

Design and Rapid Fabrication of Microneedle Patch for Targeted Drug Delivery

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Abstract

Oral administration and topical drug delivery have been the main methods of applying medication for a long time. However, both approaches usually result in low bioavailability, leading to significant drug waste. To overcome these problems, researchers have been exploring new drug delivery methods that can improve efficiency and reduce drug loss. Among these, microneedle patches have attracted great attention because of their high bioavailability and the possibility of being integrated with different medical devices or actuators. Many existing studies have focused on the mechanical design of the actuators used to deploy microneedle patches, but less attention has been paid to the integration of drug-loaded microneedles with applied actuators or surfaces. In this study, we explored several typical microneedle materials and combined them with two representative types of drugs. The prepared microneedle patches are aimed to be applied to both solid and soft surfaces in our following researches to evaluate their adhesion performance. This work aims to provide insights into the design of versatile microneedle systems that can adapt to different environments for improved drug delivery efficiency.

Keywords

Drug delivery, skin anchoring, bioavailability.

1. Introduction

Medicines are used to treat various diseases and maintain the normal function of the human body. For a long time, oral administration and topical drug delivery have been the most common and convenient ways of applying medication [1, 2]. These two approaches are still widely used today because they are non-invasive, easy to use, and generally acceptable to most patients. However, despite their convenience, both methods suffer from the same major problem — low bioavailability [3]. After being taken orally, a large portion of the drug is decomposed by gastric acid or enzymes in the gastrointestinal tract before it can be absorbed. Even when absorbed, a significant amount is metabolized by the liver before reaching the systemic circulation. Similarly, topical drug delivery, which relies on diffusion through the skin, is limited by the skin's natural barrier function. As a result, only a small fraction of the drug actually reaches the target tissue.

Because of these limitations, a high dosage is often required to achieve the desired therapeutic effect, which not only causes drug waste but can also increase the risk of side effects. Moreover, since the effect of oral medication is not always immediate and often requires repeated doses, patients tend to have poor medication adherence, which further reduces treatment efficiency [4]. Therefore, scientists have been exploring new technologies to overcome these shortcomings — technologies that can increase drug bioavailability, reduce waste, and improve patient compliance at the same time.

In recent years, transdermal drug delivery (TDD) has emerged as a promising alternative to conventional routes. TDD aims to deliver drugs directly through the skin, thereby avoiding the gastrointestinal system and first-pass metabolism in the liver [5]. However, the skin, while being the largest organ of the human body, also serves as a strong protective barrier against the external environment. Its outermost layer, the stratum corneum, is composed of tightly packed dead cells embedded in a lipid matrix, which makes it extremely difficult for most drugs to pass through. Underneath it lie multiple layers including the stratum granulosum, stratum spinosum, and stratum basal [6], which further limit penetration. This natural structure protects us from harmful substances such as bacteria, viruses, and physical irritants, but it also greatly reduces the efficiency of transdermal drug delivery.

To overcome this obstacle, researchers have developed various TDD technologies. Generally, these can be divided into passive and active methods. Passive methods, such as transdermal patches, gels, and sprays (reference), rely on concentration gradients to drive drug molecules through the skin. Although simple and low-cost, their efficiency is often limited by the skin barrier. Active methods, in contrast, make use of external energy or mechanical force to facilitate drug penetration [7]. These include iontophoresis (using electric current), sonophoresis (using ultrasound), electroporation, laser-assisted delivery, and microneedle (MN) technology. Among these approaches, microneedles stand out for their unique combination of simplicity, efficiency, and patient comfort.

