Electronic Supplementary Material (ESI) for Materials Advances.


Supplementary Information

# Monodispersed sodium hyaluronate microcapsules for transdermal drug delivery systems

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**Microchannel design**

The microchannels were designed based on a previous report by Rotem et al.[1] (Figure S1).

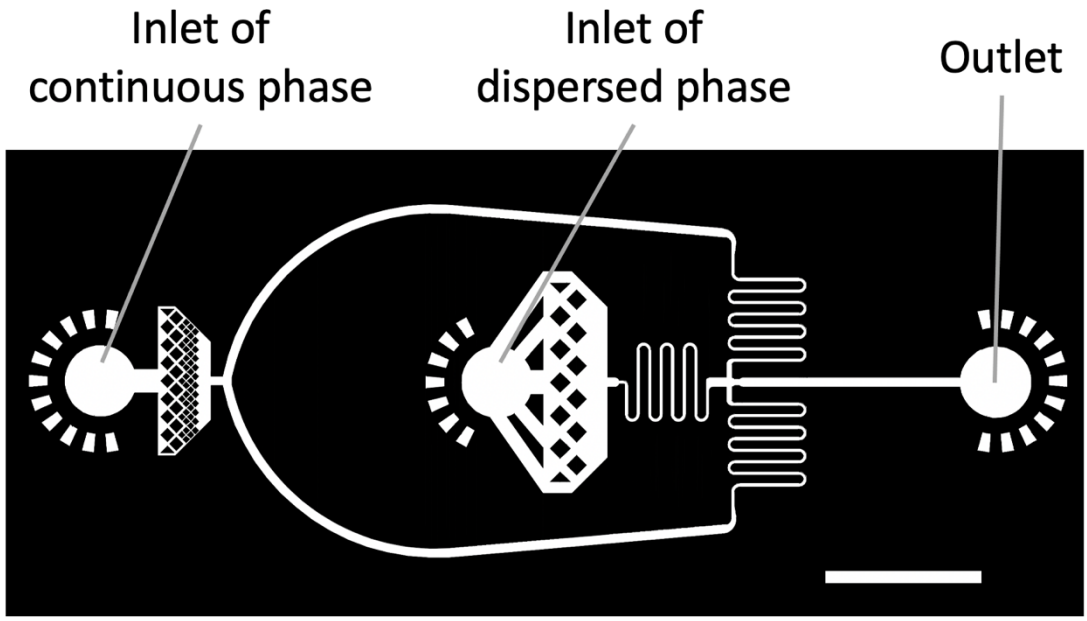



Figure S1. Microchannel design, including microchannels with a depth of 75 $\mu$m (scale bar = 2 mm).

**Microcapsule pretreatment**

The continuous phase around the microcapsules was replaced (Figure S2).

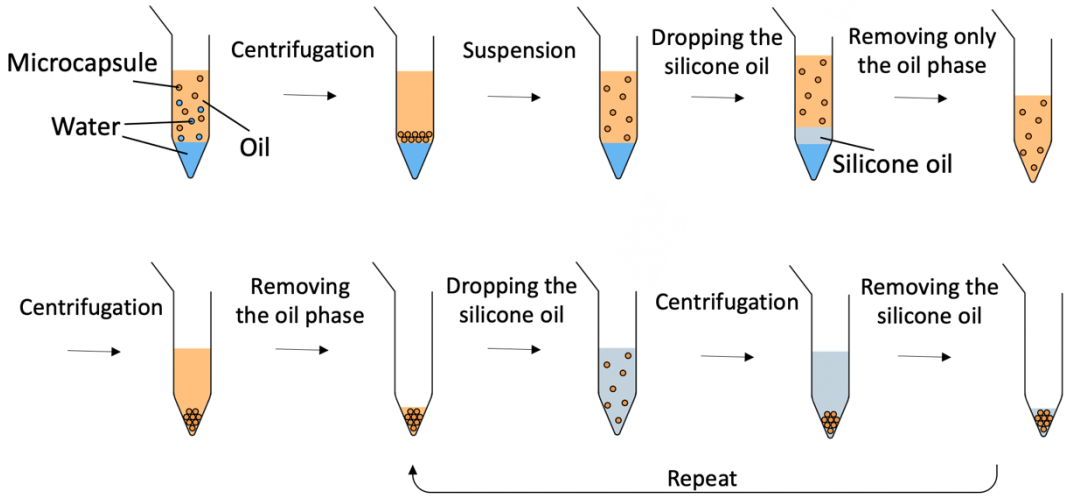



Figure S2. Microcapsule pretreatment procedure for microneedle preparation.

