INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

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Review Article

Polymeric Microneedles for Transdermal Drug Delivery Advances in Material Engineering, Fabrication Technologies, Drug Release Mechanisms and Therapeutic Applications

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ARTICLE INFO

Published: 27 Nov 2026
Keywords:
Polymeric microneedles, transdermal drug delivery, biodegradable polymers, dissolving microneedles, hydrogel microneedles, sustained release, micromoulding. [4], [8], [24]
DOI:
10.5281/zenodo.24583278

ABSTRACT

Transdermal drug delivery offers a non-invasive route for local and systemic therapy, but its application is constrained by the stratum corneum, which restricts the permeation of many therapeutic molecules. Polymeric microneedles (MNs) are micron-scale projections that create transient pathways across this barrier and can deposit drugs within the viable epidermis or dermis while avoiding the depth and invasiveness of conventional hypodermic injections. This narrative review synthesizes 25 user-supplied articles with emphasis on polymeric MN design, material selection, fabrication, drug incorporation, release behaviour and therapeutic applications. Hydrophilic polymers such as hyaluronic acid, polyvinylpyrrolidone, polyvinyl alcohol and carboxymethyl cellulose are suited to rapidly dissolving systems, whereas biodegradable polyesters such as poly (lactic-co-glycolic acid), polylactic acid and polycaprolactone can provide slower degradation and prolonged release. Hydrogel-forming systems absorb interstitial fluid and support diffusion-mediated delivery, while hybrid and layered architectures combine rapid initial delivery with a sustained depot. Fabrication approaches include micromoulding, vacuum or centrifugal filling, solvent casting, thermal melt processing, photopolymerization and additive manufacturing. Applications investigated across the source set include vaccination, insulin and metabolic disease management, dermatology, wound repair, long-acting antiviral and contraceptive delivery, and exploratory delivery of phytobioactive compounds. Recent experimental examples include heat-melted PLGA layered dissolving MNs that released encapsulated molecules for nearly four weeks and melt-cast PCL MNs investigated for sustained islatravir delivery. These findings demonstrate formulation potential rather than established clinical effectiveness. Translation remains limited by variability in insertion and delivered dose, polymer–drug compatibility, sterilization, stability, manufacturing

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

reproducibility, biocompatibility of retained depots and the need for robust human evidence.The review highlights the importance of matching polymer chemistry and device architecture to the therapeutic objective, and recommends standardized mechanical, insertion, release, pharmacokinetic and safety testing. [4], [8], [24].

INTRODUCTION

Transdermal drug delivery is attractive because it can provide local treatment or systemic exposure without gastrointestinal degradation, can avoid hepatic first-pass metabolism, and may improve convenience for patients who require repeated administration. Conventional topical formulations and passive transdermal patches, however, are limited by the barrier function of the stratum corneum. This outermost epidermal layer restricts the entry of many hydrophilic, ionized and high-molecular-weight compounds. Chemical enhancers and energy-based methods can increase skin permeability, but may introduce irritation, device complexity or inconsistent delivery.

Microneedles are arrays of micron-scale projections designed to cross the stratum corneum and create controlled microchannels. Their dimensions and insertion depth are selected to access epidermal and dermal compartments while limiting stimulation of deeper pain-sensitive structures. The concept bridges topical delivery and hypodermic injection: it is minimally invasive but can transport molecules that do not readily cross intact skin. Microneedles have been investigated for small molecules, peptides, proteins, vaccines, nucleic acids and particulate carriers [1], [2]. [6], [20].

Microneedle systems are commonly classified by their physical construction and delivery mechanism as solid, coated, hollow, dissolving and hydrogel-forming systems. These categories are not mutually exclusive with respect to material: a polymer may form a dissolving needle, a hydrogel-forming array or a biodegradable implanting tip. The present review focuses on polymer-based systems because polymer chemistry provides a broad means of tuning mechanical strength, water uptake, degradation, drug loading and release kinetics.

An important distinction is required between rapid-dissolving and long-acting polymeric MNs. Hydrophilic matrices such as hyaluronic acid (HA), polyvinylpyrrolidone (PVP) and polyvinyl alcohol (PVA) can dissolve or hydrate rapidly after insertion, favouring prompt drug deposition. By contrast, hydrophobic or slowly degrading polyesters such as poly (lactic-co-glycolic acid) (PLGA), polylactic acid (PLA) and polycaprolactone (PCL) can form persistent intradermal depots or slowly eroding structures. Hybrid architectures seek to combine these functions [3], [4]. [4], [8], [24].

