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Evaluation of ceramic passive samplers using a mixed-mode strong cation-exchange sorbent to monitor polar contaminants in river water

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ABSTRACT

Although most of the analytical methods developed for the monitoring of contaminants in environmental waters are based on discrete grab sampling, an alternative of increasing interest is the use of passive sampling. Methods based on passive sampling provide the sampling and pre-concentration of the analytes *in-situ,* which makes the sample treatment less time consuming and costly than using discrete grab sampling. In this study, ceramic passive samplers (CPSs) using mixed-mode strong cation-exchange sorbent (Oasis MCX) as retention phase were evaluated for the determination of a group of 21 therapeutic and illicit drugs and some of their metabolites in river water samples that were determined by liquid chromatography-tandem mass spectrometry. After assessing the stability of the analytes, the CPSs were calibrated for 9 days with bottled water and river water, obtaining, for the 19 stable compounds, sample rates (*Rs*) ranging between 0.180 and 1.767 mL/day and diffusion coefficients (*De*) between 2.02E-8 and 2.81E-7 cm^2/s. Once calibrated, CPSs were deployed for the determination of contaminants in the Ebre River, with good reproducibility, and some of the analytes were determined, including amongst others, gabapentin at 76 ng/L, caffeine at 203 ng/L or diclofenac amine at 57 ng/L. The passive sampling method herein presented is simple and feasible and allows the time-integrated analysis of pharmaceuticals and drugs at trace levels in river water. This study opens the possibility of using other mixed-mode sorbents or other types of sorbents as retaining phase on CPSs for the determination of very polar contaminants in water.

1. Introduction

Nowadays, the presence of contaminants of emerging concern (CECs) in water is one of the most important environmental problems. CECs comprise different groups of compounds like drugs, pharmaceuticals, flame retardants, hormones and sterols, plastic additives, amongst others [1]. These contaminants are constantly emitted into the environment because of their widespread use in many end-products [2]. The presence of illicit and therapeutic drugs in water is of concern, as these compounds are not completely metabolised in the organism and are excreted unchanged or as metabolites through urine [1]. They reach wastewater treatment plants (WWTPs) and are discharged into surface waters due to the limited capacity of the treatment process to eliminate these compounds [3]. CECs are determined at ng/L or μg/L in water [3,4] and have a high potential to negatively affect the environment and human health, although there is a limited information about the effects attributed to permanent exposure [5].

To control the presence of these compounds, different analytical methods have been developed in recent years [6,7]. These methods are based on a sample treatment followed by liquid-chromatography coupled with mass spectrometry to enable their determination at the low concentrations in which they exist in the environment.

Sampling is the most important stage of the analytical method because the samples must be homogeneous and representative and, for this reason, the errors made in this step affect the concentration reported [8]. At present, most common sampling methods are based on an active or discrete grab sampling that is usually followed by a sample treatment step to enrich the compounds and to increase selectivity [7,9,10]. Solid-phase extraction (SPE) [10,11], solid-phase microextraction (SPME) [12] or stir bar sorptive extraction (SBSE) [13], serve for this purpose.

Passive sampling is the alternative to discrete sampling and combines sampling with sample treatment steps, and can provide time-weighted average (TWA) concentration values [14]. The principal

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advantages of this type of sampling are the low cost, the ease of deployment, the capacity for performing multi-site screening, the fact that it does not require power or supervision, the easy maintenance, the reduction of matrix interferences and the obtention of a TWA during the sampling period. To allow accurate quantification of contaminants, calibration of the samplers is required for all the compounds to be determined [8,14–17]. The calibration consists of plotting mass uptake of the analyte retained in the sampler in front of time. Upon calibration, some parameters, such as the compound mass-time slope (k), the sampling rate (Rs) and the effective diffusion coefficient (De) must be calculated for each analyte. This sampling approach is increasingly used and an European directive has also recommended its implementation in the monitoring of organic contaminants in water [18].

Different passive sampling devices are available and include ceramic passive samplers (CPSs) [15,19,20], polar organic chemical integrative samplers (POCISs) [16,17,21,22], ChemCatchers [17,21,23], semi-permeable membrane devices (SPMDs) [17] and diffusive gradient in thin films (DGTs) [21]. They have different properties and Rs, and their applicability is influenced by the physicochemical properties of target compounds, the time of sampling and the water matrix.

