

Microneedle Technologies in Transdermal Drug Delivery: Improving Bioavailability and Patient Compliance

Brigitta Steven*

Department of Pharmaceutical Sciences, Princeton University, Princeton, NJ 08544, USA

Abstract

Microneedle technologies represent a transformative approach in transdermal drug delivery, offering significant improvements in bioavailability and patient compliance. This article reviews the latest advancements in microneedle technology, including its mechanisms, types, applications and future perspectives. The potential benefits of microneedles in enhancing drug absorption, minimizing pain and simplifying administration are discussed, along with challenges and opportunities for further research.

Keywords: Patient compliance • Drug delivery • Bioavailability

Introduction

Transdermal drug delivery systems (TDDS) are designed to deliver therapeutic agents through the skin for systemic effects. These systems offer several advantages over traditional methods of drug administration, including the avoidance of gastrointestinal degradation and first-pass metabolism by the liver. The fundamental principle behind TDDS is to create a controlled and sustained release of medication, which can enhance patient compliance and improve therapeutic outcomes.

TDDS typically consist of a drug reservoir, an adhesive layer to ensure the system remains attached to the skin and a backing layer to protect the drug from external conditions. Drugs are delivered through the skin's outer layer, the stratum corneum, which is the primary barrier to drug penetration. To overcome this barrier, various techniques are employed, including the use of chemical enhancers, physical methods like iontophoresis or ultrasound, and, more recently, microneedle technology.

Microneedle technology represents a significant advancement in TDDS. Microneedles are tiny needles that create microchannels in the skin, allowing drugs to bypass the stratum corneum and penetrate deeper layers of the skin where absorption is more efficient. This method not only improves the bioavailability of drugs but also reduces discomfort compared to traditional needles and invasive procedures.

The development of microneedle-based systems has expanded the range of drugs that can be delivered transdermally, including larger molecules and biologics that were previously unsuitable for this route. By enhancing drug delivery and patient comfort, these systems have the potential to transform the way medications are administered, making treatments more effective and improving adherence to therapy.

Literature Review

Bioavailability and patient compliance are critical factors in the effectiveness of drug delivery systems. Bioavailability refers to the proportion of a drug that enters the bloodstream and reaches its target tissues, impacting

the drug's therapeutic efficacy. High bioavailability ensures that an adequate amount of the drug is available to exert its intended effect, which is crucial for achieving the desired clinical outcomes. This is particularly important in drugs with narrow therapeutic windows where precise dosing is essential [1].

Patient compliance, on the other hand, involves the extent to which patients adhere to prescribed treatment regimens. High compliance rates are essential for maintaining effective drug levels in the body and achieving optimal therapeutic results. Factors influencing patient compliance include the convenience of the drug delivery method, the frequency of administration and the overall comfort and acceptability of the treatment. Poor compliance can lead to suboptimal drug levels, treatment failures and increased risk of disease progression or complications.

Combining high bioavailability with improved patient compliance can significantly enhance treatment efficacy. For instance, transdermal systems with enhanced bioavailability can ensure that a consistent and effective dose of medication is delivered over time. Simultaneously, patient-friendly delivery methods that minimize discomfort and simplify the administration process can improve adherence to the prescribed regimen. Thus, optimizing both bioavailability and patient compliance is key to maximizing the therapeutic benefits of drug treatments and ensuring better health outcomes [2].

Microneedle technology

Microneedle technology represents a pioneering advancement in drug delivery systems, offering a novel approach to administering medications through the skin. Microneedles are extremely small needles, typically ranging from 25 to 900 micrometers in length, that penetrate the outermost layer of the skin, the stratum corneum, to deliver drugs or vaccines effectively and with minimal discomfort.

The primary advantage of microneedle technology lies in its ability to bypass the skin's natural barrier function, which traditionally impedes drug absorption. By creating microchannels in the skin, microneedles facilitate the direct transport of drugs into the dermal or subcutaneous layers, where absorption is more efficient compared to traditional transdermal systems. This approach enhances the bioavailability of various therapeutic agents, including large molecules and biologics that cannot easily penetrate the skin on their own [3].

Microneedles come in several forms, each with specific applications and benefits:

- **Solid microneedles:** These are used to create microchannels in the skin, allowing drugs to be applied topically and absorbed through the skin.
- **Hollow microneedles:** These needles can deliver liquid drugs directly into the dermis or subcutaneous tissue.
- **Dissolving microneedles:** Made from materials that dissolve in

*Address for Correspondence: Brigitta Steven, Department of Pharmaceutical Sciences, Princeton University, Princeton, NJ 08544, USA; E-mail: BrigittaSteven4@gmail.com

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the skin, these needles release drugs gradually as they dissolve, providing controlled drug delivery.

- **Coated microneedles:** These are coated with a drug that is released upon insertion into the skin, allowing for precise and efficient drug delivery.

The technology not only improves drug absorption but also enhances patient comfort compared to traditional needle-based methods. Microneedles are generally less painful and less invasive, making them suitable for a wide range of applications, including vaccinations, insulin delivery and hormone treatments [4].

Despite their advantages, microneedle technology faces challenges such as the need for precise manufacturing, scalability issues and regulatory considerations. However, ongoing research and development are addressing these challenges, paving the way for broader adoption and more innovative applications in the future.