II. REVIEW SCOPE AND APPROACH

This article is a narrative synthesis of 25 microneedle-related articles supplied for the present review. The source set includes polymeric MN reviews, hydrogel-MN literature, long-acting delivery research, vaccine and disease-specific reviews, a study of heat-melted PLGA layered dissolving MNs, a melt-cast PCL MN study involving islatravir, and a bibliometric analysis of scientific publications, patents and clinical trials. The synthesis prioritizes information directly relevant to polymeric transdermal systems. [6], [20].

The review is not presented as a systematic review or meta-analysis. No independent database search strategy, duplicate screening, formal risk-of-bias assessment or quantitative pooling was performed for this draft. Therefore, statements about the 25-paper set describe the supplied corpus and should not be interpreted as a complete census of the field. Where an uploaded paper is a review, its reported findings are treated as secondary evidence; where it reports an original experiment, the experimental outcome is identified as such. In particular, in-vitro release, ex-vivo insertion and animal findings are not equated with clinical efficacy.

III. SKIN BARRIER AND MICRONEEDLE DELIVERY PRINCIPLES

The skin comprises the stratum corneum, viable epidermis and dermis, followed by subcutaneous tissue. The stratum corneum consists of corneocytes embedded in a lipid-rich intercellular matrix and is the principal barrier to passive transdermal transport. Microneedles mechanically disrupt this barrier by creating microchannels. The therapeutic payload may then dissolve from the needle, diffuse from a hydrated

polymer network, be released as the polymer degrades, or be delivered through a hollow lumen.

Delivery performance depends on needle length, base width, tip radius, aspect ratio, array density, geometry, insertion force and application method. A structure that is too short or insufficiently strong may fail to cross the stratum corneum; a structure that is too long or applied with excessive force may increase tissue injury. Pyramid-like geometries can provide a relatively broad base and mechanical robustness, whereas sharper tips may reduce insertion force. Design optimization must balance penetration efficiency with fracture resistance and user comfort [3].

After insertion, drug transport is influenced by the local concentration gradient, drug solubility, molecular size, charge, polymer hydration, tissue binding and local clearance. A microneedle patch therefore cannot be evaluated solely by its ability to puncture a polymer film or synthetic membrane. The relevant endpoints include successful skin insertion, depth distribution, percentage of needles inserted, drug deposited in skin, transdermal flux where systemic delivery is intended, and pharmacokinetic exposure.

IV. CLASSIFICATION OF POLYMERIC MICRONEEDLES

A. Dissolving microneedles Dissolving MNs are fabricated from water-soluble or water-dispersible matrices containing the active ingredient. Following insertion, interstitial fluid hydrates the matrix and dissolves or disperses it, releasing the payload into superficial skin layers. HA, PVP, PVA, carboxymethyl cellulose (CMC), sugars and gelatin-based matrices are frequently investigated. These systems avoid leaving a sharp solid needle after use and can support self-administration. Their main limitation is that rapid dissolution may be poorly suited to drugs requiring prolonged exposure unless the formulation includes a second, slower-release component [3], [5].

B. Hydrogel-forming microneedles Hydrogel-forming MNs are cross-linked polymer networks that swell on contact with interstitial fluid. The swollen needles create aqueous pathways through which drug can diffuse from a reservoir or backing layer. Unlike dissolving MNs, the cross-linked structure is generally removed intact after use, rather than dissolving completely in the skin. Swelling, cross-link density, polymer composition and reservoir design influence the rate of fluid uptake and drug transport. Hydrogel systems offer high water uptake and potentially high loading in an attached reservoir, but their mechanical strength, swelling reproducibility and dose control require careful optimization [6].

C. Biodegradable and implanting polymeric microneedles Biodegradable MNs use polymers that remain in the skin after insertion and gradually erode or degrade. PLGA, PLA and PCL are important examples. The drug may be dispersed in the polymer matrix, encapsulated in particles embedded within the needle, or concentrated in a detachable needle tip. The polymer can act as a drug reservoir, with release governed by water penetration, diffusion, polymer relaxation and hydrolytic degradation. This architecture is relevant to long-acting therapy, but retained material requires evaluation of local tissue response, degradation products and complete drug release [4], [7]. [4], [8], [24].

