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Review

Dissolving Microneedles for Psoriasis: An Intradermal Drug-Exposure Framework for Formulation Design and Clinical Translation

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Abstract

Despite increasing interest in dissolving microneedles (DMNs) for psoriasis therapy, current evaluations often emphasize device performance or therapeutic outcomes rather than drug exposure within target tissues. Psoriasis is a chronic inflammatory skin disease in which achieving sufficient and sustained local drug concentrations remains challenging because of pathological barrier alterations and limitations of conventional topical delivery. DMNs provide a promising minimally invasive approach by enabling direct deposition of therapeutic agents into skin compartments beyond the stratum corneum. This review proposes an exposure-guided framework for evaluating psoriasis-specific DMNs by integrating formulation design, device characteristics, intradermal drug exposure, and therapeutic response. The framework is based on three interconnected dimensions: amount, location, and residence time, which describe the quantity of drug delivered into skin, its spatial distribution within target compartments, and the persistence of local exposure. Current evidence regarding polymer selection, drug-loading strategies, microneedle geometry, and manufacturing processes is critically discussed according to their influence on these exposure-related parameters. Existing studies demonstrate that DMN design strategies can improve drug delivery and therapeutic outcomes; however, quantitative characterization of tissue-specific drug deposition, spatial distribution, and concentration–time profiles remains limited. The proposed framework provides a systematic approach to connect DMN formulation and device optimization with intradermal exposure, local pharmacokinetic/pharmacodynamic (PK/PD) relationships, and clinical translation. Future development of psoriasis-oriented DMNs should incorporate standardized exposure assessment, mechanistic PK/PD evaluation, and human-relevant validation to support rational dose selection and clinical application.

Keywords: dissolving microneedles; psoriasis; intradermal drug delivery; drug exposure; skin pharmacokinetics; formulation design

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1. Introduction

Psoriasis is a chronic, recurrent, immune-mediated inflammatory skin disease characterized by abnormal keratinocyte proliferation, persistent inflammation, and structural

alterations of the skin barrier [1,2]. Topical therapy remains an essential treatment strategy for patients with localized or mild-to-moderate plaque psoriasis and is also frequently used as adjunctive treatment following systemic therapy [3,4]. Clinical trials of topical roflumilast and tapinarof have demonstrated benefits [5,6]. Real-world studies have reported treatment outcomes [7], patient satisfaction [8], adherence patterns [9], and patient-reported benefits [10]. In psoriatic lesions, hyperkeratosis, epidermal thickening, and barrier remodeling may restrict drug diffusion through the stratum corneum, resulting in variable and unpredictable local drug exposure [11,12]. Therefore, improving psoriasis treatment requires not only effective pharmacological agents but also delivery systems capable of achieving reproducible drug exposure at the appropriate skin compartment.

Conventional topical formulations, including creams, ointments, and gels, mainly rely on passive diffusion across the stratum corneum. Although these formulations remain clinically important, their ability to precisely control drug deposition depth and residence time within diseased skin is limited. From a drug-delivery perspective, the therapeutic outcome of local psoriasis treatment depends on whether sufficient drug reaches the target tissue, whether the drug remains available for an adequate duration, and whether local exposure can be achieved while minimizing unnecessary systemic exposure. These considerations highlight the need for advanced delivery strategies that can overcome epidermal barriers and provide controlled intradermal drug deposition.

Dissolving microneedles (DMNs) have emerged as a promising minimally invasive platform for localized drug delivery. DMNs are composed of water-soluble or biodegradable polymer matrices that dissolve or disintegrate after insertion into the skin, enabling direct deposition of incorporated drugs beyond the stratum corneum [13–15]. Compared with conventional topical formulations, DMNs offer several potential advantages, including enhanced barrier penetration, localized drug delivery, reduced systemic exposure, and improved patient acceptability. In a psoriasis-specific example, Dai et al. developed calcipotriol nanosuspension-loaded poly(vinylpyrrolidone) (PVP)/poly(vinyl alcohol) (PVA) DMNs and evaluated their delivery performance and therapeutic effects in a psoriasiform animal model [16]. Human evidence includes a randomized trial of hyaluronic acid-based dissolving microneedles used as an adjunct to topical treatment [17]; evidence for drug-loaded DMNs in patients remains limited. Other advanced DMN designs, including tip-concentrated loading, multilayer structures, and micro/nanocarrier incorporation, have been explored to improve drug loading and release behavior [18,19].

Despite increasing interest in DMNs for psoriasis management, current evaluation approaches often emphasize device-related parameters, such as mechanical strength, insertion capability, dissolution behavior, or final therapeutic outcomes. These parameters are essential for device optimization but do not fully explain whether the drug is actually delivered to the target tissue, where it is distributed within the skin, or how long effective exposure is maintained. Consequently, successful microneedle insertion or improved disease scores alone may not sufficiently establish the relationship between DMN design and therapeutic efficacy.

Several previous reviews have summarized microneedle technologies for psoriasis treatment, dermatological applications, and transdermal drug delivery [18,19]. However, these studies have primarily focused on microneedle classification, fabrication strategies, material selection, or general therapeutic potential. A systematic evaluation of how formulation characteristics and device parameters influence tissue-level drug exposure and psoriasis-specific therapeutic outcomes remains limited. Therefore, this review proposes an intradermal drug-exposure framework based on three interconnected dimensions: amount, location, and residence time. This framework aims to evaluate DMNs from a tissue-exposure

perspective by linking formulation design, device characteristics, drug deposition behavior, pharmacokinetic/pharmacodynamic (PK/PD) relationships, and therapeutic efficacy.

In this review, we critically discuss how formulation-related factors, including polymer composition, drug-loading strategies, and carrier incorporation, as well as device-related parameters such as microneedle geometry and manufacturing processes, influence intradermal drug exposure in psoriasis. Rather than evaluating DMNs solely based on penetration capability or therapeutic outcomes, we introduce an exposure-guided perspective based on the amount–location–residence time framework to interpret how design choices determine tissue-level drug availability. Furthermore, we establish a stepwise workflow connecting DMN formulation and device optimization with drug delivery, intradermal exposure characterization, local PK/PD relationships, therapeutic efficacy, and clinical translation. This framework aims to provide a rational approach for identifying current evidence gaps and guiding future development of psoriasis-oriented DMN systems.