**Microcapsules formed from droplets**

Calcium chloride ($CaCl_2$) could not be used as a gelling agent because the sodium hyaluronate droplets were completely dissolved in its aqueous solution. (Figure S3). More than 20 h after the droplet was placed on the gel substrate, the droplet diameter became constant and shrinkage was completed (Figure S4).

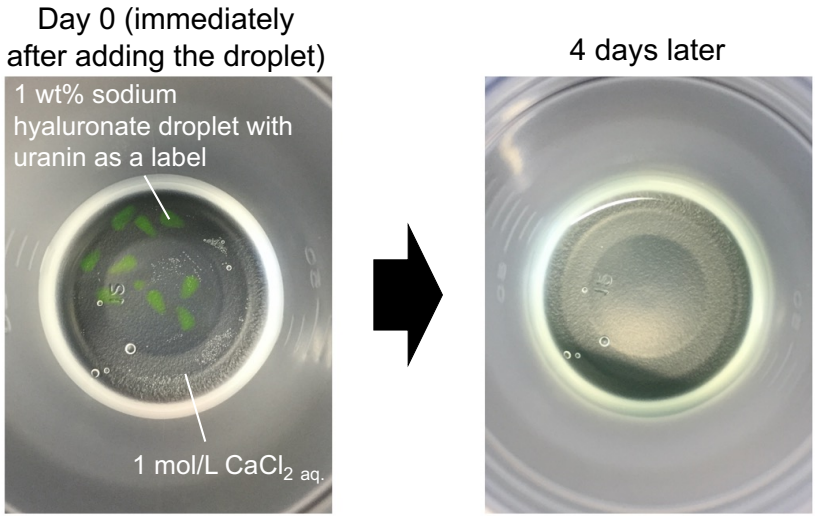



Figure S3. Images in a beaker (where $CaCl_{2\ aq.}$ was poured and sodium hyaluronate droplets were added) looking through the top. The base diameter of the beaker is approximately 4 cm.

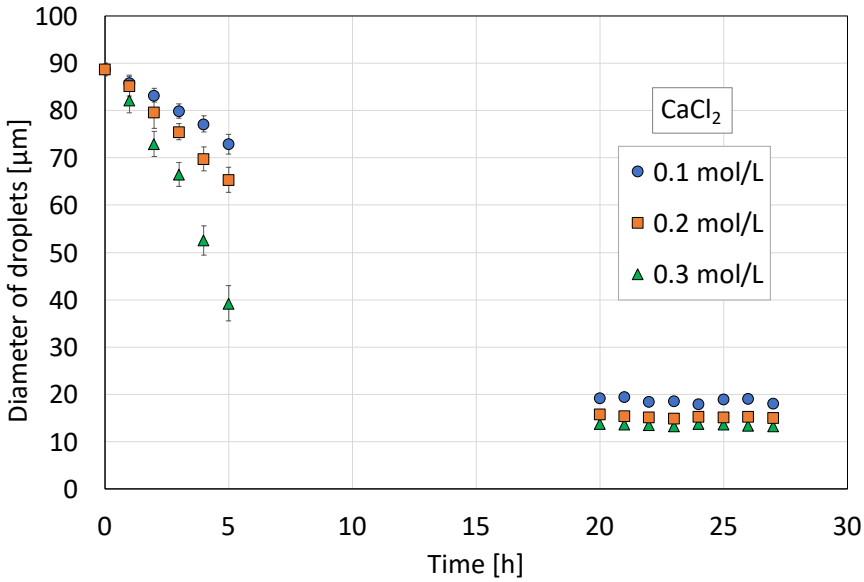



Figure S4. Diameters of the droplets on the gel plate.

**Microneedle characterization**

A section of skin could not be penetrated by the MNs (Figure S5).