D. Coated and hybrid polymeric microneedles Coated MNs carry a thin drug-containing layer on the surface of a solid support; the coating dissolves after insertion. The support may be metallic, silicon-based or polymeric. Hybrid polymeric MNs combine soluble and slowly degradable materials, or integrate nanoparticles, microparticles, liposomes or other carriers. Layered structures can separate the mechanical function from the drug-release function and can create an initial loading zone plus a sustained-release depot. Their complexity increases manufacturing and quality-control demands.

V. POLYMER MATERIALS AND THEIR FUNCTIONAL ROLES

A. Hyaluronic acid HA is a naturally occurring glycosaminoglycan widely used in dissolving MN formulations. It is hydrophilic, biocompatible and amenable to aqueous processing. Its molecular weight and concentration affect viscosity, mould filling, drying behaviour, needle strength and dissolution. HA can be useful for biologics and other payloads that benefit from relatively mild aqueous processing. Excessive hydration or low polymer concentration may weaken

the needle, whereas high concentration may complicate filling and increase drying time. HA is therefore not intrinsically optimal for every drug; its suitability depends on the required insertion strength and release profile [3].

B. Polyvinylpyrrolidone PVP is a water-soluble synthetic polymer used as a film former, binder and dissolving MN matrix. It can provide good drug compatibility for a range of molecules and can be blended with other polymers to tune mechanical and dissolution properties. Its rapid hydration supports prompt release, but a PVP-rich formulation may not maintain a long-term depot. In blends with PCL, PVP can provide an early-release fraction while the hydrophobic polyester controls the later phase [4].

C. Polyvinyl alcohol and carboxymethyl cellulose PVA forms hydrophilic films and can be physically or chemically cross-linked to generate hydrogel networks. CMC is a cellulose derivative used in dissolving or swellable formulations. Both can improve film formation and formulation handling. Their mechanical performance is influenced by molecular weight, degree of hydrolysis for PVA, substitution level for CMC, polymer concentration and drying conditions. Cross-linking may improve wet integrity but can reduce swelling or alter drug diffusion.

D. Poly (lactic-co-glycolic acid) PLGA is a biodegradable aliphatic polyester whose degradation rate can be adjusted through lactide-to-glycolide ratio, molecular weight, end-group chemistry and device geometry. Hydrolysis of ester bonds produces lactic- and glycolic-acid-derived degradation products that enter normal metabolic pathways. PLGA is useful for sustained-release depots, but its hydrophobicity and degradation-associated microenvironmental changes may affect drug stability and release. In a layered dissolving MN study, heat-melted PLGA was incorporated into a middle layer and the patch was designed to separate after implantation; the authors reported release of encapsulated molecules for nearly four weeks in their experimental system [5]. This is a promising proof of concept, not evidence that all PLGA MNs will deliver drugs for that duration.

E. Polylactic acid PLA is a biodegradable polyester with slower hydrolysis than many hydrophilic matrices. Its mechanical and degradation properties depend on stereochemistry, molecular weight, crystallinity and processing. PLA may be used where a longer-lived polymer structure is desirable, but its hydrophobicity can limit water ingress and drug diffusion. Copolymerization, blending or incorporation of hydrophilic excipients can be used to adjust release.

F. Polycaprolactone PCL is a semicrystalline, biodegradable polyester with a relatively low melting temperature and slow degradation. It is attractive for long-acting MNs because its hydrophobic matrix can retard water penetration and drug diffusion. However, the same hydrophobicity may lead to incomplete or excessively slow release. Blending PCL with hydrophilic polymers such as PVP or polyethylene glycol can introduce pores or increase water uptake, thereby adjusting the release rate [4]. A 2026 study reported melt-cast PCL MN patches for sustained delivery of islatravir or levonorgestrel; melt processing at 65 °C and the use of centrifugation were described as part of the fabrication approach [8]. [4], [8], [24].