2. Materials and Methods

2.1. Literature Search Strategy

This narrative review was informed by searches of PubMed/MEDLINE, the Web of Science Core Collection, and Scopus from database inception to 8 September 2026. The searches focused on two core concepts: psoriasis (including "psoriasis" and "psoriatic disease") and microneedles (including "microneedle," "dissolving microneedle," and "dissolvable microneedle"). Additional searches used terms related to intradermal delivery, drug deposition, skin retention, local exposure, and pharmacokinetics to identify studies relevant to the exposure assessment discussed in this review. Search strategies were adapted to the syntax of each database. The reference lists of relevant articles were screened, and forward citation tracking was used to identify additional studies. The earliest publication cited in this review is a foundational article on microneedles published on 27 March 2004. The earliest psoriasis-specific primary study of drug-loaded dissolving microneedles cited in this review was published in 2019. Publications discussed in this review span 2004–2026; the search cutoff was 8 September 2026.

2.2. Study Selection and Evidence Evaluation

Studies were selected for their relevance to psoriasis-related microneedle-mediated drug delivery and the amount–location–residence time framework. Inclusion criteria were: (1) peer-reviewed full research articles published or available online by 8 September 2026; (2) primary studies evaluating drug-loaded dissolving or biodegradable microneedles in psoriasis, psoriasiform disease models, or relevant skin models; and (3) studies of other microneedle systems or human microneedle-assisted topical treatment when they directly informed drug deposition, spatial distribution, local retention, exposure assessment, safety, or clinical translation. Relevant reviews and guidance papers were included as background or for reference-list and citation tracking, but were not counted as primary experimental evidence. Exclusion criteria were conference abstracts, non-peer-reviewed publications, duplicate reports, and studies that did not address psoriasis or a directly relevant skin-delivery question, did not involve microneedle-mediated delivery, or provided no information relevant to formulation or device performance, drug delivery, tissue exposure, therapeutic response, or translation. Studies using non-dissolving, implantable, or drug-free microneedle systems were retained only as clearly identified supporting or comparator evidence when they informed the review framework; they were not treated as core evidence for drug-loaded dissolving microneedles. This was a narrative review rather than a systematic review, and no quantitative meta-analysis or formal risk-of-bias scoring was performed. Relevant studies were assessed qualitatively for formulation and device characteristics, drug-

delivery measurements, tissue distribution, residence-time data, therapeutic outcomes, and translational limitations.

2.3. Use of Artificial Intelligence Tools

During the preparation of this manuscript, the authors used ChatGPT (OpenAI; GPT-5.6) to assist with language editing, the organization of reference information, and to provide visual references for the conceptual preparation of Figures 1–3. The AI-generated visual outputs were used solely as references during figure preparation and were not directly incorporated into the final figures. Figures 1–3 were independently redrawn and edited by the authors using Microsoft PowerPoint and Microsoft Visio 2016. All AI-assisted outputs were carefully reviewed and edited by the authors, who take full responsibility for the accuracy and content of this publication.

3. Psoriasis-Specific Requirements for Dissolving Microneedle Design

3.1. Insertion and Drug-Delivery Targets Determined by Pathological Barriers

Psoriatic lesions show scaling and hyperkeratosis, together with epidermal thickening and altered barrier parameters [11]. Lesional psoriasis is associated with changes in stratum corneum ceramide profile and barrier function [12]. Barrier differences between healthy and diseased skin have also been described [20], as have psoriasis-related epidermal barrier changes during phototherapy [21]. Studies using diseased human skin demonstrate the relevance of these changes to topical and transdermal drug delivery [22]. These alterations may affect patch–skin contact, effective needle insertion, interstitial fluid-driven needle dissolution, and subsequent drug diffusion. Consequently, insertion and dissolution performance observed in healthy skin cannot be assumed to represent performance in psoriatic lesions.

The delivery objective should not therefore be reduced to increasing needle length or maximising penetration depth. Needle geometry, mechanical integrity, and application conditions are relevant only insofar as they provide reproducible insertion and drug delivery to the intended skin compartment. For psoriasis, DMN optimisation should therefore focus on reproducible delivery to the target layer in lesional skin, rather than maximum penetration. The relationship between psoriasis-specific barriers and corresponding DMN design requirements is summarised in Figure 1.

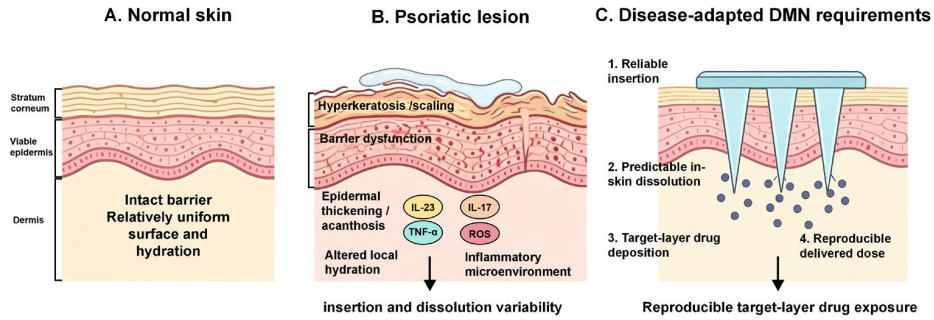


Figure 1. Psoriasis-specific skin barriers and corresponding design requirements for dissolving microneedle-mediated local drug delivery.

3.2. Anatomical Heterogeneity and Long-Term Usage Requirements

Topical treatment of psoriasis involves substantial anatomical heterogeneity. Palms, soles, face, nails, and other high-impact locations contribute to disease burden [23]; the scalp is a distinct treatment site with specific clinical outcomes and adherence considerations [24]. Skin thickness, hair coverage, surface curvature, and mechanical stress may affect patch contact, force transmission, insertion consistency, and drug delivery [25,26].

Clinical development of DMNs should therefore consider not only total lesion area but also the intended anatomical site, treatment area per application, application method, and anticipated use scenario.

The chronic and recurrent nature of psoriasis also makes repeated application an important consideration. Current human evidence primarily supports the short-term tolerability of microneedle-assisted topical treatment and is insufficient to establish the safety, dose consistency, or reliability of self-administered drug-loaded DMNs during long-term repeated use [17]. Treatment site, application area, dosing frequency, and treatment duration should therefore be considered early in product development.

These disease- and site-specific factors do not dictate a particular polymer, needle length, or device configuration. Rather, they influence patch contact, insertion, dissolution, and drug transfer and thereby affect the reproducibility of intradermal drug delivery. Formulation and device design should therefore be selected according to the intended treatment site and use conditions, with subsequent evaluation focused on actual delivery and target-layer exposure.

4. Formulation and Device Design of Dissolving Microneedles: Determinants of Intradermal Drug Exposure

From a pharmaceutical technology perspective, DMNs are integrated drug delivery systems consisting of a polymeric needle matrix, therapeutic payload, and supporting patch structure. The polymer matrix provides mechanical integrity during insertion and subsequently controls needle dissolution and drug release after contact with skin interstitial fluid. Therefore, DMN performance is determined by the combined effects of formulation composition, drug distribution within the matrix, mechanical properties, and dissolution behaviour.

