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Combining o-DGT passive sampling with UHPLC-Q-ToF MS for the analysis of 12 tracer micropollutants in the context of the European urban wastewater directive (PE-CONS 85/1/24)

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ABSTRACT

This study presents an integrated and innovative approach for monitoring the 12 tracer organic micropollutants introduced in the new Urban Wastewater Directive (PE-CONS 85/1/24) of the European Council. The proposed method combines the Diffusive Gradients in Thin Films (o-DGT) passive sampling with ultra-high-performance liquid chromatography coupled to high-resolution time-of-flight mass spectrometry (UHPLC-Q-ToF MS). The analytical procedure was validated in terms of linearity, accuracy, and limits of quantification (LOQs), which ranged from 0.05 to 0.5 μg L^{-1} for all compounds, except for hydrochlorothiazide (2 μg L^{-1}). Matrix interferences in o-DGT extracts (comprising agarose diffusive gel, HLB binding phase, and cellulose acetate membrane) exposed in treated wastewater were effectively removed after evaporation and ten-fold dilution, ensuring reliable quantification of target compounds. Following laboratory calibration, with the determination of five new diffusion coefficients, o-DGT devices were deployed at three sites along a river, including the urban wastewater treatment plant (WWTP) discharge channel. The combination of passive sampling and the developed analytical method enabled the detection of all 12 target compounds in WWTP treated waters and revealed an increased micropollutant concentrations in downstream site. Beyond confirming the method robustness and field applicability, o-DGT proved to be more sensitive and reliable than commonly used grab sampling, which failed to quantify certain compounds at low concentration in water. Moreover, o-DGT allowed the estimation of time-weighted average (TWA) concentrations and fluxes, representing a powerful tool for future monitoring of the efficiency of WWTP to remove micropollutant from water.

1. Introduction

Anthropogenic activities such as urban development, manufacturing, agriculture, and healthcare practices contribute significantly to the generation of micro-pollutants, leading to the contamination of aquatic environments [1]. Among these contaminants, pharmaceutical compounds (PCs) have raised global concern due to their potential impacts on water quality and ecosystem health [2], particularly in wastewater and natural water bodies [3]. These compounds primarily enter aquatic systems through effluents from wastewater treatment plants (WWTPs), which are often unable to completely remove them.

In response to these challenges, the European Council adopted a new Urban Wastewater Directive (PE-CONS 85/1/24), updating the previous Directive 91/271/EEC, as part of the EU Zero Pollution Action Plan. This revised framework emphasizes the importance of evaluating WWTP efficiency in removing micropollutants and identifies twelve key substances for monitoring [4].

However, analyzing these compounds remains challenging due to their typically low concentrations in environmental samples [5] and the complex nature of the matrices in which they occur, often containing salts, organic matter, and biological components. Advances in analytical chemistry, particularly in trace-level detection, have enabled the identification of diverse contaminants. High-resolution mass spectrometry (HRMS), when coupled with chromatographic techniques such as liquid chromatography (LC), has become indispensable for the sensitive and versatile analysis of micropollutants [6].

Nonetheless, the reliability of these analytical methods depends critically on appropriate sample collection. Conventional grab sampling

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often fails to provide sufficient sensitivity, as contaminants are frequently present near detection limits, requiring the extraction of large water volumes [7]. Moreover, grab sampling provides only a snapshot of contaminant concentrations at a single point in time, lacking temporal representativeness [8]. Automatic samplers can alleviate some of these limitations but still require specific deployment conditions, electrical power, and proper sample preservation. In this context, passive sampling has emerged as a robust alternative, offering more comprehensive and time-integrated assessments.

The Polar Organic Chemical Integrative Sampler (POCIS), introduced in the early 2000s [9], is the most widely employed device for sampling organic compounds, particularly those with semi-polar characteristics. However, POCIS is often considered semi-quantitative, as its accuracy depends on compound-specific corrections and can vary under different environmental conditions [10]. The Diffusive Gradients in Thin Films (DGT) passive sampler, originally developed for inorganic species, has since 2012 been increasingly applied to monitor a wide range of organic contaminants [11], including pesticides [12], endocrine-disrupting chemicals [8], and various pharmaceuticals [13] such as antibiotics [14], β-blockers [15], and psychiatric drugs [16]. This adaptation, referred to as o-DGT [17], consists of a diffusive layer positioned between the water and an adsorptive layer. Organic contaminants diffuse through the diffusive layer and are irreversibly captured by a binding material in the inner layer under deployment conditions [18]. According to Guibal et al. (2019) [19], the hydrophilic–lipophilic balanced (HLB) binding phase is commonly used for organic micropollutants due to its strong affinity for a wide range of environmental organic compounds.

