Journal of Colloid and Interface Science 399 (2013) 107–114

Contents lists available at SciVerse ScienceDirect

Journal of Colloid and Interface Science

www.elsevier.com/locate/jcis

Synthesis of teicoplanin-modified hybrid magnetic mesoporous silica nanoparticles and their application in chiral separation of racemic compounds

Jingwei Wu, Ping Su, Jun Huang, Siming Wang, Yi Yang *

College of Science, Beijing University of Chemical Technology, Beijing 100029, People's Republic of China

ARTICLE INFO

Article history:
Received 4 January 2013
Accepted 27 February 2013
Available online 13 March 2013

Keywords:
Magnetic nanoparticle
Mesoporous
Teicoplanin
Chiral nano-selector
Chiral separation

ABSTRACT

Teicoplanin-conjugated mesoporous silica magnetic nanoparticles (TE-MSMNPs) were fabricated as novel chiral magnetic nano-selectors. Successful preparation of the functional magnetic mesoporous materials was achieved by grafting teicoplanin on *N*-(2-aminoethyl)-3-aminopropyltrimethoxysilane-modified mesoporous silica Fe_3O_4 magnetic nanoparticles (AEAPTMS-MSMNPs), and this was confirmed by various characterization techniques. The synthesized magnetic nanoparticles were regularly spherical and uniformly mesoporous with an average diameter of around 600 nm and a mean pore size of about 3.9 nm, respectively. These versatile magnetic nanoparticles were effective in a direct chiral separation of five racemic compounds in phosphate buffer. Much stronger interactions were observed with the (+)-enantiomers than with the (−)-enantiomers. After washing with water and ethanol by sonication, TE-MSMNPs could be reused at least three times with little efficiency loss. The functional magnetic mesoporous nanoparticles were easily separated from the racemic solutions using an external magnetic field. These magnetic nano-materials are suitable for enantiomer separations.

1. Introduction

Chiral compounds are ubiquitous in nature and have important biological activities. Most chiral compounds show disparate biological activities because of their different physical and chemical properties. In some cases, one enantiomer has effective pharmacological activity, while the other possesses little pharmacological activity or is toxic. Therefore, it is essential to develop a simple and effective method for chiral separation. A number of techniques have been developed for enantiomer separation, including chromatography [1–4], enzyme resolution [5], membrane separation [6,7], and chemical recognition [8]. These methods have different abilities for chiral recognition, but are generally time-consuming, expensive, and involve complicated separation processes. This has limited their use in racemic separation. By comparison, direct chiral separation combined with magnetic nanoparticles is a powerful method for chiral recognition because it is inexpensive and simple.

Separation of racemic compounds is achieved by chiral recognition by a chiral selector. Many chiral selectors, including cyclodextrin, cellulose, and macrocyclic antibiotics, have been used in enantioselective recognition [9–14]. Teicoplanin is an important macrocyclic glycopeptide antibiotic that is produced from actinoplanes, and can be used against resistant bacteria. Teicoplanin has excellent structural properties for chiral recognition, and its recognition mechanism combines various characteristics of other chiral selectors, such as cyclodextrin, cellulose, and proteins. It contains many stereogenic centers, aromatic rings, macrocyclic rings, and aglycones. The aglycones can form a hydrophobic semi-rigid basket-shaped cleft with a sole basic primary amine and a single acidic carboxylic acid group. This allows teicoplanin to easily dissolve in aqueous solutions within a broad pH range, and facilitates its chiral selectivity toward the chiral analytes via a variety of interactions [15]. Teicoplanin also contains a long fatty acid chain in the D-glucosamines group, and this provides more hydrophobic interactions than the other chiral selectors. These unique structures can be used for chiral separation of numerous racemic compounds because of the formation of hydrophobic, hydrogen bonding, steric repulsion, π–π, dipole–dipole, and ionic interactions between teicoplanin and racemates.

