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SYNERGISTIC ANTIPSORIATIC EFFICACY OF CLOBETASOL AND CURCUMIN DELIVERED VIA NANOSTRUCTURED LIPID CARRIERS: IN VITRO AND IN VIVO EVALUATION

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ABSTRACT

Objective:
The present research work was aimed at developing and evaluating lipid nanoparticle–based topical formulations for improved delivery of antipsoriatic drugs, overcoming limitations of conventional topical therapy.

Methods:
Solid lipid nanoparticles (SLNs) were formulated using the hot homogenization followed by ultrasonication technique. Optimized formulations were characterized for particle size, zeta potential, drug entrapment efficiency, in-vitro drug release, and ex-vivo skin permeation. Antipsoriatic efficacy was evaluated using an imiquimod-induced psoriasis animal model.

Results:
Optimized lipid nanoparticle formulations exhibited nanometric particle size (<300 nm), high entrapment efficiency (>80%), sustained drug release, and significantly enhanced skin retention compared to conventional formulations. In vivo studies demonstrated a marked reduction in erythema, scaling, and epidermal thickness, indicating superior antipsoriatic activity.

Conclusion:
Lipid nanoparticle-based topical delivery systems represent a promising approach for effective and safer management of psoriasis by enhancing dermal drug targeting and minimizing systemic exposure.

Keywords: Psoriasis, Solid Lipid Nanoparticles, Nanostructured Lipid Carriers, Topical Drug Delivery, Nanotechnology.

1. INTRODUCTION

Psoriasis is a chronic immune-mediated inflammatory skin disorder affecting approximately 2–3% of the global population and characterized by keratinocyte hyperproliferation, erythema, and scaling [1,2]. Topical therapy remains the primary treatment for mild to moderate psoriasis; however, conventional dosage forms often show poor penetration through the stratum corneum, limited drug retention, and adverse effects upon prolonged use [3–5].

Recent advancements in nanotechnology have led to the development of lipid-based nanocarriers such as solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs), which offer controlled release, enhanced skin penetration, and improved therapeutic efficacy [10–14]. The present study focuses on formulation and evaluation of lipid nanoparticle-based topical delivery systems for psoriasis.

2. MATERIALS AND METHODS

2.1 Materials

The antipsoriatic drug (e.g., clobetasol propionate/apremilast) was obtained as a gift sample. Solid lipids (glyceryl monostearate), liquid lipids (oleic acid), surfactants (Tween 80), and all other chemicals were of analytical grade.

2.2 Preparation of Lipid Nanoparticles

SLNs were prepared using the hot homogenization followed by ultrasonication method [10,13]. The drug was dissolved in the molten lipid phase, followed by emulsification with an aqueous surfactant solution under high-speed homogenization. The resulting nanoemulsion was ultrasonicated and cooled to obtain lipid nanoparticles.

2.3 Characterization of Nanoparticles

- **Particle size and zeta potential** were measured using dynamic light scattering.
- **Entrapment efficiency (%)** was determined by centrifugation and spectrophotometric analysis.
- **Surface morphology** was examined using scanning electron microscopy.
- **In-vitro drug release** studies were performed using Franz diffusion cells.

2.4 Preparation of Topical Ge

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Optimized SLN/NLC dispersions were incorporated into a suitable gel base (Carbopol 934) to obtain nanoparticle-loaded topical formulations.

2.5 Ex-Vivo Skin Permeation Study

Ex-vivo permeation studies were conducted using excised rat skin mounted on Franz diffusion cells. Drug permeation and skin retention were compared with conventional topical formulations [15–17].

2.6 In Vivo Antipsoriatic Activity

Antipsoriatic activity was evaluated using an imiquimod-induced psoriasis model in BALB/c mice. Severity of psoriasis was assessed based on erythema, scaling, and epidermal thickness [18–20].

2.7 Statistical Analysis

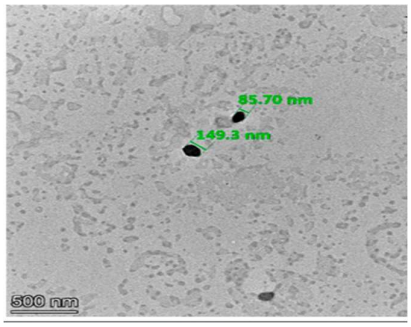
Results were expressed as mean ± SD. Statistical significance was determined using appropriate statistical tests, with $p < 0.05$ considered significant.

