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Controlled synthesis of L-cysteine coated cobalt ferrite nanoparticles for drug delivery

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ABSTRACT

In the present work, we reported a facile synthesis of cobalt ferrite ($CoFe_2O_4$) nanoparticles in the presence of L-cysteine (Lys). The morphology and size of samples were characterized by SEM and TEM. The successful coating of Lys on the surface of $CoFe_2O_4$ was confirmed by XRD, XPS and TGA. The investigation of magnetic properties showed that both bare $CoFe_2O_4$ and Lys-coated $CoFe_2O_4$ nanoparticles exhibited room-temperature superparamagnetic behavior. The results of MTT experiments revealed insignificant cytotoxicity of Lys-coated $CoFe_2O_4$ nanoparticles even after 24 h incubation. More importantly, Lys-coated $CoFe_2O_4$ nanoparticles displayed an excellent drug loading capacity and a pH-sensitive drug release behavior. In summary, the prepared Lys-coated $CoFe_2O_4$ nanoparticles demonstrated a promising application potential in controlled drug delivery.

1. Introduction

Recently, cobalt ferrite ($CoFe_2O_4$) nanoparticles with spinel structure have drawn enormous attention due to their unique properties, such as large specific surface area, high saturation magnetization and controlled magnetic behavior [1–3]. In the technological fields, they have been propagated for environmental remediation, catalysis, adsorbent and lithium ion batteries [4–7]. One of the most promising potential applications of $CoFe_2O_4$ nanoparticles is medical diagnosis and therapy of diseases, such as magnetic resonance imaging (MRI), controlled drug delivery, magnetic hyperthermia and radiotherapy [8–10]. However, there are two disadvantages confronted in the real-time biomedical applications of these nanoparticles including their destabilization effect and nonspecific uptake by the reticulum-endothelial system (RES) [11]. In both cases, the nanoparticles will be quickly removed from the blood circulation systems, which usually results in dramatic reduction in the efficiency of nanoparticle-guided diagnostics and therapeutic applications [12,13]. To realize these biomedical applications, surface modification is necessary and meaningful to make $CoFe_2O_4$ nanoparticles more stable in the RES.

Various methods have been used to synthesize $CoFe_2O_4$ nanoparticles, such as co-precipitation, sol-gel, solvothermal, thermal decomposition and microemulsion [14–16]. These strategies provide many merits in the synthesis of $CoFe_2O_4$ nanoparticles with different morphologies and structures, however, in most cases the obtained $CoFe_2O_4$ nanoparticles are clined to form severe aggregation with nonuniform shape and wide size distribution. Compared with the aforementioned methods, the ultrasonic-assisted co-precipitation method is one of the most promising techniques for the synthesis of magnetic nanoparticles [17]. Due to their excellent biocompatibility and rich functional groups, biopolymers are explored to synthesize $CoFe_2O_4$ nanoparticles, such as dextran, pullulan, chitosan, poly (ethyleneglycol) (PEG), poly (ethyleneimine) (PEI), poly (vinyl alcohol) (PVA) and poly (vinyl pyrrolidone) (PVP) [18–22].

L-cysteine (Lys), also known as cysteine, is a semi-essential biocompatible amino acid of human body, which has special physiological functions in vivo. It has three active functional groups (-COOH, $-NH_2$ and -SH), which can be easily used for the conjugation of metal atoms [23,24]. Herein, an ultrasonic-assisted co-precipitation method was adopted in this study to synthesize $CoFe_2O_4$ nanoparticles with different concentrations of L-cysteine. The morphology, microstructure, composition and magnetic properties of $CoFe_2O_4$ nanoparticles were systematically investigated using different characterization techniques. The in vitro cytotoxicity was evaluated by MTT assays with varied concentrations and incubation time. Moreover, doxorubicin hydrochloride (DOX) was used as an anti-cancer drug model to examine the drug loading capacity and drug release behavior of Lys-coated $CoFe_2O_4$ nanoparticles.

