Dynamic fabric phase sorptive extraction for a group of pharmaceuticals and personal care products from environmental waters

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ABSTRACT

This paper describes for the first time the use of a new extraction technique, based on fabric phase sorptive extraction (FPSE). This new mode proposes the extraction of the analytes in dynamic mode in order to reduce the extraction time. Dynamic fabric phase sorptive extraction (DFPSE) followed by liquid chromatography-tandem mass spectrometry was evaluated for the extraction of a group of pharmaceuticals and personal care products (PPCPs) from environmental water samples. Different parameters affecting the extraction were optimized and best conditions were achieved when 50 mL of sample at pH 3 were passed through 3 disks and analytes retained were eluted with 10 mL of ethyl acetate. The recoveries were higher than 60% for most of compounds with the exception of the most polar ones (between 8 % and 38%). The analytical method was validated with environmental samples such as river water and effluent and influent wastewater, and good performance was obtained. The analysis of samples revealed the presence of some PPCPs at low ng L^{-1} concentrations.

1. INTRODUCTION

Pharmaceuticals and personal care products (PPCPs) are extensively used in our day-to-day life and, after their consumption, they often enter into the environment, mainly from household water because of their ability to pass through the wastewater treatment plants. Their presence may affect human and aquatic life, as they are known to behazardous and may be accumulated in various

environmental compartments due to their continuous release into the environment. Consequently, these compounds are frequently found in waste, surface and even ground water [1-5]. Thus, they are considered to be contaminants of emerging concern.

Due to the growing interest in determining contaminants at low concentration levels in complex matrices, many different extraction techniques have been developed. For liquid samples In the last years, solid-phase extraction (SPE) has become the technique of choice [6-8], although some other techniques have been successfully applied, such as solid-phase microextraction (SPME) [9, 10] and stir bar sorptive extraction (SBSE) [11, 12], among others. However, the most important drawbacks of these techniques [13-15] are the low sorbent present in the fibres of SPME, and the limited number of available sorbent type and slow analyte diffusion rate through polymeric coating in SBSE.

A novel sorptive extraction technique, fabric phase sorptive extraction (FPSE), was recently introduced by Kabir and Furton [16]. This technique consists of the use of a flexible fabric substrate surface coated with different polymers/functional moieties using sol-gel technology so that high primary contact surface area is available for extraction. These unique sorbent chemistries have been developed to cover wide range of analyte polarities and include sol-gel Carbowax 20M [17], sol-gel poly(tetrahydrofuran) [18], sol-gel poly(dimethyldiphenylsiloxane) [19, 20], among others. The sol-gel coated FPSE medium (25 x 20 mm^2) can be directly introduced into the sample for the analyte extraction and, once equilibrium is reached, the analytes retained on the extraction medium can be back-extracted using a small volume of organic solvent [21].

To date, FPSE has been applied to extract several analytes from different samples, such as benzotriazole UV stabilizers in sewage samples [22], alkyl phenols in aqueous and soil samples [23], benzodiazepines in blood samples [24], estrogens in urine and environmental water samples [18], polar antibiotic in raw milk [25], non-steroidal anti-inflammatory drugs [19] and triazine herbicides in environmental water samples [20]. Our research group evaluated FPSE for the extraction of a group of PPCPs followed by liquid chromatography-tandem mass spectrometry (LC-MS/MS) with satisfactory results [17]. However, the main drawback of FPSE was the extraction time (up to four hours) required to reach the extraction equilibrium. To

overcome this long extraction time, a new mode of the FPSE approach is proposed, called dynamic fabric phase sorptive extraction (DFPSE). DFPSE uses 47 mm circular disks of FPSE media coated with sorbent material of different polarities using sol-gel coating technology. In the new extraction mode of FPSE, the sample is percolated through the FPSE disks installed on a filtration assembly. Following the extraction of the target analytes into the FPSE disks, the retained analytes are eluted by passing a volume of the elution solvent through the same assembly. This configuration may decrease the equilibrium time while maintaining the rest of features.

The present work describes for first time the use of the DFPSE technique whose performance efficiency was evaluated using a group of PPCPs in environmental water samples. In this study, different parameters affecting the dynamic extraction mode were optimized and the results were compared with those obtained with static FPSE, wherethe sol-gel Carbowax 20M coated media were also used [17]. Subsequently, a method was developed based on the new DFPSE mode followed by LC-MS/MS and it was validated for the determination of PPCPs from river and wastewater samples.

2. MATERIALS AND METHODS

2.1. Reagents and Standards

Substrates for fabric phase sorptive extraction (FPSE) media (unbleached Muslin, 100% cellulose cotton fabric) were purchased from Jo-Ann Fabric (Miami, FL, USA). Poly(ethylene glycol) (Carbowax 20M) polymers, acetone, dichloromethane, methyltrimethoxysilane (MTMS), trifluoroacetic acid (TFA) were purchased from Sigma-Aldrich (St. Louis, MO, USA). Sodium hydroxide (NaOH) and hydrochloric acid (HCl) were purchased from Thermo Fisher Scientific (Milwaukee, WI, USA).

