Microneedle-Based Transdermal Drug Delivery: Recent Advances and Future Prospects

B.Jeelani[1], A.Dinesh Raja[2*], S.Buvaneshwari[3], K.H.Ibrahim Rahathullah[3], J.Jalshiya[3], K.Karthieswari[3], K.Maries Raja Singh[3], A.Paulin Daisy[3], M.Sineha[3], S.Veeralakshmi[3],

[1]Assistant Professor,Dept of Pharmaceutics,Vinayaka Mission's college of Pharmacy, Vinayaka Mission's Research foundation (Deemed to be University), Salem-636008

[*2]Assistant Professor, Dept of Pharmaceutics, KMCH College of Pharmacy, Coimbatore-641048

[3]Department of Pharmaceutics, Arulmigu Kalasalingam College of Pharmacy, Anand Nagar, Krishanankoil, Srivilliputhur-626126

[4]Department of Pharmaceutical Chemistry, Arulmigu Kalasalingam College of Pharmacy, Anand Nagar, Krishanankoil, Srivilliputhur-626126

Corresponding author*
Assistant Professor,
KMCH College of Pharmacy,
Coimbatore-641048
Email: dineshraja.61086@gmail.com

Abstract

Microneedle (MN) systems are emerging as versatile platforms that create micron-scale pathways across the stratum corneum while limiting stimulation of deeper pain receptors and blood vessels. This minimally invasive approach expands transdermal delivery beyond the small, moderately lipophilic molecules traditionally suited to passive patches and enables administration of peptides, proteins, vaccines, poorly soluble drugs, nucleic-acid formulations and locally acting dermatological agents. This review critically examines solid, coated, hollow, dissolving, separable and hydrogel-forming microneedles, with emphasis on how material selection, needle geometry, drug localization and manufacturing method determine insertion reliability, dose capacity, release kinetics and product stability. Recent advances include pure-drug needle tips for high payloads, nanosuspension-loaded dissolving arrays for lipophilic molecules, hydrogel-forming systems coupled with engineered reservoirs, rapidly separating tips for sustained intradermal depots, and additive manufacturing for rapid design optimization. Clinical evidence from influenza, measles-rubella and osteoporosis programmes confirms the translational potential of microarray patches, although local reactions, dose delivery variability and scale-up remain important constraints. Critical quality attributes include morphology, mechanical strength, insertion depth, drug content and distribution, dissolution or swelling, permeation, sterility assurance, packaging integrity and user-applied force. Future progress will depend on integrated quality-by-design development, robust in vitro-in vivo relationships, climate-resilient packaging, human-factor engineering and clearer combination-product regulatory pathways. Microneedles are therefore positioned not merely as an alternative to injections, but as a programmable interface for localized, systemic and responsive therapy.

Keywords: microneedles; transdermal drug delivery; dissolving microneedles; hydrogel-forming microneedles; microarray patch; vaccine delivery; controlled release; pharmaceutical manufacturing

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1. Introduction

The skin is an attractive route for drug administration because it is readily accessible, supports non-invasive or minimally invasive dosing and can avoid gastrointestinal degradation and hepatic first-pass metabolism. Its protective function, however, is also the principal limitation of conventional transdermal therapy. The stratum corneum restricts passive permeation to a comparatively narrow physicochemical space, generally favouring potent drugs with low molecular mass, balanced lipophilicity and modest daily dose requirements. Microneedles address this constraint by producing short-lived aqueous pathways through the stratum corneum or by directly placing a formulation within the epidermal and upper dermal compartments [1,2].

The modern field was catalysed by microfabricated arrays that increased skin permeability without the tissue trauma associated with hypodermic needles [1]. Subsequent work established biodegradable

polymeric needles, drug-coated projections, hollow systems for liquid infusion, dissolving matrices and cross-linked hydrogel arrays [2,3]. Human studies showed that appropriately designed microneedles can be substantially less painful than conventional needles and can deliver otherwise skin-impermeant molecules [4,5]. The platform has since evolved from a permeability enhancer into a family of dosage forms capable of carrying drugs, biologics, vaccines and responsive delivery components.

