A SKIN-CONTACT-ACTUATED DISPENSER/PUMP FOR TRANSDERMAL DRUG DELIVERY

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ABSTRACT

In this paper, a skin-contact-actuated dispenser/pump is described. The dispenser consists of stacked PDMS layers mounted on a silicon substrate and operates based on the evaporation and condensation of a low boiling point liquid. Therefore, there is no need for a heater or a battery, since the only required source of energy is the heat provided by skin contact. A prototype device with overall dimensions of 14mm×14 mm×8mm is fabricated and characterized. For a perfluoro compound working fluid (3M^{TM} FC-3284), a flow rate of 60μL/min and a maximum back pressure of 4.19 psi is measured.

KEYWORDS: Micropump, transdermal drug delivery, evaporation, phase-change liquid

INTRODUCTION

Transdermal dispensing of drugs has been extensively pursued for many decades. Although patches have been used to deliver small hydrophobic molecules such as nicotine, an external pressure source (i.e., micropump) in conjunction with a direct subcutaneous access port is required to deliver the majority of therapeutically important drugs through the skin. Microfluidics has played an important role in this area by providing microneedle arrays and other micro-scale sensors and actuators for transdermal drug delivery [1, 2].

Numerous micropumps for drug delivery applications have been reported [3]. These can be categorized as mechanical (positive displacement) or non-mechanical. The most common actuation methods for mechanical micropumps are electrostatic, piezoelectric, thermo-pneumatic, and magnetic. Non mechanical pumps on the other hand, do not rely on mechanical energy in order to produce fluid momentum. Actuation methods for non-mechanical micropumps include magneto-hydrodynamic force, electro-hydrodynamic force, electro-osmosis, and electro-wetting.

Despite the differences in operation and design, a common characteristic of almost all of the reported micropumps is the requirement for a power source (usually a battery) to dispense the drug. In this paper, we present a skin-contact-actuated dispenser/pump using a low-boiling point phase change liquid in which the flow of a stored liquid is initiated by the temperature rise due to heat conduction when the device is placed in contact with the skin. This eliminates the need for a power source, thus simplifying the design and reducing the overall dimensions of the system.

STRUCTURE AND WORKING PRINCIPLE

The prototype device consists of four stacked layers of PDMS (polydimethylsiloxane, Dow Corning Sylgard 183) on a silicon substrate. Silicon base provides a good thermal interface for rapid heating and cooling of the working liquid causing evaporation and condensation. As mentioned above, a micromachined heater element is thus not required, since the low boiling point of the working liquid enables the operation of the dispenser solely by the thermal conduction of body temperature.

The structural elements of the micropump are shown in the 3D exploded sketch of Figure 1. The working liquid chamber is bonded to the silicon substrate. Two peripheral cavities are created in the perimeter of the chamber in order to facilitate the injection of the liquid and venting of the air which is trapped inside the chamber during bonding. A thin layer of PDMS is bonded on top of the chamber, acting as the membrane which deflects due to the evaporation and condensation. The membrane movement causes the pumping of the liquid in the drug chamber via a through hole in the cap layer.

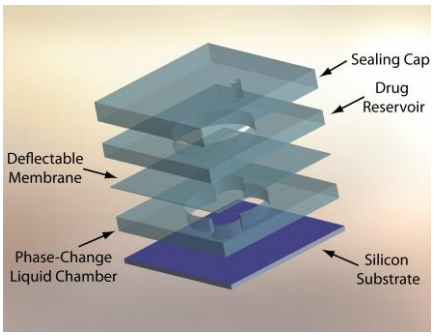

Figure 1. 3D Exploded sketch of the micro-dispenser.