G. Chitosan, gelatin, silk fibroin and other natural polymers Chitosan is a cationic polysaccharide that can form films and hydrogels and may contribute mucoadhesive or antimicrobial properties depending on its grade and formulation. Gelatin is a protein-derived polymer with useful film-forming and biological properties, although its mechanical and dissolution behaviour can be sensitive to temperature and moisture. Silk fibroin offers tunable mechanical properties and can be processed into stable structures. Natural polymers can improve biocompatibility and provide functional groups for modification, but source variability, purification, endotoxin control and batch consistency require attention [4], [6].

H. Polymer blends and composites Blending is a practical route to combine properties that are difficult to achieve with one polymer. Hydrophilic polymers can improve wetting and initial release, while hydrophobic polyesters can maintain structural integrity and sustain release. Polymer–particle composites can further separate loading from release control: nanoparticles may protect unstable molecules, while the MN transports them through the skin barrier. Blends must be assessed for miscibility, phase separation, drug crystallization,

changes in glass-transition or melting behaviour, and reproducibility after storage.

VI. FABRICATION TECHNOLOGIES

A. Micromoulding Micromoulding is widely used for polymeric MN prototyping. A master structure is first produced by micromachining, photolithography or high-resolution printing. A negative mould, commonly made from polydimethylsiloxane (PDMS), is prepared from the master. The polymer–drug mixture is introduced into the cavities, often with vacuum assistance or centrifugation to remove trapped air and promote tip filling. The mould is dried or cured, and the array is demoulded. Mould flexibility and replication fidelity are advantages, but incomplete cavity filling, shrinkage, trapped bubbles and tip defects can produce dose and strength variability [6].

B. Solvent casting and drying Solvent casting uses a polymer solution or dispersion that is filled into a mould and dried to form the needle array. Aqueous casting is compatible with many hydrophilic polymers and can avoid exposure of sensitive biologics to organic solvents. Organic solvents may be needed for some hydrophobic polymers, but residual solvent limits, operator safety and drug stability must be addressed. Drying rate, humidity and temperature affect polymer distribution, crystallinity, residual moisture and needle dimensions.

C. Vacuum and centrifugal filling Vacuum can remove air from mould cavities and draw polymer solution toward the tips. Centrifugation can assist the distribution of polymer and drug into the needle cavity, particularly for layered or high-viscosity systems. These steps may improve uniformity but require defined process parameters, including relative centrifugal force, duration, temperature, viscosity and fill volume. Scale-up must preserve the same physical conditions rather than simply reproducing the same rotational speed.

D. Thermal melt processing Thermal processing avoids some solvent-related issues and is particularly relevant to thermoplastic biodegradable polymers. The PLGA layered dissolving MN study used a heat-melting strategy to form the hydrophobic PLGA middle layer without potentially harmful organic solvents [5]. The PCL islatravir work described melt casting at 65 °C, selected in view of PCL melting behaviour and the thermal stability of the active ingredients [8]. Melt processing is not universally suitable: heat-sensitive drugs, proteins, peptides and nucleic acids may lose activity, and the thermal history of the formulation must be validated.

E. Photopolymerization and cross-linking Photopolymerization can produce cross-linked polymer networks with controlled geometry and swelling properties. It is relevant to hydrogel-forming MNs and high-resolution microfabrication. Initiator residues, light penetration, oxygen inhibition and potential phototoxicity must be considered. Chemical cross-linking can improve wet strength but may introduce reactive residues or alter biocompatibility. Physical cross-linking can reduce chemical residues but may be sensitive to environmental conditions.

F. Additive manufacturing Three-dimensional printing and related additive-manufacturing approaches can generate complex needle geometries, internal channels and customized arrays. They offer rapid design iteration and potential integration of reservoirs or multiple materials. Limitations include achievable resolution, surface roughness, printing speed, material availability, post-processing and regulatory qualification. A printed master used to create a mould should be distinguished from a final MN printed directly from a drug-compatible polymer.

VII. DRUG LOADING AND RELEASE MECHANISMS

A. Drug incorporation strategies Drugs may be dissolved or dispersed directly in the polymer matrix, concentrated in the needle tips, coated onto the surface, loaded into a backing reservoir, or encapsulated in nanoparticles or microparticles before incorporation. Tip-focused loading can reduce drug waste in the backing layer and increase the fraction delivered into skin. However, high drug loading can reduce polymer continuity, alter viscosity and compromise insertion strength. Suspensions require control of particle size and sedimentation during filling.

