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Bifunctional magnetic nanoparticles for efficient cholesterol detection and elimination via host-guest chemistry in real samples

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ABSTRACT

Cholesterol is an essential compound for maintaining cellular homeostasis and human healthy. Sensitive detection of cholesterol and efficient elimination of excess cholesterol have become the essential manipulations in clinical diagnosis and health management. To date, it is still quite challenging that cholesterol detection and elimination tasks are carried out simultaneously. In this study, bifunctional magnetic nanoparticles (Fe_3O_4@PDA-PBA-CD) are designed and fabricated to overcome this difficulty. Taking advantages of competitive host-guest interaction and magnetic separation, highly efficient, reusable and simultaneous cholesterol detection and elimination can be achieved. The limit of detection is determined to be 4.3 nM, which is comparable or even lower than existing methods. The distinguished performance may attribute to the high loading efficiency and magnetic enrichment of nanoparticles. Besides, this efficient strategy is resistant to interfering substances, thus realizing sensitive cholesterol detection in real sample. Simultaneously, the bifunctional magnetic nanoparticles also have up to 95% cholesterol elimination efficiency, which is higher than previous reported methods. Furthermore, the nanoparticles are turned out to be reusable within 5 times without noticeable loss in cholesterol elimination efficiency. Therefore, the bifunctional magnetic nanoparticles fabricated here could hold great potential for simultaneous cholesterol detection and elimination in practical applications.

1. Introduction

Cholesterol is an essential compound for maintaining cellular homeostasis and human healthy, which is responsible for the integrity of biologic membrane and serves as the sole precursor to all steroid hormones (Ikonen, 2008; Radwan and Alanazi, 2014). Abnormal cholesterol distribution or metabolism has been demonstrated as a possible linkage to various diseases, including cardiovascular disease, mental disorders and cancer (Helgadottir et al., 2016; Lin et al., 2015; Valenza et al., 2005). In humans, the main external source of cholesterol is food of animal origin such as milk and egg yolk products, so many consumers are concerned about excessive cholesterol intake. Consequently, sensitive detection of cholesterol and efficient elimination of excess cholesterol have become the essential manipulations in clinical diagnosis and health management (Li et al., 2017).

To date, the majority of cholesterol detection and elimination tasks have been performed separately. Various analytical techniques for cholesterol detection, such as HPLC (Dominguez et al., 2018), molecular imprinting (Liu et al., 2017), electrochemical analysis (Huang et al., 2018), fluorescent (Hassanzadeh et al., 2018) or colorimetric assay (Kim et al., 2015) have been developed. Most of them are high cost, time-consuming and require sophisticated instruments or natural enzymes (Gahlaut et al., 2018; Gallego et al., 2018; Semwal and Gupta, 2018). In order to attain convenient assay, more attention is paid to develop non-enzymatic approaches. Different materials including graphene, carbon nanotubes, gold nanoparticles, upconversion nanoparticles, have been used for fabricating non-enzymatic cholesterol sensors (Ding et al., 2014; Gilbert et al., 2017; Sun et al., 2017a; Zhang et al., 2008).

In addition to the efforts devoted to cholesterol detection, many methods have been developed to remove cholesterol by using physical, chemical and biological strategies (Sinha et al., 2015). Among them, β-cyclodextrin (β-CD) based approach is found to be one of the most effective method (Mahammad and Parmryd, 2015). Nonetheless, difficulty in β-CD recovery may lead to security problems and excess consumption (Su et al., 2015). Therefore, magnetic materials are good

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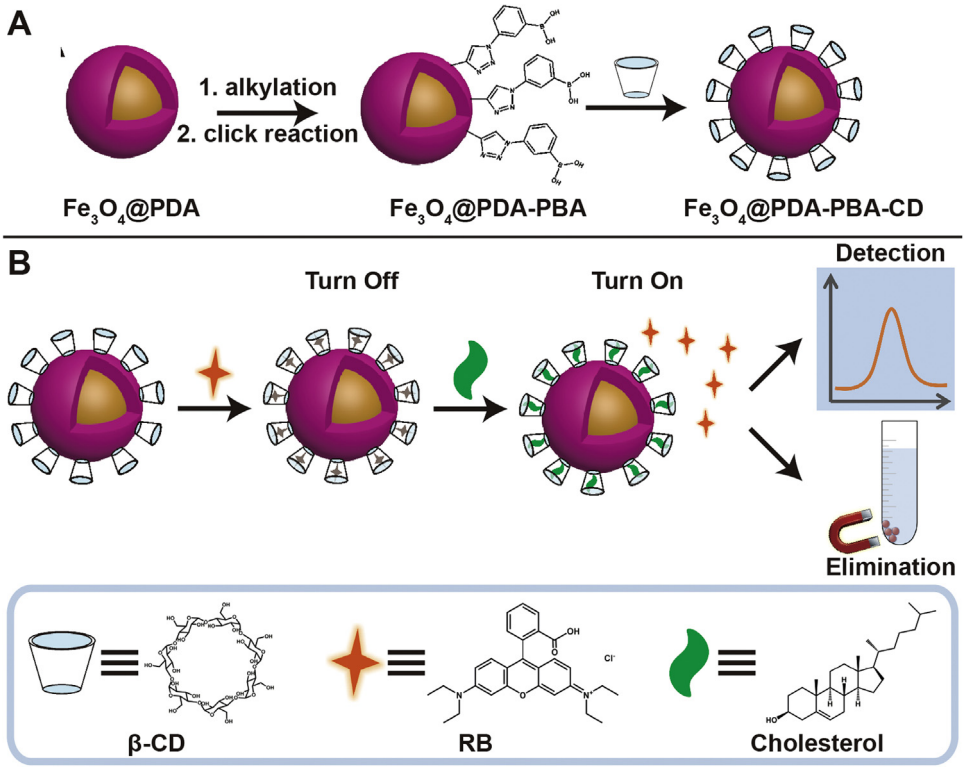

