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Solvothermal synthesis and characterization of upconversion core-shell beads and porous hollow capsules for biomedical applications

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Thesis outline

In this thesis, fabrication and characteristics of upconversion (UC) based core-shell beads and porous hollow capsules were investigated and discussed from the biomedical applications viewpoints. Two routes for synthesis of upconversion capsules were proposed. The strategy for the fabrication was based on employing hard template particles with solvothermal treatments in both synthesis routes. The formation mechanism of the UC capsules was discussed. The outline of the thesis is summarized in the following points.

1. Submicron SiO_2@$NaYF_4$:Yb/Er beads which can be converted to UC capsules by dissolving silica template particles were fabricated using solvothermal method. Both beads and capsules were inherently water-dispersible which is one of the primary requirements for biomedical applications. NaF (sodium fluoride) was successfully used as fluoride source instead of mostly used HF (hydrogen fluoride).
2. Nanosized porous shell of hollow UC capsules was synthesized without requiring the additional etching step in facile hydrothermal method. The process involved using only water as solvent making the synthesis process efficient and resulted in the fabrication of porous hollow UC capsules with simultaneous etching of silica template. It was observed that the presence of sub-critical water with NaF is necessary for the etching process. Additionally, the high pressure from sub-critical water is necessary for network shell formation. Investigation of etching process

revealed that a surface-protected type etching mechanism is responsible for the removal of template particles. By controlling the NaF amount, it was possible to synthesize partly etched and fully etched capsules used for biomedical imaging and drug delivery having 32% and 62% loading capacity respectively.

3. The size of UC capsules is template particle dependent which was verified using 100 nm silica template particles along with 300 nm size. The one step hydrothermal process successfully synthesized the UC capsule with ~180nm. The thickness of UC shell depends on precursor thickness which was tuned by controlling synthesis parameters. It was found that there is threshold amount of the precursor required for the shell formation. Additionally, the single phase of UC capsule was achieved by replacing Y (yttrium) with Gd (gadolinium).
4. To realize the true potential of the UC capsule, multi-modal imaging capability was introduced by paramagnetic elemental such as Mn and Gd doping in UC capsules. The Mn doping produced a Mn rich phase in UC capsule which enhanced the UC intensity for the capsule. Magnetic susceptibility was 5×10^{-5} emu/gOe and 20×10^{-5} emu/gOe for Mn and Gd doped UC capsules, respectively. The paramagnetic behaviors indicated the potential to be used T1 MRI agent.
5. To evaluate the suitability for biomedical applications, the drug loading and release behavior was studied using DOX as anticancer drug. The pH dependent drug release behavior was confirmed with rapid drug release in lower pH. The tumor molecular environment has acidic environment so the UC capsule drug release behavior suggests its suitability as anticancer DDS. The cell assay was conducted to verify UC capsules biocompatibility and cellular toxicity of DOX loaded capsules. The UC capsules with and without doping showed good biocompatibility even at higher

doses and DOX-loaded capsules effectively killed more than 68% cells when incubated with cells.

In summary, the upconversion core-shell beads and porous hollow capsules in this study provide a diverse and multipurpose platform as theranostic agent for biomedical applications. A new kind of theranostic system combing diagnostics (working as contrast agent and imaging probe) and therapy (by delivering the drug cargo) can be envisioned using these particles.