The CPSs are based on a ceramic membrane with a cylindrical shape that acts as a diffusion barrier and allows a free flow of contaminants from the external area to the internal area of the sampler; while flowing, the analytes are retained in the sorbent placed inside the sampler. According to the porous size of the ceramic material, different types of CPSs are available for different applications [15]. In the present study, the selected CPS is the macroporous ceramic passive sampler that have some advantages over other passive samplers since has low wall thickness and high open-porosity that facilitates a fast uptake of the contaminants; for this reason, they can be used for sampling periods from 24 h up to a few weeks without risk of clogging [15]. The morphology of the CPS used allows the sampling of water as diffusion constant of contaminants through the wall to not be affected by the water flow [19].

The sorbent placed inside, where the contaminants are retained, is a key parameter of CPS performance. In previous studies with CPSs, reversed-phase sorbents like Sepra ZT [19,20], Sepra SBD-L or PoraPak Rxn RP [20] were used to calibrate and monitor a group of pharmaceuticals and drugs in river and drinking water. Other studies used Oasis HLB sorbent, which is chemically similar to Sepra ZT, to retain the compounds by hydrophobic-lipophilic interactions, obtaining satisfactory results with other types of samplers like POCIS [16,19,24–27] or ChemCatcher [23,28]. Although Oasis HLB can retain compounds with a wide range of polarity, it showed low retention for the most polar or ionic compounds. This can be resolved by using mixed-mode ion-exchange sorbents where the compounds can be retained by ionic or reverse-phase interactions. Different studies have reported improved performance of mixed-mode ion-exchange SPE sorbents for the extraction of a group of polar or ionic compounds [9,29,30].

Therefore, in the present study, the performance of CPSs with Oasis MCX was evaluated for the first time for the determination of a group of contaminants including therapeutic and illicit drugs and some metabolites. The stability of analytes in water, the Rs, De and k are provided in bottled and river water. Finally, CPSs were deployed in the waters of the Ebre River (South Catalonia) to determine pharmaceuticals and illicit drugs. We propose the use of CPS and liquid chromatography-mass spectrometry in tandem (LC-MS/MS) for the efficient TWA monitoring of water contaminants.

2. Experimental part

2.1. Chemicals and reagents

Twenty-one pure analytical standards of drugs and metabolites (98–99% purity) were acquired from Sigma-Aldrich (St. Louis, MO, USA). They are nicotine (NIC), cotinine (COT), morphine (MOR), ranitidine (RAN), pregabalin (PRE), gabapentin (GAB), codeine (COD), caffeine (CAF), ketamine (KET), tramadol (TRA), pentoxifylline (PEN), cocaine (COC), venlafaxine (VEN), enalapril (EN), oxazepam (OXA), methadone (MET), diazepam (DIA), valsartan (VAL), diclofenac (DICLO), 4-acetamidopyridine (4-AMP) and benzoylecgonine (BE). The stock solutions were prepared at 1000 µg/mL in methanol (MeOH) and working solutions were prepared in MeOH:H_2O (5/95, v/v). All solutions are stored at −20 °C. MeOH, acetonitrile (ACN) and water of LC-MS grade were supplied by Carlo Erba Reagents (Milano, Italy). Formic acid (purity >98%), ammonium acetate (purity 28–30%) and acetic acid (purity >98%) were supplied by Sigma-Aldrich. Milli-Q water was produced from an Integral Water Purification System from Millipore (Burlington, MA, USA). Oasis MCX (500 mg) was purchased from Waters (Milford, MA, USA).

2.2. Liquid chromatography and MS/MS detection

The liquid chromatography-tandem mass spectrometry instrument was an Agilent 1200 (series LC) with a triple quadrupole analyser (QqQ) 6460 and an electrospray ionization (ESI) interface. The chromatographic column used was Luna Omega Polar C_{18} (150 mm x 3.0 mm i.d., 5 µm particle size) supplied by Phenomenex (Torrance, California, USA). The optimal mobile phase was a mixture of ultrapure water with 0.1% of formic acid (v/v) (solvent A) and ACN with 0.1% of formic acid (v/v) (solvent B).

The gradient profile started with 5% of B until minute 3, then it increased to 75% in 30 min and then to 100% in 4 min (3-minutes hold time). Initial conditions were regained in 2 min, which were maintained for another 5 min before the next analysis. The column was maintained at 30 °C and the mobile phase flow rate was 0.4 mL/min. The injection volume was 5 µL.