4.1. Polymer Selection and Dissolution-Controlled Drug Release

Polymer selection is a critical determinant of DMN performance because polymer properties directly influence mechanical strength, dissolution behavior, drug stability, and subsequent intradermal exposure. Although numerous polymers have been investigated for dissolving microneedle fabrication, their relevance for psoriasis treatment should be considered based on their ability to achieve reproducible delivery under the pathological characteristics of psoriatic skin.

Hyaluronic acid (HA), polyvinyl alcohol (PVA), and polyvinylpyrrolidone (PVP) are among the most frequently used polymers in DMN systems. HA provides excellent biocompatibility and intrinsic skin compatibility, making it attractive for dermatological applications. However, its mechanical strength and dissolution behavior depend strongly on molecular weight and formulation composition. Lower-molecular-weight HA may promote faster dissolution, whereas higher-molecular-weight HA generally improves structural integrity.

PVA and PVP are synthetic polymers commonly used because of their favorable mechanical properties and processing characteristics. PVA can improve needle strength and insertion capability, which may be particularly relevant for psoriatic lesions with increased stratum corneum thickness. However, increased polymer concentration may delay dissolution and drug release. PVP generally provides rapid water uptake and dissolution, which may facilitate fast drug release but may require optimization to maintain sufficient mechanical strength.

Therefore, polymer selection represents a balance between mechanical integrity, dissolution kinetics, and drug exposure requirements rather than simply selecting the fastest dissolving material. For psoriasis treatment, polymers should ideally provide sufficient mechanical strength for insertion into altered psoriatic skin while allowing predictable drug release within the target tissue [27].

Compared with conventional topical formulations, DMNs can overcome the stratum corneum barrier and provide more controlled intradermal deposition. Compared with non-dissolving microneedles, dissolving systems avoid residual sharp materials after administration. However, challenges including manufacturing complexity, drug loading capacity, and scale-up remain important barriers for clinical translation [28].

4.2. Drug Loading Strategies and Spatial Distribution Within DMNs

Drug-loading strategies determine not only the total amount of therapeutic agent incorporated into dissolving microneedles but also its spatial distribution within the needle matrix, which directly affects the delivered dose and intradermal exposure profile. Unlike conventional formulations in which drug distribution is relatively homogeneous, DMNs provide opportunities to control drug localization through structural and manufacturing strategies, including tip-concentrated loading, multilayer architectures, and incorporation of micro/nanocarriers [29,30]. The following sections discuss evidence for each strategy separately.

Tip-concentrated loading has been investigated as an approach to improve delivery efficiency by placing a greater proportion of drug near the region that first penetrates the skin. This strategy may increase the fraction of drug transferred from the needle matrix into the target tissue and reduce drug loss associated with incomplete dissolution or residual drug remaining in the backing layer [31]. Therefore, tip-loading may improve the relationship between nominal loading dose and actual deposited dose, which is a critical consideration for quantitative intradermal exposure evaluation.

Multilayer DMNs provide an additional strategy to regulate drug localization and release kinetics [32,33]. By separating structural and drug-containing layers, these designs can improve mechanical integrity while allowing controlled release of therapeutic agents after insertion. However, increased structural complexity may introduce additional manufacturing challenges, including layer uniformity, drug distribution variability, and reproducibility during scale-up.

Incorporation of micro- or nanocarriers into DMNs represents another approach to modify drug solubility, stability, and release behavior [34,35]. Nanocarrier-loaded DMNs may enhance the delivery of poorly soluble drugs by improving dispersion within the polymer matrix and potentially modifying local retention. However, the incorporation of complex carriers may affect polymer dissolution, drug release kinetics, and manufacturing consistency, requiring careful optimization to achieve predictable exposure profiles.

Drug incorporation is generally achieved by dissolving or dispersing the active pharmaceutical ingredient within the polymer precursor solution before micromolding. For poorly soluble drugs, micro/nanocarrier-based approaches can be incorporated into the polymer matrix to improve dispersion, stability, and release behaviour. The optimization of these systems requires balancing drug concentration, polymer viscosity, filling efficiency, carrier stability, and needle mechanical properties to ensure reproducible drug localization and delivery.

4.3. Microneedle Geometry and Manufacturing Parameters Affecting Delivery Performance

Microneedle geometry is a critical determinant of insertion performance, dissolution behavior, and subsequent intradermal drug deposition. In psoriasis, this consideration is particularly important because pathological changes such as hyperkeratosis and epidermal thickening may alter the mechanical requirements for successful insertion.

Needle height determines the achievable penetration depth and influences the skin compartment reached by the delivered drug. Increasing needle height may facilitate deeper deposition and improve access to viable epidermal or superficial dermal regions. However,

excessively long needles may increase mechanical failure risk, discomfort, and fabrication complexity. Therefore, optimal needle height should be determined according to the target tissue compartment rather than maximizing penetration depth alone [36].

Tip sharpness and shape influence insertion force and penetration efficiency. Sharper tips generally reduce the force required to disrupt the stratum corneum and improve insertion reliability. However, highly sharp structures may increase manufacturing difficulty and require precise control of mechanical strength to prevent fracture during application [36].

Needle density represents a balance between delivery area and insertion efficiency. Increasing needle density may increase the number of microchannels available for drug deposition; however, excessive density may promote skin deformation and reduce effective penetration of individual needles [36]. Consequently, array density should be optimized together with needle dimensions and mechanical properties.

Micromolding remains one of the most widely used approaches for DMN fabrication due to its scalability and ability to reproduce microscale structures. However, molding conditions can influence needle height uniformity, tip fidelity, polymer filling efficiency, and ultimately drug distribution within the needle matrix [37].

Centrifugation or vacuum-assisted filling can improve polymer solution loading into micromolds and enhance drug localization within the needle tips. Nevertheless, variations in solution viscosity, particle size, and sedimentation behavior may affect batch-to-batch consistency.

Emerging manufacturing approaches such as 3D printing provide opportunities to generate complex geometries and potentially patient-specific designs. However, limitations including material compatibility, resolution, and regulatory scalability currently restrict widespread clinical translation [37,38].

Overall, formulation and device parameters should not be optimized independently. Polymer composition, drug localization strategy, needle geometry, and manufacturing conditions collectively determine the relationship between loaded dose, delivered dose, tissue distribution, and exposure duration. Therefore, DMN optimization for psoriasis should focus on achieving reproducible intradermal exposure rather than maximizing individual device parameters.

