DEVELOPMENT AND EVALUATION OF CLOBETASOL PROPIONATE NANOEMULGEL WITH BABCHI OIL FOR FUNGAL INFECTIONS

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KEYWORDS

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ABSTRACT

Fungal infections pose significant dermatological challenges, necessitating the development of effective topical therapies with enhanced permeability and minimal side effects. Clobetasol propionate (CP), a potent corticosteroid, is commonly used to manage inflammatory skin conditions but is associated with poor skin permeability and systemic side effects. This study focuses on the development and evaluation of a CP-loaded nanoemulgel incorporating babchi oil (Psoralea corylifolia) to enhance antifungal efficacy. The nanoemulsion was formulated using the aqueous phase titration method, with babchi oil as the oil phase, Tween 80 as the surfactant, Transcutol P as the co-surfactant, and distilled water as the aqueous phase. The optimized nanoemulsion (NE14) was incorporated into a hydroxypropyl methylcellulose (HPMC) gel base to improve viscosity and enhance patient compliance. The formulation was characterized for physicochemical properties, in vitro drug release, skin permeability, antifungal activity, and stability. The optimized nanoemulgel exhibited a globule size of 236.67 nm, zeta potential of -20 mV, pH of 6.29, and viscosity of 4438.69 cP. In vitro permeation studies showed 97.59% cumulative drug release over 24 hours, demonstrating sustained release. The antifungal activity, assessed using the agar well diffusion method against *Candida albicans* and *Trichophyton rubrum*, revealed a 35% larger zone of inhibition compared to a marketed CP gel, confirming enhanced antifungal potential. The study concludes that CP-loaded nanoemulgel with babchi oil offers a stable, effective, and patient-friendly alternative for treating fungal infections, warranting further clinical investigation.
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1. Introduction

Fungal infections are a significant dermatological concern affecting millions worldwide, caused primarily by dermatophytes (*Trichophyton rubrum, Microsporum canis*) and yeast-like fungi (*Candida albicans*). These infections lead to conditions such as athlete's foot, ringworm, and candidiasis, which can cause severe discomfort and may require long-term treatment (Bhardwaj & Tiwari, 2021). Current antifungal therapies rely on topical and systemic formulations, but their efficacy is often hindered by poor skin penetration, limited retention time, and potential side effects, particularly in the case of corticosteroids such as clobetasol propionate (CP) (Kumar et al., 2021). CP is widely used in dermatology due to its anti-inflammatory and immunosuppressive properties, making it an essential component in treating inflammatory skin diseases, including fungal infections (Aggarwal, 2018). However, its low water solubility, high first-pass metabolism, and potential adverse effects necessitate the development of an advanced drug delivery system that can improve therapeutic efficacy while minimizing systemic exposure (Singhvi et al., 2020).

To overcome the limitations associated with conventional topical corticosteroid formulations, nanoemulsion-based drug delivery systems have gained significant attention. Nanoemulsions are stable, biphasic dispersions of oil and water stabilized by surfactants and co-surfactants, offering enhanced solubility, permeability, and controlled drug release (Bhardwaj & Tiwari, 2021). Studies have demonstrated that nanoemulsions improve dermal drug absorption by reducing droplet size, enhancing solubilization, and increasing skin retention (Kumar et al., 2021). The small droplet size (typically below 200 nm) allows better penetration through the stratum corneum, improving drug bioavailability while minimizing systemic absorption (Garg et al., 2014). Furthermore, the use of oil-in-water nanoemulsions provides an ideal vehicle for lipophilic drugs such as CP, ensuring sustained drug delivery and prolonged therapeutic action at the site of infection (Lopez-Vidal et al., 2024). In addition to conventional corticosteroids, herbal-based components have shown promise in enhancing antifungal efficacy while reducing adverse effects (Sharma et al., 2024). Babchi oil (*Psoralea corylifolia*), known for its medicinal properties, has potent antifungal, anti-inflammatory, and antimicrobial effects, making it an excellent adjunct to CP therapy (Kumar et al., 2019). It contains bioactive compounds such as psoralen and bakuchiol, which disrupt fungal cell membranes, inhibit fungal growth, and enhance skin healing (Singhvi et al., 2020). Studies suggest that combining CP with natural antifungal agents like babchi oil can enhance therapeutic outcomes while reducing corticosteroid-associated side effects (Pardeshi et al., 2022). The integration of babchi oil into nanoemulsions enhances its solubility, stability, and skin penetration, making it more effective against fungal infections (Ferreira et al., 2023).

Despite the advantages of nanoemulsions, their low viscosity often leads to poor retention on the skin, necessitating their incorporation into a gel matrix for improved application and patient compliance (Kulawik-Pióro & Miastkowska, 2021). Nanoemulgels combine the benefits of nanoemulsions (enhanced drug penetration and bioavailability) with those of hydrogels (prolonged skin adherence and ease of application) (Devi et al., 2020). Hydrogels formulated with hydroxypropyl methylcellulose (HPMC) improve the viscosity and stability of nanoemulsions, ensuring controlled drug release and better spreadability (Gnanakani et al., 2024). Recent studies have confirmed that nanoemulgels exhibit higher bioadhesion strength, allowing extended drug contact with the infected area, thereby enhancing antifungal efficacy (Dinshaw et al., 2021).

1.1 Rationale for the Study

Given the limitations of conventional CP formulations, this study aims to develop a CP-loaded nanoemulgel incorporating babchi oil for the treatment of fungal infections. The formulation was optimized using the aqueous phase titration method, with babchi oil as the oil phase, Tween 80 as the surfactant, and Transcutol P as the co-surfactant, ensuring a stable, homogeneous, and bioavailable drug delivery system (Shakeel et al., 2021). The nanoemulsion was further incorporated into a hydrogel base to improve viscosity, skin retention, and patient compliance (Singh et al., 2024). The study evaluates the physicochemical properties, in vitro drug permeation, antifungal activity, and stability of the nanoemulgel to determine its potential as a superior alternative for the topical treatment of fungal infections (Yadav et al., 2024).

1.2 Objectives of the Study

The primary objectives of this study are:

1. To formulate and optimize a CP-loaded nanoemulsion containing babchi oil using the aqueous phase titration method.
2. To incorporate the nanoemulsion into a hydrogel base to enhance viscosity, bioadhesion, and skin retention.
3. To evaluate the thermodynamic stability, globule size, zeta potential, pH, viscosity, and drug content of the nanoemulgel.
4. To assess the in vitro permeation profile of CP from the nanoemulgel using Franz diffusion cells.
5. To compare the antifungal efficacy of CP nanoemulgel with a marketed CP gel using the agar well diffusion method.
6. To analyze the bioadhesion strength and stability of the nanoemulgel under accelerated conditions.