The reagents for the analytical evaluation were: paracetamol (PARA), caffeine (CAFF), antipyrine (APy), propranolol hydrochloride (PROP), methylparaben (MPB), carbamazepine (CBZ), propylparaben (PrPB), 2,4-dihydroxybenzophenone (DHB),

benzylparaben (BzPB), 2,2-dihydroxy-4-4-methoxybenzophenone (DHMB), diclofenac (DICLO), 3-benzophenone (BP-3), triclocarban (TCC) and triclosan (TCS) and all of them were purchased from Sigma-Aldrich (Steinheim, Germany). Stock solutions of individual standards were prepared by dissolving each compound in methanol (MeOH) at concentration of 1,000 mg L^{-1}. A mixture of standards of all compounds at 50 mg L^{-1} was prepared in MeOH every month. Working standard solutions were prepared weekly by diluting with mixture of ultrapure water at pH 3 and ACN (80:20, v/v). All the solutions were stored at 4^{o}C. Ultrapure water was obtained from a water purification system (Veolia Waters, Barcelona, Spain) and the elution solvent was evaporated using the miVac Duo system (Genevac, Ipswich, United Kingdom). HPLC grade MeOH, acetonitrile (ACN) and ethyl acetate (EtOAc) were supplied by Scharlab (Barcelona, Spain). Sodium chloride (NaCl) and formic acid (HCOOH) (95% purity) were purchased from Sigma-Aldrich.

2.2. Preparation of FPSE media

Preparing the substrate for sol-gel coating, design and preparation of the sol-gel coating solution, applying the sol-gel coating on the pre-treated substrate, conditioning and ageing of the sol-gel coated FPSE media, and the post-coating cleaning of the FPSE media are the sequential steps that are followed to create an inherently porous sol-gel coated permeable FPSE media. A detailed account on every steps mentioned herein are described elsewhere [17]. However, a summary of the entire process is given below. Selection of the suitable FPSE media takes into consideration the hydrophobicity or hydrophilicity of the target analytes. Considering the fact that majority of the selected PPCPs are either highly polar (PARA, CAFF, APy, MPB, CBZ) or moderately polar (PROP, PrPB, DHB, BzPB), a hydrophilic substrate would have been a suitable choice as the substrate may synergistically complement to the overall polarity and the selectivity of the FPSE media. As such, 100% cotton cellulose, being a hydrophilic substrate, was selected as the substrate for sol-gel coating. The cellulose fabric support were treated with NaOH solution to activate surface hydroxide groups, neutralized with dilute HCl, washed with deionized water and dried in an inert atmosphere prior to the sol-gel coating. Due to

the good results obtained in previous study [17] using FPSE, a polar polymer Carbowax 20M was selected as the organic polymer from a large number of polymer candidates. Methyltrimethoxysilane (MTMS) was used as the sol-gel precursor in order to prevent from shrinking and cracking of the sol-gel coating often seen when trimethoxysilane or triethoxysilane are used as the sol-gel precursor. In addition to prevent the sol-gel coating from cracking and shrinking, MTMS also exerts London dispersion type of intermolecular interaction *via* methyl functional groups towards the target analytes. TFA was used as the sol-gel catalyst. Formation of a homogeneous sol solution incorporating all the sol solution ingredients is of prime importance to the success of a sol-gel coating. An equimolar mixture of dichloromethane and acetone was needed to prepare homogeneous sol solutions for sol-gel Carbowax 20M coatings. The molar ratio between the sol-gel precursor and Carbowax 20M was kept at 1:0.02. The molar ratio between sol-gel precursor, solvent, catalyst, and water was maintained at 1:3.90:1.31:0.30, respectively.

Sol-gel coating was carried out *via* dip coating technique. The pre-treated substrates were kept submerged in the sol solution for four hours and then sol solution was discarded and the coated fabrics were transferred into a desiccator for conditioning and ageing of the sol-gel coating. The coated FPSE media were then rinsed with a mixture of dichloromethane:acetone (50:50; v/v) under sonication for 30 minutes to remove unreacted sol solution ingredients as well as other sol-gel reaction intermediates or by-products from the FPSE media. Finally, after drying the FPSE media in an inert environment, they were cut into 47 mm diameter FPSE disks.

2.3. Dynamic fabric phase sorptive extraction

The DFPSE conditions were optimized using sol-gel Carbowax 20M coated FPSE media. Prior to any extraction, the FPSE disks, placed in the filtration assembly, were conditioned and equilibrated by passing 10 mL MeOH followed by 10 mL of ultrapure water, and then dried by applying vacuum. For the extraction, 50 mL of sample (25 mL for influent wastewater) adjusted to pH 3 with HCOOH and

containing 10% of NaCl (w/v) were loaded. Then, the sample was left for 10 minutes in contact with the FPSE disk for the retention of analytes. After 10 minutes, a vacuum was applied to pass the sample through the FPSE disk completely, and then to dry the FPSE media. The retained analytes were eluted by passing 10 mL of EtOAc through the same assembly and they were collected in a receiver flask. The extract was evaporated to dryness in a miVac concentrator. Prior to LC-(ESI)MS/MS injection, the residue obtained was re-dissolved in 1 mL of ultrapure water at pH 3 and ACN (80:20, v/v) solution. After each use, the FPSE disk was cleaned twice with 5 mL of MeOH in the ultrasonic bath for 5 minutes, then dried and stored in the glass vial until the next experiment.

All water samples including river water, and influent and effluent water from wastewater treatment plant (WWTP) were collected using pre-cleaned plastic bottles. Prior to the extraction, these samples were filtered through nylon supported 0.45 µm membrane filters (Fisher, Loughborough, UK) to eliminate any particulate matter present, then acidified to pH 3 with HCOOH and stored at 4^{o}C until analysis.

