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Development and Evaluation of a Ciclopirox Olamine-Loaded Nanoemulgel for Topical Antifungal Delivery

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ABSTRACT

Background and Aim: Superficial fungal infections of the skin are among the most common dermatological disorders worldwide, particularly in tropical and humid regions, and are associated with substantial morbidity, recurrence, and impaired quality of life. Conventional topical formulations of Ciclopirox Olamine (CPO) suffer from limited penetration across the stratum corneum, inadequate retention at the site of action, and the need for frequent application, which may compromise patient compliance and therapeutic outcomes. The present study was undertaken to develop and evaluate a CPO-loaded nanoemulgel intended to for enhanced dermal delivery, prolong skin residence time, and improve antifungal efficacy in topical therapy.

Methods: *Preformulation studies included determination of λmax, construction of a calibration curve in phosphate-buffered saline (PBS) pH 5.5, and drug excipient compatibility assessment by Fourier transform infrared spectroscopy (FTIR). Equilibrium solubility of CPO was determined in various oils, surfactants, and co-surfactants, and pseudo-ternary phase diagrams were constructed at different Smix ratios by the aqueous titration method. Nine nanoemulsion batches (F1–F9) were prepared by spontaneous emulsification and optimized with respect to globule size, polydispersity index (PDI), and zeta potential. The optimized nanoemulsion was incorporated into a Carbopol 940 gel base to obtain the nanoemulgel, which was evaluated for pH, viscosity, spreadability, drug content, in vitro drug release through a dialysis membrane using Franz diffusion cells, and in vitro antifungal activity against Candida albicans. Accelerated stability studies were carried out as per ICH guidelines (40 ± 2 °C / 75 ± 5% RH) for three months. All experiments were performed in triplicate (n = 3) and results are expressed as mean ± SD. Statistical analysis*

was performed using [software name/version] with one-way ANOVA followed by Tukey's HSD post hoc test; $p < 0.05$ was considered statistically significant.

Results: *CPO exhibited the highest solubility in oleic acid, Tween 80, and PEG 400, which were accordingly selected as the oil, surfactant, and co-surfactant. The optimized nanoemulsion (F5) showed a globule size of 92.4 ± 3.1 nm, PDI of 0.214 ± 0.02, and zeta potential of -28.6 ± 1.2 mV. The corresponding nanoemulgel demonstrated skin-compatible pH (6.2–6.5), suitable viscosity, good spreadability, and drug content close to 99%. In vitro release followed the Korsmeyer–Peppas model with anomalous (non-Fickian) transport and achieved 96.8 ± 2.1% cumulative release at 12 h, significantly higher than the marketed CPO cream (70.3 ± 2.2%, $p < 0.05$). The nanoemulgel produced a significantly larger zone of inhibition against C. albicans than the marketed cream and plain drug dispersion ($p < 0.05$). FTIR confirmed the absence of drug–excipient interaction, and the formulation remained physically and chemically stable over three months under accelerated conditions.*

Conclusion: *The developed Ciclopirox Olamine nanoemulgel is a stable, efficacious, and patient-friendly topical delivery system that markedly enhances drug release and antifungal activity relative to conventional CPO formulations, with potential to reduce dosing frequency and improve therapeutic outcomes in superficial fungal infections, warranting further evaluation in appropriate in vivo and clinical studies.*

KEYWORDS: *Ciclopirox olamine; Nanoemulsion; Nanoemulgel; Topical antifungal therapy; Franz diffusion cell; Candida albicans; ICH stability; Korsmeyer-Peppas kinetics.*

INTRODUCTION

Superficial fungal infections of the skin, collectively termed dermatomycoses, are among the most prevalent dermatological disorders worldwide, encompassing dermatophytosis (tinea), cutaneous candidiasis, and pityriasis versicolor. These infections affect an estimated 20-25% of the global population at any given time, with markedly higher prevalence in tropical and

subtropical regions where elevated ambient temperature and humidity favour fungal proliferation and transmission [1,2]. Although rarely life-threatening in immunocompetent individuals, dermatomycoses are associated with pruritus, cosmetic disfigurement, social stigma, and a considerable healthcare burden, compounded by high recurrence rates and emerging antifungal resistance among Candida and dermatophyte species [3].

Topical antifungal therapy remains the first-line approach for localized superficial mycoses, as it delivers drug directly to the infection site while minimizing systemic exposure. However, conventional dosage forms such as creams, ointments, and gels are frequently limited by the formidable barrier function of the stratum corneum, inadequate drug solubilization, poor retention at the target site, and the need for frequent, prolonged application-factors that predispose to subtherapeutic drug levels, treatment failure, and relapse [3,4].

Ciclopirox Olamine (CPO) is a broad-spectrum hydroxypyridone antifungal, mechanistically distinct from azoles and allylamines. It acts by chelating polyvalent metal cations (Fe^{3+}, Al^{3+}) that are essential cofactors for fungal metal-dependent enzymes involved in detoxifying reactive oxygen species; inhibition of these enzymes causes intracellular accumulation of toxic peroxides and fungal cell death [4,5]. CPO additionally exhibits anti-inflammatory activity and broad activity against dermatophytes, yeasts (including C. albicans), moulds, and select bacteria. Marketed CPO formulations (0.77% creams, gels, and lotions; 8% nail lacquer) show satisfactory efficacy in mild-to-moderate infections, but are limited by shallow stratum corneum penetration, slow onset of action, and the requirement for prolonged daily application, underscoring the need for advanced dermal delivery systems that can improve local bioavailability and therapeutic performance [4].

