Biodegradable Micro-fluidic Sheet Devices for Controlled Delivery of Growth Factor

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Statement of Purpose: Micro fabricated fluidic devices have drawn much attention for local drug delivery due to their precisely controllable drug release characteristics. However, most micro-fluidic devices have been made of non-biodegrading materials such as silicon or PDMS [1]. Thus, we propose micro-fluidic sheet shaped devices made out of biodegradable polymers in order to combine the advantages of precise programmable release with that of biodegradable materials for local drug delivery. In particular, we investigate how the release of drug is modulated by the design of micro-channels in the devices rather than the degradation of the polymers. Furthermore, the devices can be used in the delivery of a single or multiple growth factors at different rates for the investigation of the effect of the temporal release of specific growth factors on bone growth [2].

Methods: Devices were comprised of a drug reservoir ($2cm^2$) and micro-channels ($50\times50\mu m^2$ cross-sectional area) sealed by another layer (**Fig.1**). Osmotic pressure built up in the reservoir and the release was regulated by the micro-channels. The micro-fluidic structures were constructed in thin films of a biodegradable polymer, 85/15 poly(DL-lactide-co-glycolide) (M_w = 250,000), by micro-molding [3]. The second layers of the same polymer were thermally bonded on the micro-structured layers. Fluorescent red dye or bFGF mixed in a PEG600/PEG6000 (w/w=1) paste was placed in the drug reservoir of each bonded device. For the control experiments, the sample devices containing the red dye had the micro-channels of three different lengths: 2.5, 5, and 7.5mm. The sample devices for the growth factor delivery had 2.5mm long micro-channels. The loaded devices were immersed in a buffer solution and stored in an incubator. The media solution was sampled every two days. The release amounts of the dye and bFGF were measured by the fluorescent intensity and Quantikine ELISA kit (R&D Systems, Inc., Minneapolis, MN) respectively.

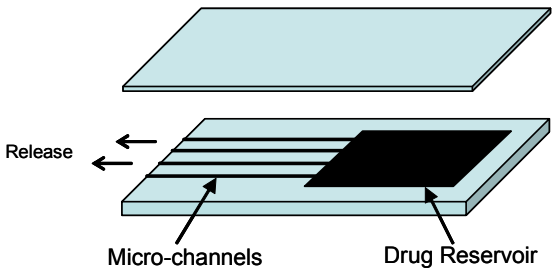

Figure 1. Device Configuration

Results/Discussion: The release profiles of the sample devices showed two different phases (**Fig.2**). For the first seven days, the release gradually increased due to the slow uptake of water through the biodegradable layer on top of the reservoir in the devices. After the osmotic pressure balanced, the release rates of the devices remained at a constant level. With all the conditions kept the same, the variation of the lengths of the micro-channels led to different release rates of the sample devices. The release rates were inversely proportional to the lengths of the release orifices which are the micro-channels in this experiment, as anticipated from osmotic pumping principle [4]. The bFGF was also released over a week at the constant rate of 30~60 ng/day, depending on the initial loading amount in the devices.

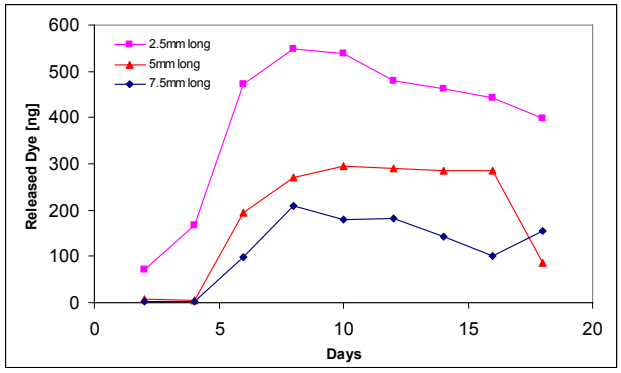

Figure 2. Release Rate Control by Micro-channel Length

Conclusions: A novel concept of foil shaped biodegradable micro fluidic devices has been developed for controlled drug delivery. The devices operated under osmotic pressure and delivered molecules at constant rates. It was shown that the release rates were modulated by the length of the micro-channels rather than polymer degradation. This elementary micro-fluidic release control indicates that more flexible and complex programmed delivery of drugs is possible by adequate design of the micro-fluidic geometry. For enhanced bone growth, in a preliminary study, the constant release of bFGF from the proposed devices was also achieved for a week. Further studies with various time-release schedules and growth factors are in progress.

Acknowledgement: Funding is gratefully acknowledged from the Musculoskeletal Transplant Foundation.

References:

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