



Microneedle Patches for Transdermal Drug Delivery: Design, Fabrication and Applications

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ABSTRACT

Transdermal drug delivery systems (TDDS) offer advantages including avoidance of first-pass metabolism and improved compliance, but transport is restricted by stratum corneum (SC) barrier. Microneedle patches (MNPs) comprising 25–2000 μm projections have emerged as minimally invasive platform that disrupts SC to create transient pathways for systemic and localized delivery of small molecules, proteins, vaccines and biologics with reduced pain and infection risk.

MNPs are classified into solid, coated, hollow and dissolving types based on architecture and release mechanism. Materials include silicon, metals (SS 304/316L, titanium), glass, ceramics and biodegradable polymers like hyaluronic acid, PVA, PVP. Geometrical optimization (150–1500 μm length, 50–250 μm width) influences penetration efficiency.

Fabrication methods such as micromolding, photolithography, laser ablation, atomized spraying and droplet-born air blowing (DAB) determine dimensional accuracy, mechanical strength and scalability. Evaluation includes dimensional, mechanical, in-vitro permeation and in-vivo studies. Despite limitations of dose variability and limited loading, MNPs show broad applications in vaccination, insulin, anesthesia, cosmetology and cancer therapy, representing a promising next-generation transdermal technology.

Keywords: Microneedle patches, Transdermal delivery, Stratum corneum, Dissolving microneedles, Fabrication

1. INTRODUCTION

Transdermal drug delivery systems (TDDS) provide major therapeutic advantages, including the avoidance of hepatic first-pass metabolism and enhanced patient compliance [1]. However, the clinical transport of most molecules across the skin is heavily restricted by the robust hydrophobic barrier function of the stratum corneum (SC) [2]. To overcome this limitation, microneedle patches (MNPs) have emerged as an innovative, minimally invasive technological platform [3]. Composed of micron-sized projections ranging from 25 to 2000 μm in length, MNPs disrupt the SC to create temporary pathways for localized or systemic delivery of broad therapeutic payloads, including proteins, macromolecules, and vaccines. By avoiding structural tissue damage and nerve contact, this technology significantly minimizes pain, reduces infection risk, and provides a highly efficient alternative to conventional hypodermic injections for clinical translation [6]

2. Microneedle definition :

Microneedle patches represent a sophisticated, minimally invasive platform designed to overcome the skin's natural barriers. These systems feature an array of microscopic projections typically ranging from 25 to 2000 μm in height [7,8]. When applied to the skin, they seamlessly penetrate the outer stratum corneum layer to establish microscopic pathways [7]. These transient channels facilitate the direct transport of incorporated pharmaceuticals, vaccines, or cosmetic agents into the viable epidermal and dermal layers [8]. Because the microprojections are engineered to remain within these superficial tissue layers, they successfully achieve efficient target delivery while avoiding deeper blood vessels and dermal nerve endings, ensuring a virtually painless Applications

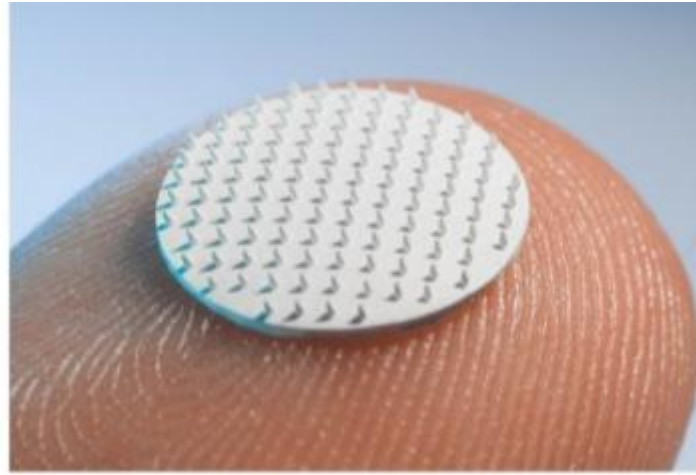


Fig. 1. Microneedle patch applied to the skin for transdermal drug Delivery

3. Classification of Microneedles

Microneedles are categorized by their structural architecture, drug-loading approach, and release mechanism into four major classes: solid, coated, hollow, and Dissolving.

