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Publication date:
2018

Document Version
Publisher's PDF, also known as Version of record

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Citation (APA):

Mazzoni, C., Antalaki, A., Jacobsen, R. D., Mortensen, J., Tentor, F., Slipets, R., ... Boisen, A. (2018). *Loading of poorly soluble drugs by supercritical CO₂ impregnation into microcontainers for oral drug delivery*. Abstract from Northern Pharma Network Meeting, Odense, Denmark.

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Loading of poorly soluble drugs by supercritical CO₂ impregnation into microcontainers for oral drug delivery

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INTRODUCTION & AIM

Microcontainers (MCs) are polymeric cylindrical microdevices with only one side open and these have been suggested as an oral drug delivery system¹. MCs can be filled with a polymer matrix followed by loading a drug into the polymer-filled MCs using supercritical CO₂ (scCO₂) impregnation².

The aim of this study was to investigate the amount, distribution and solid state form of the poorly water soluble drugs, indomethacin and naproxen loaded into three different sizes (small, medium and large with internal diameter of 110 μm, 220 μm and 440 μm, respectively) of polymer-filled MCs using scCO₂ (Fig. 1a,b). The different diameters of the MCs provided different surface areas of polymer exposed to the scCO₂ during the drug loading process.

MATERIALS AND METHODS

MCs were fabricated in SU-8 (i.e. Fig. 1a) using two-steps of photolithography. MCs were filled manually with polyvinylpyrrolidone (PVP) K10 powder keeping the amount of PVP constant for the three different sizes of MCs. Polymer-filled MCs were then impregnated with ketoprofen or naproxen by means of scCO₂ impregnation (i.e. Fig. 1b). Ketoprofen was loaded into the MCs using 100 bar, 40°C for one hour as scCO₂ impregnation parameters, whereas for the loading of naproxen, the parameters were set at 120 bar and at a temperature of 45°C for one hour. The *in vitro* release of ketoprofen and naproxen from the impregnated MCs was analyzed in PBS solution at 37 °C using a μDISS profiler. For evaluation of the solid state form and the distribution of the drug in the MCs for the different sizes, Raman Spectroscopy maps were acquired using a DXR Raman microscope.

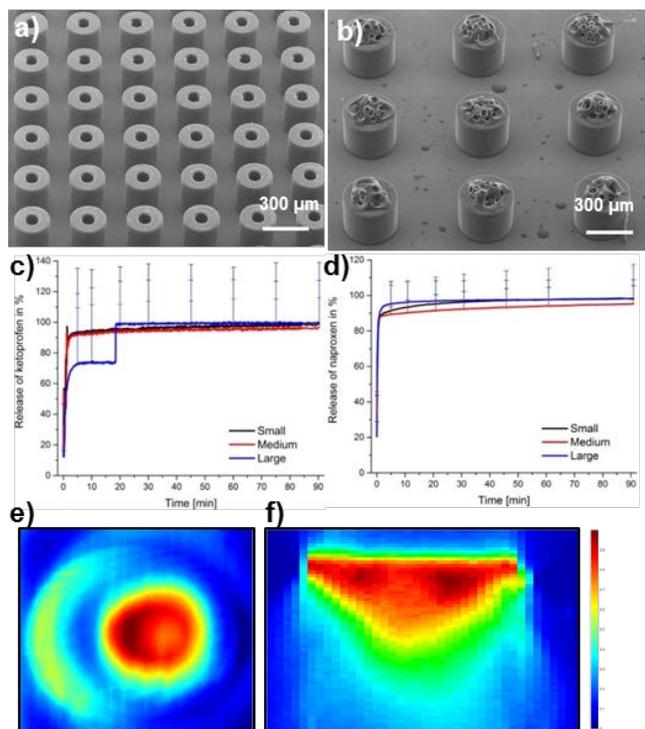


Fig. 1: SEM images of a) small empty MCs and b) drug-loaded MCs. Release of drug from small, medium and large MCs in PBS pH 7.3 for c) ketoprofen and d) naproxen. Example of a Raman map in the e) x-y and f) y-z planes of a MC filled with PVP and naproxen.

RESULTS

The amount of the drug loaded in the different sizes of MCs and for the two drugs was not statistically different. The release of naproxen or ketoprofen from the MCs showed similar kinetics for the different sizes and for the two drugs, reaching 90 % release within the first 10 min (Fig. 1c, d). By the use of Raman spectroscopy, it was evaluated if the exposed surface area influenced the distribution of the drugs in the MCs. An example with naproxen can be seen in Fig. 1e and f, where the distribution of naproxen was evaluated. It was found that the drug was mainly in the center (Fig 1e) and in the top part of the MC (Fig. 1f).

CONCLUSION

MCs having different surface areas exposed to the scCO₂ did not affect the amount and release kinetics of loaded ketoprofen or naproxen.

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2. C. Mazzoni et al. *J. Control. Release* 268, 343–351, 2017.