Hydrothermal synthesis of superparamagnetic and red luminescent bifunctional Fe$_3$O$_4$@Mn^{2+}-doped NaYF$_4$:Yb/Er core@shell monodisperse nanoparticles and their subsequent ligand exchange in water

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ABSTRACT

We report the use of an efficient hydrothermal method to synthesize superparamagnetic and red luminescent bifunctional Fe$_3$O$_4$@Mn^{2+}-doped NaYF$_4$:Yb/Er nanoparticles (NPs) with core@shell structures via a seed-growth procedure. Oleic acid coated Fe$_3$O$_4$ (OA-Fe$_3$O$_4$) NPs were initially synthesized using a coprecipitation method. The as-synthesized OA-Fe$_3$O$_4$ NPs were then used as seeds, on which the red upconversion luminescent shell (Mn^{2+}-doped NaYF$_4$:Yb/Er) was formed. Furthermore, hydrophobic to hydrophilic surface modification of the Fe$_3$O$_4$@Mn^{2+}-doped NaYF$_4$:Yb/Er NPs was achieved via a ligand exchange method where oleic acid was displaced by a PEG phosphate ligand [PEG = poly(ethylene glycol)]. These materials were characterized by means of transmission electron microscopy (TEM), X-ray diffraction (XRD), photoluminescence (PL) spectroscopy, and vibrating sample magnetometry (VSM). The Fe$_3$O$_4$ cores were uniformly coated with a Mn^{2+}-doped NaYF$_4$:Yb/Er shell, and the bifunctional Fe$_3$O$_4$@Mn^{2+}-doped NaYF$_4$:Yb/Er NPs were monodispersed. Furthermore, the Fe$_3$O$_4$@Mn^{2+}-doped NaYF$_4$:Yb/Er NPs exhibited a saturated magnetization value of 6.2 emu/g and emitted red luminescence under a 980 nm laser. The obtained bifunctional Fe$_3$O$_4$@Mn^{2+}-doped NaYF$_4$:Yb/Er NPs may find potential applications in drug targeting, bioseparation, and diagnostic analysis. The synthetic method may be employed for the preparation of other bifunctional nanomaterials.

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1. Introduction

Bifunctional magnetic and luminescent nanomaterials have received considerable attention in the past decades, as these materials hold great promise for biomedical applications such as drug delivery [1–3], diagnostic analysis [4], and multimodal imaging [5–8].

Among the various luminescent materials, lanthanide-doped upconversion nanoparticles (UCNPs), which can convert long wavelength near-infrared (NIR) radiation into a visible or NIR emission through an upconversion process, have received a growing amount of interest [9–17]. Compared with the traditionally used downconversion fluorescent materials, UCNPs exhibit higher signal-to-noise ratios, lower photodamage, and deeper tissue penetration, rendering them ideal for use as luminescent probes in biological labeling and imaging technology [9–17]. However, in vivo bioimaging based on UCNPs as luminescence probes remains limited due to the strong tissue absorption of short wavelength light (<600 nm) [18,19]. To overcome these shortcomings, a method for achieving single-band red emission is of significant importance for bioimaging [20–25]. Recently, the Zhao group presented a facile strategy for the rational manipulation of green and red upconversion luminescence (UCL), with the pure dark red emission (650–670 nm) of NaYF$_4$:Yb/Er UCNPs being achieved by doping with manganese ions (Mn^{2+}) [20,21]. The red UCL of the Mn^{2+}-doped NaYF$_4$:Yb/Er UCNPs was largely improved and its intensity was significantly enhanced (15×) compared to the Mn-free sample. These features render it an ideal nanoplatform for biological labeling [20–25]. Magnetic nanoparticles (MNPs) are another attractive material for bioimaging and actuation because they can be manipulated using external magnetic fields [26–29]. Iron oxide NPs, in particular magnetite (Fe$_3$O$_4$), are a prominent class of MNPs that can be applied in drug delivery and magnetic resonance imaging [26–30]. In recent years, much effort has been applied to designing