The present study was therefore designed to systematically develop, optimize, and evaluate a CPO-loaded nanoemulgel through a rational, stepwise approach beginning with solubility-based component selection and pseudo-ternary phase diagram construction, followed by nanoemulsion batch optimization, gel incorporation, and comprehensive physicochemical, in vitro release, antifungal, and stability evaluation with the objective of providing a stable, efficacious, and patient-friendly topical delivery platform for superficial fungal infections.

MATERIALS AND METHODS

Materials

Ciclopirox Olamine (CPO) was obtained as a gift sample. Oleic acid, Tween 80, PEG 400,

Carbopol 940, triethanolamine, methylparaben, and glycerol were of pharmaceutical/analytical grade. All other reagents and solvents were of analytical grade and used as received. Double-distilled water was used throughout the study.

Preformulation Studies

A stock solution of CPO (1000 µg/mL) was prepared in methanol and diluted with PBS pH 5.5 to obtain working solutions (2–10 µg/mL). Solutions were scanned over 200-400 nm using a UV-visible spectrophotometer to determine λmax, and a calibration curve was constructed by plotting absorbance versus concentration; linearity was assessed from the regression coefficient of determination (R^2). Drug–excipient compatibility was assessed by FTIR: spectra of pure CPO and 1:1 (w/w) physical mixtures with oleic acid, Tween 80, PEG 400, and Carbopol 940 were recorded by the KBr pellet method over 4000–400 cm^{-1}, and the principal characteristic peaks of CPO were compared for shifts, disappearance, or emergence of new peaks indicative of interaction.

Solubility Studies

Equilibrium solubility of CPO was determined in oils (oleic acid, castor oil, isopropyl myristate, liquid paraffin), surfactants (Tween 80, Tween 20, Span 80), and co-surfactants (PEG 400, propylene glycol, ethanol) by adding excess CPO to a fixed volume of each vehicle and agitating at 37 ± 0.5 °C for 72 h. Samples were centrifuged (5000 rpm, 10-15 min), and the supernatant was filtered, diluted, and analyzed spectrophotometrically at λmax. Vehicles showing the highest solubility were selected as the oil, surfactant, and co-surfactant.

Construction of Pseudo-Ternary Phase Diagrams

Pseudo-ternary phase diagrams were constructed by the aqueous titration method using oleic acid, Tween 80, and PEG 400 at Smix (surfactant:co-surfactant) ratios of 1:1, 2:1, and 3:1. For each Smix ratio, oil: Smix mixtures (1:9 to 9:1 w/w) were titrated with double-distilled water under gentle magnetic stirring at 25 ± 2 °C, and the transition from a clear nanoemulsion to a turbid emulsion or phase-separated system was visually recorded to delineate the nanoemulsion region.

Preparation of Nanoemulsion Batches (F1–F9)

Nine CPO nanoemulsion batches (F1–F9; Table 1) were prepared by spontaneous emulsification, varying the oil and Smix proportions while maintaining a fixed CPO

concentration (1% w/w). CPO was dissolved in the oil–Smix mixture with gentle stirring, and the aqueous phase was added dropwise under continuous magnetic stirring (~900 rpm) at ambient temperature until a clear, homogeneous nanoemulsion formed.

Table 1: Composition of nanoemulsion batches F1–F9

Batch	Oil (% w/w)	Smix (% w/w)	Water (% w/w)	Smix ratio	CPO (% w/w)
F1	5	30	64	1:1	1.0
F2	5	35	59	2:1	1.0
F3	5	40	54	3:1	1.0
F4	10	30	59	1:1	1.0
F5	10	35	54	2:1	1.0
F6	10	40	49	3:1	1.0
F7	15	30	54	1:1	1.0
F8	15	35	49	2:1	1.0
F9	15	40	44	3:1	1.0

Preparation of the Nanoemulgel

Carbopol 940 (1% w/w) was dispersed in distilled water and hydrated overnight at room temperature. The optimized CPO nanoemulsion was incorporated gradually into the hydrated Carbopol dispersion under gentle mechanical stirring to avoid air entrapment. Methylparaben (preservative) and glycerol (humectant) were added with continuous stirring, and the pH was adjusted to 6.0–6.5 with triethanolamine to yield a clear, smooth, viscous nanoemulgel suitable for topical application.

Evaluation of the Nanoemulsion and Nanoemulgel

Globule size, PDI, and zeta potential were measured by dynamic/electrophoretic light scattering after appropriate dilution (n = 3). The pH of the nanoemulgel was measured using a calibrated digital pH meter, and viscosity was determined using a Brookfield viscometer (spindle 64, 10 rpm, 25 ± 1 °C). Spreadability was evaluated by the parallel-plate method using $S = m \times l / t$, where m is the applied weight, l is the distance spread, and t is the time. Drug content was determined spectrophotometrically after extraction in methanol. In vitro drug release from the nanoemulgel and marketed cream was studied using Franz diffusion cells fitted

with a dialysis membrane (effective area ≈ 1.76 cm²), with the receptor compartment containing PBS pH 5.5 maintained at 37 ± 0.5 °C and stirred at 100 rpm; samples withdrawn at predetermined intervals were analyzed spectrophotometrically, and cumulative release data were fitted to zero-order, first-order, Higuchi, and Korsmeyer–Peppas models. In vitro antifungal activity against Candida albicans was evaluated by the agar well diffusion (cup-plate) method using Sabouraud dextrose agar, with zones of inhibition measured after 24-48 h incubation at 25-27 °C.