Recent progress has been driven by advances in polymer science, microfabrication, 3D printing, nanocarrier integration and clinical microarray-patch programmes. Dissolving systems have achieved higher payloads through drug localization at the needle tips; hydrogel-forming systems have separated the mechanical insertion function from the drug reservoir; and rapidly separating tips have enabled intradermal depots lasting days [14-18,23,24]. At the same time, late-stage programmes reveal that local tolerability, delivered-dose reproducibility and therapeutic equivalence cannot be assumed solely from successful skin insertion. A critical review must therefore connect device architecture with pharmaceutical development, clinical performance and regulatory expectations.

This article provides an updated narrative review of microneedle-based transdermal delivery, focusing on platform classification, materials, fabrication, critical quality attributes, therapeutic applications, clinical evidence, safety, manufacturing challenges and future research priorities. Particular attention is given to studies published from 2023 onward that illustrate high-dose delivery, nanocarrier-enabled loading, sustained release, additive manufacturing and human translation.

2. Literature Search Strategy

A structured narrative search was conducted using PubMed, publisher databases and regulatory websites. Search terms included “microneedle”, “microarray patch”, “transdermal drug delivery”, “dissolving microneedle”, “hydrogel-forming microneedle”, “coated microneedle”, “hollow microneedle”, “clinical trial”, “manufacturing”, “quality control” and “regulatory”. Foundational studies were included to describe the evolution of the field, while emphasis was placed on original research and clinical reports from 2020 to 2026. Regulatory discussion was informed by United States Food and Drug Administration guidance for transdermal and topical delivery systems, microneedling products and combination products [11,12].

3. Skin Barrier and Rationale for Microneedle Delivery

The stratum corneum is a compact, lipid-rich barrier composed of corneocytes embedded within an extracellular lipid matrix. Although appendageal pathways may contribute to the entry of selected compounds, most passive transdermal transport occurs by diffusion through this barrier. Consequently, macromolecules, hydrophilic drugs, particulate carriers and high-dose medicines generally show negligible passive flux. Chemical enhancers, iontophoresis and sonophoresis can increase permeability, but may require energy, prolonged application or excipients that irritate the skin.

Microneedles mechanically bypass the dominant barrier without reaching the depth of conventional injections. Needle length, tip radius, inter-needle spacing, array density, application velocity and backing flexibility jointly determine whether the projections insert, bend, fracture or merely indent the skin. Insertion is further influenced by anatomical site, age, hydration, disease, skin curvature and the applicator. This explains why mechanical strength measured against a rigid surface cannot alone predict delivered dose in vivo.

For systemic delivery, drug must move from the created microchannels or intradermal depot into the dermal microcirculation. For local therapy, the objective may instead be high retention within epidermal or dermal tissue with minimal systemic exposure. Vaccine applications exploit the density of antigen-presenting cells in skin. Thus, an optimal microneedle product is defined by the therapeutic objective rather than by a single universal geometry.

4. Classification and Delivery Mechanisms

Microneedle platforms are commonly categorized according to whether the needles are solid, coated, hollow, dissolving or hydrogel-forming. Separable and porous designs are functional variants that combine features of these major groups. Figure 1 summarizes their principal mechanisms, while Table 1 compares their pharmaceutical attributes.

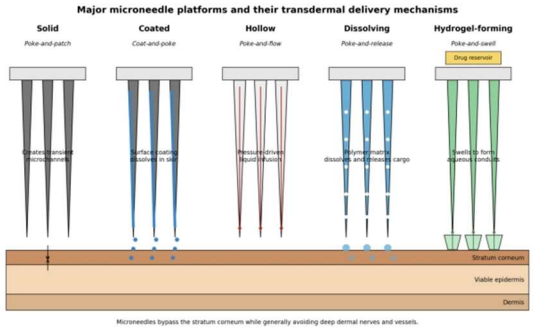

Figure 1. Major microneedle platforms and their mechanisms of transdermal delivery. The schematic is original and prepared for this review.

Table 1. Comparison of major microneedle platforms.

