

Nanoemulgel-Based Therapies for Psoriasis: Current Advances, Global Research Trends, and Future Perspectives

Dakme Papi¹, Prof. (Dr.) Niladry Sekhar Ghosh^{2*}, Dr. Pranay Wal³

¹Research Scholar, Faculty of Pharmaceutical Science, Assam Downtown University, Panikhaiti, Guwahati, Assam

^{2*}Faculty of Pharmaceutical Science, Assam Downtown University, Panikhaiti, Guwahati, Assam

³Department of Pharmacy, Pranveer Singh Institute of Technology (Pharmacy), Kanpur, Uttar Pradesh

Corresponding author: Prof. (Dr.) Niladry Sekhar Ghosh | Faculty of Pharmaceutical Science, Assam Downtown University, Panikhaiti, Guwahati, Assam

ABSTRACT

Background

Psoriasis is a persistent, immune-mediated inflammatory dermatological condition that imposes considerable clinical and psychological distress. Topical therapy continues to be a principal treatment method; however, traditional formulations frequently exhibit inadequate skin penetration and restricted therapeutic effectiveness.

Objective

This study seeks to give a thorough assessment of innovations in nanoemulgel-based drug delivery systems for psoriasis treatment, as well as to conduct a bibliometric analysis of worldwide research trends, focal points, and collaboration networks in this field.

Methods

A comprehensive literature search covering the period from 1995 to June 2025 was performed on Web of Science, Scopus, and PubMed. A bibliometric study was conducted utilizing CiteSpace, VOSviewer, R-bibliometrix, and ScimagoGraphica to evaluate publication patterns, author collaborations, keyword development, and citation networks.

Results

A substantial increase in publications post-2015 indicates accelerating research momentum. India, China, and the USA emerged as leading contributors. Nanoemulgels incorporating methotrexate, curcumin, tacrolimus, and other agents demonstrated enhanced dermal delivery, prolonged retention, and significant anti-inflammatory outcomes in preclinical models. Emerging trends include dual-drug systems, herbal combinations, and thermosensitive/bioadhesive gels.

Conclusion

Nanoemulgels offer a promising platform for targeted, sustained, and patient-compliant topical psoriasis therapy. While preclinical evidence is robust, translational hurdles such as regulatory ambiguity, long-term safety, and formulation scalability must be addressed. Future research should emphasize smart-responsive systems, AI-assisted optimization, and biomarker-driven personalization to fully harness the clinical potential of nanoemulgel-based therapeutics.

Keywords: Psoriasis, Nanoemulgel, Topical Drug Delivery, Nanocarriers, Bibliometric Analysis, Smart Systems, Personalized Therapy.

How to cite this article: Papi D, Ghosh NS, Wal P. Nanoemulgel-Based Therapies for Psoriasis: Current Advances, Global Research Trends, and Future Perspectives. *Int J Drug Deliv Technol.* 2026;16(54s): 1172-1186. DOI: 10.25258/ijddt.16.54s.102

Source of support: Nil.

Conflict of interest: None.

Introduction

Psoriasis is a chronic, relapsing, immune-mediated dermatological condition that impacts between 2–5% of the worldwide populace, primarily presenting as plaque psoriasis, but also encompassing variants such as erythrodermic, guttate, pustular, and psoriatic arthritis.[1] Psoriasis is recognized not just for its skin effects but also as a systemic inflammatory disorder linked to several comorbidities, such as

cardiometabolic diseases, psoriatic arthritis, and depression, hence increasing its overall disease burden. [2] The pathophysiological characteristic of psoriasis is the dysregulation of the Th17/IL-23/IL-17 immunological axis, characterized by activated dendritic cells secreting IL-23, which promotes Th17 cell development and the subsequent generation of IL-17A, IL-22, and TNF- α . These pro-inflammatory cytokines promote keratinocyte hyperproliferation and perpetuate persistent cutaneous inflammation. [3]

