Investigations into the Structure and Magnetic Properties of Dextran Small Particulate Gadolinium Oxide Nanoparticles

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ABSTRACT

Small particulate gadolinium oxide (SPGO) and SPGO embedded in albumin microspheres (gadolinium oxide albumin microspheres, GOAM), have previously been evaluated as contrast agents for multi-modality imaging studies [1]. However, poor solubility and particle agglomeration have resulted in uncharacteristically low SPGO r_1 values [2]. In the present study an initial attempt was made to better solubilize SPGO, prevent particle aggregation and investigate the extent of high field relaxivity enhancement.

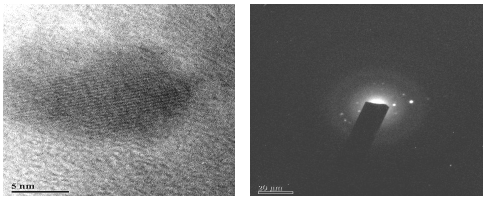

Fig. 1a & b. High resolution scanning transmission electron microscope image and electron diffraction pattern of dextran SPGO

METHOD

Dextran SPGO was prepared by adding a solution of dextran in deionized, distilled water to a base-neutralized solution of gadolinium (III) oxide (20-40 nm in size; 99.9996% pure and free of $GdCl_3$; Alfa Aesar, Inc., USA). The solution was heated to 100ºC, irradiated at 70 W/cm^2 (Misonix 2020XL sonicator, Misonix Inc., Farmingldale, NY), dialyzed, repeatedly filter centrifuged at 2700 RPM, 4ºC, collected and lyophilized. Inductively Coupled Plasma Mass spectroscopy (ICP-MS) was utilized for elemental analysis and determination of gadolinium concentration (OES Optima 2000 DV, Perkin Elmer, Norwalk, CT USA). High resolution scanning transmission electron microscopy (HR-STEM) and electron diffraction patterns were used for size and morphologic analysis of the dextran SPGO core (JEM 2010 LaB_6 STEM, JEOL, Inc., Peabody, MA, USA). X-ray powder diffraction was used to determine the crystal structure of solid, lyophilized dextran SPGO samples (GADDS, Bruker USA, Manning Park, Billerica, MA). General Electric GN300WB 300 MHz (General Electric Medical Systems, USA) and Varian Unity Inova 400, 500, 600 and 750 MHz spectrometers (Varian, Inc., Palo Alto, CA, USA) were used for relaxometry experiments. Longitudinal ($1/T_1$) and Transverse ($1/T_2$) relaxation rates were determined by IR and Carr-Purcell-Meiboom-Gill pulse sequences at 37°C with curve fitting by the least squares method assuming mono-exponential decay. Relaxivity (inverse relaxation times vs. gadolinium concentration) was then plotted against proton larmor frequency.

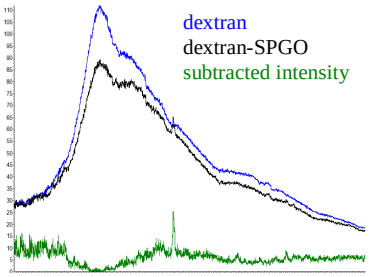

Fig. 2. X-ray diffraction patterns for dextran, dextran SPGO, and the subtracted (SPGO) spectrum.

RESULTS

Dextran SPGO appears as regular crystalline lattices in HR-STEM micrographs (Fig. 1a). The electron diffraction pattern of dextran SPGO (Fig. 1b) is consistent with that of body centered cubic geometry and corresponds with published crystal studies and X-ray powder diffraction patterns. The X-ray powder diffraction spectrum of dextran, dextran SPGO, and the subtracted spectrum are shown in Fig. 2. The subtraction pattern shows diffraction angles and intensities similar, but not identical, to that of published Gd_2O_3 diffraction patterns. Experiments were conducted to determine the relaxivity of dextran SPGO in aqueous solution at proton larmor frequencies of 300,500, 600 and 750 MHz (Fig. 3): r_1 is maintained, and slightly increases while r_2 increases with frequency. Mono-exponential decay was noted for all samples.

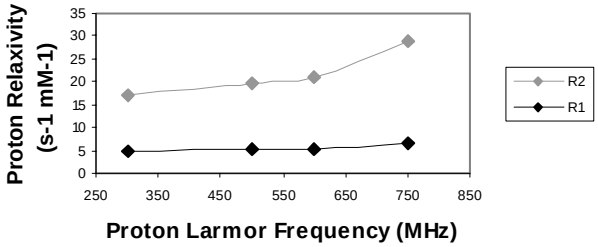

Fig. 3. Field dependence values for r_1 and r_2 of water protons of solutions of dextran SPGO at 300, 500, 600 and 750 MHz, 37°C.

CONCLUSIONS

To date, relatively few studies of the physical and magnetic properties of crystalline, nanometer-sized T_1 particulate complexes have been carried out. The r_2/r_1 ratio for dextran SPGO is in the 3 - 4 range at the proton larmor frequencies measured (between 300 and 750 MHz). High r_2/r_1 ratios would seem to indicate that SPGO compounds may behave like superparamagnetic complexes and perhaps may be classified as class II agents [3]. The observation that r_1 is maintained even at high fields indicates the potential utility of dextran SPGO as a high field T_1 contrast agent. The enhanced high field relaxivity is partly explained by the solubilization of SPGO by the surface adherent carbohydrate. It may also be the result of an ideal lattice structure of the central gadolinium oxide crystal. The symmetries and intensities of the X-ray powder diffraction spectrum confirm the crystal structure of dextran SPGO (ICSD Collection Code 40473, 1999). However, the presence of a slight shift in the lattice parameter is noted; most likely explained by surface modification by dextran or perhaps secondary to the existence of more than one phase (i.e., crystalline and amorphous). In conclusion, by increasing the solubility and limiting particulate aggregation dextran SPGO shows enhanced r_1 and r_2 even at high magnetic fields. The results from this study will aid in the synthesis of newer T_1 particulate based contrast agents for high-field MR imaging and targeted multi-modality imaging..

REFERENCES

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