Stability Studies

The optimized nanoemulgel was stored at accelerated conditions of 40 ± 2 °C / 75 ± 5% RH as per ICH guidelines, and evaluated for appearance, pH, globule size, and drug content at 0, 1, 2, and 3 months.

Statistical Analysis

All experiments were performed in triplicate and data expressed as mean ± SD. Differences between formulations were analyzed by one-way ANOVA followed by Tukey's honestly significant difference (HSD) post hoc test, with $p < 0.05$ considered statistically significant.

RESULTS AND DISCUSSION

Solubility Studies

CPO exhibited the highest solubility in oleic acid (48.6 ± 1.9 mg/mL) among the oils tested, followed by castor oil, isopropyl myristate, and liquid paraffin (Table 2, Figure 2). Among surfactants, Tween 80 showed the greatest solubilizing capacity (62.3 ± 2.2 mg/mL), and among co-surfactants, PEG 400 was superior (55.8 ± 2.0 mg/mL). The high solubility in oleic acid is attributable to favourable drug–lipid interactions and its known penetration-enhancing effect on stratum corneum lipids, while the high HLB of Tween 80 (~15) favours solubilization of moderately lipophilic drugs, and PEG 400 acts as an efficient co-solvent by partitioning into the interfacial film. Oleic acid, Tween 80, and PEG 400 were accordingly selected as the oil, surfactant, and co-surfactant for nanoemulsion development.

Table 2: Equilibrium solubility of CPO in oils, surfactants, and co-surfactants

Vehicle	Category	Solubility (mg/mL, mean ± SD)
Oleic acid	Oil	48.6 ± 1.9

Castor oil	Oil	31.2 ± 1.5
Isopropyl myristate	Oil	22.7 ± 1.1
Liquid paraffin	Oil	9.4 ± 0.8
Tween 80	Surfactant	62.3 ± 2.2
Tween 20	Surfactant	44.1 ± 1.7
Span 80	Surfactant	18.5 ± 1.0
PEG 400	Co-surfactant	55.8 ± 2.0
Propylene glycol	Co-surfactant	39.6 ± 1.6
Ethanol	Co-surfactant	33.2 ± 1.4

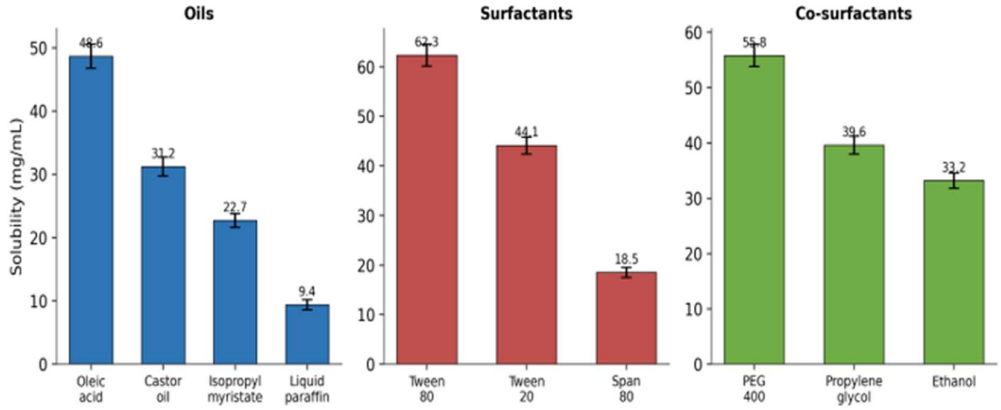

Figure 1: Equilibrium solubility of CPO in oils, surfactants, and co-surfactants

Drug–Excipient Compatibility (FTIR)

Pure CPO showed characteristic bands at ~3140 cm^{-1} (O–H stretch), ~3360 cm^{-1} (N-H stretch), ~1635 cm^{-1} (pyridone C=O), ~1545 cm^{-1} (aromatic C=C), ~1450 cm^{-1} (C-H bending), and ~1290 cm^{-1} (C-N stretch). In the physical mixture with oleic acid, Tween 80, PEG 400, and Carbopol 940, all principal peaks were retained with only minor shifts (±2-4 cm^{-1}) and no new peaks (Table 3, Figure 3), confirming the absence of chemical interaction and the suitability of the selected excipients for nanoemulgel formulation.

