A Simple *In Situ* Fabrication of Hollow Poly(n-Butyl Methacrylate) Microneedles Integrated with a Magnetic Micropump System

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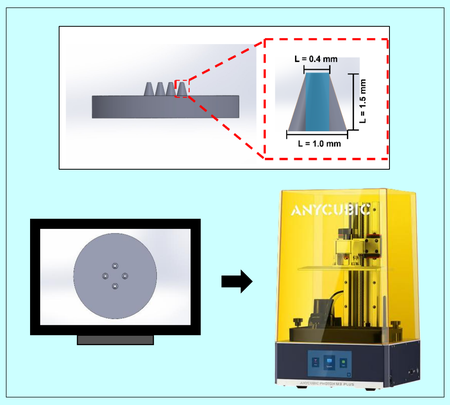
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Introduction

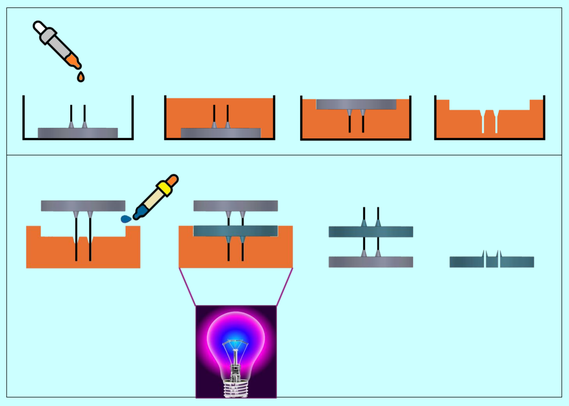
Microneedle-based transdermal drug delivery systems represent promising strategy to enhance drug bioavailability while minimizing the pain, anxiety, and tissue trauma associated with conventional hypodermic needles. Microneedles are generally classified into solid, surface-coated, soluble, swellable hydrogel, porous, and hollow types. Among these, hollow microneedles (HMNs) are of particular interest, especially when integrated with reservoir systems, as they allow for the controlled delivery of high molecular weight or labile therapeutics. In this study, PBMA-based HMNs, fabricating using this simple, low-cost, and rapid method, were easily integrated into a magnetic micropump system and demonstrated the ability to deliver defined volumes of liquid within a specific time period under varying applied voltages and frequencies.

Materials and Methods

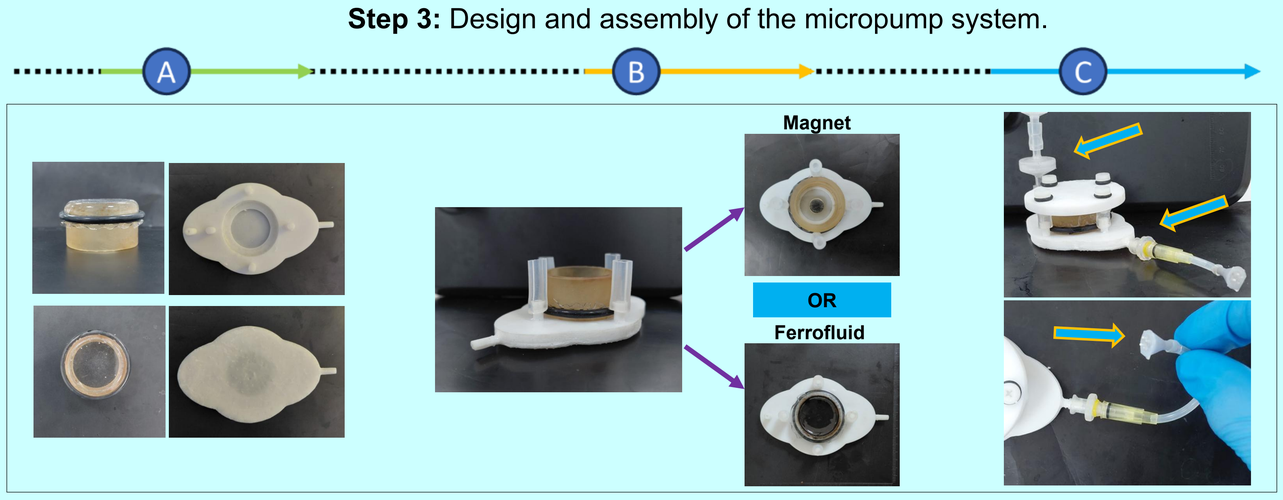
Step 1: Design and fabrication of positive mold.



