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Microneedle Drug Delivery Systems: Recent Advances, Clinical Applications, and Future Directions

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Annotation: Microneedle (MN)-based drug delivery presents an innovative technology for minimally invasive and painless transdermal/ intradermal drug administration with a various combination of drugs. This review systematically compiles recent (2021–2025) findings in the field of fabrication methods, material developments, delivery systems, clinical translations, and commercialization. There are still challenges despite the rapid progress in large-scale manufacturing, biological stability and regulatory harmonization. Highlights amongst new developments are smart MNs combining with biosensors for feedback-controlled release, combination MNs for multi-agent therapy and AI guided design optimization. Resolution of these issues will facilitate more widespread clinical translation, personalized therapy and worldwide control. The review ends with a summary of the major opportunities and research areas in next generation microneedle technologies.

Keywords: Microneedle, transdermal drug delivery, fabrication, controlled release, clinical application.

1. Introduction:

Microneedle (MN) drug delivery systems have received much attention over the last two decades as a promising alternative to conventional transdermal patches and hypodermic injections (Hu, Y., et al. 2024; Sutar, A. D., & Shukla, R. 2025). Traditional drugs beg for fashion statement delivery systems. A transdermal approach, without systemic side effects is ideal, but conventional transdermal absorption is limited by skin's outermost stratum corneum—no power for penetration. Microneedles address these issues by forming microchannels through which drug can diffuse without agitating pain receptors or rupturing blood vessels (Hassan, J., et al. 2022; Nguyen, H. X. 2025).

The early research was primarily focused on solid or coated microneedles for silicon and metal fabrication. However, the field has been rapidly advancing with introduction of biodegradable polymers, hydrogel matrixes and fabrication techniques such as 3D printing and laser micromachining. These progressions have positioned MNs as a very versatile type of delivery vehicles for a wide range of substances that include vaccines, peptides, biologics, and cosmetic ingredients (Maia, R. F., et al. 2025; Abdullah, A. C., et al. 2024).

The current world-wide search for safe, self-administered and cost-effective drug delivery systems, especially in the period of COVID-19 pandemic—has reconfirmed the importance MN technology. Multiple studies demonstrate that MN-based vaccines elicit immune responses equivalent to those produced by conventional injections and offer benefits such as increased patient comfort and storage stability (Hassan, J., et al. 2022; Nguyen, H. X. 2025).

This review offers an up-to-date and critical discussion of recent advances in the field of microneedles. They discuss current advances in design, materials and manufacturing, their clinical experience, safety applications and market potential. Thereby, attempting to provide insights into current challenges and emerging opportunities of the future generations of MN-based drug delivery systems.

2. Classification of Microneedles:

The design and performance of MNs are conditioned primarily by their structure-related features and drug administration mechanisms. Knowledge of these grading systems is critical for clinical outcome and manufacturing strategies. Commonly, MNs can be divided into five different forms; solid MNs, coated MNs, dissolving MNs, hydrogel-forming MNs and hollow MNs with specific benefits as well as technical aspects (Aldawood, F. K., et al. 2021; Avcil, M., & Çelik, A. 2021).

2.1. Solid microneedles: Solid microneedles are usually made of long lasting and biocompatible materials such as silicon, metals, or medical-grade polymers. They act primarily by generating short-lived microchannels within the stratum corneum, which facilitate topical formulation delivery. This "poke-and-patch" procedure is designed to facilitate drug permeation to a level sufficient to reach the lumenal side of epidermis but not so deep as to cause pain. However, the latter usually involves a two-step process, which is not necessarily convenient for users in self-administration environments (Aldawood, F. K., et al. 2021).

2.2. Coated microneedles: The principle of coated microneedles implies that a thin drug layer is placed directly onto the surface of needle. After insertion through skin, the coating dissolves fast in interstitial fluid and payload is released within 100 s. This design is specifically applicable to vaccines and low-dose biologics in need of rapid systemic absorption but loading efficiency is still relatively low (Avcil, M., & Çelik, A. 2021).

2.3. Dissolving microneedles: Dissolving microneedles are a big leap toward biocompatible and wasteless. MNs, composed of biodegradable polymers such as carboxymethyl cellulose (CMC), or polyvinylpyrrolidone (PVP), contain active substances within their matrix. Once the lattice is

in place, the entire structure dissolves within the skin to facilitate controlled release and leaves no sharp refuse — a crucial consideration for mass immunization efforts (Aldawood, F. K., et al. 2021).

