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Dextran-coated superparamagnetic amorphous Fe–Co nanoalloy for magnetic resonance imaging applications

Lu An [a], Yanrong Yu [a], Xuejian Li [a], Wei Liu [a], Hong Yang [a,*], Dongmei Wu [b], Shiping Yang [a,*]

[a] The Key Laboratory of Resource Chemistry of Ministry of Education & Shanghai Key Laboratory of Rare Earth Functional Materials, Department of Chemistry, Shanghai Normal University, Shanghai 200234, PR China

[b] Shanghai Key Laboratory of Magnetic Resonance, Department of Physics, East China Normal University, 3663 North Zhongshan Road, Shanghai 200062, PR China

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ABSTRACT

For magnetic resonance imaging applications, a facile approach for water-soluble dextran coated amorphous Fe–Co nanoalloy was developed. The as-synthesized nanoalloy had a diameter of 9 nm with a narrow size distribution and showed superparamagnetic property with a saturated magnetization (Ms) of 25 emu/g. *In vitro* cytotoxicity test revealed that it was biocompatible at a concentration below 120 μg/mL. It can be uptaken by HeLa cells effectively and resulted in the obvious T_2 effect after internalization. Biodistribution studies in conjunction with inductively coupled plasma-atomic emission spectroscopy (ICP-AES) confirmed that Fe–Co nanoalloy was preferentially accumulated in lung and spleen after intravenous injection for 4 h. *In vivo* MRI, dextran-coated Fe–Co nanoalloy can serve as a sensitive contrast agent for MR imaging, especially in the spleen, so we believe that it maybe hold great promise for diagnosis of splenic disease by appropriately functionalizing their surface.

1. Introduction

Magnetic resonance (MR) imaging is currently one of the most powerful diagnosis tools in medical science for imaging the brain and the central nerve system to assess cardiac function and detect tumors [1–4]. To obtain the high contrast and information-rich images for disease detection, contrast agents (CAs) play a prominent role in MR imaging. Generally, MR contrast agents must have a strong effect to accelerate longitudinal relaxation (T_1) of water and exhibit bright or positive contrast where they are localized, or to accelerate the transverse relaxation (T_2) and produce dark or negative-contrast images. Compared with conventional paramagnetic gadolinium complex-based contrast agents such as Magnevist, Prohance, and Dotarem, superparamagnetic nanoparticles (NPs) are emerging as the next generation magnetic probes for MR imaging because of their excellent magnetism and prolonged circulating time in the blood [5]. Since magnetic iron oxide NPs have been firstly reported as a liver contrast agent in 1986, many scientists have developed novel nanoparticulate contrast agents with improved contrasting ability and biocompatibility, targeting ability, and multifunctionality.

Transition metal nanoalloy is considered to be one of the most effective superparamagnetic NPs (*e.g.*, Fe_2O_3, Fe_3O_4, $MnFe_2O_4$, etc.) because of their high saturation magnetizations (Ms) [6–9]. Recently, Dai et al. reported FeCo NPs stabilized with single graphitic carbon shells for magnetic resonance imaging and near-infrared photothermal agent [10]. Yang et al. synthesized water-soluble FePt NPs of 3, 6, and 12 nm in diameter and applied them as a dual modality contrast agent for CT/MR molecular imaging [11]. Our group reported the use of monodispersed amphiphilic FePt NPs and water-soluble functionalized Fe–Ni NPs for MR imaging applications *in vitro* [12,13]. Recent advances have shown that amorphous nanoalloy (Fe–M, M = Cu, Co and Ni) has a very high magnetization and large relaxivity owing to their large magnetic spin magnitude [14,15]. However, there are no reports related to the use of amorphous nanoalloy as contrast agents for MR imaging applications.

To impart the stability and ensure the non-toxicity under physiological conditions, magnetic nanomaterials have been coated with different materials, which are required to be nonimmunogenic and nonantigenic [16]. Common biocompatible coatings including lipids, liposomes, proteins, dendrimers, and synthetic or natural macromolecules, such as polyethylene glycol (PEG), polyacrylamide, and polysaccharide-based materials were investigated [17,18]. As one of the extensively explored examples, dextran has been used in a range of biomedical applications because of its excellent aqueous solubility, biocompatibility, and nonfouling properties [19–22].

* Corresponding authors. Tel.: +86 21 64322343; fax: +86 21 64322511.
E-mail addresses: yanghong@shnu.edu.cn (H. Yang), shipingy@shnu.edu.cn (S. Yang).

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In this present paper, we developed a facile approach to prepare dextran-coated Fe–Co nanoalloy at room-temperature. Dextran is able to serve as a stabilizer to prevent its aggregation in the reaction medium, and simultaneously improve its biocompatibility. The morphology, structure, and magnetic property of Fe–Co nanoalloy were investigated by transmission electron microscopy (TEM), X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR), superconducting quantum interference device (SQUID), and relaxivity measurements. Its biocompatibility *in vitro* was evaluated by MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay of the viability of cells. To further explore its applications for MR imaging, cells treated with Fe–Co nanoalloy and the KM mice intravenously injected with Fe–Co nanoalloy were imaged by MR imaging.

2. Experimental

2.1. Preparation of amorphous Fe–Co nanoalloy

Firstly, dextran (1.00 g, 0.5 mmol) was added into 100 mL aqueous solution containing $FeSO_4{\cdot}7H_2O$ (0.278 g, 1.0 mmol), and $CoCl_2$ (0.130 g, 1.0 mmol). The mixture was stirred vigorously for 20 min to form a clear solution at 363 K. Then, 30 mL $NaBH_4$ (0.151 g, 4.0 mmol) aqueous solution was added dropwise into the above solution under vigorous stirring in nitrogen atmosphere at room temperature (25 °C). The resulting black solid was washed thoroughly with ethanol at 6000 rpm for three times and finally stored in ethanol until use.

