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# Ceramic passive samplers for determining pharmaceuticals and drugs of abuse in river and drinking water

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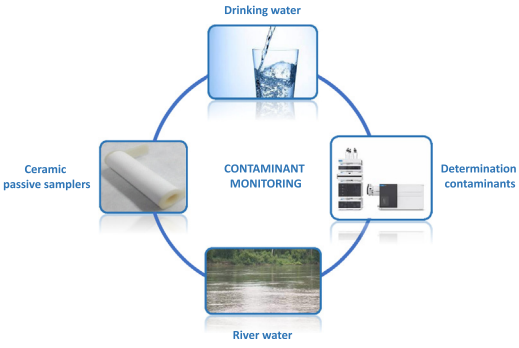
## HIGHLIGHTS

- Different materials were evaluated in ceramic passive samplers (CPSs).
- They were evaluated for the monitoring of pharmaceuticals and drugs of abuse.
- CPSs were calibrated with suitable uptake during 13 days.
- CPSs were deployed in surface and drinking water.
- Time weighted concentration was determined for some compounds at ng/L.

## GRAPHICAL ABSTRACT

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## ABSTRACT

An important challenge today is to efficiently monitor the presence of polar pharmaceuticals and drugs in surface and drinking waters to ensure its safeness. Most studies rely on grab sampling techniques, which enable the determination of contaminants at a given point and given time. In this study, we propose the use of ceramic passive samplers (CPSs) to increase the representativeness and efficiency of organic contaminant monitoring in waters. Firstly, we have assayed the stability of 32 pharmaceuticals and drugs and found that five of those compounds were unstable. Moreover, we evaluated the retention capabilities of three sorbents (Sepra ZT, Sepra SBD-L, and PoraPak Rxn RP) in solid-phase extraction (SPE) mode and found no differences in terms of recoveries for all three sorbents. We then calibrated CPSs using the three sorbents for the 27 stable compounds over 13 days, with a suitable uptake for 22 compounds with sampling rates between 0.4 and 17.6 mL/day, which indicates high uptake efficiency. CPSs with the Sepra ZT sorbent were deployed in river water ($n = 5$) and drinking water (n = 5) for 13 days. Some of the studied compounds occurred with a time-weighted concentration, for instance, of 43 ng/L for caffeine, 223 ng/L for tramadol or 175 ng/L for cotinine in river water.

## 1. Introduction

The European Union and other international bodies require regular monitoring of organic contaminants in water (European Directive, 2015). These contaminants are conventionally determined in environmental waters by grab sampling followed by sample treatment (usually solid-phase extraction, SPE) and chromatographic techniques with mass spectrometry-based detection. However, these are time-consuming methods that involve the handling of large volumes of samples, which sometimes lack representativeness. Moreover, especially in surface and drinking waters some of these contaminants are present at low concentrations (i.e., low ng/L to pg/L) that may lie below the quantification limits of the analytical methods.

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Passive sampling enables the in situ enrichment of contaminants, and, therefore, it is unnecessary to sample, handle and extract large volumes of samples. Also, since it yields time-weight average (TWA) concentration, it provides a high level of sensitivity because the contaminants accumulate over their deployment period. In addition, interference from the matrix may be substantially reduced thanks to the diffusion layer of the device (Becker et al., 2021; Harman et al., 2012; Verhagen et al., 2021). For this reason, passive sampling strategies should be considered for a more exhaustive control of water quality. Indeed, passive sampling has been proposed as a feasible alternative monitoring technique within the EU Water Framework Directive (Brack et al., 2017; European Directive, 2015).

Different types of passive sampling techniques such as silicone rubbers, semi-permeable membrane devices (SPMDs), polar organic chemical integrative samplers (POCIS), Chemcatchers, diffusive gradients in thin films (DGT) and ceramic passive samplers (CPSs) have been developed to monitor contaminants in water samples. Non-polar compounds such as polychlorinated biphenyls, organophosphorus compounds and polycyclic aromatic hydrocarbons have been monitoring using silicone rubbers (Sobotka et al., 2022), short-chain chlorinated paraffins with Chemcatchers (Godere et al., 2021), pesticides, high production volume compounds, pharmaceuticals and oestrogens with POCIS (Jeong et al., 2018; Morin et al., 2018; Nguyen et al., 2021), per- and polyfluoroalkyl compounds (Yang et al., 2022) or pharmaceuticals using CPSs (Franquet-Griell et al., 2017).

Weaknesses involved in passive sampling, however, are understanding of the uptake mechanisms and the performance of the passive sampler. To overcome these issues, careful calibration enables the calculation of the diffusion coefficients (*De*) and sampling rates (*Rs*) of target compounds. Uptake and performance depend on the properties of the compounds (solubility in water, polarity and hydrophilicity), the receiving phase of the passive sampler, and the complexity of the water to be monitored (Becker et al., 2021; Franquet-Griell et al., 2017; Vrana et al., 2021).

However, selection of the most suitable sorbent for trapping polar compounds is one of the greatest challenges in passive sampling (Becker et al., 2021; Mutzner et al., 2019; Nguyen et al., 2021; Vrana et al., 2021). In this context, three passive sampling receiving phases – namely, styrene-divinylbenzene reversed phase sulfonated (SBD-RPS) sorbents from two different brands and hydrophilic lipophilic balance (HLB) disks – were evaluated in Chemcatcher samplers for retaining a group of nine pesticides whose $\log K_{ow}$ ranged from −1 to 5 (Becker et al., 2021). The above study demonstrated that all three phases were generally suitable for monitoring the pesticides under study. However, the small differences observed between brands or phases suggest that calibration parameters should be experimented for each individual case rather than merely transferred from the literature (Becker et al., 2021). When a similar comparison of receiving phases (i.e. HLB, styrene-divinylbenzene and styrene) was conducted using POCIS, Speedisk and Sorbicell as passive samplers, respectively, to monitor 108 moderately polar compounds (mainly pesticides and pharmaceuticals; $\log K_{ow}$ ranging from −0.1 to 6), the results showed that only 43 compounds were detected in all three samplers and that the highest number of compounds was detected with the HLB receiving phase (Nguyen et al., 2021). However, the designs and surface areas of the samplers were different and the changes in retention observed could not be attributed only to the receiving phase. To monitor moderate-polar compounds, the receiving phase capabilities in passive sampling therefore require further exploration.

