



DISSOLVING MICRONEEDLE PATCHES: A NEXT- GENERATION APPROACH FOR PAINLESS AND TARGETED DRUG DELIVERY

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ABSTRACT

Dissolving microneedle patches (DMNPs) are an emerging transdermal platform designed to overcome the barrier function of the stratum corneum while retaining the convenience of a patch and avoiding the discomfort and sharps waste associated with conventional injections. In a DMNP, microscopic projections composed of water-soluble or biodegradable materials contain or carry the active pharmaceutical ingredient. After application, the projections penetrate the superficial skin layers and dissolve or disintegrate in response to tissue fluid, depositing the payload within the skin. This approach can improve access to compounds that show inadequate passive permeation, including selected peptides, proteins, vaccines, nucleic-acid cargos and potent small molecules. Recent literature has expanded the field from proof-of-

concept delivery toward disease-specific systems, combination delivery and more sophisticated material and fabrication strategies. At the same time, translation remains constrained by drug-loading capacity, dose uniformity, mechanical strength, skin insertion variability, stability, manufacturing scale-up, sterilization, packaging and the absence of fully harmonized regulatory expectations. This review discusses the design principles, materials, fabrication methods, mechanism of action, characterization, therapeutic applications, advantages, limitations and future development of DMNPs. Particular attention is given to the balance between needle mechanical integrity and rapid dissolution, formulation stability, dose reproducibility and clinically relevant manufacturing. DMNPs therefore represent a promising but still developing technology whose successful translation will depend on robust quality-by-design approaches, standardized performance testing and evidence that demonstrates reproducible clinical benefit.

Keywords: dissolving microneedles; microneedle patch; transdermal drug delivery; polymeric microneedles; targeted delivery; painless delivery; controlled release.



1. Introduction

Drug administration is strongly influenced by route, dosage form, patient acceptability and the physicochemical properties of the active ingredient. Oral delivery remains the most familiar route, but gastrointestinal degradation, variable absorption and hepatic first-pass metabolism can restrict exposure for some medicines. Conventional transdermal systems can provide sustained drug input and avoid gastrointestinal and hepatic first-pass effects, yet the stratum corneum presents a highly effective barrier. Consequently, only a limited group of molecules can cross intact skin at therapeutically useful rates without an enhancement strategy. Recent reviews describe microneedles as a physical approach for temporarily bypassing this barrier and enabling intradermal or transdermal delivery across a broader range of molecular sizes.³

Microneedles are arrays of micron-scale projections engineered to cross the outer skin barrier without reaching the depth associated

with conventional hypodermic injection. Major classes include solid, coated, hollow, dissolving and hydrogel-forming microneedles. Dissolving microneedles are particularly attractive because the needle itself can function as the drug-containing matrix: after insertion, the matrix hydrates and dissolves, releasing its cargo into the skin. This creates a one-step 'poke-and-release' process and avoids recovery of a sharp needle array after use.^{1,3}

The concept is not merely a smaller injection. DMNPs combine microfabrication, polymer science, drug formulation and skin biomechanics. Their performance depends on needle geometry, insertion force, polymer composition, drug distribution, water uptake, dissolution kinetics and the characteristics of the application site. Recent reviews published in 2025–2026 emphasize that the field is moving toward clinically relevant optimization but still faces dose-loading, manufacturing, regulatory and reproducibility barriers.