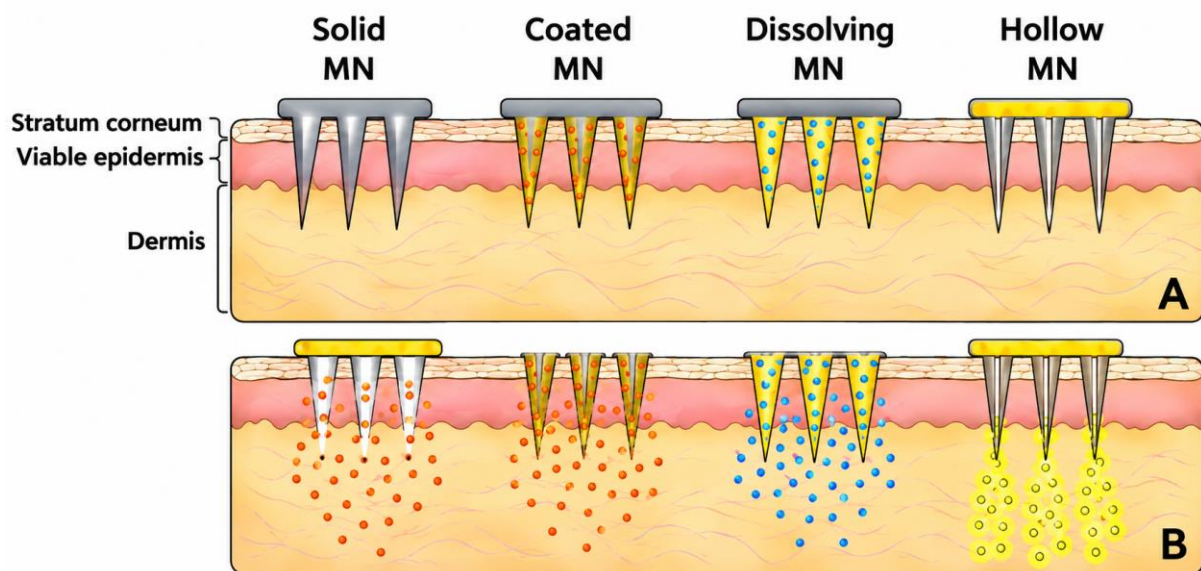


Figure.2 Types of microneedle patches and drug delivery mechanisms.

3.1 Coated Microneedles

Coated microneedles carry therapeutic payloads directly onto the external surface of sharp micro-projections. Fabrication primarily relies on controlled dip-coating into concentrated drug reservoirs or uniform spray-coating methods to achieve a thin, solid operational layer that dissolves rapidly post-insertion [11].

3.2 Solid Microneedles

Solid microneedles operate via a mechanical 'poke-and-apply' sequence, utilizing drug-free micro-projections to puncture temporary microchannels across the hydrophobic stratum corneum. A subsequent topical formulation is then applied to diffuse into the deep dermis. Due to demanding physical stress, high-strength substrates like medical metals or silicon are strictly preferred [12].

3.3 Hollow Microneedles

Hollow microneedles integrate an internal microfluidic bore within the needle shaft to resolve the dosing control limitations of solid arrays. This platform supports continuous, pressure-driven active infusion of fluid formulations spanning both small molecules and heavy biological payloads. Silicon, glass, and specialized metals are standard substrates [13].

3.4 Dissolving Microneedles

Dissolving microneedles fully incorporate therapeutic agents directly inside a water-soluble or biodegradable polymeric matrix. Upon insertion, interstitial skin fluid triggers immediate matrix breakdown, releasing embedded proteins, peptides, or biomolecules at a rate dictated by polymer erosion. This leaves zero sharp clinical bio-waste [14].

4 Skin Anatomy and barrier functions :

Human skin comprises epidermis, dermis and hypodermis, where the outermost stratum corneum (SC) with characteristic brick-and-mortar structure, in which dead, keratin-filled corneocytes are surrounded by tightly organized intercellular lipids, acts as the principal barrier to transdermal delivery. This compact hydrophobic arrangement restricts passive transport to drugs <500 Da, while hydrophilic macromolecules show poor penetration. The SC consists of piles of dead corneocytes that are the end-products of terminal differentiation of epidermal keratinocytes and performs a crucial barrier function. Microneedles overcome this by creating temporary microscopic pathways through SC to reach viable epidermis.[15][16]