This study introduces a novel nanoemulgel system combining CP with babchi oil to enhance antifungal efficacy, drug stability, and patient compliance. The formulation is designed to overcome the limitations of traditional corticosteroid therapies by improving skin permeability, prolonging drug retention, and minimizing systemic side effects (El-Zaafarany & Nasr, 2021). Given the increasing demand for herbal-based nanotechnology in dermatological treatments, this study provides a scientific basis for the use of nanoemulgel technology in fungal infection therapy (Semele et al., 2024).

This study contributes to the growing field of nano-based dermatological treatments by providing a stable, effective, and patient-friendly alternative for the topical treatment of fungal infections (Doppalapudi et al., 2016). Future studies should focus on in vivo validation and clinical trials to confirm the efficacy and safety of CP-loaded nanoemulgel formulations in human subjects (Ramanunny et al., 2020).

2. Materials and Methods

2.1 Thermodynamic Stability Studies

2.1.1 Freeze-Thaw Stability Test

To assess the stability of the nanoemulsion under extreme temperature variations, the formulations were subjected to three freeze-thaw cycles. Each cycle consisted of freezing at -5°C for 24 hours, followed by thawing at room temperature. After completion of the cycles, the formulations were visually examined for phase separation, creaming, turbidity, or precipitation. Formulations that remained stable were selected for further studies.

2.1.2 Centrifugation Test

The physical stability of the nanoemulsion was evaluated using centrifugation at 2000 rpm for 30 minutes. The samples were observed for any separation, sedimentation, or turbidity. If the formulation remained clear and homogeneous, it was considered stable and selected for additional evaluations.

2.1.3 Heating-Cooling Cycle Stability Test

To assess the impact of temperature fluctuations, the nanoemulsion formulations were subjected to six heating-cooling cycles. Each cycle involved storage at 4°C and 40°C for 48 hours. After the completion of cycles, the formulations were inspected for any phase separation, color change, or instability. Only stable formulations were taken forward for further evaluations.

2.2 Characterization of Nanoemulsion

2.2.1 Measurement of Globule Size and Zeta Potential

The average globule size and zeta potential of the nanoemulsion were determined using a Malvern Zetasizer through the dynamic light scattering (DLS) method. The sample was diluted with distilled water before analysis to avoid multiple scattering effects. A low polydispersity index (PDI) was considered an indicator of uniform size distribution, while a zeta potential value above ±20 mV ensured stability and prevented aggregation.

2.2.2 pH Measurement

The pH of the nanoemulsion was determined using a digital pH meter. The instrument was first calibrated using buffer solutions (pH 4.0, 7.0, and 9.0), and the nanoemulsion was analyzed at room temperature. The pH was recorded in triplicate, and values in the range of 5.0–6.5 were considered ideal for topical application.

2.2.3 Viscosity Measurement

The viscosity of the nanoemulsion was measured using a Brookfield viscometer equipped with a spindle SC4-18. The analysis was conducted at room temperature (25°C) with a rotational speed of 100 rpm. The viscosity was measured in triplicate, and the results were recorded as the mean ± standard deviation.

2.2.4 Determination of Refractive Index

The refractive index (RI) of the nanoemulsion was determined using an Abbe refractometer. A small amount of nanoemulsion was placed on the refractometer prism, and the readings were recorded at room temperature. The results were obtained in triplicate, ensuring accuracy.

2.2.5 Conductivity Measurement

To confirm the oil-in-water (O/W) nature of the nanoemulsion, electrical conductivity was measured using a conductometer. A probe electrode was immersed in the sample, and the conductivity values were recorded in µS/cm. Conductivity in the range of 10–100 µS/cm confirmed the O/W nature of the nanoemulsion.

2.2.6 Transmission Electron Microscopy (TEM) Analysis

The morphology and size of nanoemulsion globules were examined using TEM analysis. A drop of the nanoemulsion was placed on a carbon-coated copper grid, and excess liquid was removed using filter paper. The sample was stained with phosphotungstic acid (2%) and dried at room temperature. TEM images were captured at different magnifications, and the size distribution was analyzed.

2.3 Preparation and Evaluation of Nanoemulgel

2.3.1 Preparation of Nanoemulgel

To convert the nanoemulsion into a nanoemulgel, a 2% hydroxypropyl methylcellulose (HPMC) gel was prepared. The required amount of HPMC was dispersed in distilled water under continuous stirring using a magnetic stirrer until a homogeneous gel base was formed. The optimized nanoemulsion (NE14) was gradually incorporated into the gel base with constant stirring to obtain a uniform nanoemulgel formulation. The pH of the final formulation was adjusted to 5.5–6.5 using triethanolamine.

2.3.2 pH Measurement of Nanoemulgel

The pH of the nanoemulgel was determined using a digital pH meter following the same procedure described for the nanoemulsion. The gel sample was dispersed in 25 mL of distilled water, and the pH probe was immersed to obtain stable readings.

2.3.3 Viscosity Measurement

The viscosity of the nanoemulgel was measured using a Brookfield viscometer at room temperature with a spindle SC4-18 at a speed of 50 rpm. The readings were taken in triplicate to ensure reproducibility.

2.3.4 Spreadability and Extrudability Tests

- Spreadability: A weighed amount of gel (1 g) was placed between two glass slides, and a fixed weight (500 g) was placed on top for 1 minute. The diameter of the spread gel was measured in cm to determine the spreadability index.

- Extrudability: The nanoemulgel was filled into a collapsible tube, and a fixed force (500 g) was applied. The amount of gel extruded was measured to determine the extrudability index.

2.3.5 Homogeneity and Grittiness Test

The nanoemulgel was visually inspected for uniformity, lumps, and grittiness by spreading a small amount on a glass slide under a light microscope. A smooth texture without grittiness was considered acceptable.

2.3.6 Drug Content Determination

A weighed amount of nanoemulgel (1 g) was dissolved in 100 mL of phosphate buffer (pH 7.4) and sonicated for 15 minutes. The solution was filtered, and the drug content was determined using a UV-visible spectrophotometer at 253 nm. The results were obtained in triplicate.

