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Application of cyclodextrin-modified gold nanoparticles in enantioselective monolith capillary electrochromatography

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ABSTRACT

β-cyclodextrin modified gold nanoparticles (CD-GNP) were employed as the stationary phase in monolith capillary electrochromatography (CEC) to facilitate enantioseparation. CD-GNP were covalently bound to the surface of the thiolated porous polymer monolithic column. The fabricated enantioselective monolithic column was characterized by a variety of spectroscopic methods. The column exhibited steady EOF mobility over pH values ranging from 4.6 to 9.7. Additionally, the column was stable under CEC separation conditions over 180 min. Moreover, the column exhibited good column-to-column reproducibility. The CD-GNP-modified monolithic column was employed in the efficient CEC separation of three pairs of drug enantiomers (chlorpheniramine, zopiclone and tropicamide). The results exhibit reproducible run-to-run enantioseparations and the monolith column can maintain its enantioselectivity for more than 1 month if the column is stored in a CD-GNP solution at 4 °C.

1. Introduction

Capillary electrochromatography (CEC) exploits both the high efficiency of CE and the selectivity of liquid chromatography stationary phase; CEC is a powerful technique in separation science [1–3] and the key for the separation process is the solute–stationary phase interaction. Developing an efficient stationary phase to enhance the solute–stationary phase interaction has been a major task in CEC studies for many years. Notably, the high colloidal stability and large surface area of nanoparticles have positioned them as promising stationary phase materials for CEC separations [4,5]. Over the past decade, different types of nanoparticles, including polymer [6,7], titanium oxide [8,9] and gold nanoparticles [10] as well as carbon nanotubes [11], have been utilized as the stationary phase for CEC separations. Nanoparticles have been shown to improve separation efficiency by forming a stable and large surface that interacts with the analytes.

Among various nanoparticles, GNPs are very attractive since their easy and inexpensive to prepare, they easily form active complexes with biological substances and they have controllable particle size and narrow size distribution [12,13]. GNPs have been used as novel stationary or pseudo-stationary phases in CEC techniques to efficiently separate DNA and proteins [10]. It has been well established that organic molecules containing an thiol (–SH) or amine (–NH) group can be easily adsorbed onto gold surfaces through covalent bonding, leading to well defined and stable arrays of chemically modified GNPs. Such chemically modified GNPs can be very useful in CEC separations, including enantioseparations.

Various research fields, including the pharmaceutical, clinical, environmental and food science, rely heavily upon CEC enantioseparation [14]. In recent years, the application of nanoparticles in CEC enantioseparation has attracted increased research interest. The large surface area of nanoparticles has been shown to be a key element in improving enantioselectivity. It is expected that chiral selectors (e.g., CD and protein) can be covalently bound to the surface of GNPs to form an efficient nanoparticle-based chiral stationary phase for CEC separations. Unfortunately, reports applying GNPs in CEC enantioseparations are rare; however, capillaries and microdevices that have been chemically modified with GNPs have shown great promise in enhancing enantioseparation performance. For example, Li et al. presented the first application of BSA-GNP conjugates. These conjugates have been employed as the chiral stationary phase in fabricated chiral OTCEC microdevices [15]. Lu et al. describes the development of a silica monolith stationary phase modified with BSA-GNP conjugates; this modified stationary phase was used in the CEC separation of phenylthiocarbamyl amino acids [16]. The application of CD-GNP as chiral selectors in pseudo-stationary phase CEC and OTCEC separation have been reported for

Abbreviations: β-CD, β-cyclodextrin; GNPs, gold nanoparticles; CD-GNP, β-cyclodextrin modified gold nanoparticles; CEC, capillary electrochromatography; PDDA, poly diallydimethylammonium chloride; TMSPM, 3-trimethoxysilyl propyl methacrylate; AIBN, 2, 2′-azobis (2-methylpropionitrile); EDMA, ethylene dimethacrylate; GMA, glycidyl methacrylate; EDS, energy dispersive X-ray spectroscopy; SEM, scanning electron microscopy; TEM, transmission electron microscopy; TGA, thermogravimetric analysis.

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efficient enantioseparation of amino acid enantiomers and drug enantiomers [17,18].

In this work, a monolith stationary phase modified with CD-GNP conjugates was developed to function as the chiral stationary phase during CEC enantioseparation. The enantioselective monolithic column was prepared by introducing CD-GNP conjugates onto a poly (GMA-co-EDMA) monolith through covalent bonding. The stability and reproducibility of the enantioselective monolithic column were investigated. Three drug enantiomer pairs were separated using the modified monolithic column to demonstrate its performance during CEC enantioseparation. The results demonstrate the promise of using a monolithic column outfitted with a chiral selector comprising modified GNPs to achieve CEC enantioseparation.

