CONTAINERS FOR DRUG DELIVERY BASED ON VATERITE PARTICLES

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Key Words: vaterite, calcium carbonate, drug delivery, biomaterials, nanoparticles

Calcium carbonate is an important inorganic biomaterial thanks to its chemical stability, bioactivity, and biocompatibility. These properties have recently made it an interesting candidate for drug delivery systems. Calcium carbonate exists in three anhydrous polymorphic modifications: vaterite, aragonite, and calcite. Under normal conditions, vaterite is an unstable phase, while calcite and aragonite are stable. The transition between these phases can be exploited as a payload release mechanism. Vaterite polycrystalline particles have further favorable properties like high porosity, large surface area, and negative zeta potential.

In our work we present a novel technique for the synthesis and characterization of CaCO3 containers. Porous polycrystalline particles were fabricated with controllable average sizes from 400 nm up to 10 microns. For demonstration a wide range of particles were loaded with enzyme alkaline phosphatase (ALP) and low molecular weight fluorescent anticancer photosensitizer –“sulfonated aluminum phthalocyanines” was encapsulated to study payload release dynamics. ALP is a popular model protein as it is easily detectable spectrophotometrically. Furthermore, it is responsible for mineralization of bone tissue in vivo. Hence, ALP-loaded vaterite could be applied for bone regeneration. In addition, ALP has been applied as an anti-inflammation drug to combat certain diseases.

Several levels of control on these release dynamics could be identified:
1) The immersion medium: capsules immersed in water, showed a delayed burst release of the dye, coinciding with the crystal phase transition from vaterite to calcite. In ethanol this phase transition was inhibited, consequently only a slow desorption of the encapsulated dye was found.
2) Surface modification: Covering microcontainers with additional layers of biocompatible polyelectrolyte increases the payload release time.
3) pH value: A change of the pH from neutral to acid conditions will instead lead to a destruction of the vaterite matrix leading to an immediate release.

Moreover, we report on studies of vaterite containers in cell culture assays, evaluating their cytotoxicity, their influence on cell viability, and the particles' uptake efficiency. The prove of principle to use such particles with encapsulated photosensitizer for photodynamic therapy were demonstrated. These flexible control mechanisms and the perfect biocompatibility have proven the system’s potential for future pharmaceutical applications like drug delivery or bone reconstruction material.

We would like to thank the Russian Federation (grant number 14.Z50.31.0004 to support scientific research projects implemented under the supervision of leading scientists at Russian institutions and Russian institutions of higher education), and RFBR research project №15-29-01172. BP acknowledges support of FWO (Fonds Wetenschappelijk Onderzoek)