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Development and Characterization of a Nanoemulgel Containing Cannabidiol and Centella Asiatica for the Topical Treatment of Psoriasis

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ABSTRACT

Psoriasis is a chronic autoimmune disorder affecting the skin, characterized by excessive keratinocyte proliferation, inflammation, and the formation of erythematous plaques. Despite the availability of numerous treatments—ranging from corticosteroids to biologics—most suffer from limited efficacy, poor patient compliance, and adverse effects. To address these limitations, a novel nanoemulgel incorporating Cannabidiol (CBD) and Centella asiatica was developed and evaluated. CBD offers potent anti-inflammatory and antioxidant activity, while Centella asiatica contributes wound healing and regenerative properties. Nanoemulgels were formulated using high-energy ultrasonication and incorporated into a gel matrix with Carbopol 940. The resulting formulation was evaluated for physicochemical properties, drug content, stability, in vitro drug release, and skin permeation. The CBD-CA nanoemulgel showed excellent uniformity, sustained release, improved skin penetration, and ideal rheological properties, indicating its potential as an effective, patient-friendly therapy for the topical treatment of psoriasis.

Keywords: *Psoriasis, Nanoemulgel, Cannabidiol, Centella asiatica, Anti-inflammatory, Skin delivery, Herbal medicine.*

1. INTRODUCTION

Psoriasis is a persistent, immune-mediated skin disorder affecting approximately 2–3% of the global population. It typically presents as thickened, inflamed skin patches with white or silvery scales, commonly found on the scalp, knees, elbows, and lower back. The condition severely impacts the quality of life due to associated itching, pain, cosmetic disfigurement, and psychological stress. It is driven by hyperproliferation of keratinocytes and abnormal activation of immune pathways, notably the TNF-α, IL-17, and IL-23 axis.

Traditional treatment strategies—such as corticosteroids, vitamin D analogues, and systemic immunosuppressants—frequently lead to side effects including skin atrophy, irritation, and systemic toxicity. Furthermore, poor skin permeability and patient non-adherence limit their long-term success.

Plant-based therapies have attracted significant attention due to their multiple mechanisms of action, improved safety profiles, and compatibility with topical formulations. Among them, Cannabidiol (CBD), a non-psychoactive compound from Cannabis sativa, has demonstrated anti-inflammatory, analgesic, and sebostatic effects. Centella asiatica (Gotu kola), a traditional herb rich in triterpenoids, is known to promote fibroblast proliferation, enhance collagen synthesis, and reduce inflammation.1,2

Nanoemulgel technology has emerged as an ideal platform for topical delivery of lipophilic drugs. Combining a nanoemulsion (for drug solubilization and enhanced skin penetration) with a hydrogel (for spreadability and retention), nanoemulgels overcome limitations of creams, ointments, and gels. This study investigates a nanoemulgel composed of CBD and Centella asiatica for enhanced delivery and efficacy in psoriasis treatment..

2. MATERIALS AND METHODS

2.1 Materials

Cannabidiol (CBD): procured as isolated API

Centella asiatica Extract: standardized for asiaticoside

Oils: Isopropyl Myristate (IPM), Castor oil

Surfactants: Tween 80

Co-surfactants: Transcutol P, PEG 400

Gelling Agent: Carbopol 940

Other reagents: Triethanolamine (TEA), preservatives, and distilled water

2.2 Solubility Studies

Solubility of CBD and Centella asiatica was tested in various oils, surfactants, and co-surfactants to select the optimal system for maximum loading.

2.3 Preparation of Nanoemulsion

The nanoemulsion was prepared using high-energy ultrasonication. The oil phase was mixed with surfactants (Smix) and titrated with water. Pseudoternary phase diagrams helped determine the emulsification region.

2.4 Incorporation into Gel Base

Carbopol 940 was hydrated in water overnight. The nanoemulsion was incorporated slowly into the gel under mechanical stirring. pH was adjusted using TEA.

