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RESEARCH PAPER

Fabrication of Degradable Carboxymethyl Cellulose (CMC) Microneedle with Laser Writing and Replica Molding Process for Enhancement of Transdermal Drug Delivery

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Abstract Transdermal drug delivery system (TDDS) may provide a more reliable method of drug delivery than oral delivery by avoiding gut absorption and first-pass metabolism, but needs a method for efficiently crossing the epidermal barrier. To enhance the delivery through the skin, we have developed a biocompatible, dissolvable microneedle array made from carboxymethyl cellulose (CMC). Using laser ablation for creating the mold greatly improved the efficiency and reduced the cost of microneedle fabrication. Mixing CMC with amylopectin (AP) enhanced the mechanical and tunable dissolution properties of the microneedle for controlled release of model compounds. Using the CMC microneedle array, we observed significant enhancement in the skin permeability of a fluorescent model compound, and also increase in the anti-oxidant activity of ascorbic acid after crossing the skin. Our dissolvable microneedle array provides a new and biocompatible method for delivery of drugs and cosmetic compounds through the skin.

Keywords: microneedle, carboxymethyl cellulose (CMC), laser fabrication, transdermal delivery

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1. Introduction

Among several drug delivery methods, injection and oral delivery are considered to be the two most popular routes. Drug delivery *via* injection are highly efficient, but carries several limitations, such as bleeding, pain, risk of infection, and the need for a trained personnel [1]. Oral delivery can avoid such limitations, but the process of oral absorption and subsequent first-pass metabolism often results in unpredictable bioavailability. Transdermal drug delivery system (TDDS) can avoid such limitations of injection and oral delivery, and has been used for the delivery of small molecule drugs, proteins, and vaccines [2,3]. However, transdermal delivery requires penetration of the outer barrier of stratum corneum, which is not easily achieved with drugs with high molecular weights, and therefore requires a method for enhancing the efficiency of delivery. Iontophoresis and electroporation can enhance transdermal drug delivery by applying electrical current and creating nanoscale pores [4,5]. However, these methods create pores with the size less than 10 nanometers, which are often not sufficiently large for the penetration of high molecular weight drugs. High-voltage electric pulse can enhance the delivery of high molecular weight drugs, but

accompanies unpleasant pain and muscle contraction. Therefore, recent research efforts have been directed towards developing microneedles for minimally invasive transdermal drug delivery [6].

Microneedles were first devised in the 1970s, and have been a topic of interest since then. Microneedles can be categorized into four types, which are (1) 'poke and flow' type using hollow microneedles, (2) 'poke and patch', (3) 'poke and release', (4) 'coat and poke' types that use solid microneedles [2]. Early research works were focused on the 'poke and flow' type, which are similar to conventional needles. Hollow microneedles are fabricated and drugs to be delivered are injected through the hollow openings of the microneedles [7]. This type of microneedle device can also be used for continuous monitoring, for example of blood glucose, or as a neural probe [8,9]. This method allows efficient and continuous drug delivery through the skin, but the fabrication process is relatively difficult. In addition, continuous drug delivery through this type of microneedles requires additional devices, and there is a risk of fractured pieces remaining inside the skin tissue. Solid microneedles are relatively easy to fabricate. The 'poke and patch' type microneedles are applied onto the skin and removed to create small holes on the skin, and drugs are applied directly or *via* the form of a patch [10,11]. In case of the 'coat and poke' type microneedles, drugs are coated on the surface of the microneedles and delivered through the skin when the microneedles are applied onto the skin [12]. These two types are relatively easy to fabricate and requires less training for self-administration. However, these microneedles are also fabricated from undissolvable materials and the issue of fractured microneedles still remains. 'Poke and release' type microneedles are fabricated from biodegradable and biocompatible materials, such as hyaluronic acid, carboxymethyl cellulose, poly(D,L-latic-co-glycolic acid). Drugs to be delivered can be encapsulated inside the material and released when the microneedles are dissolved in the skin. Since these microneedles are made from biocompatible and biodegradable materials, they are free from the risk of fractured needle remaining in the body. Encapsulating drugs inside the microneedle also offers the advantage of enhancing the stability of the drugs [13]. In addition, the rate of drug release can be controlled by adjusting the degradation rate of the microneedles.

Microneedles are generally fabricated by directly etching solid materials, using photolithography techniques. The pattern for the microneedle is printed on a thin transparent film or chrome mask, and UV exposure through the mask transfers the pattern onto polymer photoresist substrate coated on a wafer. Subsequent dry or wet etching create microneedle patterns [14]. Combination of photolithography with other methods such as replica molding can produce hollow microneedles for more efficient drug injection [15]. Photolithography enables fabrication of microscale structures with high precision, but requires complex process of printing a mask, exposure, development and etching, increasing the process time and the cost. In addition, changing the size or number of microneedles requires repetition of the whole process, therefore rapid prototyping is difficult.