Microneedles (MNs) are micro-scale needle structures, usually ranging from 50 to 900 μm in length, designed to penetrate the stratum corneum without reaching deeper pain receptors. This allows painless and minimally invasive drug delivery directly into the viable epidermis or dermis, where abundant capillaries facilitate absorption. Depending on their fabrication and drug-loading mechanism, microneedles can be categorized into solid, coated, and dissolving microneedles (DMNs) [8]. Solid microneedles, often made of metals or rigid polymers, are used to create microchannels in the skin through which drugs can later diffuse. Coated microneedles carry the drug on their surface, releasing it rapidly upon insertion. Dissolving microneedles, on the other hand, are made of biocompatible, water-soluble polymers that encapsulate the drug within their structure. Once inserted, these microneedles gradually dissolve, releasing the drug directly into the tissue [8].

Thanks to advances in polymer chemistry and microfabrication, dissolving microneedles have become one of the most promising technologies for transdermal drug delivery. They combine the benefits of safety, high bioavailability, and ease of use. Moreover, since DMNs dissolve completely after administration, there is no need for removal, which minimizes medical waste and eliminates the risk of needle injury. Over the past decade, dissolving microneedles have been successfully applied to deliver vaccines, peptides, and small-molecule drugs for the treatment of various diseases, including skin disorders and metabolic diseases [9].

However, despite these advantages, some challenges still remain. One important issue that has not been fully addressed is the adhesion ability of microneedle patches when applied to different types of surfaces. Most existing studies focus on microneedles applied directly to the skin, but in many practical applications, especially for internal or complex biological environments, the target surface may not always be soft or flat. For example, it may be desirable to attach drug-loaded microneedles to solid medical devices, such as implants, or to moist and flexible tissues, such as mucosal surfaces. Under these conditions, conventional microneedle patches may not adhere effectively, which could lead to detachment or insufficient drug delivery.

In this study, we aim to address this issue by developing a microneedle patch that can adhere effectively to both solid and soft surfaces. We selected several representative microneedle materials and integrated them with two model drugs to investigate their performance. The adhesion ability of these microneedles was systematically tested on different substrates to

evaluate their mechanical stability and retention strength. Through these experiments, we hope to provide insights into the design of versatile, adhesive microneedle systems that can be applied to a wide range of medical scenarios, offering improved efficiency, reduced drug loss, and expanded application potential for future transdermal and transmucosal drug delivery technologies.

2. Result and Discussion

2.1. Microneedle Manufacturing

To integrate microneedle drug systems (MNDs) with general medical actuators, microneedle patches were designed and fabricated through a molding-based approach. Two types of model drugs were incorporated into the MNDs.

The microneedle molds were first fabricated using stereolithography (SLA) 3D printing, which provides high-resolution and flexible design capability. The geometry of each microneedle array was defined by three main parameters: the base shape, the microneedle shape, and the spacing (interval) between adjacent microneedles. The base part serves as the structural interface to the actuator. Its shape was selected according to the actuator geometry — commonly cylindrical or rectangular. In this study, a cylindrical base was adopted to match the finger-shaped actuator used for adhesion testing.

The microneedle shape was characterized by its height and diameter. Based on previous studies, a height-to-diameter ratio of 1:4 was chosen [10], which offers excellent mechanical strength and penetration ability. However, directly printing microneedles of very small size using SLA often results in deformation or incomplete formation due to limitations in printing resolution. To address this issue, a two-step printing and curing process was applied. The microneedle mold was printed in a notched platform with shallow grooves. After the initial printing was completed and cured, additional photopolymer resin was carefully filled into the grooves and cured again under UV light. This post-processing step reduced the exposed height of the microneedles and improved the overall surface smoothness and dimensional accuracy.

