

# Europium-doped gadolinium sulfide nanoparticles as a multimodal imaging agents for bio-application

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## ABSTRACT

We have prepared trivalent europium-doped gadolinium sulfide with various concentration of  $\text{Eu}^{3+}$  by simple sonochemistry method under the 1-Dodecanethiol. The maximum synthesis temperature reached to about 240 °C when treated by ultrasound for 20 min. The nanoparticles were found to be 5 nm size and highly crystalline despite their small size. Under UV excitation, these nanoparticles shows intense orange-red emission corresponding to  $^5\text{D}_0 \rightarrow ^7\text{F}_J$  ( $J=0, 1$  and  $2$ ) intra-configurational f-f transition. The magnetization measurement confirms the paramagnetic property of these nanoparticles which is commonly shared by the positive contrast agents for magnetic resonance imaging (MRI). The synthesized nanoparticles were easily water soluble by ligand exchange method with 3-mercaptopropionic acid. Based on the optical and the paramagnetic properties of these nanoparticles, it can be much attention to application of multimodal particulate agents to combine fluorescence and MRI.

**Keywords:** nanoparticles; paramagnetic contrast agents; magnetic resonance imaging; bio-imaging

## 1 INTRODUCTION

There is considerable interest in the development of quantum dots (QDs) including II - VI compounds for sensors, solar cell, optical devices, and biological applications because of their unique properties such as their size dependence, stability of light, high absorption coefficients, and bright fluorescence [1-7]. However, these QDs have limitation to industrial and biological applications due to include toxically heavy metals such as cadmium, selenium, and tellurium. Therefore, searching for nontoxic materials is an actual challenge in this field. Especially, lanthanides nanoparticles are promising labels in biological applications because of their optical properties, such as large Stokes shift, lack of photobleaching, long luminescence lifetime, and easily controlled the different emission band by controlled doping of lanthanide ions into an appropriate host material [8].

Most of the magnetic nanoparticles based on iron oxides have been widely used experimentally for numerous in vivo applications such as magnetic resonance imaging (MRI) contrast enhancement, tissue repair, hyperthermia, medical

diagnostics, and therapeutics [9-17]. These magnetic nanoparticles have high transverse relaxivity/longitudinal relaxivity ( $r_2/r_1$ ) values because of their superparamagnetic character, so that they used to negative contrast agent. In the case of paramagnetic contrast agents, such as  $\text{Gd}^{3+}$  chelates, exhibited relatively low  $r_2/r_1$  value and is revealed by a brightness which reflects the shortening of the longitudinal relaxation time  $T_1$ . However, there is a demand for new and more efficient  $T_1$ -weighted contrast agents because of their low relaxivity and high toxicity. Especially, nanoparticles combining fluorescence and MRI received much attention because they combine the high sensitivity of the fluorescence phenomenon to the high spatial resolution of MRI. Here, we report the development of a  $\text{Eu}^{3+}$ -doped GdS nanoparticles, which can be used as molecular markers and  $T_1$ -weighted MRI contrast agents. The  $\text{Eu}^{3+}$ -doped GdS nanoparticles show a strong narrow emission band at around 614 nm and paramagnetic property.