In this study, we report using replica molding technique for rapidly fabricating a microneedle array. Instead of photolithography technique, laser writing process was used to create a mold with tapered holes, which greatly enhanced the process efficiency and reduced the cost. In addition, the laser writing process does not involve toxic chemicals used in the photolithography process, and is suitable for rapid prototyping of microneedles since the writing process only takes a few minutes. To fabricate microneedles, carboxymethyl cellulose (CMC) was used as a main material with amylopectin (AP) as a material to further fine-tune the mechanical property of microneedles. Among various materials that have been used to fabricate microneedles [2,3], CMC was chosen based on its biocompatibility, relatively easy processing at low temperature, compatibility with bioactive compounds, and a low cost [16,17]. After fabrication, mechanical properties of fabricated microneedles were characterized by measuring the dissolution rate and the stiffness. We also verified that the strength and the dissolution speed of the microneedle can be tuned by combining CMC with amylopectin (AP). The permeability of a model compound, rhodamine B, through the porcine skin was measured in a Franz cell, and we verified that application of CMC microneedle enhances the drug delivery through the porcine skin approximately three-fold compared to the case where the model compound was directly applied. Ascorbic acid, which is known for its anti-oxidant activity, was used as a model cosmetic agent, and it was observed that delivery of ascorbic acid *via* microneedle improved anti-oxidant activity after skin penetration, compared to the same amount of ascorbic acid applied directly to the skin.

2. Materials and Methods

2.1. Fabrication of microneedles

The fabrication process of CMC microneedles is based on the previously developed method for fabricating high aspect ratio structures with hydrogels [18]. This method allows fabrication of microscale high aspect ratio structures with various materials, and was applied to development of an artificial intestinal villi scaffold [19,20]. The mold for the microneedles was fabricated from PDMS (polydimethylsiloxane) using a commercial CO_2 laser writer (PL-40K, Korea stamp, Seoul, Korea). Shooting laser beams at

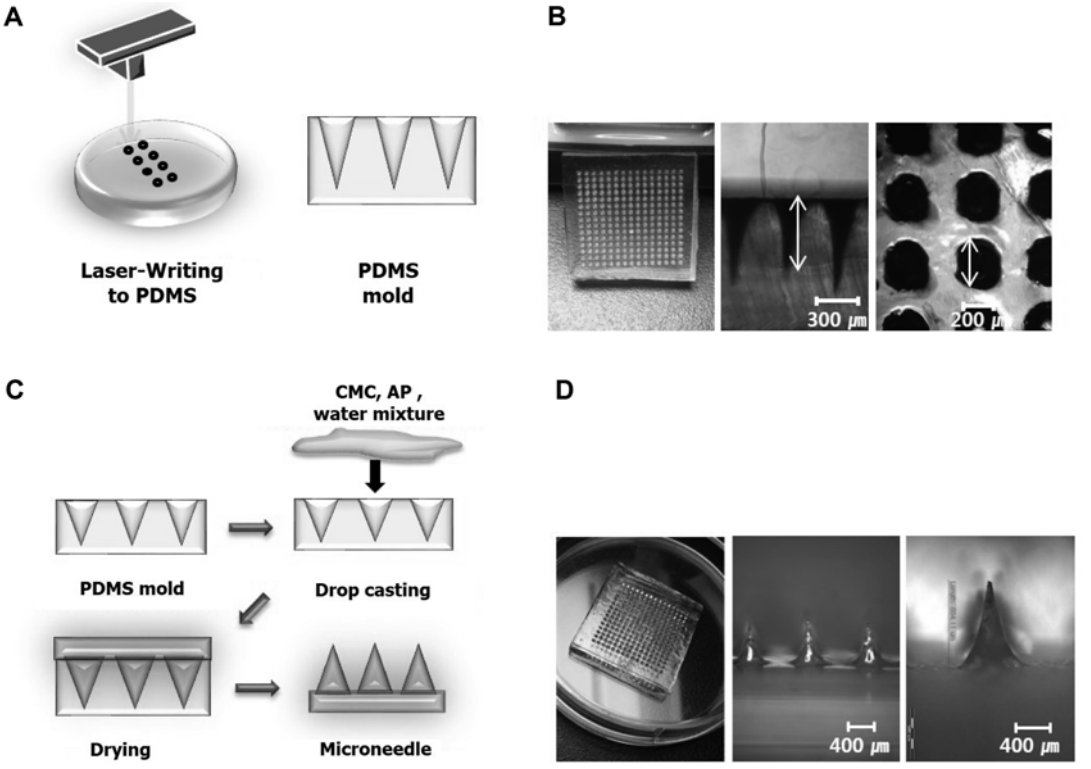

Fig. 1. Fabrication of PDMS mold and CMC microneedle array. (A) Fabrication process of PDMS mold by laser-writing. (B) Optical microscope images of the fabricated PDMS mold. (C) Fabrication process of CMC microneedle array. (D) Optical microscope images of the fabricated CMC microneedle array.