Among different passive sampling techniques, CPSs have been proven to retain contaminants of different physico-chemical properties with high efficiency (Orera et al., 2018;). They consist in ceramic cylinders where the pore size, pore density and thickness of the ceramic cylinder have been optimized to allow high diffusivity of multiple contaminants in different types of samples (Lacorte et al., 2022). CPSs were tested using Sepra ZT (a HLB receiving phase type) to determine anticancer drugs in waste water, and their performance was validated by comparing the results to those obtained with grab sampling (Franquet-Griell et al., 2017).

The aims of the present study are to develop an analytical method using CPS for monitoring a group of polar organic contaminants (pharmaceuticals, drugs of abuse and some metabolites covering a broad range of $\log K_{ow}$) in surface and drinking water. The extraction and analysis using liquid chromatography with mass spectrometry in tandem (LC-MS/MS) were optimized to determine 32 contaminants. For the passive sampling, an already tested CPS device (Orera et al., 2018) was filled with three sorbent materials evaluated in terms of sorption capabilities (using dispersive SPE approach) and uptake mechanisms (calculation of *De* and *Rs* values). Finally, the calibrated method was used in a pilot study to monitor the occurrence of the compounds studied in surface water and drinking water.

## 2. Experimental

### 2.1. Materials

The 32 compounds studied in this paper, classified by family and their main properties, are shown in Table S1. All compounds were purchased from Sigma-Aldrich (St. Louis, USA) except codeine, 2-ethylidene-1,5 dimethyl-3,3-diphenylpyrrolidine (EDDP) and morphine, which were purchased from Cerilliant (Round Rock, TX, USA). Stock solutions of individual standards at 1000 mg/L were prepared in methanol (MeOH). Working solutions of the mixture of the compounds were prepared by diluting each compound in water/MeOH (8/2, v/v). All standards were stored in amber vials at −20 °C. The ultrapure water was provided by a Synergy UV water purification system (Merck Millipore, Burlington, MA, USA), while HPLC grade MeOH, "MS grade" acetonitrile (ACN) and water were all supplied by Scharlab (Sentmenat, Barcelona, Spain). Formic acid (HCOOH) was acquired from Sigma-Aldrich.

### 2.2. Optimization of ceramic passive sampler deployment

Fig. 1 shows our analytical approach for the integrated determination of pharmaceuticals and drugs of abuse in river and drinking water. This approach comprises four mandatory steps before deployment for determining CPS performance. The parameters measured in this study are the stability of the pharmaceuticals and the drugs of abuse, the extraction efficiency of three different sorbents, calibration and calculation of the sampling rate (*Rs*) and diffusivity (*De*) of the suite of contaminants studied. These steps are described below.

#### 2.2.1. Stability of the pharmaceuticals and drugs of abuse in water

The stability of the compounds in water was evaluated to determine their potential degradability, since for labile compounds the calibration parameters cannot be accurately determined. To determine their stability, bottled water (Table S2 details its chemistry) was spiked at 20 μg/L with all the compounds, and a 0.5 mL aliquot was taken at time 0, 1, 2, 4, 6, 8, 14, 18, 24, 30, 36, 42 and 48 days and analysed by LC-MS/MS using direct sample injection.

Stability was measured as percentage relative concentration with the ratio between the concentration at $t = 0$ and the concentration measured at each time period. This value provides information on the degradability of contaminants, which directly affects the calculations of the sampling rate and diffusivity.

#### 2.2.2. Optimization of sorbent and extraction conditions

Three sorbents were evaluated in recovery tests. The bulk sorbents used to fill the CPSs were Sepra ZT (30 μm, 85 Å) and Sepra SBD-L (95 μm, 255 Å), both from Phenomenex (Torrence, CA, USA), and PoraPak Rxn RP (30 μm) from Waters (Milford, MA, USA). The sorbents (200 mg), placed in a 30 mL polypropylene falcon, were conditioned with 10 mL of MeOH followed by 10 mL of ultrapure water, which were discarded. After the sorbents were activated, 10 mL of bottled water spiked at 20 μg/L with the mixture of the compounds was added, vortexed for a few seconds and left for 15 min to enable proper contact between the analytes and the sorbent. The water was then decanted and 12 mL of MeOH was added to the tubes. The tubes were then vortexed for 1 min and placed in the ultrasonic bath for