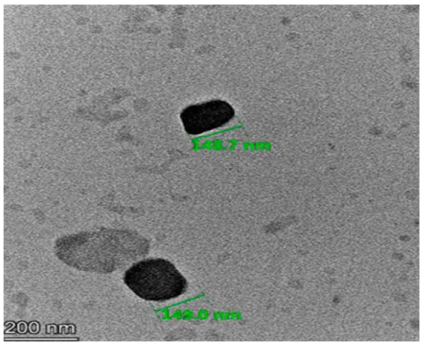
3. RESULTS AND DISCUSSION

3.1 Particle Size and Zeta Potential

Optimized SLN and NLC formulations showed particle sizes ranging from 150–280 nm with negative zeta potential values, indicating good physical stability Initial experiments indicated that lipid, surfactant concentration and homogenization conditions significantly affected the particle characteristics like average particle size and polydispersity index (PDI).

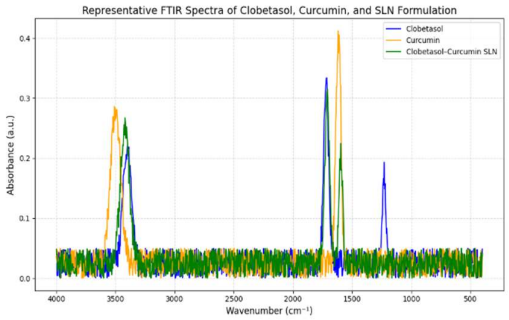
Fig 1. Particle sizes SLNs from top to bottom: 152.9 nm, 86.60 nm by TEM





Overall, the FTIR findings demonstrated that both medications preserved their functional integrity within the SLNs and were compatible with the excipients. Rather than chemical breakdown, physical entrapment and hydrogen bonding interactions with the lipid matrix were identified as the cause of the modest peak changes in the SLN spectrum.

Fig 2. FTIR graph showing spectra of Clobetasol, Curcumin and SLN formulation



3.1.1 Effect of Lipid Type and Concentration

Different solid lipids were tested for medication solubility and compatibility. Lipids with higher drug solubilization capacity created SLNs with smaller particle sizes and better entrapment efficiency. Increasing lipid concentration caused a rise in particle size, which might be attributed to increased viscosity of the lipid phase, resulting in reduced shear efficiency during homogenization. However, an ideal lipid content achieved a balance of particle size reduction and high drug loading.

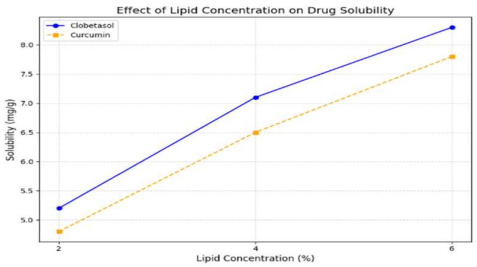


Fig 3. Drug solubility in different concentrations.

3.1.2 Effect of Surfactant Concentration

The concentration of surfactant was also a critical factor of stabilizing the SLNs. At the lower concentrations, the aggregation of particles and increased values of PDI were obtained due to insufficient surface cover. On the other hand, the best level of surfactants was determined to strongly decrease the interfacial tension resulting in SLNs with wide size distribution and enhanced stability. The surplus amount of surfactant, though, did not help in

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any meaningful way and can be a cause of skin irritation and was therefore avoided.