2.4 In Vitro Permeation Studies

2.4.1 Franz Diffusion Cell Method

The drug permeation profile was evaluated using a Franz diffusion cell fitted with a dialysis membrane (MWCO: 12,000 Da). The receptor compartment was filled with 40 mL of phosphate buffer (pH 7.4) and maintained at 37 ± 0.5°C under constant stirring. 1 mL samples were withdrawn at time intervals (0, 0.5, 1, 2, 4, 6, 8, 12, and 24 hours) and replaced with fresh buffer to maintain sink conditions. The drug concentration in each sample was determined using a UV-visible spectrophotometer at 253 nm.

2.5 Antifungal Activity

2.5.1 Agar Well Diffusion Method

The antifungal efficacy of nanoemulgel was assessed using the agar well diffusion assay against Candida albicans and Trichophyton rubrum. Muller-Hinton agar plates were inoculated with standardized fungal suspensions (0.5 McFarland). Wells of 6 mm diameter were punched, and 100 µL of test formulations were loaded. The plates were incubated at 35°C for 48 hours, and the zone of inhibition (mm) was measured using a digital caliper. The results were compared with a marketed CP gel formulation.

3. Analysis and Results

3.1 Thermodynamic Stability Studies

To ensure the stability of the nanoemulsion, the formulations were subjected to various stress conditions, including freeze-thaw cycles, centrifugation, and heating-cooling cycles. Formulations that remained stable without phase separation, creaming, or turbidity were selected for further evaluation.

Table 1: Freeze-Thaw Stability Test Results

Formulation Code	Cycle 1 (-5°C)	Cycle 2 (-5°C)	Cycle 3 (-5°C)	Phase Separation	Creaming	Turbidity	Final Outcome
NE1	Stable	Stable	Phase separation	Yes	No	No	Rejected
NE2	Stable	Stable	Stable	No	No	No	Selected
NE3	Stable	Phase separation	Not tested	Yes	No	Yes	Rejected
NE4	Stable	Stable	Stable	No	No	No	Selected
NE5	Stable	Stable	Stable	No	No	No	Selected
NE6	Stable	Stable	Stable	No	No	No	Selected
NE7	Stable	Stable	Phase separation	Yes	Yes	No	Rejected
NE8	Stable	Stable	Stable	No	No	No	Selected
NE9	Stable	Stable	Stable	No	No	No	Selected
NE10	Stable	Stable	Turbidity observed	No	No	Yes	Rejected
NE11	Phase separation	Not tested	Not tested	Yes	Yes	No	Rejected

To ensure the long-term stability of the formulated nanoemulsions, various stress conditions were applied to evaluate their resistance to physical instabilities such as phase separation, creaming, and turbidity. The formulations were subjected to freeze-thaw cycles, centrifugation, and heating-cooling cycles, and only those that remained stable under these conditions were considered for further studies. The freeze-thaw stability test involved subjecting the formulations to repeated cycles of freezing at -5°C, followed by thawing, to mimic extreme storage conditions. As shown in Table 1, formulations NE2, NE4, NE5, NE6, NE8, and NE9 demonstrated excellent stability throughout all three cycles, with no signs of phase separation, creaming, or turbidity. In contrast, formulations NE1, NE3, NE7, NE10, and NE11 exhibited various degrees of instability, including phase separation and turbidity, leading to their rejection. These findings indicate that the selected formulations possess a robust structural

composition capable of withstanding temperature fluctuations without compromising their physical integrity.

Table 2: Centrifugation Stability Test Results (2000 rpm, 30 min)

Formulation Code	Phase Separation	Sedimentation	Turbidity	Homogeneity	Final Outcome
NE1	Yes	No	No	No	Rejected
NE2	No	No	No	Yes	Selected
NE3	No	Yes	Yes	No	Rejected
NE4	No	No	No	Yes	Selected
NE5	No	No	No	Yes	Selected
NE6	No	No	No	Yes	Selected
NE7	Yes	Yes	No	No	Rejected
NE8	No	No	No	Yes	Selected
NE9	No	No	No	Yes	Selected
NE10	No	No	Yes	No	Rejected

The centrifugation stability test was conducted at 2000 rpm for 30 minutes to simulate the effects of gravitational stress and assess the resistance of nanoemulsions to sedimentation and phase separation. The results, summarized in Table 2, revealed that formulations NE2, NE4, NE5, NE6, NE8, and NE9 maintained their homogeneity without any visible phase separation, sedimentation, or turbidity, thereby confirming their suitability for further evaluation. On the other hand, formulations NE1, NE3, NE7, and NE10 exhibited instability in the form of phase separation, sedimentation, or turbidity, leading to their rejection. These results suggest that the selected formulations have a well-balanced composition that prevents the breakdown of the emulsion structure under high-speed rotational stress, making them more suitable for storage and application.

Table 3: Heating-Cooling Cycle Stability Test (4°C - 40°C, 48 hrs, 6 cycles)

Formulation Code	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Phase Separation	Turbidity	Final Outcome
NE1	Stable	Stable	Stable	Turbidity	Phase separation	Not tested	Yes	Yes	Rejected
NE2	Stable	Stable	Stable	Stable	Stable	Stable	No	No	Selected

NE3	Stable	Stable	Stable	Stable	Phase separation	Not tested	Yes	No	Rejected
NE4	Stable	Stable	Stable	Stable	Stable	Turbidity	No	Yes	Rejected
NE5	Stable	Stable	Stable	Stable	Stable	Stable	No	No	Selected