From a pharmaceutical technology perspective, DMN development involves selecting the drug and polymer matrix, incorporating the drug or a carrier into the needle-forming feed, filling the micromold, and controlling drying or cross-linking. The resulting patches should then be evaluated for drug content, mechanical integrity, insertion, dissolution, and drug deposition in skin. This formulation-to-exposure workflow is summarized in Figure 2.

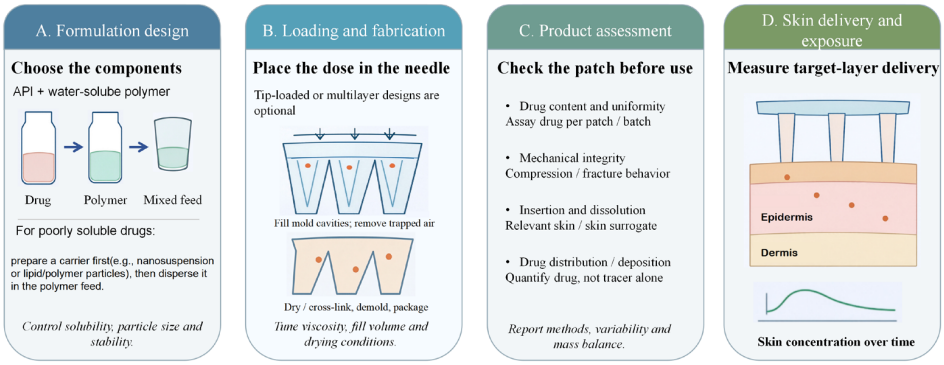


Figure 2. Formulation, fabrication, quality assessment, and skin-delivery evaluation of dissolving microneedles. For poorly soluble drugs, a micro- or nanocarrier may be prepared before incorporation into the polymer feed. Manufacturing approaches vary across formulations; vacuum-assisted filling,

centrifugation, drying, or cross-linking are used as appropriate. The nominal drug load should be distinguished from the amount released from the needles and the amount retained in skin.

4.4. Key Quality Attributes and Developability Considerations

Beyond individual formulation and device parameters, successful clinical translation of DMNs requires comprehensive control of critical quality attributes (CQAs). These attributes determine whether a DMN product can provide reproducible drug delivery and consistent intradermal exposure.

Important CQAs include needle mechanical strength, insertion efficiency, dissolution behavior, drug content uniformity, residual drug after application, and stability during storage. Mechanical properties influence whether needles can reliably penetrate psoriatic lesions, whereas dissolution behavior affects the timing and extent of drug release. Drug content uniformity and delivered dose assessment are particularly important because the nominal drug loading may not directly represent the actual amount deposited within the skin.

From a developability perspective, DMN optimization should consider not only laboratory performance but also manufacturing scalability, batch-to-batch consistency, storage stability, and clinical usability. Quality assessment should therefore be integrated with the amount–location–residence time framework to determine whether a formulation can achieve predictable intradermal exposure and support rational clinical translation [18,19,34].

These quality attributes should not be evaluated independently because each parameter contributes to a different component of intradermal drug exposure. For example, mechanical integrity and insertion performance primarily determine whether the loaded dose can enter the skin, whereas drug content uniformity, spatial distribution, and residual drug analysis determine whether the delivered dose can be accurately quantified. Dissolution behaviour and stability further influence the residence time of drug exposure. Therefore, the evaluation strategy summarized in Table 1 provides a quality-oriented approach for linking DMN product characteristics with exposure assessment.

Table 1. Key quality attributes and development-oriented evaluation strategies for drug-loaded dissolving microneedles.

Critical Quality Attribute	Major Risks and Implications	Recommended Evaluation Methods	Reporting and Interpretation Recommendations	References
Appearance and geometric consistency	Needle-tip defects or dimensional variability may cause non-uniform array performance.	Optical microscopy, SEM, 3D imaging, or machine vision.	Report the proportion of intact needles, needle length, base width, and within-batch variability.	[39–41]
Mechanical integrity	Bending, buckling, or fracture under compression.	Compression testing of single needles or full patches; change in needle height; fracture-mode observation.	Report loading rate, number of needles under compression, and ambient humidity; do not report total compressive force alone.	[39–42]
Insertion performance	A conforming patch may still fail to penetrate skin reliably.	Skin or relevant surrogate models; OCT, histology, and dye-assisted assessment.	Report effective insertion fraction and depth distribution rather than only the deepest pore.	[41–43]
Drug content and uniformity	Inter-patch dose variability may affect efficacy and safety.	Quantitative methods such as HPLC/UPLC.	Report drug content per patch, inter-patch variability, and degradation products.	[41,42]

Table 1. *Cont.*

Critical Quality Attribute	Major Risks and Implications	Recommended Evaluation Methods	Reporting and Interpretation Recommendations	References
Spatial drug distribution	Drug migration into the backing may make nominal drug load unavailable for delivery.	Sectional analysis of needle tips/backing; Raman or other chemical imaging.	Report the fraction of drug located in needle tips and provide a complete mass balance.	[16,41]
Actual delivered dose	Incomplete insertion or dissolution can cause dose loss.	Mass balance of residual drug in the used patch, on the skin surface, and recovered from skin.	Distinguish loaded dose from actual delivered dose and report dose per unit area.	[41,43]
In-skin dissolution behaviour	Rapid in vitro dissolution may not reflect performance during actual use.	Time-series observation in ex vivo skin or relevant models.	Distinguish needle dissolution, residual fraction, and drug release; acceptance criteria should match the intended application time.	[41,42,44,45]
Residual moisture and stability	Moisture uptake may cause softening; excessive drying may cause brittleness; drug crystallisation or degradation may occur.	Moisture determination; repeat mechanical and content testing; accelerated and long-term stability studies.	Establish relationships among moisture, mechanical performance, and drug stability, and evaluate packaging protection.	[18,41,46]

5. Intradermal Exposure Evidence Audit and Interpretation of Therapeutic Efficacy for Psoriasis DMNs

Unlike conventional DMN evaluation approaches that mainly focus on device performance or therapeutic outcomes, the amount–location–residence time framework provides an exposure-oriented perspective by linking formulation and device characteristics with tissue-level drug availability.

The amount–location–residence time framework proposed in this review is applied as an evidence-interpretation approach to evaluate whether reported therapeutic outcomes of psoriasis DMNs can be mechanistically linked to drug-specific intradermal exposure. Rather than replacing conventional efficacy evaluation, this framework aims to assess the completeness of exposure characterization by considering three interconnected dimensions: the amount of drug delivered into the skin, the spatial location of drug deposition within relevant tissue compartments, and the duration of local drug availability.