2.4. Hydrogel-forming microneedles: Hydrogel-forming microneedles are more advanced in concept. They are composed of hydrophilic polymers with covalent crosslinks, which swell in interstitial fluid and form a gel matrix that allows for the transport of drug from an attached reservoir. Their capacity to carry significant or multiple moieties renders them attractive for sustained-release treatments (Cao, J., et al. 2024).

2.5. Hollow microneedles: Hollow microneedles however are miniaturized hypodermic needles with an internal lumen for fluid delivery. They enable pressure-controlled infusion of liquid formulations and are thus applicable also for high-dose delivery of viscous drugs like monoclonal antibodies or enzymes. However, some technical barriers such as clogging in fabrication and the complexity of fabrication are still unreached (Aldawood, F. K., et al. 2021).

A brief description of the key characteristics of each type can be found in *Table 1* with respect to materials, mechanisms and pros and cons. The most suitable category under these categories is dependent on several factors such as physicochemical stability of drug, release kinetics, patient compliance and scale-up of production (Aldawood, F. K., et al. 2021; Avcil, M., & Çelik, A. 2021).

Table 1. Classification and Characteristics of Microneedle Types.

Type	Material	Drug Loading	Release Mechanism	Advantages	Limitations	Typical Applications
Solid	Silicon, metal, polymer	Post-application (skin pre-treatment)	Passive diffusion through created microchannels	Simple design, easy fabrication, good reproducibility	Two-step process, limited drug control	Skin pre-treatment, enhanced permeation for topical drugs
Coated	Metal, silicon	Surface coating of active agent	Rapid dissolution upon insertion	Fast onset of action, suitable for vaccines	Limited drug capacity, coating uniformity issues	Vaccines, small-molecule therapeutics
Dissolving	Biodegradable polymers (PVP, CMC, HA)	Drug encapsulated within polymer matrix	Polymer degradation and dissolution	Biocompatible, safe disposal (no sharps waste)	Fragile structure, limited mechanical strength	Vaccines, insulin, peptides, biologics
Hollow	Glass, metal, polymer	Liquid formulation within lumen	Pressure-driven infusion	Enables high-dose and viscous drug delivery	Risk of clogging, complex fabrication	Monoclonal antibodies, enzymes, fluids
Hydrogel-forming	Hydrogel polymers (cross-linked PVA, PEG)	Drug stored in attached reservoir	Swelling-mediated sustained release	Long-term controlled delivery, reusable designs	Requires prehydration, slower onset	Hormones, biologics, diagnostic sensors

3. Fabrication Techniques:

With the diverse structures of MNs, the various fabrication methods developed in last 20years are presented. After the functional type of MN is selected, such as solid, dissolving and hollow MNs, it can be important to choose the manufacturing method that specifies the performance and reproducibility of resulting devices in addition to cost. With the development of microengineering, geometry, surface finish and mechanical strength of MNs can be well controlled to move from just laboratory prototypes to potentially commercially viable medical devices (Maia, R. F., et al. 2025; Abdullah, A. C., et al. 2024).

A. Photolithography: It is one of the oldest and most accurate techniques, especially for solid and coated microneedles. It permits manufacturing silicon or metal substrates, with using patterned photoresist layers and subsequent enrichment. Such an approach provides a micron level of accuracy and is suitable for research where uniform arrays are necessary, but relatively high cost and multiple steps hinder manufacturing in large scales (Abdullah, A. C., et al. 2024).

B. Micromolding: It is the development process of choice for dissolving and hydrogel-forming MNs. In this method, molds fabricated of a flexible material such as PDMS (polydimethylsiloxane) are filled with a polymeric solution comprising the drug of interest. The resulting MN arrays are monodispersed, inexpensive and biodegradable after drying and demolding. This method is not only facile for industrial- and academic-scale synthesis but also for its application in academia and industry (Maia, R. F., et al. 2025).

C. Laser ablation: Laser ablation devices have good flexibility: on-the-fly modification is feasible with no other tools more easily than for prototyping. With the help of a tightly focused laser beam for local material elimination such MNs can be cut from sheets made out of metal or polymer with any desired shape and sharpness of their tip. Although it enables fast design iteration, it affects heat-induced surface irregularities, and the part needs to be post-processed afterwards (Abdullah, A. C., et al. 2024).