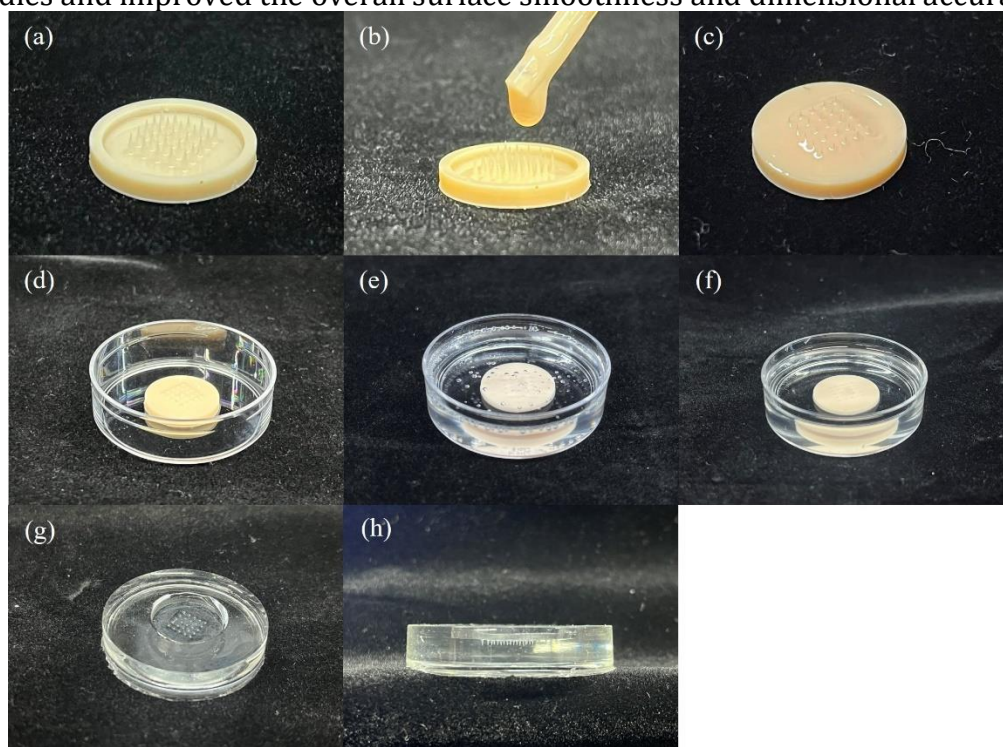


Fig. 1 Microneedle manufacturing process

2.2. Microneedle Parameters Optimization

During fabrication, the interval between microneedles was also found to significantly affect the printing quality and structural integrity of the array. When the spacing was too small, surface tension caused unwanted resin accumulation between adjacent microneedles, leading to small bumps or protrusions on the mold surface that interfered with further molding and replication(reference). On the other hand, excessively wide intervals decreased the total number of microneedles within a given base area, reducing the effective drug-loading capacity. Therefore, a balance had to be achieved between structural integrity and density. According to our experimental results, the optimal spacing for reliable fabrication and mechanical performance ranged from 1.2 mm to 1.4 mm (Fig. 2). This fabrication strategy effectively improves the precision of small-sized microneedle molds and provides a simple and efficient method for preparing microneedle arrays suitable for integration with medical actuators and adhesive layers. In this way, the drug can be taken at largest amount meanwhile shape of the MND can still remain perfectly.

The experimental results are shown in Fig. 2. As the distance between the microneedles decreases, the capillary effect of the liquid between them becomes stronger. Macroscopically, this is manifested as a more pronounced bulging of the liquid surface between the microneedles when the liquid level is kept at the same height — the denser the microneedle arrangement, the higher the liquid meniscus rises between them.

Since the final microneedle patch is fabricated through a secondary molding process using the initially produced microneedle model, the bulging of the liquid surface at this stage has a significant impact on the final shape of the microneedle patch. Based on the observations, a microneedle spacing of 1–1.2 mm was found to be optimal. This range ensures that the microneedles are dense enough to maximize drug loading capacity, while also keeping the capillary-induced deformation of the patch within an acceptable level.