Step 2: Negative mold and PBMA-based HMNs fabrication process.



Step 3: Design and assembly of the micropump system.



Results and Discussion

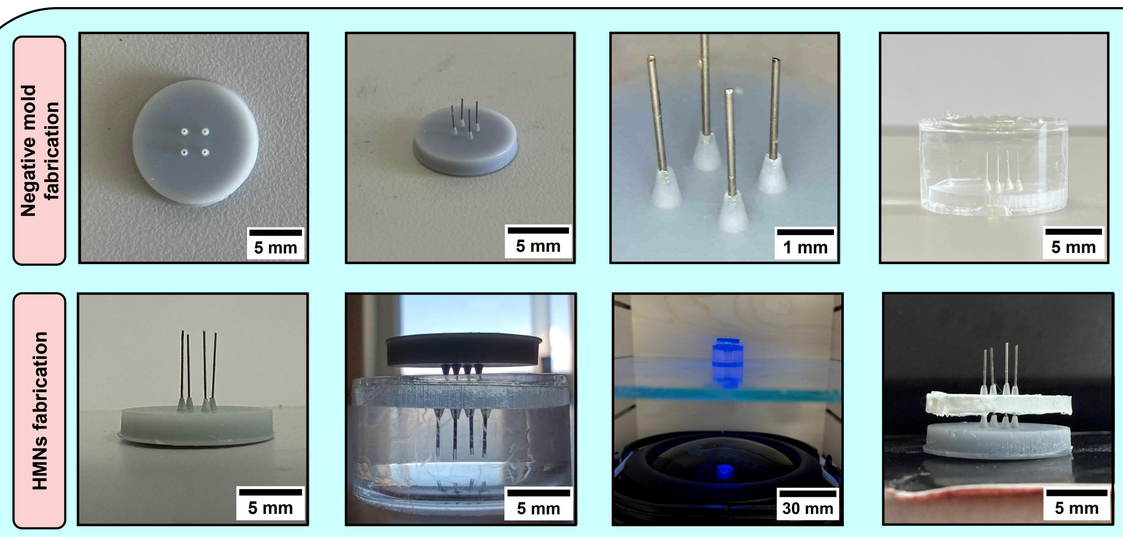


Figure 1. Images of negative PDMS mold and PBMA-based HMNs fabrication.

2 × 2 and 5 × 5 hollow microneedle (HMN) arrays were fabricated via photopolymerization of BMA (**Figure 1**). The 2 × 2 array is produced the needle length of **0.83 ± 0.02 mm** for 1.0 mm design and **1.28 ± 0.06 mm** for 1.5 mm design (**Figure 2A**). The 5 × 5 array is produced the needle length of **0.89 ± 0.06 mm** for 1.0 mm design and **1.25 ± 0.07 mm** for 1.5 mm design (**Figure 2B**).

