Journal of Chromatography A, 1338 (2014) 1–8

Contents lists available at ScienceDirect

Journal of Chromatography A

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

Magnetic nanoparticles based dispersive micro-solid-phase extraction as a novel technique for coextraction of acidic and basic drugs from biological fluids and waste water

Ali Akbar Asgharinezhad, Narges Mollazadeh, Homeira Ebrahimzadeh*, Fatemeh Mirbabaei, Nafiseh Shekari

Faculty of Chemistry, Shahid Beheshti University, G.C., Evin, Tehran, Iran

ARTICLE INFO

Article history:
Received 25 November 2013
Received in revised form 5 February 2014
Accepted 8 February 2014
Available online 18 February 2014

Keywords:
Dispersive micro-solid phase extraction
Coextraction
Cetyltrimethyl ammonium bromide-coated Fe_3O_4@decanoic acid
Diclofenac
Diphenhydramine

ABSTRACT

The coextraction of acidic and basic drugs from different samples is a considerable and disputable concept in sample preparation strategies. In this study, for the first time, simultaneous extraction of acidic and basic drugs with magnetic nanoparticles based dispersive micro-solid phase extraction followed by high performance liquid chromatography-ultraviolet detection was introduced. Cetyltrimethyl ammonium bromide-coated Fe_3O_4@decanoic acid as an efficient sorbent was successfully applied to adsorb diclofenac (DIC) as an acidic and diphenhydramine (DPH) as a basic model compound. First, appropriate amount of synthetic Fe_3O_4@decanoic acid nanoparticles was added to aqueous solution of drugs. After adjusting the pH of the solution, cetyltrimethyl ammonium bromide (CTAB) was added to the mixture being stirred at a constant rate. After the adsorption of drugs and decantation of supernatant with a magnetic field, the sorbent was eluted with methanol by fierce vortex. The parameters affecting the extraction efficiency were optimized and obtained as: pH of the sample = 9, concentration of CTAB = 0.2 mmol L^{-1}, amount of sorbent = 10 mg, extraction time = 5 min, no salt addition to sample, type and volume of the eluent = 50 μL methanol, and desorption time = 1 min. Under the optimum conditions detection limits and linear dynamic ranges were achieved in the range of 1.8–3.0, 5–1500 μg L^{-1} for DPH and 1.5–3.5, 5–1500 μg L^{-1} for DIC, respectively. The percent of extraction recovery and relative standard deviations (n = 5) were in the range of 47.3 – 60, 5.2 – 9.0 for DPH and 64 – 76.7, 5.1 – 5.8 for DIC, respectively. Ultimately, the applicability of the method was successfully confirmed by the extraction and determination of DIC and DPH in human urine, plasma and waste water samples in the range of microgram per liter and satisfactory results were obtained.

1. Introduction

The growing worldwide consumption of pharmaceuticals and their occurrence in the environment has become an important issue in recent years [1]. Therefore, the development of simple, sensitive, rapid and reliable method for the determination of drugs in human beings, animals and environment is of great importance. Herein, co-administration of diphenhydramine (DPH) and diclofenac (DIC) is in a point of view (Table 1S, Electronic Supplementary Materials). Co-administration of diphenhydramine (DPH) with diclofenac is occasionally prescribed as antihistaminic and non-steroidal anti-inflammatory drugs.

Antihistamines are widely consumed to relieve allergic symptoms caused by histamine release. Histamine causes changes within the cells which lead to symptoms such as sneezing, itching and increased mucus production [2,3]. Principal pharmacological histamine effects involve the cardiovascular system, extravascular smooth muscle and exocrine glands [4]. Diphenhydramine hydrochloride, [2-(diphenylmethoxy)-*N*,*N*-dimethylethylamine hydrochloride], is a first generation basic antihistamine drug. It is mainly used as an antiallergic, antiemetic, sedative, antitussive and hypnotic drug found in many pharmaceutical preparations [5,6]. Several analytical methods have been described for DPH analysis in pharmaceutical preparations including spectrophotometry [7–9], flow injection analysis [10], capillary electrophoresis [11–13], thin layer chromatography [14], gas chromatography [15], and high performance liquid chromatography [16–18].

