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Ag nanoencapsulation for antimicrobial applications

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Postoperative infections are a common and severe side effect in the use of biomaterials inside the human body. Their surfaces are prone to the attachment of bacteria forming persistent biofilms which neither can be successfully combated by the immune system nor treated by systemic antibiotics. Consequently, the implant has to be removed and replaced after the infection is cleared. Antimicrobial coatings of implant materials could contribute to the prevention of such infections. In the context of the rapidly emerging resistance of bacteria to traditional antibiotics, alternative antimicrobial agents are receiving more and more attention with silver being an example that is well known for conservation purposes throughout history. Especially Ag nanoparticles reach an excellent antimicrobial efficacy due to their high specific surface area, rendering them even bactericidal towards multi-resistant strains. They serve as reservoirs for the slow release of Ag^+ as actual antimicrobial active species. In the Fromm group, research is done to control this release by encapsulation and integration of the Ag nanoparticles into hollow oxide nanocontainers, creating eventually Ag@oxide nanorattles with a movable Ag core inside a bigger hollow oxide shell.

For this thesis, three different synthetic approaches towards such nanostructures were optimized. Ag@SiO_2 nanorattles could be realized firstly with a microemulsion based soft template and additionally via the surface protected etching of a common core shell particle. Thirdly, Ag-TiO_2 nanocontainers were synthesized by a hard template method comprised of the deposition of Ag nanoparticles onto a polystyrene template, a TiO_2 coating step and the subsequent dissolution of the polystyrene core. The Ag^+ release by oxidative dissolution of the Ag nanoparticles was investigated for all three materials either in water or cell culture medium. If the released ions were at least partly removed and replaced by fresh water or medium, a sustained and elevated release could be measured. As expected, all the Ag containing nanomaterials showed a strong antimicrobial effect, some even towards a methicillin-resistant *S. aureus* strain. The classical Ag@SiO_2 core shell morphology turned out to possess a superior efficacy compared to the nanorattles. For the Ag-TiO_2 nanocontainers, a calcination step, turning the amorphous shells into anatase, enhanced the antimicrobial activity. The cytotoxicity was evaluated by exposure of murine fibroblast and immune cells to the particles, with the results suggesting a good cytocompatibility. Hence, with the developed Ag@oxide nanomaterials, good candidates are available for the design of novel implant coatings or other antimicrobial biomaterials.

Besides the biomedical applications, hollow nanospheres and nanorattles have also shown advantages for other fields, which could be demonstrated by using the Ag@SiO_2 nanorattles as catalyst for a model reaction.

Additionally, a side project investigated the potential of silica nanoparticles for the treatment of dentin hypersensitivity (DH), which is a dental defect characterized by a sharp pain in the gum line induced by external stimuli such as cold or heat. It is caused by the exposure of the dentin tubules, which are opened due to gingival recession followed by the abrasion of the root cementum layer. The permanent occlusion of the tubules by silica nanoparticles could offer a way to avoid the nerve irritation by the external stimuli. The arginine catalyzed hydrolysis of tetraethylorthosilicate in a two-phase system allowed the synthesis of monodisperse silica nanoparticles in various sizes that could be grinded with water to form a paste for the application onto exposed dentin. For a future study of the tubule occlusion, cross sections of human dentin with open tubules were characterized by confocal and atomic force microscopy.

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