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REVIEW

Nanocarriers for Psoriasis Treatment: Insights from a Clinical Trial Registered on the Global Clinical Trials Registry Platform

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Abstract: Psoriasis is a chronic, relapsing inflammatory skin disease. Topical treatments are the primary choice for up to 80% of psoriasis patients; however, their effectiveness is often limited by poor penetration into the skin. Nanocarriers represent a promising advancement in drug delivery systems by enhancing bioavailability and tissue penetration and reducing the frequency of dosing. This study conducted a narrative review and analyzed the characteristics of clinical trials registered on ClinicalTrials.gov and the International Clinical Trials Registry Platform (ICTRP) that investigated the use of nanocarriers for psoriasis treatment. The findings indicate that the proportion of registered randomized controlled trials (RCTs) focusing on nanocarriers for psoriasis treatment is exceedingly limited, comprising only 0.2% (11 out of 5338) of all registered RCTs related to psoriasis treatment. Among these 11 RCTs, six types of nanocarriers were identified: microemulsion/nanoemulsion, chitosan nanoparticles, liposomes, ethosomes, micelles, and niosomes. Five trials reported complete or partial outcomes using the Psoriasis Area and Severity Index (PASI) as the primary efficacy measure. However, many trials had incomplete baseline and follow-up PASI data. Studies have shown that encapsulating APIs within nanocarriers generally yields a more significant reduction in PASI scores than administering empty nanocarriers. Additionally, no study has directly compared nanocarriers with traditional formulations. The APIs used in these RCTs primarily comprised lipophilic drugs. In conclusion, although nanocarriers for psoriasis treatment demonstrate significant potential, they continue to face challenges, including incomplete regulatory frameworks, difficulties in large-scale production, and high production costs.

Keywords: psoriasis, nanocarriers, topical drug delivery, clinical trials, ClinicalTrials.gov, liposomes, nanoparticles

Introduction

Psoriasis, a chronic immune-mediated inflammatory skin disease, is characterized by abnormal keratinocyte proliferation and immune cell infiltration into the dermis and epidermis, resulting in pruritic, scaly, and erythematous plaques on the skin.[1] This condition affects an estimated 2–4% of the global population.[1,2] Management strategies for psoriasis include topical therapy, systemic agents, and phototherapy, with treatment selection primarily determined by disease severity.[3,4] Topical medications are typically the first-line treatment for mild-to-moderate cases, whereas moderate-to-severe cases often require phototherapy or systemic therapy.[4] Systemic therapy is frequently combined with topical treatments to enhance therapeutic outcomes.[5] However, current therapeutic methods for psoriasis have notable shortcomings. Phototherapy is costly and prone to toxicities, such as photoaging, sunburn, and erythema.[6] Although systemic drugs are efficacious in many cases, they often trigger adverse reactions, including nephrotoxicity, hypertension, hepatotoxicity, skin cancer, and hyperlipidemia.[7,8] Additionally, immunosuppressants and biologics with immunosuppressive properties, although effective for moderate-to-severe psoriasis, are limited by the heightened risk of infection and adverse

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cardiovascular and hepatic effects.[9,10] Consequently, topical treatments have emerged as the predominant choice for most patients, with nearly 80% selecting them as their primary therapeutic modality.[5]

In patients with psoriasis, atypical keratinocyte proliferation and differentiation in the epidermis not only increase skin stiffness and rigidity but also markedly decrease drug permeability.[11] This dysfunction of the skin barrier further increases transepidermal water loss and decreases hydration in patients with psoriasis, thereby exacerbating skin dryness and rigidity.[12] Consequently, topical traditional formulations exhibit notable limitations in addressing these pathological changes, including restricted drug penetration, increased dosing frequency, adverse toxicological reactions, and reduced patient compliance.[13]

Nanocarriers are recognized for their ability to enhance drug penetration and overcome the skin barrier; consequently, their potential for treating skin diseases has been widely recognized.[14,15] The active pharmaceutical ingredients (APIs) encapsulated within nanocarriers can traverse different skin strata through multiple pathways, including transcellular, intercellular, and transappendageal routes.[14] The mechanism of skin penetration is markedly influenced by the physicochemical characteristics of both the active drug and its carrier, including particle size, charge, mobility, and the balance of hydrophilic and lipophilic.[14] Among the critical parameters for follicular targeting, the particle size and mobility of nanocarriers in targeted drug delivery are paramount.[16,17] Compared with conventional topical formulations, nanocarriers can substantially reduce the required API dose to achieve therapeutic efficacy, thereby mitigating the adverse effects associated with traditional treatments, enhancing drug solubility and bioavailability, and minimizing toxicity.[18,19]

Several studies[20–22] have comprehensively reviewed nanocarrier-based strategies for psoriasis therapy, including liposomes, niosomes, ethosomes, solid lipid nanoparticles, nanoemulsions, and transferosomes. However, these reviews primarily focus on formulation strategies, physicochemical characterization, and therapeutic efficacy in preclinical animal models, providing limited insight into advances in clinical application. Clinical trials are a pivotal phase of drug development, serving as the primary means of validating safety and efficacy in humans.[23–25] Well-designed clinical trials are essential for successful drug development, as their quality directly influences the efficiency of translational processes and the likelihood of regulatory approval and market entry.[26,27] Consequently, a systematic analysis of registered clinical trial data is essential for informing clinical practices and guiding future research. A narrative synthesis of the characteristics of registered trials can yield valuable information regarding clinical trial design trends and the potential market prospects of emerging therapies.[28] In this study, we conducted a comprehensive search of major clinical trial databases, including the ClinicalTrials.gov database and the International Clinical Trials Registry Platform (ICTRP), with a specific focus on topical nanocarriers for psoriasis treatment. Based on the identified studies, a narrative review was conducted to analyze the key trial characteristics and evaluate the advantages of different nanocarrier categories.

Methodology

This study used ClinicalTrials.gov (https://clinicaltrials.gov/) and the ICTRP (https://trialsearch.who.int/) to conduct a systematic search for clinical trials of nanocarrier-based psoriasis treatments. The search strategy included two terms: "psoriasis" and "liposome or nanoparticle or nanoformulation or niosomes or ethosom or nanosphere or nanocapsule or nano*". All other parameters were set to default values. After removing duplicate entries, the studies were manually screened using the following inclusion criteria: interventional study design, psoriasis as the target condition, and drug delivery via nanocarriers. Studies were excluded if they were non-interventional or if the condition addressed was not psoriasis. Subsequently, the included studies were analyzed using the "Trial ID" as the primary identifier. To further identify relevant studies, a comprehensive search was conducted in PubMed, Web of Science, Embase, Ovid MEDLINE(R), and Cochrane databases.

Results

Screening and Included Trials

On September 21, 2025, a search of the ClinicalTrials.gov and ICTRP databases identified 5,338 randomized controlled trials (RCTs) involving psoriasis treatment. Employing nanocarriers as the screening criterion, including liposomes, nanoparticles, nanoformulations, niosomes, ethosomes, nanospheres, nanocapsules, and all terms prefixed with "nano",

57 RCTs involving nanocarriers for psoriasis treatment were initially selected. Following a thorough verification process, 46 studies that did not meet the criteria for nanocarrier-based psoriasis treatment were excluded. One RCT (NCT03004339) was excluded because the submicron particle paclitaxel investigated was an uncoated nanoparticle paclitaxel produced via supercritical carbon dioxide technology, which did not meet the definition of a nanoformulation. Consequently, 11 RCTs were included in this review. Figure 1 presents a flowchart of this study.

