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Total number of authors:

11

Publication date:

2019

Document Version

Peer reviewed version

[Link back to DTU Orbit](#)

Citation (APA):

Abid, Z., Javed, M. M., Andersen, S., Mazzoni, C., Nielsen, L. H., Gundlach, C., Vaut, L., Petersen, R. S., Müllertz, A., Boisen, A., & Keller, S. S. (2019). *Fabrication and in vivo assessment of biodegradable microcontainers for oral drug delivery*. Abstract from 2019 Controlled Release Society Annual Meeting & Exposition, Valencia, Spain.

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Fabrication and in vivo assessment of biodegradable microcontainers for oral drug delivery

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Introduction: In recent years, microfabricated devices have been proposed as advanced drug delivery systems [1]. In particular, microcontainers have been demonstrated as promising new oral drug delivery systems with the potential to significantly enhance the bioavailability of drugs [2]. The state of the art of the materials are the epoxy-based SU8 prototype microcontainers. However, the microcontainers are preferentially fabricated with biocompatible or biodegradable polymers [3]. In this work, we are presenting the fabrication of microcontainers in a material that is in accordance with such requirements, namely polycaprolactone (PCL), and assessing its versatility for oral drug delivery devices.

Methods: Microcontainers with diameter of 300 µm and height of 100 µm were fabricated using hot punching, a modified hot embossing technique. The process started with the assembly of a PCL device layer and a PVA substrate. The device layer was then molded by a robust Ni stamp and finally punched due to the backpressure exerted by the PVA layer. After the hot punching process finished, the microcontainers were physically separated from the surrounding PCL film and remain on the underlying PVA substrate. microCT,

Due to their small dimensions, drug loading into the cavities of the microcontainers have been a challenge. In this work, the already existing polymer film between the containers is used as a shadow mask. This allows a fast and precise loading of the cavities without need for alignment of containers with a custom-made shadow mask.

Results: Microcontainers were successfully fabricated in arrays of 400x400 microcontainers in a single process (**fig. 1A**). They were loaded with the model drug paracetamol in a uniform manner by the modified powder embossing method (**fig 1B**). A pH-sensitive Eudragit L100 lid was spray coated on the containers (**fig. 1C**) and the PVA substrate was then dissolved in aqueous media. The containers were harvested (**fig. 1D**) and into rat capsules (**fig 1E**). The in vivo release profile of PCL microcontainers showed an increased bioavailability compared with the control capsules(**fig. 2**), supporting the findings in the present study that micron-sized biodegradable containers can successfully be used as drug delivery system and that the unidirectional release of the drug into the mucus might have a beneficial effect for the sustained release of the drug.

Conclusion: A versatile fabrication method for making biodegradable microcontainers for oral drug delivery was presented in this study. The in vitro and in vivo studies led to an increased knowledge of the behavior and release profile of PCL as a biodegradable material for microcontainers.

Acknowledgements: The Danmarks Grundforskningsfond (project DNRF122) and Villium Fondens Center for Intelligent Drug Delivery (Grant No. 9301) and Sensing Using Microcontainers and Nanomechanics (IDUN) are acknowledged for financial support.

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