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Fabrication and *ex vivo* retention study of biodegradable microcontainers for oral drug delivery

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**Abstract.** In this work, we are demonstrating successful fabrication of microcontainers intended for oral drug delivery with a highly versatile hot punching process. This method is up-scalable and can be used for various types of polymers. After successful fabrication of microcontainers in polymers such as SU-8, PCL and PLGA, *ex vivo* perfusion studies have been completed to evaluate the mucoadhesion of different materials in the intestinal tissue and the results showed a similar behavior of biodegradable materials as the state-of-the-art material (SU-8).

Microfabrication techniques have been applied to develop micron-scale devices for oral drug delivery with a high degree of control over size, shape and material composition [1]. For real life applications of these microfabricated drug delivery systems, it is necessary to move away from the prototype material SU-8 and fabricate them in biodegradable polymers approved for similar applications [2][3][4]. In this study, we for the first time fabricate and evaluate biodegradable microcontainers in three different materials, namely poly-ε-caprolactone (PCL), poly(lactic-co-glycolic acid) (PLGA) in a ratio of 50:50 and 75:25 of acid-glycolic and acid-lactic, respectively.

Microcontainers in PCL and PLGA (50:50 and 75:25) were successfully fabricated in arrays of 20x20 microcontainers in a single-step hot punching process as described in **Figure 1**. Microcontainers with a diameter of 300 µm and a height of 100 µm were produced. The process started with the assembly of a polymer device layer (either PCL or PLGA), a poly(vinyl alcohol) (PVA) substrate, and a thin Polytetrafluorethylene (PTFE) film if needed. The device layer was then molded by a robust Ni stamp and finally punched due to shear stress under the stamp that became higher than the ultimate tensile strength of the material and thus punched it. After the hot punching process, the microcontainers were physically separated from the surrounding films and remained on the underlying PVA substrate. Scanning Electron Microscope (SEM) images revealed good replication fidelity and an inner and outer diameter very close to the nominal diameter (**Figure 2**). After harvesting the empty microcontainers from the PVA substrate (**Figure 3**), *ex vivo* testing of mucoadhesion on porcine small intestinal tissue was performed (**Figure 4**). The results indicate similar adhesion properties of PLGA microcontainers compared to the conventional SU-8. PCL microcontainers seem less prone to adhere to the mucus layer when compared to the other materials of microcontainers. This means that biodegradable PLGA microcontainers could be more suitable for oral drug delivery purposes as they can have a targeted delivery through the small intestine since they perform equally well as the state-of-the-art material (SU-8).