a flat PDMS sheet created an array of tapered-cone shaped holes. The size, shape, and the angle of the holes could be adjusted by manipulating the parameters in the operating software for the laser writer. An array of 12 by 12 holes on a PDMS sheet was created, and the PDMS sheet was cleaned in an ultrasonic cleanser (DH.WUC.A03H, DAIHAN-Scientific, Korea) with 70% ethyl alcohol.

CMC was dissolved in deionized water at 3% concentration and the solution was poured onto the PDMS mold. After placing in a desiccator, the mold and the CMC solution was degassed under vacuum to completely fill the holes with CMC. After degassing for 120 min, the CMC microneedle was dried in an oven at 50°C for 15 h. The microneedles were separated from the mold after drying. The fabrication process is summarized in Fig. 1.

2.2. Measurement of mechanical properties of CMC microneedles

The dissolution rate of CMC microneedles were measured by immersing the microneedles in PBS buffer solution (pH 7.0). The microneedle array was fixed in a container so that only the tips of the microneedles were immersed in the buffer solution. Time-series pictures of microneedle tips were taken with a microscope to track the changes in the length of the tips. The fraction of microneedle tips dissolved was calculated by dividing the height of the tip by the original height.

The mechanical strength of the microneedles was investigated with custom-designed device. The device is designed so that the specific amount of weight can be applied in vertical direction to simulate the situation where the microneedle array was applied onto the skin. For each measurement, designated weight was applied on the microneedles for 1 min, after which the height of the microneedles was measured. The amount of deformation was calculated by measuring the changes in the height of the microneedles. Three different weights of 300, 500, and 1,000 g were tested.

2.3. Measurement of skin permeability

The effect of microneedle on enhancing the transdermal delivery was tested by measuring the transport of a model drug through the porcine skin. The full porcine skin containing the stratum corneum was obtained after being separated from the animal. Rhodamine B was used as a model drug since its concentration can be easily quantified by measuring the fluorescent intensity. Rhodamine B was mixed with CMC and AP before the solution was poured onto the PDMS mold to create a microneedle that contains 9 mM concentration of rhodamine B. Before measuring the

permeability, a patch of porcine skin was hydrated in 0.9% sodium chloride solution for 30 min, and was fixed in a Franz diffusion cell filled with PBS buffer. The microneedle was pressed against the porcine skin in the Franz diffusion cell, and the concentration of rhodamine B in the solution in the bottom chamber was periodically measured for 24 h. The fluorescent intensity was measured with UV-visible spectrometer (VARIAN CARY 100 UV-Visible spectrophotometer, Agilent Technologies, USA), which was then converted to concentration. The control experiment was performed by directly applying the same amount of rhodamine B (9 mM in 200 μL) on the skin in the Franz diffusion cell.

2.4. Measurement of antioxidant activity of ascorbic acid after skin permeation

Ascorbic acid was encapsulated in a microneedle array and its radical scavenging activity after skin permeation was measured by DPPH (2,2-diphenyl-1-picrylhydrazyl) assay. Ascorbic acid was mixed with microneedle pre-solution at 3% (w/v) concentration before microneedles were fabricated. The microneedles were applied on the porcine skin for 24 h in a Franz diffusion cell to allow diffusion of ascorbic acid. After 24 h, the radical scavenging activity of the solution in the receiving chamber was assessed. 100 μL of the solution in the receiving chamber was collected and mixed with 100 μL of 0.1 mM DPPH solution. The concentration of DPPH solution was measured by reading the absorbance at 517 nm wavelength. For control experiment, the same amount of ascorbic acid was directly applied to the skin, and the antioxidant activity was measured using the same method. Antioxidant activity was calculated using the following equation.

$$\mathrm{AA\%} = 100 - \frac{(Abs_{sample} - Abs_{blank}) \times 100}{Abs_{control}},$$

where Abs_{sample} = Absorbance of the sample to be measured, Abs_{blank} = Absorbance of a blank solvent (ethanol), $Abs_{control}$ = Absorbance of DPPH solution. For blank sample (Abs_{blank}), the ethanol solvent without DPPH was mixed with the sample solution in the receiving chamber of the Franz cell.