In this framework, the amount dimension refers to the quantity of active pharmaceutical ingredient successfully transferred from the DMN system into the skin, which should be distinguished from the nominal drug loading within the patch. The actual delivered amount is influenced by multiple factors, including drug-loading strategy, polymer composition, needle insertion efficiency, dissolution behaviour, and residual drug remaining within the patch after application.

Therefore, in this review, actual delivered dose refers specifically to the amount of active pharmaceutical ingredient that is successfully transferred from the DMN system and deposited within the target skin tissue after application, rather than the nominal drug loading or the total amount released from the dissolving matrix.

The location dimension describes the spatial distribution of delivered drug within skin compartments relevant to psoriasis treatment. Since psoriatic lesions are characterized by epidermal hyperplasia, altered barrier properties, and inflammatory changes involving different skin layers, therapeutic performance depends not only on whether drug enters

the skin but also whether it reaches the appropriate tissue compartment. Therefore, layer-specific drug quantification and imaging-based distribution analysis provide important evidence beyond overall delivery efficiency.

The residence time dimension represents the persistence of local drug exposure after DMN administration. This parameter is determined by polymer dissolution characteristics, drug physicochemical properties, formulation strategies, and release mechanisms. Understanding the duration of local exposure is essential for establishing relationships between drug deposition, pharmacokinetic/pharmacodynamic (PK/PD) responses, and therapeutic outcomes.

Together, these three dimensions provide a mechanistic framework for linking DMN formulation and device characteristics with intradermal exposure profiles and clinical efficacy. The following sections apply this framework to evaluate current psoriasis-related DMN studies according to the completeness of their exposure evidence. The amount–location–residence time framework is illustrated in Figure 3.

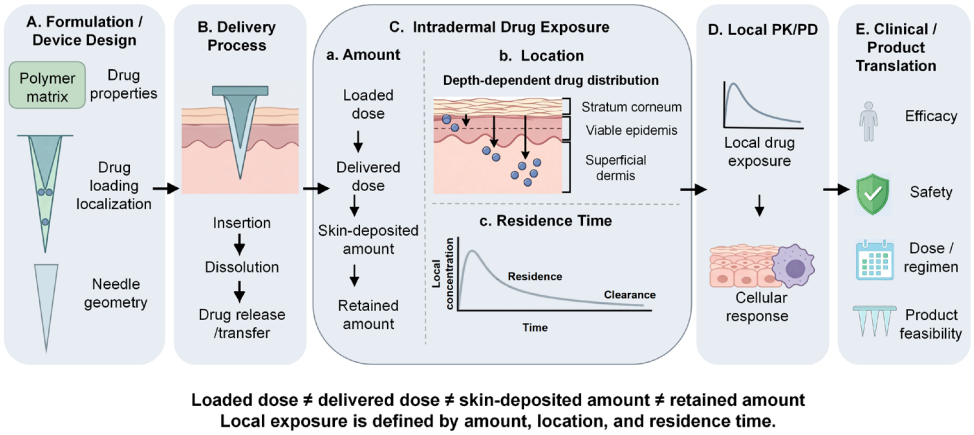


Figure 3. Conceptual amount–location–residence time framework linking dissolving microneedle formulation and device design to intradermal drug exposure, local PK/PD, and clinical/product translation.

5.1. Application of the Amount–Location–Residence Time Framework to Current DMN Evidence

Among current psoriasis-related DMN studies, only a limited number provide drug-specific evidence sufficient to establish intradermal exposure. These studies are particularly valuable because they allow therapeutic outcomes to be interpreted in relation to actual drug deposition rather than device performance alone.

Dai et al. developed calcipotriol nanosuspension-loaded poly(vinylpyrrolidone) (PVP)/poly(vinyl alcohol) (PVA) DMNs and demonstrated improved drug delivery performance and anti-psoriatic efficacy in a psoriasiform mouse model [16]. From an exposure perspective, this study provides evidence supporting the amount dimension by demonstrating enhanced delivery efficiency through nanosuspension incorporation. However, quantitative information regarding the spatial distribution of calcipotriol within different skin compartments and the time-dependent persistence of drug exposure remains limited, preventing complete evaluation across all three framework dimensions.

Similarly, other drug-loaded DMN systems have demonstrated improved therapeutic effects through enhanced skin penetration, controlled release, or incorporation of advanced formulation strategies. However, the extent to which these improvements result from increased deposited dose, altered tissue localization, or prolonged residence time remains insufficiently characterized in many studies.

Therefore, studies providing direct measurements of drug deposition, spatial distribution, and local exposure duration represent a higher level of evidence for understanding DMN-mediated psoriasis treatment. The evidence levels used to assess the completeness of intradermal drug-exposure characterization are summarized in Table 2.

Table 2. Framework for assessing the completeness of intradermal drug-exposure evidence after dissolving microneedle administration.

Level	Main Evaluation Methods	Core Question Addressed	Main Limitation	References
I-Insertion structure	Dye staining, histology, OCT, micropore counting, and insertion-depth analysis.	Do the microneedles reliably contact and enter the skin? Where are the microchannels located and how deep are they?	Demonstrates insertion or channel formation only; does not establish the actual amount of drug entering the skin, its distribution, or exposure level.	[31,43,44]
II-Tracer distribution	Fluorescent tracers, confocal microscopy, and tracking of fluorescently labelled carriers.	What is the spatial diffusion range and distribution pattern of the carrier or tracer in skin?	Tracer physicochemical properties may differ from those of the active drug, and signal intensity cannot be equated directly with drug concentration.	[47,48]
III-Drug-specific deposition	HPLC/UPLC, LC–MS/MS, whole-skin drug quantification, epidermal–dermal separation with quantification, Raman imaging, or mass-spectrometry imaging.	How much actual drug is deposited, and in which skin layers is it predominantly located?	Most studies assess only one time point, making the duration of local exposure difficult to determine.	[49–51]
IV-Space–time exposure	Multi-time-point skin drug quantification combined with assessment of patch residue, surface losses, and systemic exposure where relevant.	How do drug deposition, retention, and clearance evolve over time? Is local exposure maintained?	Experimentally demanding; complete spatiotemporal exposure profiles remain uncommon in psoriasis DMN studies.	[18,32,33,41,48]

Note: This classification describes the completeness of intradermal drug-exposure evidence established after administration with dissolving microneedles; it is not a grading system for clinical efficacy or overall study quality. A higher level indicates more complete characterisation of spatiotemporal drug exposure and does not necessarily imply greater therapeutic value.