2.4. Liquid chromatography-tandem mass spectrometry analysis

To analyze the extracts a 1200 series liquid chromatograph coupled to a 6410 series triple quadrupole mass spectrometer with an electrospray ionization (ESI) interface, and equipped with an automatic injector, a degasser, a quaternary pump and a column oven from Agilent Technologies (Waldron, Germany) was used.

The optimized parameters for LC and (ESI)MS/MS were taken from a previous study [17]. The column used for chromatographic separation was the reversed-phase Kromasil 100 C_{18} (150 mm × 4.6 mm i.d., 5 µm) from Teknokroma (Barcelona, Spain). The temperature of the chromatographic column was maintained at 40^{o}C and the flow-rate was 0.6 mL min^{-1}. The mobile phase consisted of ACN and ultrapure water adjusted to pH 3 with HCOOH. The gradient started at 20% ACN, which was increased to 80% ACN in 15 min, to 90% ACN in 7 min, to 100% in 1 min and kept constant for 8 min. Finally, it was returned to the initial conditions in 3 min, which were held for 8 min to equilibrate the column for further analysis. 50 µL of the extract were injected into LC-(ESI)MS/MS.

The analyses were performed in MRM mode in positive or negative ionization mode. The optimized ESI parameters were as follows: N_2 flow rate of 12 L min^{-1}, capillary voltage of 4,000 V, nebulizer pressure of 45 psi (N_2) and source temperature of 350^{o}C. The cone voltage and collision energies for all of the compounds were between 18 and 200 V, and 5 and 35 eV, respectively (optimal values are summarized in Table 1). The confirmation of the presence of the compound was performed by comparing the retention time and ratios of two MRM transitions with those from the standard.

Using the LC-MS/MS in MRM mode, linear range for the selected analytes was between 0.1 and 50 µg L^{-1}, except for TCS, which were between 2 and 50 µg L^{-1}. The lowest points of the calibration curve were considered as the instrumental limits of quantification (ILOQs). The instrumental limits of detection (ILODs), calculated as a signal-to-noise ratio (S/N) of 3 ranged from 0.02 to 0.5 µg L^{-1}.

3. RESULTS AND DISCUSSION

3.1. Optimization of DFPSE procedure

In our previous study, the static FPSE technique was used for the extraction of PPCPs from environmental water samples. In that study, we evaluated several FPSE media coated with sorbents having different polarities: non-polar sol-gel poly(dimethyldiphenylsiloxane) (PDMDPS), mid polar sol-gel poly(tetrahydrofuran) (PTHF), and polar sol-gel poly(ethyleneglycol)-block-poly(propyleneglycol)-block-poly(ethyleneglycol) (PEG-PPG-PEG triblock) and sol-gel Carbowax 20M). Sol-gel Carbowax 20M provided the highest recoveries for the analytes tested [17] and therefore, this extraction medium was selected for the present study.

Taking advantage of the previous information, the dynamic extraction mode was evaluated for the same group of PPCPs. In order to obtain high extraction efficiencies for the DFPSE , several parameters were optimized: extraction time, ionic strength, sample volume and number of FPSE disks. For the desorption, elution solvent and its volume were optimized. Initial experimental conditions were: 10 mL of ultrapure water adjusted to pH 3 with HCOOH spiked at 2 µg L^{-1} with the mixture of analytes percolated through the FPSE disk using the filtration assembly. For the

elution of the retained analytes, two times 5 mL of MeOH were passed. These two 5 mL fractions of the eluted solvent were evaporated and the residue was re-dissolved in 1 mL of ultrapure water at pH 3 and ACN (80:20, v/v) before injecting into LC-(ESI)MS/MS.

3.1.1. Extraction conditions

The effect of sample pH on the extraction efficiency had already been investigated in our previous study at pH 3, 5, 7 and 9 [17], with better results being obtained under acidic conditions at pH 3 for the extraction of PPCPs from water sample. Therefore, this value was selected for the current study.

At initial conditions, the recoveries were not very high, so attempts were made to increase the retention of the analytes by increasing the contact time, leaving the sample in contact with the FPSE disk before applying the vacuum. The contact time was optimized from 10 to 60 minutes. The results showed that the extraction efficiencies increased about 10% in recoveries when the extraction time was 10 minutes but they did not improve significantly with higher contact time. In addition, extended extraction time was not suitable for the desirable routine analysis method, and the aim of this new mode was to reduce extraction time. Therefore, an extraction time of 10 minutes was selected for subsequent analyses, with better results and much shorter time being necessary compared to the 4 hours needed in static FPSE [17], or even compared to some commercially available and in-house SBSE materials [11, 12, 26].

The ionic strength effect was evaluated by adding NaCl from 0% to 20% (w/v) in the sample. It was observed that the extraction efficiencies increased when the concentration of NaCl increased from 0% to 10%, but decreased when the concentration of NaCl was raised to 20%, except in the case of APy, PROP, MPB and CBZ. Extraction efficiencies increased due to the salting-out effect and electrostatic interaction between polar molecules and salt ions in the solution [27]. Therefore, the addition of 10% of NaCl was chosen to provide the best results for further studies, which also agreed with the results obtained with static FPSE [17].