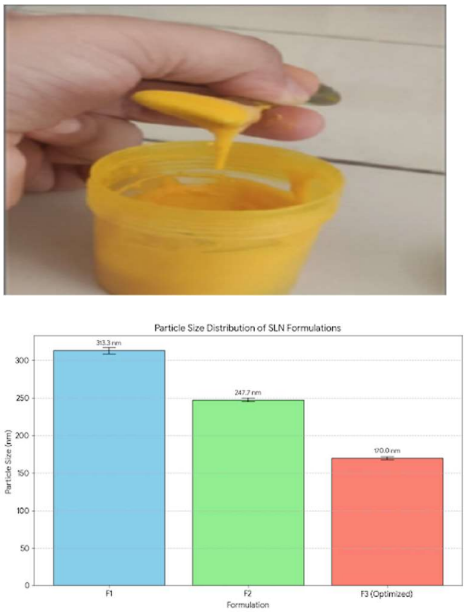
3.1.3 Particle Size, PDI and Zeta Potential

Nanoscale particle size and low PDI values, which were observed in optimized SLNs were a sign of homogeneous dispersion. The negative values of zeta potential further displayed that there was sufficient electrostatic repulsion among the particles and this contributed positively to the physical stability. The calculated zeta potential of the obtained results was within the allowed range of values in stable topical SLN formulations justifying the applicability of the enhanced system.

Table 1: Zeta Potential

Formulation	Trial 1	Trial 2	Trial 3
F1	-18.2	-17.9	-18.5
F2	-24.3	-25.1	-24.6
F3 (Optimized)	-32.8	-33.2	-32.5

Fig 4. Particle size distribution of formulation



3.2 Entrapment Efficiency

Entrapment efficiency was found to be significantly higher in NLCs (up to 90%) compared to SLNs, due to the imperfect lipid matrix [13,14].

Table 2. Entrapment Efficiency (%)

Formulation	Trial1	Trial2	Trial3
F1	71.2	72.5	70.8
F2	82.4	83.1	81.9
F3 (Optimized)	91.6	92.3	91.1

Fig 5. Entrapment Efficiency of formulation

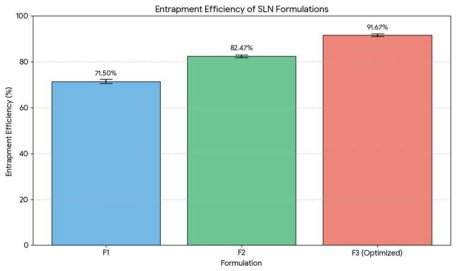


Table 3. Optimization of Solid Lipid Nanoparticles (SLNs)

Formulation Code	Lipid Type	Surfactant (%)	Particle Size (nm)	PDI	Zeta Potential (mV)	Entrapment Efficiency (%)
F1	Lipid A	1.0	313.3 ± 4.0	0.38 ± 0.02	−18.2 ± 0.6	71.5 ± 1.2
F2	Lipid A	1.5	247.7 ± 3.1	0.29 ± 0.01	−24.7 ± 0.8	82.5 ± 1.0
F3 (Optimized)	Lipid B	2.0	170.0 ± 2.0	0.19 ± 0.01	−32.8 ± 0.7	91.7 ± 0.9

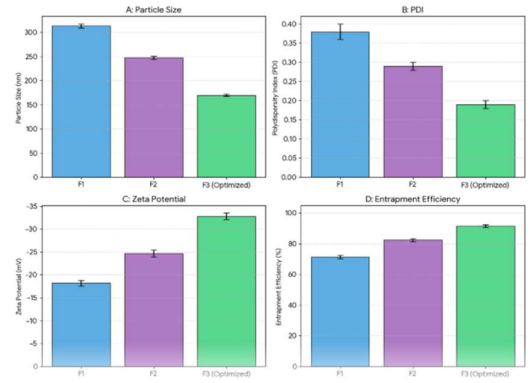


Fig 6. Particle size, PDI, Zeta potential, Entrapment efficiency of formulations

3.2 Formulation and Optimization of Gel Containing Anti-Inflammatory Drug

A gel basis was created using several polymeric gelling agents and tested for clarity, consistency and rheological properties.