In the LC-ESI-QqQ, the optimised parameters were: the ESI working in positive mode, a source gas temperature of 340 °C, a nitrogen flow rate of 12 mL/min, a nebuliser pressure of 40 psi, a capillary voltage of 2500 V, a cone voltage of 100 V and a collision energy between 8 and 40 eV. Table 1S of the Supplementary Information shows the multiple reaction monitoring (MRM) acquisition parameters for all the compounds and the collision energy applied to obtain the product ions.

2.3. Stability test

To evaluate the stability of the compounds in water during

Table 1

Constants k (ng/day), Rs (mL/day) and De (cm^2/s) when the CPSs were calibrated with bottled and river water for 9 days.

	Bottled water calibration			River water calibration		
Compounds	k (ng/ day)	Rs (mL/ day)	De (cm^2/s)	k (ng/ day)	Rs (mL/ day)	De (cm^2/s)
NIC	6.1	0.2	2.9E−8	6.3	0.3	3.1E−8
COT	32.0	1.5	1.5E−7	32.9	1.0	1.6E−7
RAN	17.3	0.9	6.5E−8	19.5	1.8	9.2E−8
PRE	25.8	1.2	1.2E−7	37.7	1.5	1.4E−7
GAB	20.8	1.1	9.9E−8	31.5	1.3	1.2E−7
COD	34.6	1.4	1.6E−7	45.7	1.7	1.6E−7
4-AMP	27.2	1.2	1.3E−7	35.4	1.3	1.3E−7
CAF	35.8	2.0	1.7E−7	32.6	1.9	1.7E−7
KET	18.1	0.9	8.5E−8	10.2	0.5	4.8E−8
BE	44.8	1.2	2.1E−7	38.3	0.8	1.8E−7
TRA	18.2	0.9	8.6E−8	21.9	1.0	9.3E−8
PEN	31.4	1.5	1.5E−7	59.6	1.6	1.7E−7
VEN	16.3	0.9	7.7E−8	22.9	0.9	8.7E−8
EN	20.9	1.1	9.8E−8	13.2	1.2	1.2E−7
OXA	12.7	0.9	6.0E−8	–	–	–
MET	6.2	0.3	2.9E−8	–	–	–
DIA	34.8	1.7	1.6E−7	45.0	1.8	1.7E−7
VAL	16.3	0.9	7.7E−8	17.8	0.9	8.0E−8
DICLO	29.3	1.2	1.4E−7	–	–	–

"-" means not calculated

calibration, 100 mL of water adjusted at pH 7 were spiked with a mixture of all the compounds at 20 µg/L and introduced into a beaker left at room temperature for 14 days. This stability study was done simultaneously with river, bottled and ultrapure water. Every working day, 1 mL of the water sample was taken, placed in a chromatographic vial and kept at −20 °C until injection. The stability was measured as the ratio expressed in% between the concentration measured at each time and the initial concentration.

2.4. Passive sampling

2.4.1. Preparation and extraction of CPS

The CPS (Patent P201530882) consists of a cylindrical ceramic shell of 45 mm length x 13 mm outer diameter and 1.5 mm of thickness of the diffusion layer. Oasis MCX was used as the sorbent in the CPS. Oasis MCX is a mixed-mode strong cation-exchange sorbent which is based on the Oasis HLB (polyvinylpyrrolidone-divinylbenzene) and is chemically modified with sulfonic groups ($pk_a < 1$).

To introduce the sorbent inside of the CPS, 200 mg of the Oasis MCX sorbent was introduced with the help of ultrapure water into a CPS with one of the ends closed with a plastic cap, then the CPS was filled with ultrapure water and finally the CPS was closed with another plastic cap placed on the other end.

After deployment, the sorbent was completely removed from the CPSs with the help of ultrapure water. The dispersed sorbent in water was packed in an empty 6 mL SPE cartridge fitted with a 10 µm polyethylene frit at the bottom of the cartridge and with a second polyethylene frit of 10 µm placed at the top of the sorbent and dried under vacuum. Finally, the analytes were eluted from the sorbent with 5 mL of 5% of NH_4OH in MeOH (v/v). The extracts were evaporated to dryness with a miVAC Duo Concentrator, Genevac (Ipswich, UK) and subsequently redissolved with 1 mL of MeOH:H_2O (5:95, v/v) for the injection to LC-MS/MS.