D. 3D printing: Last but not least is the game changing effect caused by 3D printing technologies which allowed layer-by-layer additive manufacture of complex and patient specific MN geometries. And not only waste could be minimized this way, but multi-material designs can also be connected in a similar way – even integrating sensors or drug reservoirs within the needle body. There is a resolution variation between commercially available printers; however, this gap closes as technology progresses (Maia, R. F., et al. 2025).

E. Conversely, **the microelectromechanical systems (MEMS)** fabrication technology has been developed for manufacturing high precision and reproducible needle arrays at least in silicon MNs used for diagnostic and biosensor applications. The MEMS fabrication process is well-suited to hybrid systems where mechanical robustness and electronic functionality need to be integrated (Cao, J., et al. 2024).

Material selection remains a crucial aspect for all these methods, which in turn determines biocompatibility), dissolution rate and long-term drug stability. Some common ones are silicon, titanium, stainless steel or biodegradable polymers like PLGA, hyaluronic acid and even some sugars such as mannitol or maltose in short term use (Maia, R. F., et al. 2025). The need for continued geometry-optimization—needle length, tip-radius and density—is a key reason reliable and relatively pain-free penetration has been achieved in some but not yet all subjects (Abdullah, A. C., et al. 2024; Maia, R. F., et al. 2025). In general, these diverse methods demonstrate how engineering innovation is being used to promote the evolution of MN systems. Discussing the archetype of fabrication technologies as they evolve from low throughput to mass customization fabrication types, knowing these protocols permit to predict how MN transfer drugs (Hu, Y., et al. 2024; Sutar, A. D., & Shukla, R. 2025).

4. Drug Delivery Mechanisms:

The delivery of (bio)therapeutics by MNs is strongly determined by the MNs' architectural, compositional and penetrating properties. With the recent developments in fabrication, knowledge about how MNs interact with skin has been increasingly pivotal for their optimized clinical performance. By penetrating to the stratum corneum barrier, MNs can create tiny microchannels that offer a feasible approach for controlled transdermal delivery of drugs into viable epidermis or dermis without stimulation pain receptors and blood vessels (Tan, J. Y., et al. 2021; Zhang, Y., et al. 2023).

In coated MNs, the drug molecules are coated on the surface of the solid needles in a thin film form. On penetration into the skin, the coating rapidly dissolves in interstitial fluid with consequent rapid release and systemic uptake. This renders coated MNs particularly

advantageous as vaccines and small-molecule drugs that require rapid onset of action. But the small space of each needle allows low total drug loading, which is not suitable for high dose treatment (Tan, J. Y., et al. 2021).

Dissolving MNs also overcome this drawback by incorporating the drug into a biodegradable polymeric matrix. The matrix dissolves slowly when the microneedles are inserted into the skin, therefore e.g. a sustained release over minutes or even hours are enabled. This modality is very safe for the patient as nothing sharp is left over after use, and it has a high degree of dose accuracy with respect to peptide/protein and delicate biologics delivery. The dissolution rate—and therewith release profile—depends on the polymer composition, humidity, and skin hydration (Zhang, Y., et al. 2023).

Hollow MNs serve more as microscopic hypodermic needles permitting pressurized infusion of liquid formulations. Higher drug volumes, viscous biological products (e.g., monoclonal antibodies or solutions of enzymes), can be administered. Flow rate, inner diameter and penetration depth are significant factors affecting the efficiency of administration. Despite their direct regulation capability on drug dosing, engineering development is also required for issues including clogging or non-uniform fluid release patterns (Aldawood, F. K., et al. 2021).

Hydrogel-forming MNs use different principles. When inserted, these cross-linked polymer tips swell via acquisition of interstitial fluid and form a hydrogel network allowing passive drug diffusion from an adherent reservoir. This reversible long-term swelling property is suitable for the application of therapeutic or diagnostic biosensors systems in which release and sampling are performed simultaneously (Cao, J., et al. 2024).

The general steps involved in drug penetration, diffusion and release kinetics for the four types of microneedles are depicted pictorially in ***Figure 1*** to illustrate that coated, dissolvable, hollow and hydrogel-forming MNs types exhibit specific modes of interaction with different layers of skin. The figure clearly illustrates how the drug pathway (surface diffusion, matrix dissolution, pressure driven infusion and hydrogel mediated release) is different for MN design types and insertion depth. These images are invaluable for relating structure to function and prediction in vivo pharmacokinetics (Tan, J. Y., et al. 2021; Cao, J., et al. 2024).