In order to improve analyte recoveries, the number of FPSE disks used for the extraction of PPCPs was increased. Here, the effect of extraction recovery was evaluated when one or three FPSE disks were used. It was observed that the number of FPSE disks increased the percentage of recovery (increasing between 5% and 20%) for all of the analytes. Thus, three FPSE disks were selected for the further studies.

The next step was to determine the sample volume that could be loaded. To do this, volumes of 10, 25, 50 and 100 mL of ultrapure water spiked with the analyte mixture were tested. Figure 1 shows that, when the sample volume was increased from 10 mL to 25 mL, the recoveries decreased (~8% on average) for the PARA, CAFF, APy, PROP, MPB and CBZ. When 50 mL and 100 mL of sample volume were extracted, the recoveries decreased between 5% and 25% for the all of the analytes and, therefore, 50 mL of sample volume was selected as a compromise between recoveries and the sensitivity of the method.

3.1.2. Solvent desorption conditions

Different solvents used to back-extract the analytes retained in the FPSE disks were tested. Apart from MeOH, 5 mL of other solvents such as ACN, mixture of MeOH/ACN (1:1, v/v) and EtOAc were tested. All the solvents tested showed similar results for the studied analytes, which included different polarities, but EtOAc took less time to be evaporated and, therefore, this was the selected elution solvent.

For determining the volume of the elution solvent, three fractions of 5 mL of EtOAc were passed through the FPSE disks and recoveries up to 65% were obtained in the first fraction of 5 mL. However, some analytes (recoveries ranging from 10% to 15%) still appeared in the second fraction. Furthermore, when 5 mL of solvent volume were additionally passed through the FPSE disks, no significant increase in recovery was observed. Therefore, 10 mL of EtOAc was chosen as the optimal volume for elution.

The 10 mL of EtOAc was evaporated to dryness in a miVac concentrator and the residue re-dissolved in 1 mL of ultrapure water at pH 3 and ACN (80:20, v/v)

before being injected into LC. No significant losses were observed during this step (less than 5% losses).

To check for the possible carryover effect, the FPSE disks were washed with 5 mL of MeOH in a sonication bath for 5 minutes twice and, when analyzed, after evaporation and reconstitution, no carryover was observed. In addition, each FPSE disk can be used for several times (more than 20) for the extraction of water samples.

To summarize, the optimal extraction conditions for the DFPSE-Carbowax 20M coated FPSE disks were as follows: (a) load 50 mL of sample adjusted to pH 3 with HCOOH, containing 10% of NaCl (w/v) on three FPSE disks placed in the filtration assembly; (b) let the sample be in contact with the media for 10 minutes to enhance the retention of the analytes and then apply vacuum to draw sample through FPSE disks; (c) dry the FPSE disks; (d) elute the retained analytes by passing 10 mL of EtOAc; (e) evaporate the extract to dryness, and redissolve it in 1 mL of the mixture of ultrapure water at pH 3 and ACN (80:20, v/v); (f) inject 50 µL into LC-(ESI)MS/MS instrument. When comparing these optimal conditions to the ones of static FPSE [17], these DFPSE conditions involve higher sample volume (from 10 mL in FPSE to 50 mL in DFPSE), which leads to higher sensitivity, and shorter extraction time (from 240 minutes in FPSE to 10 minutes in DFPSE).

Under the optimal conditions, the recovery values (%) for the fourteen PPCPs in ultrapure water obtained by DFPSE were comparable or even better to those obtained by static FPSE, as shown in Figure 2. DFPSE showed similar recoveries to those provided by FPSE for mid-polar and apolar analytes (between 38% and 86%) and improved recoveries for the two most polar analytes, APy and PROP (between 24% and 28%), but no improvement was observed for PARA and CAFF.

Different extraction techniques had been evaluated for the PPCPs, but they still had certain drawbacks, such as the extraction time of over an hour [11, 26, 28] and the low recoveries for the most polar analytes. For instance, when using SBSE with commercial coating based on EG/Silicone [11] the recoveries for the most polar analytes (PARA, CAFF, APy and PROP) were not higher than 2% when 50 mL of sample were extracted, whereas when in-house SBSE coating based on

335 Poly(PEGMA-co-PETRA) [26] was used to extract these analytes from 50 mL of
336 sample, recoveries were between 2 and 19%. Therefore, DFPSE mode provided
337 promising results.

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340 **3.2. Evaluation and validation of DFPSE with environmental samples**

341 After optimization, DFPSE was applied for the extraction of the PPCPs from
342 environmental water samples, such as river water, and effluent and influent samples
343 from WWTP. Due to the low recoveries obtained for PARA and CAFF, the method
344 was validated excluding these two analytes.

345 When working in the electrospray ionization mode in LC-MS/MS, the matrix
346 effect (%ME) is one of the main problems that arises in the quantification of the
347 analytes in complex samples. This can result in the suppression or enhancement of
348 analyte response, leading to erroneous quantification. %ME was calculated as the
349 ratio of the signal of each analyte when it was spiked in the sample (river water,
350 effluent or influent wastewater) after extraction by DFPSE and their signal in
351 standard solution. Apparent recovery (%R_{app}) was calculated as the ratio of the
352 signal of each analyte in the sample spiked before DFPSE and the signal of each
353 analyte in standard solution. As is known, the %R_{app} includes the extraction recovery
354 and the ME.