A comprehensive understanding of the uptake mechanisms and performance characteristics of passive samplers, combined with proper calibration, enables the determination of sampling rates (Rs, for POCIS) and diffusion coefficients (D, for o-DGT) for target compounds [20]. Compared to POCIS, o-DGT is less affected by changes in water flow due to variations in the water boundary layer at the sampler surface and allows for straightforward temperature corrections [21]. Furthermore, the diffusive layer of o-DGT substantially reduces matrix interferences [20], making it a robust and reliable tool for deployment in complex field environments.

Thus, the aims of this work were (i) to develop and validate UHPLC-QToF-MS methodologies in both positive and negative ionization modes for a simultaneous quantitative analysis of the 12 target compounds highlighted by European Directive as micropollutants tracers in wastewater systems, (ii) to adapt a sampling method and establish a reliable laboratory calibration strategy for the o-DGT passive sampler with respect to these target compound, and (iii) to conduct an in situ field deployment at river upstream and downstream locations, as well as in a WWTP discharge channel, for the target analysis of the twelve micropollutants of concern and for the validation and discussion of the overall innovative monitoring approach developed in items (i) and (ii).

2. Materials and methods

2.1. Reagents and materials

All diluted solutions in this work were prepared using ultrapure water (UPW) with a resistivity of 18 MΩcm, which was obtained from a water purificator (Franceeau). For the preparation of the stock solutions and mobile phases or elution procedures, LC-MS grade acetonitrile (ACN), methanol (MeOH), ethyl acetate (EtAc) (Carlo Erba, Val Germany), formic acid (FA) and ammonium formate (Sigma-Aldrich, Germany) were utilized. Internal standards, benzotriazole-d4, candesartan-d5, carbamazepine-d10, diclofenac-d4, hydrochlorothiazide-d2 and metoprolol-d7 were purchased from TechLab (Metz, France). For binding and diffusive gel preparation, Oasis® HLB sorbent was purchased from Waters and agarose powder was purchased from Sigma-Aldrich. Passive sampler acetate cellulose (AC) and nitrate cellulose (NC) protective membranes were purchased from Whatman and Polyesther Sulfone (PES) membrane was purchased from Pall.

2.2. Standard solutions preparation

Each compound (listed in table S1, *Supporting Information*) stock solution at 100 mg L^{-1} concentration was individually prepared by weighing and dissolving in MeOH, and stored in amber glass bottles at −18 °C. For each experiment, a freshly prepared diluted solution was prepared.

For the individual analysis of each compound, a dilution to 100 μg L^{-1} concentration in UPW was performed in clear glass vials ready for analysis, while for Q-ToF-MS analysis parameter optimization, a mix solution containing 1 mg L^{-1} of each compound was prepared in MeOH and stored in amber glass vials prior to dilution for analysis.

A mixture containing 1 mg L^{-1} of each of the six deuterated compounds used as internal standards was also prepared in MeOH and stored at −18 °C in amber glass vial. For method development and validation experiments, the internal standards were added to the analytes immediately before sample analysis.

2.3. UHPLC-Q-ToF MS method

LC separation was performed using a UHPLC Acquity H class from Waters™ coupled to a Xevo G3 Quadrupole Time-of-Flight high resolution mass spectrometer from Waters™. A chromatographic column ZORBAX Eclipse Plus C18 Rapid Resolution HD (2.1 × 150 mm, 1.8 μm) from Agilent was used.

The mobile phases were A, H_2O with 0.1 % ammonium formate, and B, ACN with 0.1 % formic acid. The flow rate used in all UHPLC-Q-ToF MS experiments was 0.4 mL min^{-1}, with the chromatographic column temperature set at 40 °C and the chromatography gradient was optimised as explained in table S2. Briefly, in ESI positive mode: 0–0.5 min, 20 % B; 0.5–4 min, 20 to 30 % B; 4–11 min, 30 to 95 % B; 11–13 min, 95 % B; 13–13.5 min, 95 to 20 % B; 13.5–15 min, 20 % B (column equilibration). For ESI negative mode: 0–0.5 min, 20 % B; 0.5–7 min, 20 to 95 % B; 7–8.5 min, 95 % B; 8.5–9 min, 95 to 20 % B; 9–10 min, 20 % B (column equilibration).