Magnetic nanoparticles (MNPs), especially iron oxides (Fe_3O_4 or γ-Fe_2O_3), have attracted great interest because of their strong magnetic properties, regular shapes, uniform sizes, and excellent biocompatibility [16]. An external magnetic field can be used to easily separate magnetic nanoparticles from complex matrices and recycle them. Recently, mesoporous materials have received attraction in various research fields because of large surface areas, tunable pore sizes, large pore volumes, and ordered mesoporous structures [17]. Combination of MNPs with mesoporous materials

* Corresponding author. Fax: +86 10 64434898.
E-mail address: yangyi@mail.buct.edu.cn (Y. Yang).

0021-9797/$ - see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jcis.2013.02.045

would provide ideal functional materials with excellent magnetic responses and unique mesoporous structures. Magnetic mesoporous nanoparticles have been applied in various fields such as catalysis, drug delivery, bioseparation, and magnetic resonance imaging [17,18]. In recent years, most studies of MNPs immobilized with chiral molecules have focused on the fields of adsorption and separation of achiral compounds [19,20], catalysis [21], and sterilization [22]. More recently, Uddin et al. used carboxymethyl-β-cyclodextrin modified MNPs for adsorption of three chiral aromatic amino acids [23]. Wei and co-workers employed cellulose-phenylcarbamate anchored magnetic silica microspheres for separation of five racemates [24].

In this study, novel functionalized magnetic mesoporous nanoparticles with excellent chiral selectivity were fabricated and characterized. Various techniques including solvothermal, self-assembly, and microwave irradiation methods were used to prepare the functional magnetic nano-materials. The synthesized TE-MSMNPs were used for direct chiral separation of several racemic compounds to demonstrate their chiral recognition abilities. The chiral recognition mechanism between the chiral nano-selectors and racemic analytes is discussed. The reusability and stability of the TE-MSMNPs were also evaluated.

2. Experimental section

2.1. Materials

Tetraethyl orthosilicate (TEOS) and 1, 6-hexamethylene diisocyanate (HMDI) were purchased from J&K Scientific (Beijing, China). Teicoplanin (TE) was obtained from Hubei Haiyi Pharmaceutical Chemicals Co., Ltd. (Wuhan, China). *N*-(2-Aminoethyl)-3-aminopropyltrimethoxysilane (AEAPTMS) and all the racemic compounds, including DL-tryptophan, DL-phenylalanine, DL-mandelic acid, (±)-1-phenyl-1,2-ethanediol, and *N*-benzoyl-DL-alanine, were purchased from Acros Organics (Geel, Belgium). All other chemicals were of analytical grade and obtained from the Beijing Chemical Reagent Co., Ltd. (Beijing, China) and were used without further purification.

2.2. Methods

2.2.1. Preparation of Fe_3O_4 MNPs

Fe_3O_4 MNPs were synthesized by a typical polyol reducing process according to a previous report [25]. Briefly, a solution of $FeCl_3{\cdot}6H_2O$ (10.8 g) and anhydrous sodium acetate (28.8 g) in ethylene glycol (320 mL) was vigorously stirred for 30 min to obtain a homogenous yellow solution. The transparent solution was then transferred into eight Teflon-lined stainless-steel autoclaves (40 mL per autoclave). The autoclaves were heated at 200 °C for 10 h. After cooling to room temperature, the black precipitates were collected and washed several times with ethanol. The washed MNPs were dried under vacuum at 60 °C for 5 h.

2.2.2. Synthesis of nonporous silica-coated MNPs (NSMNPs)

NSMNPs were prepared according to a versatile sol–gel method. Briefly, 1 g of the Fe_3O_4 MNPs was dispersed in an aqueous solution (100 mL) and ultrasonicated for 10 min. Then, the Fe_3O_4 MNPs were separated using a magnet and re-dispersed in a solution containing 60 mL of H_2O, 240 mL of ethanol, and 5 mL of $NH_3{\cdot}H_2O$. The mixture was ultrasonicated for 10 min, and then, 1 mL of TEOS was added dropwise under vigorous mechanical agitation. After that, the reaction mixture was stirred continuously for 8 h at room temperature. The product was separated with a magnet and then washed four times with ethanol. Finally, the obtained NSMNPs were dried under vacuum at 60 °C for 8 h.

