Microcontainers as oral drug delivery systems for small molecules and proteins

Rønholt, Stine; Nielsen, Line Hagner; Davidsen, Anders Bork; Keller, Stephan Sylvest; Müllertz, Anette; Boisen, Anja; Nielsen, Hanne Mørck

Publication date:
2014

Authors

*Stine Rønholt, PhD, Department of Pharmacy, University of Copenhagen, stine.roenholt@sund.ku.dk

Line Hagner Nielsen, PhD, Department of Micro- and Nanotechnology, Technical University of Denmark, lihan@nanotech.dtu.dk

Anders Bork Davidsen, BSc., Department of Pharmacy, University of Copenhagen, davidsen.anders@gmail.com

Stephan Sylvest Keller, PhD, Department of Micro- and Nanotechnology, Technical University of Denmark, Stephan.keller@nanotech.dtu.dk

Anette Müllertz, PhD, Department of Pharmacy, University of Copenhagen, anette.mullertz@sund.ku.dk

Anja Boisen, PhD, Department of Micro- and Nanotechnology, Technical University of Denmark, Anja.boisen@nanotech.dtu.dk

Hanne Mørck Nielsen, PhD, Department of Pharmacy, University of Copenhagen, hanne.morck@sund.ku.dk

* Presenting author

Title

Microcontainers as oral drug delivery systems for small molecules and proteins

Purpose (words 101)

In the present work, the potential of utilizing microcontainers as oral delivery systems for enhancing delivery of a small protein, insulin, and a poorly soluble drug, furosemide, is tested *in vivo*. The applied types of microcontainers comprise small reservoirs with a flat base and are prepared from polymers such as poly-L-lactic acid (PLLA) (Nagstrup 2011 DOI) and the epoxy SU-8 (Nielsen 2012 DOI). In previous

studies, they have shown promising properties as drug delivery systems for oral administration (Ainslie et al. doi:10.1002/smll.200901254) due to their mucus adhesive properties of the flat base material and unidirectional drug release (Tao et al. doi:10.1016/S0168-3659(03)00005-1).

Methods (words 119)

SU-8 microcontainers were prepared (Nielsen et al. doi: 10.1016/j.ejpb.2012.03.017) and filled with insulin or amorphous furosemide sodium salt (AFSS) followed by coating the cavity of microcontainers with Eudragit-L100. Microcontainers were transferred to capsules (size 9) and dosed to rats (fed state) by oral gavage (n=6), dosing 40 IU/kg insulin or 15 mg/kg AFSS. As controls, dosing of Eudragit-L100 coated capsules (2 %w/v) containing insulin or AFSS as well as subcutaneous administration of insulin (1.5 IU/kg) was used. Blood samples were collected during 6 h for insulin and 24 h for AFSS. After administration of insulin, blood glucose was monitored simultaneously. The plasma insulin concentration was evaluated using an ELISA kit and furosemide was quantified by liquid chromatography–mass spectrometry.

Results (words 49)

For insulin, no significant effect was observed in the blood glucose and plasma insulin levels by using the microcontainers as oral delivery system when compared to empty microcontainers. When dosing AFSS in microcontainers, however, a furosemide bioavailability of 220±43% was observed relative to dosing of Eudragit-coated capsules containing AFSS.

Conclusion (words 60)

No significant effect was observed for insulin. Further formulation development is therefore essential, before the full potential of utilizing microcontainers for oral protein delivery can be explored. However, microcontainers show promising properties as oral drug delivery system for the poorly soluble drug furosemide, as the bioavailability of furosemide increased 2.2-fold after oral administration in microcontainers compared to administration in capsules.

Figures

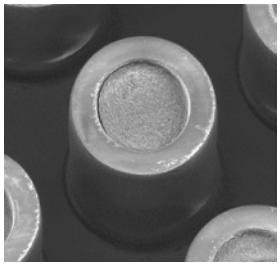

Figure 1: Image of a drug-filled microcontainer

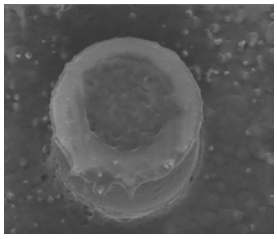

Figure 2: Image of the microcontainer after drug loading and coating on the cavity of the microcontainer with Eudragit L100