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RESEARCH PAPER

Glycine functionalized multiwall carbon nanotubes as a novel hollow fiber solid-phase microextraction sorbent for pre-concentration of venlafaxine and *o*-desmethylvenlafaxine in biological and water samples prior to determination by high-performance liquid chromatography

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Abstract A hollow fiber solid-phase microextraction method for pre-concentration of venlafaxine and *o*-desmethylvenlafaxine in biological matrices is described for the first time. The functionalized MWCNTs with an amino acid, glycine, were synthesized and held in the pore of a hollow fiber by sol–gel technique. In order to extract venlafaxine and *o*-desmethylvenlafaxine from real samples, the hollow fiber was immersed into the sample solution under a magnetic stirring for 20 min. The extracted venlafaxine and *o*-desmethylvenlafaxine from the fibers were then desorbed with methanol by sonication and analyzed using high-performance liquid chromatography. Important microextraction parameters including pH of donor phase, donor phase volume, stirring rate, extraction time, and desorption conditions such as the type and volume of solvents and desorption time were thoroughly investigated and optimized. The optimized technique provides good repeatability (RSD of the intraday precision 3.7 and 3.4, interday precision of 5.8 and 5.4 %), linearity of (0.1–300 and 0.2–360 ng mL^{-1}), low LODs of (0.03 and 0.07 ng mL^{-1}), and high enrichment factor of (164 and 176) for venlafaxine and *o*-desmethylvenlafaxine, respectively. The analytical performance of Gly-MWCNTs as a new SPME sorbent was compared with MWCNTs and carboxylic MWCNTs. The results indicate that Gly-MWCNTs are quite effective for extraction of venlafaxine and *o*-desmethylvenlafaxine. Feasibility of the method was evaluated by analyzing human urine and real water samples. The results obtained in this work show a promising, simple, selective, and sensitive sample preparation and determination method for biological and water samples.

Keywords Venlafaxine · *O*-desmethylvenlafaxine · Glycine · Functionalized multiwall carbon nanotubes · Hollow fiber solid-phase microextraction · Human urine samples

Introduction

Serotonin–norepinephrine reuptake inhibitors (SNRIs) are a class of antidepressant drugs. Venlafaxine (VEN) is the first and most commonly SNRI and was introduced in 1994 by Wyeth-Ayerst Research. VEN has been widely used in the treatment of depression by selective serotonin (5-hydroxytryptamine; 5-HT) and noradrenaline (norepinephrine) reuptake inhibitors [1]. VEN is metabolized in the liver through the cytochrome P450 system into another antidepressant drug called *o*-desmethylvenlafaxine (ODV) [2]. Like VEN, ODV has pharmacological activity and affect the reuptake of monoamines. VEN and ODV are formulated as tablet and capsules with retarded release for oral administration. They are excreted in urine by kidney [3]. The average half-life of VEN and ODV is 5 ± 2 and 11 ± 2 h, respectively. Approximately 87 % of VEN excreted in urine as the unchanged form (5 %), free ODV (29 %), coupled ODV (26 %), or inactive metabolites (27 %) within 48 h [4]. Several extraction methods coupled with HPLC for the extraction and determination of VEN and ODV in biological and other samples such as cloud point

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extraction [5], solid-phase extraction [6], stir bar sorptive extraction [7], liquid–liquid extraction [8–10], microextraction by packed sorbent [11], and ultrasound-assisted emulsification microextraction based on solidification of floating organic droplet [12] were developed.

A large number of drugs in the world are used for healing various diseases in recent years. Many of these drugs are excreted in urine or feces as either unchanged drug or as biologically active metabolites. Therefore, drugs are a serious source of biologically active environmental contamination when these compounds are eventually entered in the water sources. In order to identify sources of contamination study of behavior and fate and assess the potential risks deriving from their ubiquity, monitoring drugs in the environment is very important [13].

