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Synthesis and Characterization of PEG-Silane Functionalized Iron Oxide Nanoparticle as MRI T2 Contrast Agent

Mu-Jen Young, Cheng-Yen Wu, and Wen-Yuan Hsieh

***Abstract*—**Iron oxide nanoparticle was synthesized by reactive-precipitation method followed by high speed centrifuge and phase transfer in order to stabilized nanoparticles in the solvent.Particle size of SPIO was 8.2nm by SEM, and the hydraulic radius was 17.5nm by dynamic light scattering method.Coercivity and saturated magnetism were determined by VSM (vibrating sample magnetometer), coercivity of nanoparticle was lowerthan 10Hc, and the saturated magnetism was higher than 65emu/g. Stabilized SPIO was then transferred to aqueous phase by reacted with excess amount of poly (ethylene glycol) (PEG) silane. After filtration and dialysis, the SPIO T2 contrast agent was ready to use.The hydraulic radius of final product was about 70~100nm, the relaxation rates R2 (1/T2) measured by magnetic resonance imaging (MRI) was larger than 200(sec^{-1}).

***Keywords*—**Contrast Agent, Iron Oxide Nanoparticle, MagneticResonance Imaging, Nanoparticle Stabilization.

I. Introduction

MAGNETIC resonance imaging (MRI) technology uses nuclear magnetic resonance (NMR) principle, with energy releases in different material interior structure declines in different environment, according to gradient magnetic field examination to examine the position and the type of nucleus of objective atom, and a schematic diagram of interior structure of examined object can be plotted.According to this principle, in cooperate with contrast agent; this measurement technology can be applied in the field of medical radiography diagnosis [1].With special physical structure and magnetic properties, superparamagnetic iron oxide agents (SPIO) possess large magnetism even in the weak magnetic field, and this can vanish rapidly after the magnetic field has switched off [2]. This magnetic property enhances the accuracy and sensitivity of radiography examination [3]. Superparamagnetic iron oxide (SPIO) is the one of major magnetic resonance imaging (MRI) T2 contrast agent materials. The major advantage of this material is low toxicity of iron oxide, thus reduces side effects caused by common gadolinium based T1 contrast agents [4].This research has studied the synthesis, functionalization process and characterization of superparamagnetic iron oxide (SPIO) nanoparticles.

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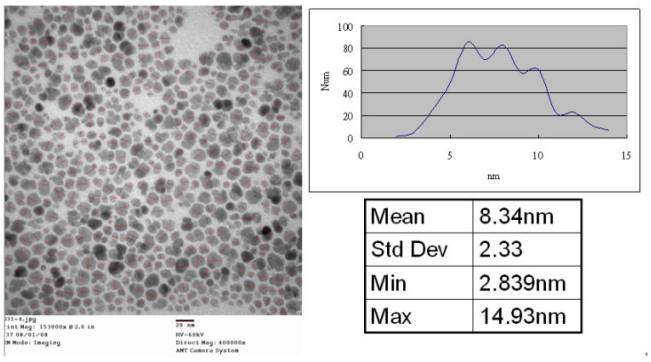
II. Material and Methods

Iron oxide nanoparticle by obtained by reactive precipitation of $FeCl_2/FeCl_3$ aqueous solution with molar ratio of Fe^{2+}/Fe^{3+} was 2/1 titrated with NaOH. After the solution pH reach 11, oleic acid was added and back titration was then performed by HCl, a dark precipitate contains mixture of iron oxide and oleic acid will formed after pH reach 2. After re-slurry in toluene and high-speedcentrifuge to remove agglomerated nanoparticles, iron oxide was dispersed and stabilized in toluene with oleic acid.Particle size and magnetic properties analysis was then employed to determine the properties of iron oxide nanoparticle [5].

Iron oxide toluene slurry was reacted with aqueous PEG-sliane to perform phase transfer functionalization. Oleic acid on surface of iron oxide nanoparticle was replaced by excess amount of PEG-sliane and dissolved back into aqueous phase again, after filtration and dialysis, the PEG-sliane functionalize was dispersed in aqueous solution and analyzed [6].

III. Results and Discussion

Transmission electronic microscopy image of iron oxide nanoparticle synthesized was shown in Fig.1. The average particle size of nanoparticle was 8.34nm with standard deviation 2.33nm. The hydraulic particle size of oleic acid functionalized iron oxide dispersed in toluene was shown in Fig. 2. The Z-average particle size was 15.99nm with PDI 0.066.This iron oxide slurry can stabilized for more than one month without agglomeration.



