Preparation of water stable methyl-modified metal–organic framework-5/polyacrylonitrile composite nanofibers via electrospinning and their application for solid-phase extraction of two estrogenic drugs in urine samples

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ABSTRACT

The nanofibers of methyl-modified metal–organic framework-5/polyacrylonitrile composite (CH_3MOF-5/PAN) were successfully synthesized and used as a solid-phase extraction (SPE) sorbent for pre-concentration of two estrogenic drugs, levonorgestrel and megestrol acetate, in urine samples. A simple, cheap and accessible electrospinning method was employed to prepare a water stable CH_3MOF-5/PAN composite. The nanofibers were packed into the mini-disc cartridges to be used as SPE devices. They were also characterized by scanning electron microscopy, thermogravimetric analysis, Fourier transform infrared spectroscopy, X-ray diffraction and N_2 adsorption–desorption experiments. The effects of different parameters influencing the extraction efficiency including the type of eluent and its volume, the amount of the sorbent, pH, the ionic strength, the sample volume and the reusability of the sorbent were investigated and optimized. Under the optimized conditions, the linearity varied in range of $0.05–100\,\mu g\,L^{-1}$ with R^2 values higher than 0.999. The limit of detection for both of the analytes was $0.02\,\mu g\,L^{-1}$. The applicability of the method was examined by analyzing the analytes in the urine samples. The recovery of the analytes varied in the range of 82.8–94.8% which shows capability of the method for the determination of the drugs in the urine samples.

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1. Introduction

The first step in any instrumental analysis is sample preparation which is one of the vital steps in the trace analysis methodologies. Solid-phase extraction (SPE) is the most popular sample preparation technique used for liquid samples before chromatographic analysis. In SPE, the sorbent type and its physicochemical characteristics such as porosity, specific surface area and surface chemistry play important roles to obtain high extraction efficiency [1–3]. Therefore, investigation for finding new sorbent materials is an important research area.

Unlike the conventional fiber spinning techniques such as dry spinning, wet spinning, gel spinning and melt spinning, which can generate polymer fibers with diameters down to the micrometer range, electrospinning is a process which can generate polymer fibers in the submicron to nanometer diameter ranges.

Electrospinning is a very simple, versatile and high-throughput method for generating continuous nanofibers from a wide range of materials including polymers, composites and ceramics with controllable diameters, compositions and morphologies [4–9]. It was observed that the electrospun nanofibers possess a great potential to serve as a good sorbent material for SPE-based techniques. The main advantage of electrospun nanofibers is their large surface area to volume ratio, which allows using small amounts of the sorbent in the SPE procedure. It reduces the volume of eluting solvents and increases the extraction efficiency for the trace analyses [10–12]. In 2007, Kang et al. reported the first use of electrospun polymer nanofibers for packed-sorbent SPE [13]. To date, most of the electrospun nanofibers used for SPE have been polystyrene [13–25] or nylon 6 [26–32] polymers and the application of other electrospun nanofibers in sample preparation has been less explored.

Metal–organic frameworks (MOFs) or porous coordination polymers are a new class of crystalline porous materials that have been first introduced by Yaghi and co-workers [33,34]. The advantages of MOFs as compared to the conventional porous materials, like zeolites or activated carbons, are their extraordinary surface

area, microporosity, remarkable low density and ability to be easily designed or modified to have different pore sizes [35–38]. These advantages make MOFs attractive for the analytical applications. Recently, MOFs were used for SPE [39–46], micro-SPE [47–50] and SPME [51–56] of some organic and inorganic analytes.

Perhaps the most famous MOF ever used is MOF-5. MOF-5 with its high surface area and great porosity has been widely used for gas adsorption studies and molecular simulation analysis [57]. However, problems arise when it is either applied for adsorption in aqueous matrices or exposed to the low amounts of moistures. This is important because generally water resistance is an important property for a SPE adsorbent in aqueous media while the mobile phase and most of the environmental and biological samples are in the aqueous phase. Recently, researchers have found that it is possible to obtain water-stable MOFs by introducing hydrophobic functional groups into their framework structures. In 2011, Yang et al. [58] synthesized the methyl modified MOF-5 (CH$_3$MOF-5) analogs using a solvothermal method. It was confirmed that the incorporation of hydrophobic methyl groups into the structure of MOF-5 improved its water resistance.

Polyacrylonitrile (PAN) is a synthetic and semi-crystalline organic polymer resin that is resistant to most of the solvents. PAN has some properties, such as low density, modulus of elasticity and good thermal, chemical and mechanical stability as well as biocompatibility. These unique properties have made it one of the most important polymers used in the electrospinning process [59].

The present study focuses on the use of CH$_3$MOF-5/PAN composite for SPE of levonorgestrel (LeV) and megestrol acetate (MA), two estrogenic drugs, as the model compounds. They are the synthetic progestational hormones. LeV is widely used in pregnancy prevention in humans [60]. MA is used mainly to treat breast, endometrial, and prostate cancers. [61,62]. The presence of different functional groups in the chemical structures of the target analytes can possibly lead to different interactions such as π–π interactions, hydrogen bonding and hydrophobic interactions between them and the sorbent. On the other hand, due to the remarkable water stability of CH$_3$MOF-5, it is distinguished from the other moisture sensitive MOFs. Therefore, it can be used as a suitable sorbent for the extraction of the analytes from the aqueous media such as biological fluids.