5.2. Therapeutic Evidence with Limited Exposure Characterization

A substantial proportion of DMN studies report improved therapeutic outcomes without comprehensive characterization of intradermal drug exposure. Although reductions in lesion severity, inflammatory markers, or histological changes provide important evidence of biological activity, these outcomes alone cannot determine whether therapeutic improvement resulted from enhanced local drug exposure, improved penetration, altered formulation behaviour, or other pharmacological effects.

This limitation is particularly relevant for psoriasis because disease models may respond to multiple biological mechanisms, and therapeutic outcomes do not always directly reflect drug distribution within target tissues. Without quantitative exposure assessment, it remains difficult to establish relationships between DMN design parameters and pharmacological effects.

Therefore, future psoriasis DMN studies should integrate efficacy evaluation with drug-specific exposure measurements to distinguish successful drug delivery from general therapeutic improvement.

5.3. The Problem of Efficacy Attribution in Complex Drug Delivery Systems

Recent psoriasis-related DMN studies have explored nanocarrier-loaded formulations [52–54], self-locking and combination-delivery designs [55,56], bilayer or ROS-responsive patches [57,58], and an additional combination-payload design [59] to improve drug solubility, loading capacity, or release behavior. These approaches may provide formulation advantages, but they also make it more difficult to attribute therapeutic outcomes to individual design factors.

For example, enhanced efficacy observed with nanocarrier-loaded DMNs may result from increased drug loading, improved skin penetration, prolonged retention, or intrinsic biological effects of the carrier system. Similarly, multilayer or controlled-release architectures may modify drug distribution and exposure kinetics, but the contribution of each component to therapeutic performance is often difficult to separate.

Therefore, comprehensive exposure characterization is essential for interpreting complex DMN systems. The amount–location–residence time framework provides a strategy to distinguish whether observed efficacy is associated with increased drug quantity, improved spatial targeting, or prolonged local availability.

5.4. Human-Relevant Models and Clinical Bridging Evidence

Although preclinical psoriasis DMN studies have demonstrated promising therapeutic potential, translation toward clinical application remains limited. Most available evidence is derived from animal models, particularly chemically induced psoriasiform models, which may not fully reproduce the structural and immunological characteristics of human psoriasis.

Human-derived skin models and clinical studies provide important opportunities to evaluate whether DMNs can achieve predictable intradermal exposure under clinically relevant conditions. However, current clinical evidence remains limited, and most human studies have focused on microneedle-assisted enhancement of topical therapy rather than drug-loaded DMN systems.

Future clinical translation will require integration of exposure-based evaluation with pharmacodynamic assessment. Establishing quantitative relationships between deposited drug amount, tissue distribution, residence time, and clinical response will be essential for rational dose selection and development of clinically meaningful DMN therapies for psoriasis.

Among reported psoriasis-related DMN studies, chemically induced psoriasiform models are the predominant preclinical approach [60,61]. The imiquimod (IMQ)-induced model is commonly used because topical IMQ application activates inflammatory pathways and produces psoriasis-like features, including epidermal hyperplasia and inflammatory responses [60,61]. However, the IMQ model represents an acute inflammatory condition and cannot fully reproduce the chronic and heterogeneous characteristics of human psoriasis [62].

Current evidence remains predominantly preclinical, with limited progression of drug-loaded DMNs into human clinical evaluation and no widely established DMN-based psoriasis products currently available in routine clinical practice.

The representative microneedle systems discussed in Sections 5.2–5.4, together with their intradermal drug-exposure evidence, therapeutic outcomes, and key evidence gaps, are summarized in Table 3.

Table 3. Intradermal drug-exposure evidence, therapeutic evidence, and key gaps in representative microneedle systems for psoriasis.

(**A**) Core drug-loaded dissolving microneedles.					
Representative System/Study	**Platform/Model**	**Intradermal Exposure Evidence (Amount–Location–Residence Time)**	**Efficacy/PK–PD Evidence**	**Key Evidence Gap**	**Ref.**
Calcipotriol nanosuspension-loaded three-layer PVP/PVA DMNs	Core drug-loaded DMN; ex vivo skin + IMQ-induced psoriasiform model	A: Drug-specific skin delivery assessed. L: Local skin delivery demonstrated. R: Multi-time-point local exposure not established.	Improved local anti-inflammatory and anti-psoriatic effects vs. conventional calcipotriol ointment.	Human lesional-skin PK, multi-time-point exposure, and clinical-dose validation lacking.	[16]
Tacrolimus nanocrystal-loaded microneedles	Core drug-loaded DMN; IMQ-induced psoriasiform model	A: Skin retention quantified per unit area (8.40 ± 0.33 μg/cm^2; ~6-fold vs. marketed ointment). L: Local deposition demonstrated. R: Multi-time-point local PK not established.	Improved histology and inflammatory markers.	Human lesional epidermal–dermal concentrations, systemic exposure, and repeated-dose evidence lacking.	[49]
Glucocorticoid-loaded microneedles (triamcinolone acetonide/clobetasol)	Core drug-loaded DMN; IMQ-induced psoriasiform model	A: Skin delivery/release assessed, but actual delivered dose incompletely characterised. L: Drug-specific layer distribution limited. R: Concentration–time profiles not established.	Improved lesion scores and inflammatory features; some comparisons with conventional topical formulations.	Actual delivered dose, target-layer PK, and systemic exposure remain insufficiently characterised.	[63,64]
MTX–HA nanoparticle/PVA microneedles	Core drug-loaded DMN; IMQ-induced psoriasiform model	A: Local delivery demonstrated. L: Local retention and nanoparticle uptake assessed. R: Sustained release/retention reported, but complete drug-specific local PK not established.	Suppressed inflammation and prolonged therapeutic effects.	Human-skin PK, quantitative multi-time-point exposure, plasma exposure, and long-term safety lacking.	[52]
MTX/cyclosporine cubic liquid-crystal nanoparticle-loaded DMNs	Core drug-loaded DMN; ex vivo skin + IMQ-induced psoriasiform model/animal PK	A: Ex vivo permeation assessed. L: Stratified local skin PK not established. R: Systemic plasma PK assessed, but local concentration–time profile lacking.	Combination therapy improved psoriasiform inflammation.	Local skin PK and attribution require monotherapy, isodose, and needle-free carrier controls.	[56]
MTX nanocrystal-loaded dissolving microneedle array (2020)	Core drug-loaded DMN; ex vivo neonatal porcine skin + healthy rats	A: ~25.1% of loaded MTX deposited in skin. L: Stratified skin quantification performed. R: Multi-time-point assessment with retention to 72 h; systemic exposure assessed.	No direct efficacy evaluation in a psoriasis disease model.	Strong exposure characterisation, but pathological human-skin and psoriasis PK/PD evidence lacking.	[65]
Anemoside B4-loaded DMNs (2026)	Core drug-loaded DMN; IMQ-induced psoriasiform model	A: Up to 193.7 μg/patch; ~10-fold higher skin retention vs. free-drug solution. L: Delivery depth > 240 μm; insertion efficiency 92.3%. R: Complete multi-time-point drug-specific local PK not established.	Improved phenotype, histology, and inflammatory markers; outperformed oral/topical AB4.	Complete local concentration–time profile and human-skin PK lacking.	[66]
MTX–HA dissolving microneedles (2019)	Core drug-loaded DMN; IMQ-induced psoriasiform model	A: Controllable drug loading and intralesional delivery demonstrated. L: Penetration into thickened psoriasiform epidermis demonstrated; stratified quantification lacking. R: Multi-time-point skin PK not established.	Outperformed the same dose of oral MTX; higher oral dose required for comparable improvement.	Quantitative amount–location–residence time relationship remains incomplete.	[67]