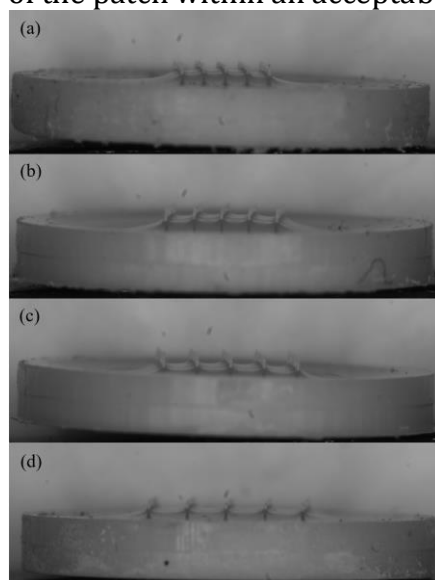


Fig. 2 Microneedle model with different distances between the microneedles.
(a)0.8mm (b)1mm (c)1.2mm (d)1.4mm

2.3. Manufacturing of Microneedle Patch Loaded with Drug

The drugs used in the microneedle device (MND) generally fall into two categories: powder-based drugs and fluidic drugs. Both types can influence the mechanical properties of the microneedles when incorporated into the MND precursor solution. Fluidic drugs are generally more compatible, as they can be directly dissolved in water during the initial preparation of the MND solution. In contrast, powder drugs can only be effectively integrated when they remain uniformly suspended during mixing, which requires that the particle and solution densities be

relatively close. Increasing the drug concentration typically reduces the mechanical strength of the microneedles, making them more brittle. Therefore, only limited amounts of each drug were added to the MND solution. Here we take amount of 1 mg of powder drug and 1 mL of fluidic drug. This amount of drug would not make an obvious change to the mechanical properties of the microneedle Patches.

Three different polymer matrices—polyvinylpyrrolidone/polyvinyl alcohol (PVP/PVA), chitosan, and carboxymethyl cellulose sodium (CMC-Na)—were tested as MND materials. Rebamipide tablets and Sucralfate oral suspension were used as model drugs. The Rebamipide tablets were finely ground and filtered to ensure uniform particle size before being incorporated into the solution. The Sucralfate oral suspension was directly mixed into the MND solution.

Each polymer solution required a distinct preparation process. For the chitosan solution, 5 wt% chitosan and 0.5 v/v% acetic acid were mixed in deionized water [11, 12]. The PVP (20 wt%) / PVA (5 wt%) solution was prepared by dissolving the polymers in deionized water with magnetic stirring at 70 °C for 1 hour [11]. The CMC-Na solution was prepared by dissolving CMC-Na in deionized water and heating at 60 °C for 90 minutes [10]. The overall preparation process is illustrated in Fig. 3.

Most of the polymer solutions were compatible with both drugs, except for the chitosan solution, which showed poor compatibility with Sucralfate oral suspension (Fig. 3g). When the two were mixed, a flocculent precipitate formed, indicating phase instability. Because drug degradation may occur at elevated temperatures, the drugs were generally added after the polymer solutions had cooled to room temperature. However, for the CMC-Na solution, the viscosity was too high to allow homogeneous mixing of the drug once the solution had been fully prepared. Therefore, the drugs were added before the CMC-Na was dissolved, which may have caused partial drug degradation during heating.

