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Preparation of upconversion nanoparticles by ultrasonic irradiation and investigation for cancer therapy

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1. Introduction

Photodynamic therapy (PDT) is one of the promising less-invasive cancer therapies. After the administration of photosensitizer to cancer cells, the irradiation with visible light to the cancer cells generates reactive oxygen species (ROS), which kills cancer cells. However, conventional PDT cannot cure large cancers and cancers in the deep portion of the skin because low transparency of visible light. The combination of upconversion nanoparticles and photosensitizer would solve it[1,2).

Upconversion phosphor material emits visible light with the excitation of near-infrared (IR) light[3,4)], while normal phosphor material emits visible light with the excitation of ultraviolet light usually. Upconversion material is useful for various applications such as solar cell[5)] and bioimaging[6-8)]. The advantage of the usage of near-IR light in the biomedical field is transparency for a living body[9)]. The irradiation with near-IR light to upconversion nanoparticles in cancer cells emits visible light and then generates ROS and kills cancer cells even in the case of large ones and those in deep portions[1,2)].

The Particle size of nanoparticles that would be used in a living body should be in the range between a few ten nm and a few hundred nm because nanoparticles less than a few ten nm are ejected from a living body through a kidney[10)] and nanoparticles more than a few hundred nm are accumulated in a liver[11)]. The nanoparticles with a particle size between a few ten nm and a few hundred nm are easily accumulated in cancer cells by the Enhanced Permeability and Retention (EPR) effect[12)].

The highest upconversion efficiency is obtained by $NaYF_4$:Er,Yb crystal, which has α and β phases[13-15)]. Er^{3+} ion is the color center and Yb^{3+} ion is co-dopant to increase the upconversion luminescence.

Nanoparticles can be prepared by ultrasonic irradiation to the suspension solution of powders[16-18)]. The physical impact of ultrasound is very effective in obtaining fine particles.

In this study, $NaYF_4$:Er,Yb upconversion nanoparticles were prepared by ultrasonic irradiation to suspension and then ROS generation was detected for cancer therapy.

2. Experimental

$NaYF_4$:Er,Yb was added to ultra-pure water (150 mL). The suspension was irradiated with ultrasound (20 kHz, 25 W). Irradiation time was varied from 5 min. to 24 hours.

The primary particle size was measured by Scanning Electron Microscope (SEM). Photoluminescence (PL) spectra were measured by a spectrometer. The generation of ROS was detected by the decrease in absorbance of 1,3-diphenylisobenzofuran (DPBF) at the wavelength of 422 nm. The prepared nanoparticles and rose bengal were irradiated with near-IR light at the wavelength of 980 nm because rose bengal emitted singlet oxygen by green light from upconversion nanoparticles excited by near-IR light.

3. Results and discussion

Figure 1 shows SEM images of raw materials and upconversion nanoparticles prepared by ultrasonic irradiation for 24 hours. Raw materials with micron size were transformed into nanoparticles with a particle size of a few ten nm by ultrasonic irradiation. The distributions of the primary particle size at each irradiation time are shown in Figure 2. The increase in ultrasonic irradiation decreased the primary particle size measured by SEM. It indicated long-time irradiation proceeded with the refinement of upconversion micron powders. Shock waves and micro-jets would repeatedly mill powders[19)].

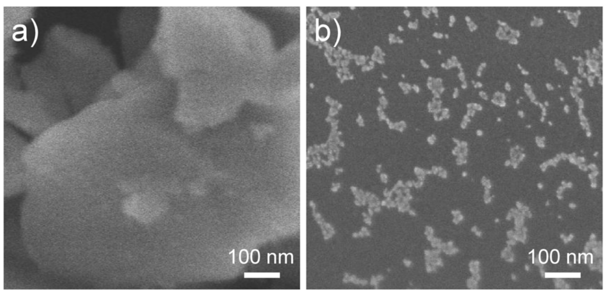

Fig. 1. SEM images of a) raw materials and b) upconversion nanoparticles.

Figure 3 shows PL spectrum of prepared upconversion nanoparticles $NaYF_4$:Er,Yb with an excitation at 980 nm. The strongest green emission is related to the following transition of color center Er^{3+} [20)];

$$^2H_{11/2}/^4S_{3/2} \rightarrow {}^4I_{15/2},$$

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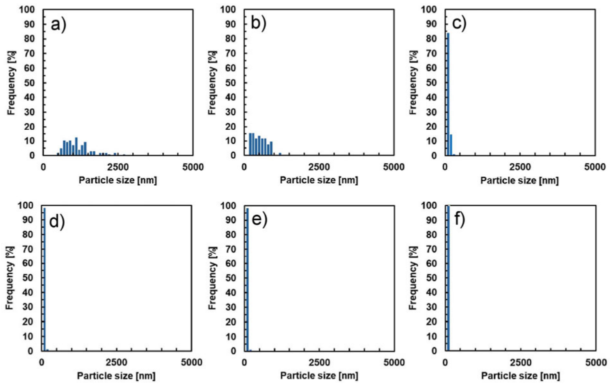

Fig. 2. Histogram of the primary particle size of upconversion nanoparticles. a) raw material. Irradiation time of ultrasound: b) 5 min., c) 2 hours, d) 4 hours, e) 6 hours and f) 24 hours.

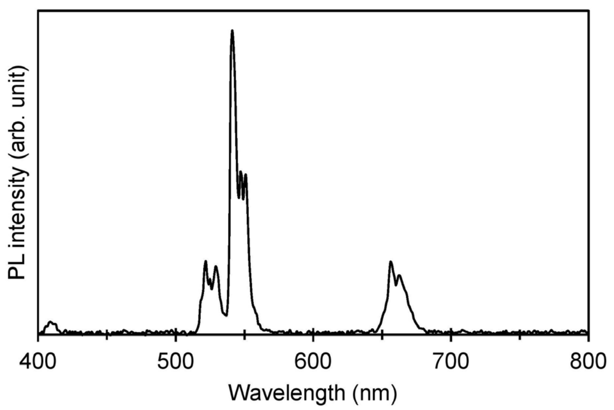

Fig. 3. PL spectrum of upconversion nanoparticles. Excitation wavelength: 980 nm.

while the red emission is related to the following transition;

$$^4F_{9/2} \rightarrow {}^4I_{15/2}.$$

Energy transfer from co-dopant Yb^{3+} to Er^{3+} increases PL intensity[3,4]. Because the PL spectrum was the same as raw material powders, the color center and the crystal structure of matrix would not be deformed by ultrasonic irradiation.

To know the effect of cancer therapy, the peak of DPBF was measured by spectroscopy. The increase in the irradiation time of near-IR light decreased the peak of DPBF, which meant the decomposition of DPBF by ROS. Therefore, the generation of ROS supports the usage of upconversion nanoparticles in low-invasive cancer therapy PDT.

4. Conclusions

Upconversion nanoparticles with a particle size of a few ten nm, which was suitable for PDT cancer therapy, were successfully prepared by ultrasonic irradiation. The emission from the nanoparticles was typical green emission of Er^{3+}. The combination of the prepared nanoparticles and rose bengal generated ROS, which was useful for low-invasive cancer therapy.

Acknowledgment

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