CPSs were reused during the study. The cleaning protocol includes immersion of CPS in a solution of H_2O:acetone (50:50, v/v) for 24 h, sonicated in an ultrasonic bath for 20 min, rinsed with water and kept completely dry.

2.4.2. Calibration of CPSs

The calibration of the CPS was performed with 10 samplers in a support made of tulle mesh that was placed in a 4 L beaker with bottled water spiked at 20 µg/L with a mixture of analytes. Figure S1 shows the set-up used. The CPSs were initially calibrated in bottled water because it is more similar to the river water than the Mili-Q ultrapure water. The calibration lasted 14 days and two CPSs were removed after 2, 6, 9, 12 and 14 days. The sorbent was removed from the CPS and the analytes extracted using the method described in the previous section.

The CPSs were also calibrated using the same conditions with river water to confirm the calibration constants using other types of waters. The calibration was done for 9 days, and two CPSs were removed after 2, 5, 7 and 9 days.

To calculate the calibration constants (*Rs, k* and *De*), Eqs. (1) and (2) were used. The *k* (ng/day) is the slope obtained by representing the mass of the analyte retained in the sorbent with respect to the time of sampling, and *Rs* (mL/day) was calculated using Eq. (1), where *Cw* is the concentration of the external solution.

The *Cw* was measured for all the compounds, because some of the analytes were present in the river water, and the concentration was higher than 20 µg/L.

$$Rs = \frac{k}{\mathrm{Cw}} = \frac{De{*}\mathrm{A}}{\Delta\mathrm{g}} \tag{1}$$

The constant *De* (cm^2/s) was calculated using Eq. (2). *Δg* is the thickness (1.5 mm) and *A* is the CPS area (18.4 cm^2).

$$De = \frac{k{*}\Delta\mathrm{g}}{\mathrm{Cw} * \mathrm{A}} \tag{2}$$

Finally, after the calibration, to calculate the concentration of the compounds in the sample, Eq. (3) was used, where *M* is the mass accumulated on the sorbent (ng) and *t* the time (days).

$$Cw = \frac{M{*}\Delta\mathrm{g}}{De * A * t} = \frac{M}{Rs * t} \tag{3}$$

2.4.3. Deployment of the CPS in river water

To evaluate the presence of these compounds in the Ebre River using the calibrated samplers, the CPSs were placed in the catchment site of the drinking water treatment plant (DWTP) of the *Consorci d'Aigües de Tarragona* (CAT) located at Camp-Redó, Tarragona (Spain), which supplies water to the region of Tarragona (more than 500,000 people).

CPSs were deployed for 9 days, from 12th of July of 2022 to 21st of July of 2022, in quadruplicate. CPSs were placed inside of a tulle mesh, immersed in water and securely tied to a fixed place. Fig. 1 shows the set-up of the samplers before (A) and after (B) sampling. After 9 days, the CPSs were taken out of the water, and contaminants were extracted and analysed using the LC-MS/MS method as described previously.

3. Results and discussion

3.1. LC-MS/MS optimisation

For MS/MS optimisation, all the parameters were optimised injecting each compound at 5 mg/L in a solution of MeOH:H_2O (50:50, v/v). Firstly, the ionisation mode was optimised for each compound. All the compounds achieved good results with the positive ionisation mode since most of them are basic analytes. DICLO and VAL, in spite of containing acidic groups in the structure, achieved a good response in both positive and negative ionisation mode but, ultimately, positive mode was selected for all compounds. Subsequently, the precursor and product ions were selected for each compound and the MRM transitions are summarised in Table S1. The selected precursor ions for all the compounds were the $[M+H]^+$. Two product ions were selected, except in the case of TRA, where only one product ion was selected corresponding to the characteristic fragment of this compound, already reported in literature [31]. Cone voltage was optimised between 50 and 150 V and it was observed that the optimal voltage for all the compounds was 100 V. Collision energy was optimised between 0 and 30 eV in 5 eV steps and after revising the results using a more accurate range in 2 eV steps. For example, for the fragmentation of PRE a more accurate inspection in the range between 5 and 15 eV allowed as optimal collision energy 8 eV and 12 eV for product ion 1 and 2, respectively, to be established. However, for MOR the range of energy was increased to 50 eV, finally fixing a collision energy of 40 eV for both product ions. All these parameters are summarised in Table S1.

