

Microneedles as Novel Drug Delivery Platforms: Fabrication Techniques, Evaluation Methods, and Clinical Potential

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ABSTRACT

Microneedle-based drug delivery has received considerable attention and is rapidly approaching commercialisation owing to the availability of different scalable techniques to yield various microneedles. Numerous materials such as metals, silicones, polymers, and carbohydrates have been employed to fabricate microneedles. Microneedles offer a range of benefits to patients, not only because of their minimally invasive and comfortable nature, but also because of their availability in various geometries. Microneedles are useful for various applications, such as topical, ocular, and nail delivery of small drug molecules, proteins, peptides, and nucleotides. Various fabrication methods for microneedles have been tested for various compounds. Different evaluation tests have been conducted to demonstrate the applicability of microneedles for the delivery of a variety of materials in a desired manner. Microneedles are used in vaccine administration, drug delivery, and cosmetic applications. However, certain issues such as the selection of suitable substances and fabrication techniques that meet the requirements of drug delivery need to be investigated.

Keywords: Cosmetic, Microneedle Fabrication, Microneedles, Mould Fabrication, Ocular Delivery, Topical Delivery.

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INTRODUCTION

Over the last 25 years, interest in nanotechnology used in healthcare has experienced exponential expansion.¹ The need for efficient drug delivery methods that reduce risk remains an ongoing challenge despite technological advances.² New drug delivery technologies are becoming increasingly important.³ Although research continues to emerge from drug discovery projects, problems persist with novel compounds.⁴ High-throughput testing identifies therapeutic molecules, but some face solubility and permeability issues, making distribution difficult using traditional methods.⁵ Many available drugs lack delivery options. While oral and parenteral formulations have been strengthened, significant challenges remain.⁶ Many oral preparations require low doses for therapeutic concentrations, though small doses increase unwanted effects.⁷ Drugs unsuitable for oral delivery due to stability issues are delivered parenterally. Biotherapeutic macromolecules are inappropriate for oral delivery due to proteolytic degradation.⁸

Recently, new methods have emerged for drug delivery. Transdermal delivery is attractive due to benefits like avoiding first-pass degradation and gastrointestinal alterations, ensuring consistent plasma levels, and enhancing patient adherence.^{9,10}

Skin serves as a crucial natural shield protecting the human body. It consists of the epidermis (50-150 μm thick), dermis (1-2 mm thick), and subcutaneous layers, forming a thickness of approximately 3 mm. The epidermis is mainly responsible for skin's obstruction qualities. The stratum corneum is the main barrier to transdermal delivery. The subcutaneous layer comprises 15 to 20 layers of stratified corneocytes, low in lipids but rich in proteins.^{9,11}

Drug particle conveyance through skin is a significant alternative to oral delivery, though skin's barrier properties limit vehicles. Various processes for improving synthetic and physical pervasion have been developed. Microneedle-based devices offer a promising approach to increase particle permeation within skin. Microneedle (MNs) arrays are non-invasive instruments that penetrate skin's microcirculation, bypass the SC barrier, and enable systemic transdermal administration.¹² Microneedles are small enough to avoid piercing dermal blood vessels or activating nerves yet reach the dermis.¹³ MNs are made from materials like steel, silicon, ceramics, biodegradable polymers, sugars, and glass, with varying shapes and lengths (25-2000 μm). The technique's various aspects and delivery mechanisms provide wide applicability. Researchers have explored these approaches



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for different tissues including gastrointestinal tract, eyes, nails and oral cavity. Microneedles have helped standardize drug transport in ocular tissues. These mechanisms for ocular and transdermal delivery can significantly benefit patients and industry, with their full potential emerging in three to five years through diligence and cooperation.⁷⁻⁹

MICRONEEDLES AS A NOVEL APPROACH FOR DRUG DELIVERY

Microneedles were conceptualized in the 1970s, but substantial research began in the 1990s due to developments in microfabrication technology enabling their production.¹⁰ Microneedles are single needles or micrometre-sized needle arrays produced using microelectronic tools.¹⁴⁻¹⁵ Their application to bio-membranes creates micro-dimensional delivery routes and increases active agent penetration through skin obstructions.¹⁶ Various manufacturing methods were developed with different shapes, sizes, and materials. Researchers investigated microneedles in ophthalmology as an alternative to intravitreal injections, exploring various designs and drug delivery pathways.¹⁷ The basic types of microneedles and their drug delivery representation are shown in Figure 1.

