

Synthesis and characterization of water-dispersible core/shell Mn-doped magnetite/Au nanoparticles for proton radiotherapy

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1. Introduction

Advances in magnetite nanoparticle synthesis have promoted research into new applications, including electronic devices, magnetic fluid, bio-imaging, and cancer therapy using high hyperthermic effects [1-4]. In order to enhance its magnetic and other attractive properties, metal-doped magnetite has been studied using various starting materials such as metal chlorides and metal acetylacetonates (acac) [5,6]. Recently metallic nanoparticles have been shown for therapeutic applications in radiation oncology [7].

The surface modification of the nanomaterials is required for the biomedical use to give physiological stability, surface reactivity and targeting properties. Among many approaches for the surface modification with materials, such as polymers, organic ligands and metals, one of the most attractive ways is to employ metals. The fabrication of metal-based, monolayer-coated magnetic nanoparticles has been intensively studied. However, the synthesis of metal-capped magnetic nanoparticles with monodispersities and controllable sizes is still challenged.

Recently, gold-capped magnetic nanoparticles have been reported to increase stability and to provide biocompatibility [8]. Gold-coated magnetic nanoparticles are an attractive system, which can be stabilized in biological conditions and readily functionalized through well-established surface modification chemistry. In addition, the Au coating offers plasmonic properties to magnetic nanoparticles. This makes the magnetic/Au core/shell combinations interesting for magnetic and optical applications.

In these studies, manganese-doped magnetite nanoparticles ($\text{Mn}:\text{Fe}_3\text{O}_4$) as core nanoparticles have been synthesized with well-controlled size. Core/shell $\text{Mn}:\text{Fe}_3\text{O}_4/\text{Au}$ nanoparticles were transferred from organic to aqueous solutions for biomedical applications. The synthesis and characterization of the core/shell nanoparticles have demonstrated.

2. Methods and Results

2.1 Synthesis of Mn-doped magnetic nanoparticles

$\text{Mn}:\text{Fe}_3\text{O}_4$ nanocrystals were prepared with a thermal decomposition method [6]. Briefly, to prepare monodisperse $\text{Mn}:\text{Fe}_3\text{O}_4$ nanoparticles, $\text{Mn}(\text{acac})_2$ and $\text{Fe}(\text{acac})_3$ were mixed in benzyl ether with 1,2-

hexadecanediol, oleic acid and oleylamine under nitrogen gas. The solutions were heated to reflux for 1 h. After cooled to room temperature, ethanol was added to the reaction mixture to precipitate the magnetic nanoparticles for the characterization. The resulting solutions were centrifuged to give 7-nm $\text{Mn}:\text{Fe}_3\text{O}_4$ nanocrystals. X-ray photoelectron spectra (XPS), shown in Fig. 1, verify Mn doping in the nanoparticles.

As shown in Fig. 2A, TEM analysis was performed with the resulting product dissolved in hexane.

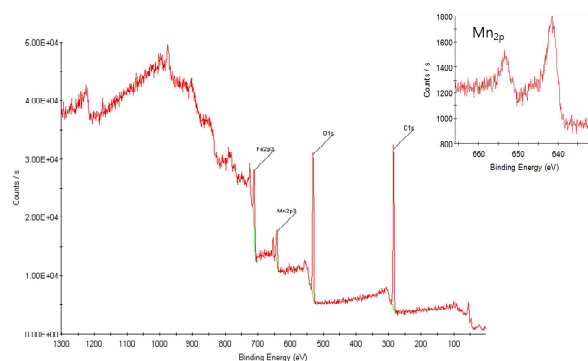


Fig. 1. XPS survey spectrum of Mn-doped magnetite nanoparticles. The inset shows high-resolution XPS spectrum for Mn_{2p} peaks.

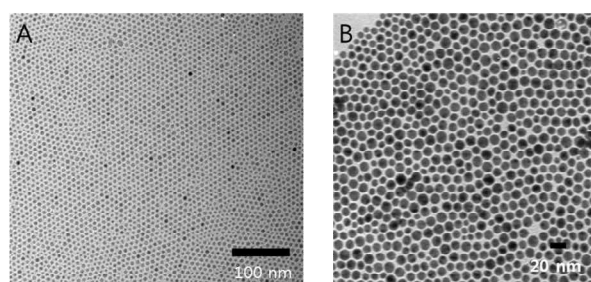


Fig. 2. TEM images of manganese-doped magnetic nanoparticles (A) and the gold-coated nanoparticles (B) in organic solvent.

2.2 Au coating of the Mn-doped magnetic nanoparticles

The resulting magnetic nanoparticles were used as seeds for gold coating. The reaction solution of magnetic nanoparticles in benzyl ether was mixed with gold acetate, oleic acid, oleylamine and 1,2-hexadecanediol [8]. Gold acetate as a gold source was added into the reaction mixture. Various ratios of gold acetate and core nanoparticles were tried to obtain uniform gold coating. The reaction solution was heated to $\sim 180^\circ\text{C}$ and was kept at this temperature for 1.5 h.