Table 3. *Cont.*

(**A**) Core drug-loaded dissolving microneedles.

Representative System/Study	Platform/Model	Intradermal Exposure Evidence (Amount–Location–Residence Time)	Efficacy/PK–PD Evidence	Key Evidence Gap	Ref.
MTX nano-/responsive drug-loaded DMNs (ROS prodrug, HA-modified liposomes, HMSN/CS)	Core drug-loaded DMNs; cell studies + IMQ-induced psoriasiform models	A: Drug delivery/release demonstrated but actual delivered dose incompletely quantified. L: Mainly penetration/carrier-uptake evidence. R: Responsive or sustained release/retention reported; limited drug-specific local PK.	Antiproliferative and anti-inflammatory effects; potential prolonged action.	Drug-specific A–L–R quantification and isodose/mechanistic controls needed to isolate effects of complex designs.	[68–70]
Biologic/nucleic-acid/antibody payload DMNs (rExo@DMF, secukinumab/Stattic, MSCNV@siPCSK9)	Core drug-loaded DMNs; cell studies + IMQ-induced psoriasiform models	A: Local delivery demonstrated; active-payload dose incompletely characterised. L: Mainly carrier/functional distribution evidence. R: Active-payload-specific local PK limited.	Improved psoriasiform inflammation and immunomodulatory outcomes.	Quantitative active-payload exposure, systemic exposure, attribution, and long-term safety require further evaluation.	[71–73]
Natural bioactive and combination-payload DMNs (daphnetin, β-elemene, hesperidin, curcumin/shikonin, etc.)	Core drug-loaded DMNs; cell studies + IMQ-induced psoriasiform models	A: Generally incompletely quantified. L: Mainly tracer distribution/local-retention evidence; stratified drug deposition limited. R: Drug-specific concentration–time data limited.	Anti-inflammatory, antioxidant, and/or antiproliferative effects.	Evidence mainly supports delivery feasibility and pharmacological activity rather than a defined exposure–efficacy relationship.	[53,54,74–81]
Photoactivated combination DMNs	Core drug-loaded DMN; cell + animal models	A: Drug delivery demonstrated but exposure incompletely quantified. L: Local delivery/photoresponsive functionality demonstrated. R: Drug-specific local PK not established.	Combined chemotherapeutic/photodynamic effects.	Exposure attribution, external-stimulation conditions, dose control, and long-term safety remain unresolved.	[82]

(**B**) Comparative and translational bridging evidence.

Representative System/Study	Platform/Model	Intradermal Exposure Evidence (Amount–Location–Residence Time)	Efficacy/PK–PD Evidence	Key Evidence Gap	Ref.
Calcipotriol/betamethasone sustained-release reservoir microneedles	Depot/degradable comparator; ex vivo human skin + minipigs	A: Local delivery assessed. L: Imaging supports local deposition. R: Sustained local-release evidence reported.	Sustained pharmacological signal after a single administration.	Reservoir/depot mechanism differs from rapidly dissolving drug-loaded DMNs; not core DMN efficacy evidence.	[83]
MTX/puerarin implantable hydrogel microneedles	Implantable/depot comparator; IMQ-induced psoriasiform model	A: Intradermal delivery demonstrated. L: Intradermal implantation demonstrated. R: Sustained release reported.	Improved psoriasiform inflammation.	Retained-implant mechanism differs from DMNs and does not permit direct comparison of delivery advantages.	[84]
Momordin Ic ROS-responsive hydrogel microneedles	Hydrogel comparator; IMQ-induced psoriasiform model	A: Local delivery demonstrated. L: Local exposure supported. R: Responsive release demonstrated, but complete drug-specific local PK not established.	Anti-inflammatory effects and reduced ROS levels.	Effects of drug, material, and responsive module are difficult to separate.	[85]

Table 3. *Cont.*

(**B**) Comparative and translational bridging evidence.					
Representative System/Study	**Platform/Model**	**Intradermal Exposure Evidence (Amount–Location–Residence Time)**	**Efficacy/PK–PD Evidence**	**Key Evidence Gap**	**Ref.**
Long-acting microneedle system in patient-derived psoriatic skin	Bridging evidence; patient-derived psoriatic skin model	A: Actual-drug exposure not established. L: Tracer/tissue distribution demonstrated. R: Sustained tracer diffusion for ~2 weeks.	Improved model histology and pharmacological markers.	Tracer persistence cannot establish sustained active-drug exposure, patient PK, or a clinical dosing interval.	[48]
Drug-free HA microneedles used with calcipotriol/betamethasone	Adjunctive unloaded DMN; randomised self-controlled study in 22 patients	A/L/R: No drug-loaded DMN exposure profile; evidence relates to microchannel formation and assisted conventional topical delivery.	Short-term mPASI improvement; human feasibility/tolerability evidence.	Microneedles did not contain the therapeutic drugs; therefore, the study cannot establish clinical efficacy or exposure–efficacy relationships for drug-loaded DMNs.	[17]

Note: A, amount; L, spatial location; R, residence time; DMN, dissolving microneedle; IMQ, imiquimod; MTX, methotrexate; PK, pharmacokinetics; PD, pharmacodynamics. "Not established" or "limited" indicates that the corresponding evidence was not sufficiently demonstrated in the cited study and should not be interpreted as evidence of absence. Comparative and bridging systems are included to inform sustained exposure, disease-relevant modelling, or clinical translation and are not treated as core drug-loaded DMN evidence.

5.5. Operational Application of the Amount–Location–Residence Time Framework in DMN Development

The practical value of the amount–location–residence time framework lies in its ability to guide rational DMN formulation and device optimization. Rather than optimizing individual formulation or device parameters independently, this framework provides an exposure-oriented approach for linking design variables with therapeutic requirements.