3. Results and Discussions

3.1. Fabrication of a CMC microneedle array

The fabrication method used in this study was previous developed to reproduce the tissue microscale structures [18]. It was previously used to reproduce the intestinal villi structure for artificial organs. We realized that this fabrication method was also applicable to various applications, and sight modification was made to the original process and the method was applied to the fabrication of microneedle structures [21]. In this study, the microneedle mold was fabricated by creating tapered cone-shaped holes in a PDMS sheet using the laser writing process. Adjusting the laser parameters allowed control of diameter and the depth of cone-shaped holes in the array. We were able to fabricate holes with a diameter between 200 and 600 μm and a depth between 300 and 1,200 μm. The PDMS mold contains an array of 12 by 12 holes, each hole approximately having the diameter of 400 μm and the depth of 800 μm. Fig. 1A shows the mold fabrication process. Fabrication of the mold with laser writing process reduces significant amount of time and cost compared to other microfabrication processes. Also, it does not involve toxic and hazardous chemicals involved in photolithography and etching processes [22,23]. Furthermore, fabricating non-vertical shapes, such as cone-shaped holes, with photolithography often requires complicated fabrication steps involving several organic solvents. On the other hand, laser writing process can create cone-shaped holes with sharp edges *via* a simple one-step fabrication process. Therefore, laser writing process provides a quicker and safer method for rapid prototyping of microneedles than conventional microfabrication methods. Fig. 1B shows the picture of fabricated PDMS molds.

Fig. 1C shows the microneedle fabrication process, where CMC solution was cast onto the mold. Casting CMC into the mold and solidifying either alone or in mixture with amylopectin resulted in solid microneedle arrays. The geometry of the cone-shaped holes and sharp edges in the PDMS mold were successfully reproduced, resulting in an array of microneedles, each with approximately 800 μm height and 400 μm diameter at the base. Fig. 1D shows the cross-section images of the fabricated microneedles. Fabrication of microneedles with CMC does not involve the use of toxic or harsh organic solvents, which might degrade or contaminate active ingredients. Therefore, CMC microneedle is suitable for encapsulation of sensitive materials as active ingredients. The images in Fig. 1 show that the structures of the microneedles are relatively uniform. Although microfabrication method enables fabrication of microneedles with much higher precision, our laser writing and replica molding process also ensures relatively high uniformity.

To assess the uniformity of microneedle fabrication, the geometry of the fabricated microneedles was examined. Fig. 2A shows the heights, diameters, and angles of ten microneedles in a single set. This result shows that within a single set of microneedle array, the geometry of the needles are relatively uniform. Fig. 2B shows the means of the heights, diameters, and angles of three different sets,