Mechanisms of microneedle technology

Microneedle technology operates by creating micro-sized punctures in the skin to facilitate the delivery of drugs or vaccines. The mechanisms through which microneedles achieve this are centered on their ability to bypass the skin's outermost barrier, the stratum corneum and access deeper layers where absorption is more efficient. Here's an overview of the mechanisms:

Physical disruption of the stratum corneum: Microneedles penetrate the stratum corneum, the primary barrier to drug absorption in traditional transdermal systems. By creating microchannels in this layer, microneedles allow drugs to pass through more easily and reach the viable epidermis and dermis, where absorption occurs more effectively. This physical disruption helps in bypassing the skin's natural barrier without causing significant pain or discomfort [5].

Enhanced drug diffusion: The microchannels created by microneedles increase the permeability of the skin. This enhanced permeability allows for more efficient diffusion of drugs across the skin barrier. As the microchannels heal, they close, facilitating the sustained release of drugs into the systemic circulation if designed for such purposes.

Types of microneedle technologies

- **Solid microneedles:** These create microchannels in the skin. The drug is then applied topically or administered through a separate system that allows it to diffuse through the microchannels. Solid microneedles are particularly useful for creating microchannels for subsequent drug application.
- **Hollow microneedles:** These needles have a hollow core through which drugs can be injected directly into the dermis or subcutaneous layers. This method allows for precise control over the volume and rate of drug delivery.
- **Dissolving microneedles:** Made from biodegradable materials, these needles dissolve after insertion into the skin, releasing the drug slowly over time. The dissolving mechanism helps in providing controlled and sustained drug delivery.
- **Coated microneedles:** These are coated with a drug or vaccine formulation. Upon insertion, the drug coating dissolves or diffuses into the skin, delivering the therapeutic agent directly into the target area.

Minimized pain and discomfort: Because microneedles are typically shorter and thinner than traditional needles, they cause minimal damage to nerve endings in the skin. This results in reduced pain and discomfort, making the microneedle approach more acceptable for patients compared to conventional injection methods [6].

Rapid healing and drug release: The microchannels created by microneedles close relatively quickly after insertion, which helps in minimizing the risk

of infection and accelerating the healing process. For systems designed for sustained release, the microneedles' dissolution or drug release is managed in a controlled manner, providing prolonged therapeutic effects.

Discussion

Enhancing bioavailability is crucial in drug delivery systems to ensure that an adequate amount of a drug reaches systemic circulation and exerts its therapeutic effect. Microneedle technology significantly contributes to improving bioavailability through several mechanisms:

1. **Bypassing the stratum corneum:** The stratum corneum, the outermost layer of the skin, acts as a major barrier to drug absorption. Microneedles create microchannels that penetrate this layer, allowing drugs to bypass this barrier and reach deeper skin layers where absorption is more efficient. By circumventing this first line of defense, microneedles enhance the drug's ability to enter the bloodstream.
2. **Increased permeability:** The microchannels created by microneedles increase the permeability of the skin. This enhanced permeability allows drugs to diffuse more readily through the skin's layers into the dermal or subcutaneous tissue, where they can be absorbed more effectively. This improved diffusion can significantly boost the amount of drug that reaches systemic circulation.
3. **Targeted delivery:** Microneedles can be designed to deliver drugs directly to specific layers of the skin or even to the bloodstream, depending on the type of microneedle used. Hollow microneedles, for instance, can inject drugs directly into the dermis or subcutaneous tissue, where they can be absorbed more efficiently. This targeted approach helps in achieving higher local drug concentrations and improving overall bioavailability.
4. **Controlled release:** Some microneedle systems, particularly dissolving microneedles, are designed to release drugs gradually over time. This controlled release mechanism helps in maintaining therapeutic drug levels in the bloodstream for an extended period, improving bioavailability and reducing the need for frequent dosing.
5. **Enhanced drug solubility:** Microneedle technology can also enhance the solubility of poorly water-soluble drugs. By creating microchannels, the technology facilitates the dissolution of these drugs in the skin, leading to improved absorption and higher bioavailability.
6. **Reduction of first-pass metabolism:** Oral drugs often undergo significant first-pass metabolism in the liver, which can reduce their effective bioavailability. Microneedles deliver drugs directly into the systemic circulation, bypassing the gastrointestinal tract and liver, thus avoiding first-pass metabolism and improving the overall bioavailability of the drug.
7. **Increased drug stability:** Some microneedle systems protect drugs from degradation due to environmental factors such as light and oxygen. This increased stability ensures that a greater proportion of the drug remains effective and available for absorption, thereby enhancing bioavailability.

By improving the drug's ability to reach systemic circulation and exert its therapeutic effects, microneedle technology addresses some of the limitations of traditional drug delivery methods and opens up new possibilities for administering a wide range of therapeutic agents.

Improving patient compliance

Improving patient compliance is a critical aspect of effective healthcare management and microneedle technology offers several advantages in this regard. Patient compliance refers to the extent to which patients adhere to prescribed treatment regimens and enhancing it can lead to better health outcomes and more efficient treatments. Here's how microneedle technology contributes to improving patient compliance:

Conclusion

In conclusion, microneedle technology holds great potential to transform the landscape of drug delivery. By offering an efficient, patient-centric approach to medication administration, it not only improves therapeutic efficacy but also enhances the overall treatment experience. As the technology continues to evolve, it is expected to play an increasingly important role in modern healthcare, contributing to more effective and accessible treatments for a wide range of conditions.

Acknowledgement

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Conflict of Interest

None.

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