Monitoring the Dissolution Behavior of Dissolving Microneedles by UV-Vis Imaging System

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Visualization of compounds released from microneedles using UV and Visible light

PURPOSE

Microneedle patches, consisting of small needles less than 1 mm in length that contain drugs, have gained attention as a novel transdermal drug delivery system (TDDS). Microneedles allow drugs to cross the skin barrier painlessly[1], making them an attractive option for delivering low-molecular compounds and vaccines[2].

In this study, we investigated a method to visually and quantitatively monitor the release behavior of drugs from microneedles.

METHOD(S)

Preparation of microneedle patches

Microneedles were prepared by melting drug powder at 180 °C under vacuum and molding it in a silicone mold. The silicone mold contained 100 needles within a 25 mm^2 area (5 mm x 5 mm). Indomethacin and nifedipine were used as model compounds. HPMCAS, with a melting point close to that of the model compounds, was used as the base material for the microneedle patches.
These steps were performed in a VCM chamber (MeltPrep GmbH).

Monitoring of dissolution behavior

Microneedle patches were placed in an SDi2 system (Pion inc.) equipped with a UV-Vis imaging system and a flow-through cell type dissolution tester. Open-loop short-duration tests (30 min) and closed-loop long-duration tests (12 h) were performed using a phosphate buffer solution with a pH of 7.2.
In all release tests, the test medium was pumped from bottom to top at a flow rate of 25 mL/min.
During the release tests, LED light at wavelengths of 255 and 520 nm was used to monitor the dissolution behavior of the drugs from the microneedles.

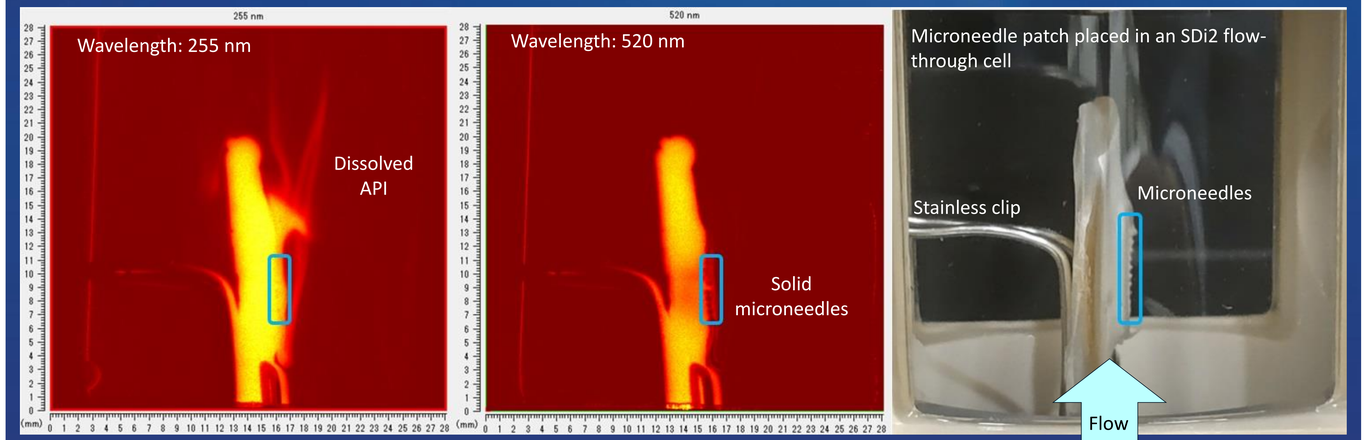

Figure 2 Imaging the release behavior of indomethacin from microneedles. The position of the needles is highlighted by a blue frame. (Left) Image acquired at a wavelength of 255 nm, visualizing the release of indomethacin into the solution. (Middle) Image acquired at a wavelength of 520 nm, showing the shape of the microneedles in their solid state. (Right) Photograph inside the flow-through cell after the release test. The microneedle patch was pressed against an artificial membrane , allowing only the tips of the needles that penetrated the membrane to come into contact with the test medium. The patch base was covered with an insoluble film.

REFERENCE(S)

1. Ziad Sartawi, Caroline Blackshields, Waleed Faisa, Dissolving microneedles: Applications and growing therapeutic potential, J. Control. Release (2022) 348,186–205.
2. Sharvari M. Kshirsagar, Thomas Kipping, Ajay K. Banga, Fabrication of polymeric microneedles using novel vacuum compression molding technique for transdermal drug delivery, Pharm. Res., (2022) 39(12), 3301-3315.

RESULT(S)

Uniform microneedle patches were successfully obtained for both indomethacin and nifedipine (Fig. 1).

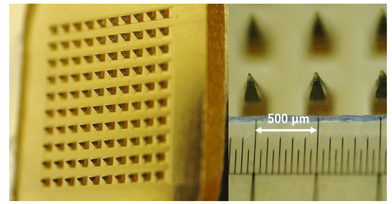

Figure 1 (Left) Overall image of microneedles molded into 5 mm x 5 mm square area.
(Right) Enlarged image of microneedles. The needles were aligned at a pitch of 500 µm and a height of 600 µm. The base of the patch was HPMCAS.

The dissolution behavior of the APIs from the microneedles was observed in real time by imaging the interior of the flow-through cell using UV and visible (Vis)light. UV imaging detected the dissolution behavior of the drugs from the microneedles (Fig. 2 - left), whereas Vis light detected the presence of undissolved microneedles (Fig. 2 - middle).

In the open-loop release test, the compound concentration in the upper part of the flow-through cell was calculated using absorbance data obtained through UV imaging. For indomethacin, the release rate peaked 10–20 min after the start of the test, followed by a gradual decrease (Fig. 3).
In contrast, nifedipine exhibited a sustained release profile in the short-duration open-loop release tests. In the closed-loop release test, with a test solution volume of 750 mL, mass release was monitored over 12 h, confirming sustained release of nifedipine (Figs. 4 and 5).

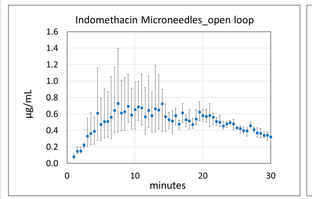

Figure 3 Indomethacin concentration in the upper area of the flow-through cell during open-loop release tests.

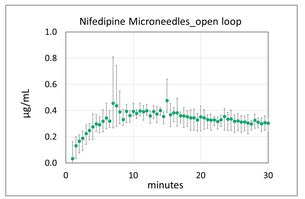

Figure 4 Nifedipine concentration in the upper area of the flow-through cell during open-loop release tests.

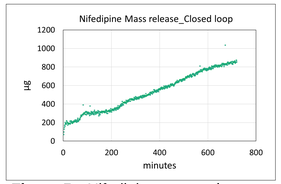

Figure 5 Nifedipine mass release during closed-loop release tests.

CONCLUSION(S)

When evaluating the dissolution behavior of drugs from microneedles, mimicking conditions similar to those of the skin is crucial. In this study, we conducted a flow-through cell type dissolution test, focusing on the drug release from the needle portion that punctured through the membrane. By combining UV and Vis imaging, we successfully visualized the dissolution behavior of the drugs. This method is applicable to both rapid and sustained-release microneedles. The combination of the flow-through cell system with UV-Vis imaging offers an effective approach for simultaneously visualizing and quantitatively evaluating the dissolution behavior of drugs from microneedles.

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