

Magnetic resonance imaging(MRI) and X-ray computed tomography(CT) dual functionality of gadolinium iodate dihydrate nanomaterials

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Introduction

We, for the first time, explored Gd(IO₃)₃·2H₂O NMs as a new type of MRI-CT dual contrast agents. This study deals with MRI-CT dual contrast agents. The multi-modal imaging modalities could be used to improve the accuracy of diagnosing diseases. In MRI-CT, MRI is a true noninvasive imaging technique because it uses low energies of radiofrequency. Since MRI uses proton signals, its sensitivity is very high due to an ample existence of protons in a living system. On the other hand, CT is somewhat harmful to a body because it uses high energies of X-ray radiation. However, CT is very useful for hard parts such as bones and hardened diseases. Therefore, MRI-CT can be used as a complementary imaging modality to cover their individual strength and weakness. As found in this study, Gd(IO₃)₃·2H₂O NMs showed very large water proton relaxivities because of hydrated water molecules which served as a reservoir for MR signals. Gadolinium itself also strongly absorbs X-ray radiation [xx] and in fact, Gd(IO₃)₃·2H₂O NMs showed enhanced CT contrasting power compared to commercial iodine CT contrast agent. Measured properties were all superior to those of commercial MRI and CT contrast agents.

Materials and Method

A mixture solution of 1 mmol of GdCl₃·6H₂O and 1mmol of D-glucuronic acid in 10 ml of triply distilled water was prepared in a 100 ml round bottom flask and magnetically stirred under atmosphere. Solution temperature was kept at 80 °C by dipping the reaction flask into a silicon oil bath. In a separate beaker, 3 mmol of KIO₃ was dissolved in 10 ml of triply distilled water, which was then injected into the above solution by using a syringe. The reaction solution was magnetically stirred for 30 minutes. After final products of surface coated Gd(IO₃)₃·2H₂O NMs were formed, the reaction solution was cooled to room temperature and transferred into a beaker containing 400 ml of triply distilled water for washing.

A high resolution transmission electron microscope (HRTEM) (JEOL, JEM 2100F, 200 kV acceleration voltage) was used to measure the particle dimension of surface coated Gd(IO₃)₃·2H₂O NMs. A copper grid (PELCO No.160, TED PELLA, INC.) covered with an amorphous carbon membrane was placed onto a filter paper and then, a sample solution diluted in triply distilled water was dropped over the copper grid by using a micropipette (Eppendorf, 2-20 µL). An inductively coupled plasma atomic emission spectrometer (ICPAES) (Thermo Jarrell Ash Co., IRIS/AP) was used to measure the Gd concentrations in sample solutions. Compositions (I and Gd) of D-glucuronic acid coated Gd(IO₃)₃·2H₂O NMs were also measured by using an X-ray photoelectron spectrometer (XPS) (ULVAC-PHI, Quantera SXM) with an Al Kα X-ray source (= 1486.6 eV). A Fourier transform-infrared (FT-IR) absorption spectrometer (Mattson Instruments, Inc., Galaxy 7020A) was used to investigate the surface coating of D-glucuronic acid coated Gd(IO₃)₃·2H₂O NMs. A superconducting quantum interference device (SQUID) magnetometer (Quantum Design, MPMS-7) was used to measure the magnetic properties of D-glucuronic acid coated Gd(IO₃)₃·2H₂O NMs. A 1.5 tesla MRI instrument (GE 1.5 T Signa Advantage, GE medical system) equipped with the knee coil (EXTREM) was used to measure both longitudinal (T₁) and transverse (T₂) relaxation times. A series of aqueous sample solutions of D-glucuronic acid coated Gd(IO₃)₃·2H₂O NMs prepared at concentrations of 0.25, 0.125, 0.0625, and 0 mM Gd were used to measure relaxation times. A CellTiter-Glo Luminescent Cell Viability Assay (Promega, WI, USA) was used to measure the cellular toxicity of an aqueous sample solution of D-glucuronic acid coated Gd(IO₃)₃·2H₂O NMs. In this assay, a luminometer (Victor 3, Perkin-Elmer) was used to quantify the intracellular ATP. Both human prostate cancer (DU145) and normal mouse hepatocyte (NCTC1469) cell lines were used as test cells. An Inveon CT (Siemens Medical Solutions) was used to measure the X-ray phantom images. Two aqueous sample solutions of D-glucuronic acid coated Gd(IO₃)₃·2H₂O NMs prepared at concentrations of 40 mM (10 mM Gd + 30 mM I) and 169.6 mM (42.4 mM Gd + 127.2 mM I) were used for phantom image measurements.