MICRONEEDLES TYPES

Solid microneedles

Solid Microneedles (SMNs) create pores on the skin for pre-treatment. The needles' projections penetrate the skin to form micrometer-sized channels, allowing drugs to reach skin layers directly through patches, increasing permeation. Capillaries absorb medications for systemic or localized effects.¹⁸ In a pick, remove, and disperse configuration, solid microneedles placed on skin disrupt the epidermis. Removing them produces temporary microchannels where drug formulations may be added as gels, creams, liquids, or patches. Drugs penetrate these channels via passive diffusion to reach appropriate sites. Solid microneedles improve transdermal transport of molecules that cannot pass through skin by passive diffusion alone, potentially increasing absorption by fourfold.^{11,12} This type can transport large molecular weight compounds, with microchannels recovering quickly without secondary infection. Gupta *et al.* studied skin recovery by modifying microneedle dimensions to estimate barrier resealing time.¹⁹ Materials for solid microneedles include silicone, metals (titanium, stainless steel, tantalum, platinum, nickel), carbohydrates (dextran, maltose, mannitol, sucrose),^{8,18} and silver, ceramics, glass, biodegradable, and synthetic polymers. Major drawbacks include the two-phase procedure requirement and sharp biohazardous residues.¹⁰ The skin's self-regeneration naturally heals and inhibits substance transfer via micropores.^{20,21} Skin-curing methods restrict drug transfer rates.²² One solution uses cyclooxygenase inhibitors to prolong pore life.²³

Coated Microneedles

Coated microneedles comprise a solid array of microneedles, usually made from silicon or metal.²⁴ Coated with medication/vaccine. After skin application, the coated microneedles allow material penetration and absorption. This approach is referred to as 'cover and poke'.^{25,26} The development of solid-coated microneedles aimed to create a standardized application framework more appropriate for patient use.^{14,27} Microneedle surfaces can be treated with aqueous solutions containing pharmaceutical compounds and polymers; however, water-insoluble drugs face challenges including tissue fluid degradation and decreased bioavailability.^{18,28} Li *et al.* coated microneedles with various formulations for co-delivering multiple agents with different properties. Coated microneedles have been used for applications including injury care, analgesic delivery, insulin, anticancer agents, nucleic acids, proteins, and neovascularization.²⁹

Coated microneedles are viable for delivering vaccines or potent medications, but unsuitable for some uses as they cannot hold large quantities of active molecules. When coated, the needles' mechanical stiffness and sharpness decrease, restricting the quantity of medication that can be applied to the surface. Thus, coated microneedles are ideal where large drug volumes, such as in vaccine delivery and cosmetic procedures, are unnecessary.^{11,30}

Hollow microneedles

The "poke and flow" technique involves inserting hollow microneedles under the skin, then delivering medications into the dermis via the microneedle channels, like conventional subcutaneous injections.^{14,31,32} Hollow microneedles contain a vacant space where medication is loaded. Once injected into the skin, the medication enters the epidermis through the tip opening. It is used for substances with high molecular weight, including oligonucleotides, vaccines, and proteins.^{28,29} Unlike solid microneedles, drug patches deliver medication continuously without repositioning. Research showed that silicon hollow MNs with various needle shapes had sufficient structural integrity and sharpness for transdermal applications.²⁵ Hollow microneedles are manufactured using micro molding, deep etching of reactive ion, laser-based micromachining, and upturned construction utilizing carbon nanotubes and LIGA technology.^{11,23,33} Jiang *et al.* demonstrated the intra-scleral distribution of sulforhodamine with microparticles and nanoparticles using a hollow glass microneedle. Hollow microneedles of borosilicate cylindrical glass were created using a micropipette tube.⁷