Due to trace-level concentrations of drugs in biological human samples and its complex matrices, a sample preparation step prior to analysis is inevitable. Sample preparation is one of the main bottle necks in drug analysis. The choice of sample preparation methodology is very effective in the quality of results. Solid-phase microextraction (SPME) has been widely used as a sample preparation technique due to its advantages such as simplicity, solvent-free, and cost effective [14–18]. However, like other analytical methods, the traditional SPME also has its drawbacks including high time-consumption, fiber breakage, stripping of coatings, low operating temperature (generally in the range of 240–280 °C for desorption with GC), instability, and swelling in organic solvents (greatly restricting their use with HPLC) [19, 20]. In order to overcome some of these drawbacks, hollow fiber SPME methods have been developed. Hollow fibers are a polypropylene or polyethylene tubes with a high porosity structure. Due to mechanical, chemical, and thermal stability and high porosity structure, hollow fiber has great ability to be applied in microextraction technique. Hollow fibers have a large surface area to volume so the contact between receiver and donor phases in microextraction is high. Use of hollow fiber has led the microextraction to be handled with ease because the receiving phase is protected by hollow fiber segment [21]. Most recent trends in SPME are on the development of new fiber coating and extraction formats in order to overcome the limitations of conventional SPME method [22]. A drawback of conventional SPME is the loss of fiber coatings due to the physical bonds between the coatings and fiber surface. The sol–gel technique has overcome some significant shortcomings of conventional SPME by chemical bonding between the sorbent and fiber surface [15]. In this process, a colloidal solution (sol) is formed from a monomer (Precursor), and then sol is converted to an integrated network (or gel) of either discrete particles or network polymers at room temperature [23–25].

A unique allotrope of carbon is carbon nanotubes (CNTs) with novel properties making them potentially useful in wide varieties of applications (e.g., electronics, optics, catalysis, biomedicine, analytical chemistry, etc.). They are always divided into two categories; single-walled carbon nanotubes (SWCNTs) and multi-walled carbon nanotubes (MWCNTs) [26, 27]. Due to their unique structures, they have extraordinary properties such as thermal and mechanical stability and high absorption capacity. In addition, their surface characteristics are easily modified by both non-covalent and covalent modification. Modified surface of CNTs are expected to exhibit higher pre-concentration factors and better selectivity in SPME [3, 28].

In this work, a new, simple, sensitive, and selective hollow fiber solid-phase microextraction combined with HPLC technique was proposed for pre-concentration and determination of VEN and ODV in human biological and real water samples. In order to achieve desirable selectivity and efficiency of SPME, novel functionalized MWCNTs were prepared and placed onto the pores of hollow fiber by the sol–gel technology. The analytical performance of the functionalized MWCNTs as SPME sorbent was compared with MWCNTs for HF-SPME of VEN and ODV. The optimum experimental conditions of the proposed HF-SPME procedure were systematically studied before validating the human urine and real water analysis.

Experimental

Chemicals and materials

VEN and ODV of pharmaceutical quality were purchased from Samisaz Pharmaceutical Co. (Mashhad, Iran). All other chemicals were of analytical grade and were obtained from Merck (Darmstadt, Germany). MWCNTs with mean outer diameter of ≤20 nm, 5–15 μm lengths, and purity greater than 95 % were purchased from the Research Institute of the Petroleum Industry (Tehran, Iran). The Q3/2 Accurel polypropylene micro porous hollow-fiber membrane (200 μm wall thickness, 600 μm inner diameter, 0.2 μm pore size, 75 % porosity) was obtained from Membrana (Wuppertal, Germany). Acetonitrile and methanol (HPLC grade, ≥99.8 %) were purchased from Merck (Darmstadt, Germany).

Apparatus

The HPLC system was a Knauer HPLC (Germany, D-14163) consisting a port sample injection valve with a 20 μL injection loop, a photodiode array detector (S2600), computer system and software EZ-Chrom Elite with integration capability. The chromatographic separation was carried out at room temperature (22 ± 0.5 °C) on a 100/

$5C_{18}$ analytical column (6.4 × 250 mm, 5.1 μm). The mobile phase was a mixture of 50 % water containing 50 mM potassium dihydrogenorthophosphate (pH 6.2), 40 % acetonitrile, and 10 % methanol. The flow rate was 1.0 mL/min and the PDA detector was set at 226 nm. A compact ultrasonic model Hiescher up 100 h (100 W, 30 kHz) was used to mix various solution ingredients thoroughly. The pH values were adjusted by a Metrohm pH-meter model 691.

MWCNT functionalization

In order to remove amorphous carbon, 0.2 g of untreated MWCNTs was weighted and poured into a flask and heated in an oven at 350 °C for 30 min. After thermal treatment, 30 mL mixture of HNO_3/H_2SO_4 (1:3, *v/v*) was added into a flask, and treated for 3 h at 40 °C in an ultrasonic bath. The resulting solution was centrifuged for 5 min at 4000 rpm. The oxidized MWCNTs (MWCNT–COOH) was washed thoroughly with tetrahydrofuran for five times and dried in an oven at 70 °C [29].