Results and Discussion

A HRTEM image shows of D-glucuronic acid coated Gd(IO₃)₃·2H₂O NMs, showing bimodal distributions in both morphologies and particle dimensions. Nearly spherical nano-sheet NMs showed a bimodal distribution in particle diameters, one ranging from 80 to 150 nm (avg. = 110 nm) and the other ranging from 500 to 1000 nm (avg. = 750 nm). Rod-type NMs showed length (l) x width (w) of 150-500 x 100-200 nm (avg. = 325 x 150 nm). An aqueous sample solution of D-glucuronic acid coated Gd(IO₃)₃·2H₂O NMs is shown in Fig. 1a. The r₁ and r₂ of an aqueous sample solution were estimated to be 52.3 and 63.4 s⁻¹mM⁻¹ from the slopes in the plots of 1/T₁ and 1/T₂ as a function of Gd concentration, respectively (Fig. 2a). r₁ and r₂ values of D-glucuronic acid coated Gd(IO₃)₃·2H₂O NMs are also larger than those of anhydrous Gd-based NMs as well as those of Gd(III)-chelates. These high water proton relaxivities are very important for MRI because strong contrast enhancements allow us to easily delineate tissues, diseases, and micro blood vessels. These high water proton relaxivities are likely related to hydrated water molecules in Gd(IO₃)₃·2H₂O NMs. Therefore, hydrated water molecules can serve as a reservoir for MR signals, producing large r₁. The X-ray absorption power of Gd(IO₃)₃·2H₂O NMs was clearly compared to that of Ultravist® by plotting X-ray absorption intensities as a function of concentration (Fig. 3b), showing that Gd(IO₃)₃·2H₂O NMs more strongly absorbed X-ray radiation than Ultravist®. One of possible reasons for this is that Gd more strongly absorbs X-ray radiation than I [xx]. Therefore, this dose-dependent and stronger X-ray absorption of Gd(IO₃)₃·2H₂O NMs than Ultravist® indicates that Gd(IO₃)₃·2H₂O NMs are potential candidates as CT contrast agents.

Conclusion

We synthesized D-glucuronic acid coated Gd(IO₃)₃·2H₂O nanomaterials and for the first time investigated their magnetic properties, water proton relaxivities, and X-ray phantom images. D-glucuronic acid coated Gd(IO₃)₃·2H₂O nanomaterials were paramagnetic, with very large longitudinal (r₁) and transverse (r₂) water proton relaxivities of 52.3 and 63.4 s⁻¹mM⁻¹, respectively, both of which were larger than those of commercial Gd-chelates. Hydrated water molecules seem to serve as a reservoir for strong MR signals. The stronger contrast enhancements in X-ray phantom images than those of commercial molecular iodine CT contrast agents were also observed. These results revealed that D-glucuronic acid coated Gd(IO₃)₃·2H₂O nanomaterials should be a potential candidate for a MRI-CT dual contrast agent.

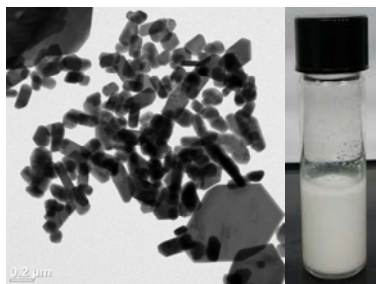


Figure 1. HRTEM images, (a) an aqueous sample solution, (b) a DLS pattern, and (c) an XRD pattern of D-glucuronic acid coated Gd(IO₃)₃·2H₂O NMs. M-H curves at T = 5 and 300 K.

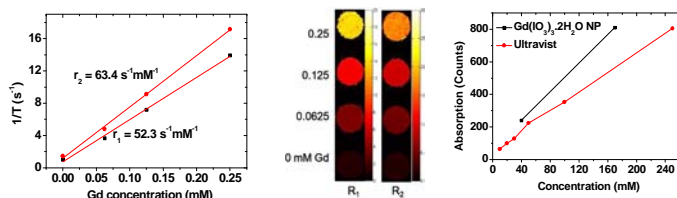


Figure 2. (a)Plots of 1/T₁ and 1/T₂ and (b) R₁ and R₂ map images of aqueous solutions of D-glucuronic acid coated Gd(IO₃)₃·2H₂O NMs as a function of Gd concentration (22°C and 1.5 tesla). The slopes correspond to r₁ and r₂, respectively.

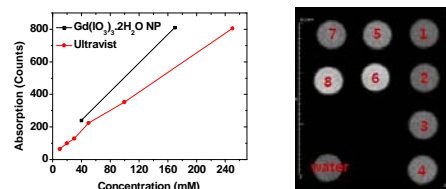


Figure 3. (a)X-ray phantom images taken at 35 kV of aqueous sample solutions of D-glucuronic acid coated Gd(IO₃)₃·2H₂O NMs (labeled as 7,8), together with those of Ultravist® (labeled as 1,2,3,4,5,6). An X-ray phantom image of water is also given as a comparison. (b) Plots of X-ray absorption intensities as a function of (Gd+I) concentration for Gd(IO₃)₃·2H₂O NMs and as a function of I concentration for Ultravist®.