A study of Lactobionic acid coated $GdEuO_3$ nanoparticles as MRI-FI dual imaging agent

Wenlong Xu[1], Badrul Alam Bony[1], Tirusew Tegafaw Mengesha[1], Cho Rong Kim[1], Sung June Kim[1], Md. Wasi Ahmad[1], and Gang Ho Lee[1]
[1]*chemistry, Kyungpook National University, Teagu, Korea*

Introduction

Dual imaging now emerges as a new and advanced imaging technique in clinical applications. $GdEuO_3$ nanoparticles are potential candidates for dual imaging experiment. A dual imaging now emerges as a new and advanced imaging technique in clinical applications. It is expected that it will play a key role to diagnose diseases by replacing conventional single-imaging techniques. For example for MRI-FI dual imaging, the fluorescence imaging can be used to locate a disease and then MRI can be used to obtain high resolution MR images around the disease. We developed a simple one-step synthesis of lactobionic acid surface-modified ultra small $GdEuO_3$ nanoparticles. It was well characterized by using MP-XRD, TEM, FT-IR spectrophotometer, TGA, confocal microscope, SQUID magnetometer and Magnetic Resonance Imaging (MRI) instrument. The capability of nanoparticles as T_1 MRI contrast agent was proved in vivo through T_1 MR images of a rat. The fluorescent images were observed in vitro by taking DU145 cells. The data suggested that the lactobionic acid coated ultrasmall $GdEuO_3$ nanoparticles can be used as a fluorescence imaging agent as well as a T_1 MRI contrast agent.

Materials and methods

Two separate solutions were prepared: one is 15 mmol of NaOH dissolved in 10 mL of methanol and the other is equal amount of 2.5 mmol of $GdCl_3.5H_2O$ and $Eu(NO_3)_3.5H_2O$ dissolved in 40 mL of triethylene glycol. In order to dissolve both $GdCl_3.5H_2O$ and $Eu(NO_3)_3.5H_2O$ in triethylene glycol, the mixture solution was heated to 100 ºC and magnetically stirred until the solution became transparent (it took ~ 2 hours). The above two solutions were then mixed together and refluxed at 200 ºC for 24 hours in air. At this point, nanoparticles were formed. After this, the solution temperature lowered to 150 ºC and 5 mmol of lactobionic acid was added to the solution. The solution was magnetically stirred for 24 hours at this temperature for surface coating. After this, the solution was cooled to room temperature. It was transferred into a 1 L beaker containing 500mL of triply distilled water and then, magnetically stirred for an hour. It was stored for a week or so until the lactobionic acid coated ultrasmall $GdEuO_3$ nanoparticles were settled down to the beaker bottom. The top transparent solution was decanted and the remaining sample solution was again washed with triply distilled water. This procedure was repeated three times. The first half volume of the sample was diluted with triply distilled water to prepare a sample solution for MR experiments.

Result and Discussion:

HRTEM images show that the diameter (d) of the $GdEuO_3$ nanoparticles in its nanocolloid is nearly monodisperse and ranges from 1 to 2 nm (fig.1). The surface coating of nanoparticles by lactobionic acid was confirmed by recording a FT-IR absorption spectrum of a powder sample. The amount of surface coating of the $GdEuO_3$ nanoparticle with the lactobionic acid in nanocolloid were estimated to be 42.1% by recording a TGA curve of a powder sample. It shows that the nanoparticles are sufficiently coated with the lactobionic acid. To characterize magnetic properties of the nanoparticles in the $GdEuO_3$ nanocolloid, both M-H and ZFC M-T curves and were recorded. The M-H curves show that both coercivity and remanence are zero. This lack of hysteresis as well as no magnetic transition down to T =3 K in the ZFC M-T curve shows that the nanoparticles are mainly paramagnetic down to T =3 K. From the M-H curve at T =5 K and at H=T, magnetizations of the $GdEuO_3$ nanoparticles were estimated to be ~ 85.3emu/g. The PL spectrum of lactobionic acid coated $GdEuO_3$ nanoparticles is shown in fig. 5. The observed peaks at 591 and 616 nm in the sample solution are due to the emission from $^5D_0$ to $^7F_0$,1,2 of Eu(III) ion respectively. Among these emission peaks, the third one corresponds to the principle emission. A fluorescent sample solution in the red region after being irradiated with a mercury lamp (365 nm and 5 watt) is also inserted in fig. 5.The R_1 and R_2 map images clearly showed dose dependent contrast changes with increasing the dose (fig.2). The r_1 and r_2 relaxivities of 11.9 and 38.7 s^{-1} mM^{-1} were obtained from the slopes in the plots of R_1 and R_2 relaxivities as a function of Gd concentration respectively (fig.3). For the $GdEuO_3$ nanocolloid to be safely applied in vivo, it should be nontoxic. We performed an *in vitro* cytotoxicity test of the nanocolloid by using the human prostate cancer (DU145) cell lines as shown in fig.4. The $GdEuO_3$ nanocolloid is not toxic for the tested concentration range up to 100 μM Gd. In vivo MR images were recorded which showed the increase of contrast enhancement on kidney of mouse after 10 minutes of injection of MRI solution. Hence, it can be inferred that ultra small single phase $GdEuO_3$ nanoparticles can be used as a dual imaging probes.

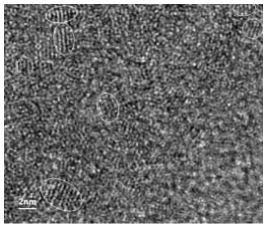

Fig. 1 HRTEM image

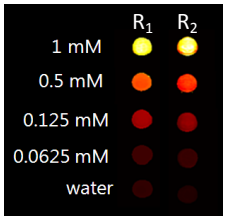

Fig. 2 Map images

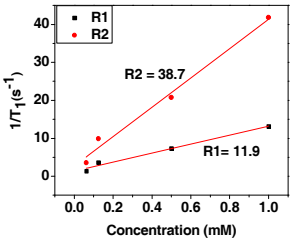

Fig. 3 Measurement of Relaxivity

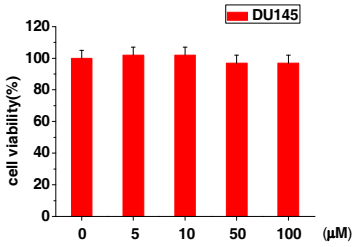

Fig. 4 *In vitro* cytotoxicity test

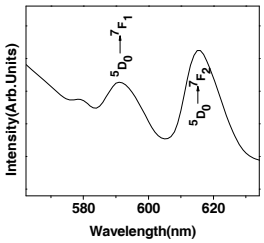

Fig. 5 PL spectra

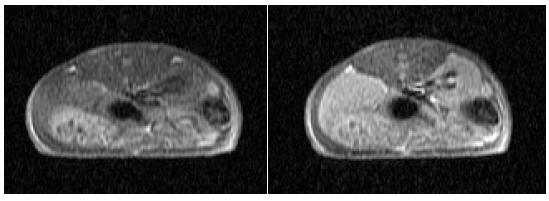

Fig. 6 *In vivo* MR images (Mouse kidney)