Platfor	Typi	Deliv	Main	Princ	Best-

m	cal materials	ery mechanism	advantages	ipal limitations	suited payloads
Solid	Silicon, stainless steel, titanium, rigid polymers	Pretreatment creates microchannels; a separate formulation is applied	Simple needles; flexible dose in external formulation; reusable applicator possible	Two-step administration; channels reseal; sharps handling; variable flux	Small molecules, macromolecules and topical formulations
Coated	Metal or rigid polymer with drug coating	Coating dissolves rapidly after insertion	Fast bolus; accurate skin targeting; limited excipient burden	Low coating capacity; coating uniformity; residual sharps	Vaccines and potent drugs requiring low doses
Hollow	Silicon, glass, metal, ceramic, polymer	Liquid is infused through a lumen under pressure	Adjustable dose and rate; compatible with liquid formulations	Clogging, leakage, back-pressure, complex fabrication	Vaccines, peptides, insulin and liquid biologics
Dissolving	PVA, PVP, hyaluronic acid, sugars, pullulan, CMC	Needles dissolve in interstitial fluid and release incorporated drug	No residual sharps; one-step use; suitable for self-administration	Moisture sensitivity; limited dose volume; drying variability; protein stress	Small molecules, peptides, proteins and local dermatological drugs
Separable/implantable	Fast-dissolving base plus slow-degrading tip; GelMA, chitosan, PLGA composites	Needle tips detach and remain as an intradermal depot	Short application time; prolonged local or systemic release	Control of tip separation; residual material safety; complex multilayer manufacture	Long-acting anti-inflammatory, metabolic and oncologic therapies
Hydrogel-forming	Cross-linked PVA/PVP, Gantrez, PEG-based or methacrylated polymers	Needles swell and form aqueous conduits from an attached reservoir	High reservoir capacity; removal leaves minimal polymer; controlled delivery	Slower onset; reservoir integration; swelling-strength trade-off	Hydrophilic drugs, high-dose small molecules and sustained delivery
Porous/stimuli-responsive	Porous silicon, conductive polymers, responsive hydro	Capillary transport or trigger-mediated release (pH, glucose,	Programmable release; potential closed-loop therapy	Complexity, sensor calibration, energy input, regulatory	Insulin, immunotherapy and precision dosing

	gels	light, heat)		burden	

4.1 Solid and coated microneedles

Solid microneedles use a "poke-and-patch" sequence: the skin is punctured and then exposed to a drug-loaded gel, cream or conventional patch. The strategy decouples needle manufacture from formulation loading, but performance depends on channel lifetime and contact between the formulation and treated area. Coated microneedles use a "coat-and-poke" approach in which a thin drug layer dissolves after insertion. They are attractive for vaccines and potent compounds, but the available coating volume is small and dose uniformity depends on controlling surface tension, drying and coating localization.

4.2 Hollow microneedles

Hollow microneedles are microscale analogues of hypodermic needles. Pressure or a pump drives liquid through the lumen, allowing dose and rate adjustment. Their main engineering difficulties are lumen blockage by tissue, leakage onto the skin surface, fracture at the hub and back-pressure within the dense dermal matrix. Bevel geometry, side openings and controlled insertion depth can reduce occlusion.

4.3 Dissolving and separable microneedles

Dissolving microneedles integrate the drug and structural polymer into a single dosage form. Interstitial fluid hydrates the matrix, causing dissolution or erosion and releasing the payload. Water-soluble polymers such as PVA, PVP, hyaluronic acid, pullulan and sugars are widely used. Drug may be dispersed throughout the needles, concentrated in the tips or placed in a multilayer architecture. Tip loading increases delivery efficiency because material remaining in the backing does not contribute to the delivered dose. A pure-drug-tip liraglutide patch achieved milligram-scale loading and measurable systemic exposure in rats and minipigs, illustrating how spatial drug localization can address conventional payload limitations [23].

Separable systems use a rapidly dissolving junction or backing to detach drug-loaded tips inside the skin. The implanted tips then act as depots. This design has sustained colchicine and stabilized uricase delivery for gout and prolonged methotrexate residence in psoriasis models [14,19]. The principal development question is whether the retained material is reproducibly implanted and safely degraded.

4.4 Hydrogel-forming microneedles

Hydrogel-forming microneedles are cross-linked, initially dry arrays that absorb interstitial fluid, swell and create continuous aqueous pathways between an external reservoir and viable skin. Because the drug can be stored in a separate reservoir, dose capacity is not restricted to needle volume. The architecture also allows removal of the swollen array after use, reducing residual polymer in the skin. However, increasing cross-link density improves strength but may slow swelling and diffusion. Recent studies have used 3D-printed moulds and experimental design to optimize this balance [24], while cellulose-based SmartReservoirs have improved delivery of hydrophobic rifampicin [18].