These devices are made from rubber, silicone, glass, polymers, ceramics, and metals.^{34,35} Hollow microneedles commonly deliver insulin.^{12,25,36} They have been used to deliver protein antigens, large molecular weight substances, vaccines, nucleic acids, and treatments like pilocarpine. Vaccination is their most common application.^{11,24,37} Notably, Suzuki *et al.* developed hollow

microneedles mimicking mosquito behaviour, showing enhanced skin penetration.²⁹

Dissolvable Microneedle

Miyano *et al.* documented the development of dissolvable microneedles in 2005.²⁵ These microneedles used the poke-and-release method to reduce sharp waste risks. Such microneedles undergo skin demolition and are made from micro-moulding soluble matrices, using biocompatible materials like carbohydrates and polymers that disperse in skin interstitial fluid. The drug payload discharges over time.^{10,21}

Dissolvable microneedles insert into skin and break down, with dissolution controlled by polymer properties, releasing product into tissues. Unlike other types, dissolvable microneedles minimize risk of damaging silicon and metal needles inside the body as they dissolve. Dissolving polymer microneedles are preferred for drug delivery due to cost-effective materials, minimal discomfort, and biological compatibility. They disintegrate within skin, eliminating biohazards after therapy.^{11,29,38,39}

Low-molecular-weight compounds like metronidazole, caffeine, theophylline, and lidocaine have been used for dissolving microneedles. Biopharmaceutical products, including insulin, low-molecular-weight heparins, erythropoietin, leuprolide acetate, and growth hormone, address medical requirements. Microneedles can dissolve using hyaluronic acid, poloxamer, polylactic acid, silk fibroin, polyvinyl pyrrolidone, polyvinyl alcohol, PLA, and PLGA.^{11,24-27}

High drug doses are difficult to administer. Matrix accumulation in skin can cause low patient adherence and health risks, particularly with daily administration.²⁷ Challenges in completely injecting pharmaceuticals and long dissolution conditions can reduce product performance.¹¹

Hydrogel-forming microneedles

Hydrogel-forming microneedles consist of non-dissolving chemically bonded hydrogels with a medication-loaded adhesive patch.³¹ These create channels connecting drug patches and capillary dispersion. These MNs penetrate skin barrier. We examined swelling as a rate-limiting membrane.²⁹ Upon injection, the array consumes interstitial fluid through swollen micro projections via skin, contributing to medication distribution from the backrest.^{2,40-41} These microneedle arrays are produced from synthetic polymers, affixed through physical or chemical techniques.^{29,41} Hydrogel-forming microneedles transmit various compounds, from tiny molecules to large molecular weight compounds. The hydrogel technique allows regulation of microneedle swelling by modifying cross-link polymer density, enabling control of drug release levels for different drugs.^{16,21}

Hydrogel-forming microneedles were extracted from intact skin without polymer traces. They are adequately soothed to avoid

reuse, reducing infection risk.¹⁰ Unlike hollow microneedles, hydrogel-forming microneedles do not block after application to compact dermal tissue. They address typical issues of coated microneedles, including minimizing load ability, proper drug coating challenges, and controlling drug discharge speed.⁴²

Other microneedles

Porous microneedles are identical to solid microneedles but have porous tips allowing medicine flow. When applied to skin, drugs pre-loaded into the pores gradually move from the microneedle structure within the skin. This method relies on diffusion, as compounds diffuse into skin through microneedles when medications deplete from the base. For dry medication, pre-loaded compounds dried using heat, vacuum, or freeze-drying are initially rehydrated by interstitial fluid as the skin is sliced. Medications absorb through skin during hydration via porous microneedle openings. Porous MNs can be fabricated using non-biodegradable substances. Silicone is widely used for non-biodegradable porous microneedles, and ceramics are used for the same purpose.^{11-12,23} Numerous microneedle fabrication techniques are listed in Table 1.

