



Micro Fabricated Devices For Oral Drug Delivery

Nielsen, Line Hagner; Müllertz, Anette; Mazzoni, Chiara; von Halling Laier, Christoffer; Tentor, Fabio; Marizza, Paolo; Petersen, Ritika Singh; Andersen, Sophie Strindberg; Keller, Stephan Sylvest; Rades, Thomas

Publication date:
2018

Document Version
Peer reviewed version

[Link back to DTU Orbit](#)

Citation (APA):

Nielsen, L. H., Müllertz, A., Mazzoni, C., von Halling Laier, C., Tentor, F., Marizza, P., ... Boisen, A. (2018). *Micro Fabricated Devices For Oral Drug Delivery*. Abstract from Controlled Release Society Annual Meeting & Exposition 2018, New York, United States.

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Micro fabricated devices for oral drug delivery

Line Hagner Nielsen¹, Anette Müllertz², Chiara Mazzoni¹, Christoffer von Halling Laier¹, Fabio Tentor¹, Paolo Marizza¹, Ritika Singh Petersen¹, Sophie Strindberg Andersen², Stephan Sylvest Keller¹, Thomas Rades², Zarmeena Abid¹, Anja Boisen¹

¹Department of Micro and Nanotechnology, Technical University of Denmark, Kgs. Lyngby, Denmark

²Department of Pharmacy, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

Learning objectives:

1. Explain the ideas behind the use of microcontainers
2. Describe which types of compounds that can be filled into microcontainers
3. Evaluate the *in vivo* performance of microcontainers as an oral drug delivery system

INTRODUCTION: Microcontainers are polymeric, cylindrical devices in micrometer size and have been proven useful in oral drug delivery¹⁻³. The hypothesis is that oral bioavailability can be improved significantly by utilizing microcontainers loaded with drug(s) and sealed with lids protecting the drug through the gastrointestinal tract. The purpose of this work was to fabricate microcontainers from either SU-8 or from biodegradable polymers such as polycaprolactone (PCL), and to load these microcontainers with either poorly water soluble drugs or particulates. Furthermore, the aim was to investigate the application of microcontainers as oral drug delivery system in terms of release, mucoadhesion and oral bioavailability in rats.

METHODS: SU-8 microcontainers were fabricated using lithography, whereas PCL microcontainers were prepared by hot punching. Subsequently, drug was loaded into the microcontainers using a variety of technologies. The SU-8 microcontainers were filled with polyvinylpyrrolidone (PVP) followed by supercritical CO₂ impregnation of e.g. ketoprofen into the PVP matrix. As an alternative filling method, the powder of amorphous sodium salt of furosemide (ASSF) or lipid particulates with ovalbumin were filled into the SU-8 microcontainers. The PCL microcontainers were loaded with drug formulation by embossing the microcontainers into a drug/polymer layer. In most cases, an enteric-resistant lid of Eudragit L100 was spray coated onto the cavity of the microcontainers. Release of drug from the coated microcontainers was investigated using a μ -Diss profiler (Pion, USA) in simulated gastric medium at pH 2 and intestinal medium at pH 6.5. Closed loop *in situ* intestinal perfusion studies as well as *in vivo* studies in rats were performed to study the mucoadhesive effect of microcontainers and oral bioavailability of the drugs loaded into the microcontainers.

RESULTS: SU-8 microcontainers had an inner diameter of 220 μ m and a cavity depth of 270 μ m (Fig. 1a, 1b), whereas the PCL microcontainers had an inner diameter of 240 μ m and a cavity depth of 65 μ m. A fast release of ASSF (88% within 3h) or ketoprofen (100% within 6h) from the microcontainers was observed and the Eudragit coating was shown not to be a hindrance for rapid release at intestinal conditions. It was shown that the microcontainers only attached to the mucus layer in the intestine and not in the stomach. For ASSF, the microcontainers were seen to increase the relative oral bioavailability by 220% within 24h, compared to the control (Fig. 2).

CONCLUSIONS: The fabricated microcontainers show considerable future potential as oral drug delivery systems.