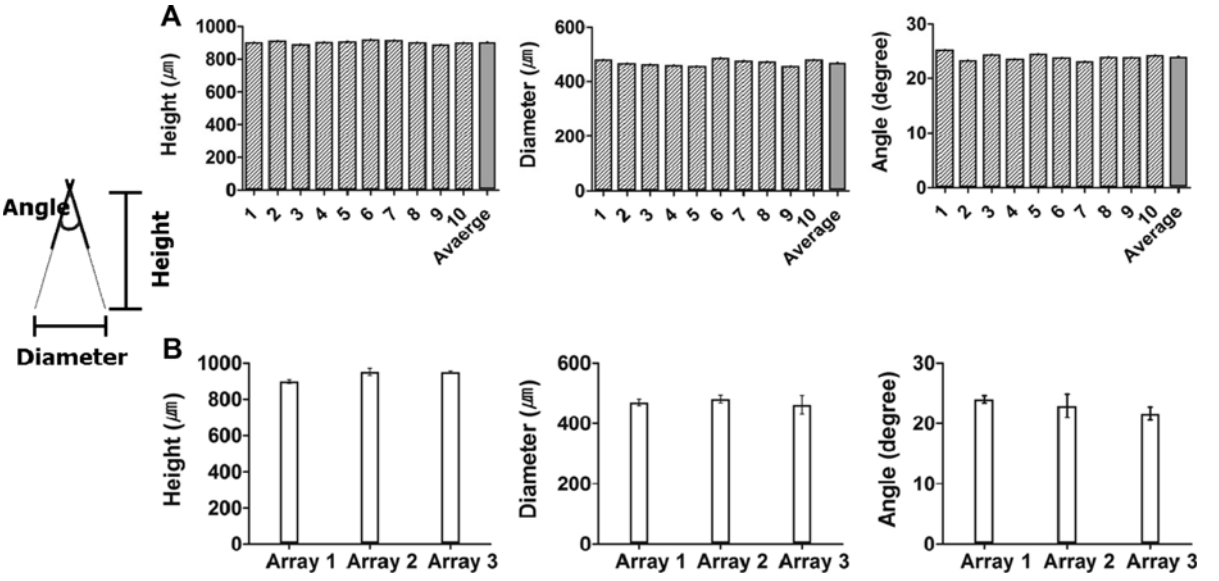

Fig. 2. Heights, diameters, and angles of CMC microneedles in a single array (A) and means of 3 different arrays (B).

each set representing the mean of ten microneedles. The difference among each set was less than 5% of the average of total set. This result verifies that the molding process was sufficiently consistent and accurate, yielding microneedles with consistent shapes and sizes. Changing the intensity of the laser during mold fabrication resulted in microneedles with different height, and we were able to fabricate CMC microneedles with three different heights (600, 800, and 1,000 μm). For subsequent studies, we used microneedles with 800 μm height. The shape of the microneedle patch can also be custom-designed to fit the target area and the purpose of microneedles (drug injection or blood collection) [24,25].

3.2. Mechanical strength of CMC microneedles

Microneedles are required to have minimum mechanical strength and tensile strength to penetrate into the skin without breaking. The solidity of the fabricated microneedles was tested by applying defined amounts of weight onto the microneedles in perpendicular direction and measuring the final amount of deformation of the microneedles. The device for applying the weight was custom-designed as shown in Fig. 3A. Microneedles made from CMC alone was mechanically weak, with significant deformation even when the minimum weight of 5 N was applied. The CMC microneedle deformed significantly to the extent that accurate and consistent measurement of the deformation was not possible, which indicated that the microneedle made of CMC only was not adequate for usage.

It has been reported that adding amylopectin (AP) increases the mechanical strength of microneedles [22]. Both CMC and AP are biocompatible carbohydrates with a history of use in FDA-approval parental formulations [26], with relatively high Young's modulus [27,28], and high water solubility for rapid dissolution. Therefore, in our study, CMC and AP were mixed in three different ratios, (1:1, 1:1.6, and 1:2.3) and the amount of deformation

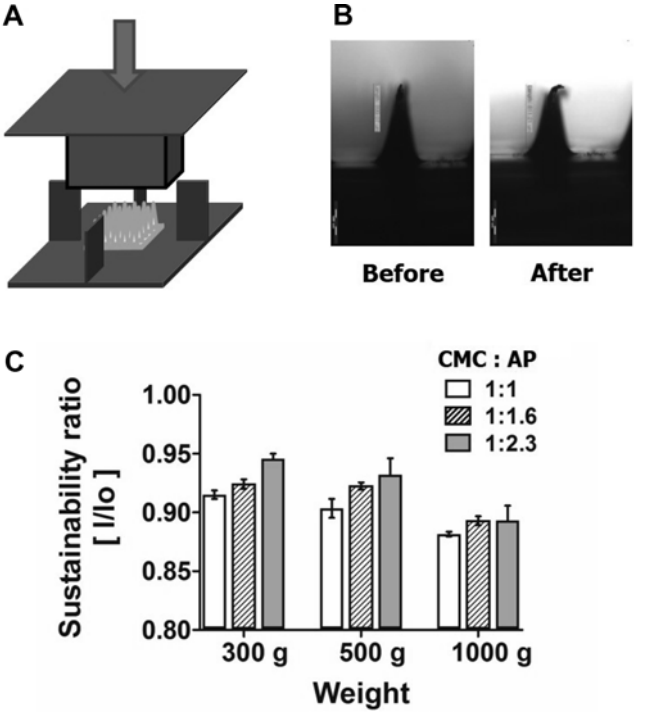

Fig. 3. Mechanical strength of CMC microneedles. (A) A schematic diagram of device for measuring the mechanical strength of microneedles. (B) Images showing the deformation of a microneedle after applying the weight. (C) The amount of deformation relative to the original structure for various mixing ratios of CMC and AP.

was measured. Three different weights were tested (3, 5, and 10 N), which was selected based on a previous study [29]. Fig. 3B presents an example of the deformation test, where the tip of the microneedle was deformed due to applied weight.