Furthermore, 0.2 g of glycine and 4 mL water was added into a conical vial in order to form the glycine suspension. MWCNT–COOH was then added to suspension and ultrasonically treated for about 1 h at room temperature to obtain MWCNT–CO-NH-CH_2-COOH [30, 31]. The mixture was washed with ethanol three times to remove excessive glycine. It was then dried in a vacuum for about 16 h at room temperature. TEM image and FTIR spectrum of Gly-MWCNTs are shown in Figs. 1 and 2.

Fabrication of the sol–gel/Gly-MWCNT/HF-SPME device

The sol solution of functionalized MWCNTs/silica composite was prepared by acid-based catalyzed method [4, 32]. One milliliter of ethanol was added to 1 mL of tetraethylorthosilicate in a glass vial and stirred for 10 min at 0 °C. In order to start the hydrolysis and condensation reactions, the HCl solution was continuously added while stirring at room temperature for 20 min. Then, 300 μL of the surfactant, poly-(ethylene glycol) 400, was added into the mixture, and the solution was stirred for 120 min. In order to form the colloidal solution (sol) of Gly-MWCNTs/silica composite, 0.04 g of the Gly-MWCNTs was added to the resulting mixture, and the mixture was stirred at room temperature for an additional 30 min [33].

The segments of polypropylene microporous hollow-fiber tubes were cut in 1.0 cm pieces. In order to remove any impurities from the fiber segments, they were ultrasonically washed in acetone for 5 min and dried in air. The fiber segments were then immerged in colloidal solution (sol) of Gly-MWCNTs/silica composite and ultrasonically treated at room temperature for 90 min. Finally, the resulting hollow fibers were washed with deionized water for three times and left to dry at room temperature for 1.0 h [34]. SEM image of sol–gel/Gly-MWCNT/hollow fiber is shown in Fig. 3.

Fig. 1 TEM image of Gly-MWCNTs

Preparation of the sol–gel/MWCNT/HF-SPME and the sol–gel/carboxylic MWCNT/HF-SPME device for comparison

The sol–gel/MWCNT/HF-SPME device was prepared by the method described in "Fabrication of the sol–gel/Gly-MWCNT/HF-SPME device" section with the exception that MWCNT (0.04 g) was used instead of Gly-MWCNT.

In order to prepare the sol–gel/carboxylic MWCNT/HF-SPME device, firstly, the carboxylic MWCNT was synthesized by the method described in "MWCNT functionalization" section. Secondly, the carboxylic MWCNT was placed on hollow fiber by sol–gel technique ("Fabrication of the sol–gel/Gly-MWCNT/HF-SPME device" section).

Extraction procedure

In order to carry out the extractions procedure, 12.0 mL of VEN and ODV standard solution (10 ng mL^{-1}) was placed in a 25 mL SPME-vial, and the pH of solution was brought to 6.0 by adding 3 mL of phosphate buffer solution. The hollow fiber containing functionalized MWCNT was then immerged into the glass vial. The vial was sealed at the cap and the mixture was stirred for 20 min at 600 rpm by a stirring bar. After the extraction procedure, hollow fiber was removed from the solution and transferred into a conical vial. Then, 1.0 mL methanol, as desorption solvent, was added to vial and ultrasonically treated for 5 min. Finally, 10 μL of the methanolic phase was measured by HPLC system. For each experiment, three replicate extractions were carried out.

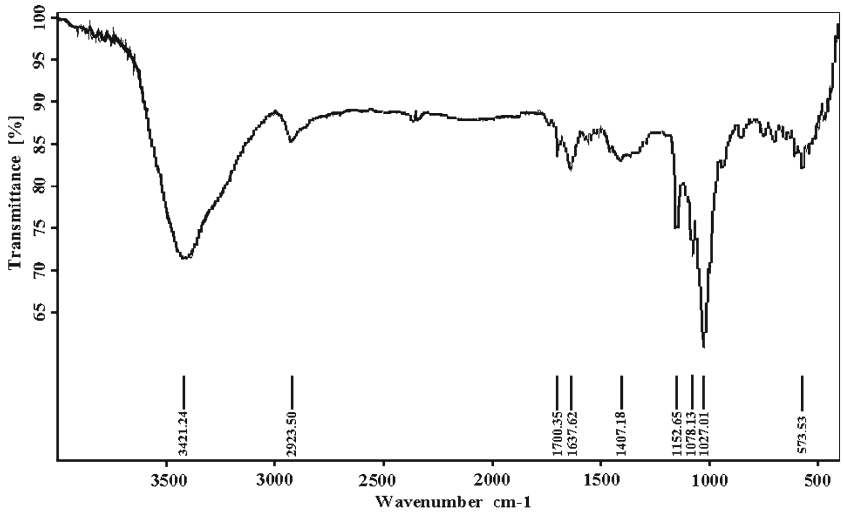

Fig. 2 FTIR spectrum of Gly-MWCNTs

Real samples preparation

Human urine samples were collected from healthily volunteers in our laboratory and stored in polypropylene tubes at 20 °C.