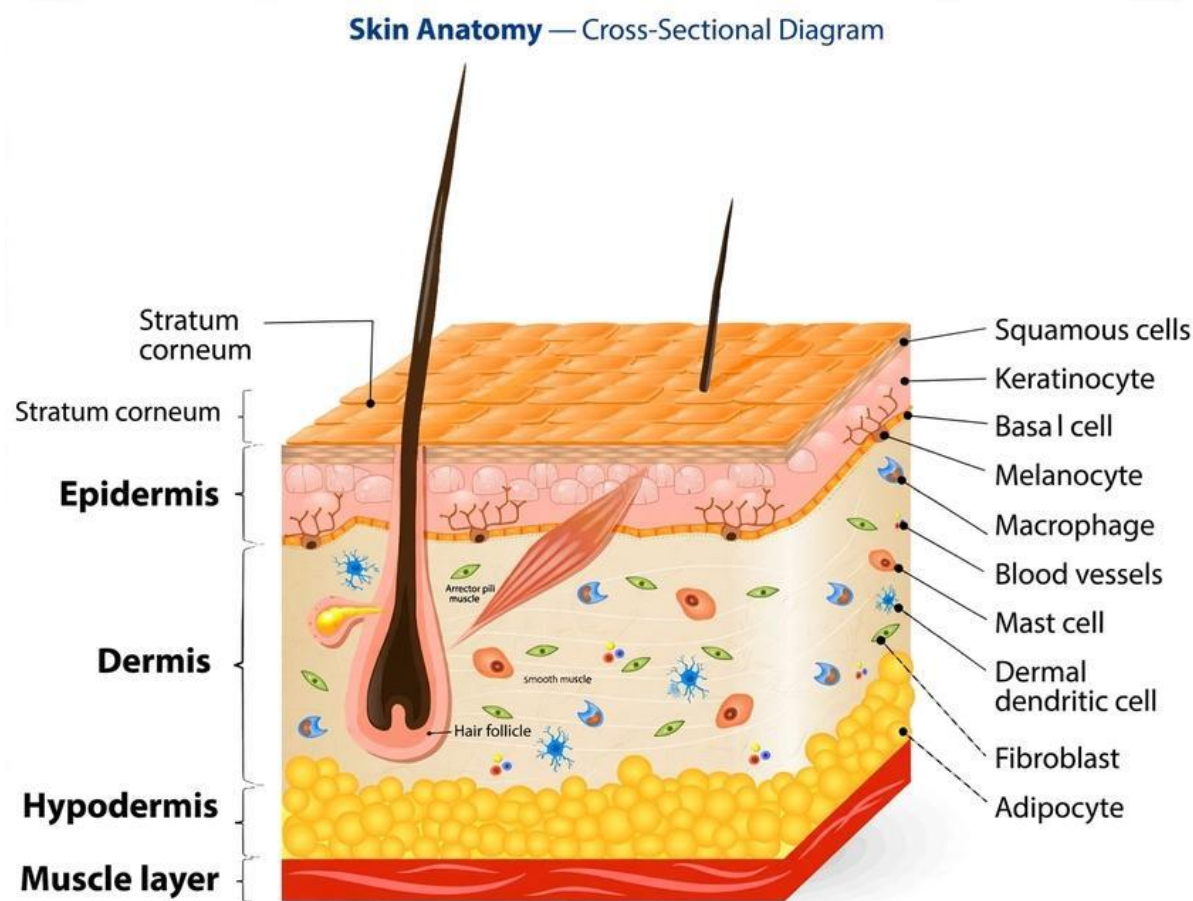


Figure 3. Cross-sectional anatomy of human skin showing its major layers and cellular components.

5. Mechanism of action

The operational mechanism of a microneedle patch relies on an array of ultra-fine, microscopic tips designed to penetrate just deep enough to bypass the skin's tough outer barrier, the stratum corneum [17]. By specifically targeting the epidermis and dermis zones, these micro-tips deploy therapeutic agents directly into the heart of a deep-seated infectious microbial biofilm [17]. Because the needles are engineered to be extremely short, they deliberately avoid reaching the lower hypodermis layer, thereby leaving the primary nerve networks untouched to ensure a completely painless treatment [18]. In stark contrast, traditional topical creams and topical patches lack the structural capability to break through the surface; their large therapeutic molecules simply

sit on top of the stratum corneum, rendering them ineffective against deep infections [17]. Meanwhile, a standard hypodermic needle can easily reach the biofilm but must plunge all the way down into the deep hypodermis layer to stabilize, which inevitably strikes the underlying nerve fibers, causing significant pain and tissue trauma [18].