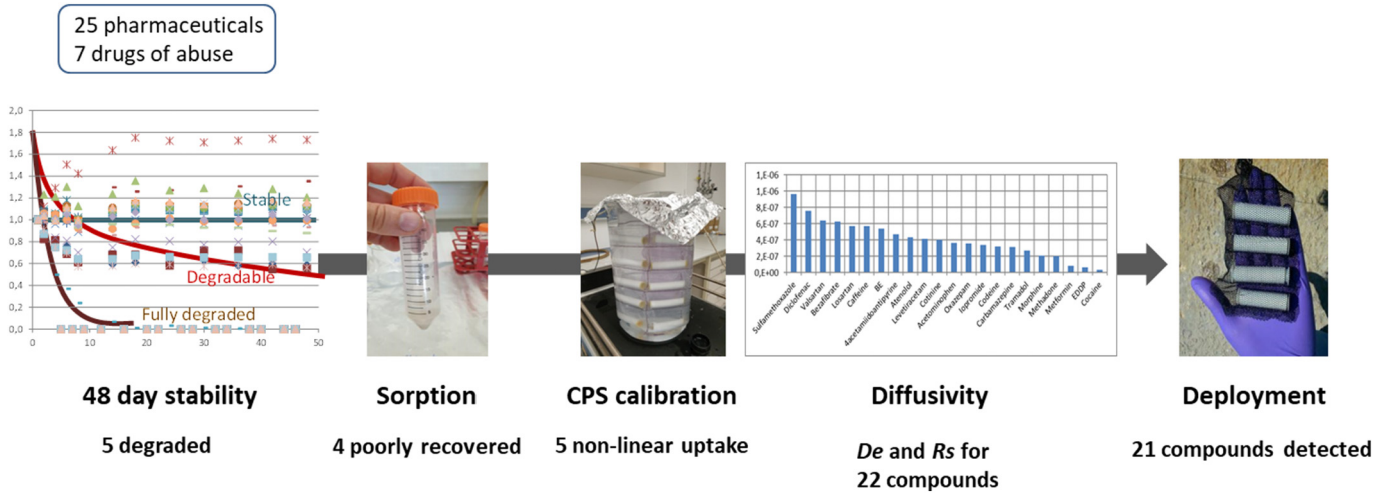


**Fig. 1.** Scheme of the procedure developed to determine 32 pharmaceuticals and drugs of abuse in water using the CPS.

5 min. This vortex-ultrasonic bath cycle was repeated three times without changing the solvent. Samples were then centrifuged for 15 min at 4000 rpm, and MeOH was recovered and placed in a 40 mL amber vial. This MeOH extract was evaporated to dryness and reconstituted in 1 mL of 0.1 % HCOOH in water/0.1 % HCOOH in ACN (20/80, v/v). This solution was then filtered through a 0.22 μm nylon filter (Phenomenex) and injected into the LC-MS/MS.

*2.2.3. Calibration of the samplers*

The CPS used (patent P201530882) consists of a cylinder ceramic shell of 45 mm length x 13 mm outer diameter and the wall thickness was 1.5 mm. This CPS contained the sorbent in the inner part. More details are described in a previous study (Franquet-Griell et al., 2017).

The CPSs were calibrated to calculate the concentration-time slope (*k*), the sampling rate (*Rs*), and the effective diffusion coefficient (*De*) for each single compound. Calibrations were performed with the three sorbents discussed in Section 2.2.2. Two hundred mg of each sorbent was conditioned with MeOH and ultrapure water, the solvents were decanted, and ultrapure water was added to the sorbent to enable proper filling of the sampler. One end of the CPS was capped (using conical thermoplastic rubber caps), the sorbent dispersion was placed inside the ceramic cylinder, and the other end of the CPS was then capped. This procedure enabled the aqueous diffusion layer to be maintained.

For the laboratory calibration, a beaker with 3.5 L of bottled water was prepared and spiked at 20 μg/L (the same concentration as in the stability tests) with the mixture of the compounds. Calibration was performed in bottled water as its pH and mineral content simulate natural waters better than ultrapure water.

Ten CPSs were placed in a tulle mesh support in the beaker and left for 13 days on an Orbital shaker to simulate flowing river conditions. The CPSs were deployed in duplicate; thus, after 3, 5, 7, 11 and 13 days, two CPSs were removed and extracted. During the period of exposure, the temperature was also controlled (22–23 °C). An aliquot of the solution was also taken to evaluate the stability of the compounds.

The sorbent was emptied from the CPS into a 30 mL polypropylene falcon tube and the inner CPS was rinsed with a small amount of water to collect all the sorbent. The sorbent was placed in a falcon tube and the extraction was carried out as explained in Section 2.2.2.

CPS can be reused as they have been used in the different steps of the study. To do so, the CPS was thoroughly rinsed with water and then placed in a beaker with MeOH and sonicated in an ultrasonic bath for 30 min, left overnight with fresh solution, and stored in ultrapure water until its next use.

*2.2.4. Calculation of the ceramic passive sampler parameters*

Different parameters were calculated to test the CPS performance. They include:

Diffusivity (*De*) is the effective diffusion coefficient of a solute measured in $cm^2/s$. The effective diffusion coefficients of compounds through the water-filled CPS were calculated from Eq. (1):

$$De = \frac{k * \Delta g}{Cw * A} \quad (1)$$

where

- *k* is the slope obtained by representing the adsorbed mass of each compound with respect to time during CPS calibration (ng/h)
- Δg is the thickness of the diffusion layer (1.5 mm)
- Cw is the concentration of the compounds quantified in the external solution calculated at $t = 0$ (20 μg/L)
- A is the area of the ceramic membrane (18.4 $cm^2$)

The sampling rate (*Rs*) was calculated from Eq. (2):

$$Rs = \frac{k}{Cw} = \frac{De * A}{\Delta g} \quad (2)$$

Once these constants were known, the concentration of compounds in the water were calculated from Eq. (3):

$$Cw = \frac{M * \Delta g}{De * A * t} = \frac{M}{Rs * t} \quad (3)$$

where

- M is the mass of each contaminant accumulated in the sorbent during the deployment period (ng)
- t is the deployment time (in days)

*2.2.5. Deployment of the ceramic passive samplers*

CPSs were deployed in river water (Llobregat River, NE Spain) and drinking water from a drinking water treatment plant (DWTP) that supplies water to Barcelona, a city with a population of three million people (Rubirola et al., 2018). The DWTP collects water from Llobregat River and treats $5 \times 10^5$ $m^3$ water per day. Table S3 collects the amin parameters of the drinking and river water analysed.

Ten CPSs (five in drinking water and five in river water) were deployed in water between 22nd July 2020 and 3rd August 2020. On retrieval, they were removed from the mesh, rinsed with water to remove any organic matter and algae. They were then transported to the laboratory wrapped

in aluminium foil and immediately disassembled and extracted as described in Section 2.2.3. Quantification was expressed in absolute amount of ng of compound per CPS and converted into ng/L in the sample by applying the *Rs* calculated from the calibration performed under controlled conditions (Eq. 3).