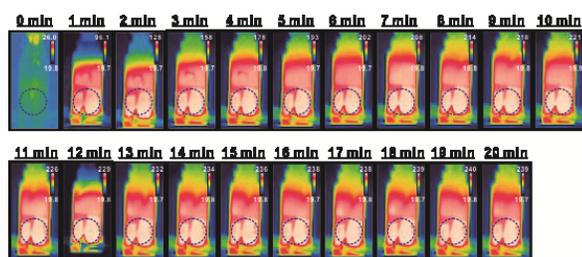
## 2 EXPERIMENTAL

In the present work,  $\text{Eu}^{3+}$ -doped GdS nanoparticles has been formed by simple sonochemistry method. The sonochemistry method using ultrasound has been attempted to obtain a rapid reaction time, milder operating conditions (e.g., lower temperatures and pressures), and reduction of synthesis steps. The effect of ultrasonic radiation on reaction is due to acoustic cavitation within collapsing bubbles, which generates localized hot spots with extreme conditions (temperature = 5000 K, pressure = 1800 atm, and cooling rate =  $10^{10}\text{K/s}$ ) [18]. Gadolinium (III) acetylacetonate hydrate (99.9%), Europium (III) acetylacetonate hydrate (99.9%), 1-Dodecanethiol ( $\text{CH}_3(\text{CH}_2)_{11}\text{SH}$ , 98%), and 3-mercaptopropionic acid ( $\text{HSCH}_2\text{CH}_2\text{CO}_2\text{H}$ ,  $\geq 99.0\%$ ) were purchased from Aldrich. Chloroform and ethanol were used in the isolation of nanoparticles. Distilled water used in synthesis was high purity grade with a conductivity of 18.2 MΩ cm. All chemicals were used without further purification. The appropriate composition of  $\text{Gd}_{1-x}\text{S}$  with various concentration of  $\text{Eu}_x$  and 10 mL of 1-Dodecanethiol were put into a 20 mL vial and ultrasound-treated for 30 min in air atmosphere. The resulting suspension was centrifuged to remove the by-products with chloroform and methanol several times. The final products were re-dispersed in chloroform. The  $\text{Eu}^{3+}$ -doped GdS nanoparticles were subjected to ligand exchange method. 10 mL methanol containing 400 μL 3-mercaptopropionic acid was controlled

pH value (over pH=13) with 1 M NaOH solution. 3-mercaptopropionic acid solution was added to the  $\text{Eu}^{3+}$ -doped GdS nanoparticles. The mixture solution was vigorously stirred for 30 min. The mixture solution was centrifuged and washed several times with methanol. The final product was re-dispersed in distilled water.

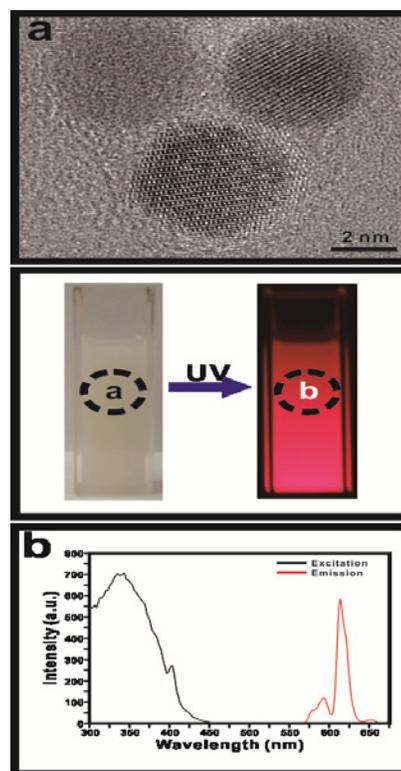
### 3 RESULTS AND DISCUSSION

To prepare the  $\text{Eu}^{3+}$ -doped GdS nanoparticles we prepared various samples by ultrasound decomposition of raw materials with ratios to give appropriate metal concentrations. Raw materials were dissolved in a 1-Dodecanethiol and treated by ultrasound for 20 min (maximum temperature reached to about 240 °C, Figure 1) and the products were obtained from centrifuge by addition chloroform and methanol and re-dispersed in chloroform.



**Figure 1. Thermal images recorded by infrared camera of  $\text{Eu}^{3+}$ -doped GdS nanoparticles with ultrasonic irradiation times.**

The transmission electron microscopy (TEM) image of synthetic  $\text{Eu}^{3+}$ -doped GdS nanoparticles revealed a spherical shape having an average core size of 5 nm (left in Figure 2). Under UV light excitation, the dispersed  $\text{Eu}^{3+}$ -doped GdS nanoparticles in chloroform exhibited bright red color (middle in Figure 2). The excitation and emission spectra are shown in right in Figure 2. Under excitation with 365 nm,  $\text{Eu}^{3+}$ -doped GdS nanoparticles yields intense orange-red emission corresponding to  $^5\text{D}_0 \rightarrow ^7\text{F}_j$  ( $J=0, 1$  and  $2$ ) intra-configurational f-f transition. As can be seen the emission spectrum, the emission spectrum of  $\text{Eu}^{3+}$  in  $\text{Eu}^{3+}$ -doped GdS nanoparticles consists of a strong peak at 614 nm and several weak peaks. The  $^5\text{D}_0 \rightarrow ^7\text{F}_1$  transition (at about 584nm) and  $^5\text{D}_0 \rightarrow ^7\text{F}_2$  transition (at about 614 nm) are to be expected magnetic and electric dipole-dipole transitions, respectively. It is known that the  $^5\text{D}_0 \rightarrow ^7\text{F}_2$  transitions depend strongly on the local symmetry of the  $\text{Eu}^{3+}$  ions.