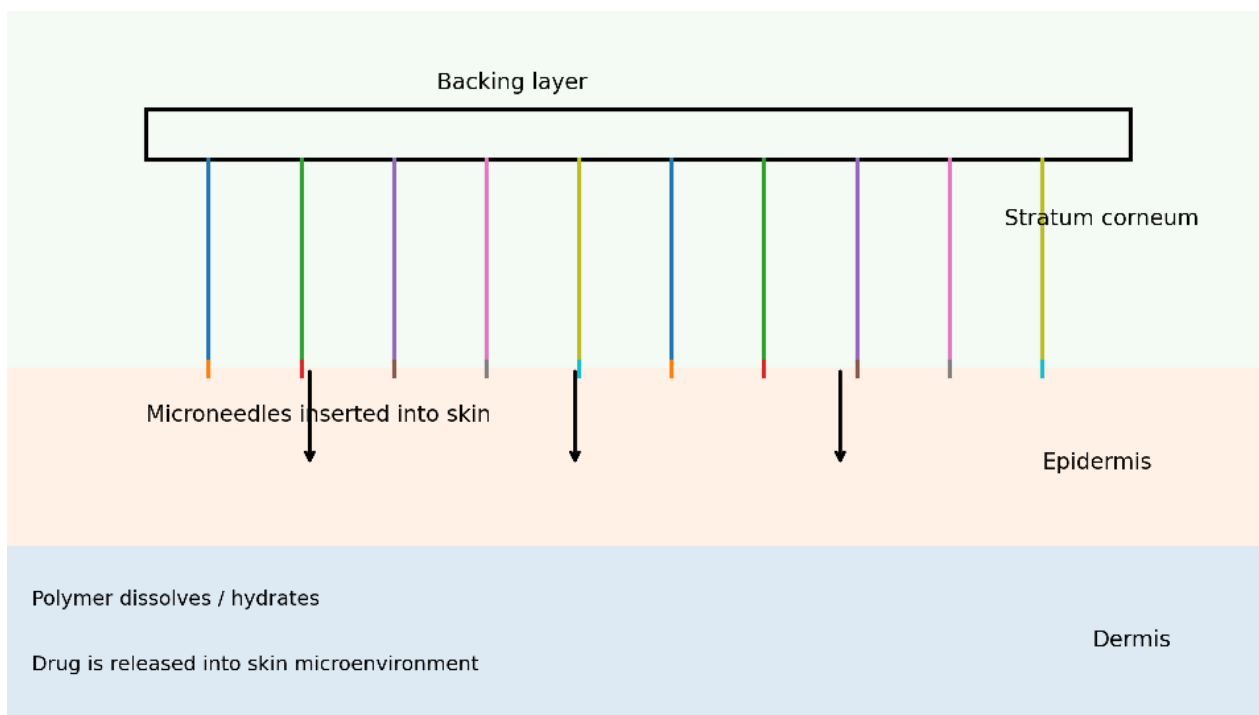


Figure 1. Schematic mechanism of a dissolving microneedle patch. The microneedles penetrate the superficial skin, hydrate and dissolve, releasing the incorporated drug within the skin.

2. Rationale for Dissolving Microneedle Technology

The principal rationale for DMNPs is to modify the path that a drug must travel. With a conventional patch, the active ingredient must partition into and diffuse across the stratum corneum before reaching viable epidermis and dermis. A microneedle array creates numerous microscopic pathways through this barrier. In a dissolving design, the polymer matrix then disappears while the payload is deposited locally. This can be especially useful when the therapeutic

molecule is too large, too hydrophilic or otherwise unsuitable for passive diffusion.

An additional rationale is patient-centered administration. Hypodermic injections can be associated with fear, pain, training requirements and sharps disposal. Properly designed microneedles are intended to produce much smaller mechanical disruption than conventional needles, and dissolving arrays leave no conventional sharp needle for disposal. These features can support self-administration and potentially improve acceptability, although 'painless' should be treated as a design goal rather than a universal clinical guarantee because sensation varies with needle dimensions, insertion force, application site and formulation.^{3,8}



3. Design and Structure of Dissolving Microneedle Patches

A typical DMNP contains a backing layer and an array of drug-loaded dissolving projections. The backing layer provides handling strength and may also be engineered to control application time or provide an additional drug reservoir. The microneedles generally have a tapered geometry, with dimensions selected to penetrate the intended skin depth while minimizing undesirable tissue injury. Array density, needle height, base width, tip radius and inter-needle spacing all influence insertion.

Drug localization within the needles is another important design variable. A homogeneous matrix can simplify fabrication, whereas tip-loaded or multilayer structures can concentrate drug near the region that penetrates skin first. Such architectures may reduce drug loss in the backing and improve delivery efficiency. However, increased structural complexity may introduce manufacturing variability. Therefore, the most sophisticated design is not necessarily the most practical; a clinically useful patch requires reproducible manufacturing, adequate dose capacity and predictable dissolution.