Well, tap, and river water samples were collected form outskirts of Mashhad and Golestan River (Mashhad, Iran), respectively.

All the human urine and real water samples were spiked with 10 and 50 ng mL^{-1} of VEN and ODV, respectively, and centrifuged at 8000 rpm for 5 min and then stored at 4 °C prior to analysis.

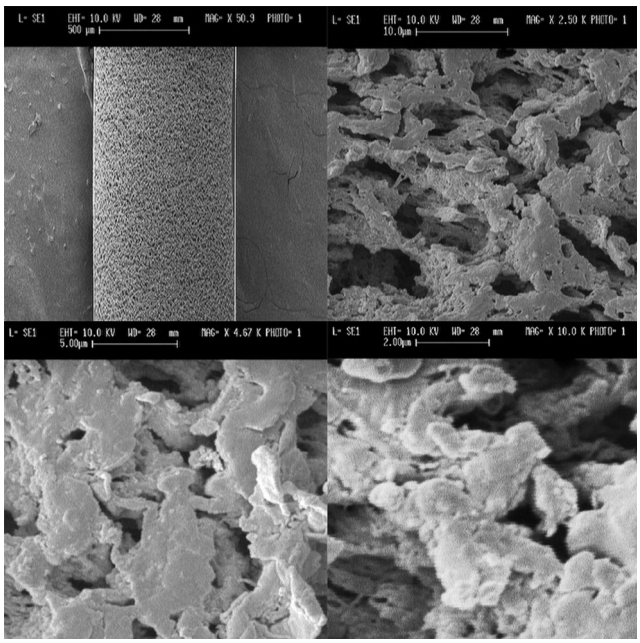

Fig. 3 SEM image of Sol–Gel/Gly-MWCNT/hollow fiber

Results and discussion

Optimization of the glycine-MWCNTs-HF-SPME procedure

In order to obtain maximal extraction efficiency, different parameters affecting the functionalized MWCNTs-HF-SPME including volume of the donor phase, pH, extraction time, desorption time, the type of desorption solvent, and stirring rate have been thoroughly investigated and optimized.

pH of sample solution

The pH of the sample solution affects the interaction between functional group on the surface of HF-SPME and target analyte. To study the effect of sample pH on the extraction efficiency of venlafaxine, the pH of solutions were adjusted at 4.0–9.0 using suitable buffer solutions, and were extracted for about 30 min at a stirring rate of 500 rpm. Figure 3 shows the effect of sample pH on the extraction efficiency of VEN and ODV. As can be seen, when the pH of the sample solution increased from 4.0 to 6.0, the peak areas were dramatically increased, and leveled off at higher pHs. This phenomenon can be explained by strong interaction between carboxylic group on the surface of Gly-MWCNTs and VEN or ODV. At pH 6.0, carboxylic group mainly exists as undissociated and neutral group. Therefore, strong hydrogen bonding is formed between the surface of hollow fiber coating and analytes and contributing to the extraction. Figure 4 shows that the highest extraction efficiency was observed at pH 6.0 for both analytes.

Donor phase volume

In the HF-SPME procedures, the ratio of donor phase volume to acceptor phase volume is an effective factor. A high pre-

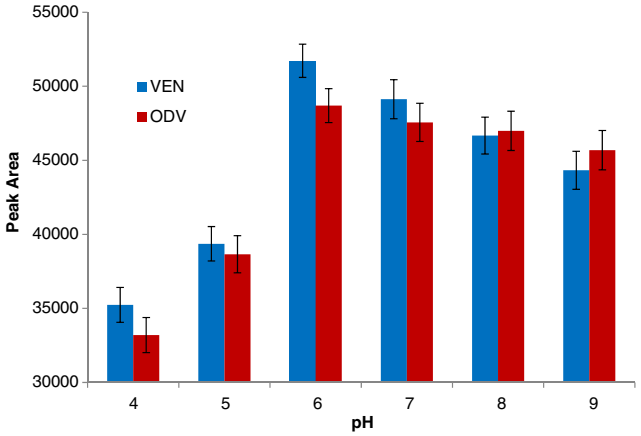

Fig. 4 Effect of feed solution pH on the extraction process. Conditions: analytes concentration, 10 ng mL^{-1}; donor phase volume, 10.0 mL; desorption phase volume, 1.0 mL; stirring speed, 500 rpm; extraction time, 30 min; desorption time, 8 min; temperature, 23 ± 0.5 °C