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The intricate immunological cascade, together with genetic predispositions like HLA-C*06:02 and environmental triggers such as infections, stress, obesity, and smoking, influences the disease phenotype and its variable clinical progression. [4] Topical treatment is fundamental in the administration of mild-to-moderate psoriasis and is essential for sustaining remission in more severe instances. In the last century, the therapeutic landscape has undergone considerable evolution: the initial documentation of coal tar in conjunction with UV radiation occurred in 1925, succeeded by the development of topical corticosteroids in 1952, emollient-based formulations in 1955, and Vitamin D analogues in 1991. [5–7] Subsequent developments encompassed tazarotene, a topical retinoid, and calcineurin inhibitors like tacrolimus, providing steroid-sparing options for delicate areas. [8–10] Notwithstanding these advancements, traditional topical formulations such as creams, ointments, and lotions are impeded by inadequate skin penetration, insufficient drug retention, and frequent dose necessities, frequently resulting in treatment non-adherence and subpar results. [11]

To address these constraints, researchers have utilized nanocarrier-based drug delivery systems that augment drug solubility, boost skin permeability, and facilitate sustained release. [12] Nanoemulgels have emerged as notably promising platforms among these advances. They integrate the exceptional solubilizing ability and nanoscale droplet dimensions (<200 nm) of nanoemulsions with the viscosity, adhesion, and controlled release characteristics of gels, resulting in greater skin penetration, extended residence duration, and better patient adherence. [13] Figure 2 This combined benefit renders nanoemulgels particularly pertinent for the administration of both traditional antipsoriatic drugs (e.g., methotrexate, corticosteroids) and innovative bioactives (e.g., herbal medicines, small-molecule inhibitors). [14]

Despite the increasing number of studies investigating nanoemulgels for psoriasis, there remains a paucity of comprehensive reviews that consolidate the technological advancements, therapeutic implications, and research trends in this field.[15] This review aims to bridge that gap by providing a systematic synthesis of the evolution, formulation strategies, and therapeutic potential of nanoemulgels in psoriasis management, supplemented by a bibliometric analysis to map global research activity and identify emerging hotspots in this domain.[16]

In addition to formulation challenges, the successful clinical translation of nanoemulgels demands attention to patient-centric design, stability, and regulatory clarity. Given that these systems straddle

the line between conventional topical agents and nanomedicines, global regulatory bodies such as the FDA and EMA have yet to provide definitive frameworks for safety and quality standards. This regulatory ambiguity, combined with formulation complexity, underscores the importance of interdisciplinary collaboration in advancing nanoemulgel technologies. [17]

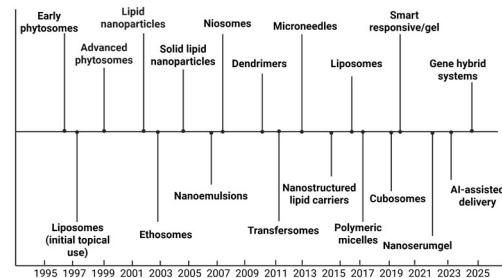


Figure 1. Timeline of novel drug delivery systems explored for the topical management of psoriasis (2000–2025). The figure highlights the chronological emergence of various advanced formulations, including hydrogels, lipid-based carriers, vesicular systems, microneedles.

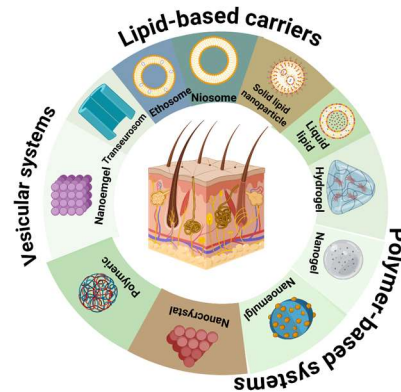


Figure 2. Schematic illustration of the anatomical structure of human skin and representative novel drug delivery systems developed for the topical treatment of psoriasis from 1995 to 2025. The figure categorizes delivery platforms into polymer-based systems, vesicular systems, and lipid-based carriers, highlighting advancements such as nanoemulgel, transfersomes, ethosomes, and Nano crystals.

Materials and Methods

Data Collection

An advanced literature search was performed in the Science Citation Index Expanded (SCI-EXPANDED) of the Web of Science Core Collection (WoSCC), as well as PubMed and Scopus, to retrieve publications related to nanoemulgels for psoriasis. The search was

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conducted on 30 June 2025 using the following strategy: TS = (nanoemulgel”) AND TS = (psoriasisOR topical drug delivery”). The time frame for the search was set between 1 January 1995 and 30 June 2025, and the document types were restricted to original research articles and review articles published in English. Records meeting the inclusion criteria were exported in Full Record and Cited References format for subsequent analysis. (Figure 3) Duplicate entries and non-relevant publications (e.g., unrelated formulations or diseases) were manually screened and excluded to ensure dataset accuracy.

