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ADVANCES IN POLYMER MICRONEEDLE SYSTEMS: A NEW ERA FOR TRANSDERMAL DRUG ADMINISTRATION

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ABSTRACT
Polymer-based microneedles (MNs) have revolutionized the field of transdermal drug delivery by offering a minimally invasive, patient-friendly, and efficient alternative to conventional routes such as oral and injectable administration. This review explores the latest advancements in polymer microneedle technologies, with a focus on their classification, material selection, drug loading strategies, release kinetics, therapeutic applications, and clinical translation. Biodegradable polymers such as polyvinylpyrrolidone (PVP), polylactic-co-glycolic acid (PLGA), chitosan, and hyaluronic acid have demonstrated superior biocompatibility and tunable mechanical properties, enabling precise and sustained drug release. Microneedles have shown significant promise in diverse therapeutic areas including vaccination, insulin delivery, cancer therapy, hormone replacement, and dermatological treatments. We also discuss the current status of clinical trials, regulatory frameworks established by the FDA and EMA, and commercial trends driving innovation. Although challenges such as manufacturing scalability and regulatory standardization persist, future directions point toward smart microneedles integrated with biosensors and digital health platforms. These advances position polymer microneedles as a transformative technology in personalized and decentralized medicine.

KEYWORDS: Polymer-based microneedles, drug loading strategies, therapeutic applications, clinical translation and Biodegradable polymers.

1. INTRODUCTION

1.1 Background on Transdermal Drug Delivery

Transdermal drug delivery systems (TDDS) represent a non-invasive route for administering therapeutics through the skin, bypassing the gastrointestinal tract and first-pass metabolism. This approach offers improved patient compliance, controlled drug release, and reduced dosing frequency, making it particularly advantageous for chronic treatments (Alkilani et al., 2022). However, the stratum corneum, the skin's outermost layer, presents a significant barrier to the permeation of most drugs, especially those with high molecular weight or hydrophilicity.

Over the past few decades, various strategies such as chemical enhancers, iontophoresis, and electroporation have been explored to improve skin permeability. Among these, microneedle (MN) technology has emerged as a transformative innovation, offering precise and minimally invasive penetration of the stratum corneum (Guillot et al., 2020).

1.2 Limitations of Conventional Methods

Traditional drug delivery methods—such as oral administration, hypodermic injections, and topical formulations—suffer from several drawbacks. Oral delivery is limited by enzymatic degradation and hepatic first-pass metabolism, leading to low bioavailability for many drugs (Singh et al., 2019). Parenteral routes, while effective, are invasive, painful, and associated with needle phobia and risks of infections or needlestick injuries.

Topical and transdermal creams often fail to deliver sufficient drug quantities through intact skin, especially for macromolecules such as peptides, proteins, and vaccines (Damiri et al., 2022). These challenges underscore the need for innovative platforms like microneedles that offer both efficacy and patient convenience.

1.3 Rise of Microneedle Technology

Microneedles are micron-scale projections that painlessly breach the stratum corneum to enable direct drug diffusion into the dermis or epidermis. This technology bridges the gap between hypodermic needles and

transdermal patches, combining the benefits of both while minimizing their disadvantages. Initially developed using metals and silicon, microneedles have evolved significantly with the advent of biocompatible and biodegradable polymers, which eliminate issues related to residual waste and safety (Park et al., 2005).

Polymeric microneedles, in particular, offer customizable mechanical strength, tunable degradation rates, and improved drug stability, making them ideal for controlled and sustained release applications (Hasan et al., 2020). This rise in MN innovation reflects a paradigm shift in drug delivery science, where engineering precision intersects with patient-centric care.

1.4 Scope and Objectives of the Review

This review aims to explore the rapid advancements in **polymer-based microneedle systems** with a focus on their application in **transdermal drug delivery**. We will assess the current material landscape, fabrication technologies, drug delivery strategies, and clinical translations. Additionally, this paper will highlight the regulatory landscape, identify ongoing challenges, and discuss future trends, including smart microneedles and personalized therapies. The overarching goal is to provide a comprehensive understanding of how polymer microneedles are reshaping the future of drug administration.