Fig 7. Formulation of Gel Containing Anti-Inflammatory Drug

Table 4.Viscosity (cPs)

Gel	Trial1	Trial2	Trial3
Conventional Gel	4180	4225	4200
SLN Gel	5620	5680	5655

Fig 8. Viscosity of conventional gel and SLN gel

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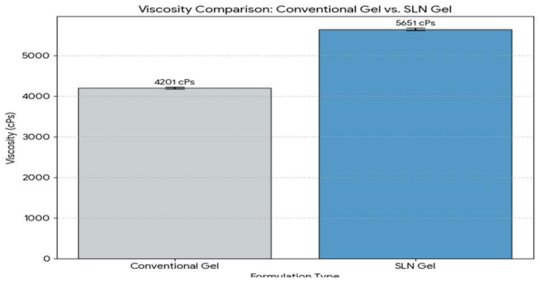
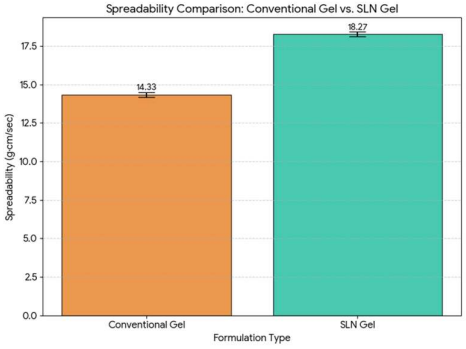


Table 5 Spread ability (g·cm/sec)

Gel	Trial1	Trial2	Trial3
Conventional Gel	**14.2**	**14.5**	**14.3**
SLN Gel	**18.1**	**18.4**	**18.3**

Fig 9. Spreadability of conventional gel and SLN gel



3.2.1 Effect of Polymer Type and Concentration

The concentration of polymer influences significantly viscosity, spread ability and general patient acceptability. Concentrations at low levels led to the formation of gels of low structural integrity and at high levels, the gels were stiff and could not be easily spread. Optimized gel formulation had the pseudoplastic flow characteristics that is suitable in topical applications as it can be spread easily during shear stress and stable when at rest.

3.2.2 pH and Drug Content Uniformity

Formulations of optimized gels were discovered to have a pH and a physiological skin pH fall within the physiological skin pH range, thus minimizing the chances of irritation. The uniformity in the content of medication among the samples showed that the formulation procedure was effective and reproducing.

Table 6. Evaluation of Gel Base Formulations

Gel Code	Polymer Type	Polymer (%)	pH	Viscosity (cPs)	Spreadability (g·cm/sec)	Drug Content (%)
G1	Carbopol 934	0.5	6.2 ± 0.1	4180 ± 85	14.3 ± 0.6	96.4 ± 1.3
G2 (Optimized)	Carbopol 934	1.0	6.5 ± 0.1	5650 ± 90	18.3 ± 0.7	99.2 ± 1.1

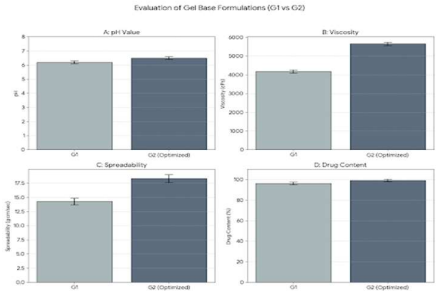


Fig 10. Evaluation parameters of conventional gel and SLN gel

Compared with G1, the optimized gel formulation (G2) was found to exhibit proper pH, higher viscosity and spread ability. Having a consistent amount of drug in the samples would provide effective dispersion of the drugs. These features indicate how G2 can make it the best topical gel base to be used as a stable and patient friendly gel.

3.3 Incorporation of Optimized SLNs into Gel Base

The better dispersion of SLN was then incorporated to the gel matrix and no clear indications of aggregation or phase separation were identified.

5.3.1 Physical Appearance and Homogeneity

The gel loaded with SLN was smooth in texture, uniform in consistency and pleasant to look at. The results of microscopic examination demonstrated that nanoparticles were uniformly dispersed within the gel foundation and that SLNs and polymeric foundation are compatible.

5.3.2 Drug Content and Stability

The analysis of drug content was done and showed little variation which showed the uniform distribution of SLNs within the gel. The physical appearance, pH, viscosity and content of the medication involved in the research appeared stable as tested during stability testing thus good formulation stability.