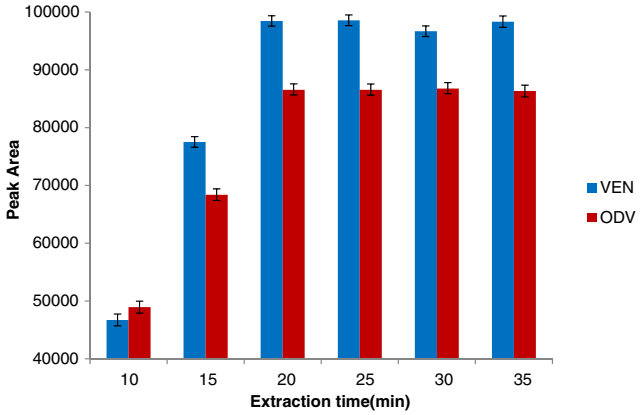

Fig. 5 Effect of extraction time on the extraction process. Conditions: analytes concentration, 10 ng mL^{-1}; donor phase volume, 15.0 mL; desorption phase volume, 1.0 mL; stirring speed, 500 rpm; desorption solvent, ethanol; desorption time, 8 min; pH, 6.0; temperature, 23 ± 0.5 °C

concentration factor is generally obtained by increasing the ratio of donor phase to acceptor phase volumes. Theoretically, the amount of analytes extracted increases by increasing in sample volume up to a point because HF-SPME is an equilibration process and analytes is reached to equilibrium between the hollow fiber coating and sample solution. Therefore, the volume of sample solution depends on the surface density of the hollow fiber coating and the size of sample vial. In order to study the extraction efficiency, sample volumes in range of 5 to 30 mL were analyzed (see Electronic Supplementary Material (ESM) Fig. S1). The results indicate that the peak areas increased with the donor phase volume up to 15 mL, and decreased afterwards. Hence, 15 mL of sample volume was selected for subsequent experiments.

Extraction time

The microextraction method is a time-dependent process and highest extraction efficiency is obtained when equilibrium is attained between the donor and acceptor phases but the time required to reach equilibrium is very long. Therefore, time of pre-equilibrium as extraction time is selected. It is shorter than the time of equilibrium but the amount of analyte extracted is time-dependent and a small error in determining the time may cause much higher relative errors in the amount of analyte extracted. The effect of extraction time on extraction efficiency was investigated in the range of 10–35 min at constant experimental conditions. According to the results shown in Fig. 5, an extraction time of 20 min was selected for further studies.

Stirring rate

Stirring was employed to increase mass transfer and reduces the thickness of boundary layer at the outer membrane surface [35]. Therefore, increasing the stirring rate reduces the time required for reaching thermodynamic equilibrium. Theoretically, the time required to reach equilibrium would depend only on the hollow fiber geometry and the diffusion coefficients of the analyte in the sample solution and boundary layer, if perfect stirring is achieved [36]. The effect of stirring rate (400–900 rpm) on the extraction efficiency was studied. It was found that the peak areas increased in the stirring rate range of 400–600 and decreased at higher rates (see ESM Fig. S2). Therefore, 600 rpm setting was selected for subsequent experiments.

Effect of desorption condition

In order to obtain the highest sensitivity, the extracted analyte must be desorbed ultrasonically by a suitable solvent at an appropriate time. Thus, the type and volume of desorption solvent and desorption time have a great influence on the extraction efficiency and should be optimized. Organic

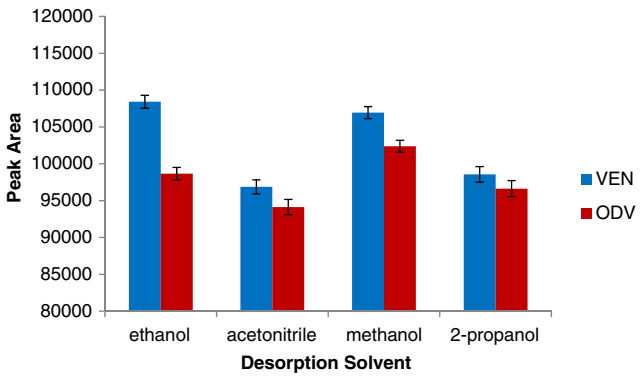

Fig. 6 Effect of desorption solvent on the extraction process. Conditions: analytes concentration, 10 ng mL^{-1}; donor phase volume, 15.0 mL; desorption phase volume, 1.0 mL; stirring speed, 600 rpm; extraction time, 20 min; desorption time, 8 min; pH, 6.0; temperature, 23 ± 0.5 °C

