)	1.5 ml	1.5 ml	1.5 ml	1.5 ml	1.5 ml	1.5 ml	1.5 ml	1.5 ml	1.5ml	1.5ml	1.5ml	1.5ml
Glycerine (5%)	0.75 ml	0.75 ml	0.75 ml	0.75 ml	0.75 ml	0.75 ml	0.75 ml	0.75 ml	0.75 ml	0.75 ml	0.75 ml	0.75 ml
Distilled Water q.s. to	15 ml	15 ml	15 ml	15 ml	15 ml	15 ml	15 ml	15 ml	15ml	15ml	15ml	15ml

Table 2: Composition of Gel Formation

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Carbopol 934 (%)	0.5% (0.075 g)	1% (0.15 g)	1 % (0.15 g)	0.75% (0.11 g)	0.75% (0.11 g)	1% (0.15 g)	0.5% (0.075 g)	1% (0.15 g)	0.75% (0.11g)	0.5% (0.075g)	0.5% (0.075g)	0.75% 0.11g)
Triethanolamine (TEA)	q.s. (pH 6.5–7)	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s	q.s	q.s	q.s
Distilled Water q.s. to	15 ml	15 ml	15 ml	15 ml	15 ml	15 ml	15 ml	15 ml	15 ml	15 ml	15 ml	15 ml

Evaluation parameters:
The following evaluations were carried out on the prepared nanoemulgels:
Measurement of pH: The pH meter was standardised using standard buffer solutions with pH values of 4, 7, and 9. The pH was determined after around 0.5 grammes of Emulgel were dissolved in 50 ml of clean water [14,15].
Viscosity*:* A Brookfield viscometer (Brookfield Engineering Laboratories, Inc., USA) with spindle number-64 was used to measure the viscosity of emulgel at various rpm. After rotating the spindle at 10, 50, 60, and 100 rpm, the viscosity (cP) and torque (%) were determined. When the torque is decreased, the viscosity will rise [14,15].
Spreadability test: Two slides were sandwiched with 500 mg of the nanomulgel. The upper slide has a 100g weight. Excess formulation was scraped off and weight was eliminated. The upper slide was attached to a non- flexible string that held a 20 g load, while the lower slide was fixed to the apparatus's board. When the upper slide came off, the time was noted [14,15].
Spreadability (S) = Applied Weight (M)×Distance Moved (L) / Time Taken(T)

Where,
S = Spreadability
M = Mass or weight placed on the top slide
L = Distance the top slide travels over the base slide
T = Time taken for the movement

Zeta Potential*:* The evaluation of stability and surface charge in colloidal dispersions and nanoformulations relies on zeta potential, indicating the electrical potential at the sliding plane of particles in a liquid. High absolute zeta potential values (exceeding ±30 mV) suggest strong electrostatic repulsion, reducing phase separation and aggregation risks. In this work, zeta potential was measured for a Butenafine 1% gel formulation containing Span 80, Tween 20, Carbopol 934, and Tea Tree Oil, using

laser Doppler electrophoresis in a Zetasizer Nano ZS. The gel was diluted 1:10 (w/v) in distilled water, homogenized, and measured thrice at 25°C to obtain an average zeta potential value [16].

Polydispersity Index: In colloidal systems, the Polydispersity Index (PDI) measures the uniformity of particle size distribution, correlating with formulation stability; lower PDI values indicate greater stability and reduced risks of aggregation. Butenafine gel formulations were analyzed for PDI using the Zetasizer Nano ZS, where gel samples were diluted with distilled water, homogenized, and measured at 25°C through dynamic light scattering. Each batch underwent three measurements, with the average recorded [17].

Particle Size: The butenafine nanoemulgel batches' particle sizes were analyzed via Dynamic Light Scattering (DLS) with a Zetasizer Nano ZS at 25°C and a 90° scattering angle. To avoid multiple scattering effects, samples were diluted with double-distilled water before analysis [17].

Drug content: A nanomulgel containing 10 mg of Butenafine HCl was prepared in a 10 ml volumetric flask by dissolving it in 5 ml of methanol to achieve a concentration of 1000 µg/ml. The volume was adjusted with methanol after transferring 1 ml of the solution to ensure accurate measurement, and the absorbance of the solution was measured at λ max 280 nm using a UV-visible spectrophotometer [18].