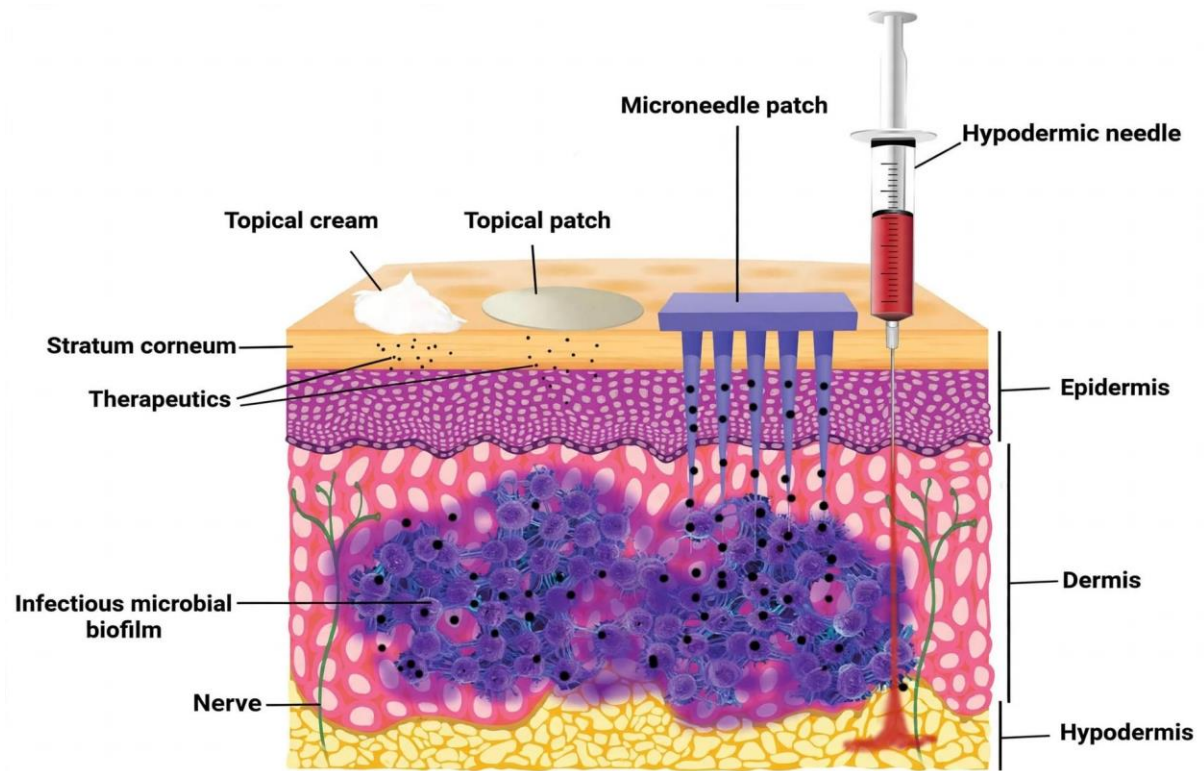


Figure:4 Comparison of microneedle patches with conventional topical and hypodermic drug delivery methods

6. Materials Used for Microneedle fabrication

6.1. Silicon:

Biocompatible and bio-inert material. Benefiting from advanced semiconductor manufacturing, it is processed via single-step wet-etching to create both solid and hollow microneedles that efficiently deliver therapeutics through the skin dermal barrier [19].

6.2. Ceramic:

Suitable for fabrication due to easy molding properties, though highly fragile.

Micro- and nanofabricated ceramic needle structures carry an inherent risk of fracturing or breaking in the tissue during manual insertion [20].

6.3. Glass:

Offers structural rigidity, chemical stability, and sterilization tolerance. Primarily used in hollow architectures via micropipette pulling or wet etching; however, its brittleness can leave fragments that induce local skin inflammation [21].

6.4. Metals:

Stainless steel (304/316L) and titanium offer excellent mechanical strength, ductility, and fracture resistance. Produced via laser cutting or electrochemical etching to yield sharp tips that minimize patient discomfort [22].

6.5. Polymers:

Flexible, cost-effective, and highly versatile materials. Natural biodegradable variants like hyaluronic acid dissolve instantly upon contact with skin interstitial fluids to release active therapeutic compounds [23].