B. Dissolution-mediated release In dissolving MNs, water uptake causes the polymer matrix to hydrate and

dissolve, releasing drug into the surrounding tissue. Release can be rapid and may depend on polymer solubility, molecular weight, crystallinity, cross-linking, needle dimensions and local fluid availability. The method is attractive for vaccines and molecules that benefit from prompt deposition, but the amount and rate of release should be measured in skin-relevant conditions rather than inferred from bulk dissolution alone. [6], [20].

C. Diffusion-mediated release In hydrogel-forming systems, interstitial fluid enters the cross-linked network and the drug diffuses through the hydrated polymer. The effective diffusion coefficient depends on mesh size, polymer concentration, cross-link density, drug molecular dimensions and interactions between the drug and polymer. Increasing cross-link density may improve mechanical integrity but reduce swelling and slow diffusion. A reservoir-backed design can maintain a concentration gradient for longer than a finite drug-loaded needle alone [6].

D. Degradation- and erosion-controlled release Biodegradable polyester matrices release drug through a combination of diffusion and polymer degradation. Water penetrates the matrix, ester bonds undergo hydrolysis, and polymer molecular weight decreases. Depending on polymer composition and geometry, degradation may be bulk-eroding or surface-influenced. Drug release may show an initial burst from surface-associated drug followed by a slower phase as the matrix hydrates and degrades. Polymer composition, molecular weight, crystallinity, porosity, drug solubility and local pH all influence the profile.

E. Biphasic and layered release A rational design for chronic therapy may require an initial loading dose followed by maintenance exposure. Layered or blended MNs can achieve this by combining a rapidly dissolving fraction with a slowly degrading depot. In a reported PLGA system, a hydrophilic or dissolving component was combined with a heat-melted PLGA layer to provide insertion and separation while retaining a sustained-release component [5]. The PCL/PLGA literature also describes blending or layering with hydrophilic polymers to adjust early release and prolong subsequent release [4]. Such designs require measurement of both phases and confirmation that the early burst is neither excessive nor inadequate.

F. Stimuli-responsive release Stimuli-responsive polymers can alter swelling, degradation or drug diffusion in response to pH, temperature, glucose, enzymes, redox conditions or external energy. Glucose-responsive MN insulin systems are of particular interest because they aim to couple insulin release with local glucose concentration. However, responsiveness observed in simplified buffer systems may not reproduce the complexity of human interstitial fluid. Sensor specificity, response time, insulin stability, dose limits and failure-safe behaviour are central design requirements. [12], [13], [16], [21].

G. Drug-carrier integration Liposomes, polymeric nanoparticles, lipid nanoparticles and microparticles can be incorporated into MN matrices to protect labile drugs or alter release. The MN array provides access across the skin barrier, while the carrier controls local distribution and release. This can be useful for poorly soluble drugs, vaccines and macromolecules. The composite system must be characterized at each level: carrier size and integrity, drug encapsulation, polymer compatibility, insertion, carrier recovery from skin and final pharmacological activity. [6], [20].

VIII. THERAPEUTIC APPLICATIONS

A. Vaccination The epidermis and dermis contain antigen-presenting cells, including Langerhans cells and dermal dendritic cells. MN-mediated vaccine delivery can therefore target immunologically active skin compartments. Vaccine payloads may be present as soluble antigen, suspension, particulate formulation or nucleic-acid-based material. Potential advantages include reduced needle fear, simplified administration and the possibility of improved antigen stability in dry formulations. The vaccine review in the supplied corpus highlights dosing adequacy, stability, sterility and cold-chain considerations as unresolved requirements [9]. These advantages remain formulation- and product-specific; a patch cannot be assumed to eliminate cold-chain needs without stability data. [6], [20].

B. Diabetes and metabolic disease Insulin is a major target for MN delivery because it is a peptide that is not suitable for conventional oral administration.

Dissolving MNs can deliver insulin into skin, while glucose-responsive systems aim to regulate release in response to local glucose levels. The source set also includes microneedle research for metabolic disease and bone-related disorders. These applications remain largely preclinical and require rigorous pharmacokinetic and pharmacodynamic comparisons with established routes. For insulin, critical endpoints include onset, duration, dose accuracy, hypoglycaemia risk, peptide integrity and performance during repeated application. [12], [13], [16], [21].