Factors influencing release kinetics from MN systems include insertion force, skin elasticity, temperature, hydration and drug molecular weight. In order to better predict these interactions, the use of computational modelling and ex vivo human skin studies in addition to in vivo pharmacokinetic trials are increasingly utilized (Tan, J. Y., et al. 2021; Zhang, Y., et al. 2023). These findings are informing the development of personalized microneedle arrays capable of specific dosing and reduced pain (Cao, J., et al. 2024). Taken together, MNs are a versatile platform that can be adapted for the target delivery as well-as illustrated with applications for rapid vaccination and sustained hormone/peptide release. The comprehension of these mechanisms forms the basis for translating them into clinical practice, as discussed in the section on clinical applications below.

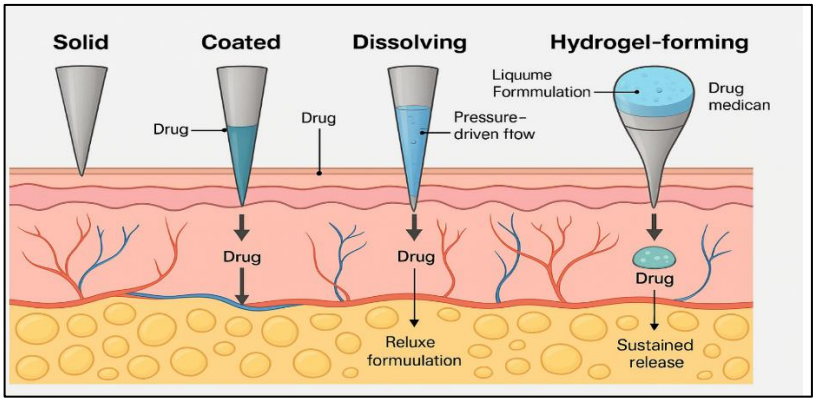

Figure 1. Schematic Diagram of Drug Delivery Routes by Various Types of Microneedles Through Skin Layers.

5. Clinical Applications:

Clinical translation of MNs technology has expanded greatly in the past decade from lab-based techniques to commercially available end-user healthcare solutions. And due to their minimally invasive and patient-administrable nature, the MNs have emerged as a promising alternative to conventional needle injection particularly for chronic diseases or preventive medicine. Throughout different therapeutic areas, MNs continue to gain importance in increased efficacy, patient convenience and compliance (Hassan, J., et al. 2022; Nguyen, H. X. 2025).

Vaccines are still most commonly applied. Indeed, microneedle delivery of vaccines has consistently produced immune responses that are equivalent to those produced by the IM route yet uniquely offers advantages (less sharps waste, facile shipping and storage; lower pain). Clinical trials of dissolving MN patches for influenza and COVID-19 vaccines have successfully demonstrated their safety and immunogenicity (Hassan, J., et al. 2022; Nguyen, H. X. 2025). Importantly, these apps allow for mass immunization programs to be performed without the need for trained personnel, which is of great significance in low resource and pandemic conditions.

In diabetes treatment, insulin-loaded dissolving MNs have exhibited high accuracy in glucose control, and patient compliance. Compared to subcutaneous injections, MN patches are less painful, enhance compliance and prevent infection. Clinical trials are currently underway to examine glucose-responsive MNs that can release insulin in response to blood glucose levels, which is a significant stride toward closed-loop management for diabetes (Zhao, J., et al., 2022).

MN platforms are also gradually accepted in oncology for locoregional chemotherapy and immunotherapy. Coated/ hallow needles MNs could facilitate site-specific delivery of agents such as doxorubicin or checkpoint inhibitors directly into tumor tissue thus by increasing local concentration while decreasing systemic toxicity. This approach could be used for many dermatological cancers or superficial cancer(s) in the future, instead of/or added to intravenous chemotherapy (Hu, Y., et al. 2024).

Outside these therapeutic areas dermatology and cosmetology are another strong developing sector. Solid and dissolving MNs are applied for deeper penetration of agents retinol, hyaluronic acid and peptides into the skin for treatment against antiaging, depigmentation and acne. With their ability for temporary disruption of the stratum corneum, dermal permeability can be enhanced without downtime which is very attractive in aesthetic medicine (Hu, Y., et al. 2024).