Mean	8.34nm
Std Dev	2.33
Min	2.839nm
Max	14.93nm

Fig. 1 TEM image of iron oxide nanoparticle

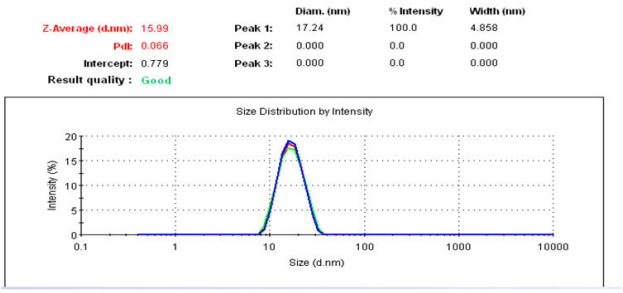


Fig. 2 DLS particle size distribution of iron oxide nanoparticle dispersed in toluene

Crystal form of iron oxide synthesized by reactive precipitation was analyzed by XRD powder reflection, reflex pattern of iron oxide nanoparticle was shown in Fig. 3. The reflex pattern was compared with the standard reflex pattern of magnetite and shows identical pattern with standard crystal form.

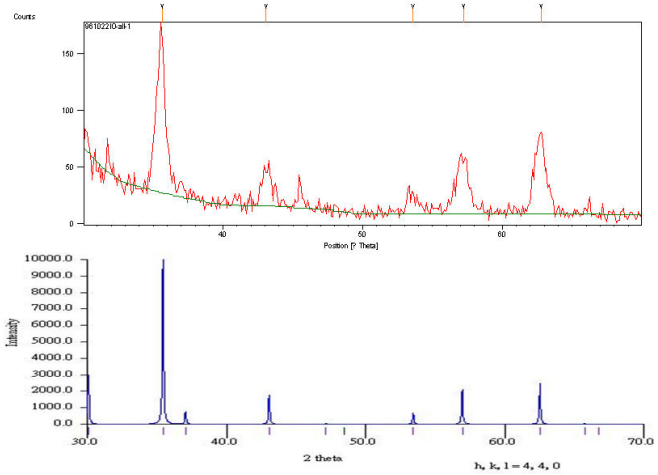


Fig. 3 XRD reflex pattern of iron oxide nanoparticle

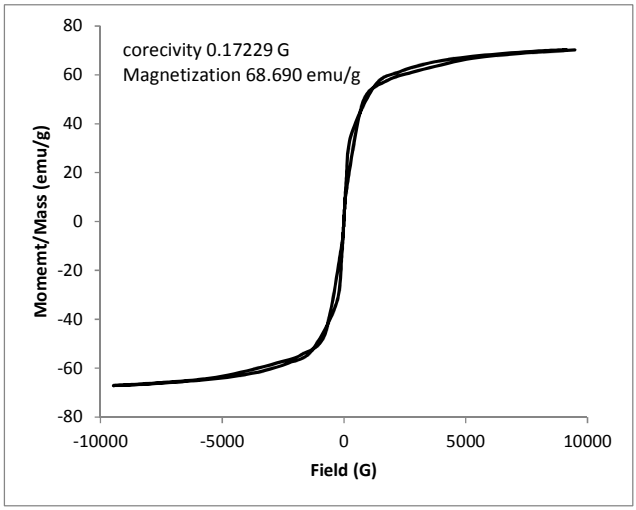


Fig. 4 Hysteresis cycle of oleic acid surface modified iron oxide nanoparticle

The major identification property of superparamagnetism is the low coercivity value.In order to determine the magnetic properties, vibrating sample magnetometer (VSM) test was performed on the iron oxide nanoparticle, the saturated magnetization value was 68.7emu/g,and coercivity was 0.17 Hc shows that the iron oxide nanoparticle synthesized is a superparamagnetic material.

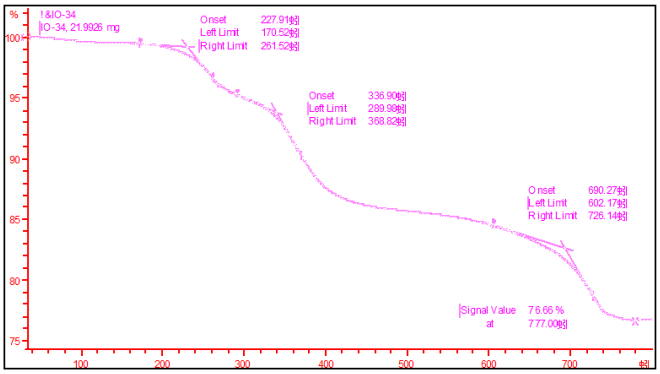


Fig. 5 TGA weight loss of oleic acid surface modified iron oxide nanoparticle

Surface property of oleic acid modified iron oxide nanoparticle was determined by thermal gravity analysis (TGA), the weight loss curve with rise of temperature was shown in Fig.5. There are two major weight loss temperature range, the first is 200~400°C,thisis the mono-dentate oleic acid on the surface of iron oxide nanoparticle, the second temperature range is 600-800°C, this is the bi-dentate oleic acid on the surface of iron oxide nanoparticle[7].