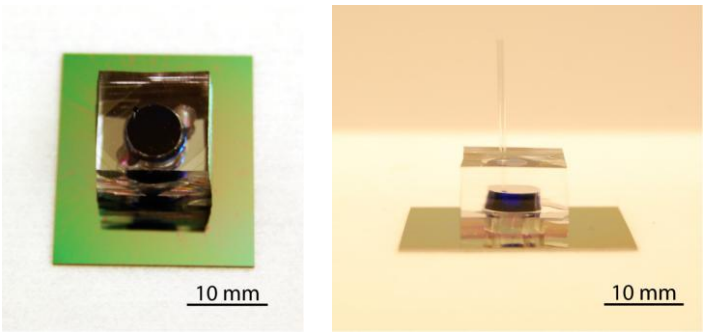

Figure 2. Side and top view of the prototype micro-dispenser.

The overall dimensions of a prototype device shown in Figure 2 are 14mm×14mm×8mm. The radius of the phase change liquid chamber is 4mm and its thickness is 2mm. The radius of the peripheral cavities is 1.5mm. The deflectable membrane is 140μm thick. The drug reservoir has a radius of 4mm and a thickness of 2mm. The silicone to curing agent ratio for the PDMS is 10:1 and the curing conditions are 120°C in a conventional oven for 15 minutes. The obtained Young's Modulus of PDMS for this mixing ratio is $7.5x10^5$ Pa.

Although a variety of phase-change liquids is commercially available, the selection of the appropriate one for this application is based on the boiling point and vapor pressure values. A low boiling point is desirable, since the temperature rise due to the skin contact is only a few degrees above the room temperature. Simultaneously, the vapor pressure should be large enough to provide adequate back pressure during the operation. Two commercial liquids from 3M™ were found to exhibit the desired values. Table 1 shows the boiling point (at 1atm) and vapor pressure (at 25°C) for 3M™ FC-3284 (a perfluoro compound) and 3M™ HFE-7000 (a methyl perfluoropropyl ether). The same table contains the values for methanol and isopropanol, which were used for comparison.

Table 1. Working Liquid Specifications

Liquid	Boiling Point (1 atm)	Vapor Pressure (25°C)
3M™ FC-3284	50°C	267.77 Torr
3M™ HFE-7000	34°C	484.53 Torr
Methanol	64.6°C	126.87 Torr
Isopropanol	82.3°C	44 Torr

EXPERIMENTAL

After fabrication and assembly, a 5.5cm capillary tube with an inner diameter of 400μm was connected to the reservoir chamber in order to measure the flow rate and back pressure. Using hypodermic syringes, the drug reservoir was filled with dyed DI-water and 10μL of low boiling point liquid was injected in the bottom chamber. In order to displace the residual air in the phase-change chamber and make sure that the deflection of the PDMS membrane occurs mainly because of liquid evaporation, a venting needle was placed in one of the peripheral cavities of the chamber, while the liquid was injected with an hypodermic syringe from the other cavity. The flexibility of PDMS allowed the temporary insertion of the hypodermic needles without permanent puncturing or formation of leakage in the channels.

Figure 3 shows time frame images of the device pumping dyed DI water when in direct contact with the skin. Although any contact with skin can initiate the evaporation of the phase-change liquid, the optimum operation occurs when the heat source is directly below the phase-change chamber, i.e., touching the bottom surface of the silicon substrate under the device. The lateral conduction case (top row in Figure 3) leads to a considerably slower rate. This is mainly due to the slower lateral thermal diffusion and simultaneous backside cooling of the silicon substrate. In order to measure the flow rate, the outlet capillary was marked and a video recorder was used to find the corresponding elapsed times for the different fluid levels. Figure 4 shows the flow rate (water level rise) vs. time for four different liquids. HFE-7000 and FC-3284 exhibit flow rates of 33.7 μL/min and 60μL/min, respectively. Despite its superior characteristics for this application, HFE-7000 was found to exhibit slower flow rate than the FC-3284. This is due to the absorption of HFE-7000 in PDMS, leading to swelling of the cavity sidewalls and stretching of the membrane. The same effect takes place for isopropanol and methanol [4] making FC-3284 the most suitable phase-change liquid for this application among the four explored ones.