Bibliometric Analysis Tools

To visualize and analyze publication trends and research networks, we employed a combination of CiteSpace (6.2.R4), VOSviewer (1.6.19), the bibliometrix package in R (version 4.4.0), and ScimagoGraphica. CiteSpace was utilized to map collaboration networks among authors, institutions, and countries, as well as to identify co-cited references and their clustering patterns. VOSviewer facilitated the generation of keyword co-occurrence maps and thematic clustering to identify emerging research hotspots. R-bibliometrix, integrated with RStudio, was applied for statistical analyses of publication output, citation counts, h-index values, and betweenness centrality, offering deeper insights into author and institutional productivity. ScimagoGraphica was used to visualize geographical distributions and collaborations at a global scale, providing an intuitive representation of country-level research activity. Although not the main focus, bibliometric filters were applied to assess studies discussing regulatory classification and safety evaluations of nanoemulgels. This included keywords like "FDA," "safety," and "toxicity," helping to map the translational bottlenecks

Statistical Models and Data Processing

To forecast research trends, linear regression models were constructed using publication year as the independent variable and annual publication volume and cumulative citations as dependent variables. Where necessary, logarithmic transformations were applied to stabilize data variance and improve model fit. Model performance was evaluated using R-squared (R^2) to assess explained variance and Mean Squared Error (MSE) to quantify prediction accuracy. Additionally, h-index values were calculated to evaluate the scholarly impact of authors and institutions, while betweenness centrality metrics were applied to identify nodes within collaboration networks.

Results

Analysis of Publication Trends and Citation Frequency

The bibliometric analysis revealed a steady and pronounced growth in research activity on nanoemulgels for psoriasis over the last decade. While early studies between 1995 and 2010 were sporadic and exploratory, a significant surge in publications emerged post-2015, aligning with global interest in nanotechnology-enabled dermatological therapies. From 2017 onward, this growth became more pronounced, reflecting increasing research investment in advanced topical drug delivery platforms.

Cumulative citation frequency also increased in parallel, peaking between 2020 and 2024, which underscores the accelerating impact and recognition of this field in scholarly communities. (Figure 4). Predictive modeling using linear regression demonstrated strong model fit for both publication counts ($R^2 = 0.89$) and citation growth ($R^2 = 0.95$). Extrapolated projections suggest that annual publications in this domain could exceed 120 articles by 2030, cementing nanoemulgels as a cornerstone in next-generation topical psoriasis therapy research (Figure 1).

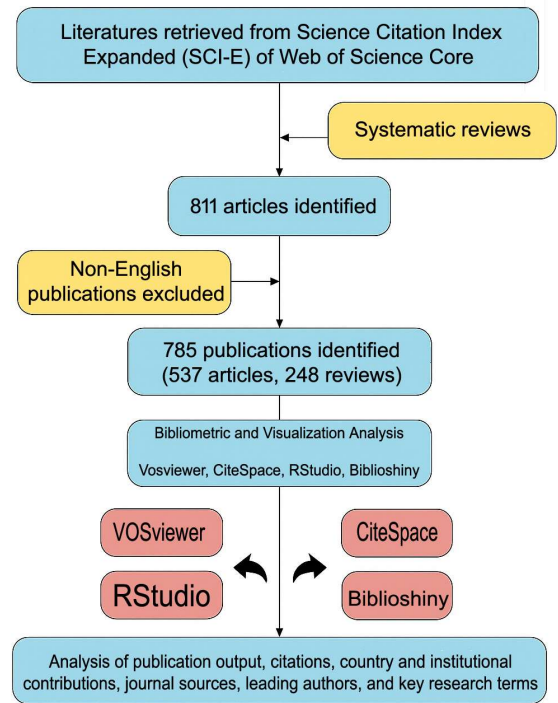


Figure 3. Schematic depiction of the literature search, screening, and analytical workflow adopted for this review.