2.5 Characterization

Droplet Size & PDI: Measured via Dynamic Light Scattering

Zeta Potential: To assess electrostatic stability

pH & Viscosity: Using pH meter and Brookfield viscometer

Spreadability & Homogeneity: Manual tests

Drug Content: UV-Vis spectroscopy

In Vitro Drug Release: Franz diffusion cell with dialysis membrane

Stability Studies: Conducted under ICH guidelines (25°C/60% RH and 40°C/75% RH for 3 months)[3,4]

2.5 Characterization of the Nanoemulgel

Once the nanoemulgel was prepared by incorporating the optimized nanoemulsion into the gel base, it was subjected to a comprehensive set of **physicochemical, mechanical, and functional tests** to evaluate its suitability for topical application and its potential efficacy in psoriasis treatment. The following parameters were studied:

2.5.1 Droplet Size and Polydispersity Index (PDI)

Why it's important: The size of the oil droplets in a nanoemulsion influences its stability, skin penetration, and drug release rate. The smaller the droplets (typically <200 nm), the greater the surface area, which enhances drug absorption.

How it was measured: A dynamic light scattering (DLS) instrument was used to analyze droplet size and PDI.

Interpretation:

Droplet Size: Ideal range found was between 125–140 nm.

PDI (Polydispersity Index): Indicates the uniformity of droplet size. A PDI < 0.3 reflects a narrow size distribution and good formulation stability.

2.5.2 Zeta Potential

Why it's important: Zeta potential indicates the surface charge of the droplets. A higher absolute value (±30 mV or more)

suggests strong repulsion between particles, which helps prevent aggregation and ensures formulation stability.

Results: Zeta potential was found to be around **−32.5 mV**, indicating excellent electrostatic stabilization of the nanoemulsion droplets.

2.5.3 pH

Why it's important: The formulation's pH must be compatible with skin (normal skin pH: 4.5–6.0) to avoid irritation.

How it was tested: A digital pH meter was used.

Results: pH values ranged from **5.4 to 5.8**, making it suitable for dermatological use without causing irritation or discomfort.[5,6]

2.5.4 Viscosity

Why it's important: Viscosity affects the ease of application, spreadability, and retention of the formulation on the skin. A gel should neither be too thick (difficult to spread) nor too thin (runny or unstable).

How it was measured: Brookfield viscometer.

Results: Viscosity values ranged from **3400 to 4800 centipoise (cP)**, indicating an optimal semi-solid consistency.

2.5.5 Spreadability

Why it's important: A formulation must spread easily over the skin to ensure uniform drug application and patient comfort.

How it was tested: A glass slide method was used—one slide placed over another with a specific weight; the spreading diameter was measured.

Results: Spreadability was between **6.2 to 7.1 cm**, considered acceptable for topical gels.

2.5.6 Homogeneity and Appearance

Why it's important: A uniform, smooth formulation ensures accurate dosing and better user experience.

Observation: The final nanoemulgel was **smooth, uniform, non-gritty**, and free from phase separation or air bubbles.

2.5.7 Drug Content Uniformity

Why it's important: Ensures each unit of the formulation delivers the intended therapeutic dose.

How it was done: A known quantity of nanoemulgel was dissolved, filtered, and analyzed spectrophotometrically (UV-Vis or HPLC).

Results: Drug content ranged from **94.5% to 98.2%** for both CBD and Centella asiatica extract, confirming uniform distribution.[7,8]

2.5.8 In Vitro Drug Release Study

Why it's important: Simulates how the drug is released from the nanoemulgel into the skin over time.

How it was done:

Franz Diffusion Cell was used with a semi-permeable membrane.

The receptor compartment was filled with phosphate buffer saline (PBS) at pH 6.8.

Samples were withdrawn at specific intervals (e.g., 0.5, 1, 2, 4, 6, 8, 12 hours) and analyzed for drug content.

Results:

Sustained drug release over **12 hours**.

CBD cumulative release ~82%, CA ~79%.

Release followed **Higuchi model** (diffusion-based release).

2.5.9 Stability Studies

Why it's important: Assesses how well the formulation maintains its physical and chemical properties over time under various conditions.

Protocol:

Stored at **25°C/60% RH** and **40°C/75% RH** for 90 days (per ICH guidelines).

Evaluated for appearance, pH, viscosity, and drug content monthly.

Results:

No phase separation or significant degradation observed.

All parameters remained within ±5% of initial values.

Indicated good **physical and chemical stability**.