### 2.3. Instrumental analysis

Sampler extracts were analysed using an Agilent 1200 series liquid chromatograph coupled with a 6460 Triple quadrupole mass spectrometer (QqQ) detector and electrospray ionization (ESI) interface, working in both positive and negative mode. The liquid chromatography (LC) separation was performed using a Luna Omega Polar $C_{18}$ (150 mm × 3 mm, 3 μm) column with a precolumn (4 mm × 3 mm) (Phenomenex) and thermostatized at 30 °C. Mobile phase was composed of (A) 0.1 % HCOOH in water and (B) 0.1 % HCOOH in ACN working in gradient elution that began at 5 % B. This was maintained for 3 min, increased to 75 % B in 25 min and then to 100 % B in 2 min, and then held for 1 min before returning to the initial conditions in 2 min. This was then maintained for 5 min for equilibration purposes. The flow rate was set at 0.4 mL/min and the injection volume was 10 μL. Optimized mass spectrometer parameters are shown in Table S1. The acquisition was performed under multiple reaction monitoring (MRM) mode using the most abundant precursor/product ion transition as the quantifier and the second most abundant transition as the qualifier. The ratio of these transitions was used for confirmation purposes, as was a retention time shift below 2 % between standards and samples.

Instrumental calibration was performed by injecting seven concentrations of the standards (ranging from 0.5 to 500 μg/L). The instrumental quantification limits (IQLs) were the lowest concentration of the calibration curve whose the signal-to-noise (S/N) ratio was ≥10. They ranged from 0.5 to 1 μg/L. The instrumental detection limits (IDLs), determined using a S/N ratio ≥ 3, ranged from 0.1 to 0.5 μg/L.

## 3. Results and discussion

### 3.1. Stability studies

Numerous studies have been conducted to check the stability of pharmaceuticals and drugs in sewage water samples and determine how the sample treatment or storage conditions affect this stability (W. Lin et al., 2021; X. Lin et al., 2021; Llorca et al., 2014; Senta et al., 2014). However, little is known about the stability of these compounds in surface waters. The first aim of this study was therefore to investigate the stability of the selected compounds in surface water to ensure a linear uptake by the CPS during the sampling period, as compounds degraded would obviously not be properly determined using CPS. To do so, bottled water spiked at 20 μg/L with the mixture of compounds with no pH adjustment (pH = 7.05) was placed in 1 L glass bottle, and kept at ambient temperature for 48 days. Aliquots were analysed at set times (see Section 2.2.1) and the results were expressed in terms of the percentage of relative concentration.

The compounds were considered unstable when the percentage of relative concentration was below 80 % (W. Lin et al., 2021; Petrie et al., 2017). Under this assumption, seven of the 32 compounds (allopurinol, ranitidine, atorvastatin, cocaine, levodopa, gabapentin and diazepam) were unstable. Fig. 2 shows that allopurinol presented the worst stability as it completely degraded after two days, whereas ranitidine, atorvastatin and cocaine presented a decrease in stability of over 50 % after four days. With levodopa and gabapentin, this loss in stability occurred after eight days. The concentrations of diazepam also decreased but only by roughly 35 % (Fig. 2). The instability of ranitidine and atorvastatin has already been reported in effluent wastewater. In most cases this was attributed to microbial degradation at ambient temperatures (i.e. 20–25 °C) compared to their reduced activity at lower temperatures (e.g. 4 °C) (Petrie et al., 2017).

Fig. 2 also shows the stability behaviours of cocaine and its main metabolite (benzoylecgonine) and of nicotine and its main metabolite (cotinine). It is widely reported that benzoylecgonine is produced from the degradation of cocaine (W. Lin et al., 2021; X. Lin et al., 2021), and for this reason has been used to estimate cocaine consumption (W. Lin et al., 2021; X. Lin et al., 2021). In our study, benzoylecgonine may be used as a biomarker for monitoring the occurrence of cocaine in surface water, since cocaine completely degraded after 14 days. As expected, a less noticeable transformation was observed for the nicotine/cotinine (nicotine's main metabolite) system, since nicotine degraded by roughly 20 % over eight days whereas cotinine experienced a proportional increase in relative concentration (Fig. 2). When calibrating the CPSs, aliquots of the spiked bottled water were analysed and the stability results were confirmed.

Other compounds included in the present study, such as acetaminophen, atenolol and morphine, have also shown instability in sewage samples (Hillebrand et al., 2013; X. Lin et al., 2021; Petrie et al., 2017). However, this instability was reliably reduced in bottled water (Hillebrand et al., 2013), a result confirmed in the present study since these compounds were stable over the 48 days.

In summary, stability tests showed that allopurinol, ranitidine, atorvastatin, levodopa and gabapentin were unstable during the monitoring period. Thus, these five compounds were discarded from the study. However, diazepam and cocaine were not discarded yet and their behaviour was further observed in later experiments.

### 3.2. Selection of the sorbent

Three bulk sorbents, namely Sepra ZT, Sepra SBD-L and PoraPak Rxn RP, were first evaluated by dispersive SPE under the conditions described in Section 2.2.2 to investigate their retention behaviour towards the studied compounds. Since all sorbents are polymeric based on styrene-divinylbenzene, they confer hydrophobic and π-π interactions. Additionally, Sepra ZT is surface-modified with pyrrolidone, which also confers hydrophilic interactions with the compounds.

Fig. 3 shows the percentage recoveries obtained for all compounds with the three sorbents. In general, Sepra ZT provided the best recoveries for most of the compounds, especially those with more polar features. This was expected because of the hydrophilic character of Sepra ZT that better interacts with the more polar compounds, whereas Sepra SBD-L and PoraPak Rxn RP cannot promote this type of interactions with the compounds during SPE extraction. For example, compounds such as cotinine, cocaine and methadone presented better recoveries with the Sepra ZT sorbent than with the other sorbents evaluated. This result is in line with previous studies (Afonso-Olivares et al., 2017; Boogaerts et al., 2021; Carmona et al., 2017; Gómez-Canela et al., 2019; Gros et al., 2012; Miossec et al., 2019; Paíga et al., 2019) in which hydrophilic-hydrophobic balanced sorbents such as Oasis HLB and Strata X (both of which present similar features to those of Sepra ZT) were selected in multi-residue analysis to extract similar polar organic compounds because they provided the best recoveries.