Table 1 Effect of hollow fiber sorbents on the extraction recovery percentage of VEN and ODV ($n = 3$)

Hollow fiber sorbent	Analytes	Venlafaxine		*O*-desmethylvenlafaxine	
	Concentration (ng mL^{-1})	50	150	50	150
MWCNTs	Found (ng mL^{-1})	24.85 ± 0.08	77.10 ± 0.06	27.44 ± 0.09	89.26 ± 0.09
	Recovery percentage	49.7	51.4	54.9	59.5
Carboxylic MWCNTs	Found (ng mL^{-1})	37.61 ± 0.07	118.12 ± 0.07	36.34 ± 0.08	116.87 ± 0.07
	Recovery percentage	75.2	78.8	72.7	77.9
Gly-MWCNTs	Found (ng mL^{-1})	43.18 ± 0.07	136.24 ± 0.07	44.13 ± 0.06	136.75 ± 0.08
	Recovery percentage	86.4	90.1	88.2	91.2

solvents such as acetonitrile, ethanol, 2-propanol, and methanol were selected and investigated as desorption solvents because they cannot dissolve polypropylene membrane and functionalized MWCNTs and also they do not interfere with the interferential peaks [37]. Experiments showed that methanol gave the highest peak areas and it was selected as desorption solvent (Fig. 6). Use of ultrasonic waves can improve desorption efficiency through acoustic cavitation and some mechanical effects caused by ultrasonic waves [38]. Due to the high power compact ultrasonic, desorption equilibrium can be achieved in a very short desorption time by decreasing viscosity desorption solvent and increasing desorption kinetics [13]. The effect of volume of desorption solvent (0.5–2 mL) on the extraction efficiency was studied. The results indicated that the peak areas increased in the volume of desorption solvent of 0.5–1.0 mL and decreased at higher rates than 1.0 mL. Hence, 1.0 mL of methanol was used as the desorption solvent for subsequent experiments. The effect of desorption time on extraction efficiency was investigated in the range of 3–8 min at constant experimental conditions. Desorption time of 5 min was selected for further studies (see ESM Fig. S3).

Comparison of the HF-SPME efficiency of the Gly-MWCNTs coated fiber with carboxylic MWCNTs and MWCNTs coated fibers

In order to compare the extraction efficiency of the Gly-MWCNTs coating with carboxylic MWCNTs and MWCNTs coatings, identical procedure as described in "Fabrication of the sol–gel/Gly-MWCNT/HF-SPME device" and "Preparation of the sol–gel/MWCNT/HF-SPME and the sol–gel/carboxylic MWCNT/HF-SPME device for comparison" sections was applied to prepare HF-SPME devices (Table 1). The results show that the Gly-MWCNTs coating provides the highest extraction recovery and the other two coatings, carboxylic MWCNTs and MWCNTs, were the next extraction recovery for the extraction of VEN and ODV, respectively. Therefore, the Gly-MWCNTs coating is quite effective as hollow fiber coating for the extraction of both analytes. This phenomenon can be explained by the difference in the type and strength of interaction as hydrogen bonding between the hollow fibers coating with analytes. In the MWCNTs coating, weak inter-molecular forces are formed between the delocalized π-electron on MWCNTs coating with functional groups in the surface of analytes, while in Gly-MWCNTs and carboxylic MWCNTs coating, strong hydrogen bonds are formed between the carboxylic groups on coating with analytes. In comparison with Gly-MWCNTs with carboxylic MWCNTs coating, amide groups on the Gly-MWCNTs coating can also participate in hydrogen bond formation. Moreover, with getting away the functional groups from the hollow fiber surface on Gly-MWCNTs coating, the space congestion is less and more interaction is possible. Therefore, due to more hydrogen bond formation and less space congestion, the extraction recovery for Gly-MWCNTs HF-SPME coating is more than carboxylic MWCNTs and MWCNTs.