Table 3: FTIR characteristic peaks drug-excipient compatibility

Functional group	**Pure CPO (cm^{-1})**	**Physical mixture (cm^{-1})**	**Inference**
O–H stretch	3140	3138	Retained

N–H (olamine)	3360	3358	Retained
C=O stretch (pyridone)	1635	1633	Retained
C=C aromatic	1545	1547	Retained
C–H bending	1450	1452	Retained
C–N stretch	1290	1288	Retained

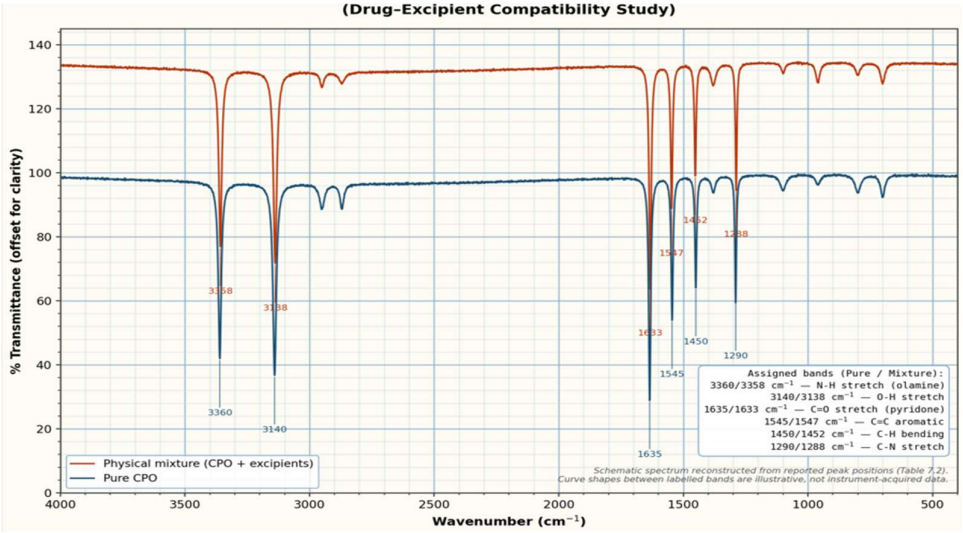

Figure 2: FTIR spectra- pure CPO vs. physical mixture

Calibration Curve

The calibration curve of CPO in PBS pH 5.5 (2–10 µg/mL, λmax 297 nm) was linear (A = 0.0588C + 0.0008; R^2 = 0.9997; Table 4, Figure 4), confirming the reliability of the UV-spectrophotometric method used for drug content and release estimation throughout the study.

Table 4: Calibration curve data of CPO in PBS pH 5.5 (λmax 297 nm)

Concentration (µg/mL)	Absorbance (mean ± SD)
0	0.000
2	0.118 ± 0.003
4	0.236 ± 0.004
6	0.351 ± 0.005
8	0.470 ± 0.006
10	0.588 ± 0.007

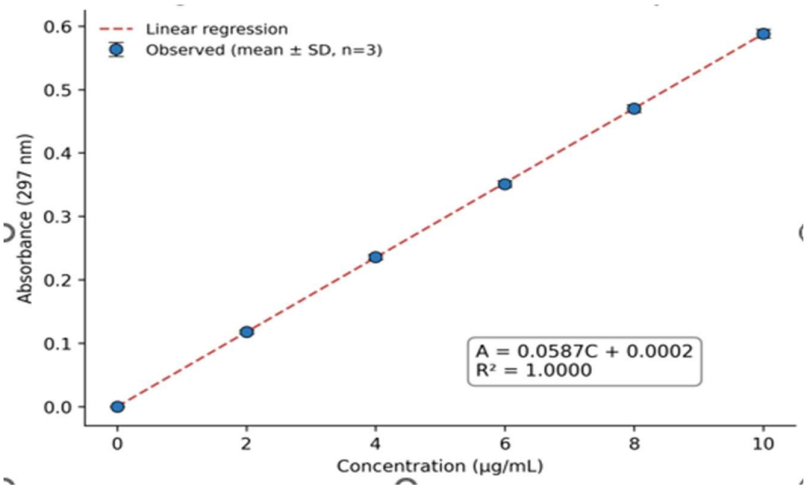

Figure 3: Calibration curve of CPO in PBS pH 5.5

Pseudo-Ternary Phase Diagram

Phase diagrams constructed at Smix ratios of 1:1, 2:1, and 3:1 showed that the 2:1 ratio produced the largest nanoemulsion existence region, reflecting an optimal balance between surfactant and co-surfactant for reducing interfacial tension and stabilizing nanometric droplets; excessive surfactant proportion (3:1) did not further expand the region, while a lower ratio (1:1) yielded a smaller region. The 2:1 Smix ratio was therefore selected for nanoemulsion development.

Globule Size, PDI, and Zeta Potential (F1–F9)

Globule size, PDI, and zeta potential of batches F1–F9 are summarized in Table 5. Smaller globule sizes and lower PDI were generally observed at intermediate oil concentrations with the 2:1 Smix ratio. Batch F5 was selected as optimized, showing a mean globule size of 92.4 ± 3.1 nm, PDI of 0.214 ± 0.02, and zeta potential of −28.6 ± 1.2 mV (Figure 4 size distribution). The nanometric size favours a large interfacial area for enhanced drug transfer, the low PDI reflects a narrow, homogeneous size distribution, and the sufficiently negative zeta potential indicates adequate electrostatic repulsion between droplets, favouring kinetic stability against aggregation.

