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Magnetic solid phase extraction of gemfibrozil from human serum and pharmaceutical wastewater samples utilizing a β-cyclodextrin grafted graphene oxide-magnetite nano-hybrid

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ABSTRACT

A magnetic solid phase extraction method based on β-cyclodextrin (β-CD) grafted graphene oxide (GO)/magnetite (Fe_3O_4) nano-hybrid as an innovative adsorbent was developed for the separation and pre-concentration of gemfibrozil prior to its determination by spectrofluorometry. The as-prepared β-CD/GO/Fe_3O_4 nano-hybrid possesses the magnetism property of Fe_3O_4 nano-particles that makes it easily manipulated by an external magnetic field. On the other hand, the surface modification of GO by β-CD leads to selective separation of the target analyte from sample matrices. The structure and morphology of the synthesized adsorbent were characterized using powder X-ray diffraction, Fourier transform infrared spectroscopy, and field emission scanning electron microscopy. The experimental factors affecting the extraction/pre-concentration and determination of the analyte were investigated and optimized. Under the optimized experimental conditions, the calibration graph was linear in the range between 10 and 5000 pg mL^{-1} with a correlation coefficient of 0.9989. The limit of detection and enrichment factor for gemfibrozil were 3 pg mL^{-1} and 100, respectively. The maximum sorption capacity of the adsorbent for gemfibrozil was 49.8 mg g^{-1}. The method was successfully applied to monitoring gemfibrozil in human serum and pharmaceutical wastewaters samples with recoveries in the range of 96.0–104.0% for the spiked samples.

1. Introduction

Applying a simple and selective sample preparation procedure prior to instrumental analysis is the most important and crucial step in an analytical process. Up to now, various sample preparation techniques based on solid phase extraction (SPE) systems have been developed to isolate various types of analytes from different matrices. However, in spite of the whole advantages of SPE, it can still be tedious, time consuming, and relatively expensive [1]. Recently, a new mode of SPE called magnetic solid-phase extraction (MSPE) has been developed [2]. MSPE is based on the combination of magnetic inorganic material and non-magnetic adsorbent material [3]. By taking advantages of the combined benefits of both the materials, the MSPE technology exhibits excellent adsorption efficiency and rapid separation from the crude sample matrix by an external magnetic field [3,4].

It is obvious that the excellent absorbent materials must have high specific surface area, chemical stability, and a lot of adsorption sites [5]. Carbon-based nanomaterials, which have unique π-electronic structure, have been used as excellent adsorbents in cleanup procedures [6]. Recently, Graphene, as a newly found carbon-based nanomaterial with fascinating two-dimensional atomic thickness structure and large theoretical specific surface area, has attracted wide attention and become a hot research tide [7]. However, there are main drawbacks in the usage of graphene as a sorbent material. Graphene nanoparticles tend to aggregate, which may lead to great reduction in the surface area and its adsorption efficiency. Moreover, graphene is an ultralight material and it is usually hard to retrieve from a suspension even by high-speed centrifugation [8,9]. Therefore, chemical modification of graphene is imperative. Graphene oxide (GO), a chemically modified graphene sheet with a giant aromatic macromolecule containing reactive oxygen functional groups on its basal planes and edges such as epoxide, hydroxyl and carboxylic acid, is a unique structure with remarkable properties such as superior dispersibility, and facile modification via its reactive groups which further enhance the selectivity of GO as a sorbent material [10]. Moreover, introducing magnetic properties into graphene or GO can combine the high adsorption capacity of these carbon based nanomaterials and the separation convenience of magnetic materials through a MSPE methodology [4,11,12]. On the other hand, the surface modification of

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magnetic GO can lead to selective separation of analytes from samples with complicated matrices.

β-cyclodextrin (β-CD) is a macrocyclic compound composed of seven D-glucose units linked together by α-(1,4)-glycosidic bonds in a torus shaped structure with a hydrophobic inner cavity, and a hydrophilic outer side [13]. β-CD can selectively bind with various organic, inorganic and biological guest molecules into its cavity to form stable host–guest inclusion complexes by a series of forces such as hydrophobic and van der Waals interactions [14,15]. Consequently, the combination of β-CD and GO simultaneously possesses the unique properties of GO (large surface area and high dispersilbility) and β-CD (high supramolecular recognition capability), providing a good opportunity for application in sample pretreatment methodology [14,16].

Gemfibrozil, 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoic acid, is a benzene derivative of valeric acid belonging to a drug group known as fibrates [17]. It is clinically effective in reducing serum cholesterol and triglyceride levels. It has also been demonstrated that this drug lowers the incidence of coronary heart disease in humans [18]. Several methods have been developed for the determination of gemfibrozil in biological samples, environmental substances and pharmaceutical formulations, including high performance liquid chromatography with fluorescence detection, liquid chromatography–tandem mass spectrometry, gas chromatography–mass spectrometry and spectrofluorometry [17–22].

The host–guest inclusion complex between β-CD and gemfibrozil has been previously proven [22], and as mentioned above, the adsorption properties and selectivity of the GO regarding the target analytes could be significantly improved in the presence of β-CD. Therefore, in this work, we report on the first application of β-CD grafted graphene oxide-magnetite nanohybrid as a novel sorbent for MSPE of gemfibrozil from human serum and pharmaceutical wastewater samples prior to spectrofluorometric determination at λ_{em}=304 nm after excitation at 276 nm.