The test result shows that a higher fraction of AP results in an increase of mechanical strength, with significantly reduced deformation. Microneedles mixed with AP retained more than 90% of original height, in all ratios tested. Since the mechanical strength was highest at the mixing ratio of 1:2.3, this mixing ratio was used for all subsequent permeability assays. When the fraction of AP was higher than 1:2.3, resulting microneedles were too stiff and brittle, causing unexpected breakage during separation from the mold or application to the skin.

3.3. Dissolution rate of CMC microneedles

CMC microneedles are intended to be a dissolvable, 'poke and release' type of microneedles, and the ability to control the dissolution rate of the microneedles is important for controllable delivery of drugs. In the case of CMC microneedles, the rate of dissolution would be limited mainly by the rate of dissolution. Water solubility of CMC microneedles was measured by immersing the microneedles in PBS (phosphate buffered saline, pH 7.0) solution for 30 sec and measuring the change in the height of the microneedles. Three different ratios of CMC and AP (1:1, 1:1.6, and 1:2.3) was tested. AP was chosen as an additive to adjust the dissolution rate based on previous studies where AP was mixed with CMC as a dissolving microneedle, and the choice of matrix material altered dissolution rate [22]. Therefore, we hypothesized that by changing the mixing ratio between CMC and AP, we could adjust the dissolution rate of the microneedles. As shown in Fig. 4A, in case of CMC microneedle with 1:1 ratio, approximately half of the original structure remained after 30 sec in PBS, and a higher fraction of AP resulted in lower dissolution rate, with more than 60% of original shape remaining in case of 1:2.3 ratio. Therefore, mixing CMC with AP changed water solubility as well as mechanical strength, which indicates that the mechanical property and the dissolution rate can be tuned by adjusting the mixing ratio of CMC and AP within this range.

Dissolution rate of microneedles when inserted into the porcine skin was also tested. We verified that increasing the mixing ratio of AP to CMC decreased the dissolution rate, although the dissolving time increased significantly compared to when dissolving in PBS (Fig. 4B). In case of a microneedle with 1:1 mixing ratio, it took approximately 8 min to dissolve half of the microneedle compared with 30 sec to dissolve the same amount in PBS. In a study by Lee *et al*., using microneedle made of CMC only, half of the microneedle dissolved in the porcine skin within 1 min [22]. In our study, 50% of a microneedle with 1:1 mixing ratio dissolved, and 30% of a microneedle with 1:2.3 mixing ratio dissolved after 8 min in the porcine skin. Fast dissolution of a microneedle results in an almost bolus delivery of encapsulated drug, whereas slower dissolution enables more sustained release of a drug, although the delivery time span is relatively short (10 ~ 20 min). We speculate that a larger time span may be achieved by mixing with other materials, such as PLGA (poly-lactic-co-glycolic acid), which is a biodegradable polymer with slower dissolution rate [30].

3.4. Skin penetration and permeability of a model fluorescent compound

The penetration depths of fabricated microneedles were tested by applying the microneedles to a porcine skin and taking section images. Fig. 5A shows the top-view image of the skin tissue after microneedle insertion and H&E staining. A microneedle with 800 μm height made a hole that is approximately 100 ~ 200 μm in diameter. Fig. 5B shows the microtome sectioned image of the porcine skin tissue. This figure shows deformation of the porcine skin, with a penetration depth of approximately 200 μm. In a study similar to our study, holes that are approximately 150 ~ 200 μm deep were created using 600 μm tall microneedles [22]. Although the depth of penetration did not reach the blood vessels, the holes contributed to a more efficient

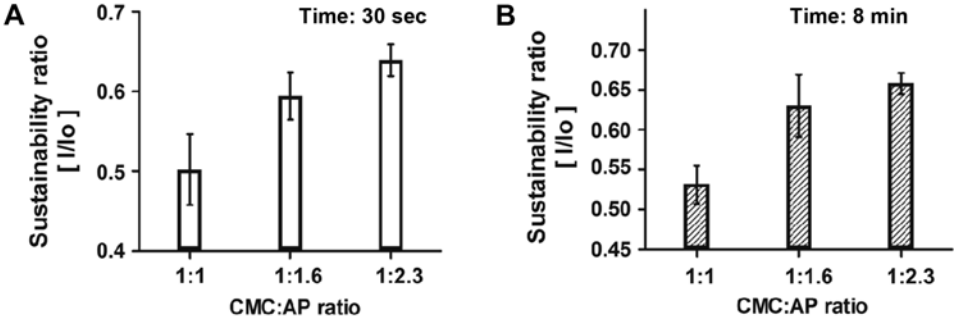

Fig. 4. Dissolution of CMC microneedles in (A) PBS buffer for 30 sec and (B) in the porcine skin for 8 min.