5. Materials and Fabrication Technologies

Material selection must simultaneously satisfy mechanical, pharmaceutical and biological requirements. Metals and silicon provide high stiffness and dimensional accuracy, but fracture, sharps disposal and cost may limit single-use drug products. Biodegradable and water-soluble polymers are attractive because they can encapsulate drugs and eliminate sharp waste. Common materials include PVA, PVP, hyaluronic acid, carboxymethyl cellulose, pullulan, maltose, dextran, gelatin, chitosan, polylactic acid, PLGA and methacrylated biopolymers. Excipients such as trehalose, surfactants, plasticizers and amino acids may stabilize proteins or improve mould filling, but can alter drying behaviour and mechanical strength.

Micromoulding remains the dominant method for dissolving and hydrogel-forming systems. A master structure is replicated in an elastomeric mould, and polymer-drug formulations are filled by centrifugation, vacuum, pressure or repeated casting. Key risks include trapped air, incomplete tips, drug migration during drying, backing-layer mixing and batch-to-batch moisture variation. Two-step casting can localize drug in the tips but adds process time and alignment requirements.

Coating methods include dip coating, spray coating, inkjet deposition and layer-by-layer assembly. Uniform coating requires control of viscosity, wetting and withdrawal speed. Hollow and rigid microneedles are commonly produced by lithography, etching, laser machining, drawing lithography or micromachining. Additive manufacturing, particularly stereolithography and two-photon polymerization, accelerates geometry screening and mould production. Tunçel and colleagues fabricated approximately 500-µm hydrogel-forming needles using stereolithographically printed master moulds and optimized formulation variables with a Box-Behnken design [24].

Freeze-drying has recently been adapted to produce porous dissolving microneedles. In an insulin model, coated freeze-dried arrays showed rapid tip dissolution, high penetration efficiency and better thermal retention of insulin than conventionally dried arrays [15]. This approach may shorten drying time and improve reconstitution kinetics, but porous

structures must still withstand packaging, transport and application forces.

6. Critical Quality Attributes and Characterization

A microneedle patch is a drug-device combination in which geometry, formulation and applicator performance collectively determine dose. Development should begin with a quality target product profile that defines the indication, intended user, anatomical site, dose, application time, storage condition and acceptable local reaction. Critical quality attributes should then be linked to material attributes and process parameters through risk assessment and designed experiments.

Morphology is assessed by optical microscopy, scanning electron microscopy or micro-computed tomography. Needle height, base width, tip radius, spacing, density and absence of defects should be quantified. Mechanical testing commonly measures axial compression, fracture force or percentage height reduction. These tests are useful for ranking formulations but should be complemented by insertion studies because skin is elastic and heterogeneous. Parafilm multilayers provide a convenient screening model, while ex vivo porcine or human skin, optical coherence tomography, histology, confocal microscopy and transepidermal water loss offer more physiologically relevant information.

Pharmaceutical tests include assay, content uniformity, drug distribution between tip and backing, residual moisture, crystallinity, protein integrity, dissolution or swelling, release kinetics, skin deposition and transdermal permeation. Raman mapping can verify tip localization, while chromatographic and spectroscopic methods detect degradation. For hollow systems, delivered volume, leakage and pressure-flow relationships are essential. For dissolving systems, the fraction of the array remaining on the backing after use can serve as an indirect measure of delivery efficiency.

Stability studies must consider humidity, polymer relaxation, tip deformation, drug migration, oxidation, aggregation and package seal integrity. Moisture-barrier pouches and desiccants are frequently required. Sterilization cannot be treated as an afterthought: heat, radiation and ethylene oxide may change polymer properties or degrade biologics. Depending on product design, aseptic manufacture, terminal sterilization of device components, low-bioburden processing or justified microbial limits may be appropriate.

Human-factor testing is a critical quality component rather than a late usability exercise. Application force, dwell time, patch adhesion, feedback that insertion has occurred and ease of removal affect actual dose. An applicator may improve reliability but adds cost and waste. Conversely, thumb application may be preferred for simplicity but requires a robust design space across users.