Table 5: Globule size, PDI, and zeta potential of nanoemulsion batches F1–F9

Batch	Globule size (nm)	PDI	Zeta potential (mV)
F1	138.6 ± 4.2	0.298 ± 0.03	−21.4 ± 1.1

F2	118.3 ± 3.8	0.262 ± 0.02	−24.7 ± 1.3
F3	126.9 ± 4.0	0.281 ± 0.03	−22.9 ± 1.0
F4	104.5 ± 3.5	0.241 ± 0.02	−26.1 ± 1.2
F5 (optimized)	92.4 ± 3.1	0.214 ± 0.02	−28.6 ± 1.2
F6	109.7 ± 3.6	0.255 ± 0.03	−25.3 ± 1.1
F7	121.8 ± 3.9	0.276 ± 0.03	−23.5 ± 1.0
F8	98.6 ± 3.3	0.228 ± 0.02	−27.4 ± 1.2
F9	133.2 ± 4.1	0.289 ± 0.03	−22.1 ± 1.1

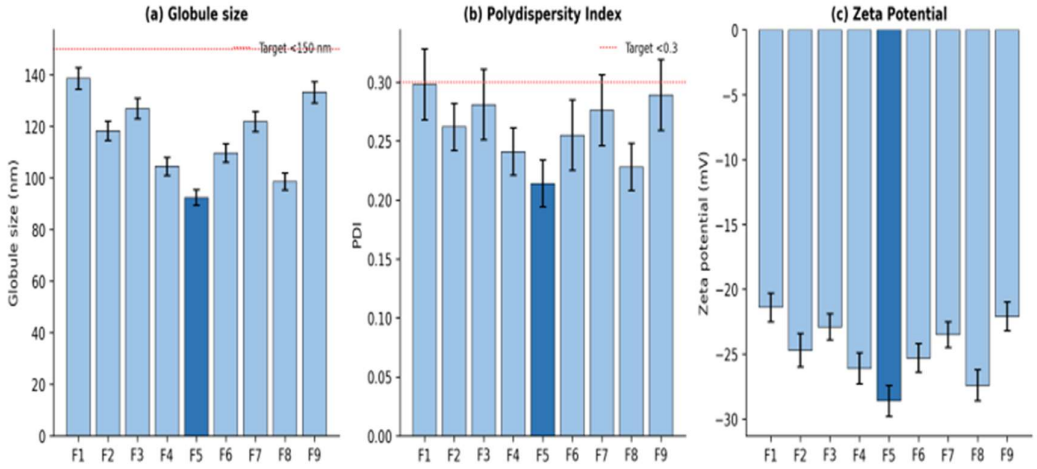

Figure 4: Globule size distribution (intensity %) of the optimized batch (F5)

Physicochemical Evaluation of the Nanoemulgel

Representative nanoemulgel batches (NEG-F2, NEG-F4, NEG-F5, NEG-F8) were evaluated for pH, viscosity, spreadability, and drug content (Table 6, Figure 5). All batches showed a pH of 6.2-6.5, within the physiological range of human skin (4.5-6.5), minimizing the risk of irritation on application; the optimized batch NEG-F5 recorded pH 6.2 ± 0.03. Viscosity values (18,420–19,880 cP) reflected suitable semisolid consistency for topical use, imparted by the pseudoplastic (shear-thinning) rheology of Carbopol 940, allowing easy spreading under applied shear while ensuring good retention at rest. NEG-F5 showed the best spreadability (7.6 ± 0.2 g·cm/s), balancing adequate consistency with ease of application. Drug content exceeded 98% in all batches, with NEG-F5 showing 99.1 ± 0.6%, confirming homogeneous drug distribution and negligible processing losses, well within pharmacopoeial limits (98-102%) for topical semisolids.

Table 6: Physicochemical properties of representative nanoemulgel batches

Batch	pH (mean ± SD)	Viscosity (cP, mean ± SD)	Spreadability (g·cm/s)	Drug content (%)
NEG-F2	6.4 ± 0.05	18420 ± 320	6.8 ± 0.3	98.2 ± 0.9
NEG-F4	6.3 ± 0.04	19150 ± 290	7.2 ± 0.2	98.7 ± 0.8
NEG-F5 (optimized)	6.2 ± 0.03	19880 ± 310	7.6 ± 0.2	99.1 ± 0.6
NEG-F8	6.5 ± 0.05	18960 ± 300	7.0 ± 0.3	98.5 ± 0.7

