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Perspectives

Microneedles: A Promising Therapeutic Strategy for Next-Generation Drug Delivery, Diagnosis and Biosensing

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Abstract: Microneedles (MNs) have emerged as a transformative drug delivery technology, offering a minimally invasive, painless alternative that bridges the gap between conventional injections and topical therapies. Initially developed for transdermal delivery, MNs have rapidly evolved into multifunctional platforms capable of administering diverse therapeutic agents, with enhanced precision and bioavailability. Recent innovations have extended MN applications far beyond the skin, enabling closed-loop therapeutic systems through integration with biosensors and stimuli-responsive release mechanisms for the treatment of chronic diseases such as diabetes and cancer. Expanding beyond human medicine, MNs are also being explored in plant science for precise agrochemical delivery and real-time physiological monitoring. Moreover, the adaptability of MNs has led to their successful deployment in challenging anatomical sites, including the oral cavity, eyes, and myocardium, enabling localized and targeted treatments. As the field advances, key challenges remain in material optimization, scalable manufacturing, and clinical translation. Looking forward, the convergence of MNs with wearable technologies and artificial intelligence holds promise for achieving personalized, data-driven therapeutic interventions. This review highlights the recent progress, diverse applications, and future potential of MNs as a next-generation delivery and diagnostic platform.

Keywords: microneedles; monitoring and diagnosis; drug delivery; closed-looped system; plant engineering

1. Introduction

Microneedles (MNs) have emerged as a groundbreaking drug delivery technology that bridges the gap between invasive injections and non-invasive topical administration. Over the past two decades, MNs have evolved from simple transdermal tools into highly versatile platforms capable of delivering a wide range of therapeutic agents, including small molecules, peptides, vaccines, nucleic acids, and even living cells [1,2]. Their minimally invasive nature, painlessness, and ability to bypass physiological barriers have positioned MNs as a transformative strategy in next-generation drug delivery.

MN-based therapy offers several notable advantages. These include minimal invasiveness, reduced pain compared to conventional injections, improved patient compliance, and the ability to bypass the gastrointestinal tract or the first-pass metabolism, which can enhance the bioavailability of drugs [3,4]. MNs also enable targeted and localized delivery, rapid onset of action, and the potential for integration with biosensors or wearable devices for real-time monitoring. However, MN-based therapy also has limitations. One major challenge is the relatively low drug-loading capacity, which can restrict the total dosage that can be delivered in a single administration [5]. Additionally, mechanical strength and skin penetration efficiency must be carefully balanced with material

biocompatibility and biodegradability. Complex or multifunctional MN systems may face manufacturing and scalability challenges, and long-term safety and stability data are still limited [6]. Addressing these limitations through optimized design, material selection, and standardized clinical protocols will be essential for the successful translation of MN-based therapies. Furthermore, the advantages and limitations of MN-based delivery vary depending on the type of therapeutic agent. For small-molecule drugs, MNs enable minimally invasive, localized, and controlled delivery, bypassing first-pass metabolism and potentially improving bioavailability. The main limitation is that low drug-loading capacity may restrict the total achievable dose. For proteins and peptides, MNs can protect sensitive biomolecules from enzymatic degradation and facilitate transdermal delivery, improving patient compliance by reducing the need for repeated injections. Challenges include maintaining protein stability during fabrication and storage, as well as achieving sufficient dosage [7]. For nucleic acids, such as DNA, siRNA, or mRNA, MNs allow targeted delivery to skin-resident immune cells, making them highly promising for vaccination or gene therapy [2,8]. Nevertheless, nucleic acids are highly sensitive to environmental conditions, and successful delivery requires careful formulation design to ensure stability, efficient cellular uptake, and effective transfection. Overall, optimizing MN design, materials, and formulation strategies is critical to fully exploit their potential for diverse therapeutic agents while mitigating inherent limitations.

Beyond conventional transdermal applications, recent innovations have broadened the utility of MNs into diverse and complex therapeutic contexts. For instance, smart MNs equipped with biosensors and stimuli-responsive release mechanisms enable real-time monitoring and controlled drug administration, paving the way for closed-loop therapeutic systems [9]. Such systems integrate diagnosis and treatment in a single platform, offering tailored interventions for chronic diseases like diabetes and cancer [10–12]. These advancements significantly enhance the precision, efficacy, and personalization of MN-based therapies, reinforcing their potential as next-generation biomedical tools. In addition to biomedical applications, MNs have recently demonstrated great potential in plant science [13]. Their minimally invasive nature enables precise delivery of agrochemicals or biomolecules directly into plant tissues, such as leaves, stems, or roots, improving uptake efficiency while minimizing environmental loss [14]. Moreover, MNs can be engineered to extract interstitial sap for real-time monitoring of plant health and metabolic status, offering a powerful tool for crop management, stress response analysis, and agricultural biotechnology [15].

In addition to their growing functional diversity, MNs are being explored for application in anatomically distinct and challenging sites. While the skin remains the most established target for MN-mediated delivery, emerging studies have demonstrated the potential of MNs for use in the oral cavity, enabling localized treatment of periodontal diseases and mucosal vaccines [16,17]; in ocular tissues, where MNs may circumvent corneal and conjunctival barriers to achieve targeted intraocular drug delivery [18,19]; and even in the myocardial tissue, where MNs may enable localized delivery of regenerative therapies post-infarction [20,21]. These advances underscore the adaptability of MN technology across tissue types with distinct structural and physiological constraints (Figure 1).

Looking forward, the development of MNs is set to intersect with several cutting-edge technologies and face critical translational challenges. The selection of biocompatible and functional materials, especially for dissolvable or bioresponsive MNs, remains a key barrier to clinical adoption. Likewise, scalable and cost-effective manufacturing processes are urgently needed to support commercial translation. Meanwhile, the rise of wearable devices and artificial intelligence (AI) opens up new frontiers for MNs, offering the possibility of real-time, personalized medicine through continuous data acquisition and AI-guided treatment optimization. In this perspective, we discussed recent advances in MN technology, its expanding applications across different tissues, and offer insight into the future directions and translational hurdles that must be addressed to fully unlock the potential of this versatile platform.