In vitro diffusion test: A Franz diffusion cell-like device was developed to measure drug release profiles from nanoemulgel. The device contained a diffusion membrane and a phosphate buffer solution. Samples were collected and diluted, and the drug content was measured using a UV spectrophotometer [19].

Antifungal Activity: *[20,21]*

Step 1: Media preparation:

For fungal organisms like *Candida albicans* and *Aspergillus niger:*

The preferred medium is Mueller Hinton Agar (MHA) supplemented with 2% Glucose and 0.5 µg/mL Methylene Blue (GMB medium) to promote fungal growth and clearer visibility of inhibition zones. Composition of Mueller Hinton Agar (per 1000 mL):

- Agar: 17.0 g;
- Starch: 1.5 g;
- Acid Hydrolysate of Casein: 17.5 g;
- Beef Extract: 2.0 g;
- Distilled Water: 1000 mL;
- pH: 7.3 ± 0.1

Preparation:

1. Accurately weigh all ingredients.
2. Dissolve in distilled water by heating with continuous stirring.
3. Add 2% Glucose and 0.5 µg/mL Methylene Blue Dye.
4. Adjust pH to **7**.3 ± 0.1**.**
5. Sterilize in an autoclave at 121°C for 15 minutes under 15 psi pressure.
6. Cool to around 45-50°C
7. Pour into sterile petri plates to a uniform depth of 4-5 mm and allow to solidify under aseptic conditions.

Step 2: Inoculum Preparation:

For Fungal Test Organisms (e.g *Candida albicans, Aspergillus niger*):

1. Pick 5 well-isolated colonies from a 24–48-hour-old culture grown on Sabouraud Dextrose Agar (SDA**)**.
2. Suspend the colonies in sterile normal saline (0.85% NaCl)**.**
3. Adjust the turbidity to match 0.5 McFarland Standard (optical density approx. 1.5×10^{8} CFU/mL for bacteria; for fungi, it's adjusted for visible turbidity ensuring a confluent lawn of growth).
4. Use immediately for inoculating the agar surface.

Step 3: Test procedure:

1. Using a sterile cotton swab dipped in the prepared inoculum, streak the entire surface of the solidified agar plate in three directions, rotating the plate approximately 60° between each streaking to ensure uniform distribution.
2. Allow the inoculated plates to dry for 5-15 minutes at room temperature with the lid closed.
3. Using a sterile cork borer (usually 6 mm in diameter)**,** punch uniform wells in the agar surface.
4. Fill each well carefully with a measured volume (typically 100 µL) of the test formulation (e.g., Butenafine Nanoemulgel F2, Standard, Marketed Preparation).
5. Allow the plates to stand at room temperature for 30-60 minutes to enable pre-diffusion of the formulations into the agar.
6. Incubate the plates at 28 ± 2°C (for fungi) for 24–48 hours**.**

7. After incubation, measure the zone of inhibition (diameter in mm) around each well using a digital Vernier caliper or millimeter scale.

RESULT AND DISCUSSION

The evaluation of formulation parameters such as pH, viscosity, and drug content, summarized in Table 3, demonstrated that the optimized Butenafine hydrochloride nanoemulgel formulation exhibited suitable topical properties, uniform drug distribution, nanoscale droplet size, good stability, and enhanced drug diffusion, indicating its effectiveness as a topical antifungal delivery system.

pH: The pH of the Butenafine hydrochloride nanoemulgel formulation ranged from 5.8 to 6.6, which is suitable for topical application and unlikely to cause irritation, as it falls within the physiological skin pH range of 4.5 to 6.5. This pH maintenance is important for patient compliance, drug stability, and dermal compatibility, confirming the appropriateness of the selected gelling agent and excipient system.

Viscosity studies: The viscosity of the prepared nanoemulgel was measured to be (insert value, e.g., 25,000–40,000 cps), demonstrating suitable rheological properties for topical formulations. This viscosity facilitates ease of application, improves retention at the site of application, allows controlled drug release, and enhances patient acceptability. The optimized viscosity is primarily due to the concentration of Carbopol (or another polymer) and the uniform dispersion of nanoemulsion droplets in the gel matrix.

