Analytica Chimica Acta 951 (2017) 68–77

Contents lists available at ScienceDirect

Analytica Chimica Acta

journal homepage: www.elsevier.com/locate/aca

Molecularly imprinted phloroglucinol–formaldehyde–melamine resin prepared in a deep eutectic solvent for selective recognition of clorprenaline and bambuterol in urine

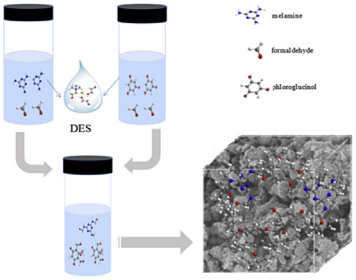
Shiru Liang [a], Hongyuan Yan [a, b, *], Jiankun Cao [a], Yehong Han [a], Shigang Shen [b], Ligai Bai [a]

[a] Key Laboratory of Medicinal Chemistry and Molecular Diagnosis, Ministry of Education & College of Pharmacy, Hebei University, Baoding, 071002, China
[b] Key Laboratory of Analytical Science and Technology of Hebei Province & College of Public Health, Hebei University, Baoding, 071002, China

HIGHLIGHTS

- Molecularly imprinted phloroglucinol-formaldehyde-melamine resin was synthesized.
- Deep Eutectic Solvent was used in the preparation of molecularly imprinted polymers.
- The prepared materials presented specific recognition to CLP and BAM in urine.
- Dummy template eliminated the influence of template leakage on quantitative analysis.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 18 August 2016
Received in revised form
17 October 2016
Accepted 8 November 2016
Available online 11 November 2016

Keywords:
Molecularly imprinted phloroglucinol –formaldehyde–melamine resin (MIPFMR)
Deep eutectic solvent (DES)
Dummy template
Urine

ABSTRACT

A new molecularly imprinted phloroglucinol–formaldehyde–melamine resin (MIPFMR) was synthesized in a deep eutectic solvent (DES) using phenylephrine as a dummy template. The MIPFMR was used as a solid phase extraction (SPE) sorbent for the selective isolation and recognition of clorprenaline (CLP) and bambuterol (BAM) in urine. Phloroglucinol and melamine were used as double functional monomers that introduced abundant hydrophilic groups (such as hydroxyl groups, imino groups, and ether linkages) into the MIPFMR, making it compatible with aqueous solvents. In addition, the formation of DES by combining the quaternary ammonium salt of choline chloride with ethylene glycol as a hydrogen bond donor was an environmentally safe alternative to toxic organic solvents such as chloroform and dimethylsulfoxide that are typically used in the preparation of most molecularly imprinted polymers (MIPs). Moreover, MIPFMR-based SPE of CLP and BAM in urine resulted in higher recoveries and purer extracts than those obtained by using other SPE materials (e.g., SCX, C_{18}, HLB, and non-imprinted phloroglucinol –formaldehyde–melamine resin (NIPFMR)). The optimized MIPFMR–SPE–HPLC–UV method had good linearity ($r^2 \geq 0.9996$) ranging from 15.0 to 3000.0 ng mL^{-1} for CLP and BAM, and the recoveries at three spiked levels ranged from 91.7% to 100.1% with RSDs ≤7.6%. The novel MIPFMR–SPE–HPLC–UV method is simple, selective, and accurate, and can be used for the determination of CLP and BAM in urine samples.

1. Introduction

Hydrophilic resins are widely used as adsorbents because of the low-cost raw materials, simple preparation processes, diverse

* Corresponding author. Key Laboratory of Medicinal Chemistry and Molecular Diagnosis, Ministry of Education, Hebei University, Baoding, 071002, China.
E-mail address: yanhy@hbu.edu.cn (H. Yan).

http://dx.doi.org/10.1016/j.aca.2016.11.009
0003-2670/

functional groups, and good porosity [1,2]. Phenolic–formaldehyde resin (PFR) is a common hydrophilic resin containing abundant hydroxyls, and it has been used as an adsorbent for separating various metal ions [3]. Melamine–formaldehyde resin (MFR) is rich in hydrophilic amino groups and has high mechanical strength, good thermal stability, and good solvent stability; therefore, MFR can be used in applications involving the adsorption of metal ions [4]. Recently, a series of melamine–formaldehyde–phenolic resins were synthesized that combine the advantages of PFR and MFR with numerous hydrophilic groups such as hydroxyls, imino groups, amino groups, and ether linkages [5]. They can be used as adsorbents to separate target molecules in aqueous solution [6]. However, the melamine–formaldehyde–phenolic resins lack specific molecular recognition ability; therefore, they show poor extraction and purification efficiency for target analytes in complicated sample matrices. Hence, it is crucial to develop new melamine–formaldehyde–phenolic resins with specific molecular recognition ability in aqueous solution.

Molecularly imprinted polymers (MIPs) can recognize target molecules by incorporating functional monomers with template molecules during polymerization. The specific molecular recognition cavities of MIPs, which can selectively rebind the template molecule or its structural analogues, are complementary to the template molecules in size, shape, and spatial distribution [7–9]. Until now, most MIPs are synthesized in organic solvents or organic-rich solvents. Consequently, they show poor compatibility with water and poor molecular recognition of analytes in aqueous environments, which significantly limit their practical application in adsorbent assays [10–12]. Moreover, various aqueous biological and environmental samples require MIPs that are compatible with aqueous media [13]. Hence, the development of MIPs that are compatible with aqueous solutions is highly desirable.