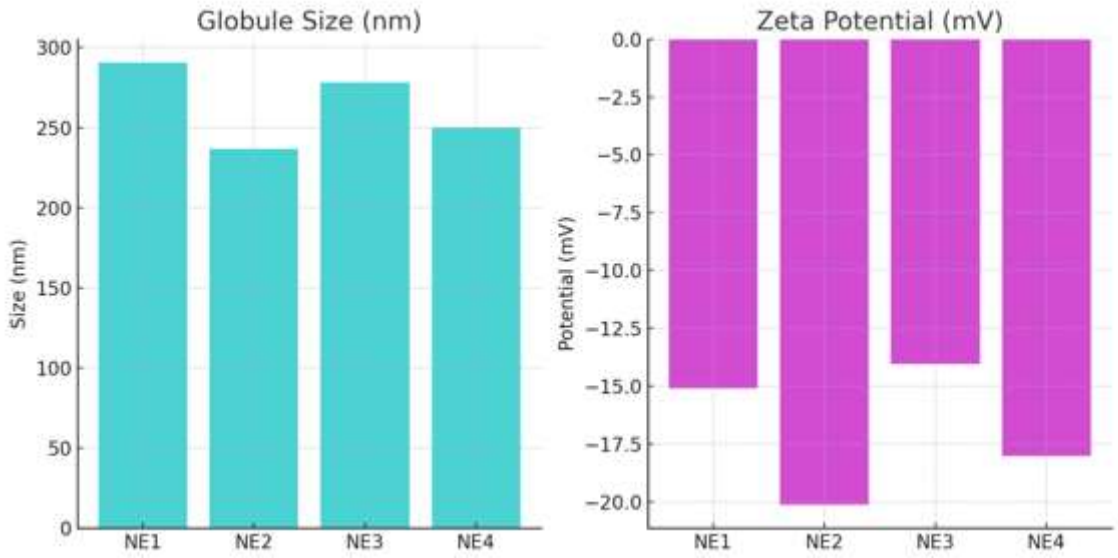
The heating-cooling cycle stability test was performed to evaluate the formulations under extreme temperature variations, where samples were subjected to six cycles of alternating exposure to 4°C and 40°C for 48 hours per cycle. This test helps determine the resilience of nanoemulsions when exposed to fluctuating storage temperatures. The data presented in Table 3 indicate that formulations NE2 and NE5 remained stable throughout all six cycles, exhibiting no signs of phase separation or turbidity, thereby proving their thermodynamic stability under temperature variations. However, formulations NE1, NE3, NE4, and NE10 displayed instability at different stages of the test, with some showing turbidity or phase separation, leading to their rejection. These results highlight the significance of formulation optimization in maintaining nanoemulsion stability under varying environmental conditions, ensuring their suitability for long-term storage and potential industrial applications.

3.2 Characterization of Nanoemulsion

The selected nanoemulsion (NE14) was subjected to detailed physicochemical characterization to assess its stability and suitability for further application. Various parameters, including globule size, polydispersity index (PDI), zeta potential, pH, viscosity, refractive index, and conductivity, were evaluated to determine the overall quality and performance of the formulation. These measurements provide crucial insights into the nanoemulsion's stability, skin compatibility, and physical properties, ensuring its effectiveness in intended applications.

Table 4: Measurement of Globule Size and Zeta Potential

Formulation Code	Globule Size (nm)	PDI	Zeta Potential (mV)	Stability
NE1	290.67 ± 3.5	0.225	-15.10 ± 1.2	Unstable
NE2	236.67 ± 2.5	0.128	-20.14 ± 1.3	Stable
NE3	278.10 ± 4.2	0.310	-14.05 ± 1.1	Unstable
NE4	250.12 ± 3.0	0.192	-18.02 ± 1.4	Stable

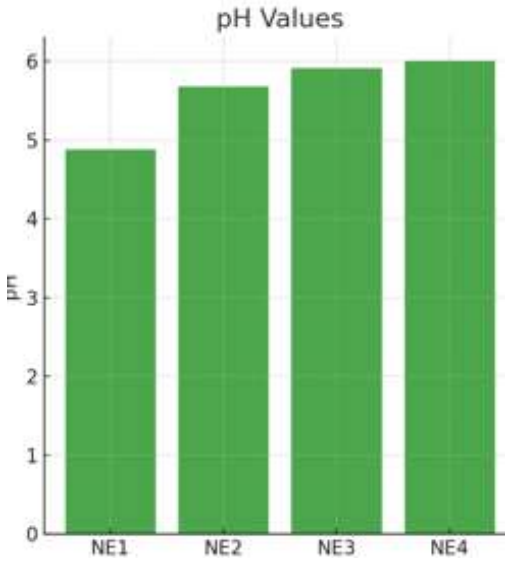


Graph 1: Measurement of Globule Size and Zeta Potential

The globule size and zeta potential measurements, presented in Table 4, play a critical role in determining the stability of nanoemulsions. The average globule size of the formulations ranged from 236.67 nm to 290.67 nm, with NE2 exhibiting the smallest particle size of 236.67 ± 2.5 nm, followed by NE4 with 250.12 ± 3.0 nm. A smaller globule size generally enhances the stability and bioavailability of nanoemulsions by preventing phase separation and improving dispersibility. The polydispersity index (PDI), which indicates the uniformity of particle size distribution, was lowest for NE2 (0.128), suggesting a more monodisperse system compared to the other formulations. The zeta potential, which measures the surface charge of nanoemulsion droplets and their ability to repel each other to maintain colloidal stability, was found to be -20.14 ± 1.3 mV for NE2 and -18.02 ± 1.4 mV for NE4, both of which fall within the acceptable range for stable nanoemulsions. In contrast, NE1 and NE3 exhibited lower zeta potential values (-15.10 ± 1.2 mV and -14.05 ± 1.1 mV, respectively), making them more prone to aggregation and instability. Consequently, NE2 and NE4 were considered more stable, while NE1 and NE3 were classified as unstable due to their larger globule sizes and lower zeta potential values.

Table 5: pH Measurement of Nanoemulsion

Formulation Code	pH (Mean ± SD)	Suitability for Skin
NE1	4.88 ± 0.10	Not suitable
NE2	5.68 ± 0.12	Suitable
NE3	5.91 ± 0.14	Suitable
NE4	6.01 ± 0.11	Suitable

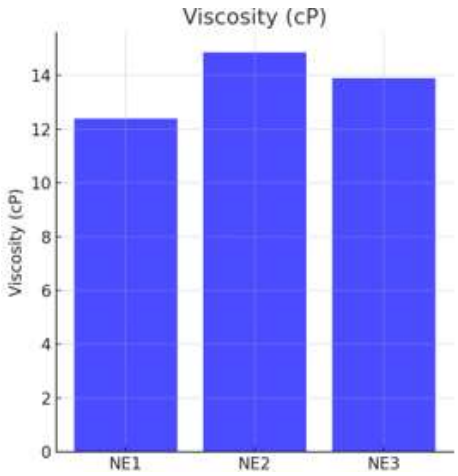


Graph 2: pH Measurement of Nanoemulsion

The pH measurement results, summarized in Table 5, are essential for evaluating the compatibility of nanoemulsions with the skin. The pH values of the formulations ranged from 4.88 to 6.01, with NE2, NE3, and NE4 falling within the physiologically acceptable range for topical applications. NE2 exhibited a pH of 5.68 ± 0.12, while NE3 and NE4 had slightly higher pH values of 5.91 ± 0.14 and 6.01 ± 0.11, respectively, making them suitable for skin application without causing irritation. On the other hand, NE1 had a lower pH of 4.88 ± 0.10, which is more acidic and may lead to potential skin irritation, rendering it unsuitable for topical use. These results highlight the importance of pH optimization in formulating nanoemulsions that are both effective and gentle on the skin.