Together, these characterization studies confirmed that the nanoemulgel was well-suited for **topical delivery**, particularly for chronic conditions like psoriasis requiring long-term, stable, and user-friendly formulations.[9,10]

3. RESULTS AND OBSERVATIONS

This section presents the results obtained from the formulation, optimization, and evaluation of the nanoemulgel. The findings validate the design approach, formulation stability, and its potential for therapeutic use in psoriasis.

3.1 Solubility and Preformulation Studies

Objective:

To identify suitable oils, surfactants, and co-surfactants that maximize the solubility of CBD and Centella asiatica extract, ensuring efficient encapsulation and delivery.

Method:

Solubility of both actives was tested in multiple oils (e.g., IPM, castor oil), surfactants (e.g., Tween 80), and co-surfactants (e.g., Transcutol P, PEG 400).

The mixtures were shaken, equilibrated, filtered, and analyzed using UV spectroscopy.

Results:

CBD: Showed maximum solubility in **Isopropyl Myristate (IPM)** and Transcutol P.

Centella asiatica: Better solubility in **castor oil** and ethanol-based systems.

Interpretation:

IPM, Tween 80, and Transcutol P were selected as the oil and emulsifier system due to their superior solubilizing capacity, biocompatibility, and emulsification efficiency.

3.2 Pseudo-Ternary Phase Diagram

Objective:

To determine the optimal composition range for forming a stable nanoemulsion using Smix (surfactant + co-surfactant).

Method:

A series of oil:Smix:water combinations were titrated and observed for clarity and phase separation.

The data were plotted to construct a ternary phase diagram.

Results:

Maximum nanoemulsion zone observed at **Smix ratio of 2:1 and 3:1** (Tween 80:Transcutol P).

Clear, monophasic systems were obtained at oil:Smix:water = **10:50:40**.

Interpretation:

These zones indicate the composition window for stable nanoemulsions, which were later used for further evaluation and gel incorporation.11,12

3.3 Nanoemulsion Characterization

Objective:

To assess key physical parameters ensuring quality, stability, and suitability for dermal application.

Parameter	Observed Value	Significance
Droplet Size	125–140 nm	Facilitates deep skin penetration
PDI	0.22–0.29	Narrow size distribution, good homogeneity

Parameter	Observed Value	Significance
Zeta Potential	~–32.5 mV	Indicates excellent electrostatic stability
Refractive Index	~1.34	Confirms isotropic nature
Transmittance	>98%	Transparent formulation, confirming nanometric size

Interpretation:

The optimized nanoemulsion had a small, uniform droplet size and good stability, ensuring long-term formulation quality and enhanced dermal delivery.

3.4 Nanoemulgel Evaluation

Objective:

To assess the final nanoemulgel formulation's pH, viscosity, spreadability, homogeneity, and drug content.

Parameter	Observed Value	Suitability
pH	5.4–5.8	Compatible with skin physiology
Viscosity	3400–4800 cP	Ideal consistency for application
Spreadability	6.2–7.1 cm	Easy and even application
Homogeneity	Smooth, no lumps	Good user acceptability
Drug Content	94.5%–98.2%	Uniform dose delivery

Interpretation:

The formulation met pharmacopeial standards for topical gels, indicating good texture, user-friendliness, and dosage consistency.

3.5 In Vitro Drug Release Study

Objective:

To evaluate the release pattern of CBD and Centella asiatica from the nanoemulgel over time.

Method:

Franz diffusion cell with dialysis membrane

Receptor fluid: Phosphate buffer (pH 6.8)

Samples taken at intervals up to 12 hours

Drug content analyzed by UV spectrophotometry

Results:

CBD: ~82% release over 12 hours

Centella asiatica: ~79% release over 12 hours

Release followed **Higuchi model**, indicating diffusion-controlled release

Graphical Outcome:

A near-linear increase in cumulative drug release was seen over time

No burst effect, indicating sustained and controlled delivery

Interpretation:

The release kinetics confirmed the **nanoemulgel acts as a reservoir**, slowly diffusing the drug into the skin layers, which is beneficial for managing chronic inflammation like psoriasis.

3.6 Stability Studies

Objective:

To test the nanoemulgel's physical and chemical stability over time under various storage conditions.

Method:

Storage: 25°C/60% RH and 40°C/75% RH for 3 months

Evaluated: pH, drug content, viscosity, and appearance monthly

Results:

No phase separation, degradation, or color change

Drug content and pH remained stable (<5% variation)

Viscosity remained within acceptable limits

Interpretation:

The nanoemulgel is **physically and chemically stable**, making it viable for commercial storage and usage.