Nevertheless, poor recoveries (between 3 and 28 %) were obtained for metformin, nicotine, EDDP and morphine with all three sorbents, which may be attributed to the high polarity of these compounds, which made their retention challenging. For example, in a previous study (Afonso-Olivares et al., 2017), nicotine recovery was 20 % and only increased to 50 % when the sample pH was optimized. Another compound that presented low recoveries is EDDP. Similar recoveries have been reported in previous studies (Boogaerts et al., 2021; Krizman-Matasic et al., 2018) in which a broad range of opioids were monitored and EDDP recoveries were roughly 20 % at most when 100 mL of tap water was percolated through an Oasis HLB cartridge. Despite this low recovery, in that study it was possible to quantify EDDP thanks to the high sensitivity and the considerable concentration of the compound in the monitored samples (Boogaerts et al., 2021). In spite of the low recoveries achieved for these four compounds, they were not removed from the study.

As the recoveries of all compounds were acceptable for the three sorbents, all the sorbents were also evaluated to calibrate the CPS.

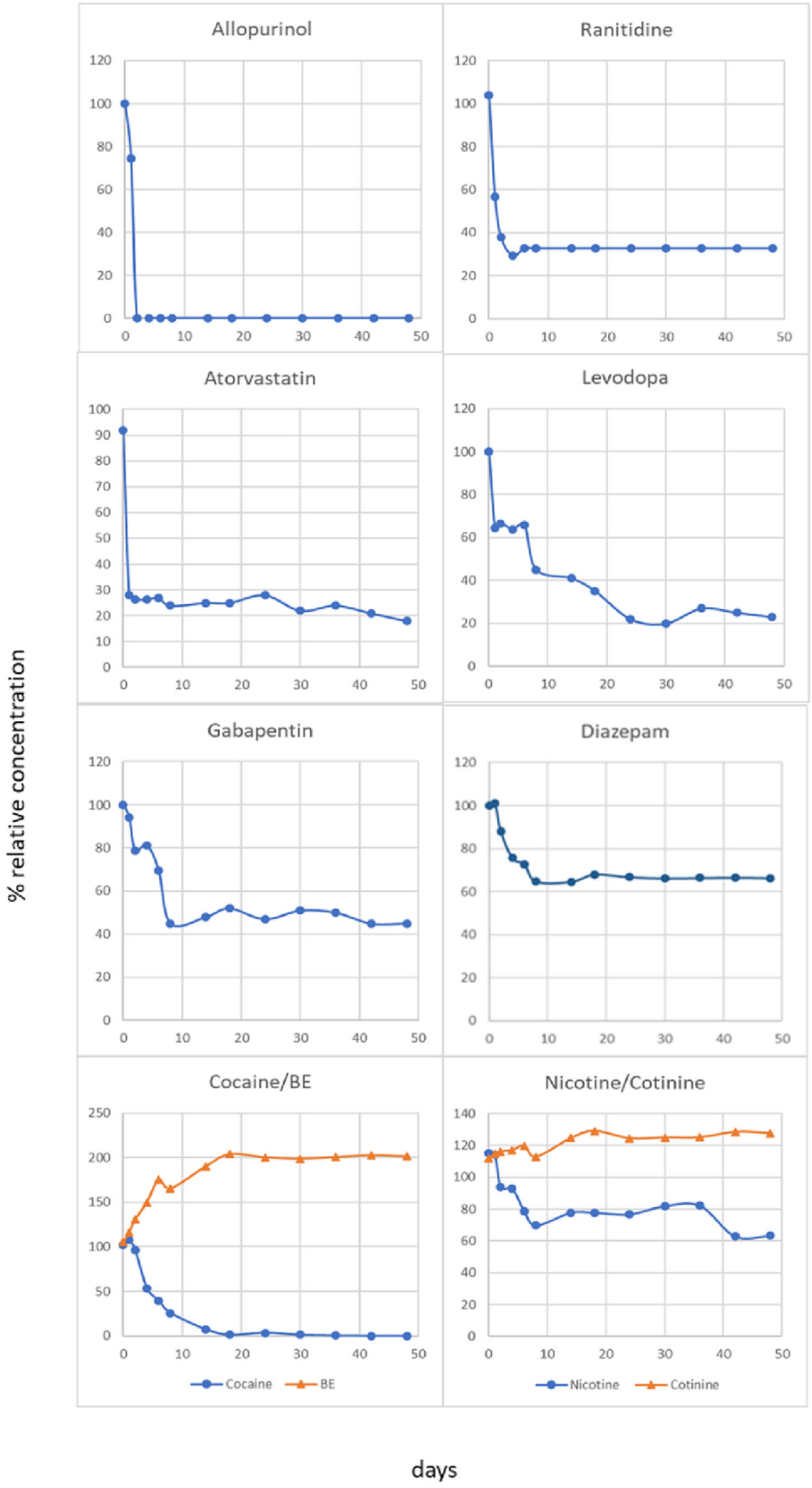


**Fig. 2.** Stability behaviour of the most unstable compound studied.

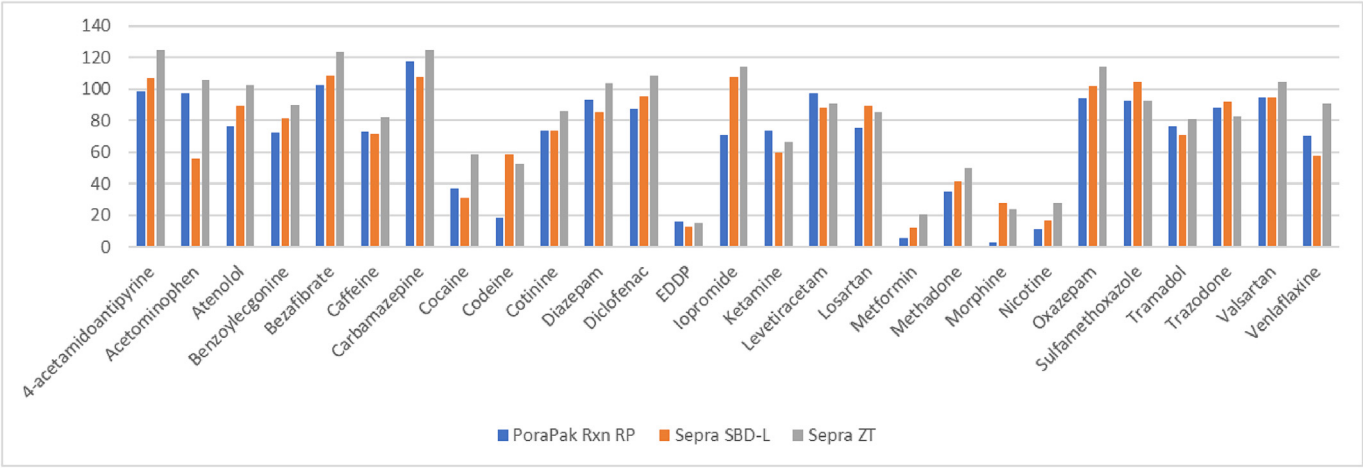


**Fig. 3.** Recovery obtained for each compound with the three sorbents evaluated. % RSD ($n = 3$) < 12 % when %$R$ > 30 %.

### 3.3. Calibration of the CPS

The CPSs were calibrated in bottled water for 13 days to determine the *k* (slope from representing the adsorbed mass of the compounds in the CPSs with respect to time) for the 27 stable compounds. From these calibrations, *De* and *Rs* were also determined. Although the values were determined in bottled water, from previous experience, these values can be applied to river water since the values found are similar. Moreover, the natural occurrence of contaminants in river water may hinder the accurate calibration. All compounds were successfully calibrated except nicotine, diazepam, ketamine, trazadone and venlafaxine, which did not show a linear mass uptake over the calibration period. In fact, diazepam had already shown instability issues (Section 3.1). Therefore, the calibration constants were not calculated for those compounds. It should be highlighted that a considerable number of compounds (22 out of the initial 27) were successfully calibrated using the CPS approach, whereas in other similar studies (Franquet-Griell et al., 2017; Morin et al., 2018; Verhagen et al., 2021; Vrana et al., 2021) where passive samplers were also set up, the number of compounds with a linear uptake were lower. Moreover, CPS enabled compounds that degraded in water to be preconcentrated, which means that although quantifying these compounds is not possible, they could still be identified at low concentration levels using CPS. With grab sampling, on the other hand, these compounds might be difficult to determine.