CHARACTERIZATION OF MICRONEEDLES

Dimensional evaluation

Methods were utilized to assess MNs shape and determine microneedle's tip diameter, length, height, and radius. Popular procedures include optical microscopy, bright field microscopy, electron microscopy, confocal laser microscope, stereomicroscope Leica MZFILL, etc.^{38,43} Microscopic examination of 3D pictures provides clear understanding of needle structure and helps in quality assurance. Confocal laser microscopy and Scanning Electron Microscopy (SEM) were employed.^{38,44} SEM uses a concentrated electron beam to generate images by interacting with sample molecules during scanning, producing signals that reveal surface structure and topography. Confocal laser microscopy generates images with exceptional resolution.^{29,44}

Mechanical properties and insertion forces

To pierce skin, a microneedle must be thin and narrow while solid enough to avoid breaking within skin. Mechanical integrity tests of microneedles were performed by examining deformation following perpendicular application of payload. Radial intensity was measured using a motorized force-measuring mechanism. The mechanical intensity was assessed using static and dynamic forces. The first tolerance measure involved placing a glass sheet on the microneedle tips and adding weights. Structural shifts were assessed using microscopy upon applying the specified load. Mechanical strength examinations used various technologies, including texture analyzers, motorized displacement-force test machines, low-force mechanical testing systems, and tensile test machines. Insertion force was used to examine surface morphology and microchannel depth using confocal laser

microscopy. Dye marking and force-displacement experiments measured insertion pressure. Confocal microscopy and optical tomography analyzed penetration depth, while histological cryo-sectioning and staining were used similarly. *In vitro* tissue injection analysis used aluminium foil folds and relevant tissues, including skin, intestine, sclera, and cornea.^{45,46}

In vitro study

Franz diffusion cells have been used to analyze medication permeation into targeted tissues. The tissue was placed between receptor and donor compartments during experiments. For transdermal examination, animal skin serves as a semi-permeable membrane, including rat cadaver skin and minipig skin tissue. The sclera, cornea, and vitreous are used as semipermeable membranes depending on the targeted area for ocular studies. The tissue was held hydrated at the correct temperature until experimentation in the appropriate medium used in further experiments.^{3,29,47}

Other evaluation parameters included

The medication may be packaged in dispersion/suspension mode or embedded form (liposomes, nanoliposomes, nanoparticles) within microneedles. The pharmaceutical compound can interact with a polymer solution or serve as a patch. Physicochemical characteristics like polydispersity index, zeta potential, viscosity, and particle size can be examined for the packed drug based on formulation type used for microneedles. Evaluation of drug release, adhesion, and permeation for patches intended for pre-treatment use is performed. The nanocarrier size, structural integrity, and crystallinity can be determined using X-ray scattering, electron microscopy transmission, and dynamic light scattering. Stability tests of the product and microneedles are conducted in physiological environments (cell line culture or tissue culture) at specific pH, temperature, and simulated *in vivo* conditions. Studies on solubility, drug content, and biocompatibility on built microneedles have also been conducted.^{34,48}

APPLICATIONS

The versatility of microneedle designs allows delivery of diverse therapeutic compounds through different routes. Their minimally invasive nature makes them an attractive drug delivery platform. Microneedles offer opportunities for combination therapies and multi-modal delivery, enabling simultaneous delivery of multiple compounds for synergistic treatments and personalized medicine. Here are the key points about applications of microneedles for drug delivery (Figure 2).

Applications in therapeutic delivery

Vaccine delivery

Parenteral vaccinations, including intramuscular, subcutaneous, and intradermal injections, have benefits and drawbacks in vaccine

administration. Therefore, developing a new delivery method took considerable time. Microneedles have gained popularity as new vaccine instruments. The microneedles perforate the skin's stratum corneum layer and transmit medications to the live epidermis and dermis beneath.^{23,27}

Arya *et al.* proposed that microneedle patches for rabies DNA vaccines could enhance vaccination reach for dogs and humans, requiring only moderately trained professionals. These sub-millimeter microneedles deliver vaccines through a patch that can be painlessly applied by minimally qualified staff. This research evaluated dissolvable microneedle patches.⁴⁹

Insulin delivery

Insulin, a peptide hormone, is a medication used to reduce blood sugar levels. MNs for insulin transport enhance the effectiveness of blood glucose level.²⁹ Key reported formulations include:

Wang *et al.* formulated microneedles using silk fibroin and proline to alter crystalline structure. The non-toxic, degradable microneedles showed slow drug release. Studies found improved