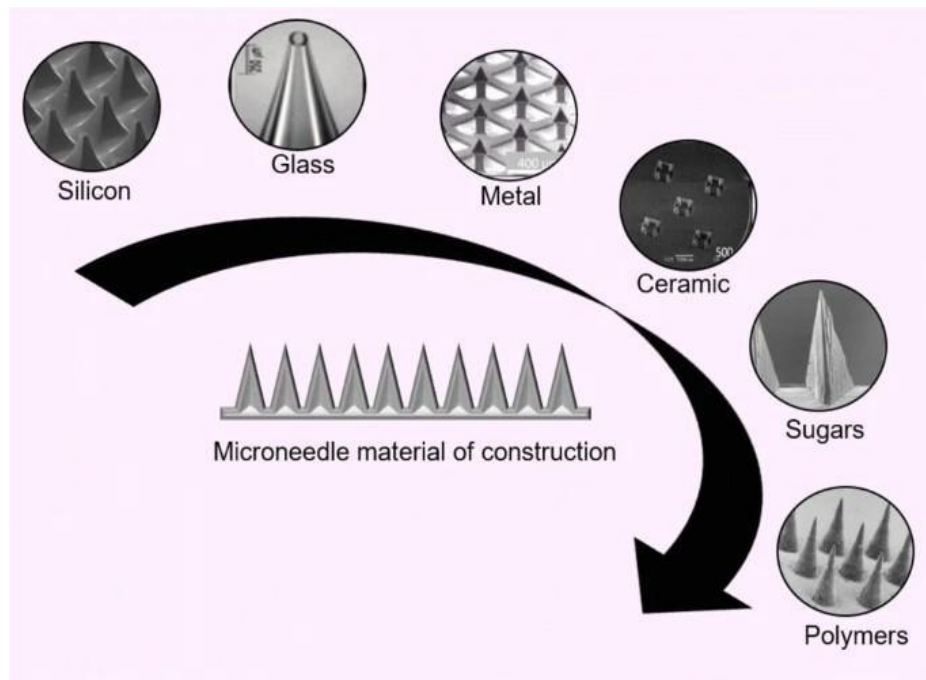


Figure:5 Materials used for microneedle fabrication.

7. Dimensions of microneedle

Geometrical optimization and specific dimensions of Microneedle patches Microneedles are generally 150–1500 μm long and 50–250 μm wide, with tip thicknesses of 1–25 μm . Their dimensions and shapes, including cylindrical, triangular, pointed, pentagonal, and octagonal designs, influence skin penetration and drug delivery [24]

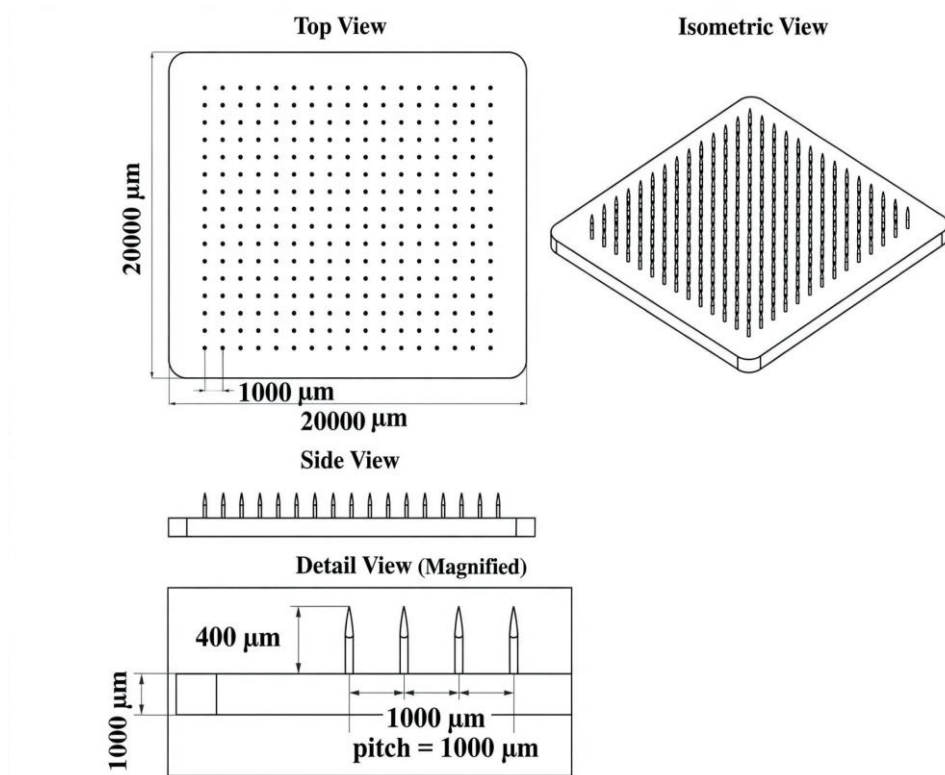


Figure.6 Geometrical Dimensions and Array Configuration of a Microneedle Patch.