Table 1 shows the calibration constants for the 22 compounds. The *k* constants were correlated among the sorbents ($R^2$ of 0.99, 0.93 and 0.94 for Porapak and Sepra SDB, Porapak and Sepra ZT, and Sepra SBD and Sepra ZT, respectively). This indicates that, irrespective of the sorbent used, the contaminants were uptaken by the sorbent during the 13-day exposure following similar sorption dynamics. In general, uptake capacity followed the order PoraPak Rxn RP > Sepra SDB > Sepra ZT for most compounds. A higher *k* means a higher *De* and *Rs*, which means a better performance since the accumulation of contaminants in the CPS will be higher, which is of special attention in the case of polar compounds whose determination is challenging. The *De* was $>1 \times 10^{-6}$ cm$^2$/s for 12 pharmaceuticals using PoraPak Rxn RP (Table 2). For those compounds, sampling rates between 11.1 and 17.6 mL/day were obtained, which indicates high CPS efficiency when deployed in the field.

As discussed in Section 3.2 (Fig. 2), compounds such as metformin, nicotine, EDDP and morphine provided low recoveries in SPE, yet could be retained with the three sorbents during CPS calibration. These compounds are highly polar and consistently produced a low *De* and low *Rs*, both of which affect the sensitivity of the CPS method.

Although PoraPak Rxn RP was the sorbent that performed best with the highest uptake capacity, Sepra ZT was selected because it provided the highest recoveries and should therefore be initially considered as the one to provide higher enrichment factors. Moreover, it is interesting to test these polar sorbents in passive samplers since it is a field where they are less explored. Sepra ZT in combination with agarose has been applied in diffusive gradients in thin films (DGT) as passive samplers for monitoring pharmaceuticals (Stroski et al., 2018). However, as in that study the amount of sorbent was larger (0.35 g compared to 0.2 g in the present study) and the sampler configuration was different from the CPS, the calibration parameters obtained are not comparable. For instance, the *Rs* for atenolol was 7.4 mL/day whereas in the present study it was 4.6 mL/day. On the other hand, the *Rs* for sulfamethoxazole was 8.4 mL/day, which is lower than in the present study (10.2 mL/day) (Stroski et al., 2018). Certain illicit drugs (including benzoylecgonine and cotinine) were also monitored using Sepra ZT in a polyethylene-based passive sampler (Pinasseau et al., 2020). Here again, however, because the amount of sorbent was larger (0.4 g) and the sampler configuration and dimensions were different from CPS, the calibration parameters cannot be compared, though *Rs* for benzoylecgonine and cotinine (analytes studied in both studies) were similar (Pinasseau et al., 2020). When CPSs were used with Sepra ZT to monitor cytostatic drugs, results in terms of calibration performance and field application were suitable (Franquet-Griell et al., 2017).