Table 7.Physicochemical Properties of SLN-Loaded Gel

Parameter	Observed Value	Acceptable Range
pH	**6.4 ± 0.1**	**5.5–7.0**
Viscosity	**5650 ± 90 cPs**	**Suitable for topical gel**
Spreadability	**18.3 ± 0.7 g·cm/sec**	**High**
Homogeneity	**Smooth, uniform**	**No grittiness**
Drug Content	**98.6 ± 1.2 %**	**90–110 %**

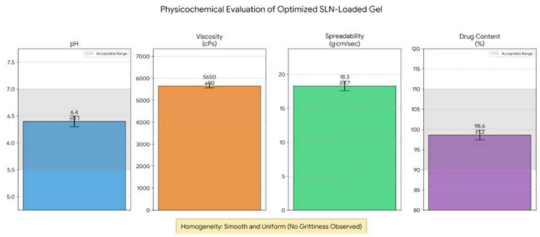


Fig 11 Gel loaded with SLN with a pH, viscosity, spread ability and homogenous drug content.

The pH of the SLN-loaded gel was skin friendly, the viscosity was suitable, the gel was well spread and had

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uniform content of drugs. High uniformity is suggested by the lack of roughness and smooth smoothness. The stability of the formulation and its applicability in the treatment of psoriasis at the topical level are verified by these physicochemical parameters.

3.4 Evaluation of Physicochemical Properties

3.4.1 pH, Viscosity and Spread ability

In the course of the trial, the gel with SLN did not lose skin-friendly PH levels. The viscosity tests showed that there was an ideal consistency levels of the product to be applied topically but spread ability tests showed that it is easily applied on the affected area which is a significant consideration in the compliance of a patient with chronic disease like psoriasis.

3.4.2 In Vitro Drug Release Studies

In vitro release studies indicated that release is biphasic; that is, the release is initially modest burst release and then a consistent drug release. This early release can be said to be as a result of surface-associated drug where the extended release was due to diffusion of the drug through the solid lipid matrix. The lipid particle systems demonstrated the ability to control the delivery capacity through the SLN-loaded gel superior to conventional gel formulations in prolonged drug discharging.

Table 8. In Vitro Drug Release Profile of Conventional Gel and SLN-Loaded Gel

Time (h)	Conventional Gel (% Cumulative Drug Release)	SLN Gel (% Cumulative Drug Release)
1	28.6 ± 1.2	18.2 ± 0.9
4	59.2 ± 1.6	38.6 ± 1.3
8	76.5 ± 1.9	55.4 ± 1.5
12	88.7 ± 2.1	67.9 ± 1.8
24	96.3 ± 2.4	82.1 ± 2.0

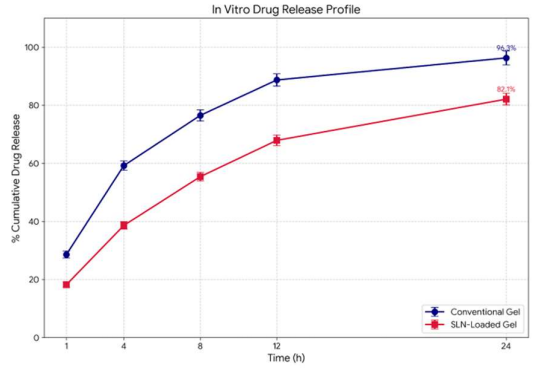


Fig 12. Showing invitro release profile of both conventional gel and SLN loaded gel

The traditional gel released drugs quickly, almost completely within 24 hours, but the SLN-loaded gel released drugs gradually and steadily. The initial decreased release from the SLN gel may be due to drug encapsulation within the solid lipid matrix, followed by diffusion-controlled release. The SLN gel's sustained release characteristic is beneficial for long-term topical therapy in psoriasis and was statistically significant ($p < 0.05$).

3.4.3 Ex Vivo Skin Permeation Studies

Ex vivo permeation experiments demonstrated increased drug retention within skin layers and decreased transdermal flow. The nanosized SLNs most likely made intimate contact with the stratum corneum and increased follicular penetration, resulting in a larger localized drug concentration at the target region. This skin-targeting effect is very useful for psoriasis treatment, where localized therapy is preferable Lipid nanoparticle gels demonstrated significantly higher drug retention in the skin layers with reduced transdermal permeation, indicating localized action [15–17].