355 The %ME and %R_{app} were calculated when 50 mL of river and effluent
356 wastewater was spiked at 0.6 µg L^{-1}. When influent sample was analyzed, the
357 sample volume was decreased to 25 mL, due to complexity of the sample.
358 Previously, each sample was analyzed without spiking and the results of the
359 analytes present in the sample were subtracted to determine %ME and %R_{app}. The
360 %ME and %R_{app} for all three samples are shown in Table 2. While dealing with
361 different water samples, ion suppression was observed, with the exception of DHMB,
362 with 9% enhancement when analyzing effluent wastewater samples. The %ME
363 values are acceptable and range from -5% to -26% for river samples, and from -7%
364 to -36% for effluent samples. As expected, when dealing with influent sample, the

%ME values were higher, up to -52%. In all of the samples, the analytes that were most affected by ion suppression were the last compounds to be eluted, due to the co-elution of these compounds with organic components of the matrix. These ME results are in line of other studies that determine these PPCPs in complex matrices, such as the one obtained in a previous study [17]. The $\%R_{app}$ (detailed in Table 2) were acceptable if the above values of %ME are taken into account. In addition, in influent samples, as expected the $\%R_{app}$ values decrease for all the compounds. In all of the samples, the compounds that showed the lowest $\%R_{app}$ were APy and PROP, since they also showed low recoveries in ultrapure water. In view of this, APy and PROP were also discarded for the validation in wastewater samples.

The analytical method based on DFPSE/LC-MS/MS was validated with effluent wastewater samples in terms of linearity, repeatability, reproducibility, limits of detection (LODs), and limits of quantification (LOQs) and results are shown in Table 3. The calibration curve was built using the matrix-matched calibration approach at 5 concentration levels in duplicate, and the analytes showed good linearity with determination coefficient (R^2) values greater than 0.993. The LOQ obtained from the lowest point of the calibration curve ranged between 20 and 50 ng L^{-1} for all compounds, with the exception of BP-3 and TCS (100 ng L^{-1}). The LODs were estimated on the basis of the instrumental LODs and $\%R_{app}$ because all of these compounds were present in the sample. The intra-day repeatability (n=5) and inter-day reproducibility (n=5) for all compounds expressed as relative standard deviation (%RSD) of 50 mL effluent wastewater sample spiked at 200 ng L^{-1} were lower than 19% and 20%,respectively.

3.3. Analysis of environmental water samples

The DFPSE/LC-MS/MS method was applied to determine the presence of these PPCPs in three kinds of matrices, which were taken on three different days and analyzed in triplicate.

In view of the differences in the $\%R_{app}$, mainly for influent wastewater samples compared to river and effluent wastewater samples, and in order to provide more

accurate results, firstly, a matrix-matched calibration curve was prepared for each kind of sample to be analysed (i.e. river water and influent wastewater samples) in a similar range to the one previously reported in the validation for effluent wastewater samples.

Table 5 includes the concentration found in river water, and effluent and influent wastewater samples. As can be seen, when analyzing river water samples, only MPB (<LOQ-64 ng L^{-1}) and DHMB (45-64 ng L^{-1}) were found, while the other PPCPs were not detected. These values are comparable to previous studies in which samples from the same river were analyzed [12, 29, 30].

Similarly, effluent and influent wastewater samples were analyzed. It can be seen that, all of the analytes were present in both wastewater samples. In effluent samples, some analytes, such as MPB, CBZ, DHMB and DICLO, were quantified in all of the samples, whereas the other analytes were found at concentrations lower than the LOQ. In influent samples, the highest concentrations found were for CBZ, PrPB, DHB and DICLO, while BzPB, BP-3, TCC and TCS were found at concentrations below the LOQ, except in the case of MPB and DHMB, which were in the ranges of <LOQ-257 ng L^{-1} and <LOQ-28 ng L^{-1}, respectively. As expected, most of the analytes were found at higher concentrations in influent rather than effluent wastewater due to the wastewater treatment, except CBZ and DICLO, which were found at similar concentrations in both effluent and influent samples. The concentrations found of these PPCPs are in line with those found in the same kind of samples [12, 17, 29, 31].

4. Conclusions

A novel dynamic mode of FPSE is presented for the first time. DFPSE with sol-gel Carbowax 20M material was successfully applied for the extraction of a group of PPCPs from environmental water samples with shorter equilibrium time and higher retention than static FPSE for some analytes extracted.

The optimization of different parameters, such as using three FPSE disks and leaving the sample for 10 minutes before applying the vacuum, was positive in terms of achieving good extraction recoveries of the analytes.

The combination of the new DFPSE with LC-MS/MS provided an efficient, rapid, simple and sensitive method for the determination of PPCPs at low levels of concentration in complex environmental samples.

The results of these studies encourage us to further test this new mode with other target compounds in different kind of samples.