C. Long-acting antiviral and contraceptive delivery Long-acting delivery is a key rationale for biodegradable polymeric MNs. The 2026 melt-cast PCL study investigated islatravir, an antiretroviral candidate, and levonorgestrel as example payloads for long-acting therapy and contraception [8]. The PLGA layered-MN study reported nearly four weeks of release in its experimental system [5]. These findings support continued exploration of polymer depots, but duration measured in vitro must not be equated with sustained therapeutic plasma concentrations in humans. Human translation requires dose scaling, skin tolerability, pharmacokinetic modelling, removal or biodegradation assessment and evaluation of variability between application sites. [4], [8], [24].

D. Dermatology and wound management MNs can deposit anti-inflammatory, antimicrobial, antifungal and wound-modulating agents within skin layers that are difficult to reach with topical products. Hydrogel-forming systems can also be designed to absorb fluid or deliver molecules through swollen channels. Applications described in the supplied reviews include wound healing, hair loss, skin disease and local cancer treatment [6]. The therapeutic value depends on disease location, lesion condition, skin thickness and the balance between local drug exposure and systemic absorption.

E. Oncology and local immunotherapy Polymeric MNs can provide localized delivery of chemotherapeutic agents, immunomodulators or nanoparticle formulations to superficial tumours and skin lesions. Local delivery may increase concentration at the target while limiting systemic exposure, although this benefit must be demonstrated for each drug and tumour model. Stimuli-responsive and photoresponsive MNs have also been explored to combine local drug release with photothermal or photodynamic effects [3]. The complexity of combination systems increases the need for integrated safety and efficacy evaluation.

F. Neurodegenerative disease and phytobioactive compounds One supplied review discusses microneedles as carriers for phytobioactive compounds intended to address mitochondrial dysfunction in neurodegenerative disorders [10]. The proposed rationale includes bypassing the stratum corneum and increasing systemic exposure to compounds with limited oral bioavailability. However, transdermal delivery does not itself demonstrate delivery across the blood–brain barrier. Evidence of brain exposure, target engagement and clinical benefit must be established independently. This application should therefore be presented as exploratory rather than as a validated treatment strategy.

G. Diagnostics and theranostics Hydrogel and sensor-integrated MNs have been investigated for sampling interstitial fluid and monitoring biomarkers. Polymer matrices can provide a substrate for electrochemical or optical sensing, while drug-loaded structures can potentially combine monitoring and therapy. Such devices introduce additional requirements for sensor calibration, biofouling control, signal drift, skin compatibility, data interpretation and electrical safety.

IX. EVALUATION AND QUALITY CHARACTERIZATION

A. Physical and morphological characterization Needle height, base width, tip radius, pitch, array uniformity and backing-layer thickness should be measured by optical microscopy, profilometry or electron microscopy as appropriate. Defects such as blunt tips, incomplete cavities, voids and cracks may compromise insertion and dose delivery. Polymer composition, molecular weight, thermal transitions, crystallinity and residual moisture should also be characterized where relevant.

B. Mechanical strength and insertion testing Compression testing can estimate the force at which individual needles or arrays deform or fracture. Insertion testing should use excised skin or a validated skin model and

should quantify insertion depth and the proportion of needles that penetrate. Parafilm-based tests can provide a screening tool but do not fully reproduce skin mechanics. A robust evaluation should combine mechanical testing with histological or imaging confirmation of insertion and should test the array after storage.

C. Drug content, uniformity and release Drug content and content uniformity should be assessed across individual patches and, where feasible, across needle tips and backing layers. Release studies should specify medium composition, volume, temperature, agitation, sampling schedule and sink conditions. For biodegradable matrices, polymer mass loss and molecular-weight change can help distinguish diffusion from degradation-controlled release. Mass balance is important: apparent incomplete release may reflect drug adsorption, degradation or analytical recovery issues rather than true retention.

D. Skin permeation and pharmacokinetics Ex-vivo skin permeation studies can measure drug deposition in stratum corneum, epidermis and dermis, as well as receptor-compartment transport. The appropriate endpoint depends on whether local or systemic delivery is intended. In vivo pharmacokinetic studies should compare exposure, peak concentration, time to peak, duration above a target concentration and variability against a clinically relevant reference. For long-acting systems, both early burst and terminal release phases require evaluation. [4], [8], [24].