Method validation

To investigate the applicability of the proposed method for determination of VEN and ODV, several validation parameters such as linearity, precision, and accuracy were evaluated under optimum conditions (Table 2). The calibration graph was linear in the concentration range of 0.1–300 and 0.2–

Table 2 Linearity, repeatability, detection limits, and pre-concentration factor of the proposed analytical procedure

Analytes	Linear range (ng mL^{-1})	R^2	%RSD ($n = 5$)		LOD (ng mL^{-1}) ($n = 5$)	LOQ (ng mL^{-1}) ($n = 5$)	Pre-concentration factor
			Intraday	Interday			
Venlafaxine	0.1–300	0.9969	3.7	5.8	0.03	0.1	164
O-desmethylvenlafaxine	0.2–360	0.9985	3.4	5.4	0.07	0.2	176

Table 3 Assay of VEN and ODV in real water and human urine samples by means of the proposed method ($n = 3$)

Analytes		Venlafaxine			*O*-desmethylvenlafaxine		
Spiked value (ng mL^{-1})		0	10	50	0	10	50
Well water	Found (ng mL^{-1})	Nd	10.67 ± 0.09	48.32 ± 0.09	Nd	9.19 ± 0.08	46.33 ± 0.07
	Recovery percentage	–	106.7	96.6	–	91.9	92.7
Tap water	Found (ng mL^{-1})	Nd	9.43 ± 0.07	47.54 ± 0.06	Nd	10.79 ± 0.08	45.86 ± 0.08
	Recovery percentage	–	94.3	95.1	–	107.9	91.7
River water	Found (ng mL^{-1})	Nd	9.23 ± 0.09	46.47 ± 0.08	Nd	8.94 ± 0.09	55.62 ± 0.08
	Recovery percentage	–	92.3	92.9	–	89.4	111.2
Human urine	Found (ng mL^{-1})	Nd	9.32 ± 0.08	54.78 ± 0.07	Nd	8.78 ± 0.09	44.73 ± 0.08
	Recovery percentage	–	93.2	109.5	–	87.8	89.5

Nd not detected

360 ng mL^{-1} of VEN and ODV, respectively. The correlation coefficients were higher than 0.997 in all cases for both analytes. The limit of detection (LOD) and limit of quantitation (LOQ) were calculated as the ratio of three and ten times of standard deviation of blank readings to the slope of the calibration curve after pre-concentration, respectively. Pre-concentration factor (CF) was calculated according to the following equation:

$$CF = \frac{PA_{final}}{PA_{initial}} \times \frac{V_{aq}}{V_O}$$

Where PA_{final} and $PA_{initial}$ are the final and initial peak area after and before the extraction of VEN and ODV, respectively, V_{aq} and V_O are volumes of sample solution and desorption solvent, respectively. The high pre-concentration factor of 164 and 176 was obtained for VEN and ODV, respectively, by the proposed extraction method (Table 2).

Real samples analysis

In order to investigate the feasibility of the proposed method, several human urine and real water samples were analyzed, and the mean extraction recoveries were calculated for three replicate analysis. The results are given in Table 3, and it is evident that VEN and ODV can be quantitatively recovered from urine and water samples by the proposed procedure and in all cases the obtained relative recoveries are between 87.0 and 111.5 %with RSD% of less than 4.5 %. These results demonstrate the applicability of the proposed procedure for VEN and ODV determination in urine and water samples. HPLC chromatogram of human urine sample after spiking with 20 ng mL^{-1} of VEN and ODV is shown in Fig. 7. No significant interfering peaks were observed at the retention position of analytes.