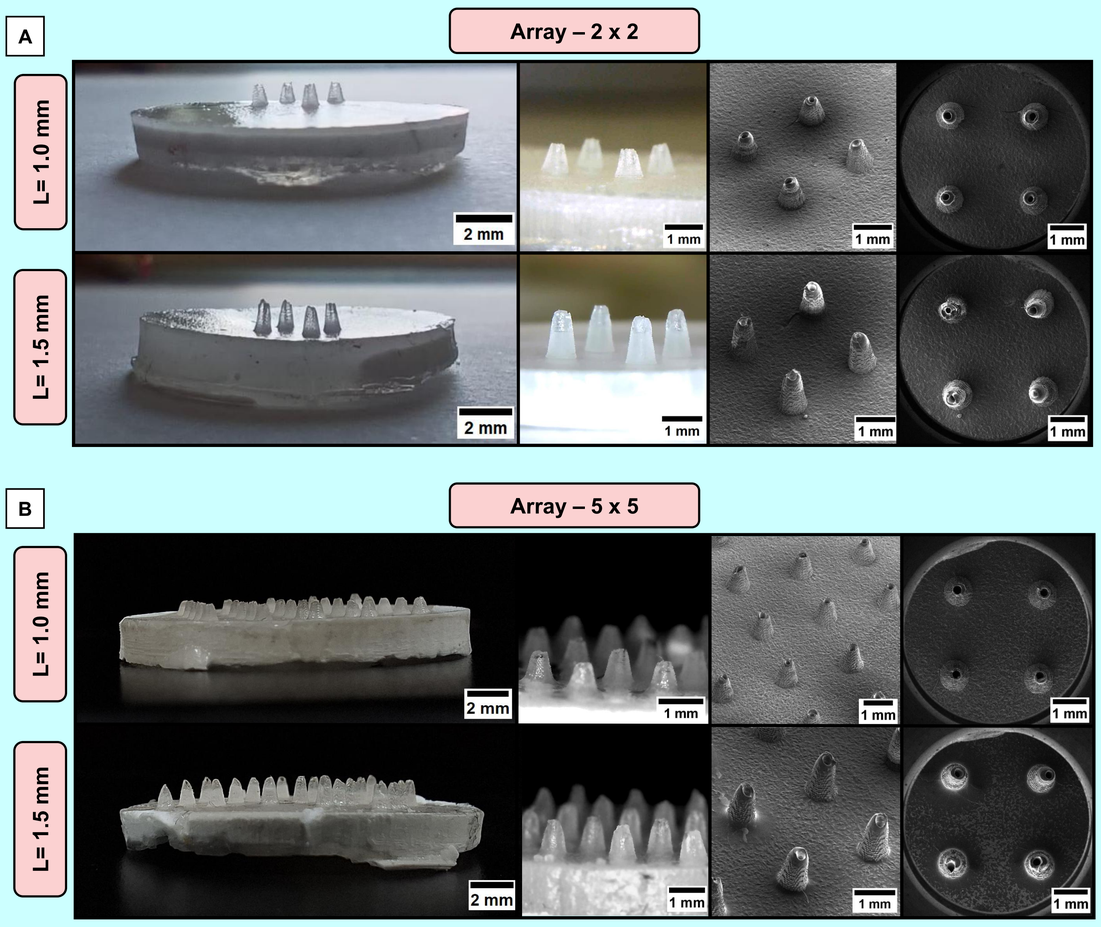


Figure 2. Digital camera, digital microspore and Scanning Electron Microscope (SEM) images of 2 x 2 **(A)** and 5 x 5 **(B)** HMNs.

In parafilm penetration tests, 1.0 mm-long HMNs exhibited efficient penetration up to approximately **380 µm**, while 1.5 mm-long HMNs achieved penetration depths up to **508 µm** (**Figure 3A**). Cytotoxicity assessment (MTT assay) revealed that HMN extracts exhibited no significant toxic effects on L929 fibroblast cell viability, maintaining values **above 85%** across all extract dilutions, comparable to the negative control (**Figure 3B**). In the skin irritation test, the microneedles caused **no edema or visible irritation** on rat skin (Ethical approval by the Ankara University Animal Ethics Committee, Approval No: 2023-3-6).

