Fabrication of Triple-labeled Polyelectrolyte Microcapsules for Localized Ratiometric pH Sensing

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Introduction

Polyelectrolyte microcapsules based on layer-by-layer (LbL) technology have emerged as novel drug delivery platforms^[1]. Their intracellular trafficking and hence the fate of the encapsulated cargo are very important for the design of the microcapsule carriers. In this study, two pH sensitive probes (fluorescein and Oregon Green) and one pH insensitive probe (rhodamine B) were covalently labeled on the microcapsules, the resulting triple-labeled microcapsules with expanding pH measurement range show great potential for realtime monitoring the localized pH during their intracellular transporting.



Fig. 1. Schematic presentation of the preparation of triple-labeled microcapsule pH sensors.

a





Fig. 2. SEM images of the CaCO₃ particles (a) and the microcapsules (b). Inset is the corresponding magnified image of the particle surface. (c) CLSM images of the microcapsule sensors dispersed in a pH 7.4 buffer.



Fig. 4. CLSM images of RAW 246.7 cells with internalized triple-labeled microcapsules after 3 h (a), 6 h (b), and 24 h (c).

Conclusions

Triple-labeled microcapsule pH sensors with extended pH measurement range were prepared. After ingested by RAW 246.7 cells, the microcapsules located in acidic organelles with a mean pH value of 5.08 \pm 0.59. The triple-labeled microcapsules with localized pH sensing ability not only facilitate our

understanding for microcapsules uptake, but also provide a base for the design of pH sensitive microcapsule drug delivery system.

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[1] Tong, W.; Song, X.; Gao, C., Layer-by-layer assembly of microcapsules and their biomedical applications. *Chemical* Society Reviews 2012, 41, 6103-6124.

Fig. 3. In vitro calibrations of the microcapsule sensors. Calibration was carried out in buffers and artificial cytoplasm.