ELECTROLYSIS-DRIVEN DRUG DELIVERY FOR TREATMENT OF OCULAR DISEASE

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Abstract
A new paradigm for treatment ocular diseases using micromachined drug delivery devices is explored as an optimal means of pharmacologic management. The device consists of a refillable reservoir, electrolysis pump, and cannula. Electrolysis-driven drug delivery provides flexible, long term treatment with only a single surgery.

Keywords: Drug delivery device, implant, electrolylsis pump, parylene, ocular

1. Introduction

Many vision-threatening diseases, including retinitis pigmentosa, age-related macular degeneration, diabetic retinopathy, and glaucoma, are incurable and yet extremely difficult to treat with currently available therapies (oral, topical, injections, and sustained-release implants). In particular, the eye wall is an effective physical barrier that obstructs intraocular delivery of therapeutic levels of drug to specific treatment sites. Intraocular injections and sustained-release implants can be effective therapies, however, repeated injections or implantations are required (typically at 6 week intervals). Furthermore, device size and drug volume are severely limited by physiological space constraints [1, 2].

While several MEMS drug delivery platforms have been explored, none are suitable for long term management of ocular diseases. Specific requirements include broad drug compatibility, ability to be refilled for chronic use, minimally invasive implantation, variable dosing (continuous or bolus), and physiological sensing for feedback controlled delivery. We previously presented a passive, mechanically-operated MEMS drug delivery which did not have variable dosing capability or feedback control [3]. An electrolysis-driven implantable MEMS drug delivery system can meet these requirements. In addition, power consumption and heat dissipation are minimal facilitating chronic operation in the body.

2. Experimental

The drug delivery system is an assembly of two parts that form a refillable silicone reservoir (~50 μL), electrolysis pump, and flexible parylene cannula (Fig. 1). During implantation, the integrated cannula crosses the sclera (eye wall) and is directed at the disease site. A pressure gradient generated by electrolysis acts on drug contained within the reservoir, forcing drug onto the disease site through the cannula. When drug is depleted from the reservoir, the chamber is repeatedly refilled by non-destructively puncturing the wall with a non-coring needle attached to a drug-filled syringe.

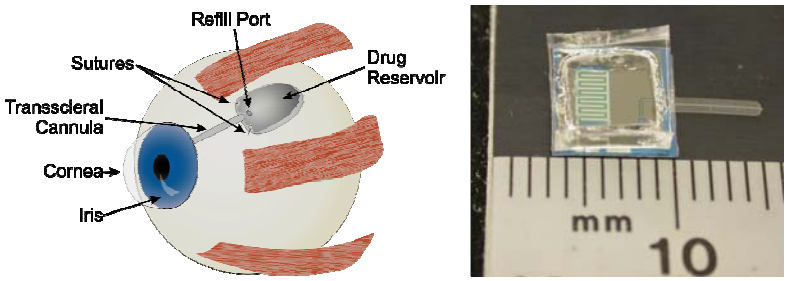

Figure 1. (a) Concept drawing of drug delivery device and (b) assembled drug delivery device

The base layer of the drug delivery device contains both the pump and cannula; a simplified fabrication process flow based on [4] (Fig. 3). The underside of the cannula is lined with an array of posts that facilitate its release from the silicon substrate. The free-standing cannula is 1 mm wide and formed from two parylene depositions (each 7.5 μm thick) (the fluid channel is only 100 x 25 μm^2 in cross section). A 70 μm thick SU-8 layer reinforces the parylene microchannel, preventing its collapse when a drug reservoir is bonded to the base chip. The top layer is a silicone rubber (Sylgard 184) reservoir fabricated by casting from conventionally machined molds. Silicone rubber can withstand multiple punctures by non-coring syringe needles (30 gauge) [3].

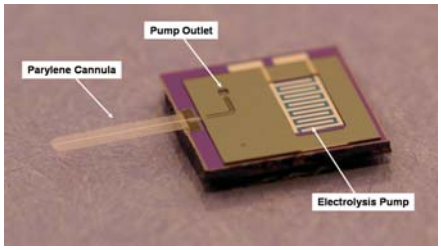

Figure 2. Electrolysis pump (Pt electrodes) and cannula integrated on base layer of drug delivery device

3. Results and Discussion

Pump performance was evaluated by using current to control DI water flow rate (Fig. 3). Data were obtained by observing movement of a meniscus in a volume-calibrated capillary over time and calculating the corresponding flow rate. Electrolysis pumping for delivering Betoptic (beta-blocker for glaucoma treatment) has been demonstrated (data not shown). In addition, the device performance is evaluated at body temperature (37°C) (Fig. 4). Finally, packaging is being developed to enable device evaluation in *ex vivo* porcine eyes and *in vivo* animal studies.

4. Conclusion

A new paradigm for intraocular drug delivery is presented in which electrolysis drives the delivery of drugs through a surface micromachined parylene cannula.

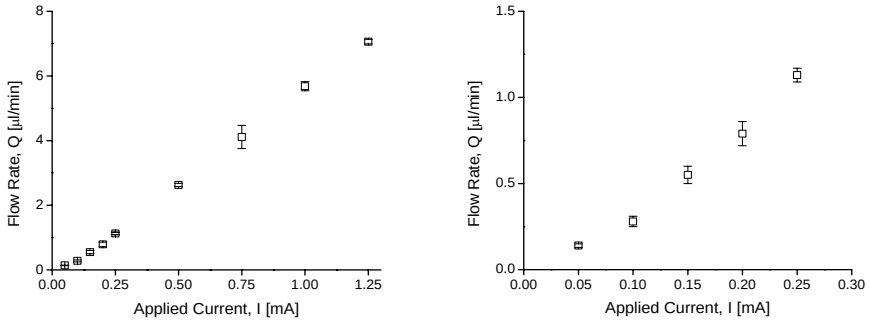

Figure 3. (a) Current-controlled pumping of DI water and (b) close-up of performance at lower flow rates (mean ± SE, n=4)

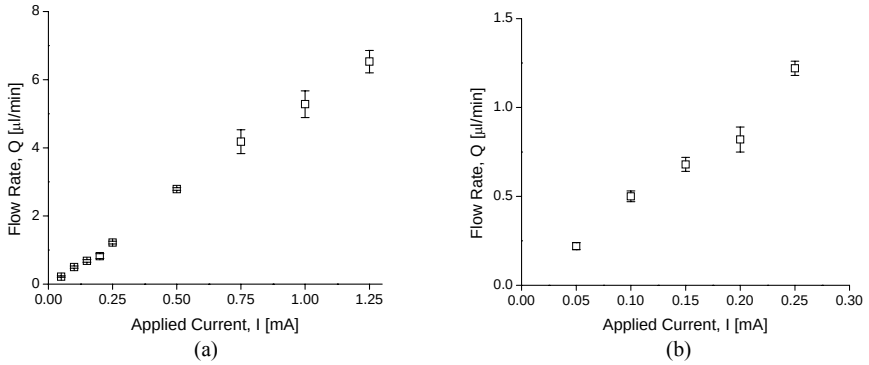

Figure 4. (a) Current-controlled pumping of DI water at 37ºC and (b) close-up of performance at lower flow rates (mean ± SE, n=4)

Acknowledgments

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