Deep eutectic solvents (DES), a class of liquids related to ionic liquids, are molecular complexes typically formed by mixing quaternary ammonium salts and hydrogen-bond donors. When alcohol-based hydrogen bond donors are used, the resulting DESs are more dipolar than other DESs such as reline and maline [14,15]. Compared with the traditional organic solvents, DESs are more environmentally safe because of their low toxicity, ease of recycling, and negligible vapor pressure [16–18]. They have other characteristics also, such as excellent solubility, nonflammability, good thermal stability, and miscibility with water and organic solvents. As a result, DESs have been successfully applied to the fields of synthesis [19–21], biochemistry [22], separation [23,24], and analysis [25,26]. However, the research on the application of DESs for preparing MIPs to enhance their affinity and selectivity is still in the initial stage.

In this work, an MIPFMR was synthesized using a hydrophilic resin and MIPs technology in a novel DES to enhance the affinity of the MIPFMR for analytes in aqueous media. MIPFMR was prepared using phenylephrine as a dummy template, phloroglucinol and melamine as double functional monomers, and formaldehyde as a cross-linker to introduce abundant hydroxyl groups, imino groups, and ether linkages into the material. The resultant MIPFMR was employed as the SPE sorbent for the selective recognition of CLP and BAM in urine, with higher recoveries and more purified extracts than those obtained using other common adsorbents such as SCX, C_{18}, HLB, and NIPFMR.

2. Experimental

2.1. Chemicals and reagents

Phloroglucinol, acetic acid (HOAc), and choline chloride were purchased from Guangfu Chemical Co., Ltd. (Tianjin, China). Ethylene glycol was purchased from Beichen Fangzheng Chemical Co., Ltd. (Tianjin, China). Melamine, formaldehyde (37 wt%), and trifluoroacetic acid (TFA) were obtained from Kermel Chemical Co., Ltd. (Tianjin, China). Clorprenaline (CLP) and bambuterol (BAM) were obtained from the National Institute for Control of Pharmaceutical and Biological Products (Beijing, China). Phenylephrine, caffeine, and thiamphenicol were obtained from Aladdin Chemical Co., Ltd. (Shanghai, China). Methanol was obtained from Xingke Biochem. Co., Ltd. (Shanghai, China). Ultrapure water was filtered using a 0.45 μm membrane before use.

2.2. Instrumentation and conditions

The specific surface area analysis was carried out by a TriStar II 3020 automated pore size and surface area analyzer (Micromeritics, Norcross, USA). The freeze dryer was purchased from SIM International Group (California, USA). The shaker was obtained from Shanghai Yiheng Scientific Instrument Co., Ltd. (Shanghai, China). The morphology evaluation was carried out via scanning electron microscopy (SEM), using a Phenom Pro SEM system (Phenom, Eindhoven, Netherlands). Fourier transform infrared spectra (FTIR) were obtained by a Vertex70 Fourier transform infrared spectrometer (Bruker, Karlsruhe, Germany) in the range 500–4000 cm^{-1}. The chromatographic analysis was performed with an LC-20A liquid chromatography system equipped with one LC-20AT solvent delivery unit and an SPD 20A UV–Vis detector (Shimadzu, Kyoto, Japan). An N2000 workstation was used as the data acquisition system (Zhedazhineng, Hangzhou, China). The C_{18} column (250 mm × 4.6 mm i.d., 5 μm) was purchased from Thermo Fisher Scientific (Massachusetts, US). The mobile phase was a mixture of 55:45 (v/v) water and methanol containing 0.1% TFA with a flow rate of 1.0 mL min^{-1}. The wavelength of the UV–Vis detector was set at 210 nm.

2.3. Preparation of the MIPFMR and NIPFMR

Ethylene glycol–choline chloride (DES) was prepared by heating ethylene glycol (0.4 mol) and choline chloride (0.2 mol) to 80 °C and stirring to obtain a homogeneous liquid. Phloroglucinol (3.0 mmol) was dissolved in 4.5 mL DES in bottle A by sonicating, and then formaldehyde (12.0 mmol) was added and stirred for 30 min at room temperature. Meanwhile, melamine (1.0 mmol), formaldehyde (2.0 mmol), and DES (1.5 mL) were combined in bottle B, and the mixture was stirred at 80 °C in an oil bath until the solution became clear. After cooling to room temperature, the solution in bottle B was poured into bottle A. Then, phenylephrine was added into bottle A and the solution was stirred for 30 min at 40 °C, heated at 60 °C for 2 h, and then heated at 80 °C for 24 h. The resultant solid was washed with water to remove DES and then freeze-dried under vacuum. After freeze drying, the solid was washed to remove the template by sonication and centrifugation with methanol–acetic acid (9:1, v/v) and water five times, respectively. The solid was freeze-dried under vacuum for 12 h to obtain the MIPFMR. NIPFMR was synthesized in an identical way, except for the addition of the template.

2.4. HPLC–UV of the MIPFMR

Twenty-one MIPFMRs were synthesized according to different parameters (Table 1). After the MIPFMRs were obtained, their adsorption amounts were determined by HPLC–UV. The MIPFMR (3 mg) was dispersed in 2 mL of 50 μg mL^{-1} standard solution (CLP and BAM) in a centrifuge tube. After shaking for 12 h, the mixture was centrifuged at 26916 × g for 15 min, and the upper layer was collected for HPLC–UV analysis to determine the adsorption