4. Materials Used in Dissolving Microneedles

Material selection is central to DMNP performance. The matrix must provide sufficient mechanical strength during insertion but dissolve or biodegrade at a controlled rate after insertion. Commonly investigated materials include polyvinyl alcohol (PVA), polyvinylpyrrolidone (PVP), hyaluronic acid, carboxymethyl cellulose, dextran, maltose and other sugars or polysaccharides. The 2021 panorama review identifies several water-soluble materials used for dissolving systems, while broader reviews describe how polymer composition influences drug release, dissolution and mechanical behavior.^{1,10,11}

Natural polymers can offer favorable biocompatibility and biological tolerability, while synthetic polymers may provide greater control over molecular weight, mechanical strength and processing. PVP can provide rapid water uptake and has been used extensively in dissolving matrices; PVA can improve film-forming and mechanical characteristics. Hyaluronic acid is attractive for skin-related applications because it is naturally present in the extracellular matrix. Blends are frequently explored to balance strength, viscosity, drying behavior and dissolution. Excipients such as sugars, surfactants or stabilizers may



be included to protect sensitive biological molecules, but each addition must be assessed for compatibility and regulatory acceptability.

For biologics, processing conditions are particularly important. Elevated temperature, organic solvents, extreme pH or prolonged drying can compromise proteins, peptides, vaccines or nucleic-acid cargos. Aqueous micromoulding and low-temperature drying are therefore attractive when the active ingredient is thermolabile. Material selection should ultimately be driven by a defined target product profile rather than by polymer availability alone.

5. Fabrication Methods

Micromoulding is one of the most widely investigated fabrication approaches for dissolving arrays. A master structure is used to produce a negative mould containing the desired cavities. A drug-polymer formulation is then introduced into the mould, often with

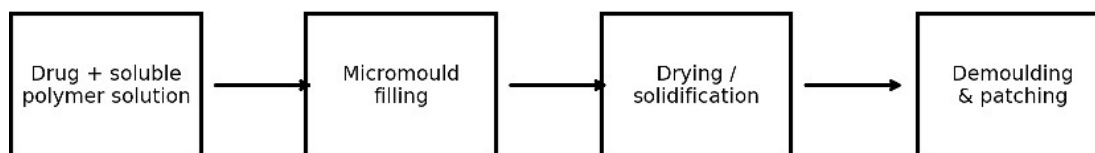
vacuum, centrifugation or pressure-assisted filling to improve cavity filling. The filled mould is dried or otherwise solidified, and the resulting microneedle array is separated from the mould and attached to a suitable backing. This approach is attractive because many needles can be produced simultaneously with controlled geometry.^{7,9}

Other fabrication approaches include drawing lithography, photopolymerization and droplet-based methods. The choice depends on the desired geometry, material, active ingredient and production

scale. Photopolymerization can offer high structural precision but requires careful evaluation of monomer and initiator toxicity and potential exposure of the drug to reactive species. Thermal processing may be unsuitable for thermolabile actives. In pharmaceutical development, the fabrication method should therefore be evaluated together with the stability-indicating analytical strategy.



Typical solvent/water-based micromoulding workflow



Critical controls: viscosity • cavity filling • drying • drug stability • needle geometry

Figure 2. Original schematic of a typical micromoulding workflow for dissolving microneedle patches.

6. Mechanism of Drug Delivery

Following application, the microneedle tips penetrate the stratum corneum and enter the superficial viable skin. Interstitial fluid and water from the tissue begin to hydrate the soluble matrix. Depending on polymer composition and environmental conditions, the needles swell, dissolve or undergo controlled degradation. The active ingredient is thereby released within the skin, from where it may act locally or enter dermal microcirculation for systemic exposure.^{7,9}

The kinetics of delivery are governed by several interacting factors: polymer hydration, drug solubility, drug-polymer interactions, matrix porosity, needle dimensions, formulation viscosity and the duration of patch application. A rapidly dissolving matrix can provide relatively

quick deposition, whereas a more slowly dissolving or layered design may extend exposure. However, prolonged retention is not automatically advantageous; the required release profile should be matched to the pharmacology of the drug and the intended site of action.