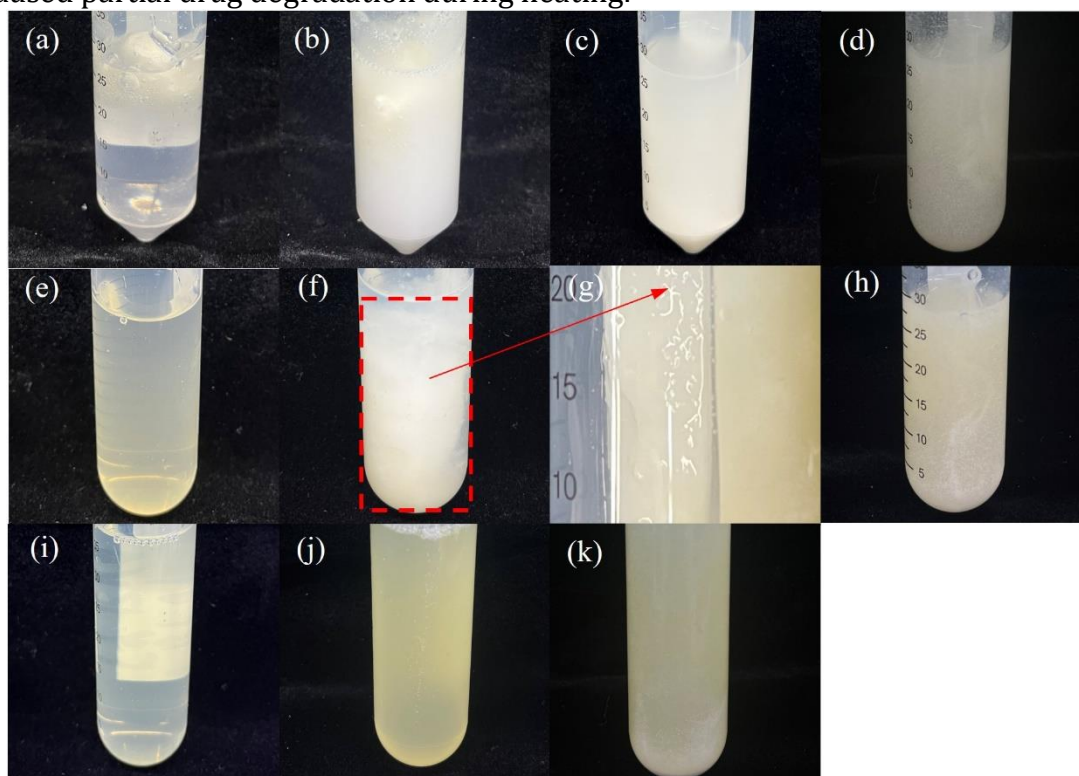


Fig. 3 (a)~(d) CMC-Na Microneedle Solution. (e)~(g) Chitosan Microneedle Solution. (i)~(k) PVP/PVA Microneedle Solution. (b) before heating, (c) after heating, (f) and (j) are loaded with Sucralfate oral suspension. (d), (h) and (k) are loaded with Rebamipide tablets

After the preparation of the microneedle precursor solution, the microneedle fabrication process begins. The prepared solution is poured into the microneedle mold, allowed to dry, and then peeled off to obtain the final microneedle patch. Ideally, drying is performed under ambient conditions, which typically takes about 8 hours, depending on the surrounding temperature and airflow. Although this method is time-consuming, it minimizes the formation of air bubbles within the microneedles and generally results in the best structural quality.

When the fabrication time needs to be reduced, the molds can be placed in an oven or a fume hood to accelerate the drying process. These methods can shorten the drying time by nearly half, but they also increase the likelihood of bubble defects forming in the microneedles. For oven-assisted drying, the heating duration should not exceed 25 minutes to prevent deformation or uneven curing. Subsequent drying in the fume hood—either after oven heating or immediately after demolding—is adjusted based on the material composition of the microneedle.

Fig. 4 shows the fabricated microneedles with and without drug loading. Microneedles without drugs tend to exhibit fewer bubble defects in the needle body compared to drug-loaded ones. Nevertheless, nearly all fabricated patches demonstrated satisfactory microneedle morphology and structural integrity.