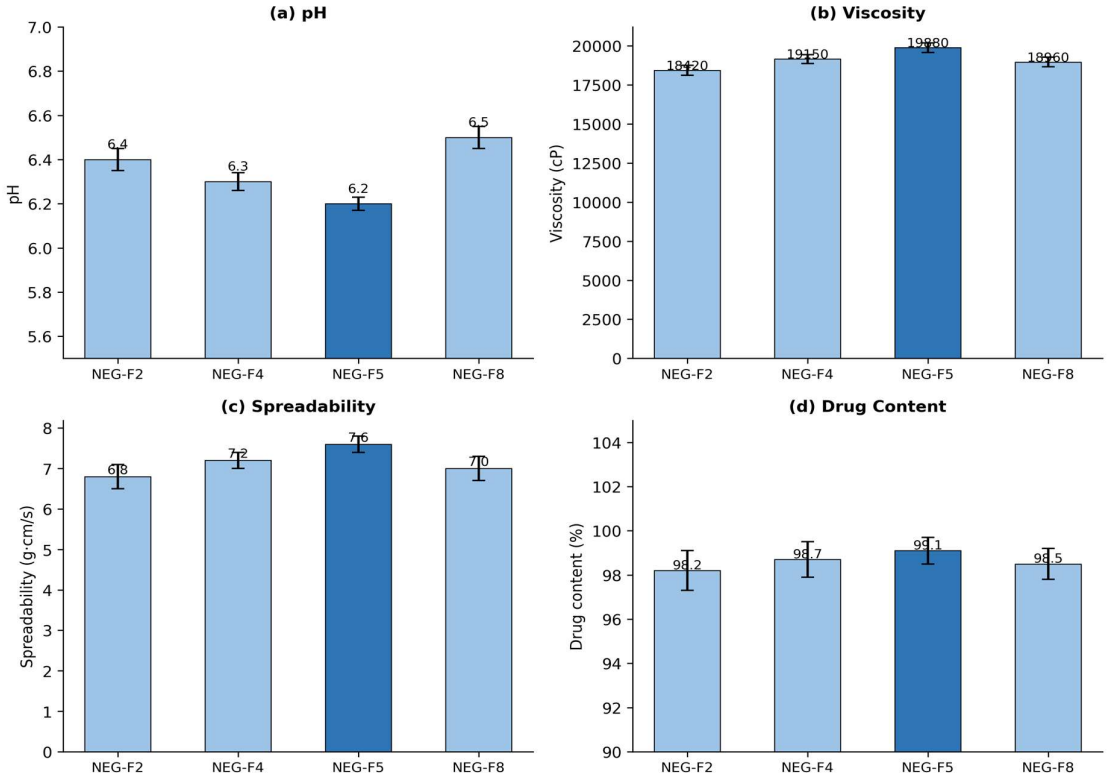

Figure 5: pH, viscosity, spreadability, and drug content of representative nanoemulgel batches

In Vitro Drug Release and Release Kinetics

The optimized nanoemulgel NEG-F5 achieved 96.8 ± 2.1% cumulative drug release at 12 h, significantly greater than the marketed cream (70.3 ± 2.2%; $p < 0.05$) and the next-best batch NEG-F4 (91.2 ± 2.0%) (Table 7, Figure 6). The enhanced release is attributable to the nanometric globule size and consequently large interfacial area, the solubilizing action of the

surfactant/co-surfactant system, and the elevated thermodynamic activity of the drug in the dispersed phase, together facilitating rapid partitioning and diffusion. The biphasic release profile an initial faster phase followed by sustained release reflects release of surface-associated drug followed by diffusion-controlled release through the gel network, consistent with 1.3–1.5-fold release enhancements reported for nanoemulgels relative to conventional creams in the antifungal literature [12,14,18].

Table 7: In vitro cumulative drug release (%)

Time (h)	NEG-F5 (%)	NEG-F4 (%)	Marketed cream (%)
0	0	0	0
0.5	12.4 ± 1.1	10.8 ± 1.0	6.2 ± 0.8
1	23.6 ± 1.5	20.1 ± 1.4	11.9 ± 1.1
2	38.9 ± 1.8	34.2 ± 1.7	20.4 ± 1.3
4	57.3 ± 2.0	51.6 ± 1.9	33.7 ± 1.6
6	72.8 ± 2.2	65.9 ± 2.1	45.1 ± 1.8
8	84.5 ± 2.3	77.4 ± 2.2	55.8 ± 2.0
10	92.1 ± 2.2	85.7 ± 2.1	63.9 ± 2.1
12	96.8 ± 2.1	91.2 ± 2.0	70.3 ± 2.2

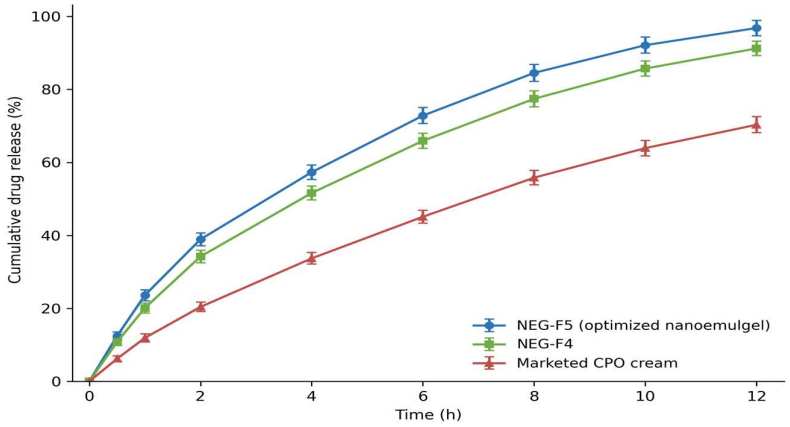

Figure 6: In vitro cumulative drug release profile - NEG-F5 vs. NEG-F4 vs. marketed cream

Release data were fitted to zero-order, first-order, Higuchi, and Korsmeyer–Peppas models (Table 8, Figure 7). The Korsmeyer–Peppas model provided the best fit ($R^2 = 0.994$) with a release exponent n = 0.62, indicating anomalous (non-Fickian) transport in which both drug

diffusion and polymer chain relaxation/erosion govern release. The strong Higuchi fit (R^2 = 0.989) further supports a predominantly diffusion-controlled mechanism through the gel matrix, consistent with kinetic behaviour widely reported for Carbopol-gelled nanocarrier systems [19–21].