8. Fabrication technologies:

Fabrication technology plays a crucial role in determining the dimensional accuracy, mechanical strength, drug loading capacity, and commercial scalability of microneedle patches. The selection of appropriate fabrication method depends on the type of material, drug characteristics, and intended therapeutic application

8.1. Micro-molding :

Micromolding is a simple and cost-effective method for fabricating microneedles. A suitable material is filled into needle-shaped mold cavities and solidified to form microneedles. This technique provides uniform dimensions, good reproducibility, and large-scale production. Polymers and hydrogels are commonly used. However, incomplete mold filling and needle damage during removal may affect quality. Vacuum-assisted filling and centrifugation can help overcome these problems. Despite these limitations, micromolding is widely used for polymeric microneedle fabrication.[25][26]

8.2 Photolithography

Photolithography is widely used to fabricate solid and hollow microneedles, including silicon, dissolving and hydrogel-forming types, by creating a negative mold. A cleaned silicon substrate is coated with a sacrificial layer and spin-coated photoresist, then aligned with a photomask and exposed to UV light. After development, the pattern serves as an etch mask, and exposed silicon is etched to form microneedles, transferring the design from mask to substrate.[27][28]

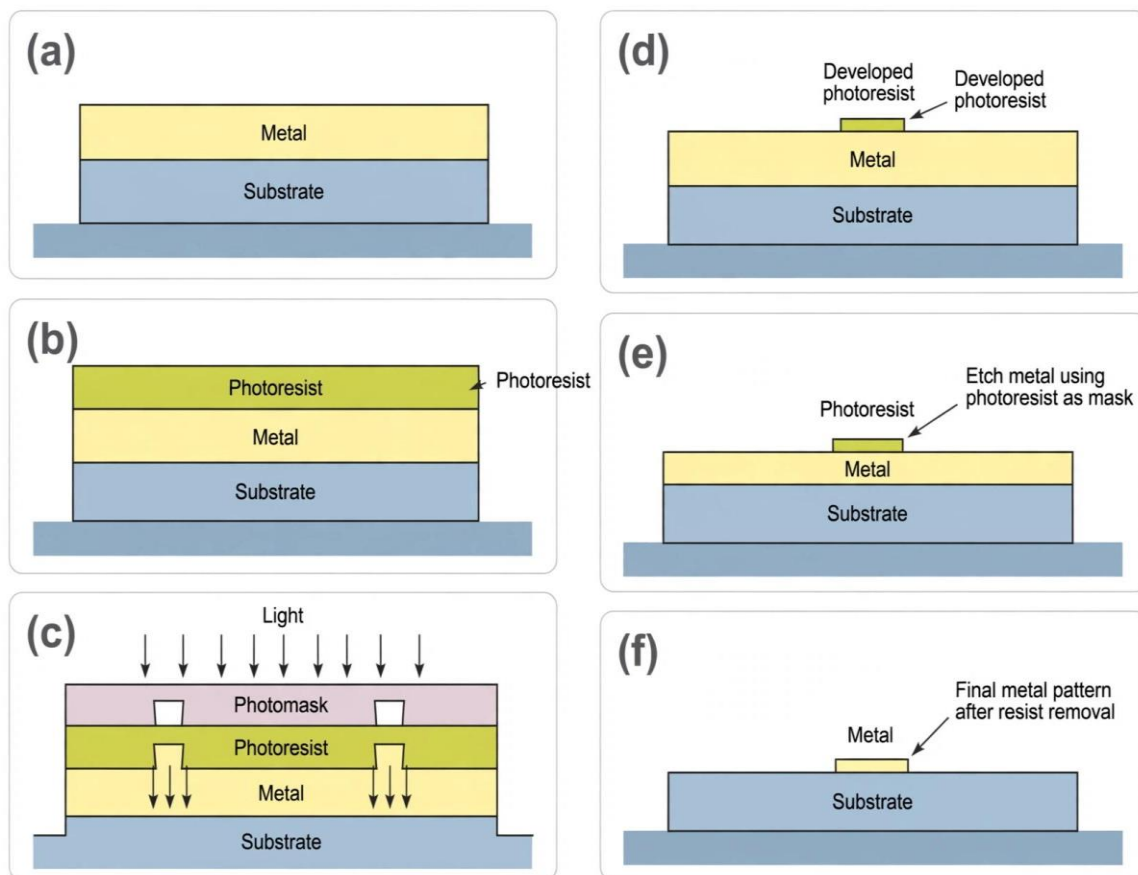


Figure:7 Photolithography process (a) Metal on substrate, (b) Photoresist coating, (c) Exposure via photomask, (d) Developed resist, (e) Metal etching, (f) Final Patterns