Characteristics of the Included Studies

A time-series analysis of the 11 included RCTs revealed an accelerating trend in the investigation of nanocarriers for psoriasis treatment. Following a period of minimal and stable trial initiation from 2000 to 2015 (9% per five-year interval), research activity increased markedly since 2016. This surge is particularly evident during the 2021–2025 period, which accounts for 45% of trials, indicating a recent and substantial intensification of research focus in this domain.

The geographical distribution of these studies was markedly concentrated, with Iran and China emerging as the predominant applicant countries for trial initiation (27% each), followed by Egypt (18%). ClinicalTrials.gov is the primary registry, encompassing 45% of these trials. Concerning trial progression, the largest proportion of studies (45%) is currently in the "Not Recruiting" phase, a percentage considerably higher than those that are completed (27%) or actively recruiting (18%). For further details, see Figure 2.

Type of Nanocarriers and Active Pharmaceutical Ingredients

Six types of nanocarriers were identified in the 11 RCTs: microemulsion/nanoemulsion (4 RCTs), chitosan nanoparticles (3 RCTs), liposomes (2 RCTs), ethosomes (1 RCT), micelles (1 RCT), and niosomes (1 RCT). Notably, one RCT (NCT03348462) incorporated two types of nanocarriers: ethosomes and liposomes. Regarding the physicochemical properties of the active pharmaceutical ingredients (APIs) used in these RCTs, six RCTs involved lipophilic drugs with Log P > 0; one RCT used a hydrophilic drug; one RCT used a plant/plant extract; and three RCTs employed traditional Chinese medicine. For details, see Table 1.

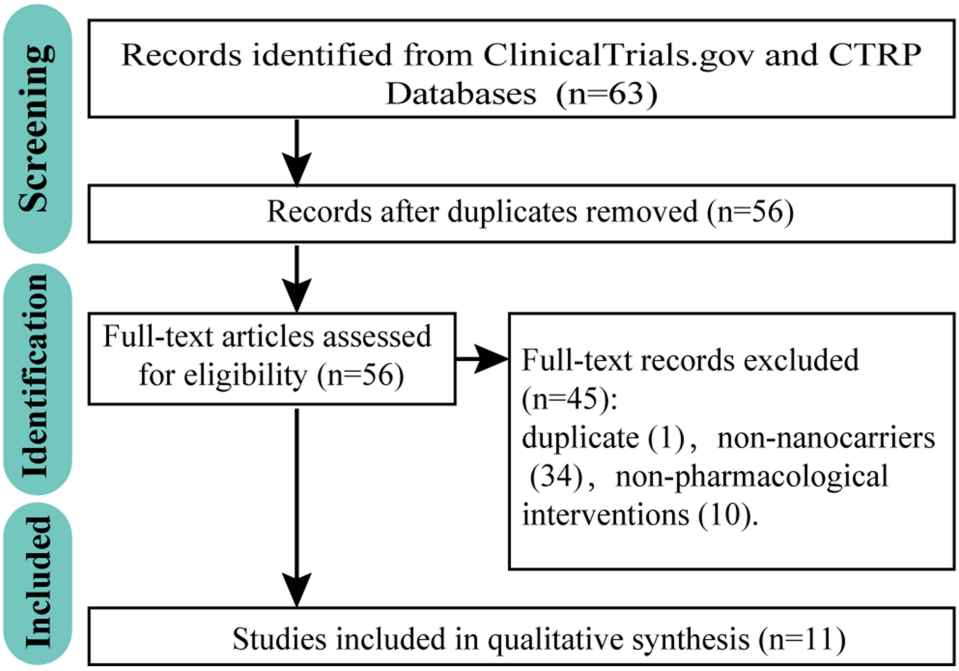

Figure 1 Flow diagram of the study.
Abbreviation: ICTRP, International Clinical Trials Registry Platform.

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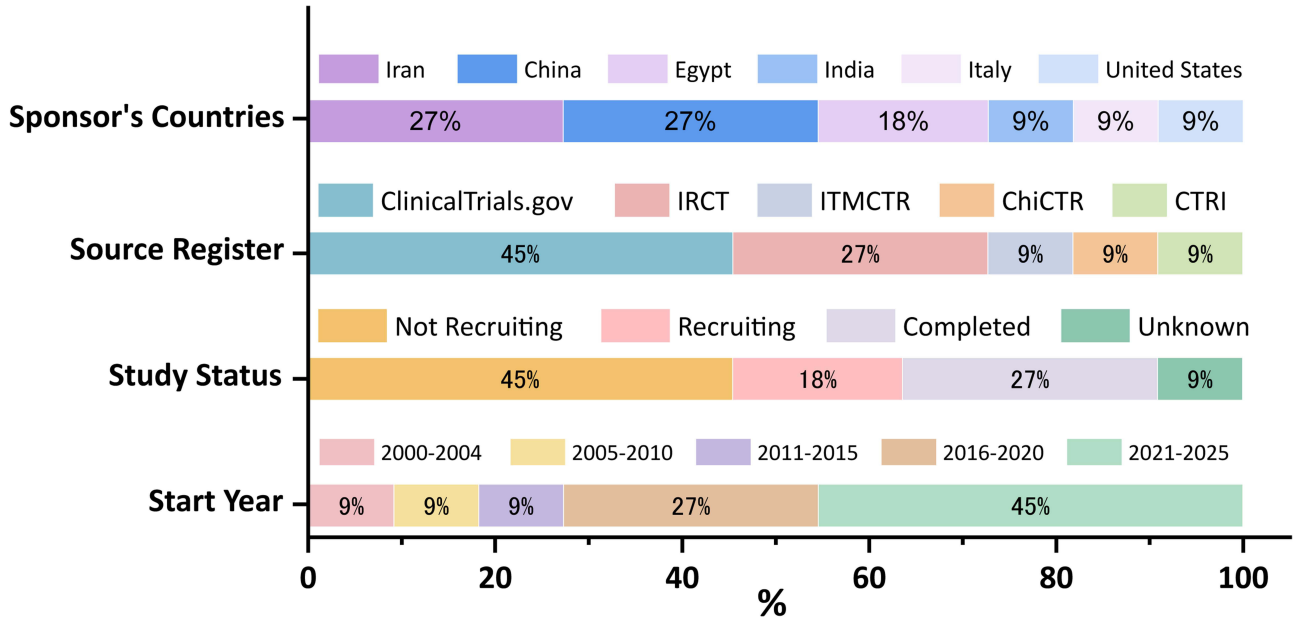

Figure 2 General characteristics of the included studies.
Abbreviations: IRCT, Iranian Clinical Trials Registry; ChiCTR, Chinese Clinical Trial Registry; CTRI, Indian Clinical Trials Registry.