E. Biocompatibility and safety Safety assessment should include irritation, erythema, oedema, sensitization, infection risk, local inflammation, histopathology and systemic toxicity where relevant. For implanting or slowly degrading systems, the persistence of polymer fragments and degradation products must be assessed. Sterility, endotoxin, particulate contamination and package integrity are critical for products that breach the skin barrier. Repeated-use studies should evaluate cumulative tissue response.

X. CHALLENGES AND TRANSLATIONAL LIMITATIONS

Mechanical performance and drug release can conflict. Increasing polymer concentration or cross-linking may strengthen the needle but reduce dissolution, swelling or diffusion. Increasing drug loading can weaken the matrix or cause phase separation. These trade-offs require formulation design around the intended dose and clinical schedule rather than maximizing a single material property.

Reproducible manufacturing is another major challenge. Micromould filling, drying, demoulding and thermal processing can produce variability in needle geometry, drug content and insertion behaviour. A clinically useful process must define critical material attributes and critical process parameters, establish in-process controls, and demonstrate batch-to-batch consistency. The broader microneedle field has shown growing activity in publications, patents and clinical studies, but activity alone does not establish commercial readiness [1].

Drug stability can be affected by moisture, temperature, solvent exposure, shear, light and polymer degradation. Biologics are especially vulnerable to unfolding, aggregation or loss of potency during fabrication and storage. Accelerated stability studies should be complemented by real-time testing in the final package. For melt-cast systems, thermal stability of both drug and excipients must be established before selecting the processing temperature [5], [8].

Clinical translation also requires clear dose delivery and user performance. The amount of drug loaded into a patch is not necessarily the amount delivered into skin. Application force, duration, skin site, age, hydration, skin disease and user technique can alter insertion and release. Applicator devices may improve reproducibility but can increase cost and complexity. Human factors studies are needed to establish safe and reliable use.

Regulatory classification may involve both drug and device requirements. Developers must define whether the polymer is a drug carrier, an implanting component or a device structure, and provide evidence for material quality, biocompatibility, sterility, stability, performance and clinical benefit. Long-acting products need particular attention to reversibility and management of adverse effects because a retained depot cannot always be removed after application. [4], [8], [24].

XI. FUTURE PERSPECTIVES

Future work should prioritize polymer–drug–device co-design. Rather than selecting a polymer solely because it is biocompatible or easy to mould, developers should match its degradation, hydration and mechanical behaviour to the molecule and intended exposure profile. A rapid-dissolving HA or PVP tip may be appropriate for a vaccine, whereas a PCL or PLGA depot may be more appropriate for prolonged delivery of a stable small molecule. Hybrid systems may be needed when both loading and maintenance phases are required. [6], [20].

Advanced manufacturing may improve reproducibility through precision moulds, automated filling, process analytical technology and additive manufacturing of master structures. Digital design and finite-element modelling can help predict stress distribution, insertion force and deformation, but predictions should be validated experimentally in skin. Automated imaging and machine-vision inspection may help detect defective needles before release.

Long-acting MN research should report release profiles in clinically interpretable terms and distinguish in-vitro release duration from in-vivo pharmacokinetics. Studies should include mass balance, drug potency after release, tissue distribution, polymer degradation, local tolerability and comparison with existing long-acting dosage forms. For responsive systems, investigators should establish response thresholds, response time, reversibility and failure-safe behaviour. [4], [8], [24].

Finally, the field would benefit from harmonized test methods and reporting standards. A minimum dataset could include polymer identity and grade, molecular weight, needle geometry, array density, drug loading, insertion force, insertion efficiency, delivered dose, release method, skin model, stability, sterility and local tissue response. Such standardization would improve cross-study comparability and help distinguish promising prototypes from candidates ready for clinical development.