7. Therapeutic Applications and Recent Advances

7.1 Vaccines

The epidermis and dermis contain abundant antigen-presenting cells, providing a biological rationale for intradermal vaccination. Dissolving influenza patches generated robust immune responses and high acceptability in a first-in-human phase 1 trial, including self-administration by participants [7]. A high-density coated microarray patch also delivered reduced influenza vaccine doses with acceptable safety and immunogenicity [8]. More recently, a phase 1/2 trial in The Gambia demonstrated that a measles-rubella vaccine microneedle patch was tolerated and immunogenic in adults, toddlers and vaccine-naïve infants [22]. The 2024 MIMIX influenza study further supported clinical feasibility of a polymeric MAP platform [21]. These programmes show the potential for dose sparing, reduced sharps waste, simplified administration and improved thermostability, although large confirmatory trials and commercial-scale manufacturing remain necessary.

7.2 Diabetes, obesity and peptide delivery

Peptides and proteins are attractive microneedle payloads because conventional oral delivery is limited by enzymatic degradation and low permeability. Insulin is frequently used as a model biologic, and recent freeze-dried dissolving arrays demonstrated rapid delivery and improved thermal stability [15]. Pure-drug-tip microneedles increased liraglutide loading to 2.21 mg per 0.9 cm^2 patch and produced relative bioavailability of 69.8% in rats and 46.3% in minipigs versus subcutaneous injection [23]. These data demonstrate that high-loading strategies can move microneedles toward clinically relevant peptide doses, but interspecies differences and incomplete bioavailability remain important.

7.3 Dermatological and inflammatory diseases

Local skin delivery can produce high concentrations at the lesion while reducing systemic toxicity. Calcipotriol nanosuspension-loaded trilayer dissolving patches improved antipsoriatic activity in vivo [25]. Tip-swellable methotrexate arrays prolonged skin retention and outperformed oral, subcutaneous and conventional dissolving approaches in a psoriasis model [19]. Eugenol-loaded hyaluronic-acid microneedles combined antibacterial delivery with photothermal action for acne [17], while cyanocobalamin-loaded dissolving microarray patches reduced inflammatory signals and histological damage in a delayed-type hypersensitivity model [20]. Hydrogel-forming arrays

have also enhanced dermal diclofenac delivery [24]. These systems illustrate the value of integrating microneedles with nanocrystals, photothermal agents or swellable depots.

7.4 Poorly soluble drugs and nanocarrier integration

Poorly soluble drugs remain challenging because dissolving matrices are generally prepared from aqueous formulations. Nanosuspensions, amorphous reservoirs, cyclodextrins and lipid carriers can increase apparent loading. A cannabidiol nanosuspension incorporated into dissolving microneedles improved intradermal delivery, pharmacokinetics and anti-inflammatory performance in a knee synovitis model [16]. SmartReservoir technology combined a cellulose matrix with hydrogel-forming arrays to increase rifampicin deposition and transdermal permeation [18]. The formulation advantage must be weighed against particle aggregation, altered mechanical properties and the need to control both nanocarrier and device attributes.

7.5 Neurological, musculoskeletal and long-acting therapy

Microneedles have been evaluated for drugs that are difficult to administer orally or require frequent injection. PVA-based dissolving arrays delivered apomorphine with rapid absorption and retained drug content during storage [26]. Hydrogel-forming arrays have been explored for esketamine delivery [10]. In gout, rapidly separating microneedles retained colchicine and stabilized uricase in skin for approximately one week, reducing disease features in acute and chronic models [14]. These examples suggest a route to short-application, long-acting therapy, although systemic dose precision and the fate of implanted polymers require careful assessment.

Table 2. Selected recent advances in microneedle drug-delivery research.

Year	Platform/ cargo	Model or trial	Key formulation feature	Main finding	Ref.
2023	Abaloparatide microstructured transdermal system	Phase 3, postmenopausal osteoporosis	Daily microprojection patch	Clinically meaningful BMD gains, but non-inferiority to injection was not met; local reactions were frequent	[13]
2023	Separable colchicine/ uricase microneedles	Acute and chronic gout models	Rapidly dissolving junction with sustained-release tips	Maintained local drug for about one week and improved gout outcomes	[14]
2024	Freeze-dried insulin dissolving patch	In vitro and diabetic mice	Porous HA needles with strengthening coat	Rapid dissolution, high insertion and improved insulin thermal stability	[15]
2024	Cannabidiol nanosuspension DMN	Rat knee synovitis and PK	Nanosuspension enabled high lipophilic-drug loading	Improved skin delivery, duration, bioavailability and anti-inflammatory effect	[16]
2024	Eugenol/photothermal HA DMN	Acne model	Combined antimicrobial drug and photothermal component	Enhanced antibacterial and anti-inflammatory treatment	[17]
2024	Rifampicin SmartRese	Ex vivo permeation	Amorphous cellulos	Approximately fourfold	[18]