**Table 1**
Calibration constant (*k*, ng/h), diffusion coefficient (*De*, $10^{-6}$ cm$^2$/s) and sampling rate (*Rs*, mL/day) values obtained for each analyte with the three sorbents evaluated during the calibration.

| Compounds | PoraPak Rxn RP | | | Sepra SBD-L | | | Sepra ZT | | |
|---|---|---|---|---|---|---|---|---|---|
| | *k* | *De* | *Rs* | *k* | *De* | *Rs* | *k* | *De* | *Rs* |
| 4-Acetamidoantipyrine | 12.3 | 1.3 | 13.5 | 8.2 | 0.8 | 9.0 | 4.5 | 0.5 | 5.0 |
| Acetaminophen | 1.3 | 0.1 | 1.3 | 1.0 | 0.1 | 1.0 | 3.9 | 0.4 | 3.8 |
| Atenolol | 11.1 | 1.2 | 12.7 | 4.6 | 0.5 | 5.2 | 4.0 | 0.4 | 4.6 |
| Benzoylecgonine | 20.3 | 1.3 | 13.8 | 13.0 | 0.8 | 8.9 | 8.4 | 0.5 | 5.7 |
| Bezafibrate | 10.8 | 1.2 | 12.2 | 7.5 | 0.8 | 8.4 | 5.9 | 0.6 | 6.7 |
| Caffeine | 12.8 | 1.3 | 13.3 | 7.9 | 0.8 | 8.2 | 5.8 | 0.6 | 6.0 |
| Carbamazepine | 12.0 | 1.4 | 15.0 | 4.3 | 0.5 | 5.3 | 2.7 | 0.3 | 3.3 |
| Cocaine | 0.6 | 0.1 | 1.2 | 0.9 | 0.2 | 1. 7 | 0.2 | 0.03 | 0.4 |
| Codeine | 11.1 | 1.1 | 11.3 | 6.8 | 0.6 | 6.9 | 3.3 | 0.3 | 3.4 |
| Cotinine | 12.6 | 1.2 | 12.4 | 4.5 | 0.4 | 4.4 | 4.3 | 0.4 | 5.2 |
| Diclofenac | 14.5 | 1.2 | 13.1 | 9.6 | 0.8 | 8.6 | 8.9 | 0.8 | 8.0 |
| EDDP | 0.9 | 0.1 | 1.1 | 0.7 | 0.1 | 0.9 | 0.5 | 0.06 | 0. 7 |
| Iopromide | 10.1 | 0.9 | 9.8 | 6.6 | 0.6 | 6.5 | 3.7 | 0.3 | 3.6 |
| Levetiracetam | 6.9 | 0.7 | 7.4 | 3.7 | 0.4 | 4.0 | 4.1 | 0.4 | 4.4 |
| Losartan | 10.8 | 1.1 | 11.3 | 7.3 | 0.7 | 7.6 | 5.8 | 0.6 | 6.1 |
| Metformin | 2.9 | 0.3 | 3.3 | 0.5 | 0.1 | 0.5 | 0.8 | 0.1 | 0.9 |
| Methadone | 2.6 | 0.4 | 3.9 | 1.4 | 0.2 | 2.2 | 1.4 | 0.2 | 2.1 |
| Morphine | 9.0 | 1.1 | 11.1 | 5.0 | 0.6 | 6.2 | 1.8 | 0.2 | 2.2 |
| Oxazepam | 5.9 | 0.7 | 7.9 | 2.8 | 0.4 | 3.8 | 2.8 | 0.4 | 3.8 |
| Sulfamethoxazole | 4.6 | 1.7 | 17.6 | 1.2 | 0.4 | 4.6 | 2.7 | 1.0 | 10.2 |
| Tramadol | 8.5 | 0.8 | 8.1 | 4.6 | 0.4 | 4.4 | 3.0 | 0.3 | 2.8 |
| Valsartan | 9.0 | 0.9 | 9.1 | 3.6 | 0.3 | 3.6 | 6.7 | 0.6 | 6.8 |

**Table 2**
Mean concentration (ng/L) with the standard deviation in parenthesis of pharmaceuticals and drugs of abuse detected in Llobregat River and drinking water using the CPS (n = 5) approach.

| Compounds | Llobregat River (n = 5) | Drinking water (n = 5) |
|---|---|---|
| 4-Acetamidoantipyrine | 99 (18) | nd |
| Acetaminophen | nd | nd |
| Atenolol | nd | nd |
| Benzoylecgonine | <LOQs | <LOQs |
| Bezafibrate | <LOQs | nd |
| Caffeine | 43 (10) | 26 (10) |
| Carbamazepine | 0.13 (0.05) | 0.1 (0.05) |
| Cocaine | nd | nd |
| Codeine | <LOQs | <LOQs |
| Cotinine | 175 (65) | 232 (101) |
| Diazepam | Retained | Retained |
| Diclofenac | 0.29 (0.02) | 0.17 (0.1) |
| EDDP | <LOQs | nd |
| Iopromide | nd | nd |
| Ketamine | Retained | Retained |
| Levetiracetam | nd | nd |
| Losartan | <LOQs | nd |
| Metformin | <LOQs | nd |
| Methadone | 0.54 (0.2) | 0.34 (0.2) |
| Morphine | nd | nd |
| Nicotine | Retained | Retained |
| Oxazepam | 0.11 (0.1) | 0.07 (0.03) |
| Sulfamethoxazole | <LOQs | nd |
| Tramadol | 223 (66) | 164 (83) |
| Trazodone | Retained | Retained |
| Valsartan | 0.09 (0.02) | nd |
| Venlafaxine | Retained | Retained |

nd: non-detected.
Retained: retained in the CPSs but not quantified due to the non-linear uptake during calibration.

### 3.4. Field application

The CPS with Sepra ZT were then applied to monitor the presence of 22 pharmaceuticals and drugs of abuse in river and drinking water. Table 2 shows the mean concentrations ($n$ = 5) of the 5 CPSs deployed in each type of sample. The concentrations were calculated from Eq. (3), in which the absolute mass of contaminants (in ng) is divided by the *Rs* obtained with the Sepra ZT CPS and by deployment time.

Nine of the 22 calibrated contaminants were quantified in river waters. The concentrations detected in river ranged from 0.09 to 223 ng/L for valsartan and tramadol, respectively. However, other compounds, including benzoylecgonine, bezafibrate, codeine, EDDP, losartan, metformin and sulfamethoxazole were detected at concentrations below their LOQs and could not be quantified. Compounds never detected were acetaminophen, atenolol, cocaine, iopromide, levetiracetam and morphine. In the case of drinking water, seven compounds were determined with concentrations between 0.07 and 232 ng/L for oxazepam and cotinine, respectively; and, two compounds (benzoylecgonine and codeine) were detected at concentrations below their LOQs. The compounds and concentrations detected are within the expected ranges according to data from the DWTP (Boleda et al., 2014).