Design Characteristics of the Included Clinical Trials

Among the 11 RCTs, the clinical design imposed no sex restrictions, with treatment as the primary objective. Eight RCTs were restricted to adults, whereas the remaining three RCTs had no age restrictions. According to the established criteria for high-quality clinical trial design, namely randomization, appropriate blinding, parallel group structure, and adequate sample size determination,[30–32] one RCT (NCT00006276) was of low quality, classified as Phase 2, and featured an open-label design, with the allocation and intervention model not reported. In contrast, the remaining 10 RCTs met the criteria for high-quality design. Regarding allocation, nine RCTs were randomized, whereas 1 RCT was not. Regarding the intervention models, 10 RCTs employed a parallel design. In terms of masking, 5 RCTs were double-blinded, 4 RCTs were open-label, and 1 RCT was single-blinded. For further details, see Figure 3.

Table 1 Type of Nanocarriers and Active Pharmaceutical Ingredients

Trial ID	Type of Pharmaceutical Formulation	APIs	CAS NO.	Log P [#]
NCT00006276	Micelles	Paclitaxel	33069-62-4	3.0
NCT00438360	Microemulsion	Cyclosporine	59865-13-3	1.4
NCT03348462	Ethosomes; Liposomes	Anthralin	1143-38-0	2.73
NCT04971239	Micoemulsion	Methotrexate	59-05-2	−1.85
NCT06396013[##]	Chitosan Nanoparticles	Qinteng Huoxue Runji Ointment*	/	/
CTRI/2025/07/090140	Liposomes	Cyclosporine	59865-13-3	1.4
IRCT20130420310 6N13	Microemulsion	Curcumin	458-37-7	3.62
IRCT20240622062209N1	Nanoemulsion Gel	Boswellia	/	/
ChiCTR2400083706[##]	Chitosan Nanoparticles	Qinteng Huoxue Runji Ointment*	/	/
ChiCTR2000034292[##]	Chitosan Nanoparticles	Runji Ointment*	/	/
IRCT20181217042030N1	Niosomes	Curcumin	458-37-7	3.62

Note: APIs, active pharmaceutical ingredients; / not applicable, or data not reported; *traditional Chinese medicine; [#]The source of data comes from Drugbank database; [##]The type of pharmaceutical formulation was determined through a website (https://www.chictr.org.cn) and published papers by an applicant.[29]

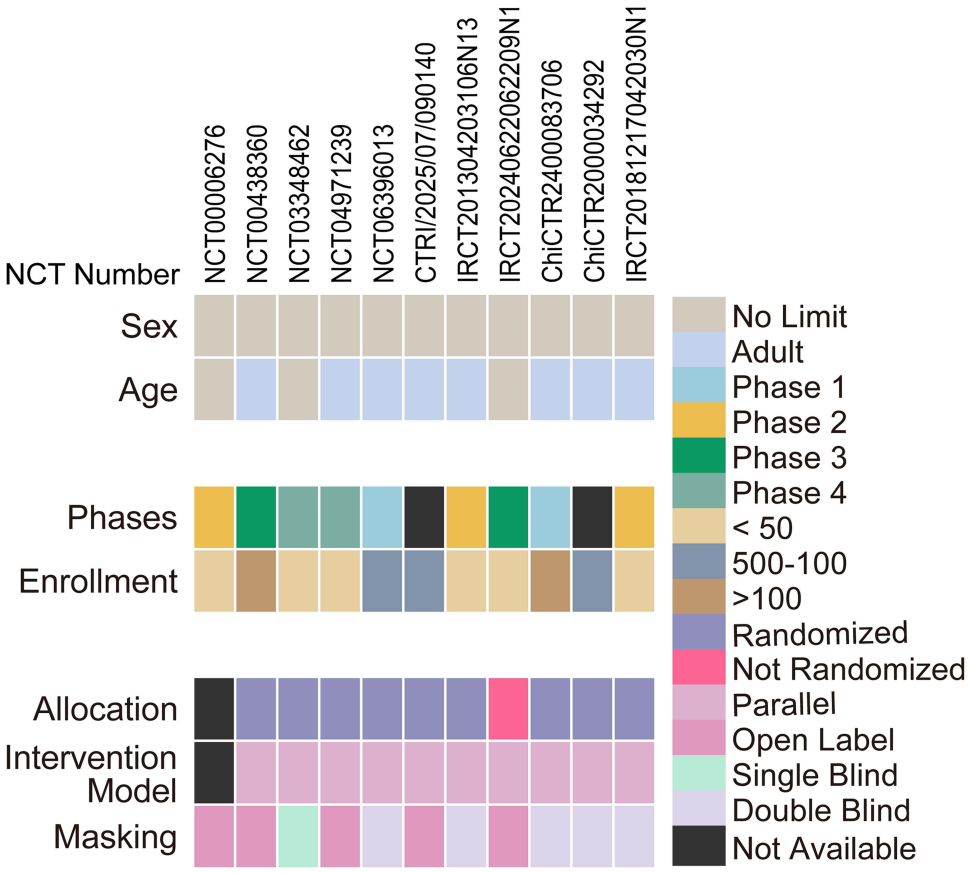

Figure 3 Design characteristics of the included clinical trials.

Primary Outcomes of the Included Trials

Among the 11 identified RCTs, five reported complete or partial outcome data. Table 2 summarizes the demographic characteristics of the enrolled participants and the primary outcomes of these trials. The participants were predominantly middle-aged, with mean ages ranging from approximately 36 to 46 years in most studies. However, the evidence base was limited by small sample sizes: only one trial (NCT00438360) enrolled more than 100 participants (160 vs 79) over 24 weeks, whereas the remaining four RCTs enrolled fewer than 50 participants. The interventions primarily involved topical drugs (four RCTs), with only one oral drug. The Psoriasis Area and Severity Index (PASI) was the principal efficacy endpoint across the studies. However, baseline and follow-up PASI data were incompletely reported in some trials. For example, the cyclosporine A microemulsion trial did not report the baseline PASI, and the curcumin niosome gel trial did not report PASI outcomes. Among trials with comparable reporting, formulations combining an active agent with a nanocarrier generally demonstrated greater PASI improvement than those with blank nanocarriers. Specifically, turmeric microemulgel reduced PASI from 3.6 to 1.4 over 9 weeks, whereas the blank nanocarrier group showed minimal change (3.7 to 3.2). Similarly, nano-modified Runji ointment reduced PASI from 23.84 ± 4.94 to 6.42 ± 4.13 in 8 weeks, exceeding the improvement observed with the blank nanocarrier (24.06 ± 5.56 to 11.06 ± 4.81). These findings suggest that nanocarrier-based topical delivery systems may decrease the severity of psoriasis. However, the strength of inference is constrained by several limitations, including small sample sizes, heterogeneity in treatment duration, baseline disease severity, and incomplete outcome reporting. Consequently, larger, rigorously designed RCTs with standardized and comprehensive PASI reporting are necessary to confirm these preliminary indications of benefit.