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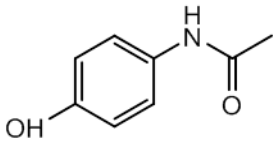
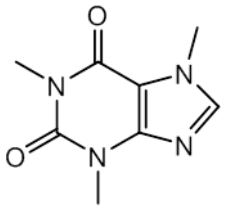
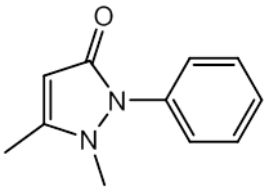
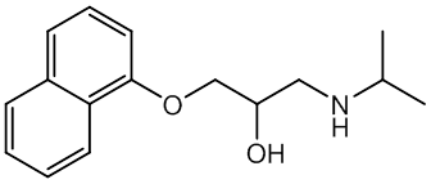
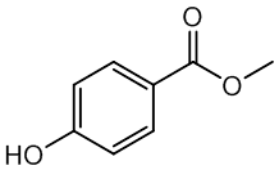
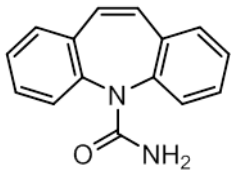
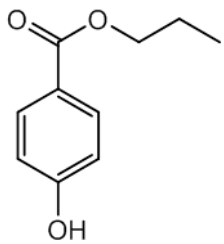
546

547 **Table 1.** General parameters of structures, t_R, log K_{ow}, pK_a and LC-(ESI)MS/MS
548 acquisition parameters in MRM mode for each analyte.

Analyte	Structure	t_R (min)	log K_{ow}*	pK_a*	Cone voltage (V)	MRM Transition (collision energy (eV))	Ionization mode
PARA		3.87	0.5	9.2	100	152 > 110 (15) 152 > 93 (25)	+
CAFF		4.37	-0.6	13.4	125	195 > 138 (15) 195 > 110(25)	+
APy		6.7	1.4	13.3	100	189 >145 (30) 189 >115 (30)	+
PROP		7.57	2.9	9.5	125	260 > 116 (15) 260 > 183 (15)	+
MPB		9.45	1.9	8.3	80	151 > 92 (15) 151 > 136 (5)	–
CBZ		11	1.9	13.7	150	237 > 193 (35) 237 > 179 (35)	+
PrPB		13.1	2.9	8.2	100	179 > 92 (15) 179 > 136 (5)	–

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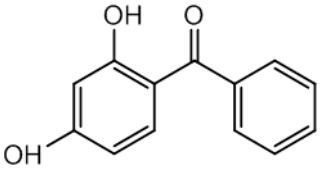
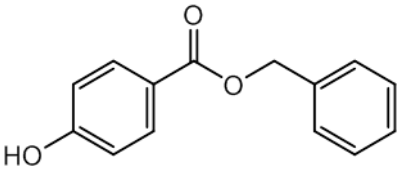
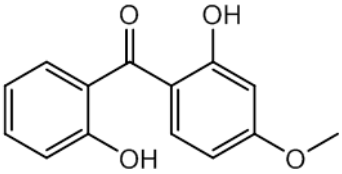
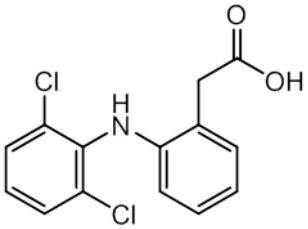
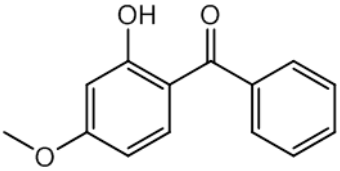
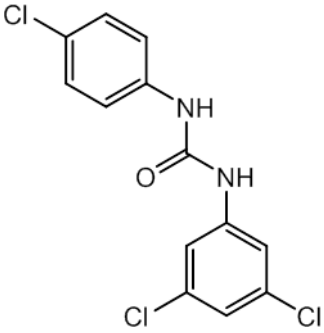
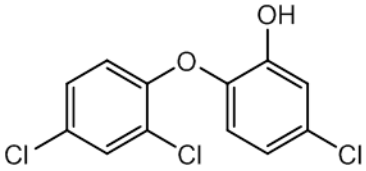
550

551 Table 1. *continue*

Analyte	Structure	t_R (min)	log K_{ow}*	pK_a*	Cone voltage (V)	MRM Transition (collision energy (eV))	Ionization mode
DHB		13.9	3.2	7.7	130	213 > 135 (15) 213 > 169 (5)	–
BzPB		14.7	3.6	8.2	100	227 > 92 (10) 227 > 136 (20)	–
DHMB		15.3	4.3	7.1	80	243 > 93 (15) 243 > 123 (15)	–
DICLO		16.4	4.5	4.2	75	294 > 250 (5) 294 > 214 (15)	–
BP-3		18	4	7.6	130	229 > 151 (15) 229 > 105 (15)	+
TCC		19.2	6.1	12.7	130	313 > 160 (5) 313 > 126 (15)	–
TCS		19.5	5.3	7.9	18	287 > 35 (18) 289 > 35 (18)	–

552 * Calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02 (© 1994–2012 ACD/Labs).

553

554 **Table 2.** %R_{app} and %ME of PPCPs in river, effluent and influent WWTP sample by
555 DFPSE extraction techniques

556

Analyte	River [(a)]		Effluent WWTP [(a)]		Influent WWTP [(b)]	
	% R_{app}	%ME	% R_{app}	%ME	% R_{app}	%ME
APy	10	-13	8	-11	3	-7
PROP	26	-15	5	-7	3	-9
MPB	30	-25	16	-13	12	-27
CBZ	53	-10	23	-26	18	-11
PrPB	64	-22	31	-28	20	-49
DHB	68	-22	38	-23	21	-52
BzPB	70	-24	50	-21	33	-46
DHMB	76	-5	64	9	39	-28
DICLO	49	-24	50	-32	23	-50
BP - 3	52	-26	52	-34	45	-37
TCC	49	-20	29	-30	15	-52
TCS	43	-26	32	-36	22	-48

557 (a) 50 mL spiked at 0.6 µg L^{-1}
558 (b) 25 mL spiked at 1.2 µg L^{-1}

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Table 3. Linear range, LODs, LOQs, repeatability, reproducibility between days obtained when 50 mL of spiked effluent wastewater sample analyzed by DFPSE followed by LC-MS/MS.