Spreadability study: Spreadability of the formulation was determined to be (insert value) g·cm/sec, indicating good characteristics, which ensures uniform drug distribution, ease of application, improved patient compliance, and enhanced therapeutic performance. The optimized nanoemulgel showed satisfactory spreadability due to balanced viscosity and polymer concentration.

Zeta Potential Measurement: Zeta potential of the optimized formulation ranged from –18 mV to –32 mV, which is crucial for predicting physical stability, preventing aggregation, and maintaining dispersion uniformity. Higher magnitude values indicate better electrostatic stabilization of nanoemulsion droplets, implying excellent formulation stability.

Table 3: Physiochemical Evaluation Results of The Formulation. (a)

Formulation No	pH Measurements	Viscosity (cP)	Spreadability (g.cm/sec)	Zeta Potential (mV)
F1	5.78 ± 0.1	4100	15.5	-17.8
F2	6.28 ± 0.1	6100	13.2	-29.4
F3	6.18 ± 0.1	5900	12.5	-25.1
F4	5.57 ± 0.1	5700	14.4	-30.2
F5	5.67 ± 0.1	4300	14.8	-27.9
F6	6.10± 0.1	5800	12.9	-16.9
F7	5.78± 0.1	3100	16.2	-24.6
F8	6.38 ± 0.1	3600	17	-18.3
F9	5.80± 0.1	4600	14.3	-22.5
F10	6.76± 0.1	3400	15.5	-31.2
F11	6.35± 0.1	3460	19	-19.6
F12	6.00±0.1	4200	15.8	-28.7

Particle size: Particle size of the nanoemulsion within the gel system is between 120–180 nm, indicating successful formation, increased surface area, improved drug solubilization, enhanced dermal penetration, and better antifungal efficacy. Smaller droplet size also leads to improved physical stability and uniform drug distribution.

Polydispersity Index (PDI): The PDI value of the optimized formulation was (insert value, e.g., 0.21–0.35), demonstrating a uniform droplet size distribution. A PDI < 0.3 indicates a monodispersed system, while a PDI < 0.5 is acceptable for nanoemulsion stability. Therefore, the obtained PDI confirms the formulation's homogeneity and stability of the nanoemulsion system.

Drug content determination: Drug content in the prepared nanoemulgel was between 96-99%, indicating uniform distribution of Butenafine hydrochloride. This high drug content reflects minimal loss during preparation, reproducibility, efficient incorporation, and reliability of the formulation process, ensuring dose accuracy and therapeutic effectiveness.

In vitro Diffusion study: In vitro diffusion studies of an optimized nanoemulgel formulation demonstrated a drug release of 85–95% within 8–12 hours. The enhanced release profile is attributed to nano-sized droplets, increased surface area, penetration enhancers like propylene glycol, improved solubilization of Butenafine hydrochloride, and a gel matrix that controls release behavior. The formulation

exhibited a sustained diffusion profile compared to conventional gels, indicating better dermal availability and prolonged antifungal activity.

Table 4: Physiochemical Evaluation Results of The Formulation. (b)

Formulation No	PDI	Particle Size (nm)	Drug Content (%)	In Vitro Diffusion (%)
F1	0.210	160.5	94.3 ±0.56	92.3
F2	0.287	189.3	101 ±0.42	95.6
F3	0.230	170.1	97.2±0.23	96.7
F4	0.265	185.7	99.8 ±0.65	94.1
F5	0.248	175.6	95.6±0.51	95.0
F6	0.200	152.8	93.9±0.42	94.1
F7	0.273	180.2	98.4 ±07	92.5
F8	0.224	168.4	96.1 ±0.34	91.6
F9	0.290	190.0	100.2±0.3	93.7
F10	0.232	150.9	93.5±0.54	93.2
F11	0.275	182.3	102.0±0.6	90.8
F12	0.260	177.5	97.7±0.73	92.9

Graphical Representation of In vitro Drug Diffusion:

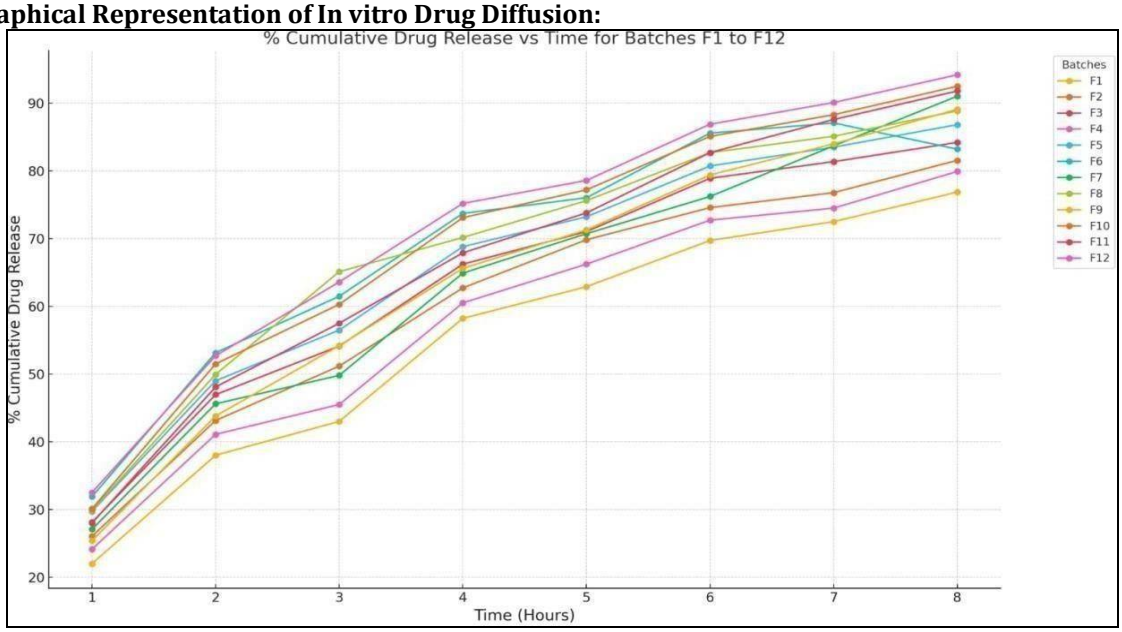

Figure 4 : % CDR vs Time for drug diffusion

The Butenafine hydrochloride nanoemulgel formulation shows skin-compatible pH, acceptable viscosity, good spreadability, nano-range particle size, low PDI, stable zeta potential, high drug content uniformity, and enhanced in-vitro drug diffusion. These attributes confirm its stability and effectiveness for topical antifungal therapy, providing improved drug penetration and sustained release compared to conventional forms.

***Antifungal activity*:**

Antifungal study was performed as per the standard procedure mentioned under experimental work. For the optimized batch zone of inhibition was found as 24 mm. On the basis of antifungal results, it was proved that optimized batch of nanoemulgel was having sufficient antifungal activity. The results were expressed as following.

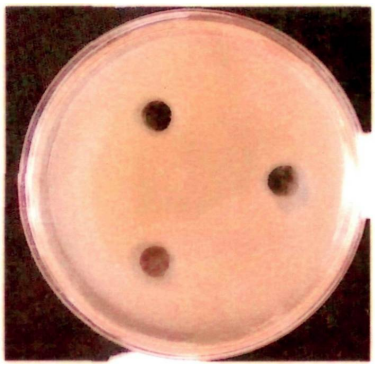

Fig. 5 Antifungal plate before application

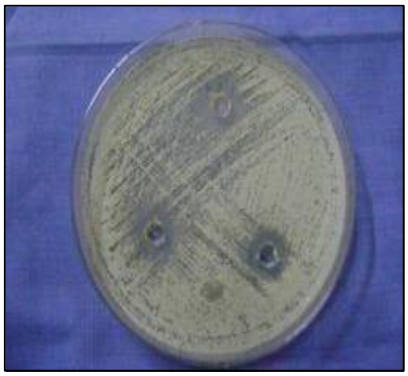

Fig. 6 Antifungal plate After application

Table 5: Comparison Of Antifungal Activity

Sr.no.	Sample	Zone of inhibition (mm)
1.	Optimized batch (F2)	24 mm
2.	Standard Butenafine HCl	20 mm
3.	Marketed Preparation	18mm