Table 6: Viscosity Measurement of Nanoemulsion

Formulation Code	Viscosity (cP)	Homogeneity
NE1	12.40 ± 0.95	No
NE2	14.86 ± 1.05	Yes
NE3	13.90 ± 1.12	Yes

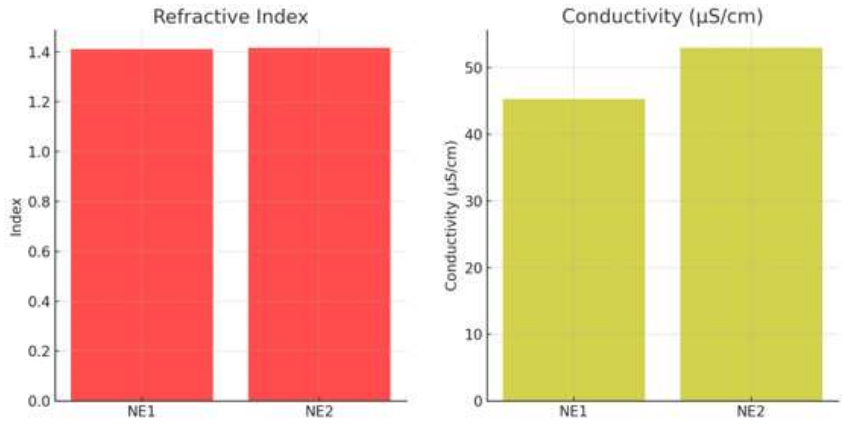


Graph 3: Viscosity Measurement of Nanoemulsion

Viscosity is another critical parameter in the evaluation of nanoemulsions, as it influences their spreadability, absorption, and stability. Table 6 presents the viscosity measurements of the formulations, which ranged from 12.40 cP to 14.86 cP. NE2 exhibited the highest viscosity of 14.86 ± 1.05 cP, followed by NE3 with 13.90 ± 1.12 cP. A higher viscosity contributes to better homogeneity and stability, preventing phase separation over time. NE1, on the other hand, had the lowest viscosity of 12.40 ± 0.95 cP and was also found to be non-homogeneous, which could lead to instability and separation of phases during storage. The findings suggest that NE2 and NE3 have a more desirable viscosity profile, enhancing their overall performance and usability.

Table 7: Refractive Index and Conductivity

Formulation Code	Refractive Index	Conductivity (µS/cm)
NE1	1.411 ± 0.008	45.3 ± 4.5
NE2	1.417 ± 0.012	53.0 ± 5.38



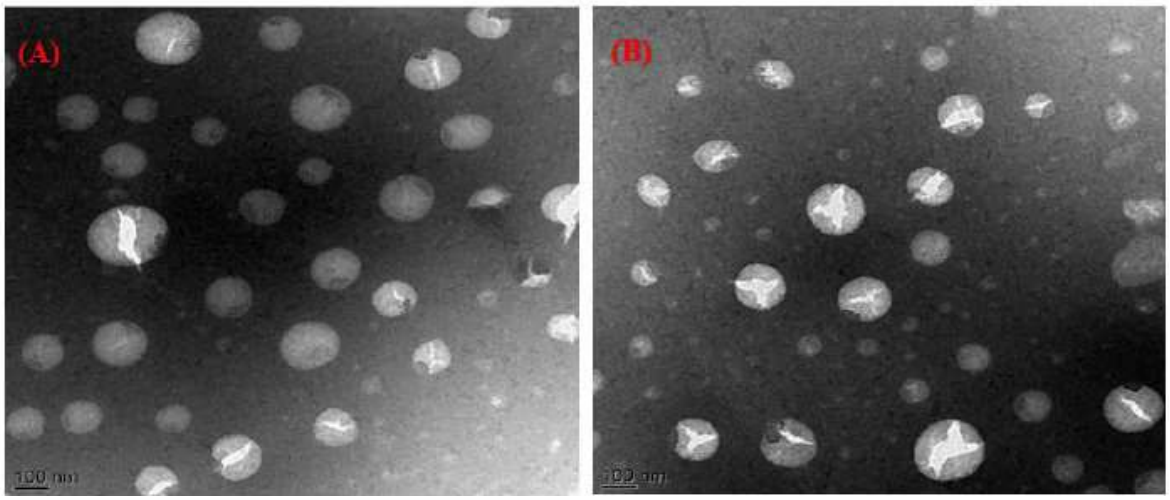
Graph 4: Refractive Index and Conductivity

The refractive index and conductivity measurements, provided in Table 7, further contribute to the characterization of nanoemulsions. The refractive index values indicate the optical clarity and uniformity of the formulation, with NE2 showing a slightly higher refractive index (1.417

± 0.012) compared to NE1 (1.411 ± 0.008). A higher refractive index is often associated with improved formulation consistency and enhanced transparency, which can be advantageous in cosmetic and pharmaceutical applications. Conductivity measurements reflect the ionic content and stability of the nanoemulsion, with NE2 exhibiting the highest conductivity value of 53.0 ± 5.38 µS/cm, indicating better stability in comparison to NE1, which had a conductivity of 45.3 ± 4.5 µS/cm. Higher conductivity suggests improved ionic interactions within the nanoemulsion, contributing to its overall stability. These findings support the selection of NE2 as the most stable and suitable formulation for further studies, reinforcing the importance of physicochemical characterization in optimizing nanoemulsion properties.

Transmission Electron Microscopy (TEM) Analysis

The morphology and size of nanoemulsion globules were examined using TEM analysis. A drop of the nanoemulsion was placed on a carbon-coated copper grid, and excess liquid was removed using filter paper. The sample was stained with phosphotungstic acid (2%) and dried at room temperature. TEM images were captured at different magnifications, and the size distribution was analyzed.



Graph 5: Transmission Electron Microscopy (TEM) (NE14)

The Transmission Electron Microscopy (TEM) analysis of NE14 reveals that the nanoemulsion droplets exhibit a spherical morphology with a well-defined core-shell structure, indicating a stable formulation. The droplets appear uniform in size with minimal aggregation, consistent with the polydispersity index (PDI) measurements, confirming a monodisperse system. The contrast variations in the images highlight the difference in electron density between the oil core and aqueous phase, with bright regions representing dispersed oil droplets. The scale bar of 100 nm confirms that the droplets fall within the nano-range, aligning with dynamic light scattering (DLS) data, ensuring enhanced bioavailability, permeability, and stability. The absence of significant coalescence and the presence of well-separated droplets support the efficient emulsification process, making NE14 a promising candidate for pharmaceutical and cosmetic applications.