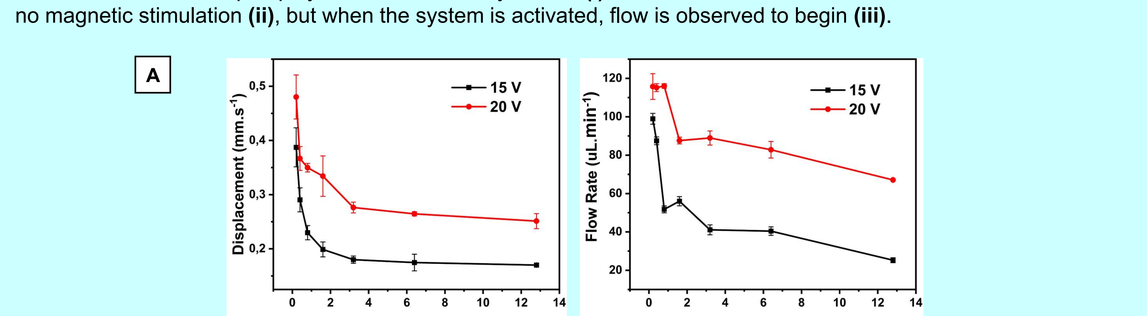


Figure 3. Microscopic images of the holes formed in the parafilm layers **(A)** and cell viability after 24 h exposure to HMN extracts at different dilutions **(B)**.

In ongoing studies, the fabricated HMNs were integrated into a magnetically actuated micropump system, and flow rates through the microneedle channels were evaluated under varying voltages (20–60 V) and frequencies (1–20 Hz) using both permanent magnet and ferrofluid-based actuation. The liquid flow rates ranged from **20 to 120 µL.min^{-1}**, demonstrating stable and controllable performance (**Figure 4 and 5**).

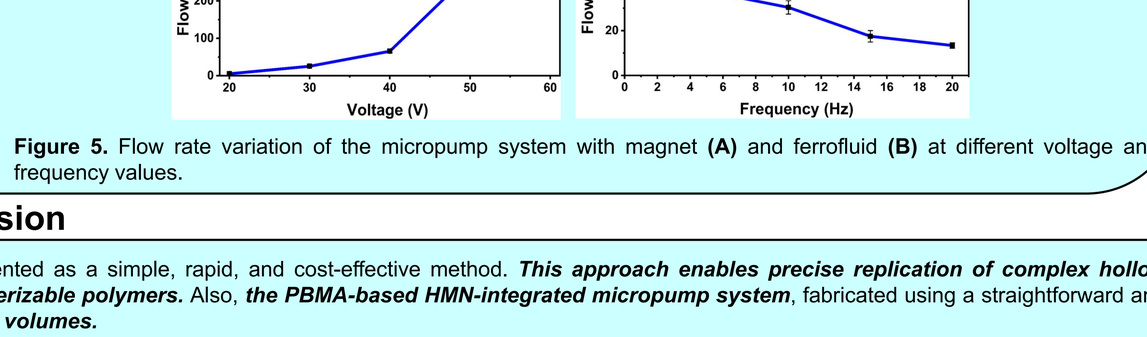


Figure 4. Setup used in the flow study: Ferrofluid micropump system, power supply, frequency regulator, electromagnet, and the ferrofluid micropump system is indicated by arrows **(i)**. No flow is observed from the microneedles when there is no magnetic stimulation **(ii)**, but when the system is activated, flow is observed to begin **(iii)**.

Figure 5. Flow rate variation of the micropump system with magnet **(A)** and ferrofluid **(B)** at different voltage and frequency values.

Conclusion

Overall, a novel one-step fabrication technique for poly(n-butyl methacrylate) (PBMA) hollow microneedles (HMNs) is presented as a simple, rapid, and cost-effective method. ***This approach enables precise replication of complex hollow geometries, maintains channel integrity, ensures mold reusability, and is compatible with a wide range of photopolymerizable polymers.*** Also, ***the PBMA-based HMN-integrated micropump system***, fabricated using a straightforward and low-cost process, ***exhibits great potential for dose-controlled and minimally invasive transdermal delivery of small liquid volumes.***

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