Each compound was individually injected at 100 μg L^{-1} concentration in the approach of determining their retention time (t_R) in both positive and negative ionization modes analysis, obtaining the Total Ion Chromatogram (TIC) and Extracted Ion Chromatogram (XIC) for each compound (figures S1 and S2, respectively).

In the interest of obtaining the highest signals for the targeted compounds, electrospray ionization source (ESI) parameters as, desolvation temperature, desolvation gas flow, capillary voltage and sample cone voltage were optimized for both positive and negative ESI ionization modes. The selected system parameters are listed in table S3 for both ESI+ and ESI- analysis.

Regarding the data acquisition by Xevo G3 Q-ToF, data independent analysis (DIA) by the Waters MS^E analysis mode was employed (also known as all ion mode) which allows to record both MS and MS^2 data in a settled range. Stablished general scan range was *m/z* 50–1200, recording MS (low collision energy) and MS^2 (high collision energy ramp) data at 6 V and 10–30 V, respectively.

To guarantee optimal analytical performance, Q-ToF calibration was performed before parameter optimization and field sample analysis. For long analytical sequences, UPW blanks together with two level QC were injected every 10 samples as QA/QC for any deviation control.

2.3.1. Validation of the UHPLC-Q-ToF analytical method

In order to ensure a quality control of the performed analysis, the analytical method was previously validated in accordance with the French national standards (NF T90–210,2018) [22].

In this context, method linearity and accuracy were studied by the preparation and analysis of the solutions by 5 different operators in

different days. While limit of quantification and interferences were studied by a single operator in a repeatability condition.

Linearity –

To evaluate the developed method linearity, a five-level calibration curve was established, with five replicates at each level conducted by five different operators on separate days as stablished by the aforementioned French national standards. These five-point calibration curve ranged between 0.1 to 100 μg L^{-1} solutions were prepared in UPW with the mixture of target compounds and with the addition of selected internal standards.

***Instrumental LOQ* & LOD –**

For the instrumental LOQ determination, 5 replicates of estimated LOQ level for each of the 12 compounds were prepared and twice injected by LC-Q-ToF for analysis, resulting in a total of 10 satisfactory injections.

The LOQ for each compound was then validated by confirming compliance with equation (Eq. 1).

$$LOQ_P - 0.6LOQ_P \langle LOQ_a - 2\sigma \;\&\; LOQ_P + 0.6LOQ_P \rangle LOQ_a + 2\sigma \quad (1)$$

where LOQ_p is the estimated LOQ_i (μg L^{-1}), LOQ_a is the average concentration found (μg L^{-1}) and σ is the standard deviation ($n = 10$).

Accuracy –

The accuracy of the method validation was assessed by injecting a minimum of five series, each with two replicates at a selected concentration (10 μg L^{-1}). To ensure robustness, five different users prepared these replicates alongside the calibration curve on separate days for accuracy evaluation. As with LOQ validation, the accuracy of the method was considered validated when compliance with (Eq. 2) was achieved:

$$[C]_r - x[C]_r \langle [C]_a - 2\sigma \;\&\; [C]_r + x[C]_r \rangle [C]_a + 2\sigma \quad (2)$$

where, $[C]_r$ is the reference concentration (10 μg L^{-1}), χ is the acceptable percentage (25, 30, 35, 40 or 50 %), $[C]_a$ is the average concentration found (μg L^{-1}) and σ is the standard deviation ($n = 10$).

Interferences –

Several approaches have been proposed to mitigate or eliminate matrix effects, including calibration by standard addition, signal correction using internal standards, and sample dilution following extraction [23–25]. In this study, the extent of potential matrix effects was systematically analyzed to ensure the proper validation of the analytical method and the generation of reliable results. To achieve this, a "loaded" matrix was selected to assess its impact on the analytes of interest. Specifically, WWTP samples were chosen for this purpose, and calibration was performed using the standard addition method, incorporating different procedures to evaluate the magnitude of the matrix effect.