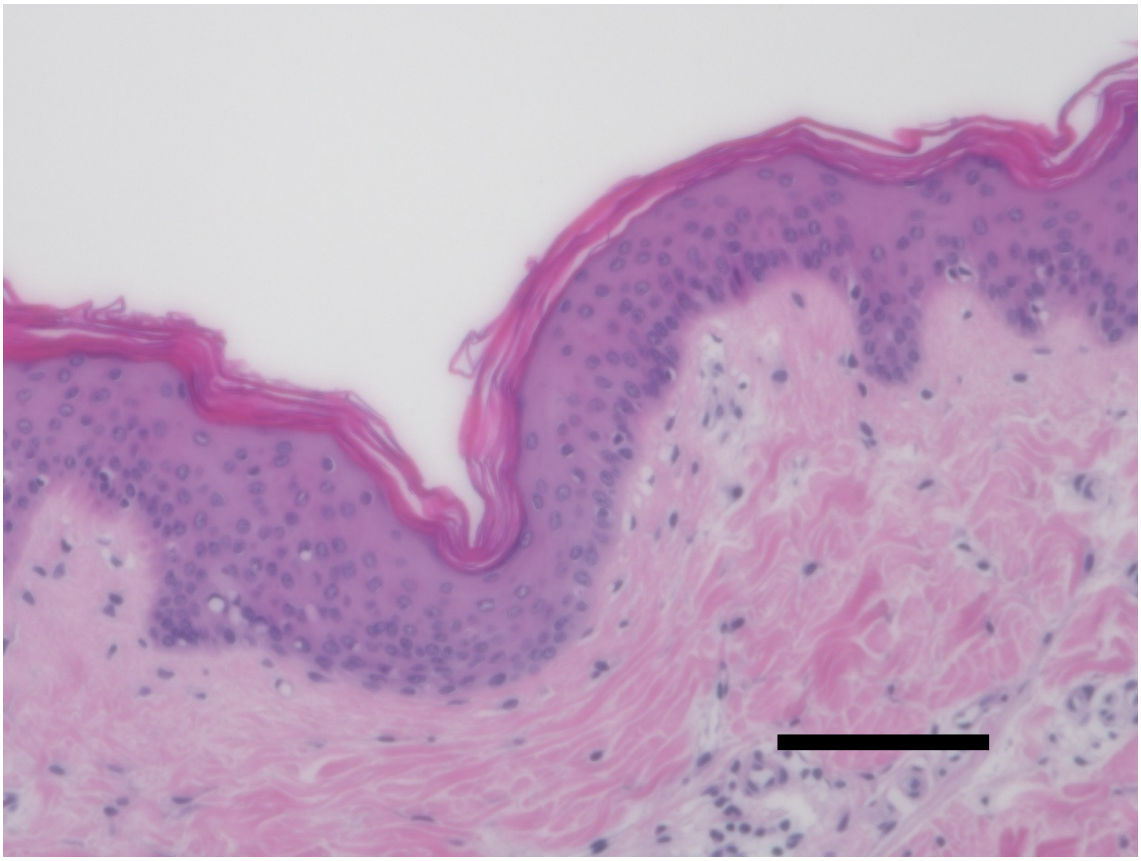
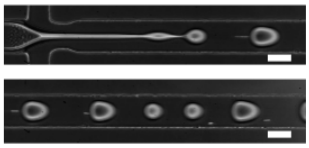


Figure S5. Histological cross-section of pig skin surface showing no penetration of the stratum corneum after MN insertion and removal (scale bar = 100 μm).

**Droplet formation stability**

A dispersed phase comprising 0.01 wt% SH aqueous solution and 0.5 mg/ml FITC-BSA was suitable (Table S1).

Table S1. Droplet formation stability at 0.1 and 0.01 wt% sodium hyaluronate. Droplets regarded as "stable" were monodispersed (CV: <10%), and those regarded as "unstable" were polydispersed (CV: >10%) (Scale bars = 100 μm).

| Concentration of sodium hyaluronate solution (wt%) | Viscosity of sodium hyaluronate solution at 25.5 ℃ (mPa·s) | Droplet generation | Stability of droplet generation phenomena |
|---|---|---|---|
| 0.1 | 21.4 |  | Unstable*1 |
| 0.01 | 3.84 |  | Stable*2 |

*1 The occurrence of transition state was observed.
*2 No occurrence of transition state was observed .

**REFERENCES**

1. A. Rotem, O. Ram, N. Shoresh, R. A. Sperling, M. Schnall-Levin, H. D. Zhang, A. Basu, B. E. Bernstein, D. A. Weitz, High-Throughput Single-Cell Labeling (Hi-SCL) for RNA-Seq Using Drop-Based Microfluidics. *PLoS One* **2015,** *10* (5).