Diazepam, ketamine, nicotine, trazadone and venlafaxine were all detected in river and drinking waters but could not be quantified as they did not show a linear uptake during CPS calibration. It should be mentioned that diazepam was qualitatively detected despite being an unstable compound. This indicates the capacity of CPS to identify contaminants present in river and drinking waters.

Fig. 4 shows a chromatogram of the detected pharmaceuticals and drugs of abuse in one CPS extract from Llobregat River. It shows the excellent chromatographic resolution of the identified compounds, which suggests that the extracts were not subject to interferences. This is because the CPS ceramic wall enables the proper diffusion of compounds and

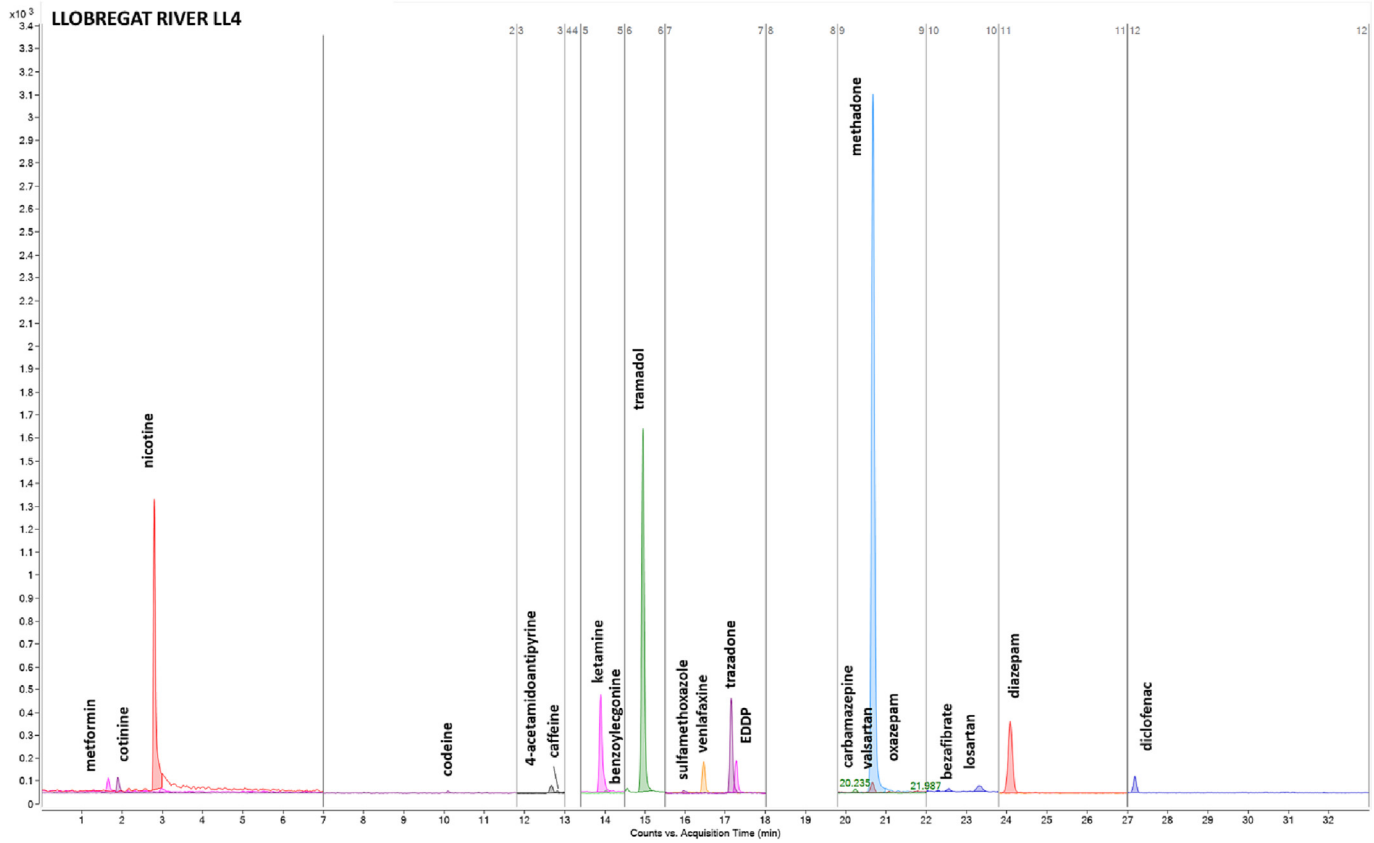


**Fig. 4.** Chromatogram obtained after analysing by LC-MS/MS one extract from the CPSs deployed in Llobregat River.

because the sorbent is retentive for polar and moderately polar contaminants. This chromatogram also shows the good sensitivity of the method.

## 4. Conclusions

In this study we have demonstrated that CPS is a suitable alternative for monitoring contaminants in water samples since it has no clogging problems, allows for high analytical sensitivity, and greatly increases the number of pollutants identified.

We have also found that preliminary studies on the stability and retention of the compounds are needed before the samplers are calibrated in order to obtain valuable information about their behaviour during CPS deployment.

In general, the three tested sorbents performed similarly in terms of retention and analyte uptake in the passive samplers. However, we selected Sepra ZT (polar properties) since it is the one most used in analytical methods for monitoring polar contaminants.

In summary, we suggest that CPS should be used to monitor water in a simple and sustainable approach allowing the time-integrated sampling, which increases representativeness and reduces cost per sample.

## CRediT authorship contribution statement

**Núria Fontanals:** Methodology, Validation, Investigation, Writing – original draft. **Maria Rosa Boleda:** Resources, Writing – review & editing. **Francesc Borrull:** Resources, Writing – review & editing, Funding acquisition. **Rosa Maria Marcé:** Methodology, Conceptualization, Writing – review & editing, Funding acquisition. **Sílvia Lacorte:** Methodology, Conceptualization, Writing – review & editing, Funding acquisition.

## Data availability

Data will be made available on request.

## 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.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2023.164267.

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