A second fast growing field is the transport of biologics and genetic materials, such as monoclonal antibodies, siRNA and mRNA-based therapies. MNs provide a potential alternative to needle-mediated injections of labile macromolecules, as the stability and bioavailability of the agent increases. It has recently been demonstrated that preclinical study for microneedle delivery of mRNA vaccines against SARS-CoV-2 and influenza and found to have excellent immunogenicity being more stable at temperatures higher than lipid nanoparticles (Sutar, A. D., & Shukla, R. 2025; Cao, J., et al. 2024). Building on these advancements, microneedle arrays are increasingly employed for the transdermal delivery of next-generation therapeutics, including biologics, immunotherapies, and genetic drugs such as mRNA vaccines. Recent innovations in nanotechnology and hydrogel-based composites have improved molecular stability, tunable release kinetics, and biocompatibility (Cao et al., 2024; Sutar & Shukla, 2025). The convergence of microneedle systems with nanocarriers and stimuli-responsive polymers represents a transformative approach to overcoming current barriers in drug transport, enabling more precise and efficient therapeutic administration. Some typical clinical trials are summarized in Table 2 based on therapeutic fields, mMTs, phase and outcome of the trial. Taking together, our results underscore the clinical readiness of MN technology for global health issues (Hassan, J., et al. 2022; Sutar, A. D., & Shukla, R. 2025).

Table 2. Selected Clinical Trials Involving Microneedle Technology.

Therapeutic Area	Microneedle Type	Drug / Vaccine	Phase	Outcome Description	Reference / Year
Vaccination	Dissolving MN	Influenza vaccine	Phase I / II	Safe and immunogenic, comparable to IM injection	Hassan, J., et al. 2022
Diabetes	Dissolving MN	Insulin	Phase I	Achieved stable glucose control, high patient acceptance	Zhao, J., et al., 2022
Oncology	Coated MN	Doxorubicin	Preclinical	Targeted drug accumulation at tumor site, reduced systemic toxicity	Hu, Y., et al. 2024
Dermatology	Solid MN	Retinol	Phase I	Enhanced transdermal delivery, improved skin penetration	Sutar, A. D., Shukla, R. 2025
Hepatitis B	Hydrogel-forming MN	HBV vaccine	Phase I / II	Immunogenicity comparable to intramuscular injection	Cao, J., et al. 2024
COVID-19 / mRNA	Dissolving MN	SARS-CoV-2 mRNA vaccine	Preclinical	Strong antibody response, good thermostability	Hassan, J., et al. 2022

The increasing evidence demonstrates the transition of MNs from research to commercially feasible medical devices. Nevertheless, widespread acceptance will depend on consistent regulatory approach, validated safety profile and standardized manufacturing processes as further detailed in the regulatory and safety considerations section.

6. Regulatory and Safety Considerations:

Regulatory oversight in driving MNs technology from the laboratory to clinic has emerged as one of the most critical issues in the path to commercialization. The above promising clinical data presented suggests that MNs have great potential, but to a large extent their application within healthcare systems is reliant on clear safety and quality standards. Present regulatory policies for MNs are still half-clear as the devices fit the junction of drugs and medical devices. Regulatory agencies such as the U.S. Food and Drug Administration (FDA) or European Medicines Agency (EMA) typically place MN-based products into combination product classification where it must comply with drug and device regulations. Such a double classification makes the clearance of each and every one of these devices difficult, for both mechanical safety and biocompatibility must be demonstrated as well as pharmacologic efficacy (WHO, 2023; EMA, 2022; FDA, 2022). (U.S. Food and Drug Administration, 2022).

Safety tests begin at the materials level. Silicon-, metal- or polymeric MNs has to be completely analyzed for biocompatibility (according to ISO 10993), including cytotoxicity, sensitization and irritation. Yet another requirement is the validation of sterility, especially for dissolving (or hydrogel forming) MNs remaining on skin tissue for a long time. In several of these procedures, such as gamma irradiation and ethylene oxide sterilization, there exist an array of special constraints in the stability of the drug (ISO, 2022; FDA, 2022). (U.S. Food and Drug Administration, 2022). Needle strength testing ensures that the needle has 'enough force' to penetrate the skin without hooking or having breakage by product pose threat for safety. In reaction to this, mechanical compression and insertion-force testing is now the norm in regulatory submissions. Post-application safety is also important: dissolving MNs are desirable from the standpoint) of biodegradability and absence or accessibility of biohazardous waste, while solid/hollow MNs require proper disposal (ISO, 2022; WHO, 2023). (U.S. Food and Drug Administration, 2022).