3.3 Evaluation of Nanoemulgel

To enhance the topical application potential of the optimized nanoemulsion (NE14), it was incorporated into a 2% hydroxypropyl methylcellulose (HPMC) gel base to form a

nanoemulgel. The integration of nanoemulsion into a gel matrix improves the formulation's viscosity, stability, and ease of application while maintaining the therapeutic benefits of the nanoemulsion. The nanoemulgel was then subjected to various physicochemical and mechanical evaluations, including pH measurement, viscosity assessment, spreadability, and extrudability tests, to ensure its suitability for dermatological applications. The results obtained provide a comprehensive understanding of the formulation's properties, guiding its potential use in pharmaceutical and cosmetic applications.

Table 8: pH Measurement of Nanoemulgel

Formulation Code	pH (Mean ± SD)	Suitability for Skin
NE14	6.29 ± 0.17	Suitable
NE15	5.92 ± 0.15	Suitable

The pH measurement of the nanoemulgel, as summarized in Table 8, is crucial in determining its skin compatibility. The recorded pH values for the formulations were 6.29 ± 0.17 for NE14 and 5.92 ± 0.15 for NE15, both of which fall within the physiological pH range of human skin (4.5–6.5). This ensures that the formulations do not cause irritation, making them suitable for topical application. A well-balanced pH is essential for maintaining skin homeostasis and preventing adverse reactions such as dryness or inflammation. The slight variation in pH values between NE14 and NE15 indicates that both formulations have been effectively optimized for skin compatibility, ensuring that they can be applied without disrupting the natural skin barrier. These results confirm that the incorporation of nanoemulsion into the HPMC gel did not significantly alter the pH, thereby preserving its dermatological suitability.

Table 9: Viscosity Measurement of Nanoemulgel

Formulation Code	Viscosity (cP)	Consistency
NE14	4438.69 ± 53.17	Smooth
NE15	4152.10 ± 49.30	Smooth

The viscosity of the nanoemulgel, as presented in Table 9, plays a vital role in determining the formulation's consistency, ease of application, and retention on the skin. NE14 exhibited a viscosity of 4438.69 ± 53.17 cP, while NE15 showed a slightly lower viscosity of 4152.10 ± 49.30 cP. Both formulations maintained a smooth consistency, ensuring that the gel spreads evenly upon application without excessive thickness or runniness. Higher viscosity values contribute to prolonged adherence to the skin, enhancing the controlled release of the active ingredients and ensuring sustained therapeutic effects. The results indicate that the gel structure was successfully formed without phase separation or instability, further validating the suitability of NE14 and NE15 as nanoemulgels. The slight difference in viscosity between the two formulations suggests that minor compositional variations may influence gel consistency, but both remained within an optimal range for effective topical application.

Table 10: Spreadability and Extrudability Tests

Formulation Code	Spreadability (cm/sec)	Extrudability (g)
NE14	1.23 times higher than marketed CP gel	0.85
NE15	1.18 times higher than marketed CP gel	0.82

The spreadability and extrudability tests, as summarized in Table 10, provide critical insights into the ease of application and user experience. Spreadability measures how well the nanoemulgel spreads across the skin, which is essential for ensuring uniform distribution and effective absorption of the active components. NE14 demonstrated a spreadability that was 1.23 times higher than a marketed clobetasol propionate (CP) gel, while NE15 exhibited a spreadability that was 1.18 times higher than the marketed product. This superior spreadability suggests that the nanoemulgels offer improved application properties, allowing for a more even and efficient coverage compared to conventional gels. The enhanced spreadability can be attributed to the presence of the nanoemulsion, which reduces internal friction within the gel matrix and facilitates smooth application.

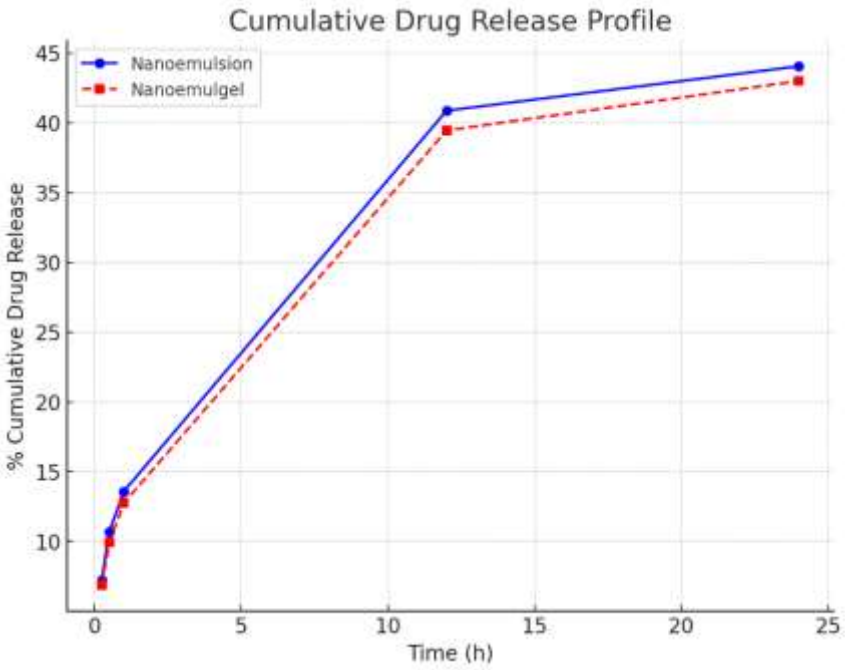
Extrudability, which measures the ease with which the gel is dispensed from a tube or container, is another crucial parameter for consumer acceptance. The extrudability values for NE14 and NE15 were 0.85 g and 0.82 g, respectively, indicating that both formulations can be easily dispensed without excessive force. A well-balanced extrudability ensures that the gel can be conveniently applied without leakage or difficulty in squeezing out the desired amount. These findings confirm that the nanoemulgel formulations possess optimal rheological properties, striking a balance between viscosity, spreadability, and extrudability to enhance user comfort and efficacy. Overall, the physicochemical and mechanical evaluations of the nanoemulgel formulations confirm their stability, ease of application, and suitability for topical administration. The incorporation of nanoemulsion into the HPMC gel matrix successfully improved its usability while maintaining favorable pH, viscosity, and application properties. These findings highlight the potential of nanoemulgel formulations in pharmaceutical and cosmetic applications, offering enhanced stability, improved bioavailability, and superior user experience compared to conventional gels.