2. Experimental

2.1. Chemicals and materials

All reagents were of the analytical grade. The double distilled water was used throughout the experiments. Methanol (HPLC grade), acetonitrile (HPLC grade), acetone, n-hexane, hydrochloric acid, sodium hydroxide, dimethylformamide (DMF), terephthalic acid, triethylamine, zinc acetate dihydrate (Zn(OAc)$_2$·2H$_2$O) and chloroform (CHCl$_3$) were obtained from Merck (Darmstadt, Germany). Polyacrylonitrile (PAN, Mw = 100,000) was prepared from Isfahan Polyacryle Co. (Isfahan-Iran). LeV and MA were obtained from Iran Hormone Drug Company (Tehran, Iran) and used without any purification. The stock solution (1000 mg L^{-1}) of each analyte was prepared in HPLC-grade methanol and stored in the refrigerator. Working solutions were prepared daily by an appropriate dilution of the stock solutions with double distilled water.

2.2. Instrumentation

All chromatographic measurements were performed using an Agilent 1100 high performance liquid chromatography (Santa Clara, CA, USA) with a C$_{18}$ column (250 mm × 4.6 mm i.d., 5 μm
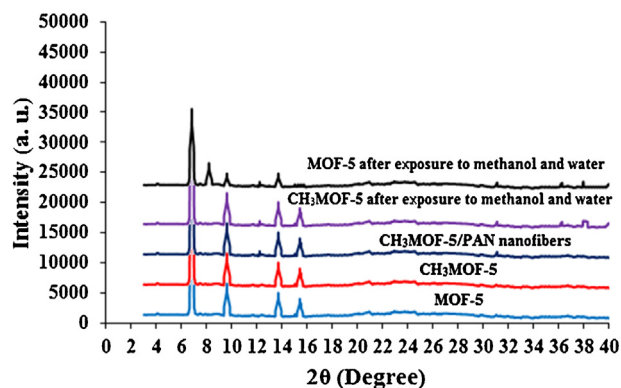
Fig. 1. XRD patterns of MOF-5, CH$_3$MOF-5, CH$_3$MOF-5/PAN nanofibers, CH$_3$MOF-5 after exposure to methanol and water and MOF-5 after exposure to methanol and water.

particle size) and UV–vis detector. The mobile phase was a mixture of acetonitrile and ultra-pure water (70:30). The detection was performed at the wavelength of 257 nm for both of the target analytes. Electrospinning machine (ANSTCO-RN/X, Asian Nanostructures Technology Co., Iran) was used for the preparation of the composite nanofibers. The pH values were adjusted with a WTW 3310 pH meter (Germany) combined with a glass electrode. The microstructure of the samples was characterized using scanning electron microscopy (SEM, KYKY EM-3200). High angle X-ray diffraction (XRD) patterns were obtained by a Philips-PW 17C diffractometer with Cu Kα radiation. Thermal gravimetric analyses (TGA) were carried out with a TGA-50 (Shimadzu, Japan) instrument. During the analysis, the sample was heated from 25 to 600 °C in the nitrogen atmosphere at a constant rate of 10 °C min^{-1}. An ABB BOMEM model FTLA 200-100 instrument was used to obtain the Fourier transform infrared (FTIR) spectra of KBr powder-pressed pellets. Brunauer–Emmett–Teller (BET) surface area analysis was measured on a Belsorp mini II (Japan Co.) using nitrogen adsorption at 77 K. ProElut ODS cartridges (200 mg, 3 mL) that were purchased from Dikma, USA.

2.3. Synthesis of MOF-5 and CH$_3$MOF-5

MOF-5 was synthesized by a new room temperature synthesis method [63]. 16.99 g Zn(OAc)$_2$·2H$_2$O was dissolved in 500 mL of DMF and then added to a mixture of 5.065 g terephthalic acid and 8.5 mL triethylamine in 400 mL DMF with stirring over 15 min to form a precipitate. The mixture was actually stirred for 2.5 h. The precipitate was also filtered and immersed in 250 mL DMF overnight. It was then filtered again and immersed in 350 mL CHCl$_3$. CHCl$_3$ was exchanged three times over 7 days: after the second day, third day, and the last day. The bulk of the solvent was decanted and the product was evacuated overnight to a pressure of 10 mTorr. MOF-5 was obtained after activation at 120 °C and 10 mTorr for 6 h.

CH$_3$MOF-5 was synthesized using a solvothermal method [58]. MOF-5 was activated by immersing in the dried CHCl$_3$ followed by heating at 160 °C in vacuum for 24 h. The obtained sample was denoted as CH$_3$MOF-5.

2.4. Preparation of PAN nanofibers

The PAN powder (10% w/v) was dissolved in DMF and stirred with a magnetic stirrer for 24 h to make the spinning solution. The prepared solution was loaded in a 5 mL-glass syringe. The syringe was fitted to a stainless needle (diameter; 0.5 mm) with a flat tip which was connected to the anode. A grounded aluminum foil served as the collection screen with an interval of 15 cm from the tip, and 18 kV voltage of 18 kV was applied between the tip and the