7. Characterization and Quality Evaluation

Characterization should address both pharmaceutical quality and microneedle functionality. Physical examination includes appearance, dimensions, needle height, base width, tip geometry and array uniformity using optical or electron microscopy where appropriate. Mechanical characterization evaluates whether the needles withstand the force required for insertion without unacceptable bending or fracture. Insertion can be studied using validated skin models or appropriate ex vivo tissue methods.^{1,2}



Drug-related tests include assay, content uniformity, encapsulation or loading efficiency where relevant, moisture content, solid-state characterization and in vitro release. Dissolution time should be measured under controlled conditions and correlated with the intended application period. Skin permeation and deposition studies can be

performed using diffusion cells and suitable biological models. Histological examination may help assess tissue response. Stability studies should evaluate both the drug and the mechanical performance of the array because moisture uptake can change polymer behavior.

Quality attribute	What it indicates	Typical evaluation
Needle geometry	Consistency of array and insertion potential	Microscopy / image analysis
Mechanical strength	Resistance to deformation or fracture	Compression / texture analysis
Insertion ability	Successful skin penetration	Parafilm or ex vivo skin model
Drug content	Dose delivered per patch	Validated assay
Dissolution time	Rate of matrix disappearance	Timed microscopy / gravimetry
Drug release	Release profile and kinetics	Diffusion/release testing
Stability	Retention of quality during storage	Accelerated and long-term studies

8. Therapeutic Applications

8.1 Vaccination

Vaccination is one of the most investigated applications of microneedles because antigen delivery into the skin can exploit the immunological environment of the dermis and epidermis. Dissolving arrays can also reduce the need for post-use sharps collection. Research has investigated vaccine delivery using different antigens and polymer matrices, with the potential advantages of simplified administration and improved stability for selected formulations. Nevertheless, vaccine-specific requirements for antigen integrity, sterility, dose

uniformity and immune response must be demonstrated for each product.^{8,9}

8.2 Peptides and Proteins

Proteins and peptides are often limited by poor oral bioavailability and can require parenteral administration. Microneedles can bypass the stratum corneum and deposit these macromolecules into skin. Insulin and other biologics have been investigated in microneedle systems. The practical challenge is maintaining biological activity throughout formulation, drying and storage while achieving an adequate dose within the small volume of an array.^{3,8}



8.3 Nucleic Acids and Advanced Therapeutics

Recent research has extended dissolving microneedles toward nucleic-acid delivery, including RNA-related cargos. A 2025 systematic review and data synthesis examined dissolving microneedles for nucleic-acid delivery and highlighted the growing interest in this area. Such applications require careful control of degradation, nuclease exposure, formulation stability and intracellular delivery.

Microneedle-based administration may become particularly valuable when local skin or immune targeting is desirable.⁴

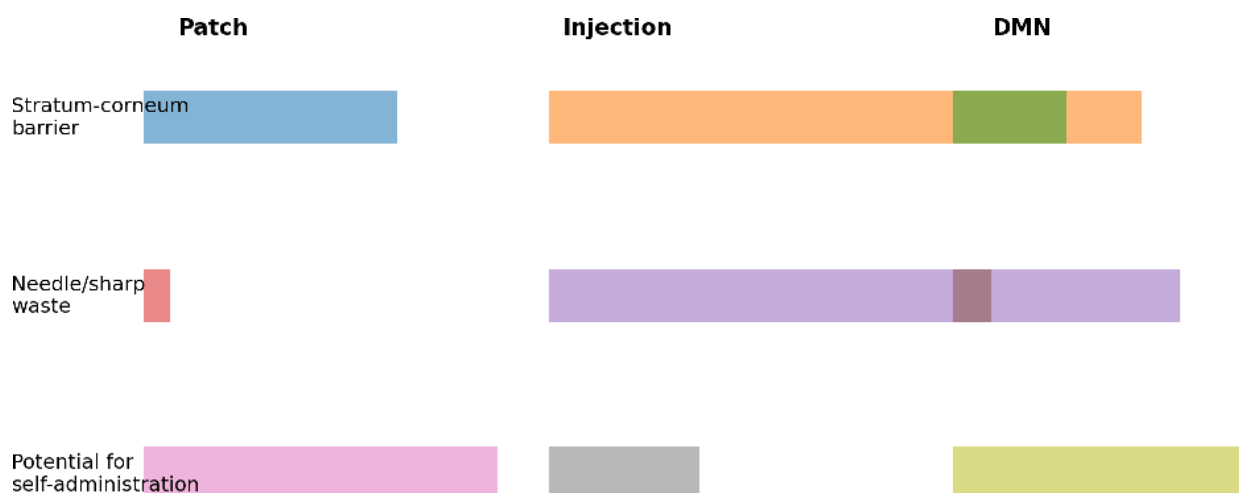
8.4 Dermatological and Local Applications