2.2. Characterization

X-ray diffraction (XRD) measurements were performed by a Rigaku DMAX 2000 diffractometer equipped with Cu/Kα radiation at a scanning rate of 4°/min in the 2θ range of 30–80° (λ = 0.15405 nm, 40 kV, and 40 mA). Transmission electron microscope (TEM), selected area electronic-diffraction (SAED) images were obtained on a JEOL JEM 2010 electron microscope at an accelerating voltage of 200 kV. Samples for TEM analysis were prepared by spreading a drop of the as-prepared products diluted in ethanol on amorphous carbon-coated copper grids and then dried in air. Fourier transform infrared (FTIR) spectra were recorded on a Perkin-Elmer Spectrum one spectrometer. Hysteresis loop was measured with a vibrating sample magnetometer VSM-236 (Lake Shore, USA). The metal ion concentrations were quantified using an Optima 5300 DV inductively coupled plasma-atomic emission spectrometer (ICP-AES) (Perkin-Elmer, USA). T_2 relaxivities and MR imaging in PBS solution and cells were measured in a 0.5 T magnet (Shanghai Niumag Corporation ration NM120-Analyst, Shanghai, China) at room temperature. Relaxivity values (r_2) were calculated through the curve fitting of $1/T_2$ relaxation time (s^{-1}) *versus* the Fe concentration (mM).

2.3. Cell culture

A human cervical carcinoma cell line (HeLa cells) and normal liver cell line (L02) were provided by Shanghai Institutes for Biological Sciences (SIBS). HeLa cells were cultured in RPMI-1640 medium supplemented with 10% FBS (Fetal Bovine Serum) at 37 °C and 5% CO_2. Normal liver cells (L02) were cultured in DMEM medium supplemented with 10% FBS at 37 °C and 5% CO_2.

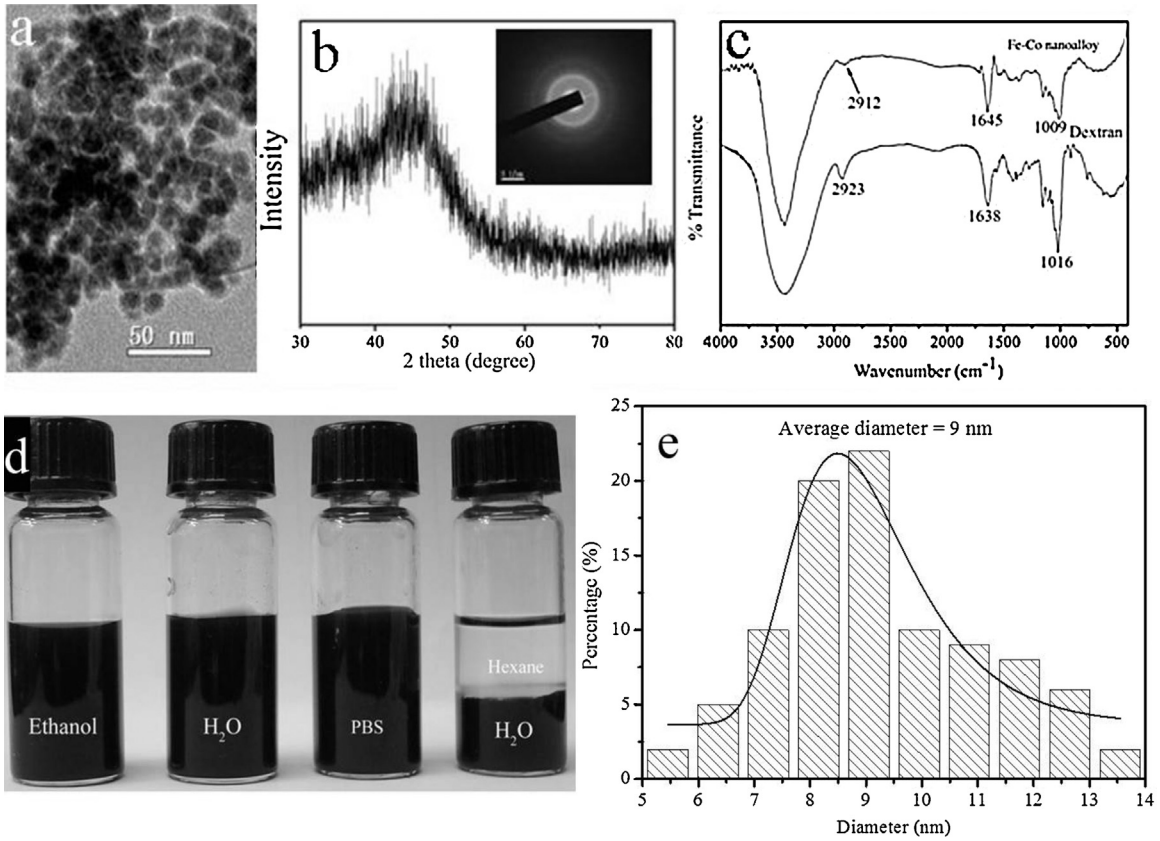

Fig. 1. TEM imaging (a), X-ray diffraction pattern (b, inset: selected area electronic-diffraction pattern), FTIR spectra (c), photographs in different solvents of as-synthesized amorphous Fe–Co nanoalloy (d, the concentration of the solution is 2 mg/mL) and the size distribution histograms of TEM imaging (e).