So, although some promising strides have been taken, there are hurdles to achieving consistent global standards. Regulation of MN In contrast to this, we find that in different regions, the rules for MNs have not been harmonized; some regard them as a transdermal patch and others consider them an injection preparation. This discrepancy complicates the global registration and access of these products to market. The FDA has begun to publish draft guidelines specifically

addressing MN manufacturing validation, sterility assurance, and performance claims and there are analogous frameworks being developed by the EMA for their Medical Device Regulation (MDR) changes as well (FDA, 2022; EMA, 2022). Importantly, in phase III sites, the MN-based influenza vaccines have shown regulatory feasibility that allows for wider uptake (Table 1). Over time, and with increasing maturity / data from the industry, it is expected that this will all be clarified by venture regulators worldwide, leading to more clarity on equipment categories and (post launch) post market surveillance processes – which should drive both public confidence in EITS equipment, as well as purchase by enterprises. However, even with the impressive advancement in technology, one of the most substantial bottlenecks for clinical implementation as well as global commercialization of these microneedle devices still remains to be regulatory harmonization. The lack of harmonized international guidance for safety, sterility, mechanical durability and manufacturing at large scale has obstructed the translation to market. The creation of collaborative platforms for the development of standardized guidelines along with regulators as FDA and EMA will be key to expedite product registration, maintain patient safety and guarantee fair access to new MN-based therapies (WHO, 2023; ISO, 2022; FDA, 2022; EMA, 2022).

Overall, while early clinical work has shown them to be safe and effective, the true proliferation of MN systems will rely on continued collaboration between industry, regulatory bodies, and researchers with respect to harmonized safety testing, sterility validation, and quality control. Such changing regulations are already influencing the speed with which new products enter the market, as discussed in the following section on commercial trends and MN products (WHO, 2023; EMA, 2022).

7. Market Trends and Commercial Products:

With growing regulatory clarity, the commercial opportunities of microneedle (MN) technology are shifting at an unprecedented rate. Once relegated to an obscure area of research, the barely invasive drug delivery market has emerged into a global market that is being driven by the need for patient-focused BALLOON SOLUTIONS Less invasive. Growing demand for self-administered therapies and developments in materials and manufacturing technology have prompted industrial investment to develop new products (Maia, R. F., et al. 2025).

A number of MN products have already moved into commercialization or are on the cusp. One of the most celebrated is Zosano Pharma Qtrypta™ (zolmitriptan) patch approved by the FDA for acute migraine intervention. Its performance illustrates the ability of microneedle technology to satisfy rigorous clinical and regulatory requirements for safety, efficacy and reliability. Another company, Micron Biomedical, has moved a collection of MN-based pediatric vaccine patches into late-stage clinical trials for diseases including measles and rubella. These progressions represent a significant transition from experimental models to products that can be taken to market (Maia, R. F., et al. 2025). In the cosmeceutical field, MN technology has been largely used in Asia (for example, in South Korea and Japan) and is commercialized by companies as the Raphas Co, Ltd., by offering a dissolving patch of MNs for anti-aging purpose, whitening purpose and acne therapy. These consumer products have facilitated the popularization and dissemination of MN-based systems that also indirectly led to breakthrough of the medical market (Hu, Y., et al. 2024).

The market opportunities of MN Technology in the future are very promising all over the world. Recent estimates forecast a CAGR of >8–10% with the market size growing over USD 1.5 billion by 2030 (Maia, R. F., et al. 2025). Growth is coming not just from therapeutics like insulin and vaccines but also from integration with new digital health platforms. Current investigations are focusing on realizing smart integrated MN patches for rapid biosensing and real-time drug release using feedback operation, along with wireless signal transmission. The combination of MN technology, biosensors, IoT and AI has the ability to transform personalized medicine in the next decade (Hu, Y., et al. 2024; Sutar, A. D., & Shukla, R. 2025).

Nevertheless, there are barriers to mass production, cost and supply chain. For worldwide utilization, particularly in resource-poor setting, still need to have the demands of production consistency and stability-during-transport. But as it becomes increasingly common for drug companies to partner with device makers — firms like 3M Drug Delivery Systems, LTS Lohmann and Micron Biomedical are touting faster launch times, cross-sector harmonization (Maia, R. F., et al. 2025).

In summary, MN technology has moved out of the status of a POC test, it is now one of industry commercialized platforms regulated by national changes, patient demands and technological advances. But as discussed elsewhere... filling the MN breadth with therapeutic payloads at "clinical" capacity is necessary to sustain this trend and ultimately reach saturation in clinical use of MN-based therapeutics (Hu, Y., et al. 2024). The developmental stages of this transition from early, basic research to large scale commercialization are shown schematically as the five stages in ***Figure 2:*** (1) Research & materials innovation (2) Fabrication and characterization (3) Preclinical evaluation (4) Clinical trials (5) Regulatory / commercialization Understanding this roadmap is fundamental in order to be able to prepare for future direction and amplify the confidence on sustained industrial growth.