* Corresponding author.
E-mail address: h-ebrahim@sbu.ac.ir (H. Ebrahimzadeh).

http://dx.doi.org/10.1016/j.chroma.2014.02.027
0021-9673/

Sodium diclofenac (DIC), a sodium salt of 2-[(2,6-dichlorophenyl)aminophenyl]-acetic acid is a relatively safe and effective non-steroidal acidic drug [19], which is widely used in the treatment of degenerative joint diseases and other arthritic conditions [20,21]. The analytical methods developed for DIC quantification, include UV–Vis spectrometry [22,23], high performance liquid chromatography [24–26], thin layer chromatography [27], capillary electrophoresis [28], LC–MS [29], voltammetry [30], and potentiometry [31].

Sample preparation procedures play a dominant role in chemical analyses. Extensive sample cleanup procedures are usually required to remove matrix components which may interfere with the analysis. Solid-phase extraction (SPE) is one of the most popular sample preparation methods due to its significant advantages such as improvements in automation, reproducibility and high-throughput capability [32–35]. Although SPE is applied broadly, it has some disadvantages such as solvent loss, large secondary wastes, a long procedure, and need for complex equipment. Dispersive micro-solid phase extraction (D-μ-SPE) is categorized as a SPE technique. The D-μ-SPE has some advantages over traditional SPE, such as convenience for efficiency of recovery; short time requirement and reduced solvent consumption [36,37]. Moreover, it is simple, economic and easy to perform [38]. Different sorbents can be employed with D-μ-SPE. Recently, magnetic nanoparticles (MNPs) have gained research interest as an extraction approach since they can be easily isolated from matrix by using an external magnetic field without retaining residual magnetization after its removal [39]. Also NPs offer a significantly higher surface area-to-volume ratio and a shorter diffusion route than conventional sorbents, resulting in high extraction capacity, rapid extraction dynamics and high extraction efficiencies [40,41]. Moreover, MNPs's surface functionality can be easily modified to achieve selective sample extraction [42,43]. All the named methods have been successfully applied for routine analysis of each drug, but none of them afford simultaneous quantification of the mentioned acidic and basic drugs in a single step.

In this context, the object is to develop a MNPs based D-μ-SPE method for simultaneous preconcentration and determination of two widely used acidic and basic drugs, DPH and DIC, in plasma, urine and waste water samples for the first time. These drugs were adsorbed on cetyltrimethyl ammonium bromide-coated Fe_3O_4@decanoic acid nanoparticles in a batch extraction procedure. The MNPs were then gathered using a supermagnet; which makes them particularly suitable for sample preparation since no centrifugation or filtration is needed after extraction. Afterward, the extracted drugs were eluted with very low amount of organic solvent from the surface of the sorbent under fierce vortex and were determined simultaneously using HPLC-UV. To the best of our knowledge, CTAB-coated Fe_3O_4@decanoic acid has not been employed yet for the simultaneous extraction and determination of acidic and basic drugs.

2. Experimental

2.1. Chemicals and reagents

DPH and DIC were kindly donated by Darou Pakhsh (Tehran, Iran) and used without further purification. Ferric chloride ($FeCl_3$), ammonium ferrosulfate ($(NH_4)_2Fe(SO_4)_2{\cdot}6H_2O$), ammonium hydroxide (28%, w/v), decanoic acid, acetone, acetic acid, ethyl acetate, 2-propanol which all were of analytical-grade were supplied by Merck (Darmstadt, Germany). HPLC grade acetonitrile (ACN) and methanol (MeOH) were purchased from Caledon (George-Town, Ontario, Canada). CTAB was purchased from Sigma–Aldrich (St. Louis, MO, USA). Ultrapure water was prepared using a milli-Q system from millipore (Bedford, MA, USA). Plasma and urine samples were obtained from the Clinic of Taleghani Hospital and waste water sample was obtained from a pharmaceutical factory (Tehran, Iran).