Analyte	Linear range (ng L^{-1})	LODs (ng L^{-1})	Repeatability[(a)] (%RSD, n=5)	Reproducibility[(a)] (%RSD, n=5)
MPB	50 - 1000	4	11	17
CBZ	50 - 1000	4	19	19
PrPB	50 - 1000	2	12	20
DHB	50 - 1000	2	11	15
BzPB	50 - 1000	2	14	15
DHMB	20-1000	2	6	13
DICLO	50-1000	2	6	7
BP - 3	100-1000	2	16	13
TCC	50-1000	8	2	13
TCS	100-1000	20	6	8

(a) spiked at 200 ng L^{-1}

584 **Table 4.** Concentration (ng L^{-1}) of found in river, effluent and influent in WWTP
585 sample (n=3)

Analyte	River	Effluent WWTP	Influent WWTP
APy	nd	-	-
PROP	nd	-	-
MPB	< LOQ-64	51 - 62	< LOQ - 257
CBZ	nd	189 - 306	119 - 343
PrPB	nd	< LOQ	425 - 660
DHB	nd	< LOQ	261 - 324
BzPB	nd	< LOQ	< LOQ
DHMB	45-64	55 - 76	< LOQ - 28
DICLO	nd	203 - 420	177 - 241
BP-3	nd	< LOQ	< LOQ
TCC	nd	< LOQ	< LOQ
TCS	nd	< LOQ	< LOQ

586 nd:- not detected

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Figure Captions

Figure 1. Effect of the sample volume on extraction recovery of analytes using sol-gel Carbowax 20M material in DFPSE.

Figure 2. Recovery obtained by FPSE and DFPSE at optimum conditions of each technique using Carbowax 20M. FPSE: 10 mL of ultrapure water spiked at 0.2 µg L^{-1} of each analyte [17]. DFPSE: 50 mL of ultrapure water spiked at 0.6 µg L^{-1} of each analyte.

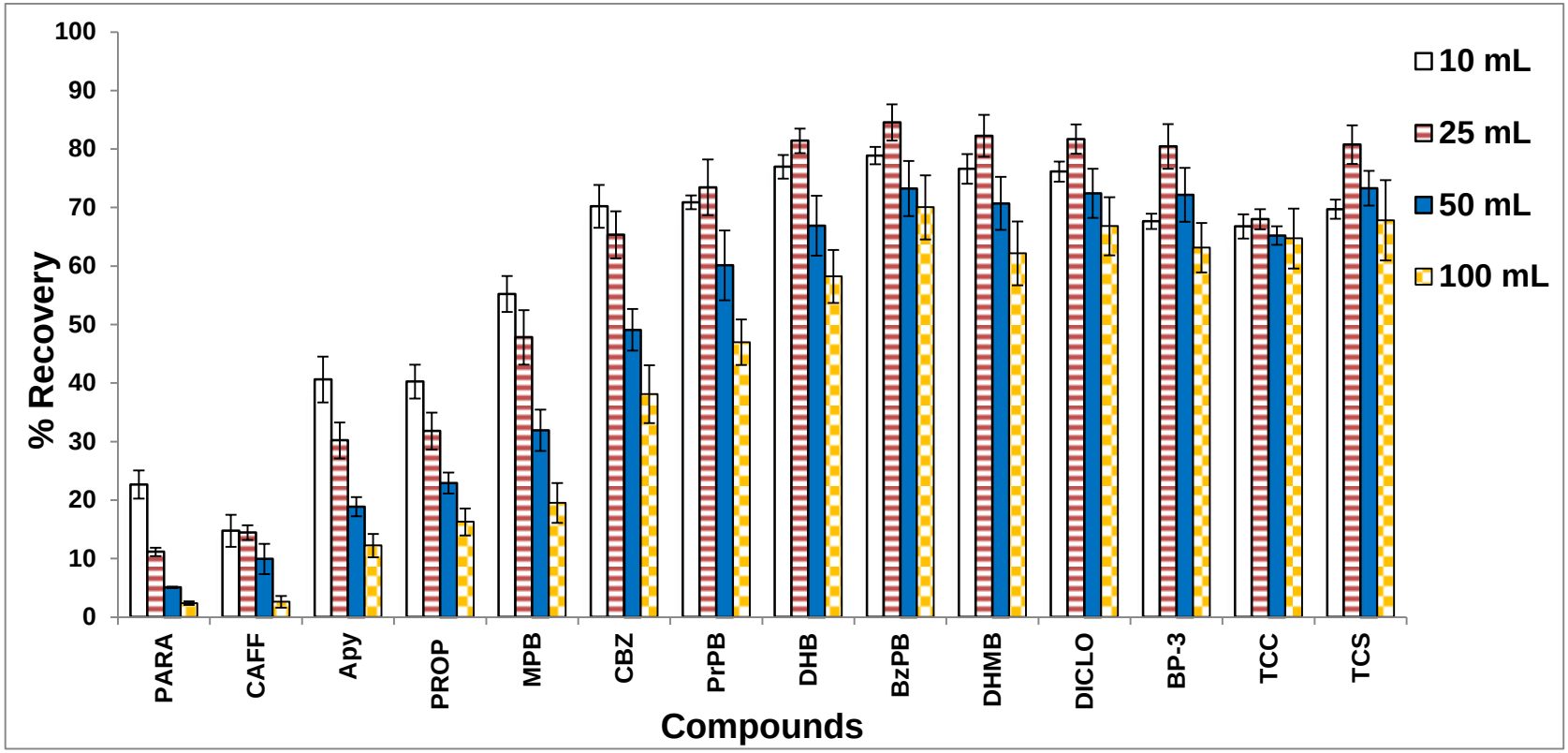
100
90
80
70
60
50
40
30
20
10
0
% Recovery
10 mL
25 mL
50 mL
100 mL
PARA
CAFF
Apy
PROP
MPB
CBZ
PrPB
DHB
BzPB
DHMB
DICLO
BP-3
TCC
TCS
Compounds