	rvoir + HF-MN		e reservoir coupled to swelling array	greater skin deposition and substantial permeation	
2024	Tip-swellable methotrexate array	Psoriasis-like mouse skin	Drug loaded into detachable swellable tips	Prolonged retention and superior antipsoriatic efficacy	[19]
2024	Cyanocobalamin DMAP	Inflammatory skin model	Antioxidant vitamin delivered through dissolving tips	Reduced inflammatory markers and tissue injury	[20]
2024	MIMIX influenza MAP	Phase 1 healthy adults	Polymeric MAP carrying H1N1 antigen	Supported safety, tolerability and immunogenicity	[21]
2024	Measles-rubella vaccine MNP	Phase 1/2 adults and children	Thermostable microarray-patch vaccine	Strong immune responses across age groups with acceptable tolerability	[22]
2025	Pure-liraglutide-tip DMN	Rats and minipigs	Needles largely composed of drug at tips	Milligram payload and measurable systemic bioavailability	[23]
2025	3D-moulded diclofenac HF-MN	In vitro, ex vivo and in vivo	SLA moulds and Box-Behnken optimization	Good penetration, skin accumulation and anti-inflammatory activity	[24]

8. Clinical Translation and Patient-Centred Performance

Clinical translation has progressed furthest for vaccines and selected peptides. Influenza trials have shown that microarray patches can be self-applied, are generally preferred over injections and can elicit immune responses comparable to intramuscular vaccination [7,8,21]. The measles-rubella trial extended this evidence to infants and toddlers, populations in whom ease of administration and reduced sharps waste could have major public-health value [22].

Transdermal abaloparatide provides an instructive example of the difference between technical feasibility and clinical equivalence. In a phase 3 study, the microstructured system increased bone mineral density but did not meet the prespecified non-inferiority criterion versus subcutaneous injection, and administration-site reactions were common [13]. This demonstrates that microneedle development must optimize not only delivery but also pharmacokinetic exposure, adherence, local tolerability and therapeutic outcomes.

Patient-centred design includes patch size, application time, pain, visible erythema, pigmentation, adhesive performance and confidence that the dose was delivered. Acceptability may be high even when mild local reactions occur, but persistent reactions can impair adherence in chronic therapy. Paediatric, geriatric and dermatological populations may require different applicators and adhesives because skin mechanics and sensitivity differ.

9. Safety, Biocompatibility and Infection Risk

Microneedles typically cause transient erythema, mild oedema or local tenderness. Pain increases with needle length, number and geometry, but remains substantially lower than that associated with hypodermic needles when projections are restricted to superficial skin [4]. Repeated application raises additional questions about sensitization, pigmentation, barrier recovery and site rotation.

Microbial entry through microchannels is a theoretical concern; however, channels produced by short microneedles generally reseal rapidly. Product sterility or bioburden specifications should be justified by invasiveness, intended population,

formulation and manufacturing process. Reusable applicators must prevent cross-contamination, while dissolving systems offer the advantage of no residual sharp needle.

Biocompatibility assessment should address not only the starting polymer but also residual monomers, photoinitiators, degradation products, extractables and leachables from moulds, adhesives and packaging. Implantable tips require evidence for local degradation and clearance. Nanomaterial-containing patches need an exposure assessment that distinguishes material retained within the patch from material delivered into tissue.

10. Manufacturing, Quality-by-Design and Regulatory Considerations

Microneedle products sit at the interface of pharmaceuticals and medical devices. A preloaded patch may be regulated as a combination product, with the primary mode of action guiding the lead regulatory centre. Development must integrate pharmaceutical CMC requirements with device design controls, risk management, human factors and packaging validation. FDA guidance for transdermal and topical systems emphasizes product design, manufacturing controls, finished-product testing, adhesion and in vivo performance [11]. Although aesthetic microneedling devices differ from drug-loaded patches, FDA guidance on microneedling products highlights the importance of intended use, invasiveness and claims [12].

Scale-up remains a major barrier. Laboratory centrifugation and manual casting are difficult to translate to continuous, high-yield manufacture. Industrial processes require automated mould filling, controlled drying, in-line inspection, rapid demoulding and validated environmental controls. Needle defects can be small yet clinically important, making machine vision and statistical process control attractive. For biologics, low-temperature processing must preserve potency while maintaining throughput.