and fabricating bifunctional magnetic upconversion NPs by combining with Fe_3O_4 NPs and UCNPs [6–8,31–43]. Such NPs can offer not only dual modal bioimaging, such as UCL imaging and magnetic resonance imaging (MRI), [6–8,32–35,39–41] but can also serve as magnetic targeted "smart" drug delivery systems [8,35,42]. Up to date, four strategies have been explored to fabricate the bifunctional magnetic upconversion NPs: using mesoporous silica as an intermediate layer to combine UCNPs with Fe_3O_4 NPs [31–33], polymer encapsulation [34,35], ligand crosslinking [36], and direct seed nucleation [37–41]. This seed-growth method can be applied to construct many kinds of hybrid magnetic nanomaterials by using a magnetic nanoparticle as a seed on which a second component can nucleate and grow [44–47]. For example, Colvin' group developed Fe_3O_4/CdSe and Fe_3O_4/ZnS NPs and explored the morphology of the structures by controlling various experimental conditions [44]. Our group developed an easy synthetic procedure for growing Au nanoshell on Fe_3O_4 superparamagnetic NP seeds under mild conditions [46]. Lin's group prepared monodisperse magnetic and upconversion luminescent NPs using the Fe_3O_4 NPs as seeds [38]. The seed-growth method proposes a novel approach to assemble magnetic bifunctional nanocomposite and offers products with a small size, homogeneous structure, and tunable stoichiometry [37–47].

We herein report a seed-growth procedure to synthesize a new type of core@shell structured NP composed of a magnetite core and red upconversion luminescent shell. Each component in the nanocomposite displays a unique function. The Fe_3O_4 core endows nanocomposites with magnetic properties, while the outer Mn^{2+}-doped $NaYF_4$:Yb/Er shell gives the red UCL. The overall synthetic procedure is illustrated in Scheme 1. Firstly, the monodispersed oleic acid coated Fe_3O_4 (OA-Fe_3O_4) NPs cores are prepared. Subsequently, a simple hydrothermal method is used to form a uniform Mn^{2+}-doped $NaYF_4$:Yb/Er layer on the surface of the Fe_3O_4 NPs through a seed-growth procedure to obtain the target oleic acid coated core@shell NPs (Fe_3O_4@Mn^{2+}-doped $NaYF_4$:Yb/Er NPs). Finally, the resulting hydrophobic Fe_3O_4@Mn^{2+}-doped $NaYF_4$:Yb/Er NPs are rendered hydrophilic via a ligand exchange process, where the oleate is displaced by a PEG phosphate ligand [PEG = poly(ethylene glycol)]. This straightforward route may be applicable to the preparation of other bifunctional core@shell NPs.

2. Experimental

2.1. Materials

All chemicals were of analytical grade and used as received without further purification. Deionized water was used throughout. Yttrium nitrate hexahydrate (99.99% trace metals basis), Ytterbium nitrate (99.99% trace metals basis) and erbium trinitrate pentahydrate (99.95% trace metals basis) were supplied by Best Chemical Reagent Co., Ltd. (Chengdu China). Oleic acid (technical grade, 98.0%), sodium fluoride (reagent grade, 98.0%), sodium hydroxide (reagent grade, 96%), tetrahydrofuran (technical grade, 99.0%), ethanol (reagent grade, 99.7%), ferric trichloride hexahydrate (reagent grade, 99.0%), manganese dichloride tetrahydrate (reagent grade, 98.0%) were supplied by Kelong Chemical Technology Co., Ltd. (Chengdu China). Toluene (reagent grade, 99.5%), chloroform (reagent grade, 99.0%) and n-hexane (reagent grade, 95.0%) were purchased from Ruijinte Chemical Technology Co., Ltd. (Tianjin China). Phosphorus oxychloride (reagent grade, 98.5%), ferrous sulfate heptahydrate (reagent grade, 99%) were supplied by Jinshan Chemical Technology Co., Ltd. (Chengdu China). Methoxypolyethylene glycol (Mw = 1000) were supplied by Aladdin company.

