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MULTILAYER MICROCAPSULES OF NATURAL AND NATURE-INSPIRED POLYMERS AS DRUG DELIVERY VESSELS

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ABSTRACT

Polyelectrolyte vesicles using layer-by-layer (LbL) were recently introduced for the encapsulation of therapeutic molecules. This work presents multilayered microcapsules of chitosan and a temperature-responsive elastin-like recombinamer (ELR) as a novel drug delivery system. The release of a pre-loaded model protein was studied at distinct temperatures and number of layers to evaluate the permeability of these structures and their potential as tunable drug delivery devices. Confocal microscopy was also performed to evaluate the size variation with the temperature.

INTRODUCTION

The pharmaceutical field is driven by the need to develop novel systems that can efficiently protect and control the release of therapeutics in a biological environment (Kreft et al. 2007). In search of a system that could fulfill such requirements, the layer-by-layer (LbL) self-assembly of polyelectrolytes emerged as a technique with the potential to address these issues.
Simple and inexpensive, LbL can be used to encapsulate sensitive biomaterials under mild conditions, such as enzymes and nucleic acids (Decher 1997). These systems exhibit a semi-permeable character, which can be tuned by using distinct materials in the capsule architecture and variable number of layers (Köhler and Sukhorukov 2007).
In this work, we report the construction of LbL microcapsules using solely natural and nature-inspired biomaterials – namely chitosan and an ELR. The capsules were pre-loaded with bovine-serum albumin (BSA) and the release profile and size variation with temperature were studied.

MATERIALS AND METHODS

Sacrificial $CaCO_3$ templates were prepared by co-precipitation of Na_2CO_3 and $CaCl_2$ in a BSA solution labeled with the fluorescent tag FICT under heavy stirring. Sequential LbL coating was performed by incubation with chitosan or ELR solutions, with a rinsing step in between. Capsules with 1, 3 and 5 bilayers were prepared and the $CaCO_3$ cores were chelated using EDTA. The capsules were suspended in phosphate buffered saline (PBS) at 25 and 37 ºC. The release profile of BSA from these systems was evaluated, as well as their size, at each temperature. Samples were taken every 24 hours during 14 days for fluorescence measurements.

RESULTS AND DISCUSSION

The graphics in Figure 1 show the zero-order cumulative release profile of chitosan/ELR microcapsules with 1, 3 and 5 bilayers, at 25 and 37 ºC. For both temperatures, the release was higher for capsules with 1 bilayer, evidencing the role played by the capsules architecture in their permeability, namely the number of layers.
By comparing each condition, the release kinetics also showed a higher cut-off at 37 ºC than at 25 ºC, for any number of layers. This result shows the effect of temperature in polyelectrolyte structures, namely when temperature-responsive materials like ELRs are used.
Confocal microscopy was also performed to evaluate the dimensions of the capsules at distinct temperatures. As depicted in Figure 2, upon increasing the temperature

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from 25 to 37 ºC, the dimaneter varies, from around 6 to 2 µm.

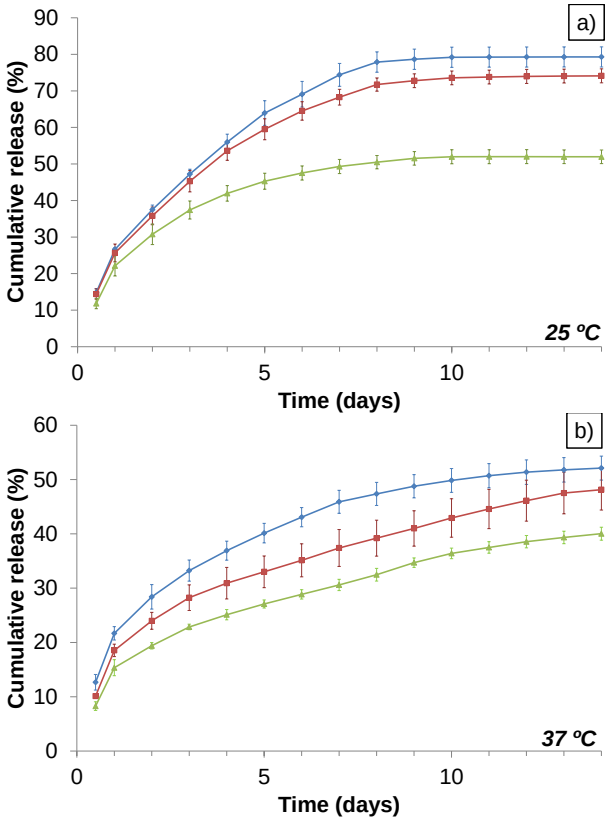

Figure 1: Zero-Order Cumulative Release Profiles of BSA Tagged with FITC at (a) 25 ºC, and (b) 37 ºC. Capsules with 1, 3 or 5 Bilayers are Depicted in Blue, Red, and Green, Respectively

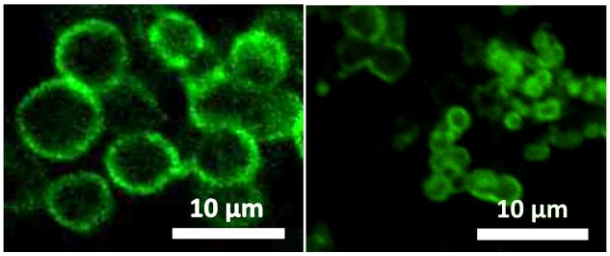

Figure 2: Confocal Microscopy of the Capsules for Size Assessment. On the Left, Capsules at 25 ºC; On the Right, at 37 ºC

CONCLUSION

Multilayered microcapsules based on chitosan and an ELR were studied as drug delivery vessels. Distinct release profiles of pre-loaded BSA at different temperatures and layer numbers demonstrated the influence of the capsules architecture and composition: more quantity of BSA was released from capsules with fewer layers and at lower temperatures. The size variation also demonstrates the effect that temperature has in this type of systems, especially when temperature-sensitive materials are used.

These microcapsules have the potential for tunable drug release in tissue engineering applications by means of design changes.

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