Table 1: Construction techniques for various types of microneedles.³²

Sl. No.	Type	Method of Construction
1.	Solid Microneedle	
	Silicon microneedle	Silicon dry-etching process, Dicing a silicon substrate
		Anisotropic wet etching, Acid etching, and Isotropic etching.
	Metal Microneedles	3D Laser ablation, Wet etching
2.		Laser cutting, Metal electroplating methods.
	Ceramic Microneedles	Ceramic micro moulding and Sintering lithography.
3.	Coated Microneedle	Dipping or Spraying, Layer-by-layer coating techniques.
	Hollow Microneedles	Micro-Electromechanical Systems (MEMS) methods include Laser micromachining, combined Lithographic moulding process, Deep X-ray photolithography, Wet chemical etching, Micro-fabrication, and Deep reactive ion etching of silicon.
4.	Dissolving microneedles	Micro molding.
5.	Polymeric (Hydrogel forming) microneedle	Photolithography, Micro molding.

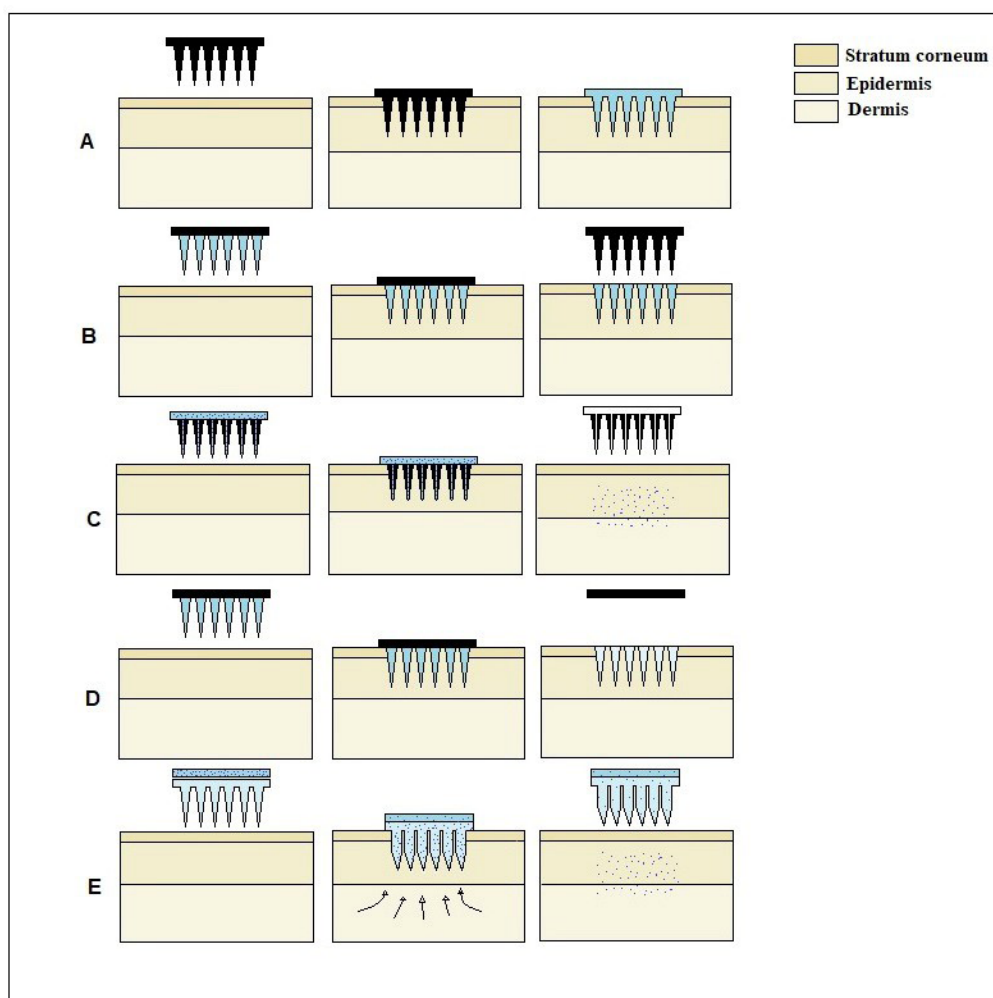


Figure 1: The diagram depicts various types of microneedles used for drug delivery, including A) Solid microneedles, B) Coated microneedles, C) Hollow microneedles, D) Dissolvable microneedles, and E) Hydrogel-forming or swellable microneedles.