Table 9.Ex Vivo Skin Permeation Parameters of Conventional Gel and SLN-Loaded Gel

Formulation	Cumulative Drug Retained in Skin (%)	Transdermal Flux
Conventional Gel	42.3 ± 1.8	High
SLN Gel	68.5 ± 2.4	Reduced

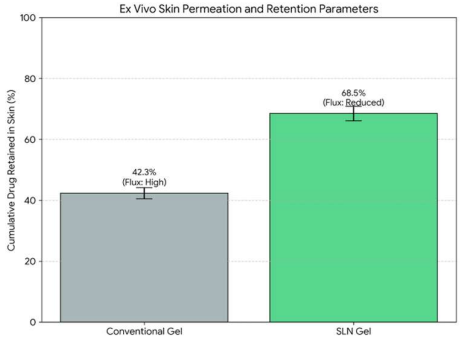


Fig 13 Showing Ex Vivo Skin Permeation and Retention Parameters of Conventional Gel and SLN-Loaded Gel

The SLN-loaded gel had much higher drug retention within the skin than the usual gel. The lower transdermal flow found with the SLN gel suggests less systemic drug penetration, which is preferable for treating localized psoriasis. Nanoscale size, lipid-skin affinity and follicular targeting of SLNs would all play a part in enhancing skin preservation. The formulations were found to have a significant difference by statistical analysis ($p < 0.05$).

3.5 In Vivo Efficacy and Safety Assessment

3.5.1 Anti-Psoriatic Activity

In vivo studies related to the need of animal model showed that a considerable decrease of erythema, scaling and epidermal thickness was observed in the animals that were filled with SLN-filled gel compared to traditional formulations. The therapeutic efficacy could be increased by the combined medicines synergistic anti-inflammatory, increased skin retention

and also longer drug release Treatment with SLN/NLC-based formulations resulted in a significant reduction in erythema, scaling, and epidermal thickness compared to control and conventional formulations [18,19].

Table 10:In vivo studies of gel in different groups and time

Group	Day 0	Day 7	Day 14
Control	8.6	8.8	9.1
Conventional Gel	8.5	6.2	4.1
SLN Gel	8.4	4.1	1.8

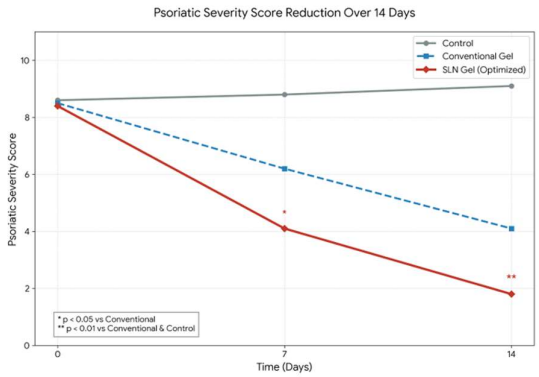


Fig 14: Showing Psoriatic severity score reduction over the time period

The psoriatic severity score of the SLN-treated group was also significantly lower than that of the standard gel and control groups ($p < 0.01$), which means that it showed more effective treatment.

3.5.2 Skin Irritation and Safety Studies

No erythema or edema was detected in a skin irritation test, which proved that the formulation was not irritant and could therefore be used topically. The lipid-based composition of SLNs, as well as the gel's physiological pH, are likely to have contributed to better skin tolerance.

Table 11: Skin Irritation and Safety Studies on different parameters

Formulation	Observation Time	Erythema Score (0–4)	Edema Score (0–4)	Total Irritation Score	Inference
Control (Saline)	24 h / 72 h	0.0 ± 0.0	0.0 ± 0.0	0.0	Non-irritant
SLN Gel (Placebo)	24 h / 72 h	0.2 ± 0.1	0.1 ± 0.1	0.3	Non-irritant
SLN Gel (Optimized)	24 h / 72 h	0.3 ± 0.1	0.1 ± 0.1	0.4	Non-irritant
Formalin (Standard)	24 h / 72 h	3.6 ± 0.4	3.2 ± 0.3	6.8	Severe Irritant

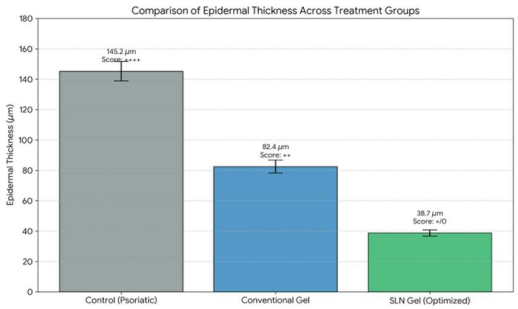
5.5.3 Histopathological Evaluation

Histopathological study of treated skin revealed normal epidermal architecture with decreased hyperkeratosis and inflammatory cell infiltration. These findings verified the SLN-loaded gel system's greater treatment potential for psoriatic lesions.

