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Loading of biodegradable microcontainers with budesonide for local treatment of inflammatory bowel disease

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Abstract: World-wide, the number of patients with inflammatory bowel disease (IBD) is continuously increasing [1]. In order to locally deliver drug to the colon for treatment of ulcerative colitis (UC), micro-reservoir based drug delivery systems can provide a more targeted release. Such reservoir based systems are characterized by small dimensions, asymmetrical geometry and unidirectional drug release [2]. In this study, we prepare these systems, known as microcontainers, in the biodegradable material poly-ε-caprolactone (PCL). The microcontainers are loaded with a budesonide-Soluplus® matrix and are tested by *in vitro* studies, indicating a faster drug release for budesonide loaded microcontainers compared to pure powder.

Microcontainers in PCL were successfully fabricated in arrays of 20x20 microcontainers in a single-step process on a poly(vinyl alcohol) (PVA) substrate in a similar fashion as described earlier [3]. The hot punching method was used to load the containers with a film matrix consisting of the synthetic glucocorticoid budesonide and the commercial polymer Soluplus®. Being both hydrophilic and non-ionic, Soluplus® is ideal for oral drug delivery [4]. A matrix consisting of budesonide (5 % w/w), Soluplus® (40 % w/w) and plasticisers polyethylene glycol (PEG) (5 % w/w) and dibetyl sebacate (DBS) (15 % w/w) was prepared by spin coating (1250 rpm, 40 s) on a PDMS coated si wafer. An ideal thickness of approximately 80 μm was achieved, corresponding to the reservoir height of the PCL microcontainers. After drying for 12 hours, the film matrix was loaded inside microcontainers by hot punching as illustrated in **Figure 1**. PDMS functioned as the soft elastic layer necessary for hot punching processes. By applying a hydraulic pressure of 1.5 bar for 680 s at 30°C, the drug polymer matrix was loaded inside the cavities. Empty microcontainers are visualized in **Figure 2** where a cavity is visible. After the hot punching process, the cavities of the microcontainers were loaded with the drug-polymer matrix, as seen after peeling off the surrounding film (**Figure 3**).

In vitro microdissolution studies were completed in an aqueous buffer medium regulated to the pH of the intestine (6.5) as seen in **Figure 4**. The samples were budesonide powder, budesonide film matrix, and budesonide film matrix inside microcontainer cavities. It was observed that the pure budesonide powder has a slower release rate than the film and microcontainers. For the final application, this drug delivery has to be further tailored by applying a pH sensitive coating on the loaded microcontainers for targeting to the desired area in the gastrointestinal tract.

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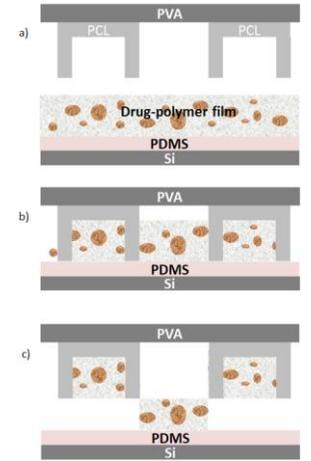


Figure 1. schematic illustration of the hot punching process for loading drug into microcontainers

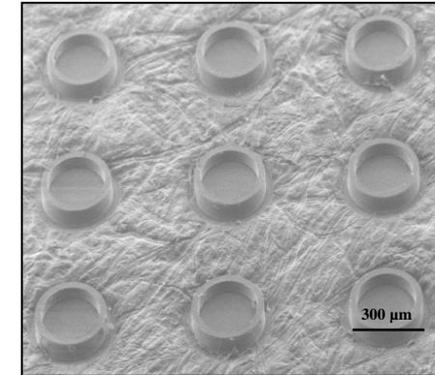


Figure 2: SEM micrograph of arrays of PCL microcontainers on a PVA substrate

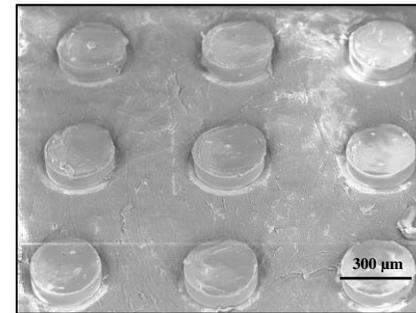


Figure 3. SEM micrograph of arrays of PCL microcontainers loaded with a budesonide-Soluplus® matrix

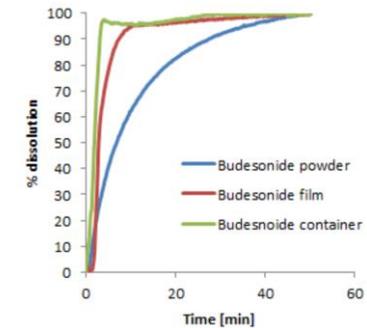


Figure 2. Cumulative release of budesonide powder, films and films loaded inside containers