During early-stage DMN development, the amount dimension can be evaluated by determining the relationship between nominal drug loading and the actual amount delivered into the skin. Relevant parameters include drug content uniformity, insertion efficiency, residual drug after application, and deposited drug quantity. These measurements help determine whether the designed formulation can achieve sufficient local drug delivery.

The location dimension can be assessed by evaluating whether the delivered drug reaches the intended skin compartment. Parameters such as penetration depth, spatial drug distribution, and tissue-specific drug quantification can provide information regarding whether drug deposition corresponds to the pathological site requiring treatment.

The residence time dimension focuses on the persistence of local drug exposure after administration. This parameter can be influenced by polymer properties, dissolution behaviour, drug physicochemical characteristics, and release strategies. Evaluation of local concentration–time profiles may help determine whether exposure duration is sufficient to maintain therapeutic activity.

Therefore, the framework enables researchers to integrate formulation design, device engineering, and exposure characterization during DMN development. However, quantitative exposure thresholds required for clinical efficacy remain to be established, and future studies should aim to define exposure–response relationships through integrated pharmacokinetic/pharmacodynamic evaluation.

6. Future Directions and Translational Challenges

6.1. Standardization of Intradermal Exposure Assessment

Despite substantial progress in psoriasis-related DMN development, the translation of promising preclinical findings into clinically meaningful therapies remains limited by insufficient characterization of intradermal drug exposure. Current studies frequently emphasize formulation design, penetration capability, or therapeutic outcomes, whereas quantitative relationships between administered dose, deposited drug amount, tissue distribution, and local persistence are often incompletely established.

Future DMN studies should therefore prioritize standardized exposure assessment strategies. The distinction between nominal drug loading and actual delivered dose requires particular attention, as the amount of drug incorporated into the patch does not necessarily represent the quantity transferred and retained within target skin compartments. Quantitative methods, including tissue drug extraction, imaging-based distribution analysis, and local concentration–time profiling, should be integrated into DMN evaluation workflows to provide mechanistic exposure information [29].

Establishing standardized approaches for measuring amount, spatial location, and residence time will facilitate comparison between different DMN platforms and enable more reliable interpretation of exposure–efficacy relationships.

6.2. Disease-Relevant Models and Clinical Translation

Another major challenge is the limited ability of current experimental models to fully reproduce human psoriasis pathology. Most psoriasis-related DMN studies rely on chemically induced psoriasiform animal models, which provide valuable information regarding anti-inflammatory activity but may not completely reflect the complex epidermal remodeling, immune dysregulation, and barrier alterations observed in human lesions.

Future research should therefore incorporate more clinically relevant models, including advanced reconstructed skin models [86,87], human psoriatic skin explants [88], and clinical microneedle evidence [17,89]. These approaches may provide more accurate information regarding drug penetration behavior, local exposure profiles, and therapeutic responses under clinically relevant conditions.

In addition, repeated-dose studies, long-term safety evaluation, and patient-oriented assessments will be essential for determining whether DMNs can provide sustained therapeutic benefits for chronic diseases such as psoriasis.

6.3. Exposure-Guided DMN Optimization and PK/PD Integration

The future development of psoriasis DMNs should move beyond empirical optimization of individual formulation or device parameters toward exposure-guided design strategies. The amount–location–residence time framework provides a potential decision-making approach by linking material selection, drug-loading strategies, microneedle geometry, and manufacturing parameters with tissue-level exposure characteristics.

For example, increasing drug loading may improve the theoretical dose capacity but may not necessarily enhance therapeutic exposure if insertion efficiency, dissolution behaviour, or tissue retention are insufficient. Similarly, optimizing needle geometry should consider not only penetration depth but also whether drug deposition occurs within the pathological skin compartment. Residence time should also be evaluated in relation to local pharmacokinetic profiles and pharmacodynamic responses to determine appropriate dosing intervals [90].

Ultimately, integration of intradermal exposure characterization with PK/PD modelling will be required to support rational dose selection and clinical translation. Rather than relying solely on lesion improvement or biomarker changes, future DMN development

should establish quantitative relationships between delivered dose, local drug concentration, biological response, and clinical outcomes.

From our perspective, the future success of psoriasis DMNs will depend not only on improving penetration efficiency but also on establishing a quantitative understanding of tissue-level drug exposure. Exposure-guided development may represent an important step toward transforming DMNs from promising experimental platforms into clinically applicable therapeutic systems.

In addition, manufacturing cost, scalability, and regulatory requirements remain important considerations for future clinical translation. Although DMNs may improve treatment convenience and patient acceptability, large-scale production and quality control strategies are required before widespread public accessibility can be achieved.

7. Conclusions

Dissolving microneedles represent a promising platform for psoriasis therapy by enabling minimally invasive intradermal drug delivery and improving access to skin compartments beyond the stratum corneum. However, despite increasing progress in DMN formulation and device development, current studies often emphasize penetration performance or therapeutic outcomes, while the relationship between device design, tissue-level drug exposure, and therapeutic response remains insufficiently defined.

This review proposes an exposure-guided framework based on the interconnected dimensions of amount, location, and residence time to provide a more systematic approach for interpreting psoriasis DMN performance. By distinguishing actual delivered drug exposure from nominal drug loading, considering spatial distribution within target skin compartments, and evaluating the persistence of local drug availability, this framework links formulation composition, drug-loading strategies, microneedle geometry, and manufacturing parameters with intradermal exposure characteristics and therapeutic outcomes.

Future advancement of psoriasis DMNs will require integration of standardized exposure assessment, tissue-level pharmacokinetic/pharmacodynamic evaluation, and clinically relevant validation models. From our perspective, the successful translation of DMNs will depend not only on improving skin penetration efficiency but also on establishing quantitative exposure–response relationships that can guide rational formulation optimization, dosing strategies, and clinical development. Exposure-guided DMN design may therefore provide an important pathway for transforming these systems from promising experimental technologies into clinically applicable therapeutic platforms for psoriasis.

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Abbreviations

The following abbreviations are used in this manuscript:

DMN	Dissolving microneedle
HA	Hyaluronic acid
IMQ	Imiquimod
MTX	Methotrexate
OCT	Optical coherence tomography
PD	Pharmacodynamics
PK	Pharmacokinetics
PVA	Poly (vinyl alcohol)
PVP	Poly(vinylpyrrolidone)
QbD	Quality by Design
QTPP	Quality target product profile
ROS	Reactive oxygen species
SEM	Scanning electron microscopy
UPLC	Ultra-performance liquid chromatography

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