Fig. 1. Schematic illustration of (A) the synthesis of RB loaded Fe_3O_4@PDA-PBA-CD NPs and (B) their application in cholesterol detection and elimination under magnetic field.

candidates for enabling the recycling of β-CD (Sinha et al., 2015; Sun et al., 2018). Although there are enormous efforts in developing cholesterol separation via magnetic materials, it is still quite challenging that cholesterol detection and elimination tasks have been performed simultaneously. Hence, an efficient strategy for cholesterol detection and elimination remains a desirable goal.

Inspired by the advantages of host-guest interaction (Wu et al., 2015; Zheng et al., 2014) and magnetic separation (Ma et al., 2014), we develop an efficient strategy for simultaneous cholesterol detection and elimination based on bifunctional magnetic nanoparticles. In virtue of host-guest reaction between β-CD and cholesterol, highly sensitive and specific detection as well as efficient and reusable elimination of cholesterol can be achieved under magnetic field. As depicted in Fig. 1A, Fe_3O_4 NPs are firstly synthesized with a polydopamine (PDA) coating layer, which provided an interface for subsequent chemical modification and acted as the fluorescent quencher (Lin et al., 2014). Next, phenylboronic acid (PBA) molecules are modified on Fe_3O_4@PDA NPs via "click reaction" as our previously reported method to obtain Fe_3O_4@PDA-PBA NPs (Zheng et al., 2015). Then, β-CD molecules are allowed to attach onto Fe_3O_4@PDA-PBA NPs spontaneously at the physiological pH through PBA/CD coupling interaction (Yang et al., 2014). Finally, competitive host-guest interaction between β-CD with cholesterol and fluorescent dyes is utilized for cholesterol detection with Fe_3O_4@PDA-PBA-CD NPs (Fig. 1B). As a proof-of-concept, rhodamine B (RB) molecules are preloaded into β-CD cavity with the fluorescence quenched due to the close contact with PDA. In the presence of cholesterol, the competitive inclusion of guest molecules in β-CD moiety gives rise to the release of RB molecules, accompanying by the recovery of fluorescence. Incorporating the magnetic property of Fe_3O_4 NPs, cholesterols could be enriched and separated from the sample solution quickly. In this way, cholesterol detection and elimination can be achieved simultaneously using the bifunctional magnetic nanoparticles.

2. Experimental

2.1. Chemicals

Ferric chloride ($FeCl_3{\cdot}6H_2O$), ethylene glycol (EG), anhydrous sodium acetate (NaAc), PEG200, dopamine hydrochloride (DA·HCl), bromopropyne, aminophenylboronic acid (APBA·H_2O), sodium azide (NaN_3), sodium nitrite ($NaNO_2$), β-cyclodextrin (β-CD), cholesterol, rhodamine B (RB) and cholesterol quantity assay kit were purchased from Sigma-Aldrich and used without further purification.

2.2. Apparatus

TEM images were obtained on a Tecnai G220 transmission electron microscopy with an acceleration voltage of 200 kV (FEI, USA). X-ray diffraction (XRD) patterns were measured using a D/MAX-3C X-ray powder diffractometer (Rigaku Co., Japan). Fluorescence (FL) measurements were performed on a Cary Eclipse fluorescence spectrophotometer (Aglient, USA). FT-IR spectra were obtained on a Nicolet FT-IR spectrometer 5700 (Thermo, USA). X-ray photoelectron spectra (XPS) were collected on an ESCALAB 250Xi XPS system (Thermo, USA). UV–vis absorption spectra were recorded using a UH4150 UV–Vis–NIR spectrometer (Hitachi, Japan). Size contribution of nanoparticles were measured by dynamic light scattering (DLS) on a Malvern Zetasizer nano ZS instrument (UK). Magnetic studies were carried out using a Model 6000 PPMS (Quantum Design, USA) with fields up to 8 T at 300 K. The thermal gravimetric (TG) assay was performed by a TG-DSC analyser (NETZSCH, STA 449 F3) from room temperature to 800 °C at a heating rate of 5 °C/min in N_2 atmosphere.

2.3. Synthesis of Fe_3O_4@PDA-PBA-CD NPs

Fe_3O_4@PDA-PBA NPs were prepared according to our previous report (Zheng et al., 2015). Then, Fe_3O_4@PDA-PBA NPs were dispersed in