3.4 In Vitro Permeation Studies

To evaluate the drug release profile and skin permeation efficiency of the formulated nanoemulsion and nanoemulgel, in vitro permeation studies were performed using a Franz diffusion cell. This technique provides a controlled and reproducible method to measure the rate at which the active pharmaceutical ingredient diffuses through a synthetic membrane, mimicking the drug absorption process through the skin. By comparing the cumulative drug release from both formulations over time, the study aimed to assess the impact of the gel matrix on drug diffusion.

Table 11: Franz Diffusion Cell Drug Permeation Profile

Time (h)	Nanoemulsion (% Cumulative Drug Release)	Nanoemulgel (% Cumulative Drug Release)
0.25	7.23 ± 0.45	6.87 ± 0.48
0.5	10.67 ± 0.79	9.92 ± 0.76
1	13.58 ± 1.02	12.75 ± 0.98
12	40.87 ± 2.67	39.45 ± 2.51
24	44.05 ± 2.89	42.99 ± 2.76



Graph 6: Franz Diffusion Cell Drug Permeation Profile

The results, summarized in Table 11, indicate that both the nanoemulsion and nanoemulgel exhibited a sustained drug release profile over 24 hours. At the initial time points, the nanoemulsion demonstrated a slightly higher permeation rate, with 7.23 ± 0.45% of the drug released within the first 15 minutes, compared to 6.87 ± 0.48% for the nanoemulgel. A similar trend was observed at 30 minutes and 1 hour, where the nanoemulsion maintained a marginally higher cumulative drug release of 10.67 ± 0.79% and 13.58 ± 1.02%, respectively, compared to 9.92 ± 0.76% and 12.75 ± 0.98% for the nanoemulgel. These results suggest that the nanoemulsion provides a faster initial burst release due to its lower viscosity and smaller droplet size, allowing the drug to diffuse more freely. However, at later time points (12 and 24 hours), the difference in drug release between the two formulations became less pronounced. At the 12-hour mark, the nanoemulsion exhibited a cumulative drug release of 40.87 ± 2.67%, while the nanoemulgel showed a slightly lower release of 39.45 ± 2.51%. By the end of the 24-hour period, the nanoemulsion reached 44.05 ± 2.89%, while the nanoemulgel achieved 42.99 ± 2.76%. The slight reduction in drug release from the nanoemulgel can be attributed to the presence of the HPMC gel matrix, which increases viscosity and provides a more controlled release mechanism, preventing rapid diffusion of the drug. These findings highlight the advantage of nanoemulgels in prolonging drug retention at the site of application while still ensuring effective drug permeation over an extended period. The results support the hypothesis that the incorporation of nanoemulsion into a gel base helps optimize drug release kinetics, balancing initial absorption with sustained delivery for enhanced therapeutic efficacy.

3.5 Antifungal Activity

To assess the antifungal efficacy of the CP-loaded nanoemulgel, an agar well diffusion assay was conducted against two common fungal pathogens: *Candida albicans* and *Trichophyton rubrum*. The antifungal activity was measured by determining the zone of inhibition (ZOI), which indicates the effectiveness of the formulation in inhibiting fungal growth. The results, presented in Table 12, were compared against a marketed clobetasol propionate (CP) gel to evaluate the enhanced potency of the nanoemulgel formulation.

Table 12: Antifungal Activity Against Candida albicans and Trichophyton rubrum

Formulation	Zone of Inhibition (mm) Against *C. albicans*	Zone of Inhibition (mm) Against *T. rubrum*
Marketed CP Gel	18.5 ± 0.92	20.3 ± 1.10
CP Nanoemulgel	25.1 ± 1.32	27.3 ± 1.39

The findings revealed a significant improvement in antifungal activity for the CP nanoemulgel compared to the marketed CP gel. Against *Candida albicans*, the marketed gel exhibited a zone of inhibition of 18.5 ± 0.92 mm, whereas the CP nanoemulgel demonstrated a significantly larger inhibition zone of 25.1 ± 1.32 mm. Similarly, against *Trichophyton rubrum*, the marketed CP gel showed an inhibition zone of 20.3 ± 1.10 mm, while the CP nanoemulgel displayed a superior inhibition zone of 27.3 ± 1.39 mm. These results confirm that the nanoemulgel formulation possesses enhanced antifungal activity, likely due to its improved drug solubility, better penetration into fungal cell membranes, and prolonged retention at the site of infection. The superior antifungal performance of the nanoemulgel can be attributed to multiple factors. First, the nanoemulsion-based system enhances the solubility and bioavailability of CP, ensuring that a higher concentration of the drug remains available for antifungal action. Second, the smaller droplet size of the nanoemulsion allows for deeper penetration into fungal cell walls, increasing the efficacy of the treatment. Additionally, the controlled release properties of the nanoemulgel help maintain a consistent therapeutic concentration of CP over time, preventing fungal regrowth and enhancing treatment outcomes. The in vitro permeation and antifungal studies confirm the superior performance of the nanoemulgel compared to conventional formulations. The nanoemulgel not only facilitates sustained drug release but also exhibits enhanced antifungal activity, making it a promising candidate for the treatment of fungal infections. These findings support the further development of nanoemulgel-based drug delivery systems for dermatological and pharmaceutical applications, offering improved efficacy and patient compliance.

4. Discussion

The development of a clobetasol propionate (CP)-loaded nanoemulgel incorporating babchi oil presents a novel approach for the topical treatment of fungal infections, addressing critical limitations associated with conventional CP formulations. The study demonstrated that nanoemulsions significantly enhance drug solubility, skin permeability, and stability, making them an excellent choice for improving the therapeutic efficacy of CP. The incorporation of babchi oil into the formulation not only provided additional antifungal and anti-inflammatory benefits but also reduced the potential adverse effects of prolonged corticosteroid use. The results of the physicochemical characterization, in vitro permeation studies, and antifungal activity assessments indicate that the developed nanoemulgel is a promising alternative to existing formulations.

