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Synthesis of Fe_3O_4–$ZnS/AgInS_2$ Composite Nanoparticles Using a Hydrophobic Interaction

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Magnetic nanoparticles and fluorescent quantum dots (QDs) can make many effective applications in biomedical system. Here, we demonstrated one way of synthetic method and its surface modification to use for biomedical applications. Fe_3O_4 nanoparticles are well known as magnetic materials and its magnetic property can be used in magnetic resonance imaging (MRI), cell detection. QDs as a fluorescent probes, make cell labeling and *in vivo* imaging possible. $ZnS/AgInS_2$ QDs have a lower toxicity than other QDs (CdSe, CdTe, CdS). We combined two nanoparticles by hydrophobic interaction in their ligands. The prepared fluorescent magnetic composite particles were modified with CTAB-TEOS. The surface modified composite has a low cytotoxicity and these biocompatible particles will provide many possibilities in biomedical system.

Keywords: Multifunctional Particle, Fe_3O_4, Quantum Dots, Hydrophobic Interaction.

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1. INTRODUCTION

Nano-Technology is most interest parts in recent research field. Many utilized inorganic nanoparticles for biomedical applications have advanced very quickly due to their unlimited potentials. So, these materials are affecting nano-bio fusion technology also. Among these functional materials, Quantum dots (QDs) is an important materials as fluorescent probes. The QDs have found increased bio-applications for cell labeling, tracking of cell migration, and *in vivo* imaging.[1–3] The QDs have fairly broad excitation spectra from ultraviolet to red that can be tuned depending on their size and composition. At the same time, QDs have narrow emission spectra, making it possible to resolve the emission of different nanoparticles simultaneously and with minimal overlap. Finally, QDs are highly resistant to degradation, and their fluorescence is remarkably stable.[4,5] A magnetic nanoparticles (MPs) are also important in fusion research. It is possible to incorporate the sufficient amount of superparamagnetic iron oxide (SPIO) nanoparticle into cells, enabling their detection *in vivo* magnetic resonance imaging (MRI).[6,7] Because of their small size, they are easily incorporated into various cell type (stem cells, phagocytes etc.) allowing the cells to be tacked *in vivo*.

The recent development of multifunctional nanostructure has attracted increased attention because of their advantage properties. The combination of fluorescent QDs and MPs has led to new applications in biomedical systems. These features could lead to effective ways to probe specific functions of bioactive molecules in localized domain or compartments of living cells without disturbing other parts of the cell.[8–10]

In this article we report the design and characterization of multimodal imaging agent. The bimodal nanoparticle, Fe_3O_4–$ZnS/AgInS_2$ composite nanoparticles, was synthesized and provided both ^{1}H-based MRI and fluorescence imaging capabilities. The Fe_3O_4–$ZnS/AgInS_2$ nanoparticles are fabricated superparamagnetic core Fe_3O_4 and $ZnS/AgInS_2$ located at core surface. We developed new approach of synthetic technique of multifunctional nanoparticles by hydrophobic interaction between MPs and QDs. Ying's group have studied this method but did not make mention of its cytotoxicity test for bio-applications, just focused on their synthetic methods.[11] Hydrophobic interface of composite changed to hydrophilic surface by well known cetyltrimethylammonium bromide (CTAB)/tetraethylorthosilicate (TEOS)

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method. Synthesized composites have low cytotoxicity and other applications will be possible.

2. EXPERIMENTAL DETAILS

2.1. Synthesis of 13 nm Fe_3O_4 Nanoparticle

$Fe(acac)_3$ (2 mmol), 1,2-hexadecandiol (10 mmol), oleic acid (6 mmol), oleylamine (6 mmol), and octyl ether (15 mL) were mixed and magnetically stirred under a flow of nitrogen. The mixture was heated to 200 °C for 30 min and then, under blanket of nitrogen, heated to 265 °C for another 60 min. The black mixture was cooled room temperature by adding ethanol (20 mL) and removing heat source. The black material was precipitated and separated via centrifugation (17,000 rpm, 15 min). The product was dissolved in hexane. Centrifugation was applied to remove unreactive residues with ethanol (20 mL).