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Table 2 Demographic Information of the Patients and Primary Outcomes of the Included Trials

Trial ID	Groups	Interventions	Mode of Administration	Participants	Sex (Female%)	Age	Time Frame	Pre-Treatment PASI Score	Post-Treatment PASI Scores	References
NCT00438360	Treatment	Cyclosporine A Microemulsion	Oral	160	55 (34.4%)	/	24 weeks	/	5.70±8.0	ClinicalTrials.gov
	Control	Placebo		79	32 (40.5%)			/	6.86±8.4	
NCT03348462	Treatment	Ethosomal Anthralin	Topical	10	3 (30%)	43.1±15.1	8 weeks	3.6	0.4	[33]
	Control	Liposomal Anthralin		10	1 (10%)	36.3±16.3		3.4	0.6	
IRCT201304203106N13	Treatment	Turmeric Microemulgel	Topical	34*	14 (41.2%)	/	9 weeks	3.6	1.4	[34]
	Control	Blank Carriers						3.7	3.2	
ChiCTR2000034292	Treatment	Nano-modified Runji Ointment	Topical	19	8 (42.1%)	46.2±10.3	8 weeks	23.84±4.94	6.42±4.13	[29]
	Control	Blank Carriers		18	8 (44.4%)	45.7±10.2		24.06± 5.56	11.06±4.81	
IRCT20181217042030N1	Treatment	Curcumin-Niosomes Gel	Topical	5*	4 (80%)	45.6±5.18	4 weeks	/	/	[35]
	Control	Blank Carriers						/	/	

Note: * Symmetric plaque psoriasis; / not applicable, or data not reported. IRCT20181217042030N1 provides only a comparison of psoriasis severity before and after treatment, based on image descriptions, without specifying the psoriasis area and severity index.

Abbreviation: PASI, Psoriasis Area and Severity Index.

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Discussion

Advantages of Nanocarriers for Psoriasis Treatment

The present study identified the nanocarriers employed in RCTs for psoriasis treatment, including microemulsions/nanoemulsions, chitosan nanoparticles, liposomes, ethosomes, micelles, and niosomes. The structures of these nanocarriers are illustrated in Figure 4. Compared to traditional formulations, nanocarriers provide numerous advantages, including enhanced solubility, bioavailability, targeted drug delivery, controlled release, and reduced toxicity.[36,37] Nanocarriers have been widely investigated for the treatment of skin diseases.[5,38] Distinct nanocarriers exhibit unique advantages and disadvantages; hence, the choice of an appropriate nanocarrier must be determined by the therapeutic aim and the drug's physicochemical properties during the design phase.[39] Additionally, nanocarrier design should incorporate key physicochemical characteristics, including size, shape, surface chemistry, porosity, and flexibility, as these parameters significantly govern their biological behavior and interactions with biological barriers.[39] Table 3 outlines the primary advantages and disadvantages of nanocarriers used in RCTs for psoriasis treatment.

Characteristics of the Active Pharmaceutical Ingredients

Of the 11 RCTs, the active pharmaceutical ingredients (APIs) employed in the interventions were classified mainly into three categories: lipophilic drugs (Paclitaxel, Cyclosporine, Anthralin, Curcumin), hydrophilic drugs (Methotrexate), and botanical agents (Boswellia, Qinteng Huoxue Runji Ointment, Runji Ointment). Owing to their favorable skin permeability, lipophilic APIs generally demonstrate superior efficacy in topical formulations.[48] In contrast, hydrophilic APIs such as Methotrexate are primarily indicated for systemic administration.[52] Although Methotrexate is effective against psoriasis, prolonged use may lead to adverse events, including hepatotoxicity.[53] These data are consistent with the findings of the current study. Only one RCT in this analysis employed a hydrophilic API.

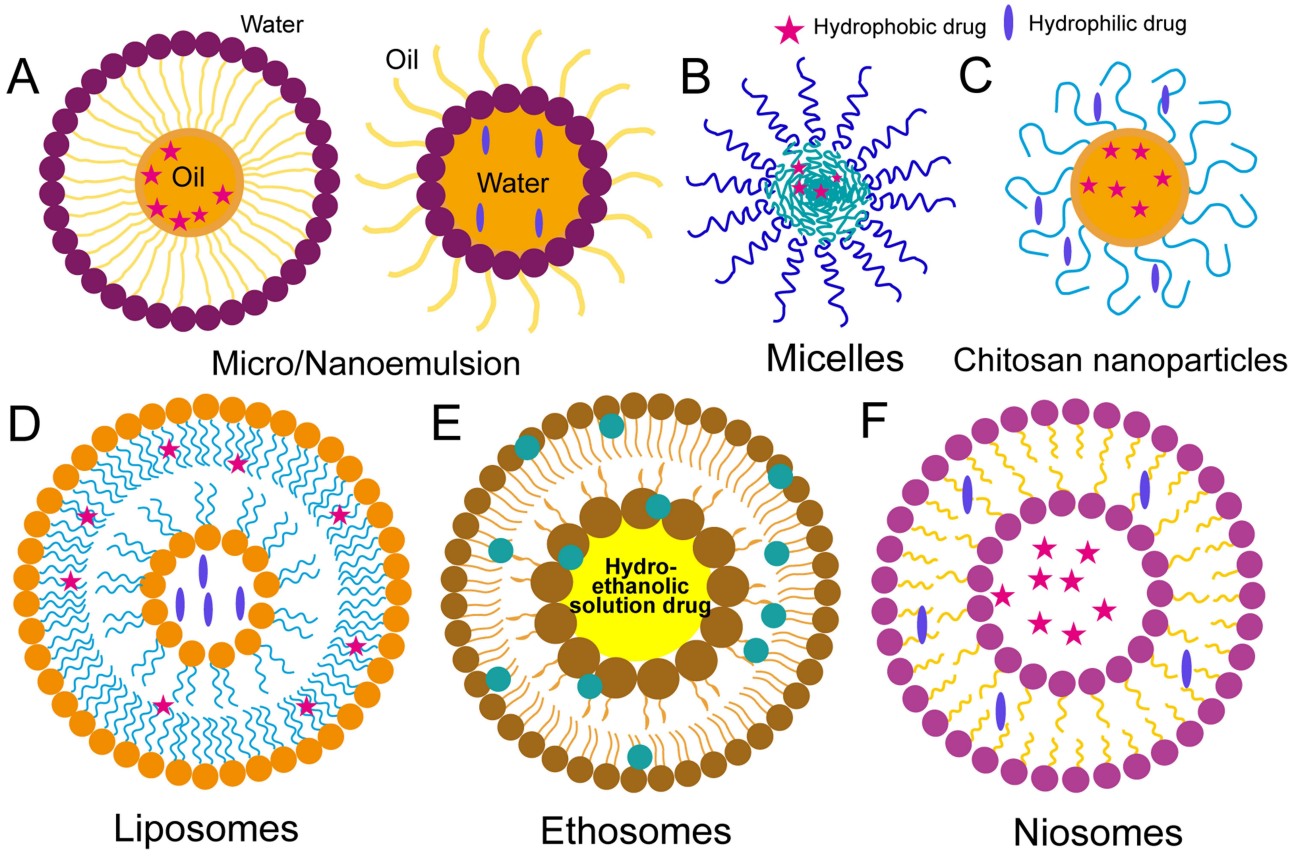

Figure 4 Types of nanocarriers used for drug delivery in psoriasis treatment. (**A**) micro/nanoemulsion; (**B**) micelles; (**C**) chitosan nanoparticles; (**D**) liposomes; (**E**) ethosomes; (**F**) niosomes.