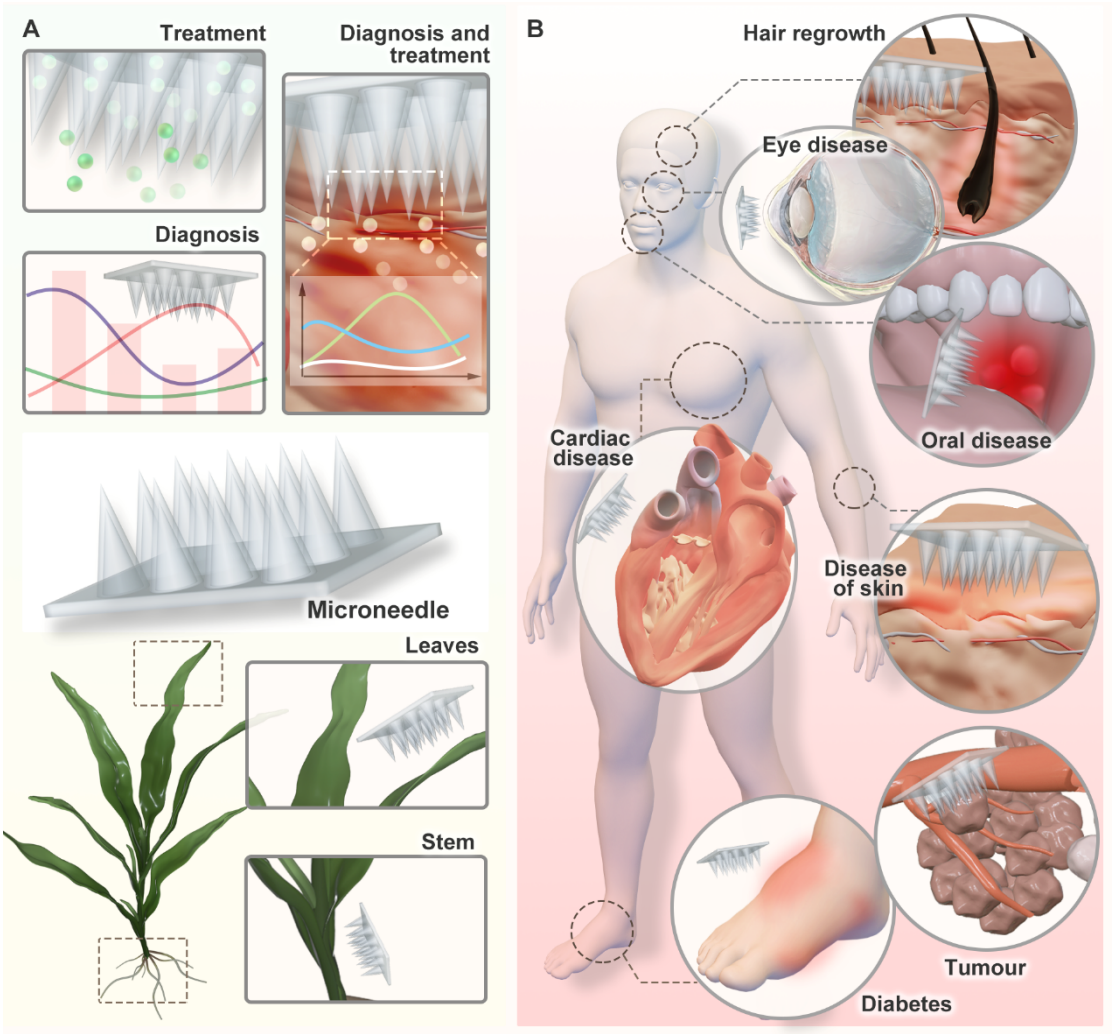

Figure 1. (**A**) Schematic illustration of MN applications in diagnostics, closed-loop diagnosis and treatment systems, and plant-based delivery and sensing. (**B**) Overview of MN applications across various medical and therapeutic scenarios, including hair regeneration, ocular drug delivery, oral delivery, tumor therapy, myocardial infarction treatment and wound healing, diabetes management.

2. Applications

2.1. Monitoring and Diagnosis

Although MNs were initially developed with a strong focus on transdermal drug delivery, recent advances have significantly expanded their utility into the realm of diagnostics. Leveraging their minimally invasive access to the interstitial fluid (ISF), a physiological medium rich in electrolytes, metabolites, proteins, and signaling molecules, MNs offer an attractive alternative to conventional blood sampling for continuous, real-time monitoring of human health [22,23] (Figure 2B). Given the compositional similarity between ISF and blood plasma, MN-based diagnostics are emerging as a powerful platform for point-of-care (POC) sensing, personalized medicine, and closed-loop health management [24].

Among the most promising advancements in MN-enabled monitoring and diagnostics are smart MN systems integrated with biosensors, which facilitate the real-time detection of a broad range of biochemical markers with minimal invasiveness [25]. Unlike traditional diagnostics that rely on invasive blood collection and centralized laboratory analysis, MN-based sensing systems allow for on-site, user-friendly, rapid and POC testing [26]. A representative example is the ion-sensing MN array (ISMA), engineered for continuous and multiplexed monitoring of essential electrolytes such as calcium (Ca^{2+}), potassium (K^{+}), and sodium (Na^{+}). This fully integrated system comprises three core components: a MN array functionalized with ion-selective membranes and a reference electrode, a printed circuit board (PCB) for signal acquisition and system control, and a smartphone-based interface enabling real-time data visualization and user interaction. In vivo experiments in rats confirmed the system's capability to dynamically monitor electrolyte fluctuations in ISF, highlighting its potential for clinical applications