release frequency of fibroin/proline microneedles based on swelling extent.⁵⁰

Zhang *et al.* prepared Ca^{2+} /Alg-Mal MNs for insulin delivery and transdermal absorption in diabetes care. Alginate/maltose polymer microneedles cross-linked with calcium ions were created to reduce subcutaneous needle discomfort. They studied insulin stability and biological activity in microneedles.⁵¹

Peptide delivery

Once delivered orally, peptides are enzymatically degraded. Transdermal delivery prevents this, as less peptide enters the skin. Microneedles can help counteract low peptide diffusion.²⁹

Van der maaden *et al.*, created a cationic liposome-based synthetic peptide from human papillomavirus as a therapeutic cancer vaccination. The DC-hMN-iSystem administered this intradermally. Silica hollow MNs with 50 μm interior diameter were created using hydrofluoric acid etching, providing potential for minimally invasive cancer treatment.³⁷

Zhao *et al.* introduced a microneedle coating composition of auto-antigenic lipophilic peptides for type 1 diabetes Antigen-Specific Immunotherapy (ASI). These findings guide formulation characteristics and delivery systems for effective microneedles.⁵²

Oligonucleotide delivery

Various preclinical experiments suggest that microneedles must be applied to distribute oligonucleotides via the skin, DNA, vaccines, desmopressin, insulin, and growth hormones. Oligonucleotides are small DNA or RNA molecules that are difficult to deliver to intracellular active regions. An effort was made to generate 20-merphosphorothioated oligodeoxynucleotides using the microneedle method.²⁹

Jain *et al.* evaluated coated MNs in improving skin distribution of 5-Aminolevulinic Acid (5-ALA), which cells transform into Protoporphyrin IX (PPIX), a Photosensitizer. Coated microneedles could distribute 350 μL of 5-ALA, compared to topical administration of 20% w/w 5-ALA in cream (25 mg),

which produced a 3.2-fold increase in PPIX production after 4 hr. Using coated microneedles for 5-ALA delivery could be suitable for treating photodynamic skin tumors.⁵³

Golombek *et al.* tested intradermal distribution of synthetic mRNA using a hollow microneedle. A porcine skin *ex vivo* model assessed the synthetic mRNA-intervene protein sequence. Synthetic mRNA administered without transfection reagent reached cells, leading to protein expression.⁵⁴

Ophthalmic applications

Treating the eye poses challenges as it is well-protected by multiple barriers, and removal of ocular techniques due to accessibility from outside the body. Drug distribution to the eye can occur via systemic delivery, surgical implantation, injecting medication carriers for sustained drug discharge, and directed topical application through injections in the eyeball or surrounding tissues.^{2,55-57}

Microneedles show promise due to their small size, allowing penetration within the eye but not via sclera or cornea. This provides an accurate, minimally invasive method for drug injection that can diffuse to disease locations.⁵⁸

Microneedles of 25-2000 μm height avoid invasive hypodermic needles. Studies show microneedles effectively distribute pharmaceuticals to anterior and posterior eye parts. Among

five transdermal microneedle types, hollow, coated, and soluble microneedles have been studied for ocular applications.⁷

Jung *et al.* reported that microneedle iontophoresis promises targeted drug delivery to the posterior point. An Ag/AgCl electrode in a syringe connected to MNs for delivery. They assessed the distribution of this iontophoretic suprachoroidal space injection system.⁹

Kim *et al.* demonstrated particle distribution in suprachoroidal space using polymer formulations following hollow microneedle injection in white rabbit sclera. MNs were made from 33-gauge cannulas, reduced to 750 μm length, with laser-formed aperture angles. Microneedles were electropolymerized using E399 electropolisher and filtered water.⁵⁷

Topical application

Transdermal application

The key benefit of hypodermic needle distribution is preventing gastrointestinal first-pass metabolism and deterioration that minimize clinical output; however, alternatives exist.²⁸ Transdermal pharmaceutical administration combines oral delivery convenience with avoiding pre-systemic metabolism of parenteral drug distribution.⁴³ The skin, the body's largest organ, serves multiple biological purposes and offers a comfortable platform for systemic and topical medication administration.⁵⁹ However, the stratum corneum, the skin's uppermost defence, impedes