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Table 3 The Main Advantages and Disadvantages of Nanocarriers Used in RCTs for Psoriasis Treatment

Type	Advantages	Disadvantages	References
Nanoemulsion	Encapsulation of both lipophilic and hydrophilic APIs; increases drug permeation and deposition; lower-cost production; suitable for large-scale production	Thermodynamic instability; lower permeation compared to liposomes	[40,41]
Micelles	Flexibility in structure by chemical modification; High capacity to incorporate molecules; Encapsulation of both lipophilic and hydrophilic molecules; Higher deposition in the skin than liposomes.	Lower accumulation in the dermis compared to the nanoemulsion.	[42,43]
Liposomes	Encapsulation of both lipophilic and hydrophilic APIs; Better drug release; Higher accumulation in the stratum corneum compared to the nanoemulsion	Difficulties of large-scale production; High-cost production	[14,44]
Niosomes	Encapsulation of both lipophilic and hydrophilic APIs; Lower-cost production; Reduced transepidermal water loss; Higher stability and lower cytotoxicity compared to liposomes	Difficulties of large-scale production; Lower permeation compared to liposomes	[14,45–47]
Ethosomes	Encapsulation of both lipophilic and hydrophilic APIs; High elasticity, deformability, and malleability; high permeability into the deep-rooted layers of skin	Predisposition to degradation; High-cost production; Ethanol induces dryness and irritation of the skin	[48,49]
Chitosan nanoparticles	Biocompatibility, biodegradability, mucoadhesive properties, easy surface modification;	Difficulties of large-scale production; Requirement of purification processes	[50,51]

Abbreviation: APIs, active pharmaceutical ingredients.

When designing and applying nanocarriers for psoriasis treatment, the physicochemical properties of APIs should be carefully considered. First, transdermal drug delivery for psoriasis is considerably more challenging than for non-keratotic skin disorders. This is attributed to the intrinsic barrier function of the skin, which limits drug penetration,[54] and to the pathological features of psoriatic skin, including hyperproliferation, hyperkeratosis, and reduced hydration, which further hinder API permeation and exacerbate therapeutic limitations.[54,55] Moreover, the molecular weight and partition coefficient of APIs significantly influence the self-assembly and physicochemical characteristics of nanocarriers, which in turn affect their penetration efficiency and biodistribution.[56,57] Therefore, a careful consideration of API properties is essential for the selection and rational design of nanocarriers to achieve optimal therapeutic outcomes.

Challenges in Regulatory Frameworks

Our study revealed that the proportion of registered RCTs focusing on nanocarriers for psoriasis treatment is notably limited, comprising only 0.2% (11 of 5,338) of all registered RCTs for psoriasis intervention. This observation highlights the significant paucity of clinical investigations directly involving human subjects, as most existing research employs animal models or cell lines to replicate experimental conditions.[42]

Nanocarriers are used in the topical treatment of dermatological conditions; however, they are challenged by incomplete regulatory frameworks. US The Food and Drug Administration (FDA), European Medicines Agency (EMA), and Chinese Food and Drug Administration (CFDA) have not issued guidance on the use of topical nanocarriers. Moreover, the regulatory frameworks for nanomedicines vary across countries. The FDA has not established regulatory definitions for “nanotechnology”, “nanomaterial”, “nanoscale”, or other related terms. Instead, it continues to utilize the considerations proposed in 2014. A drug product or material was defined as nanoscale if its particle size is within 1–100 nm or if it exhibits size-dependent physical, chemical, or biological properties, even if its size may extend beyond the nanoscale to the micrometer range (1000 nm).[58,59] The EMA defines nanotechnology as follows: “Nanotechnology is defined as the production and application of structures, devices, and systems by controlling the shape and size of materials at the nanometer scale. The nanometer scale ranges from the atomic level at approximately 0.2 nm (2 Å) to approximately 100 nm”.[60] The CFDA characterizes nanomedicine as nanoparticles synthesized through nanotechnology or as nanoparticles resulting from combining raw pharmaceuticals with suitable carrier materials, including final drug formulations. The external dimensions, internal configuration, and surface architecture of the final product or carrier material in nanomedicine are at the nanoscale, specifically 100 nm or smaller. Alternatively, the particle size of the final product or carrier material generally remains below 1000 nm, and these entities demonstrate notable size-dependent effects.[61]

Challenges in Large-Scale Production and Long-Term Stability

Large-scale production and long-term stability remain significant challenges in the translational development of nanocarriers. In particular, the scalability and reproducibility of nanocarrier formulations pose substantial technical hurdles, as maintaining physicochemical stability, structural uniformity, and consistent drug-loading capacity under industrial manufacturing conditions is challenging. One contributing factor is the wide variety of polymeric materials used in nanocarrier preparation, which can substantially influence the formulation's uniformity and overall quality. Moreover, the absence of standardized manufacturing protocols further exacerbates these challenges. Different research groups often employ distinct preparation methods, leading to considerable variability in nanocarrier size, morphology, surface characteristics, and drug loading efficiency.[62,63] This lack of standardization complicates cross-study comparisons and undermines the reproducibility required for large-scale production. Consequently, the development of advanced manufacturing equipment and platforms with robust scale-up capabilities has become a significant focus in nanomedicine, aiming to facilitate the reliable and consistent industrial production of nanocarrier-based formulations.[64]

Nanocarriers possess a large specific surface area and are therefore highly susceptible to aggregation, precipitation, and degradation under various environmental conditions,[65,66] which may lead to the deterioration or complete loss of their nanoscale properties.[67,68] Consequently, effective strategies are required to enhance nanocarrier stability during storage. A commonly employed approach to improve the storage stability of nanoparticles involves the use of cryoprotectants, particularly at low temperatures. For example, Zhao et al 56 demonstrated that nanoparticles loaded with mRNA retained their delivery efficiency for at least three months when cryoprotectants were applied during freezing or lyophilization and the formulations were stored in liquid nitrogen.

Challenges in Potential Toxicity

The potential toxicity of nanocarriers is another major challenge in the development of nanomedicine. Evidence suggests that smaller nanoparticles are associated with increased toxicity, enhanced chemical reactivity, and heightened biological activity.[69,70] Following systemic exposure, nanocarriers may accumulate within the organ phagocytic system, where they can exert toxic effects on organs such as the liver, spleen, and kidneys.[71] Significantly, nanocarrier toxicity is strongly influenced by the route of administration, level, and duration of exposure.[72] Although the transdermal delivery of nanocarriers is generally considered safer than oral or injectable administration,[73] their potential long-term toxicity cannot be disregarded. Notably, there remains a significant knowledge gap regarding the chronic and cumulative effects of persistent nanocarriers, leading some researchers to propose that they should be regarded as "potentially hazardous" and handled with caution.[74]

From a pharmacokinetic perspective, APIs can penetrate the skin via multiple pathways, including transcellular and intercellular routes. Skin penetration is strongly governed by the physicochemical properties of both APIs and their associated nanocarriers, such as particle size, surface charge, mobility, and the balance of hydrophilicity and lipophilicity.[14] In this context, the use of biocompatible and biodegradable polymeric materials represents a promising strategy for designing safer nanocarriers.