Because DMNPs deposit the active ingredient directly within the skin, they are

attractive for dermatological applications. Potential uses include acne, inflammatory skin disorders, pigmentation disorders, localized infection and cosmetic or aesthetic indications. Local deposition may permit lower overall exposure for selected agents, but this depends on the pharmacology and must be established experimentally rather than assumed.

8.5 Systemic Drug Delivery

After deposition in viable skin, some drugs can enter the dermal microcirculation and reach systemic circulation. This may provide an alternative to oral or injectable administration for potent drugs that require relatively small doses. However, the limited drug-loading capacity of microneedle arrays remains an important constraint, especially for medicines requiring milligram-to-gram quantities.



Schematic comparison (qualitative; not a quantitative performance score)

Figure 3. Qualitative comparison of key design considerations for conventional patches, injections and dissolving microneedles. The graphic is conceptual and is not a quantitative ranking.

9. Advantages of Dissolving Microneedle Patches

DMNPs offer several potential advantages. First, they can temporarily bypass the stratum corneum and expand the range of molecules considered for transdermal or intradermal delivery. Second, application can be simpler than injection and may support self-administration after appropriate instructions. Third, dissolving systems avoid leaving conventional sharp needles behind, reducing the specific sharps-disposal issue associated with injection devices. Fourth, the platform can be engineered for local or

systemic delivery and can accommodate different release profiles. Fifth, the dry state of many dissolving formulations may offer opportunities for improved stability of selected biological products compared with aqueous formulations, although this must be demonstrated for each active.^{1,3,8}

These advantages should not be interpreted as proof that DMNPs are universally superior to established dosage forms. Their value depends on the drug dose, stability, therapeutic window, intended site of action, required release duration and manufacturing constraints.

10. Limitations and Translational Challenges

Drug-loading capacity is one of the most important limitations. The total volume of



the microneedle projections is small, so DMNPs are best suited to potent agents or applications in which relatively low doses are required. Increasing needle size or density can increase loading but may compromise comfort, insertion or manufacturing. The 2025 critical analysis of dissolving microneedles identifies low loading capacity, dose consistency and clinically meaningful concentration as major barriers to translation.²

Mechanical performance and insertion variability are also critical. A patch must be strong enough to penetrate skin but not so rigid or sharp that it produces unnecessary tissue injury. Skin properties differ with age, anatomical site, hydration and disease state, meaning that laboratory performance does not always translate directly to human use. Standardized insertion tests and clinically relevant application protocols are therefore essential.

Manufacturing and quality control present another major challenge. Industrial production requires reproducible cavity filling, drying, drug distribution, packaging and environmental control. Residual moisture can change dissolution and mechanical behavior. Sterilization is particularly difficult for some polymer-drug combinations because heat, radiation or chemical exposure can damage the active or

alter the matrix. A robust aseptic manufacturing strategy or validated terminal sterilization method may be required depending on the product.^{2,3}

Regulatory uncertainty can slow translation. Microneedle products combine characteristics of a drug, a delivery device and a polymeric material, and regulatory expectations may vary according to the product and jurisdiction. The development pathway therefore needs early consideration of dose uniformity, extractables/leachables where relevant, biocompatibility, microbial quality, stability, packaging and human factors.

