DTU Health Tech
Department of Health Technology

Design, characterisation and *in vitro* evaluation of a multicompartment carrier in the submicron range

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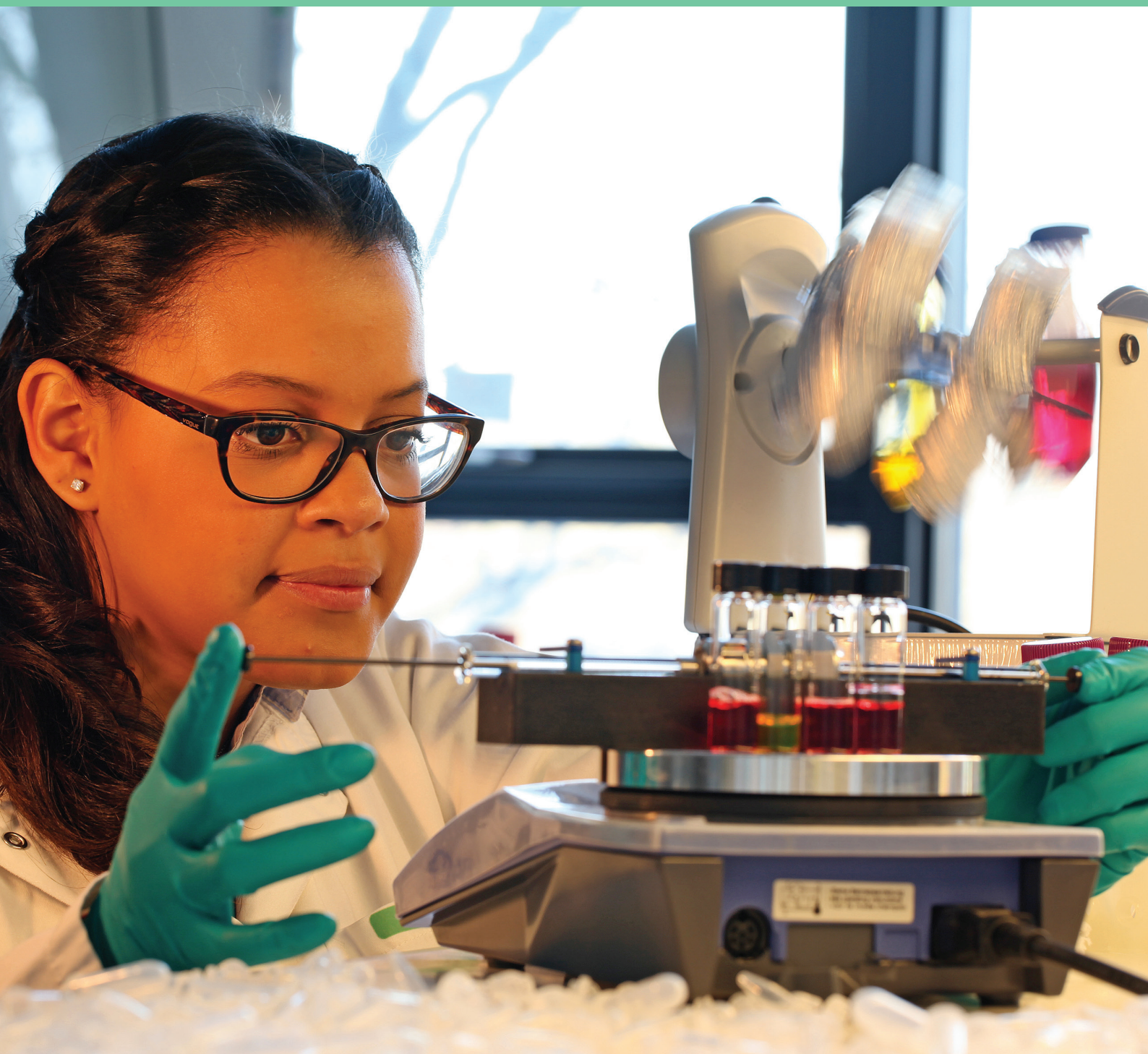

ABSTRACT

The compartmentalized structure of eukaryotic cells allows them to perform independent metabolic functions in a simultaneous manner while protecting them from unwanted side reactions. Inspired by this strategy, multicompartment carriers have emerged as a powerful tool for biomedical applications.

Their multiple sub-compartments offer the possibility to load incompatible therapeutic molecules, ensuring their co-localization at the target site, which is of particular interest in the drug delivery field. What is more, they can also act as reusable microreactors (at the intracellular- or extracellular level) for the removal of toxic compounds in the body, by loading the appropriate enzymes.

In this PhD thesis a novel multicompartment carrier is presented, thoroughly characterized, and its application as dual-cargo delivery carrier and extracellular microreactor is evaluated. In particular, hydrogels and liposomes are used as building blocks in order to achieve a different release profiles from the loaded cargo within separated/distinct compartments. Next, the system is protected with a polymer deposited by self-polymerization, which offers antioxidant properties to the carrier and it is easily functionalized with anti-fouling polymers.

Its application as dual-cargo delivery carrier was successfully confirmed by loading model molecules in the hydrogel and liposome core. The findings revealed a faster release from the hydrogels than from the liposomes, indicating the suitability of the carrier for tandem release. Next, the carrier interaction with relevant cell lines (*i.e*., macrophages, endothelial cells, and cancer cells as example of therapeutic target) was thoroughly evaluated taking the dynamics of the human physiology into account (*i.e*., blood flow and interstitial fluid flow). The results highlight the importance of including the dynamics of the human physiology when studying a new carrier in *in vitro* set ups. Their interaction (by means of cell internalization, uptake/association and uptake pathway) is highly affected by the presence of dynamic conditions in a cell type dependent manner.

Finally, its application as extracellular microreactor was evaluated by its potential to scavenge reactive oxygen species through a two-step reaction. The test tube studies indicate that the designed microreactor is able to successfully scavenge these species. What is more, the microreactor can be reused up to five times, which is of particular interest for a microreactor envisioned to scavenge these species in blood.

All in all, although the project is still at its infancy the findings presented in this PhD thesis point towards the promising design of a multicompartment platform with potential in the drug delivery and extracellular microreactor fields.

POTENTIAL PUBLICATION

The chapter five of the thesis should not be published in the department website since it is a manuscript in preparation. Therefore, this chapter must be deleted before being submitted to the website.

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