2.2. Synthesis of ZnS/$AgInS_2$ Quantum Dots

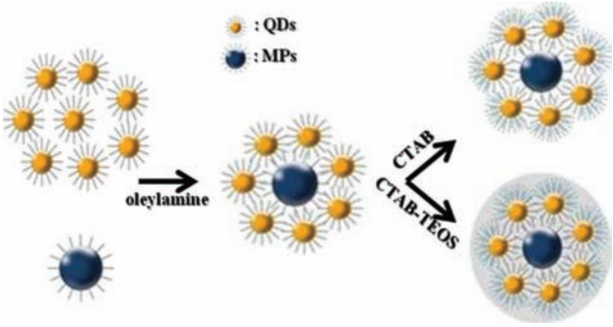
For manufacturing the bluish green quantum dot $Zn(NO_3)_2 \cdot 6H_2O$ (1.25 mmol), $AgNO_3$ (0.062 mmol), $In(NO_3)_3 \cdot 3H_2O$ (1.188 mmol) were dissolved in H_2O. $C_5H_{10}NNaS_2$ (5 mmol) was partially dissolved in H_2O. Two solutions were dropped in H_2O (50 mL). The precipite was filtered and dried. The precipite was added in 200 °C dodecylamine and heated for 60 min. Yellow mixture was cooled at room temperature by adding chloroform (10 mL) and removing heat source. Washing with methanol (10 mL) two times, and redispersed in chloroform (10 mL). In a similar fashion, orange QD was synthesized from $AgNO_3$ (0.375 mmol), $In(NO_3)_3 \cdot 3H_2O$ (0.875 mmol) and orange-red QD from used $AgNO_3$ (0.625 mmol), $In(NO_3)_3 \cdot 3H_2O$ (0.625 mmol). Green QD was synthesized from $AgNO_3$ (0.125 mmol), $In(NO_3)_3 \cdot 3H_2O$ (1.125 mmol) and $Zn(NO_3)_2 \cdot 6H_2O$ (1.25 mmol) in contrast to other QDs.

2.3. Synthesis of Fe_3O_4–ZnS/$AgInS_2$ Composite Particles

The Fe_3O_4 (5 mg) was dissolved in $CHCl_3$ (10 mL) was added to oleylamine (15 mmol). After vigorous stirring of resulting solution, 9.5 mM of ZnS/$AgInS_2$ (2 mL) was added to the solution. Then final solution was heated at 50 °C for 24 hours with vigorous stirring. The precipitate was collected by external magnet and centrifugation. Finally, the solution was washed with chloroform and methanol for 2 times.

3. RESULTS AND DISCUSSION

Scheme 1 shows the fabrication steps of Fe_3O_4–ZnS/$AgInS_2$ FMP and its surface modifications. To combine QDs and MPs, we use the hydrophobic interaction between them with oleylamine. There were some researches about hydrophobic combination of organic molecules on nanocrystal surface.[11,12] Ying et al. studied about one-pot synthesis of Fe_2O_3–CdSe nanocomposites but its surface modification could not confirm.[11] In our procedure, as prepared hydrophobic FMP was transferred to the hydrophilic FMP by mixing CTAB solution. And then, TEOS was added into aqueous CTAB-coated composite crystal solution with CTAB and sodium hydroxide.



Scheme 1. Preparation and surface modification of composite nanopaticles.

The fluorescence peaks of FMP were measured using fluorescence spectrometer (Fig. 1). The FMPs emit various wavelengths from 495 nm bluish green to 590 nm orange-red. This will be able to make variety of cell labeling and so on. The FMPs could collect by external magnet. Because of Fe_3O_4 nanoparticle core, composite particles were aggregated to the magnet side and still emit their original emissions.

We presents X-ray diffraction pattern of Fe_3O_4–ZnS/$AgInS_2$ composite particles to characterize its crystal structures at Figure 2. Fe_3O_4, ZnS, and $AgInS_2$ correspond with JCPDS nos. 98-0073, 80-0020 and 25-1328. The magnetic measurement of FMPs were studied by superconducting quantum interference device (SQUID) magnetometry (Fig. 2). The FMPs show superparamagnetic at room temperature. Field-dependent saturation magnetization (M_s) of Fe_3O_4 and Fe_3O_4–ZnS/$AgInS_2$ were 35 and 17 emu·g^{-1},

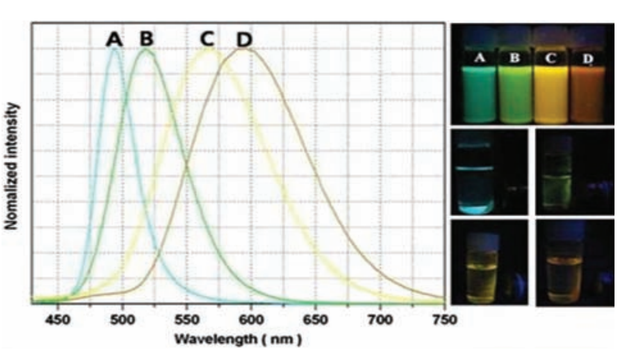


Fig. 1. The PL spectra of composite particles (left) and its fluorescent images with the magnet (right) under 365 nm UV light excitation (ratio of Ag/In: (A) 0.05, (B) 0.11, (C) 0.43, (D) 1).

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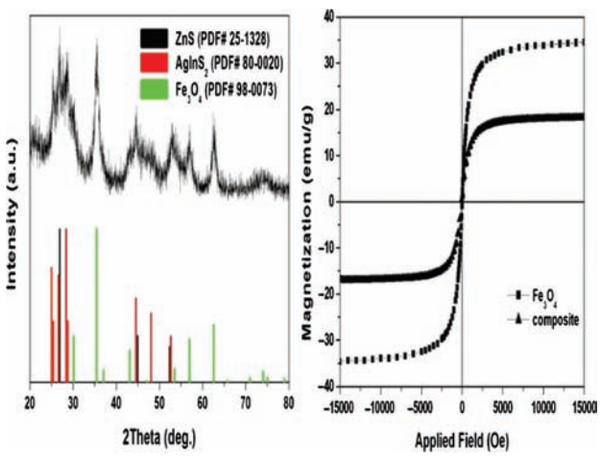

Fig. 2. The XRD patterns of composite particles (left) and magnetic characterization of the Fe_3O_4 and composite particles (right): magnetization versus magnetic field at room temperature.