For the LC separation, the gradient of the mobile phase was optimised to obtain a good separation of the compounds. Most of the compounds have a good separation, but some of them have similar retention

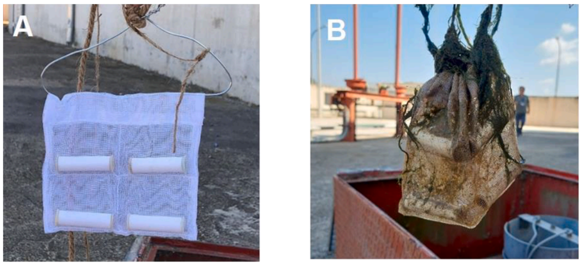

Fig. 1. Set-up for sampling with CPSs on Ebre River: before sampling (A) and after 9 days of sampling (B).

times, as can be observed in Table S1. However, they could be identified and quantified correctly because the selected transitions were different.

When the method was validated (details are summarised in Table S2), all the analytes showed a good linearity ($r^2 > 0.995$), between 1 and 250 μg/L, except NIC, CAF, TRA and MET, which were between 5 and 250 μg/L, and PRE, GAB, DIA and VAL, which were between 0.5 and 250 μg/L. The limit of quantification (LOQ) was the lowest value of the linear range. The limit of detection (LOD) was defined as the lower concentration with the presence of all ions with a signal-to-noise ratio of at least 3. The LOD for most of the compounds was 0.5 μg/L, except for PRE, BE, COC and EN, where it was 0.1 μg/L, and for GAB, TRA, MET, DIA, VAL, which was 0.05 μg/L. The precision of the method was good because the percentage of relative standard deviation (%RSD) ($n = 3$) of the method was lower than 6% (except for CAF, 14.4%).

3.2. Stability study

Before CPS calibration and deployment, a stability test was performed to evaluate the degradability of the compounds in water as this can affect the analyte uptake during the sampling and the quantification with the CPSs. According to literature [32], a compound is considered unstable if it shows a loss higher than a 20%.

Stability was tested in ultrapure, bottled and river water. The results obtained did not show differences between the different types of water. All the analytes, except COC, MOR and RAN, were stable for 14 days. Fig. 2 shows the results of the stability tests with river water for the most unstable analytes. As shown in Fig. 2, COC was completely degraded after 3 days, while the concentration of BE (its main metabolite [32]) increased to almost 200%. In addition, MOR was unstable since it degraded over 50% in 7 days. MOR is principally degraded to apomorphine, pseudomorphine or morphine-N-oxide [33]; nevertheless, in this study these compounds were not determined. RAN was also unstable, and degraded over 30% in 10 days.

Although RAN and MOR are unstable, they were initially included in the calibration of CPSs, because they are stable for some days and the period of sampling might be shorter than their stable period. COC was not included in the calibration because it was completely degraded after 3 days.

3.3. Retention study of Oasis MCX

To evaluate the retention of the compounds and the elution conditions of the sorbent Oasis MCX at sampling conditions, 500 mL of bottled water at pH 7 spiked at 2 μg/L with a mixture of the compounds were percolated through a 500 mg SPE cartridge. After loading the sample, the compounds were eluted using 5 mL of 5% of NH_4OH in MeOH (v/v), then the extracts were evaporated to dryness and subsequently redissolved with 1 mL of MeOH:H_2O (5:95, v/v).

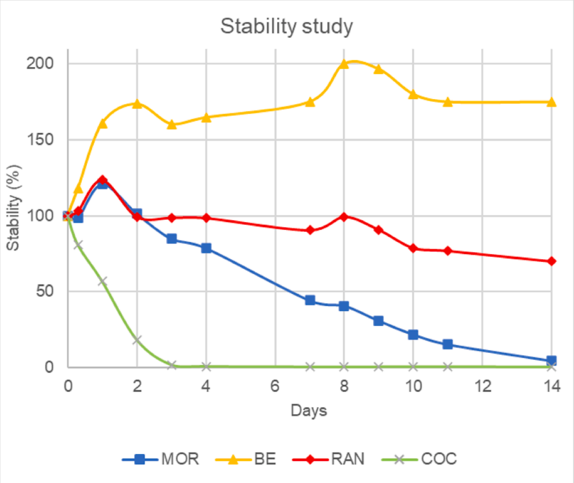

Fig. 2. Stability study results for MOR, BE, RAN and COC in river water.