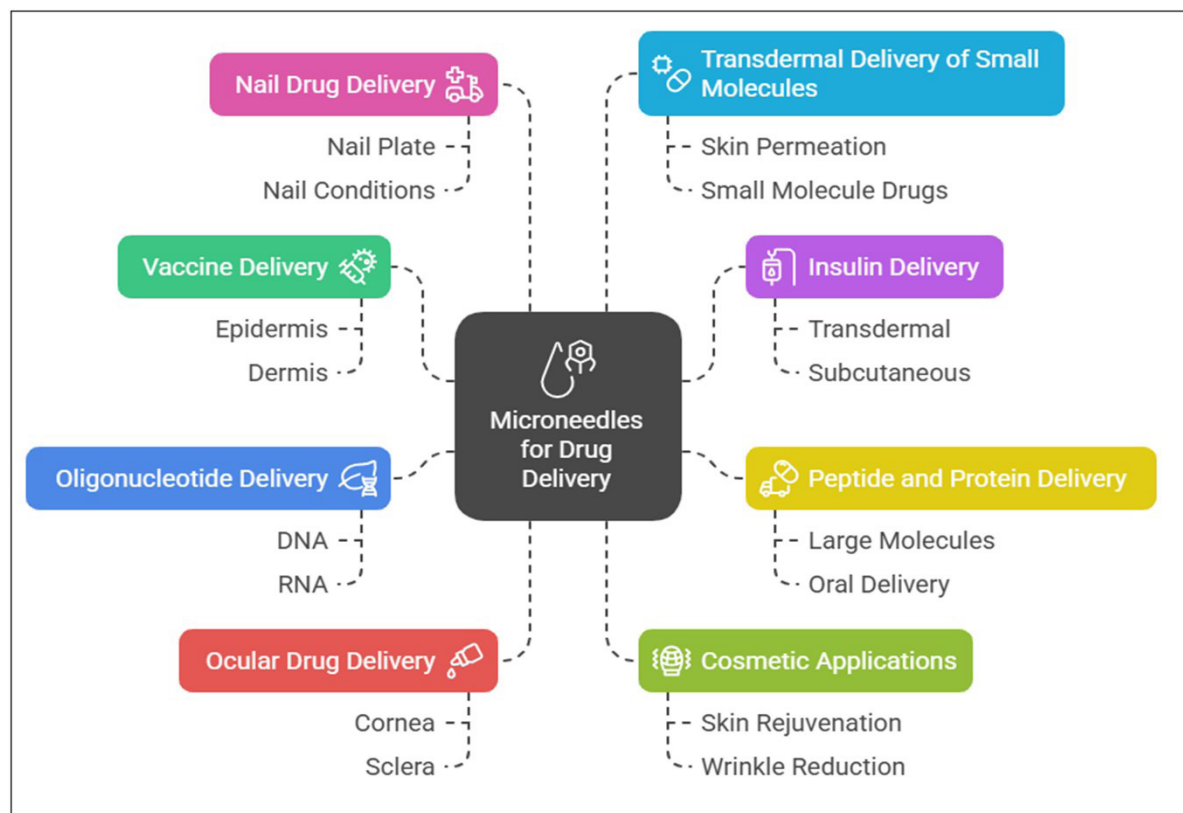


Figure 2: Applications of microneedles for drug delivery.

transdermal drug diffusion. Since the hydrophobic stratum corneum permeates few lipophilic compounds, most hydrophilic compounds were unsuitable for transdermal delivery.^{24,60} Researchers are improving the transdermal distribution of these substances. Microneedles facilitate transdermal distribution of both large and small molecules. With microfabrication technology evolution, laboratories and pharmaceutical industries have established microneedles.^{61,62} Microneedle development has become viable for delivering biotherapeutic substances transdermally. Microneedles are mini-dimensional protrusions on a base plate that penetrate the stratum corneum and provide dermal tissue exposure for medications. Research teams have shown effective drug transmission through the stratum corneum into dermal microcirculation. González-Vázquez *et al.* developed microneedles for gentamicin distribution to treat neonatal infection.⁶³ Yu *et al.* created insulin-containing biodegradable polymer microneedles for diabetes care. Biodegradable hybrid microneedle patches from gelatin and calcium sulfate were designed to reduce subcutaneous injection discomfort.⁶⁴