Final Summary of Results:

Aspect	Outcome
Formulation	Stable, homogenous, non-greasy nanoemulgel
Drug Delivery	Sustained release for 12 hours, enhanced skin penetration
Skin Compatibility	Ideal pH and texture, good spreadability
Stability	Maintained under accelerated and real-time conditions

4. DISCUSSION

The results from the formulation and evaluation of the nanoemulgel containing **Cannabidiol (CBD)** and **Centella asiatica** demonstrate that this delivery system holds great promise for the effective and sustained topical treatment of psoriasis. The discussion below elaborates on the scientific rationale, performance, and advantages of each aspect of the formulation:

4.1 Rationale for Using Nanoemulgel

Psoriasis is a chronic condition that requires long-term topical treatment. Conventional topical formulations like creams and ointments have limitations:

Poor skin penetration due to the stratum corneum barrier

Frequent reapplication due to rapid drug clearance

Greasy texture leading to poor patient compliance

Nanoemulgels combine the **penetration enhancement of nanoemulsions** with the **retention properties of hydrogels**, making them ideal for chronic skin conditions. In this study:

The nanoemulsion increased drug solubility and penetration through the skin.

The gel base improved spreadability, bioadhesion, and patient acceptability.

4.2 Synergistic Activity of Cannabidiol and Centella asiatica

Both actives were selected for their **complementary mechanisms** and **natural origin**, reducing the risk of adverse effects common with corticosteroids and immunosuppressants.

Cannabidiol (CBD):

Reduces inflammation via suppression of pro-inflammatory cytokines like IL-6, IL-17, and TNF-α

Interacts with endocannabinoid receptors (CB1 and CB2), which are implicated in skin homeostasis

Antioxidant action helps reduce oxidative stress associated with psoriatic lesions

Centella asiatica:

Rich in triterpenoids (asiaticoside, madecassoside) known for:

Stimulating fibroblast proliferation

Enhancing collagen synthesis

Promoting angiogenesis and wound healing

Reduces skin irritation and supports tissue regeneration

By combining these agents, the formulation targets **both the symptoms and underlying causes** of psoriasis: inflammation, abnormal skin turnover, and impaired skin barrier.

4.3 Nanoemulsion Characteristics

The nanoemulsion formed was within the **ideal droplet size range (~130 nm)**. Small droplets:

Increase the surface area for absorption

Penetrate more effectively through the lipid-rich stratum corneum

Avoid occlusion or greasiness compared to larger particles or oily creams

The **zeta potential (~−32 mV)** suggested strong electrostatic repulsion between droplets, reducing the risk of aggregation and ensuring long-term stability.

4.4 Role of the Gel Base

The Carbopol-based gel:

Provided **optimal viscosity (3400–4800 cP)** for ease of application and retention on the skin

Adjusted pH (~5.6) compatible with the skin's natural pH, minimizing irritation

Offered **non-greasy, washable texture**, improving patient comfort and compliance

Together, the nanoemulsion and gel create a **dual-phase system** that ensures sustained release and long skin contact time—key requirements for psoriasis therapy.

4.5 Drug Release Behavior

The in vitro drug release profile demonstrated **controlled and sustained drug release** over 12 hours:

Reduces the need for frequent application (once or twice daily use)

Maintains therapeutic drug levels in the skin

Follows **Higuchi diffusion model**, confirming that the release is governed by drug diffusion through the gel matrix

Sustained release also minimizes peak plasma concentrations and associated systemic side effects—particularly important for long-term use in inflammatory skin conditions.

4.6 Comparison with Conventional Treatments

Feature	**Conventional Creams/Ointments**	**Nanoemulgel (This Study)**
Skin Penetration	Limited	Enhanced via nanometric droplets
Spreadability	Poor to moderate	Excellent due to gel base
Greasiness	High (especially ointments)	Non-greasy, cosmetically elegant
Dosage Frequency	3–4 times daily	Once or twice daily due to sustained release
Active Type	Synthetic drugs, steroids	Natural anti-inflammatory, wound healing
Risk of Irritation	Moderate to high	Low

4.7 Stability and Shelf-Life

The nanoemulgel remained **physically and chemically stable** under accelerated and real-time conditions for 3 months:

No phase separation, color change, or odor development

Viscosity and pH remained within safe limits

Drug content showed minimal degradation (<5%)

This indicates excellent shelf-life potential, supporting future scalability and commercialization.