Table 8: Release kinetic model fitting parameters for NEG-F5

Model	R^2 (NEG-F5)	Inference
Zero-order	0.962	Good fit
First-order	0.978	Good fit
Higuchi	0.989	Diffusion-controlled
Korsmeyer–Peppas (n = 0.62)	0.994	Best fit; non-Fickian (anomalous) transport

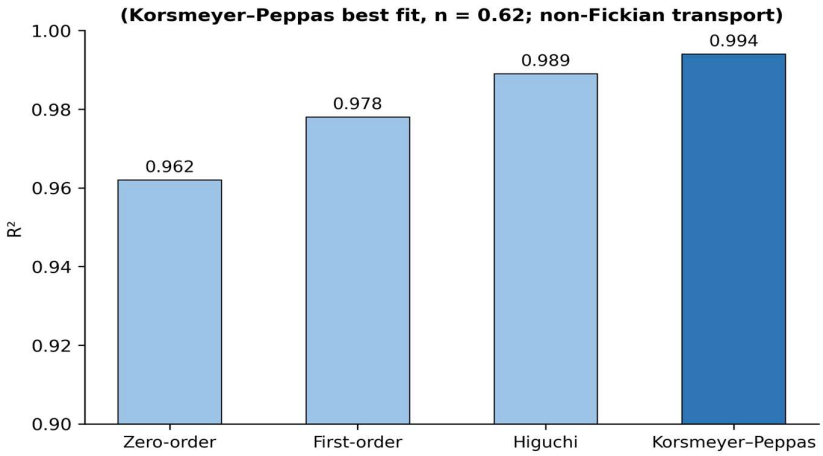

Figure 7: Release kinetic model fitting for NEG-F5

In Vitro Antifungal Activity

The CPO nanoemulgel produced a significantly larger zone of inhibition (25.4 ± 0.8 mm) against Candida albicans than the marketed cream (18.6 ± 0.7 mm) and plain drug suspension (14.2 ± 0.6 mm), while the blank nanoemulgel showed no inhibition, confirming that the observed activity is drug-mediated (Table 9, Figure 8). The rank order nanoemulgel > marketed cream > plain drug mirrors comparative antifungal data reported for azole and allylamine nanoemulgels [18,19] and is attributable to the greater availability of solubilized, finely dispersed CPO at the site of action, facilitating more efficient fungal cell penetration and chelation of essential metal cofactors.

Table 9: In vitro antifungal activity (zone of inhibition) against C. albicans

Test sample	Zone of inhibition (mm)
Plain CPO suspension	14.2 ± 0.6
Marketed cream	18.6 ± 0.7
CPO nanoemulgel (NEG-F5)	25.4 ± 0.8
Blank nanoemulgel (control)	No inhibition

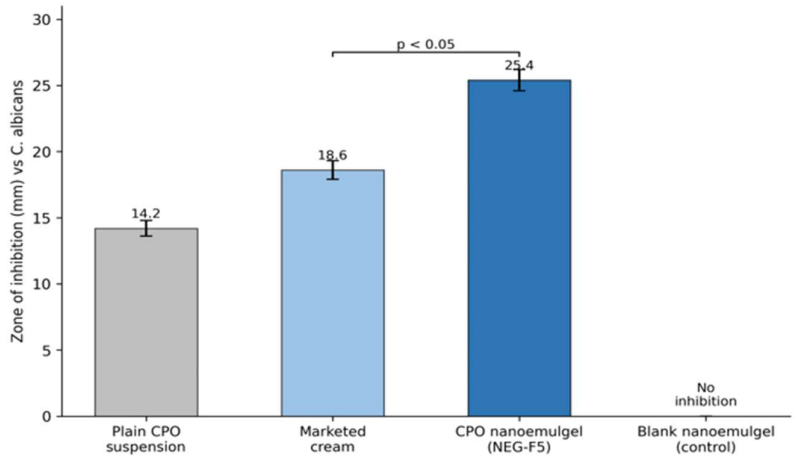

Figure 8: In vitro antifungal activity (zone of inhibition) - comparative bar chart

Statistical Analysis

One-way ANOVA of cumulative drug release at 12 h across the three formulations returned $F = 146.8$ ($p < 0.001$), indicating a statistically significant difference among groups (Table 10). Tukey's HSD post hoc test (Table 11, Figure 9) confirmed that NEG-F5 released significantly more drug than both the marketed cream ($p < 0.001$) and NEG-F4 ($p < 0.05$). As $p < 0.05$ for all pairwise comparisons, the null hypothesis was rejected and the alternative hypothesis accepted the optimized nanoemulgel provides significantly superior release performance.

Table 10: One-way ANOVA summary cumulative drug release at 12 h

Source of variation	SS	df	MS	F	p-value
Between groups	1142.6	2	571.3	146.8	< 0.001
Within groups	23.4	6	3.89	–	–
Total	1166.0	8	–	–	–

Table 11: Tukey HSD post hoc pairwise comparison

Pairwise comparison	Mean difference (%)	Significance (p)
NEG-F5 vs. marketed cream	26.5	< 0.001 (significant)
NEG-F5 vs. NEG-F4	5.6	< 0.05 (significant)
NEG-F4 vs. marketed cream	20.9	< 0.001 (significant)