Limitations and Future Perspective

The present study had two primary limitations. First, the number of included RCTs was limited, which may constrain the generalizability and robustness of our findings. Second, as a narrative review, this study did not conduct a systematic assessment of the risk of bias in the included studies, nor did it integrate such evaluations into the overall synthesis, which may have affected the rigor and reliability of its conclusions.

This review focuses on the design characteristics and clinical applications of RCTs involving nanocarriers for psoriasis treatment. Future studies should adopt a broader perspective by systematically examining the design characteristics of RCTs investigating nanocarriers for transdermal delivery systems across a wide range of diseases, thereby providing robust evidence to support the evaluation of the safety and therapeutic efficacy of topical nanocarriers. Particular attention should be paid to clinical trial design considerations and to the risks of nanomedicine use in the context of potential tissue injuries. Finally, interdisciplinary collaboration among materials scientists, pharmacologists,

and dermatologists is strongly advocated, as integrative efforts can foster innovative approaches and accelerate the clinical translation of nanocarrier-based therapies for psoriasis.

Conclusion

Nanocarriers are a promising alternative to conventional drug therapies owing to their ability to enhance the delivery of active pharmaceutical ingredients (APIs) to the skin layers via interactions with skin lipids, thereby increasing transdermal penetration. However, the clinical application of nanocarriers in psoriasis treatment faces numerous challenges, including inadequate regulatory frameworks, difficulties in large-scale production, and issues related to long-term stability. Consequently, only 0.2% of registered RCTs on psoriasis treatment focus on nanocarrier-based therapies. Moreover, existing studies have not directly compared nano- and non-nano formulations. Because nanomedicines differ fundamentally from conventional preparations, a rigorous clinical design necessitates the incorporation of three parallel arms: blank nanocarriers, conventional formulations, and nanoformulations. Therefore, future research should focus on overcoming these translational barriers by optimizing nanocarrier stability, developing robust and scalable production methods, and conducting thorough, long-term safety evaluations. This strategy is essential for bridging the gap between laboratory potential and clinical application.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Grayson M. Psoriasis. *Nature*. 2012;492(7429):S49. doi:10.1038/492S49a
2. Cao F, He Y-S, Wang Y, et al. Global burden and cross-country inequalities in autoimmune diseases from 1990 to 2019. *Autoimmunity Reviews*. 2023;22(6):103326. doi:10.1016/j.autrev.2023.103326
3. Li N, Qin Y, Dai D, et al. Transdermal delivery of therapeutic compounds with nanotechnological approaches in psoriasis. *Front Bioeng Biotechnol*. 2021;9:804415. doi:10.3389/fbioe.2021.804415
4. Mantovani L, Medaglia M, Piacentini P, et al. Burden of moderate-to-severe plaque psoriasis and new therapeutic approaches (Secukinumab): an Italian perspective. *Dermatol Ther*. 2016;6(2):151–167. doi:10.1007/s13555-016-0114-9
5. Pradhan M, Alexander A, Singh MR, et al. Understanding the prospective of nano-formulations towards the treatment of psoriasis. *Biomed Pharmacother*. 2018;107:447–463. doi:10.1016/j.biopha.2018.07.156
6. Matsumura Y, Ananthaswamy HN. Toxic effects of ultraviolet radiation on the skin. *Toxicol Appl Pharmacol*. 2004;195(3):298–308. doi:10.1016/j.taap.2003.08.019
7. Pradhan M, Singh D, Singh MR. Novel colloidal carriers for psoriasis: current issues, mechanistic insight and novel delivery approaches. *J Control Release*. 2013;170(3):380–395. doi:10.1016/j.jconrel.2013.05.020
8. Yeung H, Wan J, Van Voorhees AS, et al. Patient-reported reasons for the discontinuation of commonly used treatments for moderate to severe psoriasis. *J Am Acad Dermatol*. 2013;68(1):64–72. doi:10.1016/j.jaad.2012.06.035
9. Conway R, Carey JJ. Risk of liver disease in methotrexate treated patients. *World J Hepatol*. 2017;9(26):1092–1100. doi:10.4254/wjh.v9.i26.1092
10. Rapalli VK, Singhvi G, Dubey SK, Gupta G, Chellappan DK, Dua K. Emerging landscape in psoriasis management: from topical application to targeting biomolecules. *Biomed Pharmacother*. 2018;106:707–713. doi:10.1016/j.biopha.2018.06.136
11. Xu R, Li X, Huang X, et al. Translation-dependent skin hyperplasia is promoted by type 1/17 inflammation in psoriasis. *J Dermatol Sci*. 2023;110(1):10–18. doi:10.1016/j.jdermsci.2023.03.007
12. Lee Y, Je YJ, Lee SS, et al. Changes in transepidermal water loss and skin hydration according to expression of aquaporin-3 in psoriasis. *Ann Dermatol*. 2012;24(2):168–174. doi:10.5021/ad.2012.24.2.168
13. Pradhan M, Singh D, Singh MR. Influence of selected variables on fabrication of Triamcinolone acetonide loaded solid lipid nanoparticles for topical treatment of dermal disorders. *Artif Cells Nanomed Biotechnol*. 2016;44(1):392–400. doi:10.3109/21691401.2014.955105
14. Ghasemiyeh P, Mohammadi-Samani S. Potential of nanoparticles as permeation enhancers and targeted delivery options for skin: advantages and disadvantages. *Drug Des Devel Ther*. 2020;14:3271–3289. doi:10.2147/dddt.S264648
15. Shao M, Hussain Z, Thu HE, et al. Drug nanocarrier, the future of atopic diseases: advanced drug delivery systems and smart management of disease. *Colloids Surfaces B*. 2016;147:475–491. doi:10.1016/j.colsurfb.2016.08.027
16. Ghasemiyeh P, Azadi A, Daneshamouz S, Heidari R, Azarpira N, Mohammadi-Samani S. Cyproterone acetate-loaded nanostructured lipid carriers: effect of particle size on skin penetration and follicular targeting. *Pharm Dev Technol*. 2019;24(7):812–823. doi:10.1080/10837450.2019.1596133
17. Lauterbach A, Müller-Goymann CC. Comparison of rheological properties, follicular penetration, drug release, and permeation behavior of a novel topical drug delivery system and a conventional cream. *Eur J Pharm Biopharm*. 2014;88(3):614–624. doi:10.1016/j.ejpb.2014.10.001
18. Mascarenhas-Melo F, Carvalho A, Gonçalves MBS, Paiva-Santos AC, Veiga F. Nanocarriers for the topical treatment of psoriasis - pathophysiology, conventional treatments, nanotechnology, regulatory and toxicology. *Eur J Pharm Biopharm*. 2022;176:95–107. doi:10.1016/j.ejpb.2022.05.012
19. Sevgi G, Meriem R. Nanocarriers mediated topical drug delivery for psoriasis treatment. *Current Drug Metabolism*. 2017;18(5):454–468. doi:10.2174/1389200218666170222145240