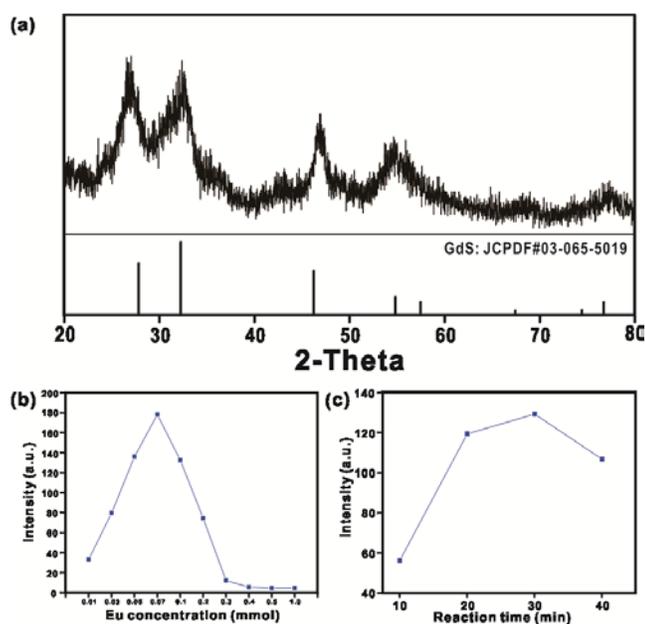


**Figure 2. Photographs of chloroform-dispersed  $\text{Eu}^{3+}$ -doped GdS nanoparticles (middle), TEM image of the 5 nm nanoparticles (a : upper), and PL spectra (b : lower).**

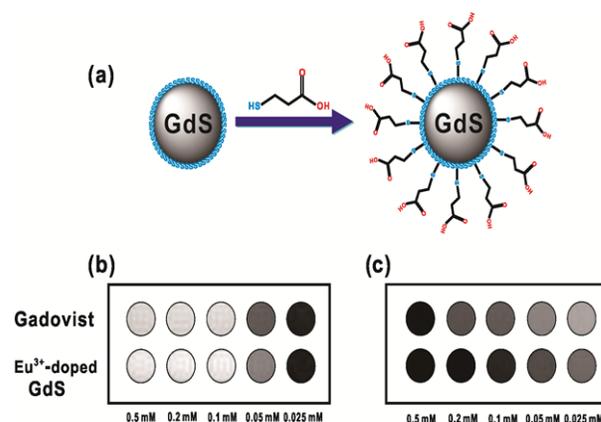
The X-ray diffraction (XRD) peak positions these  $\text{Eu}^{3+}$ -doped GdS nanoparticles show good agreement with a crystalline body-centered-cubic GdS with no evidence of secondary phases particularly  $\text{Gd}_2\text{O}_3$  (Figure 3a) which indicate that the well-formed single crystals. The concentration quenching data of the  $^5\text{D}_0 \rightarrow ^7\text{F}_2$  transition with respect to the different amounts of added  $\text{Eu}^{3+}$  in GdS are shown in Figure 3b. The results show typical concentration quenching and the critical  $\text{Eu}^{3+}$  concentration is determined to be about 0.07 mmol. According to Mahalley *et al.* [19] the concentration quenching may be due to the cross relaxation or the energy migration to quenching centers where the excitation energy is lost nonradiatively. Concentration quenching is obviously not possible by a simple multipolar transfer process since the gap in energy between the  $^5\text{D}_0$  level and the top of the  $^7\text{F}_{0-6}$  multiplet. For this reason, we assumed that the quenching of  $\text{Eu}^{3+}$  in this system is associated with exchange interaction. The optimum ultrasonically irradiated time to synthesis  $\text{Eu}^{3+}$ -doped GdS nanoparticles in 1-Dodecanethiol was determined to 30 min as shown in Figure 3c. In this system, the Dodecanethiol was used as a sulfur source to metal sulfide as well as the protecting group of nanoparticle surface.