The binding gel of the o-DGT device, which had been deployed in the WWTP, was extracted and eluted following the protocol described in the Materials and Methods section. Prior to standard addition and subsequent analysis by LC-MS, three distinct processing techniques were examined, as previously outlined: (i) direct dilution of the matrix by a factor of 10 (d10), (ii) preconcentration of the matrix by nitrogen evaporation with previously added internal standards (Evap), and (iii) a combination of preconcentration by nitrogen evaporation and subsequent dilution by a factor of 10 (Evap + d10). In all cases internal standards were present in analysis solution.

2.4. Preparation of HLB-DGT passive sampler

In this approach, a 3.14 cm^2 o-DGT passive sampler was employed. Corresponding diffusive (agarose) and binding gel (HLB-agarose) were prepared according to Challis et al. 2016 with 1.5 % agarose content (m/v). In the case of the binding gel, during the preparation, a 7 % of the Oasis® HLB solid phase powder was added to the agarose containing solution. The HLB phase displays two types of binding sites that induce a high capacity to bind strong organic compounds with different chemical properties such as the 12 tracers selected by the new European Directive.

The agarose-based diffusive gel was carefully prepared to ensure compositional homogeneity, whereas the HLB-containing binding gel, due to its more complex nature, required an even more meticulous preparation to achieve a uniform surface. To this end, the gel was left to solidify on a flat surface, ensuring that the HLB interface remained as consistent as possible. After cooling, both the diffusive gel and the binding gel were carefully inspected visually with a light beam and verified the obtention of a homogeneous gel. In addition, to verify uniformity, the thickness of randomly chosen gels from the same batch was measured to ensure it met the desired specifications. The thickness of the agarose diffusive gel was 0.75 mm (± 0.01 mm, $n = 3$), while for the HLB-agarose binding gel was 0.50 mm (± 0.01 mm, $n = 3$). Both diffusive and binding gels were stored in 10^{-2} M $NaNO_3$ solution at 4 °C before their use. Prior to their use in the o-DGT passive sampler, the gels were re-examined visually to ensure that no damaged or defective ones were used.

The passive sampler was completed by enclosing the binding and diffusive gels, followed by a protective AC membrane (0.2 μm pore size), which was chosen after the test of 3 different types of membrane (*see* Section 3.4. *Uptake and desorption from o-DGT materials*), in the o-DGT plastic holder purchased at DGT Research LTD.

2.5. Calculation of capacity, elution and adsorption of o-DGT

To complete the calibration of o-DGT towards the 12 target compounds, a series of experiments were carried out in laboratory conditions prior to field deployment (figure S3).

2.5.1. Binding gel capacity

The capacity of the binding gel was investigated to determine the maximum amount or concentration of each compound that the gel was capable of absorbing when exposed to a natural medium. To this end, a 10^{-2} M $NaNO_3$ solution was prepared, containing 1 mg L^{-1} of each compound. The binding gel ($n = 5$) was immersed in 20 mL vials containing this solution with the aim of achieving saturation. The solution was analyzed immediately after the gel immersion (designated as $t = 0$), and again after 4 h of exposure ($t = 4$ h). The difference between these two analyses allowed the determination of the binding gel absorption capacity. Furthermore, a control sample without the binding gel was analyzed to evaluate any potential degradation or sorption on vial of the compounds over the experimental period. Throughout the experiment, the vials were kept in continuous motion using an orbital shaker (140 rpm) and maintained at a constant temperature of 20 ± 1 °C, occasionally checked with a thermometer in the climatized room.

2.5.2. Elution from binding gel

An elution procedure has been developed and tested following previous work [26]. The elution of the compounds from the binding gel was performed by immersing the gel ($n = 5$), which was pre-loaded with the 12 compounds (*as explained in the previous section,* i.e.*, Binding Gel Capacity*), in 3 mL of MeOH LC-MS grade, and then placed in a sonication bath (210 W) for 2 min ($n = 3$). Before injection, the solutions were filtered using a 0.20 μm polytetrafluoroethylene (PTFE) filter and subsequently diluted with ultrapure water.

The recovery rate of the compounds was determined by comparing the elution value with the amount absorbed by the binding gel.

This elution procedure was used for o-DGTs deployed in the field (*river and treated wastewater – see part 2.9*).

2.5.3. Investigation of compound adsorption to o-DGT materials

In this experiment, the adsorption of the target compounds onto the various materials comprising the o-DGT device was investigated. However, other components of the device were evaluated in this study to assess potential adsorption, which could lead to inaccurate

quantification of the compounds if not considered.