in electrolyte management and disease monitoring [27] (Figure 2A). In addition to monitoring electrolytes, researchers have developed a miniaturized, high-precision wearable MN device for continuous glucose detection in human ISF. This fully integrated electrochemical sensing platform features individually addressable, spatially separated electrodes within a single MN array, allowing the incorporation of both a glucose sensor and a differential reference sensor within the same patch. The results demonstrated a strong correlation between ISF glucose readings obtained from the device and those measured by conventional blood-based assays, validating its clinical reliability [28]. Beyond ISF analysis, MN technology has also been adapted for the direct detection of protein biomarkers in capillary blood. A notable example involves the development of nanopillar array-embedded MNs designed for clinical POC diagnostics. These MNs leverage the high surface area of the nanopillar architecture to enhance antibody–antigen interactions, enabling rapid, specific, and highly sensitive detection of clinically relevant protein biomarkers directly within the skin. By eliminating the need for conventional blood extraction and ex vivo processing, this platform achieves ultrafast intradermal sampling and on-site analysis, significantly simplifying the diagnostic workflow [29] (Figure 2C).

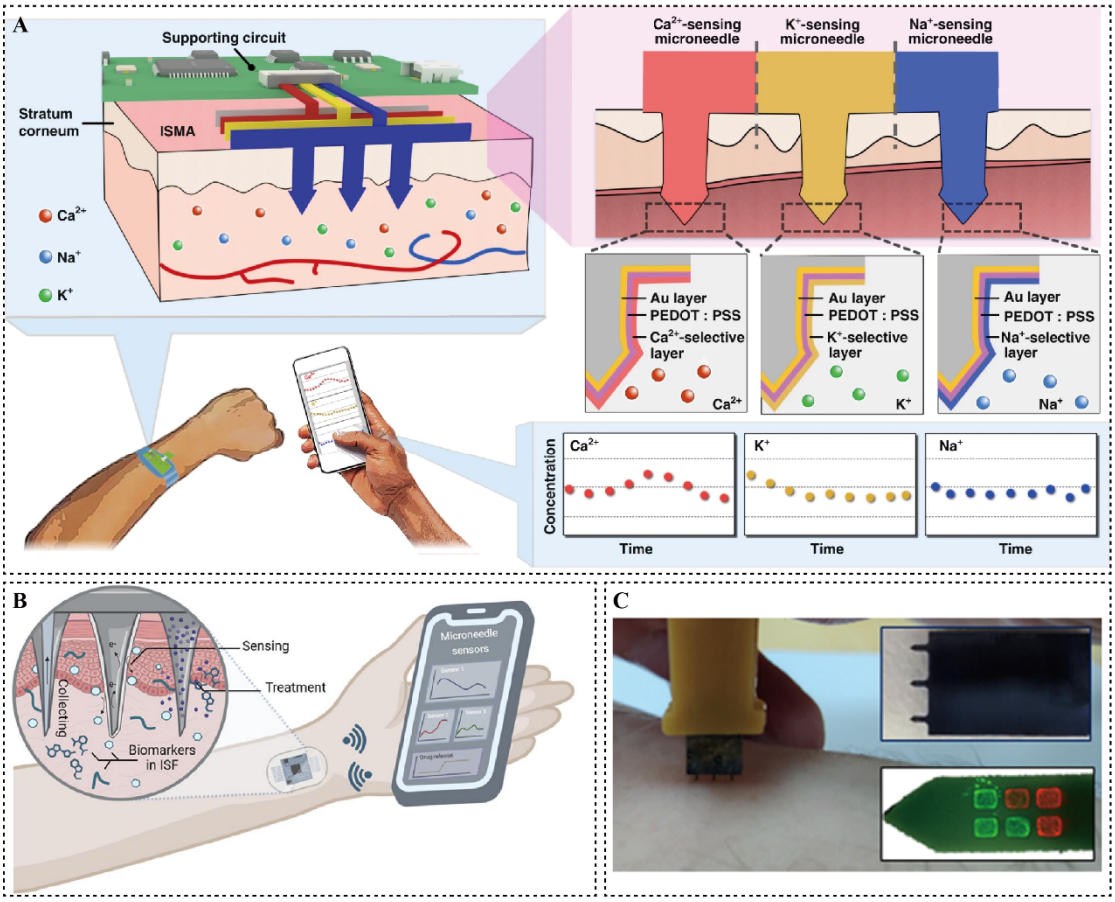

Figure 2. (**A**) Schematic illustration of a MN-array sensor for ion detection. The wearable MN-array sensor is designed for minimally invasive transdermal measurement of ion concentrations in ISF. Upon insertion into the skin, the sensor detects target ions and transmits the signals via a PCB to a microprocessor for real-time signal processing and display. The system enables simultaneous monitoring of multiple physiologically relevant ions, including Ca^{2+}, K^{+}, and Na^{+}. Reproduced with permission [27]. Copyright 2023, Springer Nature. (**B**) Overview of the MN sensing platform [30]. Copyright 2024, Springer Nature. (**C**) The figure shows the pricking step using a 3D-printed holder to assist precise skin insertion of nanopillar array-embedded MNs, which are designed for the direct detection of protein biomarkers in capillary blood for clinical POC applications. The device enables efficient, minimally invasive sampling and real-time diagnostic capabilities. Reproduced with permission [29]. Copyright 2024, ACS Publications.

2.2. Close-Looped Diagnosis and Treatment

Closed-looped diagnosis and treatment (CLDT) systems represent a transformative shift in modern medicine by mimicking the body's natural physiological feedback mechanisms to achieve autonomous, real-time therapeutic regulation [31]. In healthy individuals, complex biological feedback loops precisely regulate critical functions such

as glucose homeostasis, coagulation, and thermoregulation. However, in many pathological conditions, such control systems are disrupted, necessitating repeated manual interventions through timed drug administration, such as insulin injections or oral chemotherapy. These conventional open-loop approaches often lead to suboptimal outcomes, as drug concentrations fluctuate outside the therapeutic window due to metabolism and clearance, requiring constant re-dosing [32]. In contrast, CLDT systems integrate biosensing and actuation components to form an intelligent, responsive interface between the human body and therapeutic agents. By continuously monitoring specific biomarkers and autonomously adjusting drug release in response, these systems aim to maintain physiological parameters within target ranges, reduce dosing frequency, and improve clinical outcomes in managing dynamic and time-sensitive diseases such as diabetes, cancer, and inflammatory disorders [33,34].