2.2. Equipment

HPLC analysis was conducted using a Wellchrom HPLC system from Knauer Company (Berlin, Germany). The instrument consists of a K-5020 degasser, a K-501 pump, a 6-port/3-channel injection valve equipped with a high pressure manual injection valve (20 μL loop), and a K-2501 UV detector. Eurochrom 2000 was used for the data acquirement and processing. Chromatographic separations were performed by a Capital HPLC column (Braburn, UK) ODS-H C18 (250 mm × 4.6 mm I.D., 5 μm). The mobile phase was a mixture of sodium dihydrogen phosphate dihydrate buffer (0.01 M, pH = 2.5) and ACN (40:60, v/v) at the flow rate of 1 mL min^{-1} in isocratic mode with the detector wavelength set at 225 nm. The pH of mobile phase and all other solutions was adjusted by using a Metrohm digital pH meter 827 (Herisau, Switzerland) equipped with a glass calomel electrode. In the extraction procedure, a 6 mL conical sample vial, a MR 3001 heating-magnetic stirrer from Heidolph Company (Kelheim, Germany) and a MS3 digital vortex agitator from IKA Company (Staufen, Germany) were used to mix the MNPs with the sample. EBA 20 Hettich centrifuge (Oxford, England) and a 50 μL Hamilton HPLC syringe (Reno, NV, USA) were employed, too. The morphology and dimension of the Fe_3O_4@decanoic acid nanoparticles were explored by transmission electron microscopy (TEM) using a Zeiss 900 TEM at a voltage of 150 kV and a scanning electron microscope (SEM) model VEGA TESCAN (Brno, Czech Republic). Magnetic nanoparticles were sputter coated with gold prior to the SEM measurement. A Nd-Fe-B strong magnet (15 cm × 12 cm × 5 cm, 1.4 T) was used for sorbent collection and magnetic decantation.

2.3. Preparation of standard solutions and real samples

Stock standard solution of drugs (1000 mg L^{-1}) was prepared in HPLC grade methanol and stored in a fridge at 4 °C and brought to ambient temperature just prior to use. Mixed working solutions containing DIC and DPH at different concentrations were prepared by dilution with ultra-pure water for optimization of parameters. The plasma and urine samples were collected into test tubes and stored at −20 °C prior to use. Before extraction, for plasma samples: (1) 1.5 mL spiked plasma sample was mixed with 100 μL hydrochloric acid (37%) and 100 μL trifluoroacetic acid in order to precipitate proteins, (2) the obtained solution was vortexed and centrifuged for 5 min at 3000 rpm, and (3) the supernatant was removed and diluted at the ratio of 1:3, v/v, with ultrapure water. For spiked/real urine samples: 2.5 mL urine sample was diluted at the ratio of 1:1, v/v, with ultrapure water, and 5 mL spiked waste water sample was used without dilution.

2.4. Preparation of the Fe_3O_4@decanoic acid nanoparticles

The synthesis strategy of Fe_3O_4@decanoic acid was described by Shen et al. [38]. Briefly, in a typical synthesis to obtain 1.0 g Fe_3O_4 NPs precipitate, 1.69 g of ammonium ferrosulfate and 1.41 g of ferric chloride (molar ratio of $Fe^{3+}/Fe^{2+} = 2$) were dissolved under N_2 atmosphere in 40 mL of ultra-pure water with vigorous stirring at 2000 rpm using a mechanical stirrer. As the solution was heated to 80 °C, another solution containing 100 mg of decanoic acid in 5 mL of acetone was added, followed by the addition of 5 mL of 28% (w/v) NH_4OH. Thereafter, further decanoic acid (five 0.2 g portions) was successively added to the obtained suspension during 5 min. The crystal growth was allowed to proceed for