To this end, the diffusive gel, the plastic assembly (holder), and the protective membrane covering the gels, were examined. For the protective membrane, three types of membranes were tested to identify the one with the least adsorption issues for use in the o-DGT device. The membranes investigated were acetate cellulose, nitrate cellulose, and polyethersulfone membranes.

Each of the materials mentioned was immersed in 20 mL vials ($n = 6$) containing a solution of 20 μg L^{-1} of each of the 12 compounds in 10^{-2} M $NaNO_3$. As in the binding gel capacity study, an aliquot was taken immediately after immersion (t0) and after 4 h (t4) in the aim of calculating the concentration ratio. The vials were continuously agitated, maintaining a constant temperature of 20 °C ± 1 °C. Simultaneously, three replicates of blank samples for each material were prepared and analyzed at t0 h and t4 h.

2.6. Diffusion coefficient

The diffusion coefficients of the 12 target compounds were investigated using the previously described agarose diffusion gel. A diffusion cell, as previously detailed by Guibal et al. (2017) [27], was employed to monitor the transfer of these compounds between two compartments separated by the diffusion gel. The donor cell, designated as the source, contained the compounds at a concentration of 1 mg L^{-1} in a $NaNO_3$ solution (10^{-2} M), while the receptor cell contained only the $NaNO_3$ solution (10^{-2} M). Over a 4 h period, the concentration of the compounds concentration in the receptor cell were analyzed every 30 min, allowing the generation of diffusion curves characterizing the transfer of the compounds from one cell to the other.

This experiment was carried out at 20 ± 0.5 °C and at a pH = 5.9 ± 0.2 conditions.

Finally, diffusion coefficient was estimated using (Eq. 3):

$$D = \frac{\mathrm{qm} * \Delta g}{\mathrm{Cs} * \mathrm{A}} \tag{3}$$

Where, D is diffusion coefficient, q_m is the compound transfer between two compartments, Δ_g is the diffusive gel thickness (0.75 mm), C_s is the compound concentration in source compartment (1 mg L^{-1} each compound), and A is the diffusion area.

Diffusive coefficient values were determined at 20 °C, while when needed, the Stokes–Einstein (Eq. 4) was employed to correct D values to a different temperature.

$$\frac{D_1 * \eta_1}{T_1} = \frac{D_2 * \eta_2}{T_2} \tag{4}$$

Where, η is the water viscosity (taken from NIST chemistry Web Book [28] and T is the temperature (°K).

2.7. Concentration calculation in o-DGT

To quantify the concentration of the target compounds in the solution using the DGT technique, an estimation was performed based on the mass accumulated in the receiving gel of our device. For this purpose, previously described by Davison and Zhang (1994) [18] (Eq. 5) was applied. This equation enables the determination of the time-weighted average concentration of the sample, which in our study corresponds to the water sample concentration (C_w):

$$C_w = \frac{m * \Delta_g}{t * D * A} \tag{5}$$

Where, m is the accumulated mass on the binding gel (calculated from analyte elute concentration and considering the elution yield), Δg is the thickness of diffusive layer (combining the diffusive gel and the acetate cellulose protective membrane), t is the duration of exposure, D is the diffusion coefficient (previously calculated for a given experimental value), and A is the exposure area.

2.8. Field deployment for grab and passive sampling

o-DGT passive samplers were exposed for 10 days in a river in southwest France. As general characteristics, this river presented a pH slightly above 7 and a relatively high flow rate of around 180,000 m^3 h^{-1}. For more information of the physico-chemical properties of the river, table S4 presents the parameters measured both at the time of passive sampler deployment (Initial) and upon their retrieval (End). Parameters such as water flow, grab samples, and those collected for suspended matter analysis were obtained facing against the river current at a height of 5 cm above the riverbed.

Two sampling points separated of 600 m distance were selected along this river an upstream (Up) ($n = 3$) and downstream (Dw) ($n = 3$) points of urban WWTP close to 300 000 equivalent inhabitants which employs activated sludges technology with a biological treatment of nitrogen and injection of $FeCl_3$ to remove phosphorus (further information regarding the water-treatment employed in the WWTP is explained in *supporting information*). Another sampling point was located in the WWTP, specifically in the treated wastewater discharge channel to the river (average flow rate per year 1800 m^3 h^{-1}).

