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COMMENTARY

Microneedle-based delivery for autoimmune diseases: Emerging opportunities and unresolved questions

KEY WORDS

Microneedle;
Autoimmune diseases;
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Autoimmune diseases are receiving increasing global attention, driven by population aging and the rising burden of chronic disease worldwide[1]. Epidemiological studies estimate that autoimmune diseases affect approximately 4%−10% of the global population[2]. Although therapeutic options have expanded substantially in recent decades, most autoimmune diseases still require long-term intervention[3], and repeated treatment frequently compromises patient adherence. Delivery systems that improve tolerability, convenience, and long-term compliance therefore remain clinically important[4−6].

Microneedle (MN) technology offers a practical response to this need. By creating transient microchannels across the stratum corneum with minimal tissue disruption, MN arrays enable minimally invasive delivery into the epidermis and superficial dermis. Compared with conventional injection and oral administration, MN systems may reduce pain, improve patient acceptability, and bypass first-pass metabolism. More importantly, the skin is not merely a passive route of administration. It constitutes an immunologically active tissue containing Langerhans cells, dermal dendritic cells, macrophages, and resident memory T cells, thereby offering a biologically relevant interface for therapeutic intervention in immune-mediated disease[7].

Against this backdrop, the review by Chen et al.[8] provides a timely and valuable overview of recent advances in MN technology for autoimmune disease treatment. Its significance lies not only in summarizing device platforms and therapeutic applications, but also in drawing attention to the broader possibility that MNs may serve as tools for immune modulation rather than as drug-delivery devices alone. At the same time, the field remains at an early stage of clinical translation, and several key biological, clinical, and manufacturing issues merit further consideration.

1. The advances of MN technology for autoimmune disease treatment

Despite these advantages, MN application in autoimmune disease remains fragmented, without a clear framework linking disease characteristics, payload selection, and immune targets. Chen et al. provide a timely overview of current MN-based strategies in this area.

A notable strength of the review is its systematic classification of MN systems according to fabrication strategy and drug release mechanism, encompassing both established and emerging platforms. This organizational approach is particularly useful because it links device design to therapeutic function, rather than treating MNs as purely mechanical carriers. In doing so, it helps clarify how distinct MN architectures may be matched to payload characteristics, disease contexts, and desired release kinetics.

The review also effectively situates MN technology within the broader landscape of unmet clinical need in autoimmune disease management. Current autoimmune therapies remain broadly divided into topical and systemic approaches. Topical therapies, including glucocorticoids, vitamin D3 analogues, calcineurin inhibitors, and ultraviolet phototherapy, are widely used but frequently associated with local adverse effects such as irritation, erythema, and hyperpigmentation. Systemic therapies, including non-steroidal anti-inflammatory drugs, immunomodulators, and biologics, remain central for many autoimmune diseases but are

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limited by systemic toxicity, immune-related adverse effects, organ burden, and high treatment cost. In this context, MN-based delivery is attractive not only because it may enhance local drug deposition, but also because it may reduce systemic exposure while preserving, or in some settings, improving therapeutic benefit.

Another important contribution of the review is its synthesis of evidence across a wide range of autoimmune indications, including psoriasis, psoriatic arthritis, rheumatoid arthritis, and atopic dermatitis, where multiple preclinical studies report superior outcomes compared with conventional administration routes. Importantly, applications have also extended to systemic autoimmune diseases such as type 1 diabetes and multiple sclerosis, indicating that transdermal delivery may generate systemic immunomodulatory effects rather than purely local responses.

The review's discussion of clinical studies is likewise informative. The inclusion of investigations in psoriasis, rheumatoid arthritis, vitiligo, and type 1 diabetes provides a more concrete sense of how far the field has advanced beyond proof-of-concept experimentation. Vitiligo currently accounts for the largest number of MN-related clinical studies, likely because controlled epidermal injury induced by MNs facilitates melanocyte migration and repigmentation. Nevertheless, these early studies also underscore the persistent gap between technical feasibility and robust clinical translation. Major unresolved barriers also include material biocompatibility, manufacturing cost, and long-term safety under repeated administration in chronic disease settings.

2. Key challenges and future directions

Based on these encouraging findings summarized by Chen et al., several additional questions deserve further discussion. First, autoimmune skin lesions rarely resolve uniformly in clinical practice: most lesions improve, but small refractory areas often persist and later become sites of relapse. This gives MN systems a practical advantage by enabling spatially selective treatment of residual lesions.

Second, the clinical applicability of MN-based therapy is likely to vary according to disease extent and treatment context. Future studies need to examine whether MN-mediated delivery can actively reshape local immune memory, particularly through modulation of resident memory T cells or restoration of local Treg balance. Durable remission may depend more on reprogramming local immune networks than on transient suppression of inflammation. Limitation also appears in patients with extensive skin involvement, where patch-based treatment alone may not be sufficient. Combination with systemic therapy may therefore be unavoidable, raising practical questions regarding dosing strategy, treatment cost, and accessibility.

Third, as biologic therapies continue to expand in autoimmune medicine, increasing evidence suggests that MN platforms may support transdermal delivery of large therapeutic molecules, including monoclonal antibodies and immune regulators. Under these conditions, dose precision, storage stability, and transport logistics become critical determinants of feasibility. Gene therapy represents another direction that remains largely unexplored. For several inherited skin disorders, gene therapy is already among the few potentially curative options. Whether MN systems can support local delivery of nucleic acids or gene-editing payloads in autoimmune settings remains uncertain, but conceptually attractive. Progress here may depend less on increasing penetration alone and more on integrating MN platforms with cell-selective delivery strategies capable of targeting defined immune populations.

Lastly, as highlighted by the authors, the discontinuation of clinical trial NCT02955576 because of inconsistent therapeutic outcomes further illustrates a major translational barrier: manufacturing reproducibility. Batch-to-batch consistency and scalable production are likely to determine whether promising MN systems can move beyond early clinical testing.

3. Conclusion

In conclusion, this review provides a comprehensive and timely overview of MN technologies for autoimmune disease treatment and clearly highlights their translational potential in immune-targeted drug delivery. More importantly, it suggests that future progress should not only focus on improving delivery efficiency, but also on defining how MN-based systems can actively reshape local immune networks to promote durable immune tolerance and achieve long-term disease control.

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