Fig. 3 shows that the recoveries of most of the compounds were higher than 70%. The recoveries of NIC, BE, EN, MET and DICLO were lower than 50%. PRE, GAB and OXA showed the lowest recoveries, which might be attributed to their low pk_a value, which might hinder the compounds retention. In the present study, the sample pH was maintained at pH 7 to simulate the natural pH of surface water. However, at pH 7 not all the compounds could be at their cationic form; for this reason, some compounds have lower recoveries in comparison with the values obtained in other studies [34–36], where the loading conditions were optimal to retain the compounds on the sorbent.

These results confirm the hypothesis that the sorbent Oasis MCX could be a good candidate to act as retention phase inside of the CPS for the sampling of these compounds, because the compounds are retained on the sorbent.

3.4. Calibration of the CPS

The CPSs were calibrated initially in bottled water and later in river water to confirm the calibration parameters.

In bottled water the calibration was performed for 14 days, which was successful for all the analytes except for MET because it did not show a linear mass uptake. All other analytes showed a linear uptake trend (ng vs day) at 9 days with r^2 values ranging between 0.933 and 0.999. After 9 days, in all cases, the uptake did not increase significantly, and the linear trend was lost for all the compounds. For this reason, the calibration time was set at 9 days. Considering this, MOR could not be calibrated because it degraded significantly after 7 days.

The *Rs* and *De* were calculated for all the analytes with Eqs. (1) and (2) and using the *k* values obtained for 9 days. All the constant values are summarised in Table 1. The *k* values obtained are between 6.1 and 44.8 ng/day, *Rs* ranged between 0.2 and 2.2 mL/day and *De* values are between 2.9E-8 and 2.1E-7 cm^2/s.

After calibration with bottled water, the CPSs were calibrated in river water to confirm the results. In this case, the period of calibration was reduced from 14 days to 9 days, because this was the linear uptake time with bottled water. Most of the compounds showed a linear trend and r^2 values ranged between 0.846 and 0.987, except MET, OXA and DICLO, which did not have a linear uptake of mass.

Fig. 4 shows the uptake trend with respect to time for 2 therapeutic drugs (PEN and DIA), 2 illicit drugs (KET and COD) and 2 metabolites (4-AMP and COT), with different polarities, for which a linear mass uptake for 9 days in river water can be observed. The *k* values obtained are between 6.3 and 59.6 ng/day, the *Rs* ranged between 0.3 and 1.9 mL/day and the *De* values are between 1.7E-8 and 3.1E-7 cm^2/s.

From the results detailed in Table 1, it can be observed that there were no significant differences between the constants obtained with the two different types of water for most of the compounds. In fact, they show good correlation ($r^2>0.900$) for most of the compounds. However, the k for MET, OXA and DICLO could not be calculated correctly in river water and the *k* values obtained for bottled water were used because of the good correlation.

For the calibration with river water, CAF shows the highest values of *Rs* (1.9 mL/day) and *De* (1.7E-7 cm^2/s), and NIC shows the lowest values of *Rs* (0.3 mL/day) and *De* (3.1E-8 cm^2/s).

The *Rs* values obtained in the present study are lower than those reported using POCIS samplers with Oasis HLB as retaining phase [24, 25,37–39]. A lower value of *Rs*, indicates that the compounds are less retained on the sorbent. Han et al. [24] obtained *Rs* values between 0.041 and 0.227 L/day when a group of nine illicit drugs and some metabolites (including COT and CAF) were determined using POCIS (with Oasis HLB) followed by LC-MS/MS. However, these values are not comparable due to the differences in geometry of the samplers, which greatly affected the calculated parameters. The *Rs* obtained are also