20. Shetty K, Sherje AP. Nano intervention in topical delivery of corticosteroid for psoriasis and atopic dermatitis-a systematic review. *J Mater Sci Mater Med*. 2021;32(8):88. doi:10.1007/s10856-021-06558-y
21. Mitra R, Sharma DK, Ghosh A, Senapati S. Recent advancements in nanoparticle-based topical drug delivery systems for psoriasis treatment. *J Drug Target*. 2025;1–18. doi:10.1080/1061186x.2025.2544783
22. Husain A, Kushwaha P, Kapoor A, Singh P. Exploring the therapeutic potential of lipid nanocarriers in psoriasis management: advances and applications. *AAPS PharmSciTech*. 2025;26(7):195. doi:10.1208/s12249-025-03188-3
23. Feizabadi M, Fahimnia F, Mosavi Jarrahi A, Naghshineh N, Tofighi S. Iranian clinical trials: an analysis of registered trials in International Clinical Trial Registry Platform (ICTRP). *J Evidence-Based Med*. 2017;10(2):91–96. doi:10.1111/jebm.12248
24. Chen L, Su Y, Quan L, Zhang Y, Du L. Clinical trials focusing on drug control and prevention of ventilator-associated pneumonia: a comprehensive analysis of trials registered on ClinicalTrials.gov. *Front Pharmacol*. 2019;9. doi:10.3389/fphar.2018.01574
25. Jacobsen PB, Wells KJ, Meade CD, et al. Effects of a brief multimedia psychoeducational intervention on the attitudes and interest of patients with cancer regarding clinical trial participation: a multicenter randomized controlled trial. *J Clin Oncol*. 2012;30(20):2516–2521. doi:10.1200/JCO.2011.39.5186
26. Sverdlov O, Ryeznik Y, Wong WK. On optimal designs for clinical trials: an updated review. *J Stat Theory Practice*. 2019;14(1):10. doi:10.1007/s42519-019-0073-4
27. Curtin F, Heritier S. The role of adaptive trial designs in drug development. *Expert Rev Clin Pharmacol*. 2017;10(7):727–736. doi:10.1080/17512433.2017.1321985
28. Feng Z, Gu Y, Yuan M, Xiao R, Fei Z. Clinical trials of liposomes in children's anticancer therapy: a comprehensive analysis of trials registered on ClinicalTrials.gov. *Int J Nanomedicine*. 2022;17:1843–1850. doi:10.2147/ijn.S359666
29. Qiu Y, Lu C, Li G, Sun L. Efficacy of modified moisturizing muscle ointment based on chitosan nanotechnology on psoriasis vulgaris of blood dryness syndrome. *Modern J Integrat Trad Chin Western Med*. 2023;32(21):2935–2940. doi:10.3969/j.issn.1008-8849.2023.21.003
30. Zwierzyna M, Davies M, Hingorani AD, Hunter J. Clinical trial design and dissemination: comprehensive analysis of clinicaltrials.gov and PubMed data since 2005. *BMJ*. 2018;361:k2130. doi:10.1136/bmj.k2130
31. Zhang C, Kwong JSW, Yuan R-X, et al. Effectiveness and tolerability of different recommended doses of PPIs and H(2)RAs in GERD: network meta-analysis and GRADE system. *Sci Rep*. 2017;7:41021. doi:10.1038/srep41021
32. Oh ES, Fong TG, Hshieh TT, Inouye SK. Delirium in older persons: advances in diagnosis and treatment. *JAMA*. 2017;318(12):1161–1174. doi:10.1001/jama.2017.12067
33. Fathalla D, Youssef EMK, Soliman GM. Liposomal and ethosomal gels for the topical delivery of anthralin: preparation, comparative evaluation and clinical assessment in psoriatic patients. *Pharmaceutics*. 2020;12(5):446. doi:10.3390/pharmaceutics12050446
34. Sarafian G, Afshar M, Mansouri P, Asgarpanah J, Raoufinejad K, Rajabi M. Topical turmeric microemulgel in the management of plaque psoriasis: a clinical evaluation. *Iran J Pharm Res*. 2015;14(3):865–876.
35. Kolahdooz H, Khori V, Erfani-Moghadam V, Livani F, Mohammadi S, Memarian A. Niosomal curcumin suppresses IL17/IL23 immunopathogenic axis in skin lesions of psoriatic patients: a pilot randomized controlled trial. *Life*. 2023;13(5):1076. doi:10.3390/life13051076
36. Petrovic S, Bita B, Barbinta-Patrascu ME. Nanoformulations in pharmaceutical and biomedical applications: green perspectives. *Int J Mol Sci*. 2024;25(11). doi:10.3390/ijms25115842
37. Karabasz A, Bzowska M, Szczepanowicz K. Biomedical applications of multifunctional polymeric nanocarriers: a review of current literature. *Int J Nanomedicine*. 2020;15:8673–8696. doi:10.2147/ijn.S231477
38. Khan I, Saeed K, Khan I. Nanoparticles: properties, applications and toxicities. *Arabian J Chem*. 2019;12(7):908–931. doi:10.1016/j.arabjc.2017.05.011
39. Zhao Z, Ukidve A, Krishnan V, Mitragotri S. Effect of physicochemical and surface properties on in vivo fate of drug nanocarriers. *Adv Drug Deliv Rev*. 2019;143:3–21. doi:10.1016/j.addr.2019.01.002
40. Pandey P, Gulati N, Makhija M, Purohit D, Dureja H. Nanoemulsion: a novel drug delivery approach for enhancement of bioavailability. *Recent Pat Nanotechnol*. 2020;14(4):276–293. doi:10.2174/1872210514666200604145755
41. Wiemann S, Keck CM. Are lipid nanoparticles really superior? A holistic proof of concept study. *Drug Deliv Transl Res*. 2022;12(6):1433–1444. doi:10.1007/s13346-021-01021-5
42. Fereig SA, El-Zaafarany GM, Arafa MG, Abdel-Mottaleb MMA. Tackling the various classes of nano-therapeutics employed in topical therapy of psoriasis. *Drug Deliv*. 2020;27(1):662–680. doi:10.1080/10717544.2020.1754527
43. Soni KS, Desale SS, Bronich TK. Nanogels: an overview of properties, biomedical applications and obstacles to clinical translation. *J Control Release*. 2016;240:109–126. doi:10.1016/j.jconrel.2015.11.009
44. Kalpana P, Nimisha. An overview on promising nanotechnological approaches for the treatment of psoriasis. *Recent Patents Nanotechnol*. 2020;14(2):102–118. doi:10.2174/1872210514666200204124130
45. Amoabediny G, Haghiralsadat F, Naderinezhad S, et al. Overview of preparation methods of polymeric and lipid-based (niosome, solid lipid, liposome) nanoparticles: a comprehensive review. *Int J Polymeric Mater Polymeric Biomaterials*. 2018;67(6):383–400. doi:10.1080/00914037.2017.1332623
46. Witika BA, Bassey KE, Demana PH, Siwe-Noundou X, Poka MS. Current advances in specialised niosomal drug delivery: manufacture, characterization and drug delivery applications. *Int J Mol Sci*. 2022;23(17):9668. doi:10.3390/ijms23179668
47. Sainz-Ramos M, Villate-Beitia I, Gallego I, et al. Non-viral mediated gene therapy in human cystic fibrosis airway epithelial cells recovers chloride channel functionality. *Int J Pharm*. 2020;588:119757. doi:10.1016/j.ijpharm.2020.119757
48. Jafari A, Daneshamouz S, Ghasemiyeh P, Mohammadi-Samani S. Ethosomes as dermal/transdermal drug delivery systems: applications, preparation and characterization. *J Liposome Res*. 2023;33(1):34–52. doi:10.1080/08982104.2022.2085742
49. Paiva-Santos AC, Silva AL, Guerra C, et al. Ethosomes as nanocarriers for the development of skin delivery formulations. *Pharm Res*. 2021;38(6):947–970. doi:10.1007/s11095-021-03053-5
50. Ataide JA, Gérios EF, Cefali LC, et al. Effect of polysaccharide sources on the physicochemical properties of Bromelain-Chitosan nanoparticles. *Polymers*. 2019;11(10):1681. doi:10.3390/polym11101681
51. Abul Kalam M, Khan AA, Khan S, Almalik A, Alshamsan A. Optimizing indomethacin-loaded chitosan nanoparticle size, encapsulation, and release using Box–Behnken experimental design. *Int J Biol Macromol*. 2016;87:329–340. doi:10.1016/j.ijbiomac.2016.02.033