CONCLUSION

The investigation developed and optimized a Butenafine hydrochloride 1% w/w nanoemulgel using Carbopol 934, tea tree oil, and a surfactant-cosurfactant system (Span 80 and Tween 20). A 3^3 factorial design assessed the impact of formulation variables on quality attributes such as particle size, viscosity, spreadability, drug content, and in-vitro diffusion behavior. The optimized formulation exhibited nanosized droplets, low polydispersity, and physical stability, along with suitable viscosity and high drug content uniformity, improving patient compliance. In-vitro studies showed enhanced drug release compared to conventional formulations due to smaller droplet size and surfactant effects, suggesting increased dermal permeation and antifungal activity. This nanoemulgel delivery system provides controlled drug release and increased residence time, enhancing therapeutic effectiveness. Further research is recommended for clinical evaluation and long-term assessment for treating superficial fungal infections.

FUTURE SCOPE

The formulation and evaluation of Butenafine hydrochloride 1% w/w nanoemulgel using a 3^3 factorial design presents opportunities for further research in topical drug delivery systems. Future studies should include in vivo and clinical evaluations to confirm efficacy and safety, incorporation of additional therapeutic agents, advanced characterization techniques like TEM and confocal microscopy, assessments of patient acceptability and sensory properties, and exploration of synergistic herbal actives. These efforts may enhance the clinical translation and commercialization of nanoemulgel-based topical antifungal drug delivery systems.

REFERENCES

1. Hamed R, Alkilani AZ, Al-Adhami Y, Musleh B, Aburayya R. (2003). Advances in Transdermal Delivery Systems for Antifungals: Current Approaches and Future Perspectives. Microbial Pathogenesis. https://doi.org /10.1016/j.micpath.2025.107776.
2. Ahmed MG, Biju P, Shenoy MM, Shafeeh AR, Mustafa M, Kanekar S, Fathima Z. (2025). Navigating Effective Therapeutic Strategies for Dermatophytosis. Journal of Young Pharmacists. 17(1): 7-12.
3. Shah P, Bhargava S, Chakrabarty S, Damodaran RT, Saikia PK, Shenoy M, Bangale N. (2025). Rising burden of superficial fungal infections in India and the role of Clotrimazole for optimal management. IP Ind. J. Clin. Exp. Dermatol. 9[1]:1-16. https://doi.org/10.18231/j.ijced.2023.001.
4. Hammoudi Halat D, Younes S, Mourad N, Rahal M. (2022). Allylamines, benzylamines, and fungal cell permeability: a review of mechanistic effects and usefulness against fungal pathogens. Membranes. https://doi.org/10.3390/membranes12121171
5. Patel RB, Patel MR, Thakore SD, Patel BG. (2017). Nanoemulsion as a valuable nanostructure platform for pharmaceutical drug delivery. InNano-and Microscale Drug Delivery Systems . https://doi.org/10.1016/B978-0-323-52727-9.00017-0.
6. Wróblewska M, Szymańska E, Winnicka K. (2021). The Influence of Tea Tree Oil on Antifungal Activity and Pharmaceutical Characteristics of Pluronic® F-127 Gel Formulations with Ketoconazole. Int J Mol Sci. 22(21):11326. doi: 10.3390/ijms222111326. PMID: 34768755; PMCID: PMC8582737.
7. Szunerits S, Boukherroub R. (2018). Heat: a highly efficient skin enhancer for transdermal drug delivery.