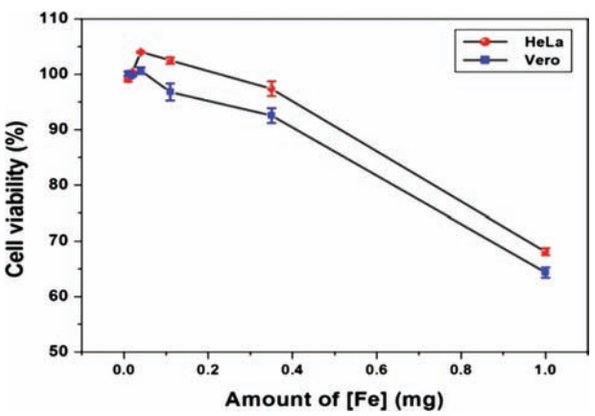

Fig. 4. *In vitro* cytotoxicity of the FMPs in HeLa and Vero cells. Cells were incubated with the FMPs for 24 h at 37 °C and the viability of the cells were evaluated with increasing concentrations of the Fe amounts ranging from 0.01 to 1 mg using an MTT assay.

respectively. There must be a magnetic quenching by QDs. The QDs shells decrease the total magnetization of composite particles. So FMPs decreased M_s value compared with original Fe_3O_4 nanoparticles.

Figure 3 shows the TEM images for oleylamine-capped 6 nm ZnS/$AgInS_2$ nanoparticles (3(a)) and 13 nm Fe_3O_4 nanoparticles (Fig. 3(b)). A size difference between MPs and QDs defines individual particles in composite structures. Figure 3(c) presents a large area TEM image of FMPs and its HRTEM image in Figure 3(d). The 13 nm MPs located at the center and combined with more than one QDs particle. In Figure 3(d), center of Fe_3O_4 and other ZnS/$AgInS_2$ nanoparticles could confirm its lattice planes {311} of Fe_3O_4 and {121} of ZnS/$AgInS_2$.

A cell cytotoxicity assay was conducted to confirm whether the FMPs damage the cells or not. Different doses (0.01, 0.02, 0.04, 0.11, 0.33 and 1 mg) of FMPs were used for *in vitro* cytotoxicity tests with Vero (African green monkey kidney) and HeLa (human cervical carcinoma) cells. Cell viability of the FMPs by MTT assay was shown in Figure 4. After incubation for 24 h, the residual FMPs were removed and a MTT solution was added to each well. The absorbances at dual wavelength were measured with microplate reader. The data revealed that the FMPs were not toxic over a broad range of concentration (CC_{50}) of >1 mg, indicating the suitability of thses nanoparticles for biological applications. Also, the FMPs has low cytotoxicity compared with conventional nanoparicles.

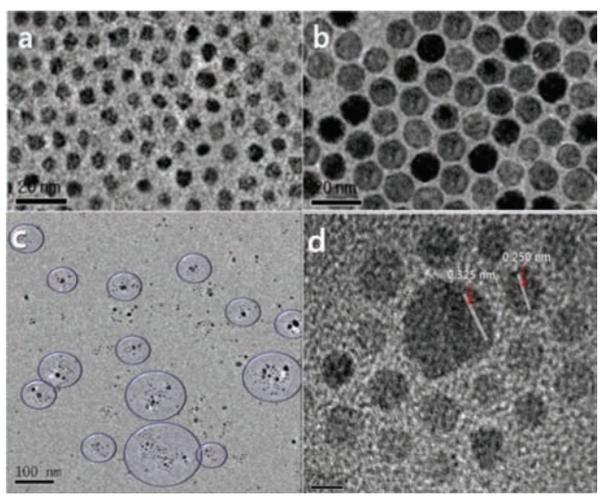

Fig. 3. The TEM images of QDs (a), MPs (b), FMP (c) and HRTEM images of FMP (d) with {311} direction of Fe_3O_4 (center) and {110} direction of ZnS–$AgInS_2$ (outer).

4. CONCLUSION

We have described a facile synthesis of multifunctional nanocomposite particles combine with Fe_3O_4 and ZnS/$AgInS_2$ nanopaticles. Prepared individual nanocrystal attached each other by hydrophobic interaction. Its surface was modified with CTAB and TEOS. This composite nanoparticle has some advantages, (i) synthetic method is very simple and can be easily revival, (ii) it has low cytotoxicity and composite particle was bio-compatible. We will continue this study to make MPs core and QDs shell structure by modified synthetic method.

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RESEARCH ARTICLE

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