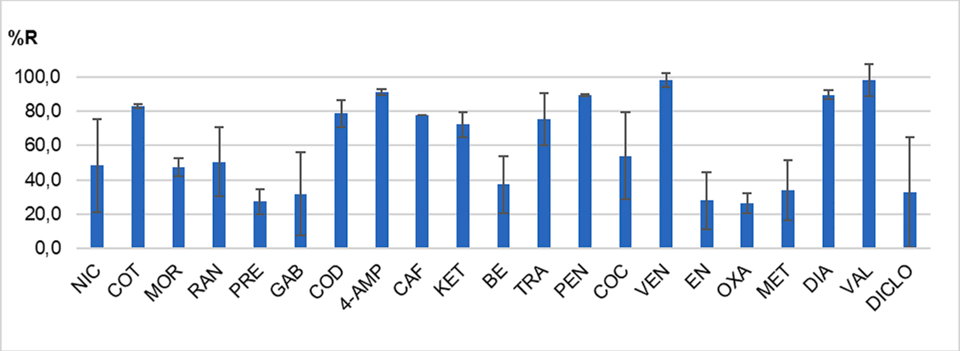

Fig. 3. Recoveries from the SPE extraction of 500 ml of bottled water at pH 7 with the Oasis MCX for all the compounds.

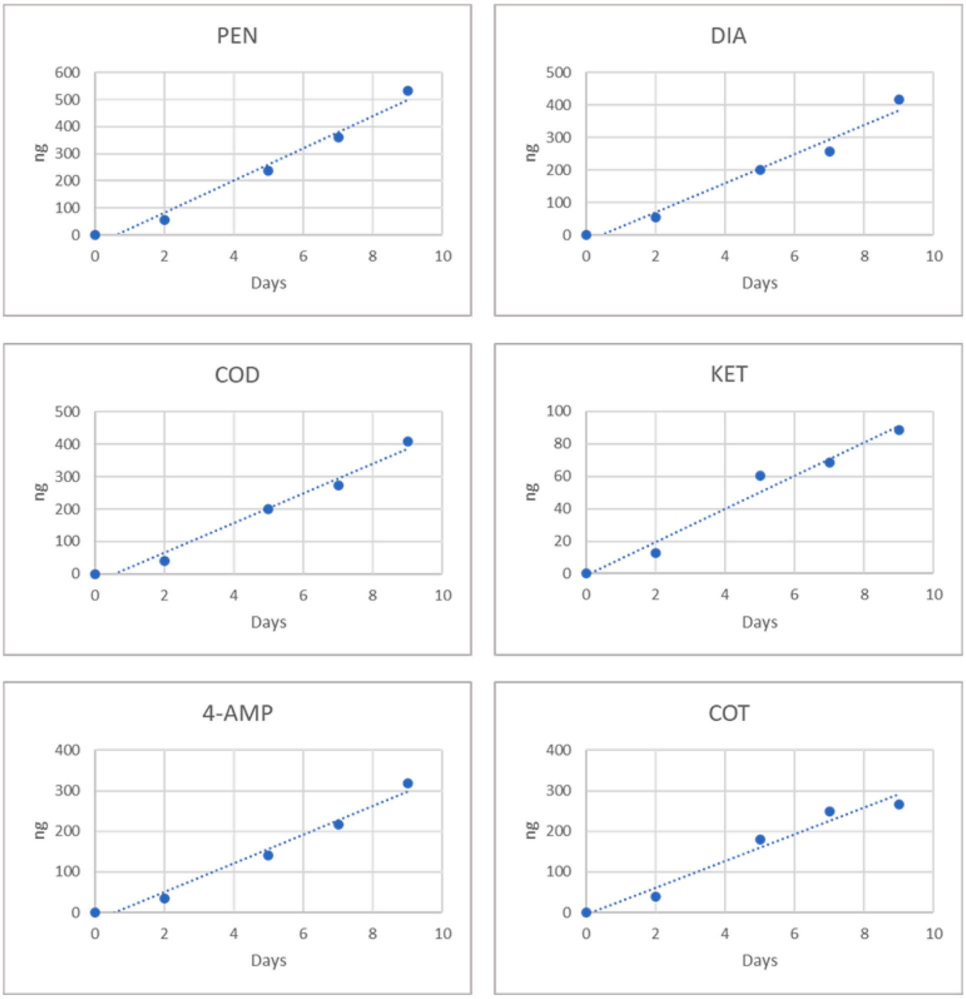

Fig. 4. Representation of the uptake mass (ng) with respect to the sampling time in river water for selected analytes.

lower than those obtained with a CPS using other retaining phases like the sorbents PoraPak Rxn RP, Sepra SBD-L and Sepra ZT [20]. For example, for COT, the *Rs* values obtained with bottled water with the Oasis MCX are 1.46 mL/day and with the Sepra ZT sorbent the values are 5.2 mL/day [20]. This fact was expected because the sampling pH is not optimal for the retention of most of the compounds on the sorbent.

