Microfabricated containers for oral drug delivery

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Oral drug delivery with microfabricated containers

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In the past years, microfabricated containers were introduced as new concept for oral drug delivery [1,2]. Here, we present the fabrication of microcontainers with a cavity filled with drug formulation and sealed with a pH sensitive polymer lid. In this way degradation of the drug in the stomach is prevented and the drug release is triggered by dissolution of the lid in the intestine. The drug release is studied *in vivo* by analysis of the drug concentration in the blood of rats.

For the preparation of the microcontainers, a fluorocarbon coating was deposited on a Si wafer serving as release layer for the final devices. Next, prototype microcontainers with inner diameters of 230 µm, a height of 270 µm and a volume of 10 nL were fabricated. For this purpose, a first step of SU-8 photolithography was performed to define the bottom of the containers and a second step to pattern the container walls [3]. The microcontainers were filled with Furosemide drug powder prepared by spray drying and the drug between the structures was removed using pressurized air. A lid of pH sensitive polymer (Eudragit L100, Evonik Industries, Germany) sealing the open side of the microcontainer cavity was deposited using spray coating [4]. Figure 1 shows a microcontainer filled with Furosemide drug powder before and after deposition of the polymer lid. Finally, the containers were mechanically removed from the fluorocarbon layer and filled into gelatin capsules (Figure 2).

The gelatin capsules are designed for oral dosage to rats (length 8.4 mm) and dissolve in the stomach of the animals during the first 10 min. The capsules were orally administered to rats (N=6) and the bioavailability of Furosemide was measured during 24 h by analysis of the drug concentration in the plasma. For comparison, capsules were directly filled with drug powder as it is conventionally done in the pharmaceutical industry. Additionally, the capsules were filled with drug powder and coated with Eudragit L100 by dipping into the polymer solution, to prevent absorption of Furosemide in the stomach.

Figure 3 shows that drug absorption is fastest for the control sample with the drug powder. This can be explained by the absence of a polymer coating that prevents drug release and absorption in the stomach. The coated capsules and the coated microcontainers have a similar release profile during the first 3 hours. However, for the complete duration of the experiment (24h) the microcontainers show a considerably higher total amount of drug absorbed in the blood of the rats than the coated capsules, as indicated by the area under the curve (AUC) summarized in figure 4. The AUC value recorded for the microncontainers is even slightly higher than the one for the drug powder in the uncoated capsules.

In conclusion, we demonstrate for the first time *in vivo* drug release using microfabricated containers coated with a pH sensitive lid. The results indicate a prolonged release of Furosemide compared to traditional dosage forms with drug powder in capsules.

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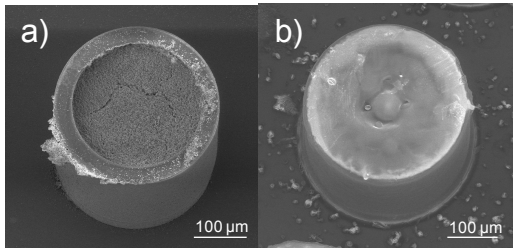

Figure 1. SU-8 microcontainer filled with Furosemide drug powder (a) before and (b) after coating with Eudragit L100

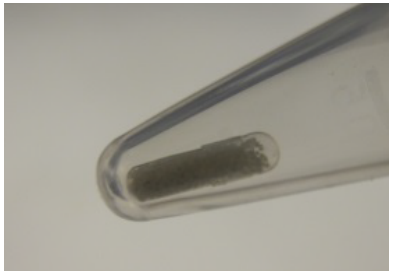

Figure 2. SU-8 microcontainers in gelatin capsule prepared for oral dosage in rats

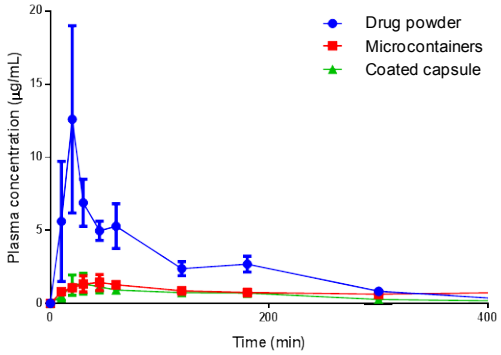

Figure 3. Concentration of Furosemide in plasma of rats at variable time after oral dosage (n=5-6)

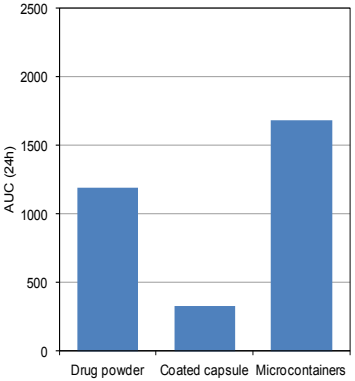

Figure 4. Total Area under curve (AUC) for the plasma concentration of Furosemide measured during 24h