Accepted Manuscript

Ultrasound-Mediated Cavitation-Enhanced Extravasation of Mesoporous Silica Nanoparticles for Controlled-Release Drug Delivery

Juan L. Paris, Christophoros Mannaris, M. Victoria Cabañas, Robert Carlisle, Miguel Manzano, María Vallet-Regí, Constantin C. Coussios

PII: S1385-8947(17)32172-1
DOI: https://doi.org/10.1016/j.cej.2017.12.051
Reference: CEJ 18212

To appear in: *Chemical Engineering Journal*

Please cite this article as: J.L. Paris, C. Mannaris, M.V. Cabañas, R. Carlisle, M. Manzano, M. Vallet-Regí, C.C. Coussios, Ultrasound-Mediated Cavitation-Enhanced Extravasation of Mesoporous Silica Nanoparticles for Controlled-Release Drug Delivery, *Chemical Engineering Journal* (2017), doi: https://doi.org/10.1016/j.cej.2017.12.051

Ultrasound-Mediated Cavitation-Enhanced Extravasation of Mesoporous Silica Nanoparticles for Controlled-Release Drug Delivery

Juan L. Paris[1,2,+], Christophoros Mannaris[3,+], M. Victoria Cabañas[1], Robert Carlisle[3], Miguel Manzano[1,2], María Vallet-Regí[1,2], Constantin C. Coussios[3,*].

1. Dpto. Química Inorgánica y Bioinorgánica, Facultad de Farmacia, UCM, Instituto de Investigación Sanitaria Hospital, 12 de Octubre i+12, 28040-Madrid, Spain.

2. Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Spain.

3. Institute of Biomedical Engineering, University of Oxford, Old Road Campus Research Building, Oxford OX3 7DQ, UK.

[+]Authors contributed equally to the work

*Corresponding author: constantin.coussios@eng.ox.ac.uk

Abstract

Mesoporous silica nanoparticles have been reported as suitable drug carriers, but their successful delivery to target tissues following systemic administration remains a challenge. In the present work, ultrasound-induced inertial cavitation was evaluated as a mechanism to promote their extravasation in a flow-through tissue-mimicking agarose phantom. Two different ultrasound frequencies, 0.5 or 1.6 MHz, with pressures in the range 0.5-4 MPa were used to drive cavitation activity which was detected in real time. The optimal ultrasound conditions identified were employed to deliver dye-loaded nanoparticles as a model for drug-loaded nanocarriers, with the level of extravasation evaluated by fluorescence microscopy. The same nanoparticles were then co-injected with submicrometric polymeric cavitation nuclei as a means to promote cavitation activity and decrease the required in-situ acoustic pressure required to attain extravasation. The overall cavitation energy and penetration of the combination was compared to mesoporous silica nanoparticles alone. The results of the present work