Global Contributions: Countries and Institutions

A total of 80+ countries have contributed to the literature on nanoemulgels for psoriasis. India leads in overall publication volume, showcasing a strong workforce and infrastructure in pharmaceutical nanotechnology. The United States ranks highest in average citations per article, reflecting broader international visibility and high-impact contributions. China occupies the second position in publication volume, highlighting its rapid advances in dermatology-oriented nanomedicine.

Leading institutions include JamiaHamdard University, Birla Institute of Technology and Science (BITS) Pilani, and Chang Gung Universitythe latter distinguished by extensive international collaborations. Visual network mapping of institutional collaborations reveals well-connected multi-country clusters, particularly between India–USA, China–Australia, and India–Europe, indicating robust global research linkages.

Authors and Co-Cited Researchers

Analysis of over 3,000 authors identified Madhulika Pradhan (India) as the most frequently co-cited author, reflecting her seminal contributions to nanoemulgel drug delivery systems. GautamSinghvi (BITS Pilani) leads in total publications, while Jia-You Fang (Chang Gung University) holds the highest h-index, underscoring his influence in transdermal nanocarrier research. Author collaboration maps depict strong national clusters especially in Indiacross-linked with interdisciplinary teams worldwide, reinforcing the field’s international and collaborative nature.

Journals and Publication Outlets

The majority of articles were published in high-impact, Q1-ranked journals, with the International Journal of Pharmaceutics, Drug Delivery and Translational Research, and AAPS PharmSciTech emerging as the most prolific. According to Journal Citation Reports (JCR), over 70% of the journals represented fall into the top quartile (Q1), emphasizing the field’s high scholarly visibility and recognition.

Co-Cited References and Knowledge Clusters

Co-citation analysis highlighted several landmark studies that have shaped the field, focusing on nanoemulsion formulation techniques, enhanced skin permeation strategies, and hybrid delivery systems for anti-psoriatic agents. Timeline clustering reveals a clear thematic evolution: from basic exploratory formulations in the 2000s, through skin-targeting optimization in the 2010s, to multifunctional,

multi-drug nanoemulgel platforms post-2020, incorporating biologics, herbal actives, and advanced anti-inflammatory compounds.

Keywords and Emerging Research Hotspots

Keyword co-occurrence analysis identified nanoemulgel, methotrexate,curcumin, targeted delivery,and Th17 inhibitionas dominant research nodes. Emerging hotspots include multi-drug nanoemulgel systems, bioadhesive and thermosensitive formulations, photodynamic therapy adjuncts, and herbal-integrated delivery platformsindicating a paradigm shift from monotherapy to personalized, multi-mechanistic topical strategies for psoriasis management. Overlay keyword mapping from 2010–2025 further reveals a transition from early single-drug systems toward multi-functional, patient-responsive nanoemulgels. Recent entries such as smart delivery, thermo-responsive gels,and AI formulation designreflect a shift toward personalized and predictive therapy models

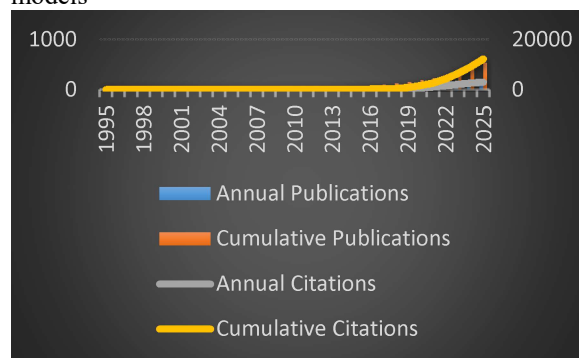


Figure 4. Visualization of annual publication trends and aggregate citation counts for articles related to nanoemulgel-based research in topical psoriasis therapy. The blue and gray bar graphs indicate annual publications and citations, respectively, while the orange and yellow lines depict the cumulative annual volumes of publications and citations.

| S · N o · | Del iver y Sys tem | Co mp osit ion | Pa rti cle Siz e (n m) | Pre par atio n Tec hni que | Dr ug / Act ive | In -vi vo / M od el | Res ult | R ef er ence |
|-----------|--------------------|-------------------------------|------------------------|----------------------------------|-----------------|---------------------|----------------------------------|--------------|
| 1 | Na noe mu lge l | Tw een 80, PE G 4 00, Car bop | 15 2.2 4 ± 0.4 2 | Hig h-e ner gy emu lsifi cati on | Met hotr exate | I M Q-mi ce | PAS I scor e & cyto kine (IL-17, | [2 7] |