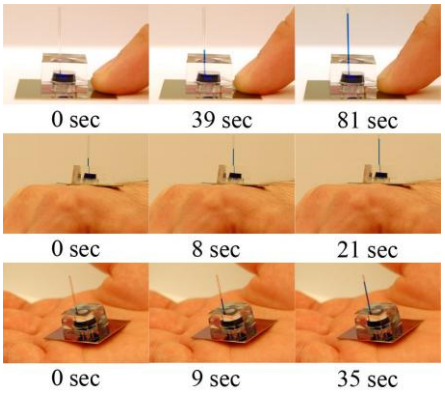

Figure 3. Time frame images of the device, pumping when in direct contact with the skin.

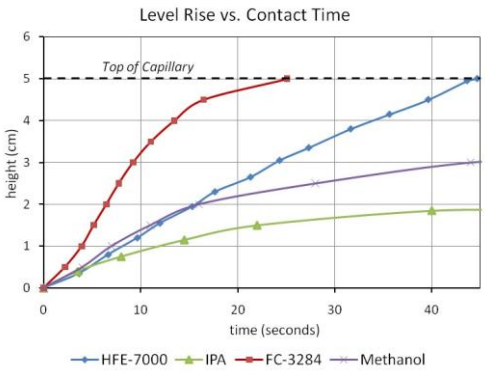

Figure 4. Water level rise due to skin contact.

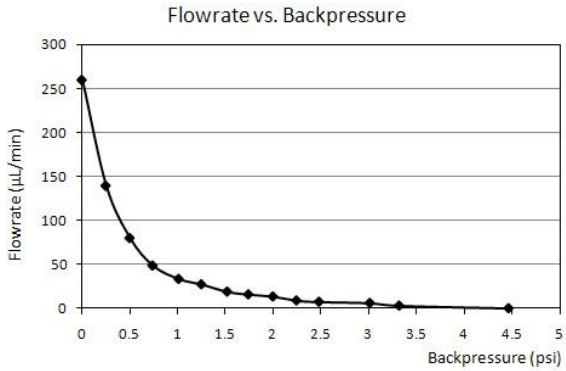

Figure 5. Flowrate vs. backpressure for FC-3284 phase change liquid.

In Figure 5, the flow rate versus backpressure is plotted with FC-3284 as the working liquid. The testing was performed using a hotplate set to 31°C in order to achieve controlled heating. The setup was comprised of a pressure regulator (Porter Instrument Company Inc., Hatfield, PA, USA) with the inlet connected to nitrogen gas supply and the outlet connected to a digital pressure gauge (Omega Engineering Inc., Stamford, CT, USA) and to the capillary outlet of the micropump. Initially, the flow rate was measured at atmospheric backpressure, i.e. the capillary end was open. The zero backpressure flow rate was calculated to be 260μL/min, a value much higher than the one calculated with thermal conduction due to finger contact. This is due to the fact that upon contact with the hotplate surface, the entire backside area of the micropump is rapidly and uniformly heated to 31°C as opposed to the near-linear and localized temperature increase upon finger contact.

An exponential decrease of the flow rate is observed with the increase of backpressure. The maximum backpressure when the micropump is heated with a hotplate is 4.46 psi. The same test setup was used to measure the maximum backpressure when pumping was initiated by a finger touch. The measured value for this case was 4.19 psi. It should be noted that the theoretical maximum backpressure that the phase-change liquid can provide at 31°C is 6.59 psi. However, the PDMS membrane used for the fluid displacement limits the attained backpressure to the value that corresponds to its maximum deflection.

CONCLUSIONS

In this paper, a skin-contact actuated dispenser/pump for transdermal drug deliver applications was described. The micropump did not require a power source, since the evaporation of a low boiling point liquid upon contact with the skin initiated the flow. The micropump consisted of four bonded PDMS layers on a silicon substrate. A flow rate of 60μL min^{-1} and a maximum backpressure is 4.19psi was measured for a 14mm×14 mm×8mm prototype.

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