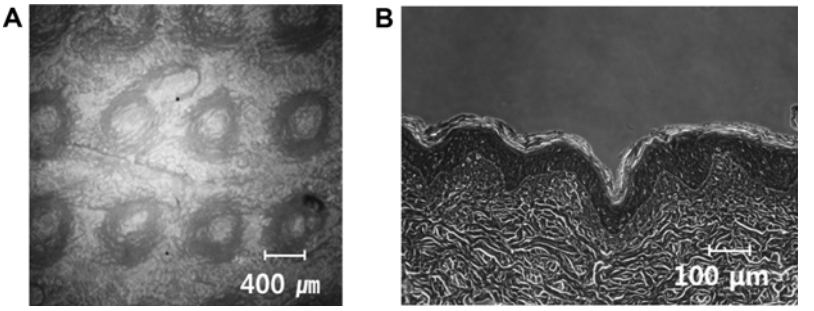

Fig. 5. (A) Top view image of the porcine skin after microneedle insertion and H&E staining and (B) microtome section image of the skin after microneedle insertion and H&E staining.

mass transfer across the skin layer, as verified by the skin permeation experiment.

The main purpose of developing a soluble microneedle is to improve the skin permeability of target molecules, either in the form of chemicals, proteins, vaccines and nucleic acids. To examine if the application of a microneedle results in the enhancement of drug delivery, we used fluorescent rhodamine B as a model compound. Rhodamine B was encapsulated inside a microneedle during the fabrication process, and the microneedle was inserted in a Franz diffusion cell to measure the amount of rhodamine B that diffused through the porcine skin, as shown in Fig. 6A. The microneedle fabricated with rhodamine B is shown in Fig. 6B. For control experiment (skin permeability of rhodamine B without a microneedle), the same total amount of rhodamine B was placed on the surface of the skin. In both cases, the amount of rhodamine B in the receiving chamber was measured after 24 h. The result in Fig. 6C shows approximately three-fold enhancement of skin permeability by using the microneedle. In a study by Kim *et al*., the permeability of rhodamine B across the skin was tested using disk rollers having microneedles with various lengths (0.15, 0.25, and 0.5 mm) [31]. In this study, 'poke and patch' method was used, where disk rollers were pressed against the skin and the model drug was applied. A disk roller with 0.5 mm microneedles improved the skin permeability about four-fold compared to the control, when measured after 24 h. In another study, 'poke and patch' method was tested using microneedles made of Gantrez^{TM} polymer [32]. In a 24 h experiment, about three-fold improvement in skin permeability was observed. In comparison with these studies, our result provides comparable improvement in skin permeability, while offering the advantage of dissolving microneedles, simpler fabrication procedure, and tunable dissolving kinetics, compared to the aforementioned 'poke and patch' method.

3.5. Anti-oxidant activity measurement

Ascorbic acid (vitamin C) is known for its anti-oxidant activity and has been widely used in various cosmetic products. It is also known to inhibit excessive formation of melanin, which contributes to its skin whitening effect [33], and is accountable for stimulating collagen formation in the skin [34]. Since ascorbic acid cannot be produced *de novo*, it has to be taken orally, and consequently has to go through gut absorption and first-pass metabolism. Therefore,

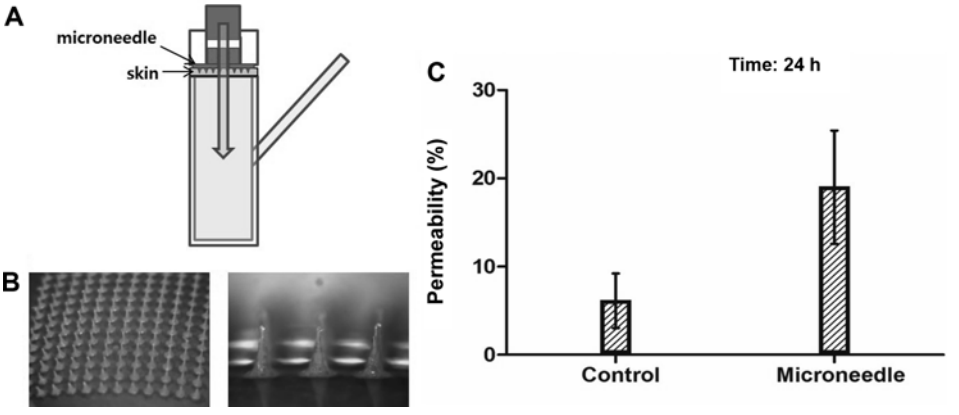

Fig. 6. Skin permeability measurement of rhodamine B loaded in the CMC microneedle. (A) A Franz diffusion cell for measuring the skin permeability. (B) Images of a microneedle array with rhodamine B encapsulated. (C) The permeability of rhodamine B through the porcine skin in the Franz diffusion cell.