52. Yan K, Zhang Y, Han L, et al. Safety and efficacy of methotrexate for Chinese adults with psoriasis with and without psoriatic arthritis. *JAMA Dermatol*. 2019;155(3):327–334. doi:10.1001/jamadermatol.2018.5194
53. Malayeri A, Badparva R, Mombeini MA, Khorsandi L, Goudarzi M. Naringenin: a potential natural remedy against methotrexate-induced hepatotoxicity in rats. *Drug Chem Toxicol*. 2022;45(2):491–498. doi:10.1080/01480545.2020.1719132
54. Singh D, Pradhan M, Shrivastava S, Murthy SN, Singh MR. Chapter 11 - Skin autoimmune disorders: lipid biopolymers and colloidal delivery systems for topical delivery. In: Grumezescu AM, editor. *Nanobiomaterials in Galenic Formulations and Cosmetics*. William Andrew Publishing; 2016:257–296.
55. Pischon H, Radbruch M, Ostrowski A, et al. Stratum corneum targeting by dendritic core-multishell-nanocarriers in a mouse model of psoriasis. *Nanomedicine*. 2017;13(1):317–327. doi:10.1016/j.nano.2016.09.004
56. Schreiner J, Rindt C, Wächter J, Jung N, Vogel-Kindgen S, Windbergs M. Influence of drug molecular weight on self-assembly and intestinal permeation of polymer-based nanocarriers. *Int J Pharm*. 2023;646:123483. doi:10.1016/j.ijpharm.2023.123483
57. Wani TU, Mohi-Ud-Din R, Majeed A, Kawoosa S, Pottoo FH. Skin permeation of nanoparticles: mechanisms involved and critical factors governing topical drug delivery. *Curr Pharm Des*. 2020;26(36):4601–4614. doi:10.2174/1381612826666200701204010
58. Guidance for Industry: Considering Whether an FDA Regulated Product Involves the Application of Nanotechnology; 2014.
59. Guidance Document: Drug Products, Including Biological Products, that Contain Nanomaterials - Guidance for Industry; 2022.
60. Reflection Paper on Nanotechnology-Based Medicinal Products for Human Use; 2006.
61. Huang F, Shao X, Geng X, Wang Q. Interpretation of guidance on non-clinical safety evaluation for nanomedicines. *Acta Pharmaceutica Sinica*. 2023;58(4):805–814. doi:10.16438/j.0513-4870.2022-1111
62. Xu PW, Yu M, Xiao ZH, Chen R, Zhang XY. Engineered hydrogels for gastrointestinal therapeutics: preclinical breakthroughs and clinical translation barriers. *J Biomater Appl*. 2026;40(6):633–649. doi:10.1177/08853282251366027
63. Bhardwaj H, Sarthi S, Jangde RK. Advanced preparation techniques for polymeric nanoparticles and their application in drug delivery. *Pharm Nanotechnol*. 2025;13. doi:10.2174/0122117385366838250314110525
64. Makoni PA, Wa Kasongo K, Walker RB. Short term stability testing of Efavirenz-loaded Solid Lipid Nanoparticle (SLN) and Nanostructured Lipid Carrier (NLC) dispersions. *Pharmaceutics*. 2019;11(8):397. doi:10.3390/pharmaceutics11080397
65. Hogarth C, Arnold K, Wright S, Elkateb H, Rannard S, McDonald TO. Navigating the challenges of lipid nanoparticle formulation: the role of unpegylated lipid surfactants in enhancing drug loading and stability. *Nanoscale Adv*. 2024;6(2):669–679. doi:10.1039/d3na00484h
66. Fan Y, Yen C-W, Lin H-C, et al. Automated high-throughput preparation and characterization of oligonucleotide-loaded lipid nanoparticles. *Int J Pharm*. 2021;599:120392. doi:10.1016/j.ijpharm.2021.120392
67. Li H, Lv K, Huang X, Lu Z, Dong X. The synthesis of polymeric nanospheres and the application as high-temperature nano-plugging agent in water based drilling fluid. *Front Chem*. 2020;8:247. doi:10.3389/fchem.2020.00247
68. Kaewbanjong J, Wan Sia Heng P, Boonme P. Clotrimazole microemulsion and microemulsion-based gel: evaluation of buccal drug delivery and irritancy using chick chorioallantoic membrane as the model. *J Pharm Pharmacol*. 2017;69(12):1716–1723. doi:10.1111/jphp.12809
69. Dong X, Wu Z, Li X, et al. The size-dependent cytotoxicity of amorphous silica nanoparticles: a systematic review of in vitro studies. *Int J Nanomedicine*. 2020;15:9089–9113. doi:10.2147/ijn.S276105
70. Crisponi G, Nurchi VM, Lachowicz JI, Peana M, Medici S, Zoroddu MA. Chapter 18 - toxicity of nanoparticles: etiology and mechanisms. In: Grumezescu AM, editor. *Antimicrobial Nanoarchitectonics*. Elsevier; 2017:511–546.
71. Najahi-Missaoui W, Arnold RD, Cummings BS. Safe nanoparticles: are we there yet? *Int J Mol Sci*. 2021;22(1):385. doi:10.3390/ijms22010385
72. Missaoui WN, Arnold RD, Cummings BS. Toxicological status of nanoparticles: what we know and what we don't know. *Chemico-Biological Interactions*. 2018;295:1–12. doi:10.1016/j.cbi.2018.07.015
73. Zhao QH, Zhang Y, Liu Y, et al. Anticancer effect of realgar nanoparticles on mouse melanoma skin cancer in vivo via transdermal drug delivery. *Med Oncol*. 2010;27(2):203–212. doi:10.1007/s12032-009-9192-1
74. Dobrovolskaia MA, Germolec DR, Weaver JL. Evaluation of nanoparticle immunotoxicity. *Nat Nanotechnol*. 2009;4(7):411–414. doi:10.1038/nnano.2009.175