Miscellaneous applications

Cosmetic applications

In cosmetology, MNs enhance topical medicament distribution by eliminating the subcutaneous obstacle. Active cosmetic ingredients are typically administered topically or by injection. Microneedles efficiently deliver medicinal products to the skin painlessly and minimally invasively. MNs are increasingly important in cosmetics to improve skin appearance and imperfections, with efforts focused on delivering ingredients like ascorbic acid, eflornithine, and retinyl retinoate.^{8,18,54,63}

Dermaroller® is widely used in cosmetic products, while Dermapen® serves as a motor-controlled microneedling device. The FDA-authorized MTS Roller™ treats conditions like hyperpigmentation, aging, and scarring. Innoture Limited developed Drop-on-Solid and Drop-on-Demand approaches for microneedle formation and launched Radara® Directed Skincare, a microneedle patch for distributing hyaluronic serum.^{2,32,48,65}

Nail application

Due to low permeability around the nail plate, topical medication efficacy is limited by the plate's dense keratinized nature. Drug permeation is hindered by medication retention on the nail plate, leading to carrier evaporation and drug immobilization. Methods are needed to develop efficient topical therapies for nail problems. Chiu *et al.* promoted rare substance permeation. These studies suggested a microneedle design method. Topical therapy effectively treats nail diseases, particularly onychomycosis and psoriasis, avoiding adverse effects while improving patient adherence and reducing dosage.²

CONCLUSION

In the past, drugs could only be delivered through skin if they had properties facilitating passage through subcutaneous tissue into viable epidermis. The push to improve topical delivery of peptides, vaccines, proteins, and conventional molecules has driven the development of microneedle products. Microarrays were developed earlier, evolving into a versatile analytical method for drug development and delivery. Microneedles have emerged as a promising solution addressing patient concerns, though uncertainties remain. Despite their potential, commercial systems have only recently appeared, with clinical trials ongoing worldwide, particularly with Soluvia® and MicronJet®.

Recent progress in microneedle drug delivery systems has garnered significant interest from researchers in the drug delivery field. Various materials are used in microneedle production, including metals, silicon, carbohydrates, and polymers, without fully addressing safety concerns. General standards for material selection must be established. Due to lack of legislative guidance on production standards and validation, reproducibility remains problematic. Formulation scientists face several unresolved fabrication questions. Safety evaluations of microneedles for delivering drugs, peptides, proteins, vaccines, and cosmetics have established groundwork for market introduction of microneedle-based products.

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ABBREVIATIONS

MNs: Microneedle(s); **SMNs:** Solid Microneedles; **µm:** Micrometre; **nm:** Nano Metre; **mm:** Millimetre; **API:** Active Pharmaceutical Ingredient; **NXT:** Naltrexone; **PLA:** Poly Lactic Acid; **PLGA:** Poly Lactic Co-Glycolic Acid; **µL:** Micro Litter; **2D and 3D:** Two-Dimensional and Three-Dimensional; **DNA:** Deoxyribonucleic Acid; **RNA:** Ribonucleic Acid; **mRNA:** Messenger Ribonucleic Acid; **ASI:** Antigen-Specific Immunotherapy; **PPIX:** Protoporphyrin IX.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

SUMMARY

Microneedles are a promising drug delivery approach offering minimally invasive and painless administration of therapeutic agents. They are micron-sized needle arrays that penetrate the skin's stratum corneum barrier to deliver drugs to dermal layers. Microneedles can be fabricated from metals, polymers, and carbohydrates using techniques like micromolding, etching,

and 3D printing. They are classified into solid, coated, hollow, dissolvable, and hydrogel-forming types based on design and drug loading. Characterization involves evaluating dimensions, mechanical properties, insertion forces, and *in vitro* performance. Microneedles have applications in transdermal delivery of small molecules, proteins, peptides, and vaccines; ocular drug delivery; cosmetic treatments; and nail delivery. They have shown promising results in delivering insulin, oligonucleotides, and antigens for immunotherapy. Despite advancements, challenges remain in selecting materials, ensuring reproducible manufacturing, and establishing regulatory guidelines for microneedle-based products.

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