Due to the potential saturation of the samplers at the WWTP, two time series were monitored at this point. A first deployment of 6 days with 4 o-DGT, and a second deployment of 4 days with 3 o-DGT. During the 10 days experiment, temperature was constantly monitored by Tinytag device (providing a temperature value every hour) in each sampling point, attached together with the passive samplers to a substantial weight (concrete block) to ensure the stability of the devices at a height of approximately 5 cm above the riverbed, where the physico-chemical measurements at the sampling points were also performed.

Moreover, an o-DGT blank was also prepared in the laboratory and exposed in the sampling point environment to check for any contamination during o-DGT preparation, transport and field deployment time. However, none of targeted compounds were detected in o-DGT blanks.

Water grab samples were also collected from the three sampling points using 0.5 L and 1 L bottles, designated for the analysis of target compounds and the determination suspended matter (SM), respectively. These samples were collected at the beginning (Grb_1) and at the end (Grb_2) of the o-DGT passive sampler exposure at upstream and downstream sites; while in the WWTP they were collected not only at the beginning and at the end, but also when the second o-DGT deployment (for 4 days) was performed (Grb_Bis_WWTP). Sampling at all points was conducted at the same time to minimize any potential external variability in the samples. Given that wastewater was sampled, collecting samples at different times could have resulted in variable concentrations, potentially affecting the reliability and comparability of the data.

Water samples and o-DGT passive samplers were transported from the field to the laboratory in a cool box and subsequently stored if needed at 4 °C until extraction.

2.9. Grab and passive sample extraction for analysis

On one hand, grab samples utilized in this study were processed using solid-phase extraction (SPE) with Chromabond® HR-X cartridges (60 mg, 3 mL, 85 μm) purchased from Macherey-Nagel. The SPE protocol included the filtration of 100 mL water samples through 0.7 μm GF/F filters (Whatman) to remove particulates. The pH of the filtered solutions was then adjusted to 7.0 ± 0.2 using 1 M HCl or NaOH, depending on the initial sample conditions. Previously described by Guibal et al. (2015) [29], cartridges were conditioned sequentially with 5 mL of MeOH followed by 5 mL of UPW prior to passing sample through it. Cartridges were dried under nitrogen stream and stored at 4 °C if needed. Finally, elution of analytes from SPE cartridge was performed with 3 mL of MeOH, followed by 3 mL of a 75:25 (v/v) MeOH:EtAc mixture.

On the other hand, after 10 days exposure (where as expected no biofouling was observed), the o-DGT devices were dismantled and the

binding gels were recovered for elution. As previously described (Section 2.5.2. *Elution from binding gel*) the elution of the compounds from the binding gel was performed by immersing the gel in 3 mL of MeOH and then placed in a sonication bath (210 W) for 2 min. This process was repeated three times, resulting in a total volume of 9 mL from the successive elution. Obtained solutions were then filtered using a 0.20 μm PTFE filter.

Post-elution, 10 μL of the internal standards solution was introduced into the collected extracts (grab and passive sample). These extracts were subsequently evaporated to dryness under a nitrogen stream and reconstituted in 1 mL of 80:20 (v/v) UPW:MeOH solution. To obtain the actual concentrations of the studied compounds in the analysed samples, the recoveries of both the DGT extract evaporation and the grab sample SPE preconcentration processes were evaluated using target compound standards, and the results are summarized in table S5.

Sample analyses were then conducted by UHPLC-Q-ToF MS.

2.10. Data treatment

All acquired data was treated by UNIFI posttreatment software from Waters connect. Target analysis of the 12 compounds was carried out using a mass tolerance of 10 ppm. For the statistical analysis of obtained results, such as t-student or p-value calculations in the Uptake and desorption from o-DGT materials (Section 3.4), ANOVA from Excel spreadsheet (Microsoft Office) was used. Daily rainfall data were obtained from Meteo France database, while WWTP and river water flow was acquired from Hydroportail by Eaufrance.

3. Results and discussion

3.1. Validation of the analytical method

Linearity –

Quantification was performed using the area of the parent ion peaks ([M + H]) and normalized to the signal of the selected deuterated internal standard within a solvent matrix (table S6). Six of the twelve target compounds had a corresponding deuterated compound used as an internal standard. As shown in Table S6, for the remaining compounds, the most appropriate internal standard among the six available was selected based on chemical family or retention time similarity. The linear calibration range extended from 0.1 μg L^{-1} to 100 μg L^{-1}, with an intercept of zero. The calibration curves demonstrated coefficients of determination (r^2) $\geq$ 0.9735 for all 12 compounds analyzed (Table 1), with RSDs range 4–8 %. These results indicate robust performance, considering also that a consistent linear calibration was achieved across different operators, different analysis days, and each user prepared different stock solutions.