MNs-based CLDT systems have recently emerged as a promising strategy for continuous glucose monitoring and responsive insulin delivery [35]. For example, Xie et al. developed an integrated wearable closed-loop system (IWCS) utilizing mesoporous MNs, which incorporates three key components: (1) a glucose-sensing module, constructed by combining mesoporous MNs with reverse iontophoresis to enhance interstitial glucose extraction and electrochemical detection; (2) a PCB serving as the control unit; and (3) a therapeutic module, in which mesoporous MNs are coupled with iontophoresis for electrically triggered insulin delivery. This IWCS demonstrated the ability to accurately monitor dynamic glucose fluctuations and autonomously deliver insulin in response, effectively regulating hyperglycemia in a diabetic rat model [36] (Figure 3A). In addition to glucose monitoring, a MN-based voltammetric sensor was developed and integrated with an iontophoretic hollow MNs to enable continuous monitoring of methotrexate levels and on-demand drug delivery [37] (Figure 3B). Another example is a self-powered skin patch that integrates hydration monitoring with on-demand drug delivery for CLDT of atopic dermatitis. The system incorporates a piezoelectric generator, hydration sensor, MN module, and flexible circuit, enabling autonomous detection of abnormal skin hydration and real-time release of therapeutic agents. This approach provides an innovative and noninvasive strategy for effective management of the disease [38] (Figure 3C).

2.3. MN-Based Delivery and Sensing in Plants

Foliar spray is currently the most widely adopted method for delivering agrochemicals in plant systems, including micronutrients, pesticides, plant growth regulators (PGRs), and stimulants. This technique is favored for its rapid deployment, low cost, and ease of use. However, its application efficiency is severely limited by significant off-target losses, studies report at least 30–40% of the sprayed substances are lost to the air [39], while others are rapidly washed off or degraded by environmental factors such as rain or sunlight [40]. Furthermore, foliar sprays often suffer from poor translocation due to the barrier properties of the plant cuticle and may cause environmental harm through water and soil contamination, loss of biodiversity, and risks to public health [41–43]. These drawbacks have driven the search for more precise and sustainable delivery approaches in plant science and agriculture.

MNs have recently emerged as a promising alternative, offering minimally invasive, localized, and highly efficient delivery of functional molecules directly into plant tissues. Due to their unique structure, MNs can physically penetrate the plant epidermis, bypassing surface barriers and enabling targeted, controlled release of active compounds [13,44]. For example, the silk-based MNs were fabricated to incorporate gibberellic acid. Experimental studies have demonstrated that MN-mediated delivery of GA_3 in *Arabidopsis thaliana* and multiple crop species induces physiological responses more effectively than traditional foliar spray, while causing minimal tissue damage or wound-related stress responses [45] (Figure 4A). Cao et al. designed MN-based devices, termed the “phytoinjector” and “phytosampler”, to enable the precise delivery of payloads into plant vasculature for studying material transport in the xylem and phloem, conducting complex biochemical reactions in situ, and accurately sampling plant sap [46] (Figure 4B). MN-based biosensors have also emerged for the combination of monitoring of plant growth and disease treatment [47]. MN biosensors can extract DNA from plant leaves within one minute, enabling rapid detection and timely intervention for plant diseases [48]. In addition, these devices are capable of real-time monitoring of various physiological indicators. By interfacing with computer systems, they can not only detect viral infections but also assess plant growth and maturity, thereby supporting precision agriculture and contributing to increased crop yield [49,50] (Figure 4C).