2. Experimental

2.1. Apparatus and instruments

Fluorescence spectra and intensity measurements were carried out using a FP-6200 JASCO Corporation (Tokyo, Japan) spectrofluorometer with a wavelength range of 220–730 nm (with 1 nm intervals) for excitation and emission. The instrument equipped with a 150 W xenon lamp, 1.0 cm quartz cell, Peltier thermostatted single cell holder (model ETC-272), and supported with PC-based Windows® Spectra Manager TM software for JASCO Corporation version 1.02. The slit widths for both excitation and emission were set at 5 nm and the fluorescence spectra were recorded at a scan rate of 250 nm min^{-1}.

In order to structural study of the nano-particles, XRD measurements were performed on a Bruker AXS model D8 Advance (Karlsruhe, Germany) instrument with Cu-K_α radiation source (1.54 Å) between 2 and 70° generated at 40 kV and 35 mA at room temperature. Samples for XRD were ground into powder and then pressed flat in the sample slot. In addition, FT-IR spectra (4000–400 cm^{-1}) were recorded on a Bruker model Vector 22 (Ettlingen, Germany) Fourier transform infrared spectrometer using the KBr disk method with a ratio sample/KBr of 1:100 by mass. A scanning electron microscope (SEM), model LEO1430vp (Carl Zeiss, Geramany), was additionally used to examine the morphological characteristics of the sorbent. An ultrasonic bath (SONICA, Italy) was used to disperse the adsorbent in sample solution vials. A shaker (Pars Azma Co., Iran) was used for controlled stirring the sample solution vials in adsorption and desorption steps. The pH values were measured with a Metrohm digital pH-meter model 827 (Herisau, Switzerland) supplied with a glass-combined electrode. An electronic analytical balance, Mettler Toledo model PB303 (Greifensee, Switzerland) was used for weighting the solid materials.

2.2. Standard solutions and reagents

All chemicals used were of analytical reagent grade and all solutions were prepared with high purity deionized water obtained from Shahid Ghazi Co. (Tabriz, Iran). Graphite flakes (99.99%) $FeCl_3 \cdot 6H_2O$, $FeCl_2 \cdot 4H_2O$, $NH_3 \cdot H_2O$ and other chemical reagents was purchased from Merck (Darmstadt, Germany). β-cyclodextrin was purchased from Acros organics (Geel, Belgium). A stock standard solution of 400 mg L^{-1} gemfibrozil (Sigma-Aldrich, St. Loius, MO, USA) was prepared in a 100 mL volumetric flask by dissolving 40.0 mg of gemfibrozil in approximately 10 mL of 0.1 mol L^{-1} sodium hydroxide and diluting to the mark with deionized water.

2.3. Preparation of the nano-sorbent

GO was prepared by oxidizing graphite with acid by a modified Hummers' method [23]. GO/Fe_3O_4 nano-hybrid was synthesized by the *in situ* chemical precipitation of Fe^{2+} and Fe^{3+} in alkaline solution in the presence of GO. For this purpose, 80 mg $FeCl_2 \cdot 4H_2O$ and 216 mg $FeCl_3 \cdot 6H_2O$ were added to 20 mL deionized water containing 40 mg well-distributed GO suspension at 50 °C under a nitrogen atmosphere. After the solution was ultrasonicated for 20 min, 1 mL solution of $NH_3 \cdot H_2O$ was added dropwise into the mixture with vigorous stirring and then heated to 50 °C for 40 min under a nitrogen atmosphere. After cooling to room temperature, the precipitate was isolated by a commercial magnet and washed several times with the deionized water. The resulting product was dispersed in 20 mL water and the homogeneous product of 4 mg mL^{-1} GO/Fe_3O_4 suspension was obtained. For the grafting of GO/Fe_3O_4 nano-hybrid with β-CD, 10 mL of 4 mg mL^{-1} GO/Fe_3O_4 suspension was mixed with 10 mL of 4 mg mL^{-1} β-CD aqueous solution. After being vigorously shaken, the vial was put in a water bath at 60 °C for 3.5 h [10]. The resultant material was precipitated and separated by a magnetic field for several cycles to remove excess β-CD.

2.4. Sample preparation

2.4.1. Human serum samples

All experiments on humans were performed in compliance with the relevant laws and institutional guidelines approved by the Medical Ethics Committee of Tabriz University of Medical Sciences, Tabriz, Iran. Required consent was obtained. Human serum samples were selected as real samples for analysis by the presented method. To precipitate and remove interfering proteins, the serum samples were diluted 1:4 with acetonitrile and centrifuged for 10 min at 4000 rpm [22]. Then, 1 mL of the supernatant was diluted 200 times and subjected to extraction and determination by following the procedure described in Section 2.5.

2.4.2. Pharmaceutical wastewater samples

Pharmaceutical wastewater samples were collected from Pharmaceutical Manufactory effluents in Tehran, Iran. These samples were filtered through Black band filter paper and centrifuged to remove any suspended particulate. Then, aliquots of 200 mL from samples were analyzed within 24 h of collection without other treatments.