11. Recent Research Directions

Recent literature indicates a shift from demonstrating that microneedles can deliver a drug toward optimizing systems for clinically relevant performance. Current research includes multilayer and tip-loaded structures, combination delivery, responsive materials, long-acting formulations and nucleic-acid therapeutics. Advanced modeling and imaging are also being used to understand insertion and dissolution. These developments can improve efficiency, but additional complexity can make scale-up and quality control more difficult.^{1,2,4}

An important future direction is quality-by-design development. Instead of optimizing



each formulation variable independently, researchers can define critical quality attributes such as needle geometry, fracture resistance, insertion force, drug content and dissolution time, then identify critical material and process parameters that control them. This approach may improve batch-to-batch consistency and provide a clearer path toward regulatory documentation.

12. Future Perspectives

The future of DMNPs will likely depend on convergence between pharmaceutical formulation, microfabrication, biomaterials engineering and clinical science. Materials that combine high mechanical strength with predictable dissolution could expand the range of deliverable drugs. Better stabilization strategies may make the technology more suitable for vaccines, proteins and nucleic acids. Scalable manufacturing methods capable of maintaining dose uniformity across large arrays will be equally important.^{1,2,3}

Personalized and site-specific delivery is another promising direction. Microneedle geometry, drug loading and release behavior could potentially be adjusted for different skin types or therapeutic objectives. Integration with biosensing and responsive delivery systems may eventually permit feedback-controlled therapy. However, these

concepts require rigorous clinical validation, and practical simplicity should remain a central design principle.

From a patient perspective, the strongest value proposition is likely to be a compact, stable and easy-to-use patch that delivers a precisely controlled dose without the burden of conventional injections. Demonstrating that value in well-designed clinical studies, rather than relying solely on laboratory permeation data, will be essential for widespread adoption.

13. Formulation Development and Product Optimization

Successful DMNP development requires integration of formulation variables with device performance. During preformulation, the selected active should be evaluated for solubility, dose requirement, molecular stability, compatibility with the polymer and sensitivity to water or processing conditions.

Polymer concentration affects viscosity and mould filling, while solids content and drying conditions can influence shrinkage, porosity and needle strength. The drug-to-polymer ratio must therefore be optimized rather than selected solely on the basis of maximum loading. Recent reviews emphasize that practical development should focus on reproducible dose delivery and clinically meaningful performance rather



than increasing structural complexity alone^{1,2}.

For a pharmaceutical development program, critical quality attributes may include appearance, microneedle dimensions, fracture resistance, insertion efficiency, drug content uniformity, residual moisture, dissolution time, release profile and stability. These attributes can be connected to critical material attributes and process parameters through a quality-by-design framework. Design-of-experiments approaches can help identify interactions among polymer concentration, drug loading, drying temperature, drying time and mould-filling conditions. Such systematic optimization can reduce batch variability and provide stronger justification for process controls. Packaging is also important because moisture can soften water-soluble microneedles during storage; moisture-barrier packaging and appropriate desiccant strategies may therefore be required depending on formulation characteristics^{2,3}.

Another important consideration is dose verification. The nominal amount of drug added to a formulation does not necessarily equal the amount delivered into skin. Drug may remain in the mould, backing layer or residual formulation, and incomplete insertion can reduce delivered dose.

Consequently, analytical recovery studies should distinguish total drug content from the fraction that is actually deposited following application. For clinical translation, human factors such as patch orientation, application force, application time and removal should also be considered. A user-friendly patch should ideally require minimal steps and provide a clear indication of successful application^{2,3}.

14. Conclusion

Dissolving microneedle patches represent an important evolution of transdermal drug delivery because they combine microscopic skin penetration with dissolution of the drug-containing matrix. Their ability to create transient pathways through the stratum corneum, deliver selected macromolecules and avoid conventional sharps waste makes them attractive for vaccines, peptides, proteins, nucleic acids, dermatological therapy and selected systemic medicines. Nevertheless, the technology remains developmental for many indications. Limited loading capacity, mechanical and insertion variability, drug stability, manufacturing scale-up, sterilization and regulatory requirements continue to influence translation. Future progress should therefore prioritize reproducible manufacturing, clinically meaningful performance testing



and rational formulation design. With these advances, DMNPs have the potential to become a practical platform for patient-friendly, targeted and minimally invasive drug administration.

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