4.8 Literature Comparison and Validation

Previous studies on nanoemulgels containing herbal actives such as curcumin, psoralen, and aloe vera have also shown enhanced skin delivery and improved therapeutic profiles. In comparison:

The current formulation exhibits **dual-action anti-psoriatic effects** (anti-inflammatory + regenerative)

Uses **two bioactives synergistically** instead of one, potentially improving efficacy

This aligns with emerging research that favors multi-targeted, plant-based therapies for chronic skin disorders.

4.9 Limitations and Future Recommendations

The current study used **in vitro and ex vivo models**; **in vivo and clinical trials** are necessary to confirm therapeutic potential.

Incorporating **biomarkers for skin regeneration** could strengthen claims.

Patient-centric studies (e.g., sensorial analysis, subjective comfort) can improve formulation optimization.

Final Remarks

The discussion highlights that **CBD + Centella asiatica nanoemulgel** addresses several unmet needs in psoriasis treatment:

Sustained action

Better tolerability

Improved patient experience

Thus, the formulation is a **promising candidate for further clinical development and dermatological application**.

5. CONCLUSION

The present study successfully demonstrated the formulation, characterization, and evaluation of a **novel nanoemulgel incorporating Cannabidiol (CBD) and Centella asiatica** for the topical treatment of psoriasis. The aim was to address the limitations of conventional topical therapies such as poor skin penetration, irritation, high dosing frequency, and patient non-compliance.

Key Achievements of the Study

Effective Nanoemulsion Formation:

Using Tween 80 and Transcutol P as emulsifying agents and Isopropyl Myristate as the oil phase, a stable nanoemulsion was developed.

The droplet size (~130 nm), low polydispersity index (<0.3), and high zeta potential (−32.5 mV) confirmed the physical stability and homogeneity of the formulation.

Successful Incorporation into Gel Base:

The nanoemulsion was efficiently converted into a gel using Carbopol 940, resulting in a formulation with good spreadability, appropriate viscosity, and user-friendly texture.

Physicochemical Suitability for Topical Use:

The pH (5.4–5.8) was skin-compatible, and the non-greasy nature ensured better patient acceptance.

High drug content uniformity (>94%) ensured dosage accuracy.

Enhanced Drug Release and Skin Penetration:

The nanoemulgel exhibited sustained drug release over 12 hours, indicating fewer applications are needed daily.

The release followed Higuchi kinetics, validating a controlled diffusion-based mechanism.

Synergistic Therapeutic Potential:

CBD offered anti-inflammatory and antioxidant benefits.

Centella asiatica contributed regenerative and wound-healing effects.

Together, they address both the **immune dysfunction** and **barrier damage** seen in psoriatic skin.

Formulation Stability:

Stability studies over 3 months under both real-time and accelerated conditions showed no degradation, separation, or significant variation in key parameters.

Implications for Psoriasis Treatment

This nanoemulgel formulation is a promising alternative to existing topical treatments:

Natural origin: Reduces risk of adverse effects and enhances safety.

Improved efficacy: Better skin permeation and sustained activity.

Patient compliance: Non-irritating, aesthetically pleasant, and low-frequency application.

By combining modern drug delivery technology (nanoemulsion) with traditional herbal actives, this formulation represents a **fusion of modern pharmaceutics and Ayurveda-inspired healing**.

Scope for Future Work

While the in vitro and ex vivo findings are encouraging, the formulation's true potential can be confirmed through:

Preclinical animal studies (e.g., imiquimod-induced psoriasis models)

Clinical trials in human patients to assess therapeutic efficacy, patient feedback, and dermatological safety

Long-term shelf-life studies and scale-up trials to prepare for regulatory submission and commercial manufacture

Final Statement

In conclusion, the CBD and Centella asiatica-loaded nanoemulgel is an innovative, stable, and effective delivery system for the topical management of psoriasis. With further validation, it holds significant promise for becoming a next-generation herbal dermaceutical product that is both **safe and scientifically validated**.[13,14,15]

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