Microcontainers as an oral drug delivery system.

Nielsen, Line Hagner; Keller, Stephan Sylvest; Jacobsen, J.; Rades, Thomas; Boisen, Anja; Müllertz, A.

Publication date:
2014

Document Version
Peer reviewed version

Microcontainers as an oral drug delivery system

Line Hagner Nielsen[a,b], Stephan Sylvest Keller[b], Jette Jacobsen[a], Thomas Rades[a], Anja Boisen[b], Anette Müllertz[a,c]

[a]Department of Pharmacy, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark
[b]Department of Micro- and Nanotechnology, Technical University of Denmark, Kongens Lyngby, Denmark
[c]Bioneer:FARMA, Department of Pharmacy, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

Objective. The purpose of this study was to evaluate microcontainers *in vitro* and *in vivo* as an innovative oral drug delivery system for the poorly water-soluble drug, furosemide.

Methods. Microcontainers, with an inner diameter of 223 µm, were fabricated in SU-8 through two steps of photolithography. The microcontainers were filled with amorphous sodium salt of furosemide (prepared by spray drying). Subsequently, a 10 µm layer of Eudragit® L100 was spray coated on the cavity of the drug-filled microcontainers. The release of the drug from the microcontainers was evaluated in a biorelevant gastric medium (pH 1.6) and a biorelevant intestinal medium at pH 6.5. The intestinal permeability of the amorphous furosemide salt loaded into the microcontainers was evaluated using a Caco-2 cell model. Furthermore, drug-filled and Eudragit-coated microcontainers were dosed orally to rats and blood samples were taken over 24 h.

Results. The release experiments revealed that the Eudragit® layer prevented drug release in the gastric medium, while an immediate release of the amorphous furosemide salt was seen in the intestinal medium. The Caco-2 cell studies showed a fast permeability of the amorphous furosemide salt with no significant differences between the microcontainers (P_{app} $1.79 \cdot 10^{-5}$ $\pm 0.068 \cdot 10^{-5}$ cm/s, mean±SD, n=11) and powder of amorphous furosemide salt (P_{app} $1.62 \cdot 10^{-5}$ $\pm 1.04 \cdot 10^{-5}$ cm/s, mean±SD, n=11). The rat study demonstrated that the amorphous furosemide salt dosed in microcontainers showed an oral relative bioavailability of 220.2±43.2% (mean±SEM, n=6) compared to amorphous furosemide salt filled into capsules and coated with Eudragit® L100.

Conclusions. Microcontainers show considerable potential as a future oral drug delivery system.