The  $\text{Eu}^{3+}$ -doped GdS nanoparticles were surface functionalized with 3-mercaptopropionic acid (MPA) via ligand exchange method to make them soluble in water

(Figure 4a). Briefly,  $\text{Eu}^{3+}$ -doped GdS nanoparticles were subjected to ligand exchange method. Methanol solution containing 0.2 M 3-mercaptopropionic acid (MPA) was controlled pH value with 1 M KOH solution. After control of pH, 0.2 M 3-MPA acid solution was added to the  $\text{Eu}^{3+}$ -doped GdS nanoparticles dispersed chloroform solution. The mixture solution was stirred for 30 min, followed by centrifugation. The wet precipitate of MPA-capped  $\text{Eu}^{3+}$ -doped GdS nanoparticles were washed several times with methanol, and re-dispersed in 1 mL of distilled water. The MR images of the various  $\text{Eu}^{3+}$ -doped GdS nanoparticle concentrations as well as the commercially available positive Gadovist as a reference are shown in Figure 4b. The  $T_1$ -weighted images of  $\text{Eu}^{3+}$ -doped GdS nanoparticles gradually become brighter with higher concentrations analogous to Gadovist. On the other hand, the  $\text{Eu}^{3+}$ -doped GdS nanoparticles become more darker as increased the concentrations than the Gadovist in the  $T_2$ -weighted images.

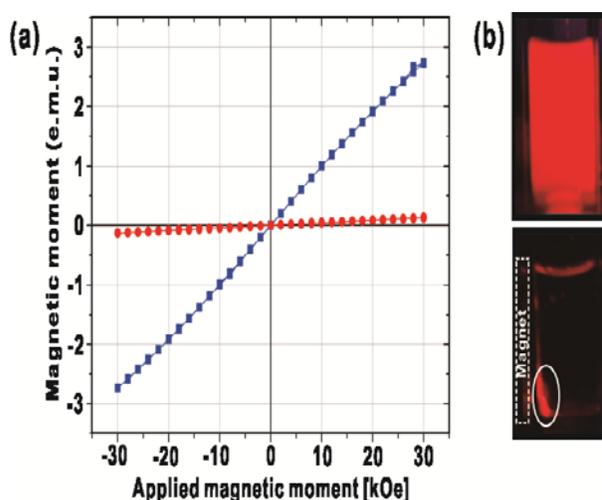


**Figure 3.** Structural and photoluminescence analysis of  $\text{Eu}^{3+}$ -doped GdS nanoparticles. (a) X-ray diffraction pattern of 5 nm nanoparticles. (b) The photoluminescence emission intensities as a function of  $\text{Eu}^{3+}$  concentrations. (c) The photoluminescence emission intensities as a function of ultrasonically irradiated time.



**Figure 4.** (a) Schematic diagram of a MPA functionalized  $\text{Eu}^{3+}$ -doped GdS nanoparticles, (b)  $T_1$ -weighted, and (c)  $T_2$ -weighted MR images of various concentration of commercially available Gadovist and  $\text{Eu}^{3+}$ -doped GdS nanoparticles.

The field dependencies of the magnetization (M-H curve) of  $\text{Eu}^{3+}$ -doped GdS nanoparticles at 5K and 300K are recorded as shown in Figure 5a. The magnetization curves at 5K and 300K show that both coercivity and remanence are zero, which indicated that the paramagnetic character. In other words, these water soluble nanoparticles can be used to the positive contrast agents for MRI. The optical measurements were performed upon  $\text{Eu}^{3+}$ -doped GdS nanoparticles dispersions in water that were red color and almost all of the nanoparticles were attracted towards the magnetic bar when a permanent magnet was applied beside the quartz cuvette (Figure 5b)



**Figure 5.** (a) Magnetization curves at temperature (T) 5K (red line) and 300K (blue line) of  $\text{Eu}^{3+}$ -doped GdS nanoparticles, (b) Water-dispersed  $\text{Eu}^{3+}$ -doped GdS nanoparticles are paramagnetic and shows a drift towards a permanent magnet.

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