

Microneedles: As a Novel Carrier for Transdermal Drug Delivery System

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Abstract

Microneedles offer a novel method for drug delivery by blending the benefits of conventional injections and transdermal patches, while reducing the limitations associated with both. These tiny needles can gently poke through the top layer of the skin without hurting. This helps medicine go straight into the skin where it works best. Because they avoid the stomach and liver, microneedles are great for giving medicines that don't work well when taken by mouth. Depending on the application, microneedles can be fabricated in various forms—solid, coated, dissolvable, or hydrogel-based, each tailored for specific delivery goals such as rapid release or sustained delivery. Their ease of use, potential for self-administration, and reduced risk of infection make microneedles a promising tool in fields like vaccination, chronic disease treatment, and cosmetic therapy. This abstract explores the design principles, benefits, and emerging applications of microneedle technology, as well as the challenges that must be addressed for its broader clinical adoption.

Keywords: microneedles; drug; mouth

Introduction

Oral drug delivery is easy and convenient, allowing patients to take medications on their own. However, it poses challenges when used for delivering biopharmaceuticals. Injections provide fast-acting drug effects and ensure high bioavailability. However, administering injections typically requires trained personnel, and patient adherence is often limited [1,2]. Thus, the perfect drug delivery system would combine the ease of oral administration with the high bioavailability achieved by injections. Transdermal delivery helps drugs bypass the liver's first-pass metabolism and allows for extended release over time. However, the outermost layer of the skin, the stratum corneum, serves as a barrier that makes it difficult for drugs to penetrate.

Microneedles

The idea of microneedles was first proposed in 1976 but did not become practical until the development of microelectromechanical systems (MEMS) technology in 1998, which also marked the issuance of the first U.S. patent for microneedles designed for transdermal drug delivery. Microneedles offer a patient-friendly method for drug administration with high bioavailability, enabling painless and minimally invasive penetration through the skin's outermost layer, the stratum corneum. They are engineered to pierce the epidermis and deliver drugs directly into

the subepidermal blood vessels. Typically, microneedles have a sharp, tapered tip with lengths ranging from 150 to 1500 micrometers, widths between 50 and 250 micrometers, and tip thicknesses of 1 to 25 micrometers. Common materials used for their fabrication include metals, silicon, polymers, glass, and ceramics. The medication is generally incorporated onto or inside the microneedle tips, which are arranged in arrays attached to a base substrate. This array is then fixed onto a patch with an adhesive backing to ensure secure skin contact and convenient application.

Advantages

- Drug effects begin quickly after administration.
- Microneedles circumvent the first-pass metabolic process.
- Controlled microneedle formulations ensure accurate dosing.
- Their minimal size and length make microneedles both safe and painless.

Disadvantages

- Temporary inflammation and allergic reactions may occur.
- Advanced manufacturing techniques are required to produce microneedle patches consistently.
- Proper storage containers are necessary to keep microneedle patches hygienic and intact during transport from manufacturers to patients.

- When using solid microneedles, fragments can sometimes break off or remain embedded in the skin.

Types of Microneedles

The microneedles are typically classified into four types:

Solid microneedles.

Coated microneedles.

Dissolving microneedles.

Hydrogel microneedles.

(i) Types of microneedles

Solid Microneedles

Solid microneedles are usually made from metal or silicon, making them strong and without any medicine inside. They have many small, sharp tips made from one material that can poke the skin to make tiny holes. After that, medicine can be applied on the skin using a regular patch or cream over the area.

Coated Microneedles

Coated microneedles are placed directly on the skin and deliver the drug right away. These microneedles have a solid surface covered with a water-soluble layer that melts quickly and releases the drug when inserted. The coating needs to stay stable on the needle and stick well during storage and use. To do this, the coating must have the right thickness or thickness level. This design helps the drug dissolve fast in the skin, so it works quickly.

