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Europium-doped gadolinium sulfide nanoparticles as a dual-mode imaging agent for T_1-weighted MR and photoluminescence imaging

Jongjin Jung [a,1], Mi Ae Kim [a,1], Jee-Hyun Cho [b,c,1], Seung Jae Lee [a], Ilseung Yang [d], Janggeun Cho [b,c], Seong Keun Kim [d,e], Chulhyun Lee [b], Joung Kyu Park [a,*]

[a] Research Center for Convergence Nanotechnolgy, Korea Research Institute of Chemical Technology, Daejeon 305-600, Republic of Korea
[b] Division of Magnetic Resonance Research, Korea Basic Science Institute, Ochang 363-883, Republic of Korea
[c] Department of Chemistry, Chung-Ang University, Seoul 156-756, Republic of Korea
[d] Department of Chemistry, Seoul National University, Seoul 151-747, Republic of Korea
[e] WCU Department of Biophysics and Chemical Biology, Seoul National University, Seoul 151-747, Republic of Korea

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ABSTRACT

We present a facile synthesis of europium-doped gadolinium sulfide ($GdS:Eu^{3+}$) opto-magnetic nanoparticles (NPs) via sonochemistry. Their photoluminescence and strong paramagnetic properties enable these NPs to be utilized as an *in vitro* cell imaging and *in vivo* T_1-weighted MR imaging probe. The $GdS:Eu^{3+}$ NPs have a prominent longitudinal (r_1) relaxivity value, which is a critical parameter for T_1-weighted MR imaging. Here, we showed not only their strong positive contrast effect to blood vessels and organs of mice, but also blood half-life and biodistribution including clearance from organs, in order to assess the $GdS:Eu^{3+}$ NPs as a competent nanocrystal-based T_1 contrast agent. We further showed confocal images of breast cancer cells containing $GdS:Eu^{3+}$ NPs to evaluate as a photoluminescence probe. Dual-mode imaging capability obtained from the $GdS:Eu^{3+}$ NPs will allow target-oriented cellular imaging as well as the resulting disease-specific MR imaging.

1. Introduction

Nanoparticles (NPs) in which magnetic and optical properties coexist have been explored intensively for diverse biomedical applications, ranging from *in vivo* imaging and therapy [1,2] to cellular imaging and manipulation [3–5]. Several approaches studied to date have mainly focused on combining two different systems, such as magnetic materials and organic dyes [6,7], or on formulating magnetic nanoparticles and fluorescent materials via polymers [8,9]. However, increased size, difficulty controlling size and homogeneity, and complicated synthetic routes have limited their potential and application. Therefore, there is urgent need for the development of high-performance dual-mode imaging agents with a simple and novel synthetic method.

Binary rare-earth chalcogenides, such as gadolinium or europium with sulfur have drawn much attention because of their intrinsic magneto-optical, semiconducting, magnetic, and luminescent properties [10–12]. For example, gadolinium-doped europium sulfide ($EuS:Gd^{3+}$) nanocrystals were prepared to enhance the low Curie temperature of EuS (16.6 K) via the magnetic coupling through carrier electrons by doping low concentrations of gadolinium. The thermal decomposition at 265 °C was applied to synthesize $EuS:Gd^{3+}$ nanocrystals with a cubic morphology using dithiocarbamate precursors of europium and gadolinium for the careful control of the gadolinium concentration and improvement of homogeneity [12]. Recently, we introduced the synthesis of europium-doped gadolinium sulfide ($GdS:Eu^{3+}$) nanocrystals via thermal decomposition at 200 °C and a facile reduction process of Eu^{3+} to Eu^{2+} in GdS host NPs using a mixture of oleic acid/hexadecylamine for the color tuning from red to green emission [13]. The thermal decomposition of gadolinium and europium acetylacetonate hydrate, and 1-dodecanethiol induced the burst of nucleation and the subsequent growth at the specific temperature until their growth was saturated by several factors such as growth temperature and dynamics of capping agents [14]. Here, we developed europium-doped gadolinium sulfide ($GdS:Eu^{3+}$) nanocrystals as an agent for T_1-weighted magnetic resonance (MR) imaging and photoluminescence (PL) imaging via the sonochemical synthesis which utilizes high acoustic energies and pressure for the formation of cavities and hot spots (roughly 5000 K and 500 atm) causing the rupture of chemical bonds and crystallization [15]. The synthesis of $GdS:Eu^{3+}$ in the form of NPs is valuable for the advanced dual-mode imaging, given that these materials enable to

* Corresponding author. Tel.: +82 42 860 7373; fax: +82 42 860 7508.
E-mail address: parkjk@krict.re.kr (J.K. Park).
[1] The first three authors contributed equally to this study.

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