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Microcontainers - an oral drug delivery system for poorly soluble drugs

Hagner Nielsen L.[1], Petersen R.S.[1], Marizza P[1]., Keller S.S.[1], Melero A.[2], Rades T.[3], Müllertz A.[3],Boisen A.[1]
[1]*Department of Micro and Nanotechnology, Technical University of Denmark, Kgs. Lyngby, Denmark*
[2]*Department of Pharmacy and Pharmaceutical Technology, University of Valencia, Valencia, Spain*
[3]*Department of Pharmacy, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark*

In oral delivery, it can sometimes be necessary to employ drug delivery systems to achieve targeted delivery to the intestine. Microcontainers are polymeric, cylindrical devices in the micrometer size range (Figure 1), and are suggested as a promising oral drug delivery system [1],[2]. The purpose of these studies was to fabricate microcontainers in either SU-8 or biodegradable poly-L-lactic acid (PLLA), and fill the microcontainers with poorly soluble drugs. Furthermore, the application of the microcontainers as an oral drug delivery system was investigated in terms of release, *in situ* intestinal perfusion and oral bioavailability.

SU-8 microcontainers were fabricated using lithography resulting in microcontainers with an inner diameter of 220 µm. The PLLA microcontainers were prepared by hot embossing with inner diameter of 240 µm (Figure 1). In terms of drug filling, the SU-8 microcontainers were filled with polyvinylpyrrolidone (PVP) by inkjet printing followed by supercritical CO_2 impregnation of ketoprofen into the PVP matrix. As an alternative filling method, the powder of amorphous sodium salt of furosemide, (ASSF) was filled into the SU-8 microcontainers. The PLLA microcontainers were filled with drug formulation by embossing the microcontainers into a polycaprolactone (PCL) and furosemide (4:1 w/w) layer. For the ASSF-filled microcontainers, an enteric-resistant lid of Eudragit L100 was spray coated onto the cavity of the microcontainers. From coated ASSF-filled microcontainers, a fast release in simulated intestinal medium at pH 6.5 was observed. *In situ* intestinal perfusions were performed in rats of the Eudragit-coated ASSF-filled microcontainers and compared to a furosemide solution. At the end of the study, the small intestine was harvested from the rat and imaged under a light microscope. The absorption rate constant of ASSF was 1.5 fold higher, when ASSF was confined in the microcontainers compared to a furosemide solution. Micrographs of the small intestine after the perfusion showed that the microcontainers were engulfed by the intestinal mucus. For the *in vivo* studies, the rats were dosed orally with capsules containing ASSF-filled microcontainers coated with Eudragit L100. As control, capsules were filled with the powder of ASSF and the capsules were coated with Eudragit L100. The oral bioavailability study showed that the relative oral bioavailability of ASSF in microcontainers is 220±43% when compared to drug-filled capsules coated with Eudragit (Figure 2).

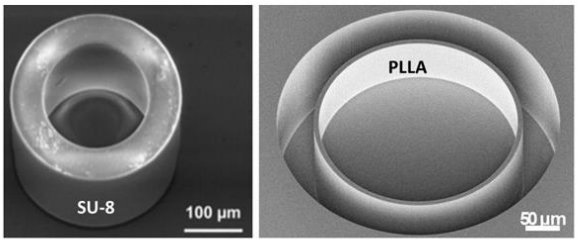

Figure 1: SEM images of SU-8 (left) and PLLA (right) microcontainers

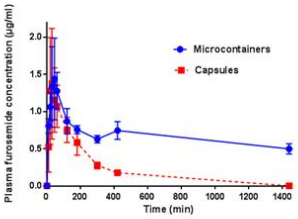

Figure 2: Plasma concentrations of microcontainers filled with ASSF coated with Eudragit L100 and filled into capsules and ASSF dosed in capsules with Eudragit coating after orally dosing to rats

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