Dissolving Microneedles

Dissolving microneedles are made from materials that can dissolve in water or break down in the body, and they carry the medicine while being strong enough to pierce the skin. Once they are inserted, these microneedles quickly dissolve when they touch the moisture in the skin, so there is no sharp waste left behind. They are often made from biodegradable materials like cellulose-based polymers such as carboxymethyl cellulose (CMC) and methyl cellulose. The base part that holds the needles usually does not contain the drug and may be thicker, weaker, or made from materials that don't dissolve in water.

Hydrogel Microneedles

In hydrogel microneedles, the medicine is spread throughout the needle tips, base, and patch, and it is released slowly while the patch stays on the skin. These patches are mostly made of hydrogel, which soaks up moisture from the skin but doesn't dissolve. A good amount of the medicine moves into the skin

by slowly spreading from the hydrogel. Because the medicine is spread all over the patch, this method works well for giving larger doses, but it takes longer, so the patch needs to stay on the skin for a while.

Microneedles Technology Applications

Microneedles anti-cancer agents

Recently, cancer vaccines, including immune-based and gene therapies, have shown promising anti-cancer results and attracted significant attention within the scientific community. Microneedles are capable of penetrating the skin's stratum corneum to depths typically greater than 200 μm , releasing their drug payload when they come into contact with interstitial fluid. This characteristic makes microneedles valuable tools for transdermal delivery in cancer treatment. Unlike traditional hypodermic needles, which can cause pain, irritation, and generate hazardous waste, microneedle drug delivery systems greatly reduce these side effects.

Moreover, microneedles can deliver vaccines in a dried solid form, improving their thermal stability and simplifying administration to the target area.

(a) For the combined treatment of superficial tumors, dissolvable microneedles made from hyaluronic acid (HA) were loaded with DOX. These drug-loaded microneedles were integrated with gold nanocages and then exposed to near-infrared light, enabling a synergistic effect of chemotherapy and photothermal therapy.

(b) In melanoma immunotherapy, an anti-PD1 antibody was incorporated into an HA-based microneedle system, combining PD1 blockade with 1-MT to inhibit the enzyme IDO, offering a novel immune-based treatment approach for melanoma.

Diabetes

In studies with diabetic rats, insulin given through microneedles was absorbed by the skin within one hour after the needles dissolved. In one test, insulin-coated metal microneedles were put on the skin to lower blood sugar in diabetic rats. Results showed these microneedles helped insulin get into the skin better and lowered blood sugar by 80%. Dissolving microneedles break apart in about five minutes, quickly releasing insulin into the skin. One study tested these in diabetic rats. About 92% of the insulin stayed effective after being delivered by dissolving microneedles.

Bacterial Disease

Studies have found that a patch that can stop bacterial infections and help tissue heal is very useful for wound care.

Chitosan, a common material used in wound treatment, has natural antibacterial properties. Researchers created a patch made from chitosan microneedles (CSMNA) that uses a smart, temperature-sensitive system to improve wound healing. The tiny needles in the patch help deliver medicine directly to the wound while reducing unwanted sticking between the skin and the patch. The patch also contains a growth factor called VEGF inside a temperature-sensitive gel within the microneedle pores. This gel releases the medicine based on temperature changes caused by inflammation at the wound, allowing the drug to be released only when needed. Tests showed that the CSMNA patch helps new blood vessels grow and supports tissue repair, showing promise for use in real wound treatments.

Ocular Microneedle Delivery

Eye conditions are commonly managed with eye drops or ointments, but these methods have drawbacks such as the need for frequent application, low bioavailability, and difficulty penetrating various ocular barriers. Microneedles offer a promising new delivery system aimed at improving treatment outcomes for a variety of eye diseases. Advances in pharmaceutical technology have enabled microneedles to deliver drugs locally in a targeted, effective, and minimally invasive manner to the eye. Studies have shown that the developed microneedle devices possess adequate stiffness for reliable insertion into ex vivo rabbit corneas. Furthermore, these microneedles demonstrated the ability to increase drug loading capacity by up to five times compared to solid microneedles of similar dimensions, as well as enhanced drug release beneath the surface of the rabbit cornea. Dissolving microneedles have been found to improve the delivery of large ocular molecules. Various molecular weights of polyvinylpyrrolidone (PVP) polymer were used to fabricate these microneedles. Conical PVP microneedle arrays, approximately 800 μm tall with a base diameter of 300 μm , containing the drug model, were produced, with an average drug load ranging between 0.96 and 9.91 μg per array. Detachable microneedle technology is especially promising for