2.2. Synthesis of poly(ethylene glycol) phosphate ligand

The PEG-phosphate ligands were synthesized using a modified version of the previously reported procedure [48,49]. In a typical synthesis, 18.5 mmol of poly(ethylene glycol) methyl ether (mPEG) was dried by heating to 70 °C under a vacuum overnight. The dried mPEG was then dissolved in 60 mL of dry tetrahydrofuran (THF). The resulting solution was added dropwise to 18.5 mmol of phosphoryl trichloride ($POCl_3$) mixed with 10 mL of dry THF. The resulting clear solution was then stirred at room temperature for 6 h 5 mL cold water was added dropwise to the reaction mixture and left to react for 1 h to quench the reaction. The product was extracted with chloroform which then were removed on a rotary evaporator to obtain the product. The product was dried in a vacuum oven. The ^1H and ^{31}P NMR spectra of the PEG-phosphate were used to help confirm the formation of the desired products. PEG(2000)-phosphate ^1H NMR: δ($CDCl_3$) 3.68-3.60 (m, 178H, (-CH_2OCH_2-)n of the PEG), 3.36 (s, 3H, $-OCH_3$). ^{31}P NMR: δ ($CDCl_3$) 0.52 (s, $(RO)_2PO_2$), −0.01 (s, $ROPO_3$).

2.3. Preparation of oleic acid coated Mn^{2+}-doped $NaYF_4$:Yb/Er NPs

Mn^{2+}-doped $NaYF_4$:Yb/Er NPs were prepared according to the literature reported previously [20,22].

2.4. Synthesis of oleic acid coated Fe_3O_4@Mn^{2+}-doped $NaYF_4$:Yb/Er NPs

First the hydrophobic OA coated Fe_3O_4 NPs were prepared according to our previously reported procedure [50], which were dispersed in toluene for using in the next step. The as-prepared Fe_3O_4 NPs were used as seeds and covered with an red UCL shell by a facile hydrothermal method which was similar with the preparation of Mn^{2+}-doped $NaYF_4$:Yb/Er NPs [20,22]. In a typical procedure, 2.0 mL of 0.5 M $MnCl_2$, 3.33 mL of 0.5 M $Y(NO_3)_3$, 3 mL of 0.2 M $Yb(NO_3)_3$, and 0.33 mL of 0.2 M $Er(NO_3)_3$ water solution were added to a mixture of NaOH (0.99 g), a ml toluene dispersion of OA-Fe_3O_4 (10 mg/L), (5.04-a) ml toluene, OA (16.65 mL) and ethanol (33.3 mL) under stirring. Then 6.66 mL of deionized water containing 8 mmol NaF was then drop wisely added into the mixture. After vigorous stiring at room temperature for 30 min, the colloidal solution was transferred into a 100 mL Teflonlined autoclave, which was sealed and heated at 200 °C for 8 h, and then the mixture was cooled down to room temperature. The final product was collected by centrifugation and magneticseparation, and then washed with ethanol and deionized water for several times to remove any possible remnants. The obtained OA coated Fe_3O_4@Mn^{2+}-doped $NaYF_4$:Yb/Er NPs were dispersed in hexane. In this work, various amounts of Fe_3O_4 nanoparticles (a = 0.63 mL, 1.26 mL, 2.52 mL, 5.04 mL) were added in the reaction mixture to prepare the Fe_3O_4@Mn^{2+}-doped $NaYF_4$:Yb/Er NPs. The sample was denoted as x% Fe_3O_4@Mn^{2+}-doped $NaYF_4$:Yb/Er NPs, where the x is the molar ratio of Fe_3O_4 to Mn^{2+}-doped $NaYF_4$:Yb/Er calculated on the basic of the initial amount of Fe_3O_4 and rare earth nitrates. In this work, the 1.2% Fe_3O_4@Mn^{2+}-doped $NaYF_4$:Yb/Er (a = 0.63 mL), 2.4% Fe_3O_4@Mn^{2+}-doped $NaYF_4$:Yb/Er (a = 1.26 mL), 4.8% Fe_3O_4@Mn^{2+}-doped $NaYF_4$:Yb/Er (a = 2.52 mL) and 9.6% Fe_3O_4@Mn^{2+}-doped $NaYF_4$:Yb/Er (5.04 mL) NPs were prepared by tuning the amounts of Fe_3O_4.

2.5. Ligand exchange on Fe_3O_4@Mn^{2+}-doped $NaYF_4$:Yb/Er NPs with PEG-Phosphate ligands

Here ligand exchange method was used to prepare waterdispersable Fe_3O_4@Mn^{2+}-doped $NaYF_4$:Yb/Er NPs. For ligand