Instrumental LOQ & LOD –

The LOQ_{inst} (Table 1) results ranged from 0.05 to 0.50 μg L^{-1} in ESI+ mode and from 0.05 to 5.00 μg L^{-1} in ESI- mode, with amisulpride exhibiting the highest LOQ (5.00 μg L^{-1}). However, compounds such as amisulpride and candesartan showed responses in both ESI+ and ESI- modes (table S6), with significant differences in LOQ between the two ionization modes: 0.1 and 5.0 μg L^{-1} for amisulpride, and 0.50 and 0.05 μg L^{-1} for candesartan in ESI+ and ESI-, respectively. These values were crucial for selecting the appropriate ionization mode for the analysis of these compounds, with preference given to the ionization mode that yields the lowest LOQ_{inst}.

Furthermore, the instrumental LODs were determined, with values ranging from 0.02 to 0.20 μg L^{-1} in ESI+ mode and from 0.02 to 1.70 μg L^{-1} in ESI- mode.

The LOQ_{inst} values acquired by this analytical method were in a comparable range to those reported in literature in the analysis of pharmaceuticals by LC-Q-ToF MS [30,31].

Accuracy –

To evaluate the accuracy of validated method, also considering the lack of certified reference materials for the target compounds in o-DGT passive sampler extracts, it was determined with standard spiked solutions at 10 μg L^{-1} concentration.

Table 1 shows the percentage results of accuracy at 10 μg L^{-1}. The results illustrate that 9 of the analyzed compounds were validated at 25 %, in accordance with the French AFNOR standard [22] used, while the 3 other compounds (candesartan, clarithromycin and diclofenac) were validated at 30 %, considered the lowest range of admissible percentages. Nevertheless, at this concentration level, vale up to 50 % may still be deemed acceptable. In comparison, R. Guibal et al. (2015) [23] reported acceptance levels between 25 % and 30 % for the highest quantification level (100 μg/L).

Interferences –

The analytical method was ultimately validated by assessing potential interferences or matrix effects, using o-DGT extracts from WTTP discharge channel deployment, that could arise during field application. This evaluation is particularly critical for methods such as LC—HRMS, employed in this study, as the presence of matrix effects can lead to a significant impact in quantitative analysis [24].

The results of these experiments are presented in Fig. 1, with Fig. 1A specifically illustrating as example the different internal calibration curves results of candesartan. This figure compares the outcomes obtained from the three aforementioned processing methods against the theoretical calibration curve, providing insight into the influence of matrix effects on quantification accuracy. Internal calibration curves regarding the analysis of interferences for the rest 11 compounds are represented in figure S4.

Fig. 1B presents the slope results for the twelve compounds analyzed following calibration by standard addition. The slopes for all compounds were close to 1, indicating a minimal or negligible matrix effect, as the calibration curves closely resembled the theoretical model. However, when only a single 10-fold dilution was performed (d10), not all compounds (i.e. citalopram, clarithromycin and venlafaxine) exhibited an intercept equal to zero as result of a possible matrix effect, and therefore,

Table 1
Validation results for the UHPLC–Q-ToF analytical method: calibration equation, relative standard deviation (%RSD), instrumental limit of quantification (μg L-1) and accuracy (%) at 10 μg L-1 concentration level.

Target compounds	Linearity	r^2	RSD (%)	LOQ_{inst} (μg L^{-1})	Accuracy (%)
4 & 5-methylbenzotriazole	$y = 0.0067$	0.9981	4	0.5	25
Amisulpride	$y = 0.2625$	0.9861	8	0.1	25
Benzotriazole	$y = 0.0104$	0.9978	6	0.5	25
Candesartan	$y = 0.0111$	0.9963	5	0.05	30
Carbamazepine	$y = 0.0155$	0.9972	4	0.05	25
Citalopram	$y = 0.0356$	0.9735	6	0.05	25
Clarithromycin	$y = 0.0448$	0.9826	4	0.5	30
Diclofenac	$y = 0.0094$	0.9918	7	0.5	30
Hydrochlorothiazide	$y = 0.0094$	0.9908	5	2.0	25
irbesartan (Avapro)	$y = 0.0754$	0.9850	4	0.1	25
Metoprolol	$y = 0.0115$	0.9925	7	0.1	25
Venlafaxine	$y = 0.2657$	0.9902	7	0.1	25