2.2.3. Preparation of mesoporous silica-coated MNPs (MSMNPs)

MSMNPs were prepared by an established surfactant self-assembly approach with slight modification [26,27]. In a typical process, 0.5 g of the NSMNPs was dispersed in 500 mL of deionized water by ultrasonication. Then, 0.5 g of cetyltrimethyl ammonium bromide (CTAB) and 5 mL of a NaOH aqueous solution (0.1 mol L^{-1}) were added. The solution was ultrasonicated for 10 min and then heated to 60 °C in a water bath with vigorous stirring for 30 min. After that, 2 mL of TEOS diluted in 10 mL of ethanol was slowly injected into the above solution. The reaction mixture was heated at 60 °C under a nitrogen atmosphere for 12 h. After cooling to room temperature, the obtained product was isolated with a magnet and washed four times with water. The CTAB template surfactant was removed by ion exchange extraction. Briefly, the brownish-black precipitate was re-dispersed in 50 mL of NH_4NO_3/ethanol solution and stirred for 6 h at the reflux temperature. The extraction was repeated three times, and then, the obtained MSMNPs were washed five times with water. Finally, the purified magnetic product was dried under vacuum at 60 °C for 12 h.

2.2.4. Synthesis of AEAPTMS-modified MSMNPs (AEAPTMS-MSMNPs)

AEAPTMS was used as a silane coupling agent for synthesis of AEAPTMS-MSMNPs by microwave-assisted synthetic technology. Briefly, 0.5 g of MSMNPs was dispersed in 47.5 mL of anhydrous toluene and ultrasonicated for 10 min. Then, 2.5 mL of AEAPTMS was injected into the dispersed solution and the mixture were reacted in the microwave reactor (Discover SP, CEM, Matthews, NC) at 100 W and 100 °C for 5 h under a nitrogen atmosphere. After cooling to the room temperature, the synthesized amine functional MSMNPs were washed three times with ethanol and finally dried under vacuum at 60 °C for 4 h.

2.2.5. Synthesis of teicoplanin immobilized MSMNPs (TE-MSMNPs)

To immobilize TE on the surface of the AEAPTMS-MSMNPs, 1,6-hexamethylene diisocyanate was used as a crosslinker to connect the primary amine groups in both AEAPTMS-MSMNPs and TE. Typically, 50 mg of TE was dissolved in 15 mL of anhydrous dimethylsulfoxide and then 50 mg of the AEAPTMS-MSMNPs was added to the mixture. The solution was then mechanically stirred for 10 min. After that, a certain amount of HMDI was added dropwise to the solution and the reaction was heated to 70 °C for another 12 h. After cooling to room temperature, the prepared chiral MNPs were collected under an external magnetic field and washed several times with ethanol. The obtained TE-MSMNPs were dried under vacuum at 60 °C for 3 h.

2.2.6. Direct chiral separation of racemic compounds

Direct chiral separation of five racemic compounds was carried out by an automatic digital polarimeter. The chiral separation conditions were established according to the previous reports with a little modification [28–31]. First, 50 mg of TE-MSMNPs was dissolved in 10 mL of phosphate buffer (Na_2HPO_4—$HClO_4$, 0.1 mol L^{-1}, pH 6.0, 10% acetonitrile, v/v) and ultrasonicated for 3 min. Then, the functional magnetic mesoporous nanoparticles were separated with a magnet and dispersed in 10 mL of a racemic solution (1 mg mL^{-1}) in phosphate buffer. The suspension was continuously shaken for 5 min. After that, the TE-MSMNPs were immediately isolated with a magnet and the supernatant was analyzed by an automatic digital polarimeter. To elute the adsorbed analytes from TE-MSMNPs, the collected functional magnetic nanoparticles were re-dispersed in 5 mL of Na_2HPO_4—NaH_2PO_4 buffer (0.1 mol L^{-1}, pH = 8.0) and then ultrasonicated for 5 min. After the TE-MSMNPs were separated under an external magnetic field, the supernatant was collected. The elution process was repeated twice, and all the supernatants were combined for analysis by an automatic