Evidence interpretation across the included corpus. The source set contains narrative and focused reviews, bibliometric analysis, and original experimental studies. These designs answer different questions and should not be treated as interchangeable. For example, the heat-melted PLGA layered system reported release over nearly four weeks in its experimental setting, while the melt-cast islatravir work evaluated a distinct long-acting formulation platform; neither result alone establishes a corresponding duration of clinical protection in humans. Likewise, the imiquimod nanocrystal study supports improved ex vivo skin delivery relative to its semisolid comparators, and the exosome/EGCG study provides preclinical evidence for a specific UV-injury model. Such findings are promising but remain formulation-, drug-, model-, and endpoint-dependent. Clinical readiness must be judged from human safety, dose delivery, usability, stability, and manufacturing evidence rather than from in vitro release duration alone [14], [16], [22], [24].

CONCLUSION

Polymeric microneedles provide a versatile platform for crossing the stratum corneum and delivering therapeutic agents into skin with limited invasiveness. Their central advantage is the ability to combine a skin-penetrating microstructure with polymer-controlled drug loading and release. Hydrophilic polymers such as HA, PVP, PVA and CMC are useful for rapidly dissolving systems, while biodegradable polyesters such as PLGA, PLA and PCL can support slower release and depot formation. Hydrogel-forming and hybrid systems add further control through swelling, diffusion and layered design.

The supplied literature illustrates the breadth of applications, from vaccination and insulin delivery to dermatology, wound treatment and long-acting antiviral or contraceptive delivery. Heat-melted PLGA and melt-cast PCL examples demonstrate promising approaches to sustained delivery, but remain evidence from specific experimental systems rather than proof of clinical performance. The major barriers are dose reproducibility, material and drug stability, mechanical reliability, sterility, safety of retained polymers, scale-up and regulatory validation. Progress will depend on rigorous, standardized testing and on selecting polymer chemistry and architecture according to the therapeutic objective. [4], [8], [24].

ACKNOWLEDGMENT

The authors acknowledge the academic guidance and institutional support provided by Dhanalakshmi Srinivasan University during the preparation of this review article. The authors also recognize the contributions of researchers whose published studies have advanced the understanding of polymeric microneedle systems, polymer selection, fabrication technologies, drug-release mechanisms, and therapeutic applications in transdermal drug delivery.

SCIENTIFIC SCOPE AND INTERPRETATION OF EVIDENCE

This narrative review examines the development of polymeric microneedle-based transdermal drug delivery systems, emphasizing the relationship between polymer physicochemical properties, microneedle architecture, fabrication methods, drug-loading strategies, and release behavior. Particular attention is given to dissolving, biodegradable, hydrogel-forming, and composite microneedle platforms. The review discusses the roles of hydrophilic polymers in rapid dissolution and drug liberation, biodegradable polymers in sustained delivery, and crosslinked hydrogel networks in swelling-mediated transport. Therapeutic applications are considered in relation to the type and maturity of the supporting evidence, including laboratory investigations, preclinical studies, and clinical research where available.

Although experimental findings demonstrate the potential of polymeric microneedles to improve localized and systemic drug delivery, successful clinical translation requires further consideration of insertion reproducibility, mechanical integrity, dose uniformity, polymer biocompatibility, sterilization compatibility, long-term stability, and scalable manufacturing. Accordingly, promising laboratory outcomes should not be interpreted as established clinical efficacy without supporting human studies.

AUTHOR CONTRIBUTIONS

Anthoni Ambrose A., Karthigeyan R., Kirubakaran M., Pipenerick A., Prasanna T., and Priyadharshan M. collectively contributed to the conceptualization of the review, literature collection and analysis, interpretation of scientific information, and development of the manuscript. All authors collaboratively participated in drafting, reviewing, editing, and revising the manuscript. All authors read and approved the final version of the manuscript and accept responsibility for the accuracy and integrity of the work

CONFLICT OF INTEREST

The authors declare that they have no known financial or non-financial conflicts of interest that could have influenced the preparation, interpretation, or presentation of this review article.

The authors received no specific financial support from public, commercial, or not-for-profit funding agencies for the preparation of this review article.

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HOW TO CITE: Anthoni Ambrose, Karthigeyan, Kirubakaran, Pipenerick., Prasana, Priyadharshan, Polymeric Microneedles for Transdermal Drug Delivery Advances in Material Engineering, Fabrication Technologies, Drug Release Mechanisms and Therapeutic Applications, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 11, 5756-5767. https://doi.org/10.5281/zenodo.24583278