ACKNOWLEDGEMENTS: The authors would like to acknowledge the Danish National Research Foundation (DNRF122) and Villum Fonden (Grant No. 9301) for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics (IDUN).

REFERENCES:

1. Fox CB. *et al.* Micro/nanofabricated platforms for oral drug delivery. *J. Control. Release*, 2015, 219: 431–44.
2. Mazzoni C. *et al.* From concept to in vivo testing: Microcontainers for oral drug delivery. *J. Control. Release*, 2017, 268:343–51.
3. Nielsen LH. *et al.* Polymeric microcontainers improve oral bioavailability of furosemide. *Int. J Pharm.* 2016, 504(1-2):98-109.

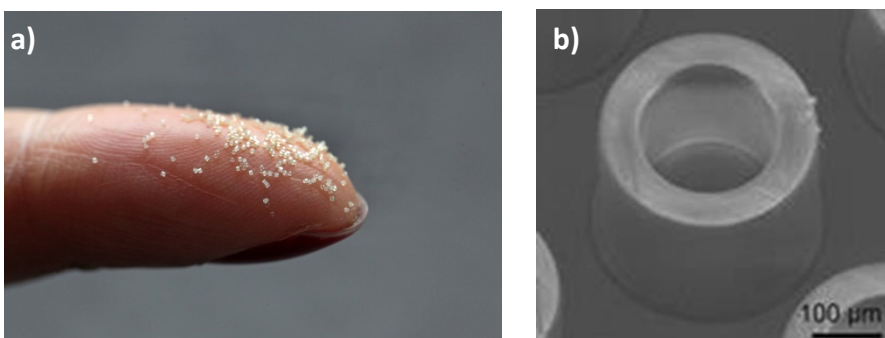


Fig 1. a) Photograph of microcontainers placed on a finger. The microcontainers have a size comparable to sugar grains. b) Image of an SU-8 microcontainer.

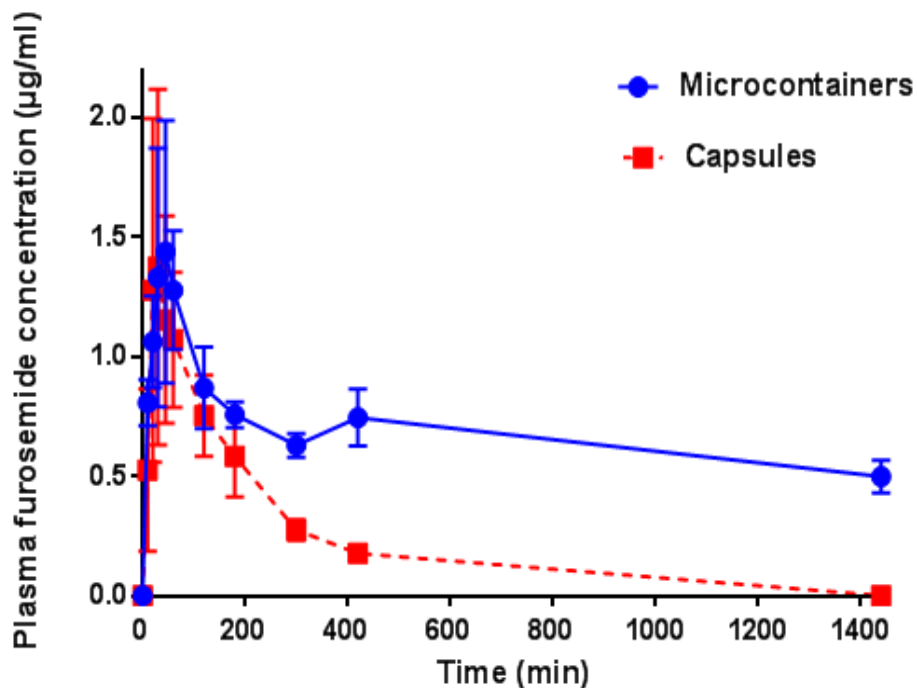


Fig. 2: Plasma concentrations of microcontainers filled with ASSF coated with Eudragit® L100 and filled into capsules and ASSF dosed in capsules with Eudragit coating after orally dosing to rats