treating eye disorders like keratitis and glaucoma, offering consistent drug delivery with reduced invasiveness. However, reducing the time needed for microneedle administration into target tissues remains a challenge, despite efforts to address this through various mechanical and chemical separation techniques.

Vaccine Therapy

A vaccine is a biological substance that helps the body build immunity against certain diseases. It usually contains a weakened or dead form of the germ, its toxins, or parts of its surface. Vaccines work by activating the immune system to protect against future infections, and microneedle technology has been effective in helping with this. DNA vaccines given through microneedles have triggered stronger immune reactions than regular injections. Scientists are also working on microneedle patches to deliver flu vaccines. Using hollow microneedles means less vaccine is needed compared to regular muscle injections. Research has also tested giving anthrax and rabies vaccines using hollow microneedles.

Cosmetics

Microneedles are becoming more popular in beauty treatments, especially for improving skin look and treating scars and blemishes. Researchers have worked on using microneedles to deliver active cosmetic ingredients like vitamin C (ascorbic acid), eflornithine, and retinyl retinoate. Melanin was put inside tiny fat-based particles called nanoliposomes to help it mix better with oils. When applied with a microneedle roller, more pigment was found near hair follicles. Microneedles also helped improve the delivery of other skin-care compounds like melanostatin, rigin, and pal-KTTKS.

Lidocaine Delivery

Lidocaine is often used to numb areas of the body. Using microneedles to deliver lidocaine causes less pain than regular injections, making it easier for patients to accept. These microneedles can reliably penetrate the skin in lab tests and deliver the drug quickly, within 2 minutes. This makes microneedles a fast and painless way to provide local anesthesia. In one study, microneedles coated with a PEG-lidocaine mix delivered the drug faster within 3 minutes compared to traditional creams or gels.

Table 1: Approved Microneedle Products

Product name	Company name	Description of the product	Use
Dermaroller®	Dermaroller Germany, White Lotus	A cylindrical roller with solid or metal microneedles, 0.2–2.5mm in length.	Improve skin texture, treat scars and hyperpigmentation.
C-8(Cosmetictype)	The Dermaroller Series by Anastassakis K	A needle length of only 0.13mm(130µm)	Used to enhance penetration of topical agents.
CIT-8(Collagen Induction Therapy)	The Dermaroller Series by Anastassakis K.	A needle length of 0.5mm (500µm)	Used in collagen induction and skin remodeling.
Soluvia®	Sanofi Pasteur Europe	Hollow micro needle attached to a syringe	Influenza vaccination
LiteClear®	Nanomed skincare	Solid silicon microneedles are used as pre-treatment and then drug applied topically.	Treats acne and skin blemishes
h-patch	Valeritas	Small adhesive machine like patch is used	To deliver drugs in subcutaneous tissue (insulin)
MF-8type	The Dermaroller Series by Anastassakis K	A needle length of 1.5mm (1500µm)	Treat scars.

Conclusion

Microneedles represent a rapidly advancing transdermal drug delivery technology, offering improved patient access by serving as an alternative to traditional administration methods. These microneedles can be categorized into solid, coated, dissolving, and hydrogel types, and are fabricated from materials such as silicon, metals, polymers, glass, and ceramics. A variety of manufacturing methods are employed to create microneedles with specific shapes, sizes, and characteristics. The technology is continuously progressing through clinical research involving different medications. Most research findings have been positive, indicating that microneedles hold promise for delivering therapeutic benefits across a wide range of medical applications.

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