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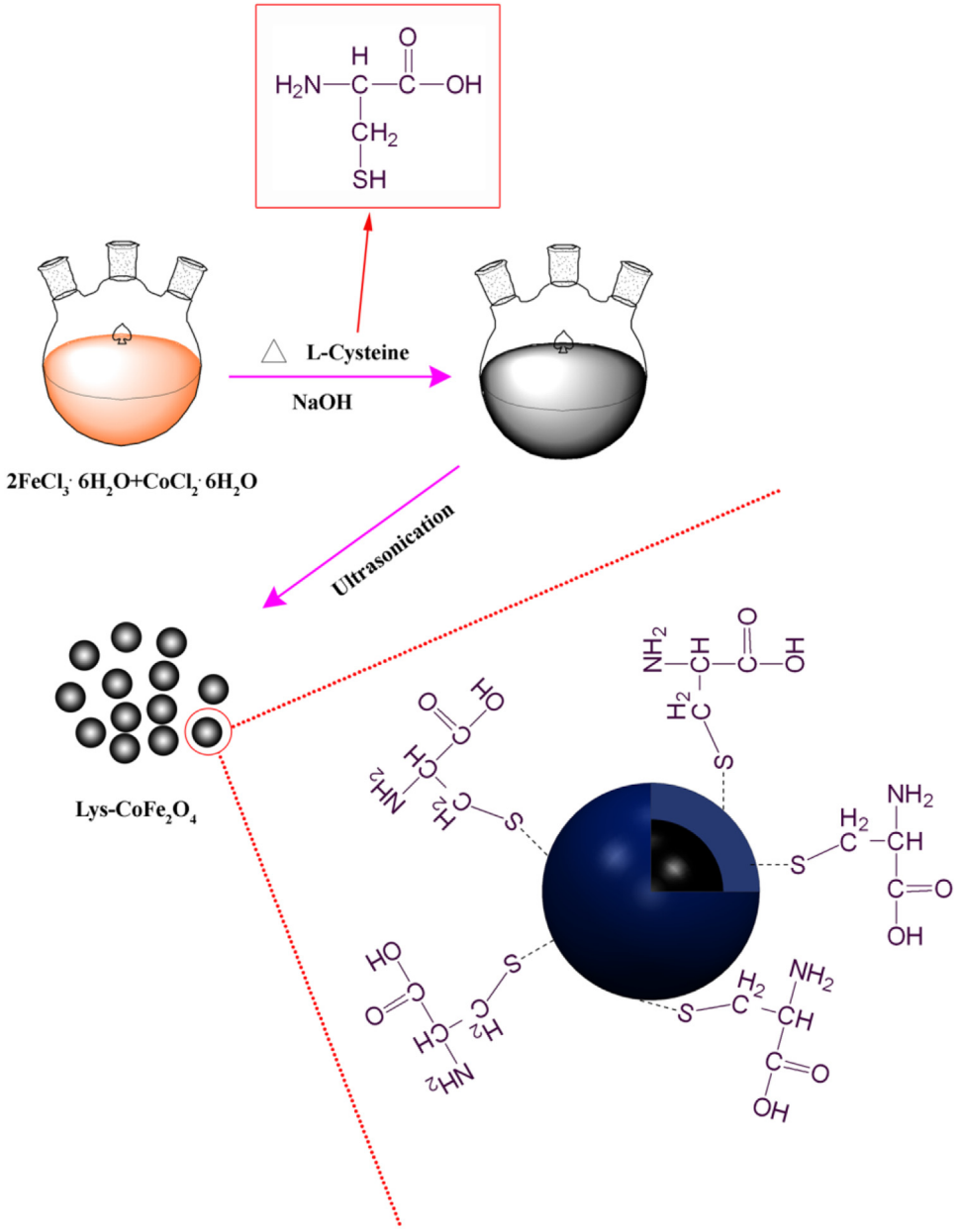

Fig. 1. Schematic representation of the synthesis for L-cysteine coated $CoFe_2O_4$ nanoparticles.

2. Experimental

2.1. Materials

$FeCl_3{\cdot}6H_2O$, $CoCl_2{\cdot}6H_2O$ and NaOH were of analytical grade and L-cysteine (Lys) was of biochemical grade. They were purchased from Sinopharm Chemical Reagent (Shanghai, China). Doxorubicin hydrochloride (DOX, > 99%) was obtained from J&K Chemical (Beijing, China). All reagents were used without further purification.

2.2. Synthesis of L-cysteine coated $CoFe_2O_4$ nanoparticles

L-cysteine coated $CoFe_2O_4$ nanoparticles were synthesized by an ultrasonic-assisted chemical co-precipitation method. In a typical experiment, $FeCl_3{\cdot}6H_2O$ (1.621 g, 6.0 mmol), $CoCl_2{\cdot}6H_2O$ (0.714 g, 3.0 mmol) and Lys (0.363 g, 3.0 mmol) were dissolved in deionized water under magnetic stirring. Then 25 mL NaOH solution (1.5 mol/L) was added dropwise into the uniform solution. After 30 min of stirring, the mixture was transferred to a self-made ultrasonic bath. The power and frequency of ultrasonic bath were 200 W and 20 kHz, respectively. The pH value was adjusted to 12 and the reactants were treated by ultrasonication for 60 min. The final products were collected by a strong magnet and rinsed with absolute ethanol and deionized water for several times. According to the mole ratio of L-cysteine and cobalt salt, the as-prepared samples were named as Lys-$CoFe_2O_4$-0.1, Lys-$CoFe_2O_4$-0.5 and Lys-$CoFe_2O_4$-1, respectively. For comparison, bare $CoFe_2O_4$ nanoparticles were synthesized in the absence of Lys following the same experiment procedure.

2.3. Characterization

The morphology was observed by a Zeiss Merlin scanning electron microscopy (SEM) and a Tecnai G2 F20 transmission electron microscopy (TEM). The crystal structure was characterized by a Rigaku Dmax-Ultima$^+$ X-ray diffractometer (XRD) with Cu-K_a radiation. The surface information was collected by a Thermo Scientific Escalab 250Xi