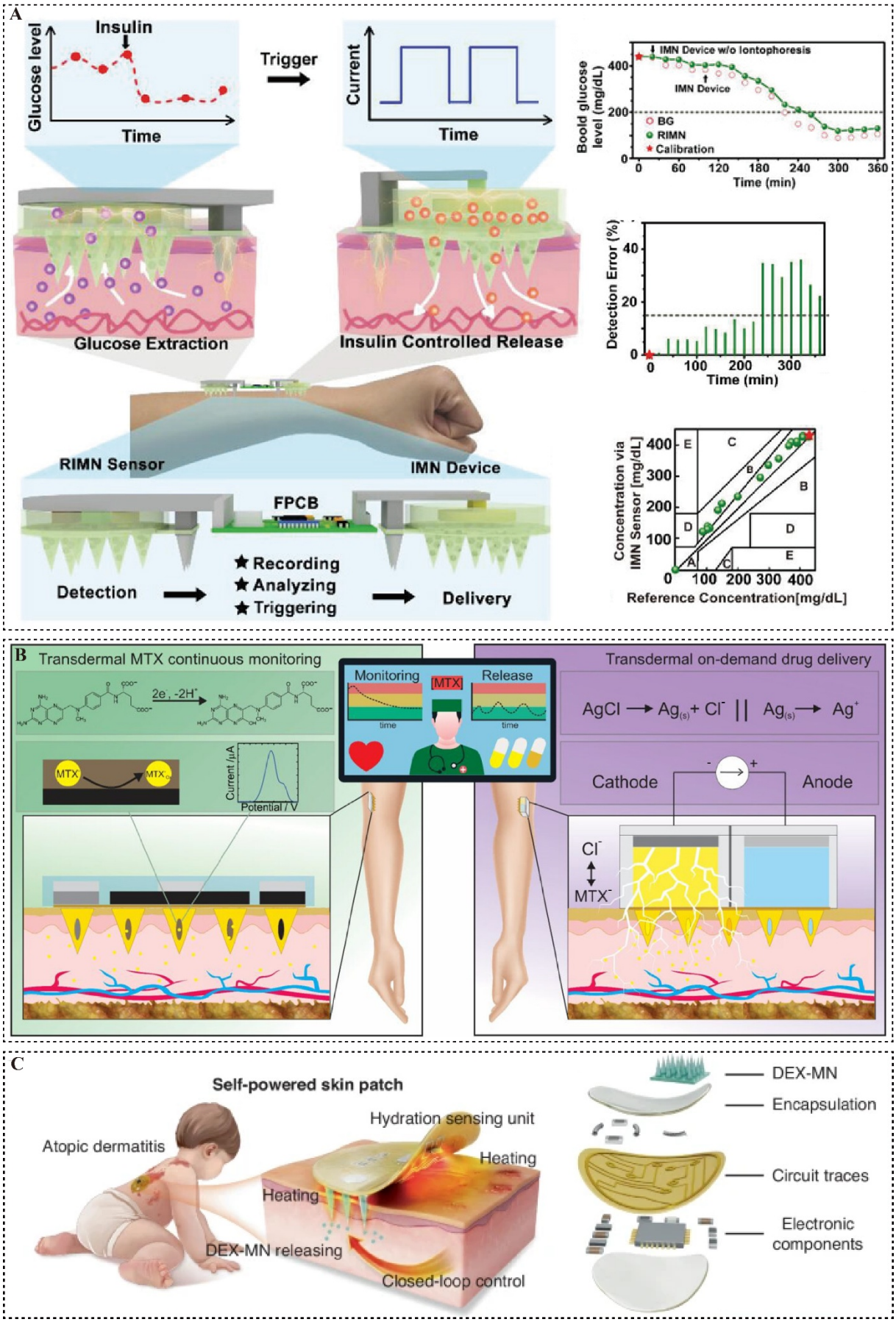

Figure 3. (**A**) Schematic illustration and performance characterization of the IWCS based on the MNs platform for diabetes management. The figure depicts the design of the IWCS, which enables real-time and in situ monitoring of glucose levels and on-demand insulin delivery via a MN-based interface. The system integrates sensing, control, and actuation components to achieve closed-loop diabetes therapy. Performance evaluations of the entire IWCS are

also shown, demonstrating its responsiveness, accuracy, and therapeutic efficacy. Reproduced with permission [36]. Copyright 2021, Wiley-VCH. (**B**) Wearable MN array patch for continuous electrochemical monitoring and on-demand transdermal delivery of methotrexate. Reproduced with permission [37]. Copyright 2023, American Chemical Society. (**C**) Schematic illustration of the MN-based system designed for atopic dermatitis therapy. Reproduced with permission [38]. Copyright 2025, Springer Nature.

