Supercritical impregnation of polymer matrices spatially confined in microcontainers for oral drug delivery: Effect of temperature, pressure and time

The present study is aimed to enhance the oral bioavailability of ketoprofen by inserting it into the matrix of poly(vinylpyrrolidone) (PVP) K10 spatially confined into microcontainers, by means of supercritical CO2-aided impregnation. Microcontainers are cylindrical reservoirs, with typical sizes in the micrometer range, with a cavity open on one side, where the drug formulation is loaded. Differently to traditional tablets, microcontainers have a higher surface area per unit volume, and release the drug only in one direction. This design is meant to enhance the absorption of problematic drugs, like those with poor solubility in water. In a previous study we introduced a novel technique for drug loading of microcontainers, based on inkjet printing and supercritical impregnation (SCI). We showed that SCI produces accurate and reproducible drug loading for large arrays of microcontainers. In the attempt of enhancing the throughput of the loading methods, we propose the replacement of polymer inkjet printing with an easier manual compression of the PVP powder into the microcontainers. As the second step, the polymer powder-filled microcontainers were submitted to SCI. The separate role of different impregnation parameters (temperature, pressure, time, drug concentration in the supercritical phase) was elucidated with respect to the loading capacity. The microcontainer filling was observed by means of optical macroimaging, X-ray microtomography and scanning electron microscopy. The physical state of the drug was investigated by means of Raman spectroscopy and compared with selected representative PVP-ketoprofen physical mixtures. Finally, the drug loading was estimated by means of in vitro dissolution tests. The characterization study shows that the present loading method is a valuable alternative to the one previously described. The drug loading can be controlled with high accuracy and reproducibility and the impregnated drug is in an amorphous state. These results demonstrate that SCI can be used as a highthroughput loading technique for microfabricated devices for oral drug delivery.

General information
Publication status: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Biomaterial Microsystems, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, University of Trieste, University of Cambridge
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Pages: 145-152
Publication date: 2016
Peer-reviewed: Yes

Publication information
Journal: Journal of Supercritical Fluids
Volume: 107
ISSN (Print): 0896-8446
Ratings:
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 3.01 SJR 0.982 SNIP 1.278
Web of Science (2016): Impact factor 2.991
Web of Science (2016): Indexed yes
Original language: English
Electronic versions:
Marizza_et_al._2015.pdf

Bibliographical note
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Source: PublicationPreSubmission
Source-ID: 116712679
Research output: Contribution to journal › Journal article – Annual report year: 2015 › Research › peer-review