2. Experimental

2.1. Chemicals and instruments

β-CD, p-toluenesulfonyl chloride, hydrogen tetrachloroaurate hydrate, sodium disulfite, trichloroethylene and sodium borohydride were obtained from Sigma Chemical (St. Louis, MO, USA). Poly dially dimethylammonium chloride (PDDA) (20%, w/w in water, MW= 200,000–350,000) was purchased from JingChun Reagent Inc. (Shanghai, China). 3-trimethoxysilyl propyl methacrylate (TMSPM), 2,2′-azobis (2-methylpropionitrile) (AIBN) and ethylene dimethacrylate (EDMA) were purchased from J&K Chemical Ltd. Glycidyl methacrylate (GMA), 1-dodecanol and cyclohexanol were purchased from Alfa Aesar. 2-Aminoethanethiol was obtained from TCI Co. Ltd. Chlorpheniramine, zopiclone and tropicamide were purchased from local pharmaceutical stores. Other reagents were of analytical grade and used without further purification.

The phosphate buffer was prepared by dissolving NaH_2PO_4 in deionized water; the pH of the buffer was adjusted by adding H_3PO_3. Stock solutions (1 mg/mL) of the bulk drug samples were prepared in deionized water. All the solutions were prepared daily and filtered through an inorganic 0.22-μm nylon membrane prior to use.

CE experiments were carried out on a CE apparatus (CL1020, Bei-jing Cailu Science Apparatus, China) equipped with a UV detector set at 214 nm. The scanning electron microscopy (SEM) and energy dispersive X-ray spectroscopy (EDS) spectra of the monoliths were obtained using an XL30ESEM-FEG SEM microscope (SEI) integrated with an energy dispersive X-ray spectrometer. UV–vis and Fourier-transform infrared (FT-IR) spectra of the synthesized CD-GNPs were obtained on a Cary 500 UV–vis-NIR spectrophotometer (Varian, CA, USA) and a fluorescence spectrophotometer. Transmission electron microscopy (TEM) images were captured on an H-7500 TEM spectrometer (Hitachi, Japan). Porosity measurements were carried out using an ASAP 2020M automatic micropore and mesopore analyzer (Micromeritics, Norcross, GA, USA). Thermogravimetric analysis (TGA) was conducted using a Perkin-Elmer TGA-2 thermogravimetric analyzer.

2.2. Preparation of CD-GNP-modified monolithic columns

The inner wall of the capillary was first vinylized to enable covalent attachment of the monolith [19]. A bare capillary was

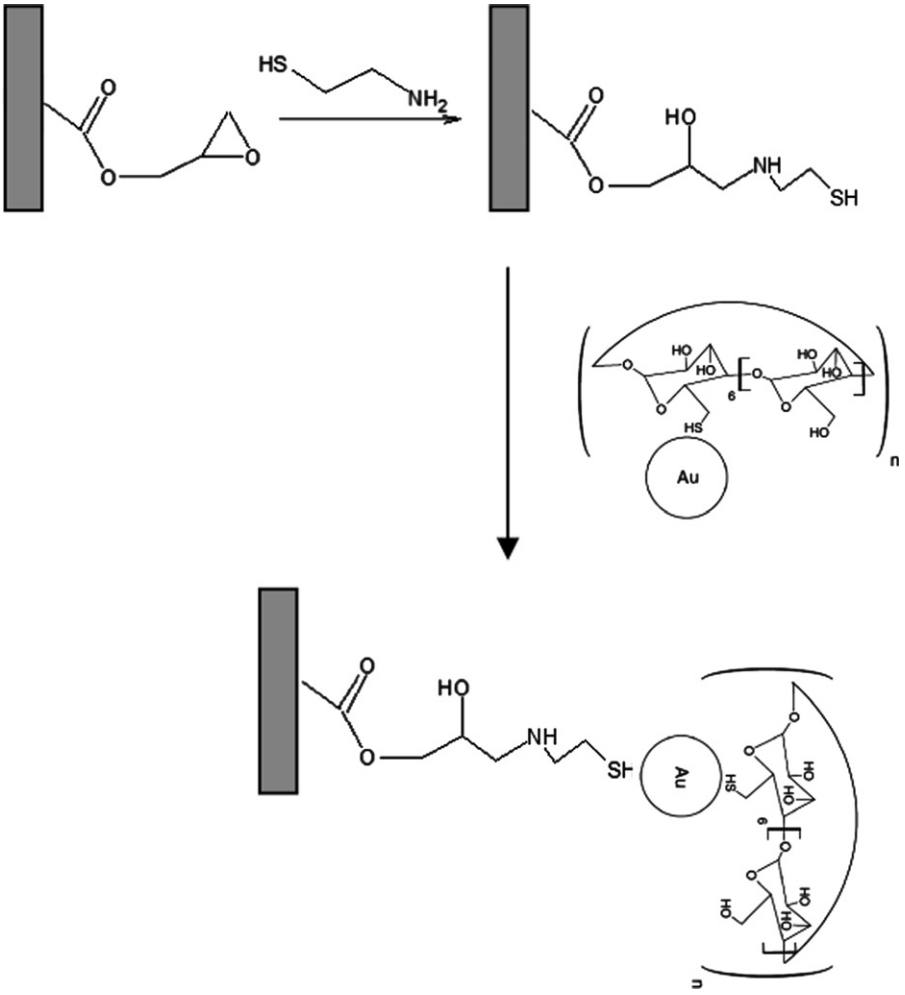

Fig. 1. Reaction scheme for the fabrication of the CD-GNP-modified monolithic column.