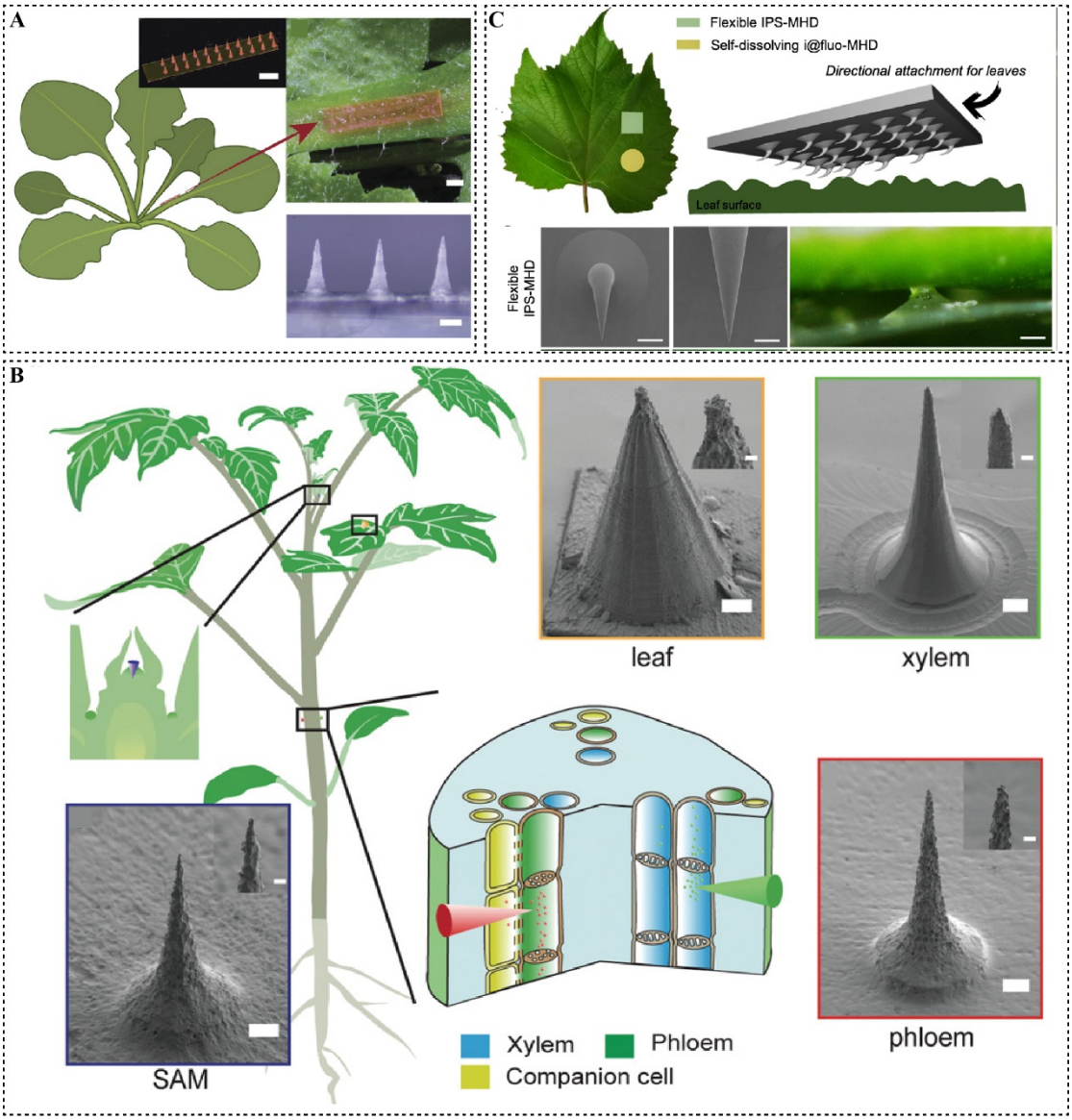

Figure 4. (**A**) Silk-based MNs for targeted GA_3 delivery in Arabidopsis mutant ft-10. Schematic illustration of GA_3-loaded silk MNs designed for precise delivery into the petiole of Arabidopsis mutant ft-10 plants. Representative image shows the petiole following administration with an array of GA_3-loaded MNs. Reproduced with permission [45]. Copyright 2022, Wiley-VCH. (**B**) Schematic illustration showing the use of silk fibroin MNs to fabricate phytoinjectors of specific shapes and sizes for precise payload delivery into foliar tissue, shoot apical meristem (SAM), and plant vasculature. Green and red phytoinjectors represent targeted delivery to xylem and phloem, respectively. The left inset highlights injection into the SAM. Scanning electron microscope images of phytoinjectors designed for delivery to the SAM, leaf tissue, xylem, and phloem. Reproduced with permission [46]. Copyright 2020, Wiley-VCH. (**C**) Artificial hooks of flexible IPS-made MH-based devices (IPS-MHDs) and their interlocking with the leaf surface [50]. Copyright 2021, Nature Publishing Group.

3. Application Sites

MN technology has demonstrated remarkable versatility in delivering therapeutic agents and diagnostics across a wide range of anatomical sites. By leveraging their minimally invasive structure, MNs can bypass physiological barriers and directly access target tissues with high precision and efficiency. Depending on the disease type and treatment goal, MNs have been engineered to suit various application sites, including the skin,

scalp, heart, eyes, and oral cavity, each with unique physiological challenges and therapeutic opportunities [51–54] (Figure 5).