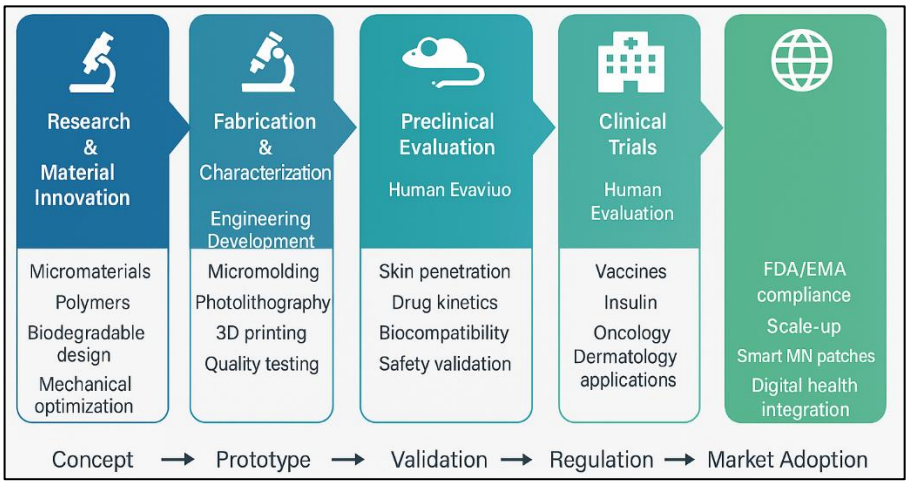

Figure 2. Research-to-Clinical Translation: Microneedle Technology Map.

8. Challenges and Future Prospects:

Microneedle technology has advanced significantly and developed rapidly; however, several challenges remain before it is fully implemented clinically or commercially. Recent advances in microneedle technology have increasingly shifted toward *smart and integrated systems*, where artificial intelligence (AI) and machine learning (ML) play essential roles in optimizing design, fabrication, and clinical translation. AI-assisted modeling allows automated material selection, geometric optimization, and adaptive calibration of microneedle specifications according to individual patient skin characteristics and therapeutic profiles (Sutar & Shukla, 2025). Moreover, the integration of biosensors within microneedle arrays enables real-time monitoring of drug diffusion and physiological responses, facilitating feedback-controlled or “closed-loop” drug delivery platforms that could redefine future personalized therapeutics (Hu et al., 2024). These hurdles are multi-layered, including scale-up of manufacture, formulation stability of the drug product, regulatory convergence and potentially patient-to-patient variability. Addressing these issues is critical in moving MN systems from innovative prototypes to robust medical products. Technological bottlenecks continue to concentrate in manufacturing and scale-up. This calls for precision engineering and tight process control to create identical high-quality MN arrays on an industrial scale. Advances in reproducibility have been achieved by micro-molding and additive manufacturing, but variability in tip sharpness, mechanical strength, and drug loading continue to be reported (Maia, R. F., et al. 2025). Automation and quality-by-design concepts are being investigated for increasing throughput and lower production cost per device, while not reducing performance.

Lack of effective drug stability for biologics, peptides and RNA-based therapies is another significant constraint. Precise temperature and humidity control are necessary during manufacturing, storage and transportation to preserve molecular integrity. Formulations and freeze-drying techniques to maintain bioactivity have been studied including stabilizing excipients, polymer cross-linking processes (Lv, X., et al. 2024). On-demand or cold-chain-autonomous MN patches may significantly broaden the availability of biologic therapies in low-resource settings.

In addition, skin differences among ethnic groups add an additional layer of difficulty in the clinical field. Variations in hydration, induration depth and penetration of the skin are influenced by dermoelastic properties of skin (Gupta, M., et al. 2025). Beyond these biophysical differences, a growing body of research emphasizes the role of ethnic and anatomical variation in determining microneedle penetration efficiency and transdermal permeability. Personalized microneedle systems, tailored to patient-specific skin elasticity, thickness, and hydration characteristics, have the potential to significantly enhance therapeutic outcomes across diverse populations (Gupta et al., 2025). Future investigations should therefore prioritize comparative clinical trials evaluating penetration depth and pharmacokinetic behavior in distinct demographic groups to advance the field toward truly individualized transdermal therapeutics. Such variabilities highlight the requirement for both MNs and intelligent insertion systems to be adaptable to in vivo conditions by adjusting parameters on-the-fly. This combination with "minifyable" sensors and digital feedback systems could help personalize dosing and increase the similarity patient to patient. Similar regulatory considerations have been addressed by the World Health Organization (WHO) and the International Organization for Standardization (ISO), which emphasize standardized testing for transdermal and microneedle-based products. WHO's recent guidelines and the ISO 10993 series remain key references for evaluating biocompatibility, sterility, and animal welfare requirements in microneedle development (WHO, 2023; ISO, 2022).