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|---|-------------|--------------------------------------|-------------------|--------------------------------------|-----------------------|----------------------|--|---------|
| | | ol940 | | | | | TNF- α suppression; prolonged retention | |
| 2 | Nanoemulgel | Tween 20, PG, Carbopol 934 | 138.15 \pm 0.51 | Ultrasound | Curcumin | BALB/c mice | Reduced erythema & thickness; antioxidant activity increased | [28] |
| 3 | Nanoemulgel | Span 80, Transcutol P, Poloxamer 407 | 145.62 \pm 0.39 | Low-energy emulsification | Tacrolimus | Ex vivo human skin | Improved dermal delivery; sustained release profile | [29-30] |
| 4 | Nanoemulgel | Tween 80, Olive oil, Carbopol 940 | 165.48 \pm 0.44 | Spontaneous emulsification | Dithranol | IMQ-rats | Reduced scaling, TNF/IL-17; better tolerability vs conventional gels | [30-31] |
| 5 | Nanoemulgel | Tween 20, Gly | 130.38 \pm 0.4 | Ultrasound | Resveratrol | BALB/c | Potent antioxidant | [32-32] |
| 6 | Nanoemulgel | Tween 80, PEG 200, Chitosan gel | 148.92 \pm 0.36 | Solvent evaporation + emulsification | Apramycin | Swiss albino mice | High SC retention; decreased epidermal hyperplasia | [33-34] |
| 7 | Nanoemulgel | Tween 80, Oleic acid, Carbopol 974P | 160.27 \pm 0.47 | High-shear homogenization | Tazarotene | IMQ-mice | Enhanced permeation, controlled release, minimal irritation | [35-36] |
| 8 | Nanoemulgel | Tween 80, PEG 400, Carbopol 940 | 155.14 \pm 0.43 | Spontaneous emulsification | Clobetasol propionate | Ex vivo porcine skin | Dramatic skin deposition; minimal systemic absorption | [37-38] |
| 9 | Nanoemulgel | Tween | 140.8 | Low-e | Alone | BA | Synergist | [39-] |

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|----|-------------|--|---------------|------------------------------|-----------------------------------|----------------|--|---------|
| 17 | Nanoemulgel | Tween 20, Caprylic triglycerides, Carbopol 940 | 146.27 ± 0.36 | Ultrasound | Tacrolimus + Apremilast | Swissalbinomic | Dual-drug gel outperforming single-agent systems | [54-55] |
| 18 | Nanoemulgel | Tween 80, PEG 200, Carbopol 940 | 154.85 ± 0.39 | High-energy emulsification | Curcumin + Vitamin D ₃ | IMQ-mice | Enhanced anti-proliferative & antioxidant response | [56] |
| 19 | Nanoemulgel | Span 20, PG, Carbopol 974P | 148.54 ± 0.41 | Low-energy emulsification | Dithranol + Resveratrol | BALB/c mice | Synergy in scaling reduction; elevated IL-22 suppression | [57-60] |
| 20 | Nanoemulgel | Tween 80, Ole | 150.42 ± 0.3 | Ultrasound | Metformin + | IMQ-mice | Broad suppression | [61] |
| 21 | Nanoemulgel | Tween 80, Ethanol, Carbopol 940 | 142.68 ± 0.33 | Ultrasound | Bexarotene | BALB/c mice | Suppressed IL-17 & IL-22; epidermal thickness normalized | [62] |
| 22 | Nanoemulgel | Span 80, PEG 400, Carbopol 934 | 147.12 ± 0.41 | High-pressure homogenization | Pso-ralen | IMQ-rats | Enhanced phototherapeutic retention; reduced oxidative markers | [63-64] |
| 23 | Nanoemulgel | Tween 80, Olive oil, Carbopol 940 | 156.91 ± 0.44 | Spontaneous emulsification | Vitamin E + Curcumin | BALB/c mice | Strong synergistic antioxidant & anti-inflammation | [65-67] |
| 24 | Nanoemulgel | Tween 20, Transc | 138.47 ± 0.35 | Ultrasound | Curcumin + Res | IMQ-mice | Decreased PAS I; | [68-70] |