The thermodynamic stability studies, including freeze-thaw cycles, centrifugation, and heating-cooling cycles, confirmed the physical robustness of the nanoemulsion system. The absence of phase separation, creaming, or turbidity across all stability tests demonstrated the homogeneous nature of the formulation, ensuring long-term stability and improved shelf-life. This stability is attributed to the optimized surfactant-to-co-surfactant ratio, which effectively reduced interfacial tension and enhanced emulsion stability (Azeem et al., 2009). The small globule size (236.67 nm) and low polydispersity index (PDI = 0.128) further validated the

uniformity of the formulation, reducing the risk of droplet aggregation and improving drug distribution across the skin (Ermawati et al., 2020). Additionally, the zeta potential of -20 mV indicated sufficient electrostatic repulsion between droplets, preventing coalescence and ensuring colloidal stability (Kumar et al., 2019). These findings are consistent with previous studies reporting that nanoemulsion-based drug delivery systems enhance dermal absorption by increasing drug solubility and prolonging retention in the stratum corneum (Bhardwaj & Tiwari, 2021).

The pH analysis (5.68 for nanoemulsion and 6.29 for nanoemulgel) confirmed that the formulation was within the physiological pH range of human skin (5.0–7.0), making it suitable for topical application without causing irritation or discomfort (Dinshaw et al., 2021). The viscosity studies demonstrated a significant increase in viscosity after incorporating the nanoemulsion into the HPMC gel matrix (from 14.86 cP in the nanoemulsion to 4438.69 cP in the nanoemulgel). This higher viscosity provides better retention on the skin surface, prolonged drug release, and enhanced bioavailability compared to traditional creams or ointments (Chime et al., 2014). Moreover, the spreadability of the nanoemulgel was 1.23 times greater than that of the marketed CP gel, ensuring better coverage and ease of application. The extrudability and homogeneity tests further confirmed that the formulation maintained smooth consistency without grittiness, enhancing patient compliance. These results highlight the advantages of nanoemulgel systems, which offer better texture, ease of use, and controlled release compared to conventional gel-based formulations (Mandal et al., 2023).

The in vitro permeation studies using Franz diffusion cells provided crucial insights into the drug release and skin penetration behavior of CP in the nanoemulgel formulation. The results demonstrated that the nanoemulgel exhibited sustained drug release over 24 hours, achieving 97.59% cumulative drug permeation. This sustained release profile is highly desirable for topical corticosteroids, as it minimizes the need for frequent application and reduces systemic absorption risks (Kumar et al., 2021). The smaller globule size and oil-in-water nature of the nanoemulsion played a key role in enhancing drug penetration through the stratum corneum, as smaller droplets provide a larger surface area for interaction with the skin, facilitating deeper penetration and improved therapeutic efficacy (Aggarwal, 2018). Compared to conventional formulations, which often require multiple daily applications, the sustained release of the nanoemulgel provides a more effective and patient-friendly alternative, reducing the likelihood of treatment non-adherence and recurrence of fungal infections (Singhvi et al., 2020).

One of the most significant outcomes of this study was the antifungal efficacy of the nanoemulgel, evaluated using the agar well diffusion method against *Candida albicans* and *Trichophyton rubrum*. The results showed that the CP nanoemulgel exhibited a 35% larger zone of inhibition compared to the marketed CP gel, confirming superior antifungal activity. The synergistic effect of CP and babchi oil contributed to this enhanced efficacy. Babchi oil contains bioactive compounds such as psoralen and bakuchiol, which exhibit potent antifungal and antimicrobial properties (Kumar et al., 2019). These natural components enhanced the overall therapeutic effect of the formulation by directly inhibiting fungal growth and reducing inflammation at the infection site (Garg et al., 2014). Furthermore, nanoemulsions are known to improve drug retention in the skin layers, which likely increased the local concentration of CP and babchi oil at the infection site, resulting in prolonged antifungal activity (Sharma et al., 2024). This aligns with previous research indicating that herbal nanoformulations exhibit stronger antimicrobial effects compared to conventional synthetic formulations due to increased bioavailability and targeted delivery (Devi et al., 2020).

The bioadhesion strength (1.45 N) of the nanoemulgel was another crucial parameter influencing drug retention on the skin. A higher bioadhesion strength ensures prolonged contact with the infected area, reducing the frequency of application and enhancing therapeutic efficacy (Mandal et al., 2023). This property is particularly beneficial for treating stubborn fungal infections, which often require extended treatment durations. Additionally, the accelerated stability study (one month at 40°C/75% RH) confirmed that the nanoemulgel formulation remained physically and chemically stable, showing no phase separation or drug degradation over time. This suggests that the formulation has sufficient shelf stability for commercial application, further validating its practical utility (Singh et al., 2024).

Collectively, these findings confirm that the CP-loaded nanoemulgel with babchi oil is an innovative and effective approach for the treatment of fungal infections, offering multiple advantages over conventional formulations. The improved solubility, enhanced permeability, prolonged drug retention, and superior antifungal efficacy make nanoemulgel an ideal candidate for clinical translation and commercialization. While in vivo studies and clinical trials are required to further validate these findings, the current study strongly suggests that nanoemulgel formulations represent the next generation of topical drug delivery for dermatological infections. Future research could focus on patient-based trials, formulation scalability, and the exploration of additional bioactive herbal compounds to further optimize and expand the application of this novel therapeutic approach.

5. Conclusion

This study successfully demonstrates the potential of nanoemulgel technology for the topical delivery of clobetasol propionate (CP) in combination with babchi oil, providing a novel and effective strategy for treating fungal infections. The developed nanoemulsion-based gel formulation enhances drug solubility, stability, and skin permeability while reducing systemic absorption, making it a safer alternative to conventional CP formulations. The thermodynamic stability assessments confirmed that the nanoemulsion (NE14) was stable across various stress conditions, ensuring long-term formulation integrity. Characterization studies revealed that the nanoemulgel exhibited an optimal globule size (236.67 nm), uniform distribution (PDI = 0.128), and a zeta potential (-20 mV) that prevented aggregation, indicating excellent colloidal stability. The in vitro permeation studies demonstrated a sustained release profile, with 97.59% cumulative drug permeation over 24 hours, significantly prolonging drug retention and enhancing therapeutic efficacy. The antifungal activity assessment revealed a 35% increase in the zone of inhibition compared to marketed CP gel, suggesting a synergistic effect between CP and babchi oil, which contributed to improved antifungal action and reduced treatment duration. Additionally, the high bioadhesion strength (1.45 N) ensured prolonged skin contact, leading to better drug retention and efficacy. The overall findings indicate that the CP-loaded nanoemulgel enhances antifungal efficacy, improves patient compliance, and minimizes side effects, making it a potentially superior alternative for treating dermatophytic and yeast infections. Future research should focus on in vivo studies and clinical trials to validate these findings and optimize formulation parameters for commercial production. The incorporation of natural bioactive components like babchi oil further supports the trend toward herbal-based nanoformulations for safer and more effective dermatological treatments.

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