Microcontainers for Unidirectional Release in the Upper Intestine

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MICROCONTAINERS FOR UNIDIRECTIONAL RELEASE IN THE UPPER INTESTINE

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Introduction

In the last decade, microcontainers were introduced as a new concept for oral drug delivery [1,2]. Microcontainers are designed with a cylindrical shape having a cavity which is filled with drug formulation and sealed with a polymer membrane. The main features of microcontainer are the protection of the API from degradation in the stomach and the unidirectional drug release aimed to reduce the waste of drug released in the GIT. The drug release from microcontainers is triggered by the application of an enteric coating, which is dissolved/degraded in the upper intestine. Here we present recent developments in the fabrication of microcontainers with particular focus on the drug loading.

Results and Discussion

Prototypes of microcontainers were fabricated using epoxy resin (SU-8, Microchem, USA) patterned by UV exposure (see figure 1a) or in alternative by means of hot embossing with a biodegradable polymer such as poly(L-lactic acid) (PLLA) (Natureworks, USA) (figure 1b). Microcontainers are loaded following two methods: 1) filling with powder formulations of furosemide and cinnarizine, 2) deposition of poly(vinylpyrrolidone) (PVP) in the cavities by inkjet printing, followed by supercritical impregnation of ketoprofen (figure 2) [3]. Finally a lid of enteric polymer (Eudragit L100, Evonik Industries, Germany) is deposited on top of drug laden-containers using spray coating through a shadow mask [4] (figure 3). In figure 4 the *in vitro* drug release profiles are shown for containers loaded at different impregnation conditions. The drug impregnation is enhanced by increasing either fluid pressure or time. At 200 bar and 4 h a drug content corresponding to 32 wt.% is loaded into the polymer matrix. Up to 87% of the drug can be released within 30 min. Furthermore, pH-triggered release was demonstrated by in vitro experiments with microcontainers filled with drug solid dispersions and coated with Eudragit L100.

Conclusion

We present a novel concept for oral drug delivery, characterized by cylindrical microcontainers filled with drug formulation and providing a unidirectional release. Microcontainers are filled either with drug solid dispersion or by the combination of inkjet printing and supercritical drug impregnation. The latter method shows high accuracy and a loading yield of 32% wt. and *in vitro* release tests show an accelerated drug release. The use of inkjet printing and sc impregnation shows significant improvements and promising perspectives in the framework of the microfabricated devices for oral therapeutics.

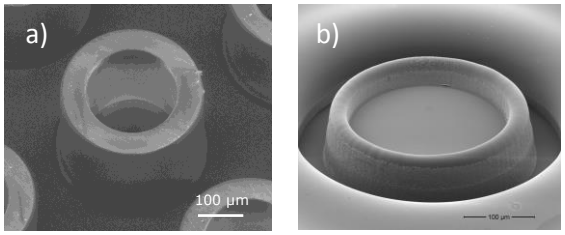

Figure 1: Microcontainers fabricated by a) UV exposure of SU-8 and b) hot embossing of PLLA.

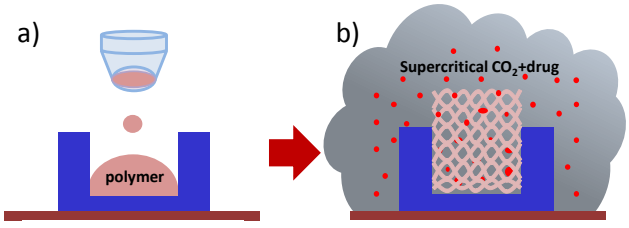

Figure 2: Drug loading: a) inkjet printing, b) supercritical drug impregnation

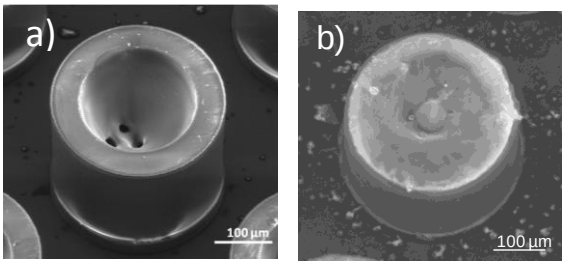

Figure 3: Drug laden microcontainers (a) before and (b) after lid deposition of Eudragit L100.

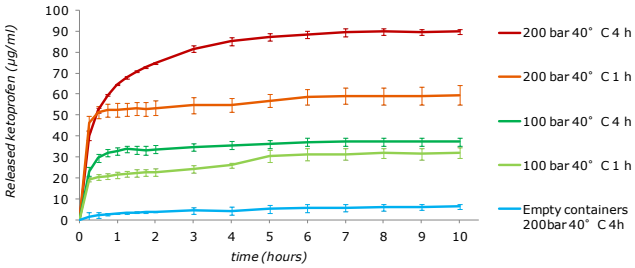

Figure 4: *In vitro* dissolution tests in 10 mL aqueous medium for 625 microcontainers filled with PVP and loaded with ketoprofen by supercritical impregnation at different conditions (N=3).

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