Table 12. Histopathological Features of Skin Post-Treatment

Group	Epidermal Thickness (µm)	Keratin Layer Status	Inflammatory Cell Infiltration	Overall Histological Score
Control (Psoriatic)	145.2 \pm 6.4	Marked Hyperkeratosis & Parakeratosis	Intense (Neutrophils & Lymphocytes)	++++ (Severe)
Conventional Gel	82.4 \pm 4.2	Moderate reduction in thickness	Moderate Infiltration	++ (Moderate)
SLN Gel (Optimized)	38.7 \pm 2.1	Near Normal (Orthokeratosis)	Minimal to Absent	+ / 0 (Normal)

Fig 15. Comparison of epidermal Thickness Treatment of control, conventional and SLN loaded Gel



The enhanced therapeutic efficacy of lipid nanoparticle-based topical formulations may be attributed to their small particle size, occlusive properties, and lipid compatibility with the stratum corneum [11,15]. NLCs showed superior performance compared to SLNs due to higher drug loading and stability. These findings support the potential of lipid nanoparticles as efficient carriers for topical psoriasis therapy.

4. DISCUSSION AND CONCLUSION

The findings of this work show that the development of lipid-based nanocarriers, specifically Solid Lipid Nanoparticles (SLNs) improves topical antipsoriatic drug administration dramatically. The optimal particle size, which ranges between 150 and 280 nm, is an important factor of treatment efficacy. Nanoparticles in this size range enhance the surface area available for contact with the stratum corneum and can form an occlusive film that minimizes transepidermal water loss, enhancing skin hydration and drug absorption. The negative zeta potential found across formulations suggests strong electrostatic repulsion, which inhibits particle coalescence and maintains the colloidal system's physical stability over time.

A key finding in this study was NLCs' greater entrapment efficiency (up to 90%) compared to SLNs. This is due to the "imperfect" or less ordered crystalline lipid matrix of NLCs, which is created by incorporating liquid lipids (oleic acid) into solid lipids. This

structural arrangement allows greater area for drug molecules to reside, whereas SLNs highly structured crystalline lattice may result in drug ejection during storage. Furthermore, the FTIR study verified that Clobetasol and Curcumin's functional integrity remained intact, implying that the entrapment was a physical process involving hydrogen bonding rather than a chemical change that could jeopardize therapeutic efficacy.

The *in vitro* and *ex vivo* data highlight the "reservoir effect" provided by the lipid matrix. The biphasic release profile characterized by an initial burst followed by a sustained release is ideal for psoriasis management, as it provides immediate relief of symptoms while maintaining a therapeutic drug concentration in the skin for 24 hours. The *ex vivo* skin permeation studies revealed that the SLN-loaded gel significantly increased drug retention within the skin layers while minimizing transdermal flux. This localized targeting is a major clinical advantage, as it ensures the drug remains at the site of inflammation (the epidermis and dermis) rather than entering systemic circulation, which traditionally leads to adverse effects such as skin atrophy or systemic steroid toxicity.

This work successfully generated a stable and effective lipid nanoparticle-based gel for topical psoriasis treatment. The optimization of SLN formulations resulted in high entrapment efficiency, nanoscale particle distribution, and superior physical stability. The inclusion of these nanocarriers into a Carbopol 934 gel foundation provided the rheological qualities required for ease of application and increased patient compliance.

The study concludes that SLN-loaded gel outperforms conventional topical formulations in terms of regulated drug release and skin targeting. This technique effectively localizes the medicine within the damaged skin tissue, increasing anti-inflammatory effectiveness while lowering the risk of systemic absorption. As a result, this nanomedicine technique offers a viable option for improving the clinical outcomes of psoriasis therapy, providing a safer and more potent alternative to conventional treatments.

5. ACKNOWLEDGMENT

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