8.3 Laser Ablation:

Laser ablation uses a femtosecond laser to selectively remove material and create microneedle cavities in a mold insert. Laser parameters such as wavelength, pulse energy, and repetition rate are optimized, and a cross-hatching scan produces well-defined circular cavities. The insert is then used for injection molding under controlled mold temperature, injection rate, and pressure. Mold cavities are examined by micro-CT and replicated microneedles by microscopy.[29]

8.4 Atomized Spraying Method:

Atomized spray filling is used to fabricate dissolving microneedles with controlled geometry. The formulation is atomized into a fine mist and sprayed into a PDMS mold, then dried, which minimizes filling issues from interfacial tension and uneven thickness. Materials like PVA, PVP, CMC, HPMC, and sodium alginate are suitable. Repeated spraying enables multilayered microneedles by adjusting conditions and layers.[30]

8.5 Droplet-born air blowing (DAB)

Droplet-born air blowing (DAB) is a mold-free method that forms polymeric microneedles without heat or UV. Polymer droplets on two plates are contacted and separated at controlled speed, then solidified by air blowing. With cyclic contact and drying (CCDP), dissolvable patches detach easily. It controls droplet size and drug loading without waste in ~10 min.[31]

Table:1 Overview of microneedle fabrication techniques, principles and materials[25-31]

S.no	Technology	Principle	Materials	Applications
1	Micro-molding	PDMS mold filling And solidification	Polymers PVP PVP,Hydrogels	Dissolving hydrogel patches for vaccine and insulin
2	Photolithography	Photoresist + photomask UV Etching	Silicon ,SU -8 Dissolving polymers	Solid hollow high Precision molds
3	Laser Ablation	Femtosecond laser for mold inserts	Mold inserts	Mass production cavities by micro CT
4	Atomized Spraying	Fine mist spray in to PDMS mold dried	PVA,PVP,CMC,HHPM C alginate	Multilayer Dissolving for vaccines and cosmetics
6	Droplet born air blowing	Two plates contact separate air solidification	Polymer Sugars	Mold free,~10 min,no drug waste

9.Administration of Microneedle Patches

Before application, assess patient for comorbidities. Procedure:

1. Skin preparation: Clean and disinfect site to remove dirt, oil.
- 2.Application: Place patch on recommended site, press gently for good contact.
- 3.Follow-up: Monitor for irritation, discomfort or local reactio

Table Adherence: Follow prescribed instructions for site, duration and replacement

10.Evaluation of microneedle patches :

1. Drug evaluation: Particle size, PDI, viscosity, zeta potential for stability; release, adhesion and penetration profiles.
2. Dimensional: Height, base width, tip radius; optical microscopy, SEM and confocal for 3D morphology.[32]
3. Mechanical: Strength and insertion force to ensure integrity against tissue resistance.
4. In-vitro permeation: Diffusion cells to track drug transport across dermis.
5. In-vivo studies: Hairless rodents for systemic response; TEWL for barrier disruption/healing measured by VapoMeter.[33]

11.Advantages of Microneedles

- Minimally invasive, reduces pain and discomfort

- Bypasses first-pass metabolism, improves bioavailability
- Rapid onset, higher plasma levels and faster healing
- Precise epidermal deposition via microchannels, enhances permeation
- Delivers wide range from small drugs to Biologics[34]
- Controlled, sustained release - reduces dose, side effects and frequency
- Lowers infection, needle-stick injury and tissue trauma risk
- Superficial penetration - less microbial contamination
- Self-administrable, improves compliance, useful in emergencies
- Well-tolerated with minimal edema or erythema [35]

12.Limitations of Microneedles

- Dose accuracy and reproducibility difficult compared to hypodermic injections
- Requires proper handling and application to avoid drug loss and ensure uniform penetration
- Skin thickness and stratum corneum variation affects insertion and transport
- Hydration level alters permeability and Absorption[36]
- Hollow type fails to penetrate thick, keratinized skin
- Tip breakage during insertion/removal may leave fragment in skin
- Limited drug loading capacity, not suitable for high-dose therapies
- Design and fabrication with adequate strength, loading and release is technically complex
- Some formulations need specialized design, increasing development costly[37]