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| | | | | | | | | |
|----|-------------|----------------------------------|------------------------------|---------------------------|-----------------------------------|-------------|--|---------|
| | | utol P, Carbopol 940 | | | veratrol | | greater skin deposition compared to Curcumin alone | |
| 25 | Nanoemulgel | Tween 80, PEG 200, Carbopol 974P | 15 1.5 8 ± 0.3 7 | High-shear homogenization | Clobetasol propionate + Aloe vera | BALB/c mice | Combined reduction in IL-17, IL-23; excellent skin compatibility | [71-72] |

Discussion

This work represents the first comprehensive bibliometric and content-focused review of nanoemulgel-based approaches for psoriasis management, providing insights into research growth, global collaboration networks, and evolving scientific priorities in this field. Our analysis shows a substantial escalation in publications after 2015, coinciding with the rising interest in hybrid nanocarrier systems that combine the solubilization efficiency of nanoemulsions with the viscosity and retention properties of gels. [18-19] Similar to patterns observed in broader nanomedicine research, India, China, and the United States emerged as the leading contributors, with Jamia Hamdard University and BITS Pilani dominating publication output in India and Chang Gung University achieving higher global collaboration and citation impact. These findings reflect not only regional research capacities but also differential prioritization of pharmaceutical nanotechnology and dermatological translational research across countries [20-21].

From a formulation perspective, the advantages of nanoemulgels are clear. Their nanoscale droplets (typically <200 nm) enhance the solubility and

thermodynamic activity of hydrophobic agents, enabling improved penetration through the stratum corneum and sustained retention at psoriatic plaques [23]. These droplets are incorporated into a gel matrix composed of Carbopol, poloxamers, or chitosan, providing structural stability, bioadhesion, and ease of application, which collectively improve pharmacological outcomes and patient compliance [24]. The versatility of formulation strategies including oil-in-water vs. water-in-oil emulsions, use of non-ionic surfactants like Tween, Span, Transcutol, and PEG, and incorporation of bioadhesive gelling agents has enabled the delivery of a broad spectrum of drugs such as methotrexate, tacrolimus, dithranol, and herbal bioactives like curcumin, resveratrol, and aloe vera [25-26]. Notably, several studies have explored dual-drug systems to enhance therapeutic synergy, highlighting the platform's potential for multifunctional therapy (Table 1).

Table 1. Applications of Single and Dual & Multi-Drug Nanoemulgel-Based Topical Drug Delivery Systems in Psoriasis

Preclinical studies strongly support the therapeutic promise of nanoemulgels. Experiments using imiquimod (IMQ)-induced psoriasis models consistently demonstrate improved Psoriasis Area and Severity Index (PASI) scores, histopathological recovery, and downregulation of inflammatory cytokines including IL-17, IL-23, and TNF- α [73]. These outcomes indicate that nanoemulgels not only improve drug delivery but also modulate immunological pathways, aligning with the central role of the Th17/IL-23 axis in psoriasis pathogenesis (Figure 5). Although clinical data remain limited, early-phase studies suggest enhanced tolerability, reduced irritation, and improved efficacy compared to conventional topical formulations, supporting the need for multicenter randomized trials to validate these findings [74-75].

Despite encouraging progress, several challenges remain. Physical and chemical stability, particularly phase separation and droplet coalescence, threaten the shelf-life and scalability of these formulations. [76-77] Additionally, the requirement for relatively high surfactant concentrations increases the risk of cutaneous irritation, underscoring the need for optimized surfactant/co-surfactant systems. Furthermore, regulatory uncertainty persists as nanoemulgels occupy a gray zone between conventional topical drugs and nanomedicines, necessitating the development of clearer safety, efficacy, and quality control frameworks before clinical translation. [78-80]

Looking forward, the next generation of nanoemulgels may evolve into smart systems,

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capable of responding to pH, temperature, or enzymatic triggers to achieve on-demand, site-specific drug release. Multi-drug nanoemulgel systems, designed to simultaneously target multiple inflammatory pathways, could provide synergistic disease control and reduce the burden of polypharmacy. [81-83] Incorporating biomarker-driven clinical endpoints (e.g., IL-17 and IL-23 levels) into trial designs could further personalize therapy, optimizing treatment for diverse patient subgroups. To achieve these goals, enhanced academic-industry partnerships and cross-disciplinary collaborations will be essential, enabling the translation of nanoemulgels from experimental innovations into patient-centered, regulatory-approved therapies for psoriasis. [84-85]