Iron oxide nanoparticle was transfer back into aqueous phase after PEG-silane functionalization, the hydraulic particle size of PEG-silane functionalized iron oxide was 78.03nm, with PDI 0.167. Molecular weight of PEG-silane is 2000, so the hydraulic particle size of PEG-silane functionalized SPIO is much large than that of oleic acid surface modified. After PEG-silane functionalization process, the iron oxide nanoparticle can be used as contrast agent with sterilization.

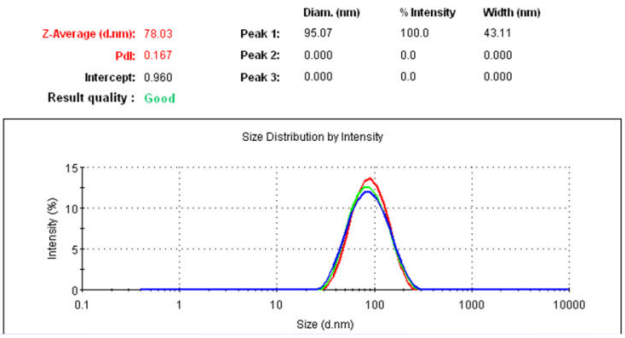


Fig. 6 DLS particle size distribution of aqueous phase PEG-Silane functionalized iron oxide nanoparticle

Magnetic property of iron oxide nanoparticle after PEG-silane functionalization was shown in Fig.7, the saturated

magnetization value was 65.8emu/g, and coercivity was 2.55 Hc, indicates that the magnetic properties changes little after PEG-silane functionalization process.

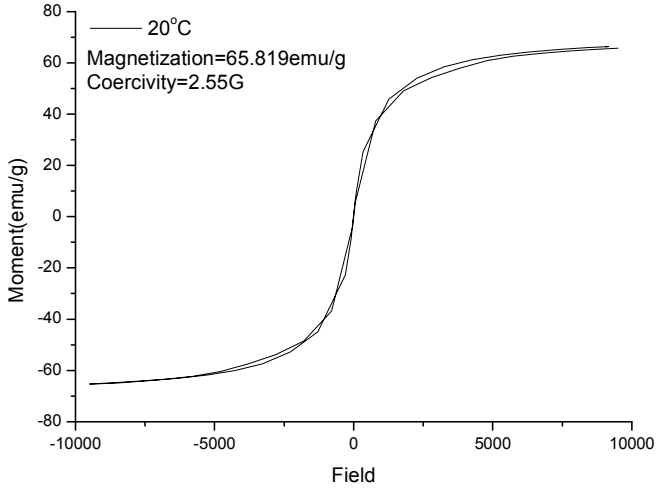


Fig.7 Hysteresis cycle of PEG-Silane functionalized iron oxide nanoparticle

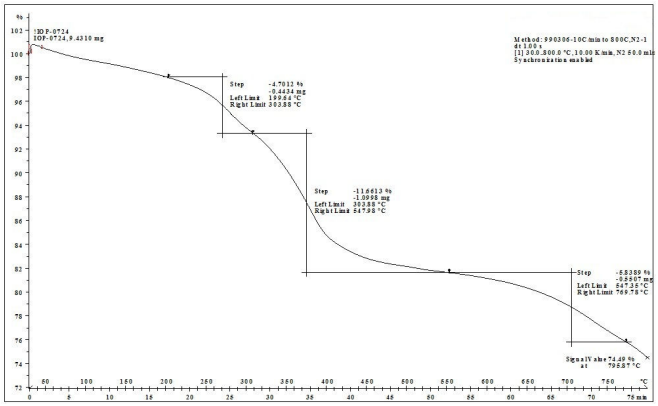


Fig. 8 TGA weight loss of PEG-Silane functionalized iron oxide nanoparticle

TGA weight loss curve of PEG-silane functionalization iron oxide nanoparticle was shown in Fig.8.The shape and weight loss ratio of temperature 200-400°C was changed after PEG-silane functionalization, implies the mono-dentate oleic acid was replaced by PEG-silane, but 600-800°Cchanges little withPEG-silane functionalization, means that bi-dentate oleic acid remains in the surface of iron oxide nanoparticle.

Relaxivity of PEG-silane functionalized iron oxide nanoparticlewas obtained by NMR relaxometer, the R2 value was in the range of 202~229 (sec^{-1}), higher than the reported value of other contrast agents [8].

IV. Conclusion

The higher relaxation rate R2 implies that this contrast agent will be more sensitive in MRI scan; the smaller particle size makes it easier uptake by macrophage.

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