P-21

An MRI-Guided HIFU-Triggered Wax-Coated Capsule for Supertargeted Drug Release

A. Romagna[1], S. Matoori[2], M. Roveri[2], O. Wuerthinger[1], P. Tiefenboeck[2], O. Kolokythas[3,4], J. M. Froehlich[1,2]

[1] Clinical Research Unit, Klus-Apotheke, 8032 Zürich, Switzerland
[2] Institute of Pharmaceutical Sciences, Department of Chemistry and Applied Biosciences, ETH Zurich, 8093 Zürich, Switzerland [3] Institute for Radiology and Nuclear Medicine, Kantonsspital Winterthur, 8401 Winterthur, Switzerland
[4] Department of Radiology, University Washington, 98190 Seattle, USA

Introduction: Compared to the systemic administration of drugs, controlled drug release reduces systemic toxicity while enhancing drug concentrations at the required site [1]. A variety of galenic formulations pursuing this goal exists, but methods to externally control the release of the active substance temporally and spatially as well as to monitor the process have not yet been developed and would be of great advantage [2].
Aims: To develop a thermoresponsive drug delivery system for personalized non-invasive therapy with magnetic resonance imaging (MRI)-guided high-intensity focused ultrasound (HIFU) as an externally controlled heat trigger and the possibility of monitoring the release of the active substance using MRI.
Methods: Mixtures composed of lanolin and cetyl alcohol in different ratios were characterized regarding their thermoresponsiveness. Capsules were loaded with lyophilized gadolinium-based contrast agent (GBCA), coated with a wax layer of lanolin/cetyl alcohol 1:1 and placed in a HIFU gel phantom. The release of GBCA was triggered by an MRI-guided HIFU pulse (200 W, 1195 kHz) and monitored using T1- and T2-weighted MRI before and after the HIFU pulse.
Results: The mixture of lanolin and cetyl alcohol in a ratio of 1:1 showed a suitable melting point of approximately 43°C. The T2-hypointensity of the wax-coated capsule allowed tracking of the drug delivery system. While T1-hyperintensity was lacking pre-exposition, a T1-hyperintense signal was observed in close proximity to the capsule after the application of a HIFU pulse (200 W, 1195 kHz), indicating that the HIFU pulse lead to melting of the wax coating and in consequence to the hydration and outflux of the GBCA. Visual examination of the capsule revealed that the HIFU pulse melted a localized distinct hole into the capsule.
Conclusions: We developed a thermoresponsive wax-coated capsule for supertargeted release of any active substance at a specific time point at the required site in the gastrointestinal tract. Also, we provide the proof-of-concept for the application of MRI-guided HIFU as an externally controlled heat trigger for drug release in a non-invasive manner. Furthermore, we introduced a method to visualize and monitor the capsule and its active principle release based on its specific T1- and T2-MRI signal pattern. We therefore provide a novel externally controllable and monitored drug delivery system which may open up new perspectives in the personalized treatment of gastrointestinal diseases.

Keywords: High intensity focused ultrasound, drug delivery system, magnetic resonance imaging, gastrointestinal tract, contrast agent

References:

[1] Weiser JR, Saltzman WM. J Control Release 2014; 190: 664-673.
[2] McDaniel JR, Dewhirst MW, Chilkoti A. Int J Hyperthermia 2013; 29(6): 501-510.