A quality-by-design strategy should identify critical material attributes such as polymer molecular weight, viscosity, moisture content and degree of cross-linking, and critical process parameters such as filling pressure, vacuum, drying temperature, drying time and demoulding force. Design-of-experiments methods can define a region in which mechanical strength, insertion, dissolution and assay are simultaneously acceptable. The translation pathway in Figure 2 emphasizes that dose capacity, insertion reliability, stability, human factors and regulatory evidence must be addressed early rather than after formulation optimization.

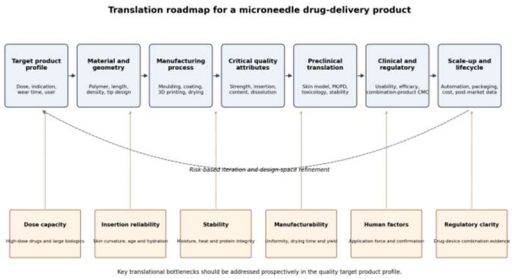

Figure 2. Risk-based translation roadmap for a microneedle drug-delivery product. The schematic is original and prepared for this review.

11. Current Challenges

First, dose capacity remains limited for high-dose systemic products. Larger patches, higher drug concentration and pure-drug tips can increase payload, but may worsen brittleness, dissolution time or application force. Reservoir-based hydrogel systems provide an alternative, although they may require longer wear.

Second, delivered dose is sensitive to incomplete insertion, skin deformation and user technique. Mechanical testing against rigid substrates can overestimate performance. Standardized skin models, validated applicators and quantitative post-use indicators are needed.

Third, stability and packaging are central to commercialization. Water-soluble matrices are hygroscopic, and many biologics are sensitive to drying and interfaces. The apparent thermostability advantage of a dry patch must be demonstrated through long-term, in-use and transport studies.

Fourth, manufacturing cost and yield remain uncertain. Complex multilayer casting, nanosuspension preparation and individualized applicators can erode the simplicity advantage. Platform standardization and modular manufacturing may reduce development time.

Fifth, the evidence base is still dominated by animal models. Differences in skin thickness, hair follicles and immune architecture limit translation. Larger-animal pharmacokinetics, ex vivo human skin studies and early human pharmacology should be incorporated sooner.

12. Future Prospects

Future microneedles will increasingly combine delivery with sensing, feedback and spatial control. Glucose-responsive insulin systems, pH-responsive antimicrobial patches, light-triggered reservoirs and electroactive arrays could provide on-demand dosing. The central challenge will be to prove trigger specificity, dose accuracy and fail-safe behaviour.

High-resolution additive manufacturing may enable patient- or site-specific geometry, but pharmaceutical use will require reproducible materials, validated

post-processing and scalable inspection. Artificial intelligence and mechanistic modelling can support geometry optimization, predict insertion and integrate formulation variables, provided models are trained on relevant skin and manufacturing data.

Combination with nanoparticles, liposomes, nanocrystals and nucleic-acid complexes will broaden the therapeutic space. Formulation scientists should avoid treating the microneedle as a passive carrier: nanocarrier size, surface chemistry and physical state can change needle strength, release and tissue fate.

Commercial success is most likely where microneedles provide a clear system-level advantage: eliminating trained administration, reducing cold-chain burden, enabling a differentiated pharmacokinetic profile, improving adherence or localizing therapy. Future clinical programmes should therefore compare the complete care pathway and health-economic value, not merely bioavailability.

13. Conclusions

Microneedles have evolved from microfabricated permeability enhancers into sophisticated pharmaceutical systems capable of bolus, sustained, localized and responsive delivery. Dissolving, separable and hydrogel-forming platforms are particularly promising because they integrate patient-friendly administration with flexible drug loading. Recent clinical vaccine studies and the experience of transdermal abaloparatide confirm that translation is achievable but also show that insertion alone does not guarantee therapeutic equivalence. Progress toward routine clinical use will require product-specific quality target profiles, scalable manufacturing, predictive skin models, robust human-factor engineering, stability-indicating control strategies and coordinated drug-device regulation. With these elements in place, microneedle patches can become an important bridge between conventional transdermal systems and injectable medicines.

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