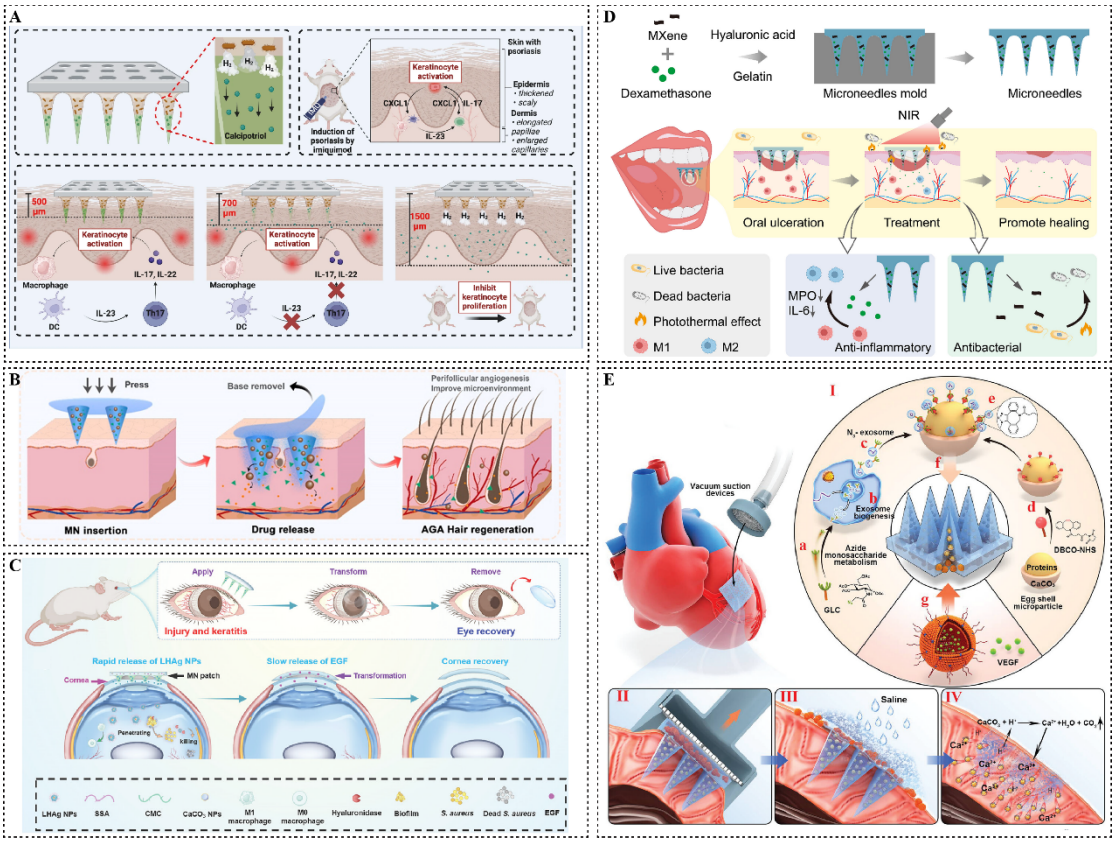

Figure 5. (**A**) Schematic illustration of a microbiota-assisted gas-propelled MN system for psoriasis treatment. Enterobacter aerogenes (E.A.) residing in the skin microbiota generates gas that facilitates the detachment and propulsion of the drug-loaded MN layer. The gas-driven dynamics enable calcipotriol to penetrate deeply into psoriatic lesions, thereby enhancing intradermal drug release and improving therapeutic efficacy. Reproduced with permission [55]. Copyright 2024, Springer Nature. (**B**) Schematic illustration of the VEGF–Ritlecitinib–Microneedle (V-R-MN patch) for promoting hair regrowth through vascular and immune microenvironment modulation. The V-R-MN patch delivers mild mechanical stimulation to the skin and enables the sequential release of VEGF to remodel the microvascular network around hair follicles and Ritlecitinib to modulate the local immune microenvironment. This synergistic approach enhances follicular regeneration and effectively promotes hair regrowth. Reproduced with permission [56]. Copyright 2024, KeAi Publishing Communications. (**C**) Schematic illustration of the transformative corneal MN patch for ocular injury and infection treatment. The diagram depicts the application of the corneal MN patch to the eye and its working mechanism: upon insertion, the dissolvable MN tips release antibacterial agents into the corneal stroma, while the backing layer transforms into a contact lens for sustained delivery of therapeutic factors, promoting infection control and tissue healing. Reproduced with permission [57]. Copyright 2025, Wiley-VCH. (**D**) Schematic illustration showing the fabrication of MXene-integrated MNs with near-infrared (NIR) responsiveness and their application at the oral ulcer site to achieve localized antibacterial effects, anti-inflammatory drug release, and accelerated tissue healing. Reproduced with permission [58]. Copyright 2025, Wiley-VCH. (**E**) Schematic illustration of the secondary drug-loaded MN patch design and therapeutic process. The MN patch features VEGF-loaded nanoparticles in the effervescent base and N_3-exosome–eggshell microparticle complexes in the needle tips. Upon insertion into the ischemic heart, VEGF is rapidly released into infarcted tissue, while self-propelled eggshell microparticles deliver exosomes to deeper myocardial regions. Reproduced with permission [59]. Copyright 2025, Wiley-VCH.

3.1. Skin

The skin is one of the most accessible and extensively studied sites for MN application [60]. As a novel transdermal drug delivery system, MNs work by penetrating the stratum corneum, the outermost barrier of the skin, to create micron-scale channels that enable the direct delivery of therapeutics into the epidermis or upper dermis [61]. This approach not only bypasses the limitations of the skin's natural barrier but also facilitates

localized or systemic drug absorption without significant pain or tissue damage. In the field of skin disease treatment, MN-based therapies have demonstrated potential in managing atopic dermatitis, wound healing, and acne, by enabling targeted delivery of anti-inflammatory agents, antibiotics, or regenerative molecules directly to affected skin layers [55,62,63] (Figure 5A).

3.2. Scalp and Hair

The scalp represents another promising site for MN-based therapeutic intervention, particularly in the treatment of hair-related disorders such as alopecia (hair loss) and folliculitis. Conventional topical therapies, such as sprays or lotions, often suffer from low delivery efficiency and poor drug absorption due to the barrier properties of the scalp and hair follicles, as well as rapid drug evaporation or runoff. MNs offer a compelling alternative by penetrating the scalp's stratum corneum and delivering drugs directly to the dermal layer, where hair follicles and associated structures reside [64]. This not only enhances drug bioavailability and therapeutic efficacy, but also enables minimally invasive and painless administration, improving patient compliance [56] (Figure 5B). As a result, MNs are gaining traction as a superior approach for localized, targeted, and efficient treatment of scalp-related dermatological conditions.

3.3. Ocular Tissue

The eye is a delicate and highly protected organ, yet it is susceptible to a wide range of chronic diseases that can affect both the anterior and posterior segments [65,66]. Anterior segment diseases, such as glaucoma and amebic keratitis, are commonly treated with topical drug formulations like eye drops. However, while eye drops are noninvasive and easy to administer, they suffer from significant limitations including low bioavailability (typically less than 5%), rapid tear clearance, limited drug penetration across the corneal epithelium, and poor patient adherence due to frequent dosing requirements [67]. In contrast, posterior segment diseases, such as age-related macular degeneration (AMD) and diabetic retinopathy, often necessitate intraocular injections to achieve effective drug concentrations in the retina or vitreous [68]. Although this method ensures direct delivery to deep ocular tissues, it is highly invasive, requires skilled medical professionals, and poses risks such as infection, retinal detachment, and patient discomfort.

MN technology presents a promising alternative for ocular drug delivery, offering several advantages over conventional methods. With a length typically less than 1 mm, MNs can penetrate ocular tissues in a minimally invasive manner, enabling targeted delivery to specific eye compartments with reduced tissue trauma and improved patient compliance [18]. For anterior segment conditions, MNs can bypass the corneal barrier to enhance local drug absorption, while for posterior segment diseases, specially designed MNs can deliver therapeutics across the sclera or into the suprachoroidal space, offering a less invasive and potentially safer alternative to intravitreal injections [69,70]. For instance, Jiang et al. developed a wearable corneal MN patch composed of water-soluble tips encapsulating antibacterial nanoparticles (NPs) and a transformative backing layer loaded with epidermal growth factor (EGF). Upon insertion into the corneal stroma, the MN tips rapidly dissolve, releasing the antimicrobial NPs to effectively eliminate bacterial pathogens. Simultaneously, the remaining backing layer undergoes an in-situ transformation upon contact with the mildly acidic fluid characteristic of infected corneal edema. This transformation results in the formation of a conformal contact lens that adheres to the ocular surface, enabling the sustained release of EGF for over 8 h, thereby promoting corneal repair and regeneration [57] (Figure 5C). MNs, as an innovative approach holds great potential for sustained, precise, and patient-friendly treatment of a broad spectrum of ocular diseases across both eye segments.

3.4. Oral Cavity

The oral cavity presents a unique and challenging environment for local drug delivery due to the presence of dynamic physiological barriers such as saliva flow, enzymatic degradation, and the mucosal epithelium [71]. Traditional oral dressings or hydrogel systems often suffer from limited adhesion, poor permeability, and imprecise drug localization. In contrast, MN systems offer a promising alternative for the treatment of oral diseases, such as oral ulcers, mucositis, and oral microbial infections [72,73]. By penetrating the mucosal epithelium and reaching the lamina propria, MNs can construct transient microchannels that bypass the mucosal barrier and facilitate precise, site-specific drug delivery directly to the lesion. This approach not only enhances drug bioavailability and retention at the target site but also significantly improves therapeutic efficiency compared to conventional oral formulations [74]. For example, a MXene-integrated responsive hydrogel MN system was developed for the targeted delivery of dexamethasone in the oral cavity to promote the healing of oral ulcers. This smart MN platform

can generate localized hyperthermia to exert antibacterial effects, while simultaneously releasing dexamethasone to suppress inflammation and facilitate tissue regeneration [58] (Figure 5D).