2. OVERVIEW OF MICRONEEDLE TECHNOLOGY

2.1 Types of Microneedles

Microneedles (MNs) are broadly categorized into five types based on their structure and function, each offering unique drug delivery mechanisms:

- **Solid Microneedles:** Used to create microchannels in the skin. Drugs are applied post-insertion, relying on passive diffusion. They are simple to manufacture but limited in controlling dose (Yadav et al., 2022).
- **Coated Microneedles:** These have a drug-coated surface that dissolves upon skin insertion, releasing the drug rapidly. They allow precise dosing but require careful formulation to maintain drug stability (Shriky et al., 2023).
- **Dissolving Microneedles:** Made of biodegradable polymers that encapsulate the drug within the needle structure. Upon insertion, the needle dissolves in the skin, providing both delivery and biodegradation (Tian et al., 2025).
- **Hollow Microneedles:** Function like hypodermic needles to inject liquid formulations directly into the dermis. They offer controlled infusion but are structurally more complex (Dang et al., 2022).
- **Hydrogel-Forming Microneedles:** Swell upon insertion and create a conduit for drug diffusion from a connected patch or reservoir. They are reusable and do not leave residues, making them safe and sustainable (Alex et al., 2024).

2.2 Mechanism of Transdermal Penetration

Microneedles physically breach the **stratum corneum**, the main barrier of the skin, without reaching the pain receptors located deeper in the dermis. The created microchannels allow hydrophilic and high-molecular-weight drugs to pass through, enabling localized or systemic drug absorption. Drug diffusion occurs via:

- **Capillary action** (in hydrogel-forming MNs)
- **Passive diffusion** (in coated or dissolving MNs)
- **Active infusion** (in hollow MNs with pump systems)

Their precision targeting also reduces systemic side effects and ensures high local drug concentrations (Parhi, 2022).

2.3 Advantages Over Traditional Delivery Systems

Compared to oral and parenteral routes, microneedles offer:

- **Minimally invasive delivery** with little or no pain
- **High patient compliance**, especially for chronic treatments
- **Bypassing of gastrointestinal and hepatic metabolism**, enhancing bioavailability
- **Enhanced delivery of macromolecules** like peptides, proteins, and vaccines
- **Elimination of sharps waste**, especially with dissolving and hydrogel-forming MNs

These benefits make MNs a promising platform for both therapeutic and diagnostic applications (Mahato, 2017; Migdadi & Donnelly, 2019).

3. POLYMER MATERIALS FOR MICRONEEDLES

3.1 Biodegradable vs. Non-Biodegradable Polymers

Polymers used in microneedle fabrication are generally classified into **biodegradable** and **non-biodegradable** categories based on their degradation behavior within biological tissues. Biodegradable polymers gradually break down into nontoxic byproducts and are ideal for **dissolving microneedles**, eliminating the need for needle removal after administration. Common examples include **PLGA**, **chitosan**, and **hyaluronic acid**. In contrast, **non-biodegradable polymers**, such as **polycarbonate** or **silicone**, are primarily used in **solid microneedles**, and require post-application disposal (Mdanda et al., 2021).

3.2 Commonly Used Polymers

3.2.1 Polyvinylpyrrolidone (PVP)

PVP is a water-soluble, non-toxic polymer widely used for **dissolving microneedles**. It has high mechanical strength, is easy to mold, and allows for fast dissolution upon insertion (Kulkarni et al., 2023). It is especially suitable for heat-sensitive and biologically active molecules due to its gentle processing requirements.

3.2.2 Poly (lactic-co-glycolic acid) (PLGA)

PLGA is a US-FDA approved **biodegradable polymer** known for its sustained drug release capabilities. It provides excellent encapsulation for vaccines, peptides, and small molecules. PLGA's degradation rate can be

tuned by altering the lactic to glycolic acid ratio (Malek-Khatabi et al., 2023).

3.2.3 Chitosan

Derived from chitin, **chitosan** is a natural, biocompatible polymer with **mucoadhesive and antimicrobial** properties. It is particularly advantageous in skin and wound-related applications due to its wound healing potential (Damiri et al., 2022). Chitosan microneedles are often used in conjunction with other polymers to improve mechanical stability.