Figure 1

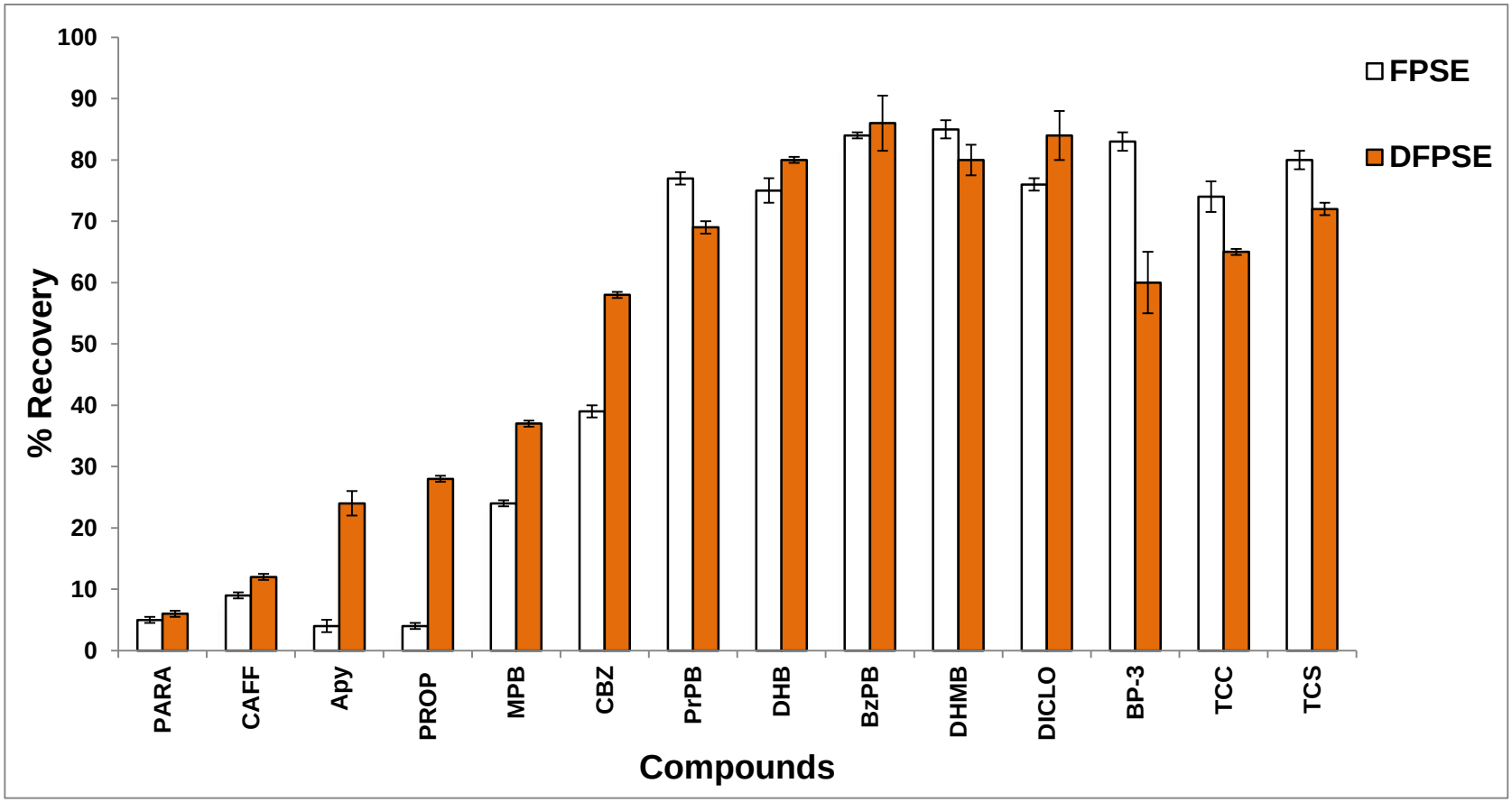
100
90
80
70
60
50
40
30
20
10
0
% Recovery
FPSE
DFPSE
PARA
CAFF
Apy
PROP
MPB
CBZ
PrPB
DHB
BzPB
DHMB
DICLO
BP-3
TCC
TCS
Compounds

Figure 2