Synthesis, Characterization, *In vitro* and *In vivo* MR Studies of Dy(OH)$_3$ Nanostructures for T_2 MRI Contrast Agent

Krishna Kattel[1], Ja Young Park[1], Wenlong Xu[1], Badrul Alam Bony[1], Woo Choul Heo[1], Tirusew Tegafaw Mengesha[1], and Gang Ho Lee[1]
[1]*Department of Chemistry, Kyungpook National University, Daegu, Korea, Republic of*

Introduction

Lanthanide (Ln)-based inorganic materials with their outstanding optical and magnetic properties are interesting alternatives for the applications such as contrast agent in magnetic resonance imaging (MRI). Except La^{3+} and Lu^{3+}, all trivalent lanthanide ions possess unpaired electrons resulting in paramagnetic behavior. Currently, some of the gadolinium compounds are in clinical use as MRI contrast agents due to high magnetic moment of Gd (7.9 μ_B). Dy-compounds are another promising candidate for this purpose. Dy^{3+} has the shortest electronic relaxation time and highest magnetic moment (10.6 μ_B) which induce water proton relaxation that primarily affect T_2. It increases significantly with the external magnetic field, and is proportional to the square of the magnetic moment of the Dy^{3+} ion. Here, Dy(OH)$_3$ nanostructures were examined for their possible use in MR imaging and tracking of cells by investigating their cytotoxic behaviors.

Materials and Methods

To synthesize Dy(OH)$_3$ nanocolloid, 5 mmol of Dy(III) precausor was added to 40 mL distilled water in a round-bottom flask. 15 mmol of aq. NaOH (10 mL) was prepared and added slowly into the reaction mixture. It was heated at 80℃ and magnetically stirred for 24 hours. For surface modification, 5 mmol of D-glucuronic acid was added and the reaction was continued for another 24 hours. The reaction solution was cooled to room temperature. The unreacted coating ligand, unreacted Dy(III) ions etc. were removed from the solution by washing it with nano pure water for three times. The reaction solution was stored for a week until Dy(OH)$_3$ nanostructures were settled down to the bottom. The top transparent solution was decanted. Half of the Dy(OH)$_3$ nanocolloid was dispersed in distilled water to prepare a MRI solution and the remaining half was dried in air to prepare a powder sample for characterizations.

Result and Discussion

HRTEM micrographs revealed uniform nanorods with an average diameter 20 nm and an aspect ratio between15-20 (fig. 1). The XRD pattern confirmed high crystallinity of the materials with hexagonal lattice (JCPDS card no. 19-0430), as shown in figure 2. The changes in surface chemistry of Dy(OH)$_3$ nanorods after coating with D-glucuronic acid were characterized by FT-IR spectra. The magnetic properties of Dy(OH)$_3$ nanostructures were also characterized. The saturation magnetization of paramagnetic nanostructures at 5 K was measured to be 159.88 emu/g. The longitudinal (T_1) and transverse (T_2) relaxation times were measured at various Ln^{3+} ion concentration and, r_1 and r_2 values were calculated from the respective slopes, as shown in figure 4. MRI contrasting capability of the nanomaterials was tested by measuring R_1 and R_2 map images and a clear dose dependent contrast enhancement on R_2 map images was observed (fig. 3). As observed from in vitro assays, the investigated Dy(OH)$_3$ nanostructures do not induce any significant cytotoxic effect, as shown in figure 5. In vivo T_2 MR images of mouse were recorded by using 3 tesla MRI scanner. A clear negative contrast can be seen on liver and kidneys after 15 minutes of injection as shown in figure 6. Hence, it clearly reflects that surface modified Dy(OH)$_3$ nanostructures may function as sensitive T_2 MRI contrast agent at high MR field.

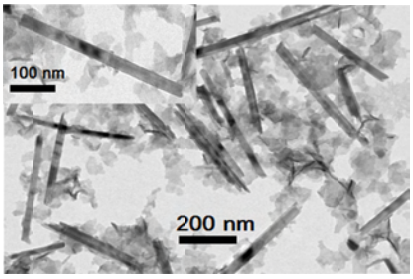

Fig. 1 HRTEM images of D-glucuronic acid coated Dy(OH)$_3$ nanostructures.

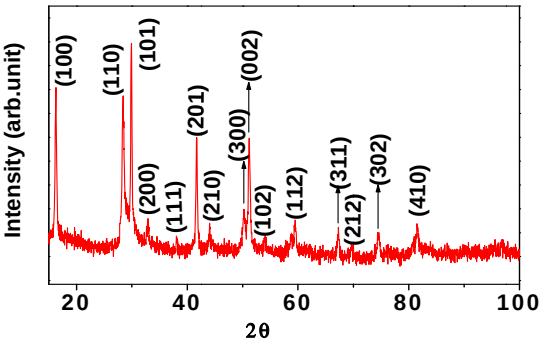

Fig. 2 XRD curve

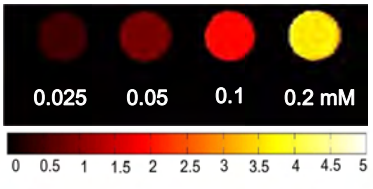

Fig. 3 R_2 map images.

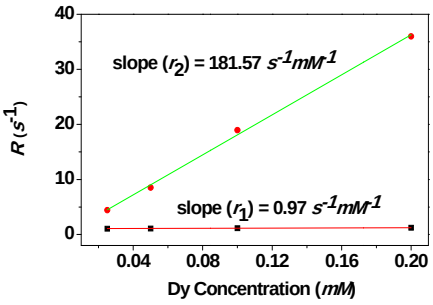

Fig. 4 Plot of $1/T_1$ and $1/T_2$ inverse relaxation times of sample solution of Dy(OH)$_3$ nanocolloid.

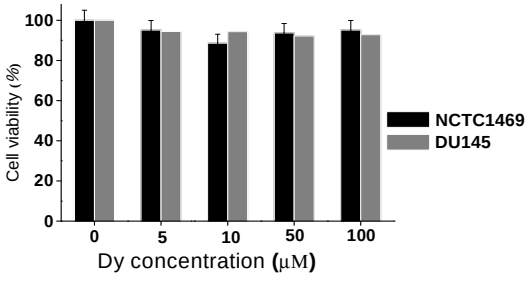

Fig. 5 *In vitro* cytotoxycity test of Dy(OH)$_3$ MRI sample solution by using DU145 and NCTC1469 cell lines.

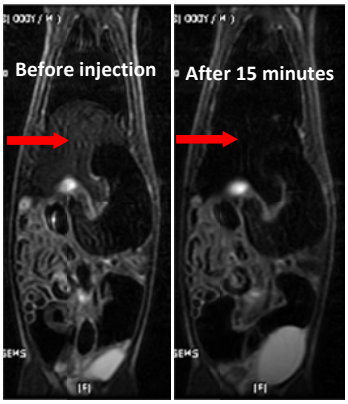

Fig.6 3-tesla T_2 MR images of mouse liver, (indicated with arrow) before and after 15 minutes of injection of Dy(OH)$_3$ nanocolloid.