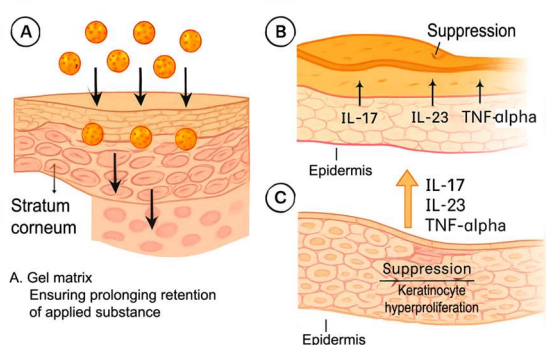


Figure 5. Proposed mechanism of nanoemulgel action in psoriasis: (A) Nano-sized droplets enhance penetration through the stratum corneum; (B) Gel matrix ensures prolonged retention; (C) Delivered agents suppress inflammatory cytokines (IL-17, IL-23, TNF- α), reducing keratinocyte hyperproliferation.

Challenges in Regulation and Safety

The regulatory classification of nanoemulgels remains inconsistent globally, with differing interpretations under cosmetics, drugs, or nanomedicine. High surfactant/co-surfactant loads, though essential for stability, pose skin irritation risks in long-term use. Additionally, limited long-term toxicity and microbiome interaction studies present barriers to mainstream approval. Addressing these will be critical for successful clinical transition.[86-88]

5. Conclusion

Nanoemulgel-based drug delivery systems represent a significant advancement in the topical management of psoriasis, addressing limitations associated with conventional formulations such as poor dermal penetration, inadequate drug retention, and suboptimal patient adherence. The integration of nanoemulsion droplets within gel matrices enhances solubility, prolongs skin residence time, and

facilitates controlled release of both synthetic and phytopharmaceutical agents.

The present bibliometric analysis reveals a marked escalation in research activity post-2015, with considerable contributions from India, China, and the United States, reflecting a global shift toward nanotechnology-enabled dermatotherapeutics. Emerging formulation strategies emphasize dual-drug systems, bioadhesive and thermosensitive matrices, and the incorporation of herbal actives to achieve synergistic therapeutic effects and improved biocompatibility.

However, the clinical translation of nanoemulgels remains constrained by challenges including physical and chemical stability, surfactant-associated cytotoxicity, and ambiguous regulatory categorization. These limitations necessitate the development of optimized formulation protocols, long-term safety assessments, and clear regulatory frameworks.

Future directions should focus on the design of stimuli-responsive (e.g., pH-, enzyme-, or temperature-sensitive) nanoemulgels, integration of artificial intelligence for predictive formulation modeling, and adoption of personalized medicine approaches using biomarker-guided therapies. Such innovations are critical to realizing the full clinical potential of nanoemulgels as next-generation therapeutics for psoriasis.

Future Discussion

The advancement of nanoemulgel technology for psoriasis therapy has opened up promising avenues for improving treatment outcomes; however, its translation from preclinical success to widespread clinical application requires further exploration. Future research should focus on the development of smart, stimuli-responsive nanoemulgels that can adapt to changes in skin pH, temperature, or enzymatic activity, ensuring precise and controlled drug release at the psoriatic site while minimizing systemic exposure.[89-93] In addition, integrating multi-drug combinations, including anti-inflammatory agents, biologics, and natural bioactives, within a single delivery platform could enhance therapeutic synergy and reduce the overall dosage requirements. Long-term safety studies, particularly assessing chronic use and potential immunological implications, remain critical for establishing clinical reliability. [93-97] Furthermore, the integration of advanced imaging and omics-based tools will allow deeper insights into drug-skin interactions and therapeutic responses at the molecular level. Finally, collaborations between pharmaceutical scientists, dermatologists, and regulatory bodies will be essential to streamline product development, optimize large-scale

manufacturing, and establish clear regulatory pathways, ultimately ensuring that these innovative formulations reach patients efficiently and effectively.[97-100]

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