13.Applications of Microneedles

- Vaccine delivery: Avoids hypodermic injections, improves compliance and stimulates skin immune cells for effective immunization
- Insulin delivery: Creates microchannels for systemic absorption, improves convenience and glucose control
- Parathyroid hormone: Alternative transdermal route for osteoporosis, shows promising bone health outcomes
- Anesthetic delivery: Lidocaine via microneedles makes minor procedures more comfortable
- Cosmetics: Microchannels stimulate collagen, improves texture, wrinkles and acne scars [38]
- Naltrexone: Sustained transdermal delivery for substance dependence management
- Diagnosis and biosensing: Samples interstitial fluid for glucose, lactate, alcohol and biomarker monitoring
- Iron supplementation: Ferric pyrophosphate patches as alternative for anemia
- Protein delivery: Transports albumin, ovalbumin across skin barrier
- Cancer therapy: Localized delivery of drugs, proteins, vaccines and photodynamic agents like 5-aminolevulinic acid near tumors with minimal systemic exposure
- Ophthalmic delivery: Alternative to intravitreal Injections and reduce complication[39]

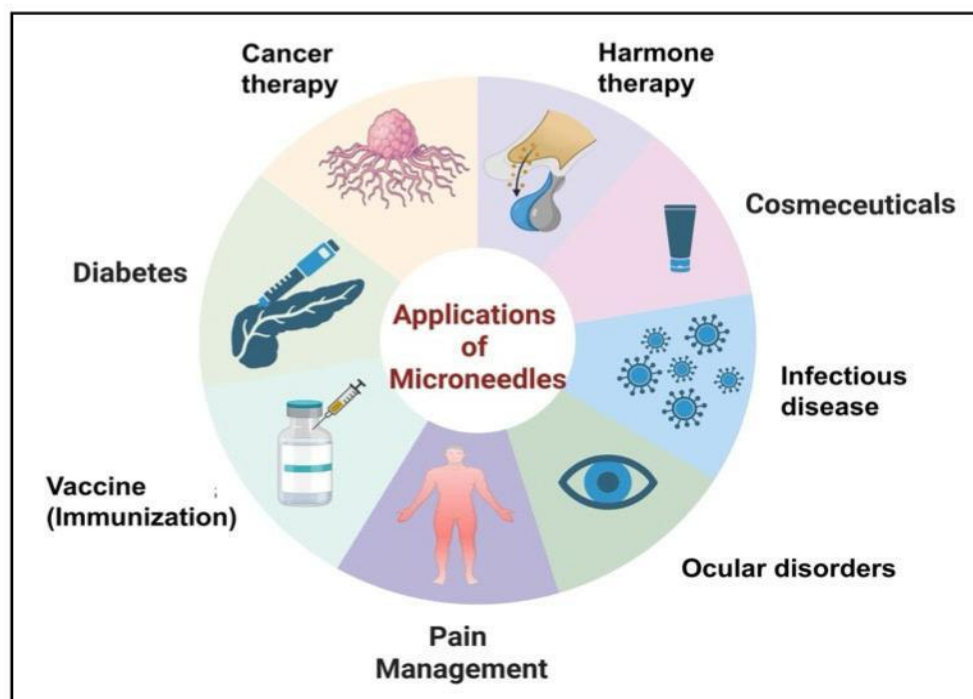


Figure applications of microneedles

14. Current Research, Challenges and Future Trends

Initially microneedles focused on silicon structures to overcome skin barrier and deliver macromolecules like albumin and insulin. Cadaver skin permeation studies confirmed enhanced transport, encouraging advanced designs and patient-friendly systems.[40]

However challenges remain before clinical and commercial translation. Safety, efficacy and regulatory acceptance need extensive evaluation. Skin reactions such as redness, irritation and allergy may occur. Drug loading capacity is limited, and hydrophilic, high-molecular-weight compounds show poor transdermal delivery. Fabrication material must provide sufficient mechanical strength to avoid failure during insertion. Ideal system should enhance permeation with minimal pain and tissue damage. Application and proper placement may be difficult for some patients. Incomplete microchannel closure after removal may increase microbial entry and infection risk.[41]

15. Conclusion

Microneedle patches (MNPs) have emerged as a minimally invasive platform that overcomes stratum corneum barrier while ensuring patient compliance and painless delivery. With dimensions of 25–2000 μm , they create transient microchannels for precise deposition of small molecules, proteins, vaccines and biologics, bypassing hepatic first-pass metabolism and enhancing bioavailability.

Four architectures — solid, coated, hollow and dissolving — fabricated from silicon, metals, ceramics, glass and biodegradable polymers like hyaluronic acid, provide versatility. Techniques such as micromolding, photolithography, laser ablation, atomized spraying and DAB enable scalable production with controlled loading and zero bio-waste in dissolving systems.

Despite advantages, challenges including dose reproducibility, limited loading, skin variability and tip breakage require optimization. With demonstrated potential in vaccination, insulin, anesthesia, cosmetology and cancer therapy, continued advances in materials and fabrication will drive clinical translation of MNPs as next-generation transdermal systems.

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