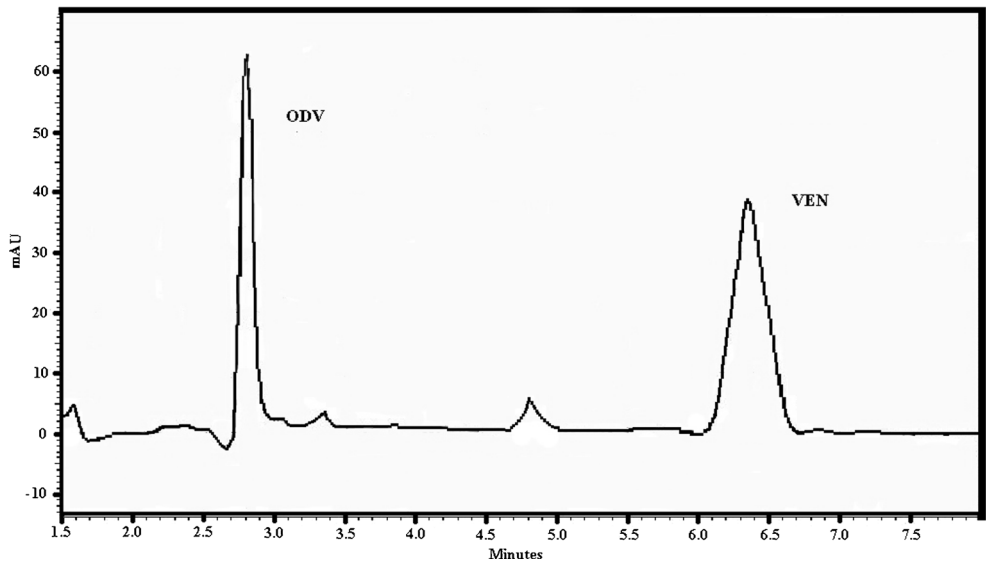

Fig. 7 Chromatogram of human urine sample at 20 ng mL^{-1} for VEN and ODV under optimum conditions

Table 4 Comparison of the proposed method with other reported methods for VEN and ODV determination

No.	Date	Matrix	Extraction method	Detection	LOQ (ng mL^{-1})		DLR (ng mL^{-1})		r		RSD%				Ref.
											Interday		Intraday		
					VEN	ODV	VEN	ODV	VEN	ODV	VEN	ODV	VEN	ODV	
1	2007	Human plasma	SPE	HPLC-Flu	1.0	1.0	1–1000	1–1000	0.9990	0.9990	1.8	2.2	3.6	4.4	[39]
2	2008	Human plasma	CPE[a]	HPLC-Flu	10	–	10–800	–	0.9995	–	0.6	–	1.3	–	[5]
3	2010	Plasma	SBSE[b]	HPLC-FLD	0.2	0.5	0.2–2000	0.2–2000	0.999	0.994	7.9	6.8	6.9	4.0	[7]
		Urine			2.0	5.0			0.999	0.998	6.8	7.3	4.9	5.3	
		Brain tissue			1.0	2.5			0.999	0.999	4.3	6.2	6.2	4.6	
4	2010	Plasma	LLE	UPLC-MS/MS	0.2	0.2	0.2–200	0.2–200	0.996	0.997	>3.2	>4.0	>4.6	>5.2	[40]
5	2013	Saliva	LLE	HPLC-UV	10.2	9.4	1–1000	1–1000	0.9996	0.9998	–	–	–	–	[10]
6	2014	Plasma	MEPS[c]	HPLC-Flu	10	20	10–1000	20–1000	0.9976	0.9987	<5.1	<5.1	<5.1	<5.1	[41]
7	–	Urine Real water	HF-SPME	HPLC-DAD	0.1	0.2	0.1–300	0.2–360	0.9969	0.9985	5.8	5.4	3.7	3.4	–

[a] Cloud-point extraction

[b] Stir bar sorptive extraction

[c] Microextraction by packed sorbent

Comparison to other methods

A comparison of the proposed method with other reported pre-concentration methods coupled by HPLC is given in Table 4. This method has many advantages such as very wide dynamic range, low LOD and LOQ, and high pre-concentration factor with low sample consumption, free of solvent and cost effective compared to other techniques. Moreover, the extraction time (20 min) is less and the relative standard deviation (interday and intraday) and extraction recovery is better than most other reported microextraction methods (data is not in Table 4). Hollow fiber segment is also used as an individual device and directly applied for extraction, so its usage is very simple without any memory affect. These characteristics demonstrate that the proposed method is very suitable for routine laboratory analysis of VEN and ODV for biological and water samples.

Conclusions

A simple, rapid, and sensitive HF-SPME method has been developed for analysis of VEN and ODV in human urine and water samples. In this mode, the Gly-MWCNTs was prepared by the reaction of oxidized multiwall carbon nanotubes and amino acid (glycine) and held in the surface of hollow fiber with sol–gel technique as solid-phase sorbent. The analytical performance of Gly-MWCNTs as new SPME sorbent was compared with MWCNTs and carboxylic MWCNTs. The results indicate that the prepared fiber was found to be the most suitable coating for extraction of VEN and ODV. Several parameters influencing the adsorption and desorption of the analytes on this fiber have been studied. The application of the method to real samples confirmed that this procedure is suitable for quantitative determination of VEN and ODV in biological and water samples for routine laboratory analysis.

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Compliance with ethical standards This article does not contain any studies with human or animal subjects.

Conflict of interest The authors declare that they have no conflict of interest.

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