After cooled to room temperature, ethanol was added to the solution. The dark-purple materials were precipitated and separated by centrifuging. The resulting product was washed with ethanol and redissolved in hexane solutions to give 10-nm core/shell Mn:Fe₃O₄/Au nanocrystals (Fig. 2B).

2.4 Phase transfer of the core/shell nanoparticles

Poly(maleic anhydride-alt-1-octadecene) (PMAO) and primary amino group functionalized poly(ethylene glycol)methyl ether (mPEG-NH₂) were employed to transfer the nanoparticles from organic solvents to aqueous solutions. PMAO-PEG polymers were prepared by simply mixing PMAO and mPEG-NH₂ in chloroform at room temperature overnight [9]. FT-IR spectra showed the formation of PMAO-PEG as shown in Fig. 3. The hexane solutions containing Mn:Fe₃O₄/Au nanoparticles were removed and then the resulting nanoparticles were dispersed in 4 mL of chloroform. The core/shell nanoparticles and PMAO-PEG polymers dispersed in chloroform were mixed overnight at room temperature. The next day, chloroform was slowly removed by rotary evaporation at room temperature. When the core/shell nanoparticles in chloroform were mixed with the PMAO-PEG polymer solution rapidly, water-dispersible nanoparticles were aggregated during phase transfer as shown in Fig. 4A. When the nanoparticles were added to the polymer solutions dropwise, Mn:Fe₃O₄/Au nanoparticles were successfully transferred from an organic phase to an aqueous phase.

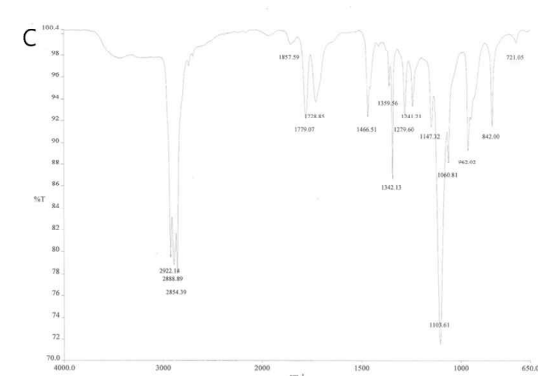
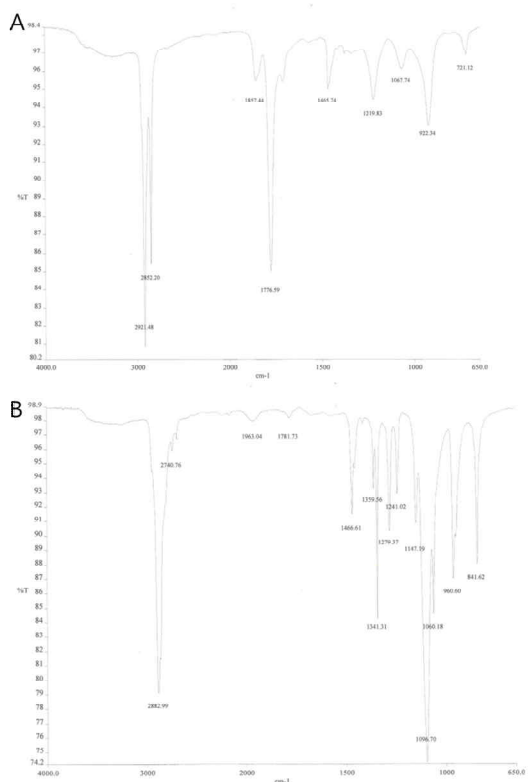


Fig.3. FT-IR spectra of PMAO (A), mPEG-NH₂ (B) and PMAO-PEG (C).

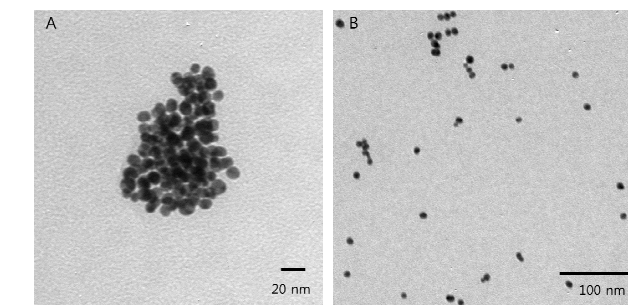


Fig.4. Aggregated Mn:Fe₃O₄/Au nanoparticles (A) during phase transfer and the well-dispersed nanoparticles (B) after phase transfer.

3. Conclusions

The monodisperse Mn:Fe₃O₄/Au nanoparticles have been prepared in organic solvent first and then transferred from an organic phase to an aqueous solution. The resulting core/shell-structured nanoparticles may be an attractive system for biomedical applications, which are needed both magnetic resonance imaging and optical imaging. In addition, the resulting nanoparticles may be useful for proton radiotherapy due to the enhanced therapeutic effects of secondary radiation stemmed from gold and proton beam bombardment [7]. The proton therapy study with the resulting Mn:Fe₃O₄/Au nanoparticles is undergoing.

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