In any case, CPS using Oasis MCX was properly calibrated and it is ready to be applied for the monitoring of these challenging compounds in the Ebre River. In addition, this opens up the possibility of using the mixed-mode ion-exchange sorbents in the passive sampling.

3.5. Application in sampling of environmental water

Once CPSs were calibrated, they were deployed in quadruplicate to determine the presence of the analytes in the Ebre River. Fig. 1 shows the samplers before and after the sampling period, and it can be observed that the tulle mesh was completely dirty with the presence of some algae, but this prevented the CPSs from becoming clogged.

The concentrations of the compounds were calculated using the *Rs* in river water, except for DICLO, MET and OXA, where the constants obtained with bottled water were used. Table 2 shows the concentrations of the compounds using the sampling method developed in the Ebre

Table 2
TWA concentrations (ng/L) and standard deviation of the compounds determined with the CPSs in the Ebre River.

Compounds	Concentration (ng/L)
NIC	422 ± 102
COT	312 ± 38
RAN	n.d.
PRE	n.d.
GAB	76 ± 26
COD	n.d.
4-AMP	136 ± 15
CAF	203 ± 58
BE	204 ± 65
TRA	n.d.
PEN	73 ± 13
VEN	n.d.
EN	n.d.
OXA	324 ± 15
MET	n.d.
DIA	535 ± 302
VAL	172 ± 11
DICLO	57 ± 20

River. Eleven out of 19 contaminants were determined in the Ebre River at concentrations ranging from 27 to 535 ng/L. NIC and DIA are the compounds found at the highest concentration in the Ebre River, followed by OXA and COT. RAN, TRA, PRE, VEN, EN, MOR, COD and MET could not be detected during the sampling period. Figure S2 shows a chromatogram obtained after deployment of one of the CPSs in Ebre River, where it can be seen the presence of the mentioned compounds.

Regarding the precision, it should be mentioned that for most compounds, like 4-AMP, COT, PEN or VAL, as can be observed in Table 2, precision was good, the RSD ($n = 4$) being lower than 30% for most of them. For instance, RSD for 4-AMP was 11%, for COT 12% or 4.6% for OXA. However, lower precision was obtained for DIA (RSD 56%) and the concentrations of KET in the four CPSs were not reproducible and therefore, KET could not be quantified.

The concentrations found are in line with those previously determined in the grab samples from the Ebre River and also with some predicted values from pharmaceutical consumption [40], which demonstrate the proper applicability of the developed method based on CPS using Oasis MCX followed by LC-MS/MS. For instance, the concentration of DICLO was between 23 and 30 ng/L [41], between 12 and 70 ng/L [42], 25 ng/L [43] and up to 148 ng/L [44]. Other concentrations found in the Ebre River that were similar to those found in the present study were 240 ng/L of caffeine [43], up to 24 ng/L of MET [41, 42] RAN and EN were not detected in most of samples [44]. As regards BE, maximum values of 94.6 and 129 ng/L were found in 2010 and 2011 [45], respectively, which are lower as compared to the concentration found in the present study (204 ng/L) probably due to an increase in cocaine consumption. The wide ranges of concentrations found for some compounds in other rivers [46–48] make it difficult to compare them, although consistency is found for compounds such as DICLO and VAL in rivers of South Wales [46].

4. Conclusions

In this study, we successfully pioneered the use of a mixed-mode strong cation-exchange sorbent (Oasis MCX) as retaining phase of CPS for the determination of a group of therapeutic and illicit drugs and some metabolites in river water. The CPSs were successfully calibrated in bottled and river water for 9 days. Both the stability and calibration studies using different types of water disclosed similar results. The passive method presented here is simple and feasible for the monitoring of CECs at trace levels in river water. This study opens the possibility of using other mixed-mode sorbents or other types of sorbents as retaining phase on CPSs or other passive samplers.

CRediT authorship contribution statement

Pol Clivillé-Cabré: Investigation, Validation, Writing – original draft. **Sílvia Lacorte:** Investigation, Conceptualization, Methodology, Funding acquisition, Writing – review & editing. **Francesc Borrull:** Conceptualization, Methodology. **Núria Fontanals:** Conceptualization, Methodology, Writing – review & editing, Supervision. **Rosa Maria Marcé:** Conceptualization, Methodology, Writing – review & editing, Supervision, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.chroma.2023.464348.

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