it can be quite challenging to deliver sufficient amount of ascorbic acid to the skin through oral intake. Application of ascorbic acid directly through the skin *via* cosmetic products can also be quite challenging, due to rapid degradation in the air, low absorption efficiency through the skin, and effective metabolism by the skin [35]. Encapsulation of ascorbic acid in microneedles and delivery through the skin may improve dermal delivery by protecting ascorbic acid from degradation and enhancing the skin permeability. To test this hypothesis, we encapsulated ascorbic acid in our microneedle array which was applied to the skin, and measured the antioxidant activity of the buffer in the receiving chamber of a Franz cell.

One of the most widely accepted *in vitro* method for evaluation of anti-oxidant activity uses DPPH as a model free radical and measures the reduction in DPPH concentration by changes in the absorbance of DPPH in solution. As a model compound for cosmetic products, ascorbic acid was encapsulated in the CMC-AP microneedle array and the radical scavenging activity of ascorbic acid that crossed the skin was evaluated. Fig. 7 shows that applying the microneedle improved the observed radical scavenging activity by about six-fold, compared to the case of direct application of the same amount of ascorbic acid. It is interesting to note that the antioxidant activity of ascorbic acid increased about six-fold when applied with microneedles, while the skin permeability of rhodamine B increased about three-fold when microneedles were used. It may be explained by the difference in the molecular weights and the chemical properties of the two molecules. Ascorbic acid, having smaller molecular weight compared with rhodamine B, is likely to have experienced faster delivery across the skin. Therefore, the increase in the permeability offered by the microneedle may have been greater for the case of ascorbic acid than the case of rhodamine B. In a study by another group, a microneedle made of chondroitin sulfate was used to delivery ascorbic acid through the skin. About 95% of ascorbic acid was delivered after six hours, whereas direct application of ascorbic acid resulted in non-detectable amount of absorption [36]. The stability of ascorbic acid was also improved by encapsulating in the chondroitin sulfate microneedle, even at 60°C. Our results also indicate that the microneedle fabrication process did not compromise the stability of ascorbic acid, since the application of microneedle resulted in higher antioxidant activity compared to the control. In our study, observation of a low (12%) antioxidant activity in the control experiment probably resulted from longer incubation time (24 h) as opposed to 6 h used in the study by Ito *et al.* [36]. The enhanced antioxidant activity of ascorbic acid after crossing the skin probably resulted from the higher concentration of ascorbic acid in the receiving chamber due to increased permeability, as well as the protective effect by being encapsulated in the CMC microneedle. Our study verifies that the CMC microneedle can be useful for delivering cosmetic ingredients or pharmaceutical compounds. However, the extent of advantages will also depend on the chemical property and the stability of materials to be delivered. In our future studies, we plan to test the usefulness of CMC microneedles for delivering various pharmaceutical compounds.

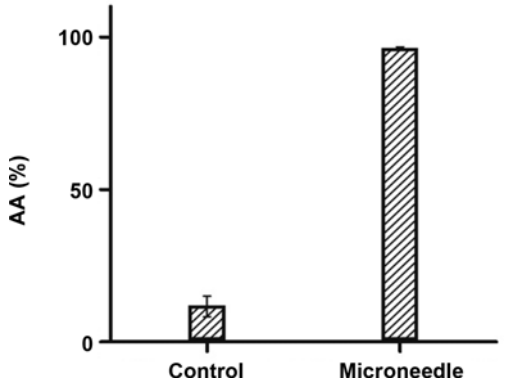

Fig. 7. Antioxidant activity of ascorbic acid after dermal delivery for 24 h, measured by DPPH assay. Control is the antioxidant activity of the same amount of ascorbic acid directly applied to the skin and after dermal delivery.

4. Conclusion

In this study, we used a laser writing process to fabricate a PDMS mold for a microneedle array made of CMC. Rapid prototyping of various sizes of microneedles was possible, while providing reasonable consistency in the fabricated microneedles. The mechanical property and the dissolution rate could be controlled by mixing with AP at various ratios. Using fluorescent molecules as a model drug and the porcine skin, improvement of about three-fold in the skin permeability was observed, whereas the antioxidant activity of ascorbic acid encapsulated in the microneedle showed about six-fold increase, compared to the direct topical application. The fabrication method reported in this paper may be useful for rapid prototyping of microneedles using materials other than CMC, and improving the dermal delivery efficiency of various drugs as well as cosmetic products.

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