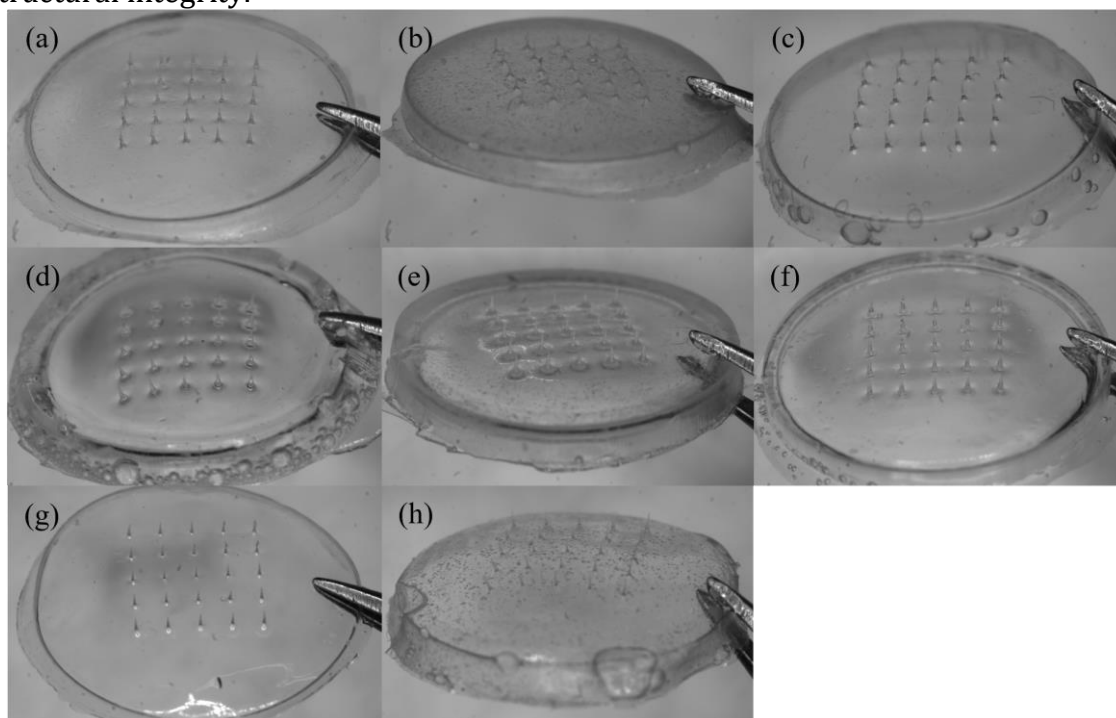


Fig. 4 Microneedle Patches made from, (a)~(c) CMC-Na Solution, (d)-(f) PVP/PVA Solution, (g) and (h) Chitosan Solution. (b), (e) and (h) are loaded with Rebamipide tablets. (c) and (f) are loaded with Sucralfate oral suspension

3. Conclusion

Since their introduction in the late 1990s, microneedles have evolved from simple solid microstructures used to pierce the skin into highly sophisticated, drug-loaded delivery systems. Advances in microfabrication, polymer chemistry, and biomedical engineering have continuously expanded their applications from vaccine delivery to pain management, metabolic therapy, and tissue regeneration. Among various types, dissolving microneedles have attracted particular interest because of their safety, biocompatibility, and ability to deliver precise doses without leaving hazardous residues.

In this study, we developed a rapid microneedle patch system that builds upon these advancements to enable efficient and targeted drug delivery. Using a molding-based fabrication process, we optimized critical parameters including microneedle geometry, spacing, and material composition. Three biocompatible polymers—PVP/PVA, chitosan, and CMC-Na—were evaluated for their suitability in drug incorporation, with PVP/PVA exhibiting superior mechanical integrity and compatibility with both model drugs, Rebamipide and Sucralfate. The optimal microneedle spacing was determined to be 1.0–1.2 mm, which ensures both high drug-loading capacity and stable structural formation.

The developed process offers a reliable and time-efficient approach to producing dissolving microneedle patches with excellent uniformity and mechanical strength. This work contributes to the continuous evolution of microneedle technology by providing design and fabrication strategies adaptable to diverse biomedical environments. In the future, further studies on drug release kinetics, penetration depth, and in vivo therapeutic performance will advance the clinical translation of rapid microneedle systems toward practical and personalized drug delivery solutions.

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