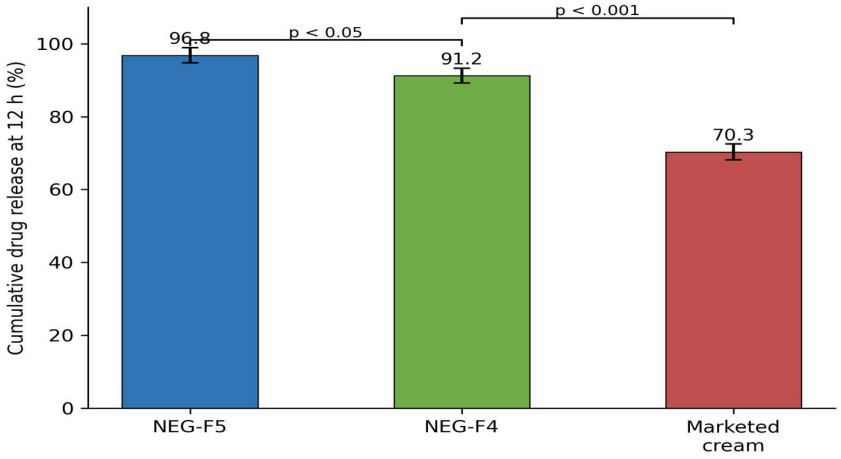

Figure 9: Tukey HSD post hoc pairwise comparison of cumulative drug release

Stability Studies

Under ICH accelerated conditions (40 ± 2 °C / 75 ± 5% RH) for three months, the optimized nanoemulgel retained a translucent, uniform appearance, with pH, drug content, and globule size remaining within acceptable limits (Table 12, Figure 10). Drug content decreased only marginally from 99.1% to 98.0%, and globule size increased slightly from 92.4 to 99.2 nm a change consistent with slow Ostwald ripening that does not compromise product quality. No phase separation, creaming, or significant drug degradation was observed, corroborating stability profiles reported for optimized Carbopol-based nanoemulgels under ICH conditions [24].

Table 12: Stability study data (40 ± 2 °C / 75 ± 5% RH, 3 months)

Parameter	Initial	1 month	2 months	3 months
Appearance	Translucent, uniform	Translucent, uniform	Translucent, uniform	Translucent, uniform
pH	6.2 ± 0.03	6.2 ± 0.04	6.1 ± 0.03	6.1 ± 0.04

Drug content (%)	99.1 ± 0.6	98.8 ± 0.7	98.4 ± 0.6	98.0 ± 0.8
Globule size (nm)	92.4 ± 3.1	94.1 ± 3.3	96.8 ± 3.5	99.2 ± 3.6

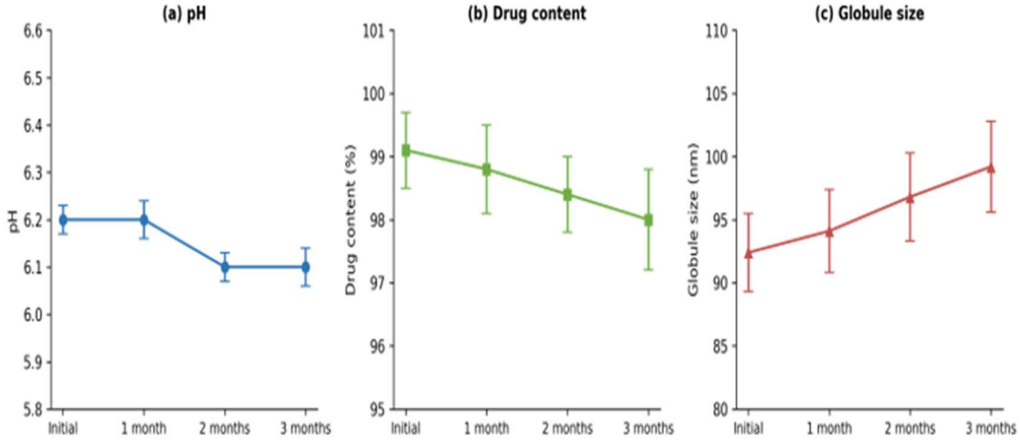

Figure 10: Stability study data over three months under ICH accelerated conditions

CONCLUSION

A Ciclopirox Olamine-loaded nanoemulgel was successfully developed and comprehensively evaluated for enhanced topical antifungal therapy. Solubility studies guided the rational selection of oleic acid, Tween 80, and PEG 400 as the oil, surfactant, and co-surfactant, respectively, and pseudo-ternary phase diagram analysis identified the 2:1 Smix ratio as optimal. Among nine nanoemulsion batches, F5 was optimized on the basis of its small globule size (92.4 nm), low PDI (0.214), and adequate zeta potential (-28.6 mV). The corresponding nanoemulgel exhibited skin-compatible pH, suitable viscosity, good spreadability, and high drug content, together with significantly enhanced in vitro drug release (96.8% at 12 h, following the Korsmeyer–Peppas model with non-Fickian transport) and a markedly larger antifungal zone of inhibition against Candida albicans compared with the marketed cream (ANOVA, $p < 0.001$; Tukey HSD, $p < 0.05$). FTIR confirmed the absence of drug–excipient interaction, and the formulation remained physically and chemically stable over three months under ICH accelerated conditions. Collectively, these findings establish the CPO nanoemulgel as a stable, efficacious, and patient-friendly topical delivery platform capable of overcoming the penetration and retention limitations of conventional CPO formulations, warranting further evaluation through in vivo efficacy, skin-irritation, dermatokinetic, and clinical studies.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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