3.2.4 Carboxymethyl Cellulose (CMC) and Hyaluronic Acid (HA)

Both **CMC** and **HA** are natural polysaccharides with excellent biocompatibility. CMC is frequently used in **dissolving microneedles** due to its structural flexibility and hydrophilic nature, while HA is valued for **cosmetic and dermatological applications** because of its role in skin hydration (Tsung et al., 2023).

3.3 Material Properties Influencing Performance

Key properties that determine the selection and performance of polymers in microneedle systems include:

- **Mechanical Strength**: Ensures proper skin penetration without breaking.
- **Hydrophilicity/Hydrophobicity**: Influences drug loading and release.
- **Degradation Rate**: Affects duration and control of drug release.
- **Biocompatibility**: Ensures safety and minimizes immune response.

Optimization of these properties often involves polymer blending or crosslinking strategies to balance mechanical and biological functions (Berillo et al., 2021).

3.4 Fabrication Techniques and Scalability

Several fabrication techniques are employed to manufacture polymeric microneedles:

- **Micromolding**: The most common technique involving polymer casting into microstructured molds.
- **Drawing Lithography**: A precision method suitable for rapid prototyping and scale-up.
- **3D Printing and Laser Cutting**: Advanced methods enabling custom designs and smart integration (Azizi Machekposhti et al., 2023).

  Scalability remains a significant challenge, especially for multilayer and drug-loaded MNs. However, the integration of **robotic automation** and **continuous casting systems** shows promise for industrial-scale production.

4. DRUG LOADING AND RELEASE KINETICS

4.1 Drug Incorporation Strategies

Drug loading in polymeric microneedles (MNs) is a critical step that influences dosage precision, release kinetics, and therapeutic efficacy. Strategies for incorporation vary depending on the MN type and therapeutic target:

- **Matrix embedding** is commonly used in dissolving and hydrogel-forming MNs, where the drug is uniformly distributed within the polymer matrix.
- **Surface coating**, often used in solid microneedles, allows rapid drug release upon insertion but may suffer from limited drug capacity.
- **Encapsulation in nanoparticles** or **liposomes**, followed by integration into the MN matrix, enhances stability, controls release, and enables co-delivery of multiple agents (Alkilani et al., 2022).

Some recent innovations also use **layer-by-layer assembly**, allowing spatial control over drug deposition within the microneedle length for **multi-stage release** (Jamaledin et al., 2020).

4.2 Controlled and Targeted Drug Release

Controlled release from MNs is influenced by **polymer composition**, **needle geometry**, and **drug-polymer interactions**. Polymer microneedles like those made from **PLGA** or **hyaluronic acid** can provide **sustained release** for days to weeks depending on polymer degradation profiles (Vora et al., 2023).

Approaches include

- **Time-controlled release** using multilayered microneedles or cross-linked networks
- **Stimuli-responsive systems** such as **pH-sensitive** or **temperature-responsive polymers**, which release the drug upon encountering a specific microenvironment (Syafika et al., 2023).

These systems ensure precise dosing, reduce side effects, and improve therapeutic efficiency—especially in chronic disease management and vaccination.

4.3 Stability and Bioavailability Considerations

Microneedles significantly enhance the **stability** and **bioavailability** of therapeutics by:

- Avoiding the harsh conditions of the gastrointestinal tract
- Reducing enzymatic degradation common in oral routes
- Protecting labile compounds like proteins and peptides through **encapsulation**

Studies have shown up to **4- to 10-fold increases in bioavailability** for macromolecules delivered via microneedles compared to oral or topical formulations (Tang et al., 2024). Encapsulation in polymer matrices also helps **preserve the structural integrity** of sensitive drugs, extending shelf life under ambient storage conditions (Xu et al., 2024).

5. APPLICATIONS IN THERAPEUTICS

5.1 Vaccination

Polymeric microneedles (MNs) offer an innovative platform for **needle-free, painless, and stable vaccine**

delivery. They improve antigen stability, enhance immune responses by targeting skin-resident antigen-presenting cells, and simplify mass immunization logistics. Recent studies demonstrated that microneedle patches loaded with **virus-like particles** or **mRNA vaccines** can induce strong humoral and cellular immunity, outperforming conventional injections in some cases (Guillot et al., 2020; Kim et al., 2012).

