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題目(和文)	バイオ医療応用を目指したアップコンバージョン・コアシェル粒子および多孔質中空カプセルの水熱合成と特性評価
Title(English)	Solvothermal synthesis and characterization of upconversion core-shell beads and porous hollow capsules for biomedical applications
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（博士課程）
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論 文 要 旨

THESIS SUMMARY

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要旨（英文800 語程度）

Thesis Summary （approx.800 English Words ）

The present thesis "Solvothermal synthesis and characterization of upconversion core-shell beads and porous hollow capsules for biomedical applications" is composed of five chapters. The purpose of this work is to establish fabrication protocols of upconversion core-shell beads and porous hollow capsules using green chemistry methods and their evaluation particularly for the biomedical applications.

Chapter 1, "General introduction", describes the current challenges regarding fabrication and applications of upconversion core-shell beads and porous hollow capsules particularly with respect to biomedical applications. Based on the previous studies, it was identified that fluoride-host based submicron sized upconversion core-shell beads and porous hollow capsules with water dispersibility are suitable materials for biomedical applications. To meet this challenge, two synthesis routes have been proposed in this thesis. Both methods use silica as a hard template to synthesize core-shell beads as well as porous hollow capsules.

In Chapter 2, "SiO_2@$NaYF_4$:Yb/Er beads and $NaYF_4$:Yb/Er capsule", a solvothermal approach for the synthesis of water dispersible SiO_2@$NaYF_4$:Yb/Er core-shell beads has been investigated. Furthermore, the core-shell beads can be converted to $NaYF_4$:Yb/Er porous hollow capsules by etching the silica template. In this method, the amorphous silica nanoparticles with ~300 nm in size were used as a sacrificial template. Solvothermal method (using ethylene glycol as a solvent) was employed to obtain composite particles using sodium fluoride (NaF), which is comparatively a safer fluoride source. The effect of thermal treatments on morphology of composite particles was studied by subjecting the particles to i) supercritical water, ii) supercritical ethanol, and ii) air annealing under ambient pressure. The results show that high pressure supercritical treatments destroy the shell structure, whereas annealing in air successfully facilitated the formation of upconversion core-shell beads having network porous shell. Moreover, the silica template was dissolved using alkaline treatment to obtain porous hollow capsules. The network shell was shown to maintain its structural integrity after the dissolution of the silica core. Both the core-shell beads and porous hollow capsule have size of ~ 390 m and are inherently water dispersible. The upconversion characterization shows that both upconversion beads and capsules have typical green Yb/Er emission properties. This fabrication method can be used to successfully synthesize core-shell beads and porous hollow capsules but require template etching as an additional step.

In Chapter 3, "Upconversion capsule synthesis using H_2O based etching", a comparatively efficient synthesis route requiring no additional silica-etching step is described. A simple hydrothermal method using

NaF/H_2O (sodium fluoride/water) system was used to obtain the porous hollow upconversion capsules. The hydrothermal process can simultaneously synthesize upconversion shell and dissolve silica cores. The etching of the silica cores by the hydrothermal process was investigated in detail and it was found that the amount of NaF plays an important role in etching of the silica cores. By controlling the ratio of NaF to initial rare-earth precursors, partly-etched and fully-etched upconversion capsules were obtained. A typical surface protected type etching was observed in the silica-etching process. The smaller sized upconversion capsules were achieved using 100 nm silica template particles, showing the size tenability in this synthesis protocol. The tuning of the shell thickness of the upconversion precursor was realized by changing the ratio of precursors to silica template particles. Moreover, the effect of different fluoride precursors on the crystallinity and upconversion properties was also investigated. It was found that by addition of a fluoride pre-treatment step (using ammonium NH_4F) with polymer protection, highly crystalline upconversion capsules can be achieved. Furthermore, using $NaBF_4$ (sodium boro-fluoride), which can provide sustained release of fluoride ions, instead of NaF, a much higher crystalline upconversion capsules were obtained but at the cost of some aggregation. The porous hollow capsules having upconversion as well as paramagnetic properties can have dual imaging modalities i.e. additional MRI imaging contrast agent properties. Incorporating a paramagnetic character to upconversion capsules was achieved by replacing Yttrium (Y) with Gadolinium (Gd) and Manganese (Mn). The magnetization at 1.0 T for Gd-doped capsules was 1.91 emu/g as compared with Mn-doped capsules which was 0.58 emu/g. The Gd doping resulted in a single phase upconversion capsules, controlling the crystal phase.

In Chapter 4, “Applications to drug delivery system”, the potential of the core-shell beads mentioned in Chapter 2 and porous hollow capsules mentioned in Chapter 3 for biomedical applications was investigated through *in-vitro* studies. The MTT assay of core-shell beads and porous hollow capsules showed excellent biocompatibility even at a high concentration (100 μg/mL). The drug loading and release characteristics were evaluated using Doxorubicin (DOX) as a model drug. The porous hollow capsules exhibit high drug-loading capability with pH dependent drug release characteristics. The cytotoxicity of DOX-loaded capsules using MCF-7 cell line and MTT assay showed that ~ 68% cells were killed using 5 μg/ mL of DOX concentration. From these studies-, it can be inferred that upconversion core-shell beads and porous hollow capsules obtained in this study possess excellent biocompatibility with imaging capabilities. Moreover, porous hollow capsules are equipped with drug loading, release and cytotoxic characteristics when employed as drug delivery system.

In Chapter 5, "General conclusions", the findings obtained in this study have been summarized with conclusions. An outlook and suggestions for further studies have also been described.

Briefly the thesis describes new fabrication protocols to obtain upconversion, sub-micron, water dispersible core-shell beads and porous hollow capsules with tunable characteristics. These core-shell beads and porous hollow capsules exhibit excellent potential for biomedical applications.