From a regulatory and clinical perspective, the lack of standardized testing procedures continues to restrict global uptake. The FDA and EMA are increasingly providing MN guidance documents; however, differences in device class assignment and post-market surveillance are still the case (U.S. FDA, 2022). Setting international harmonized requirements for biocompatibility, sterility assurance and performance verification will be required to facilitate registration of products and the safe usage of regenerative medicine interventions globally.

Future Now, the future of MN technology seems very promising. Recently developed profiles in research suggest future smart MN platforms, integrating biosensing, wireless data transmission and feedback-controlled release to transform the naïve patch into an all-in-one therapeutic system. Multi-drug or multi-vaccine component delivery combination MNs are increasingly attracting attention too, especially in the contexts of oncology and immunotherapy (Hu, Y., et al. 2024; Sutar, A. D., & Shukla, R. 2025). Furthermore, developments in flexible and biodegradable (or even self-healing) materials may increase comfort and safety for prolonged use.

Lastly, artificial intelligence (AI) and computational modeling are changing the landscape of MN optimization design. In silico, these AI-driven algorithms can predict the mechanics of insertion, the ideal geometry and even simulate drug diffusion profiles across different skin types - massively shortening development time (Cao, J., et al. 2024). These technologies should facilitate the translation of MN research to clinics. Somehow, if we could overcome the issues of manufacturability, stability and regulation – at present which are highly challenging to address- it will pave new way to a true patient-centric personalized data-driven drug delivery approach. The second conclusion reflects on how this collective advance pitched microneedle systems as a bridgehead of the therapeutics regimen of the future (Hu, Y., et al. 2024).

9. Conclusion and Future Outlook:

Drug delivery using microneedles has evolved from an idea to one of the most attractive contemporary therapeutic approaches. Due to low invasiveness, dosing accuracy and simple use and with good biocompatibility, jet injectors have become known as the new driving force for dispensing traditional needle needles. Over the past decade, developments in microfabrication, materials engineering and formulation science led to a wide variety of MN devices that could deliver various therapeutics including vaccines/peptides, biologics, cosmetics. The current body of clinical evidence continues to grow with efficacy, and the level of safety has been established following MN-based treatment. Commercial achievements, such as the FDA-approved Qtrypta™ patch and late-phase testing of MN-based vaccines underscore maturation of this technology from bench to bedside. In addition, the combined concept of accurate MN-assisted biosensors and digital health systems facilitates personalized-tailored and feedback-controlled therapeutic protocols. However, there is work to be done for MN systems to reach their full potential in terms of standardization of manufacturing, achieve the long-term stability of biologics, and coordinate regulatory pathways across global jurisdictions. Implementation of uniform test protocols to accelerate market translation will require collaboration with academia, industry and health authorities.

Future Outlook:

In order to achieve further advances and facilitate the translation of these microneedle technologies into clinical practice, future experimental work should fully explore the link between microneedle geometry, insertion mechanics and drug distribution profiles in vivo. Comparative clinical trials including various skin types and ethnicities are necessary to confirm device efficacy regardless of ethnicity. Furthermore, developing standardized application protocols and universal deployment tools will be critical in improving device reliability, patient comfort, and long-term regulatory compliance. In the future of healthcare, MN technology will be expected to have a major role. Smart microneedle patches within situ sensor and AI enabled on-demand release profiling ability would soon be available and determine a new paradigm for on-chip, data-driven drug delivery. The wide intersection today of material science, bioengineering and computational design is surely to deliver devices that are safer and more efficient while also being deployable in tens of thousands of patients worldwide. With the ongoing interdisciplinary research efforts and regulation, microneedles will be widely accessible and make personalized medicine a reality in ten years.

Finally, MN platform technologies propose a logistic in drug delivery characterized with comfort, safety and convenience. As technology and the link between clinical practice and engineering continue to advance, these tiny tools of destruction could very well revolutionize how people are healed around the world.

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