5.2 Pain Management

Transdermal delivery of analgesics like lidocaine, ibuprofen, and opioids via MNs allows **rapid onset and prolonged pain relief**. MNs help avoid gastrointestinal complications and bypass hepatic metabolism. Some systems have been developed with **responsive release mechanisms**, such as pain-triggered or thermally activated microneedles (Nazary Abrbekoh et al., 2022).

5.3 Hormone Replacement Therapy

Microneedles are now being explored for delivering hormones like **estradiol**, **testosterone**, and **growth hormone**. These systems ensure **stable plasma levels**, reduce injection frequency, and avoid peak-trough fluctuations that occur with injections. They're particularly promising for **menopausal therapy** and **contraceptive applications** (Nguyen & Nguyen, 2023).

5.4 Insulin Delivery for Diabetes

One of the most prominent and clinically advanced applications of MNs is **transdermal insulin delivery**. Dissolving microneedles fabricated with biocompatible polymers have shown **efficient glucose control** in diabetic models and human trials, offering a **pain-free alternative** to subcutaneous injections (Singh et al., 2019; Liu et al., 2024). Innovations include **glucose-responsive MNs** that release insulin only when blood sugar rises, enabling smart self-regulation (Syafika et al., 2023).

5.5 Cancer Therapy and Chemotherapy

Microneedle systems have shown potential in **targeted transdermal chemotherapy**. Drugs like doxorubicin and 5-FU have been incorporated into dissolving MNs, enabling **localized delivery** to skin tumors while minimizing systemic toxicity. Combinations with nanocarriers and **immune checkpoint inhibitors** are under development for melanoma and breast cancer treatments (D'Amico, 2025; Lima et al., 2021).

5.6 Cosmetic and Dermatological Use

Microneedles have surged in popularity in the cosmetic sector, especially for **anti-aging**, **scar reduction**, and **skin lightening**. Active ingredients like **hyaluronic acid**, **retinoids**, and **vitamin C** are delivered directly into the dermis, improving efficacy and user satisfaction. Some MN patches are now **commercially available** for under-eye brightening and acne treatment (Xu et al., 2024).

6. Challenges and Future Perspectives

The future of polymer microneedle (MN) technology lies in overcoming current limitations through advances in materials science, fabrication scalability, and regulatory harmonization. To fully realize their clinical potential, MNs must achieve consistent mechanical strength, precise drug dosing, and long-term stability, particularly for biologics and complex molecules. Innovations in 3D printing, automated micromolding, and smart materials are expected to streamline manufacturing and enable large-scale production. Regulatory frameworks are beginning to evolve, but clearer guidance from agencies like the FDA and EMA will be essential to accelerate approval pathways. Moreover, the integration of MNs with digital health technologies—such as biosensors, microfluidic systems, and feedback-responsive drug release—opens the door to intelligent, closed-loop delivery systems tailored to individual patient needs. Equally important is addressing affordability and accessibility, especially for use in low-resource settings where MNs could revolutionize at-home treatments and preventive care. As research converges across engineering, medicine, and biotechnology, polymer microneedles are poised to play a transformative role in the future of personalized, decentralized healthcare.

7. CONCLUSION

In conclusion, polymer microneedles have emerged as a groundbreaking platform in transdermal drug delivery, combining the benefits of minimally invasive administration, controlled release, and enhanced patient compliance. Their ability to bypass biological barriers like the stratum corneum while maintaining drug integrity makes them especially suitable for delivering a wide range of therapeutics, including vaccines, peptides, hormones, and chemotherapeutic agents. Significant advancements in polymer engineering, fabrication technologies, and drug-loading strategies have propelled microneedles from experimental prototypes to clinically viable systems. Despite ongoing challenges related to scalability, regulatory approval, and long-term safety validation, the rapid progress in this field signals a strong trajectory toward commercialization and widespread adoption. As interdisciplinary collaboration continues to drive innovation, polymer microneedles are expected to play a pivotal role in the next generation of precision medicine and self-administered healthcare solutions.

8. Author's Contribution

All Authors Contributed Equally.

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