3.5. Heart

The heart presents a unique challenge for therapeutic delivery due to its constant dynamic contraction, which leads to the rapid extrusion of injected drugs from the myocardium. Studies have shown that only 5–15% of therapeutics are retained in the myocardial tissue following conventional injection, significantly limiting treatment efficacy [75]. To address the limitations of conventional cardiac therapies, researchers have developed MN patches as an innovative strategy for targeted drug and cell delivery to the heart. For example, a MN patch integrated with cardiac stromal cells (MN-CSCs) was designed to promote myocardial regeneration following acute myocardial infarction [76]. To further enhance delivery efficiency, a MN-based cardiac patch (MN-MSCF-NP) was developed, incorporating mesenchymal stromal cell-secreted factors (MSCF) encapsulated in poly(lactic-co-glycolic acid) (PLGA) nanoparticles at the MN tips. Both in vitro and in vivo studies demonstrated that the MSCF-NP formulation effectively promoted the proliferation of injured cardiomyocytes, reduced cardiomyocyte apoptosis, and enabled direct, localized delivery of MSCF into the myocardium [77]. Recently, a microrobot-mounted MN patch was proposed by Zhu et al. for the treatment of myocardial infarction. In this design, exosomes and VEGF-loaded nanoparticles were separately incorporated into the tips and base of the MNs. Upon injection, the patch base released VEGF-loaded nanoparticles, which adhered to the infarcted myocardium to promote angiogenesis. Meanwhile, exosome-modified eggshell microparticles were propelled into deeper myocardial regions by carbon dioxide bubble generation, facilitating targeted delivery to the infarct core [59] (Figure 5E).

4. Future Perspective

MN technology has demonstrated remarkable potential across a wide range of biomedical and agricultural applications. According to clinicaltrials.gov website, 81 clinical trials related to MNs have been registered over the past five years. These trials have primarily focused on the topical delivery of small-molecule drugs to the skin, oral cavity, and eyes. In addition, MNs have been utilized to enhance the administration of peptides, proteins and vaccines. Clinical studies have also explored MN-based biosensing applications, such as real-time monitoring of lactose and blood glucose levels. Furthermore, MNs are being investigated in the clinical diagnosis of various diseases, including psoriasis, food allergy, and allergic rhinitis. Commercially, MNs are particularly prominent in aesthetic applications, such as the SkinPen® Precisio. Market leaders have also advanced therapeutic applications: Zosano Pharma developed the Adhesive Dermally-Applied Microarray (ADAM) Technology for the delivery of zolmitriptan, and Debioject™ has been introduced for intradermal vaccine administration. The regulatory landscape for MN-based medicinal products is complex, as these systems are typically classified as drug-device combination products. In the United States, the FDA categorizes MN arrays under 21 CFR 3.2(e), requiring comprehensive oversight of both the device and the therapeutic agent.

However, several challenges must be addressed to fully translate laboratory success into clinical and commercial reality. Currently, materials commonly used for MN fabrication can be broadly categorized into four types: metallic materials, inorganic materials, natural polymers, and synthetic polymers. Inorganic and metallic materials, such as silicon and stainless steel, are widely applied in the preparation of solid and hollow MNs. Natural polymers, including hyaluronic acid and polysaccharides, as well as synthetic polymers, such as poly(lactic-co-glycolic acid) (PLGA), are mainly utilized for fabricating dissolving and hydrogel MNs. However, one major obstacle lies in the selection and optimization of MN fabrication materials. Ideal materials must balance mechanical strength for skin or tissue penetration, biocompatibility, biodegradability, and cost-effectiveness, a combination that remains difficult to achieve, particularly for multifunctional or stimuli-responsive systems. In addition, the scalable and reproducible mass production of MNs, especially those with complex structures or integrated sensors, remains a significant manufacturing bottleneck. Standardized, automated fabrication technologies will be essential to ensure quality control and regulatory compliance. To address these challenges, several feasible measures can be considered. Expanding the use of biocompatible and biodegradable materials, together with rigorous long-term preclinical and clinical safety evaluations, will be essential to reduce risks and increase patient acceptance. In surgical and diagnostic applications, proper training of healthcare professionals, standardized operating protocols, and comprehensive monitoring of postoperative outcomes will minimize adverse events and improve reliability. Collectively, these measures can help bridge the gap between laboratory research and real-world clinical adoption of MN technologies.

Looking ahead, the integration of MN systems with wearable electronics represents an exciting frontier, enabling continuous health monitoring, real-time feedback, and even closed-loop therapeutic interventions. The

miniaturization of sensing and actuation components, coupled with advances in flexible electronics, can transform MNs into truly intelligent and user-friendly platforms. Moreover, the convergence of MN technology with AI is poised to revolutionize personalized healthcare. AI algorithms can analyze large volumes of real-time biosignal or biomarker data collected via MNs, enabling early disease detection, predictive diagnostics, and optimized therapeutic regimens tailored to individual patients. This synergy between MNs and AI will also facilitate adaptive drug delivery systems capable of autonomous decision-making based on physiological cues.

In conclusion, while technical and translational challenges remain, the future of MNs lies in their convergence with smart materials, wearable systems, and AI-driven analytics, paving the way toward next-generation platforms for precision medicine, remote health management, and sustainable agriculture.

Author Contributions

Y.T. and Y.C. wrote the manuscript, Y.T. illustrated the figures. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

This study does not involve humans or animals.

Informed Consent Statement

This study does not involve humans.

Data Availability Statement

No new data were generated or analyzed in this study.

Conflicts of Interest

Given the role as the Editor-in-Chief, Yu Chen had no involvement in the peer review of this paper and had no access to information regarding its peer-review process. Full responsibility for the editorial process of this paper was delegated to another editor of the journal.

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