BIOCERAMIC MICRO AND NANOPARTICLES AS FUNCTIONAL BIOLOGICAL MATERIALS

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Introduction

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 [1]. Calcium carbonate exists in three anhydrous polymorphic modifications: vaterite, aragonite, and calcite. Under normal conditions, vaterite is an unstable phase [2,3], 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.

Materials and Methods

Spherical calcium carbonate microparticles (with a mean diameter of 3.0 ±0.3 μm) were synthesized via the protocol of Volodkin et al. [4] The same procedure of $CaCO_3$ particle synthesis was used for the formation of calcium carbonate microparticles with the mean diameter of 1.0 ±0.1 μm using the protocol described by Svenskaya et al. [5] briefly, but there is the only difference that stirring of the reaction mixture was carried out with ultrasound (US) with a frequency of 20 kHz and power density 1 W/cm^2 during 1 min. For the formation of calcium carbonate microparticles with the mean diameter of 0.5 ±0.2 μm the protocol developed by Parakhonskiy et al. was used [6].

Results and Discussion

In our work we present a novel technique for the synthesis and characterization of $CaCO_3$ containers. Porous polycrystalline particles were fabricated with controllable average sizes from 400 nm up to 10 microns. Fluorescent anticancer drug - photosensitizer was encapsulated to study payload release dynamics. 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.

Conclusions

The demonstrated flexible control released mechanisms, mild loading conditions and the perfect biocompatibility have proven the system's potential for future applications as drug delivery system, bioimplants and tissue engineering area.

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