Frontiers in bioengineering and biotechnology. https://doi.org/10.3389/fbioe.2018.00015.
8. Pawar A, Dere S, Pandhare R, Mohite P, Alharbi HM, Subramaniyan V, Kumarasamy V, Maitra S, Ahamed FM, Uti DE, Kumer A. (2025). Enhancing solubility and dissolution of felodipine using self- nanoemulsifying drug systems through in vitro evaluation. Scientific Reports. https://doi.org/10.1038/s41598-025-90962-9.
9. Garcia CR, Malik MH, Biswas S, Tam VH, Rumbaugh KP, Li W, Liu X. (2021). Nanoemulsion delivery systems for enhanced efficacy of antimicrobials and essential oils. Biomaterials Science. 10:633-653. https://doi.org /10.1039/D1BM01537K.
10. Anegundi R. (2022). Formulation and optimization of process variables of a model water insoluble drug using nanoemulsion technology (Master's thesis, Rajiv Gandhi University of Health Sciences (India).
11. Ferreira SC, Bruns RE, Ferreira HS, Matos GD, David JM, Brandão GC, da Silva EP, Portugal LA, Dos Reis PS, Souza AS, Dos Santos WN. (2007). Box-Behnken design: An alternative for the optimization of analytical methods. Analytica chimica acta. https://doi.org/10.1016/j.aca.2007.07.011.
12. Kraisit P, Yonemochi E, Furuishi T, Mahadlek J, Limmatvapirat S. (2022). Chitosan film containing antifungal agent-loaded SLNs for the treatment of candidiasis using a Box-Behnken design. Carbohydrate Polymers. https://doi.org/10.1016/j.carbpol.2022.119178.
13. Fasolo D, Pippi B, Meirelles G, Zorzi G, Fuentefria AM, von Poser G, Teixeira HF. (2020). Topical delivery of antifungal Brazilian red propolis benzophenones-rich extract by means of cationic lipid nanoemulsions optimized by means of Box-Behnken Design. Journal of Drug Delivery Science and Technology. https://doi.org/10.1016/j.jddst.2020.1015732020 Apr.
14. Phagna M, Badhwar R, Singh M, Alhalmi A, Khan R, Noman OM, Alahdab A. (2023). Development and characterization of terbinafine- loaded nanoemulgel for effective management of dermatophytosis. Gels. 9[11]: 894. https://doi.org/10.3390/gels9110894.
15. Maslii Y, Ruban O, Kasparaviciene G, Kalveniene Z, Materiienko A, Ivanauskas L, Mazurkeviciute A, Kopustinskiene DM, Bernatoniene J. (2020). The influence of pH values on the rheological, textural and release properties of Carbomer Polacril® 40P-based dental gel formulation with plant-derived and synthetic active components. Molecules. 25(21). doi: 10.3390/molecules25215018.
16. Souza ID, Saez V, Mansur CR. (2023). Lipid nanoparticles containing coenzyme Q10 for topical applications: An overview of their characterization. Colloids and Surfaces B: Biointerfaces. doi: 10.1016/j.colsurfb.2023.113491.
17. Danaei MR, Dehghankhold M, Ataei S, Hasanzadeh Davarani F, Javanmard R, Dokhani A, Khorasani S, Mozafari YM. (2018). Impact of particle size and polydispersity index on the clinical applications of lipidic nanocarrier systems. Pharmaceutics. 10(2):57. https://doi.org/10.3390/pharmaceutics10020057.
18. Savva M. (2019). Dilution and Concentration of Pharmaceutical Solutions and Other Physical Mixtures. In Pharmaceutical Calculations: A Conceptual Approach. DOI:10.1007/978-3-030-20335-1_5
19. Gómez-Lázaro L, Martín-Sabroso C, Aparicio-Blanco J, Torres-Suárez AI. (2024). Assessment of In Vitro Release Testing Methods for Colloidal Drug Carriers: The Lack of Standardized Protocols. Pharmaceutics. 12;16(1):103. doi: 10.3390/pharmaceutics16010103. PMID: 38258113; PMCID: PMC10819705.
20. Seneviratne CJ, Rosa EA. (2016). Antifungal drug discovery: new theories and new therapies. Frontiers in microbiology. doi: 10.3389/978-2-88919-950-1.
21. Xu WL, Peng GY, Qin SL, Zheng YQ, Huang JC, Zhou JM, Zheng MY, Zheng DY, Zhang X. (2026). Antifungal susceptibility testing and clinical efficacy observation of methylene blue photodynamic therapy in treating trichophyton indotineae infections. Photodiagnosis Photodyn Ther.;58:105363. doi: 10.1016/ j.pdpdt.2026.105363. Epub 2026 Jan 21. PMID: 41577315.