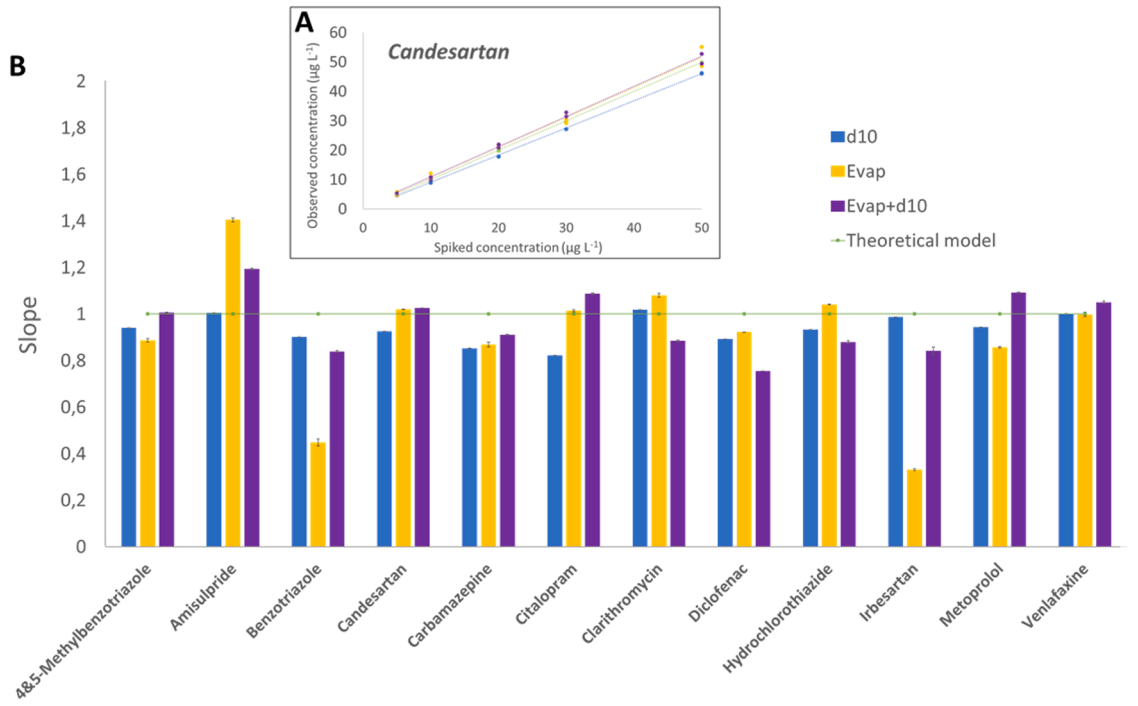

Fig. 1. Representation of studied o-DGT extracts interferences results for the 12 compounds corrected by internal standard. A) Example of candesartan internal calibration curves compared to theoretical curve. B) Interference results for the studied 12 compounds after dilution of extracts and with or without evaporation step compared to theoretical model.

preventing the validation of the method. In the case where the sample underwent preconcentration step without subsequent dilution (Evap), all compounds except for benzotriazole, irbesartan (Avapro) and venlafaxine met the validation criteria, slope equal to 1 and intercept equal to zero. Examination of the signals for these three non-validated compounds revealed that their concentrations in the matrix were inherently high, and consequently, the application of standard addition did not yield reliable concentration determinations due to a possible signal saturation. To address this limitation, a supplementary 10-fold dilution step was incorporated [32] into the previously tested preconcentration process (Evap+d10). Finally, the combination of evaporation followed by a 10-fold dilution enabled the successful validation of all 12 compounds meeting the validation criteria slope equal to 1 and intercept equal to zero.

Quantification of the percentage deviation from the theoretical slope (value = 1) showed that the deviation after the d10 treatment ranged from −17.7 % to +1.9 %. The Evap condition exhibited the greatest variability (−66.9 % to +40.5 %), indicating significant ion suppression or enhancement effects. Finally, the combined Evap + d10 treatment resulted in deviations between −24.6 % and +19.3 %, with an average deviation below 10 %. These results confirm that incorporating a 10-fold dilution after evaporation effectively minimizes matrix effects and was therefore selected as the optimal procedure for subsequent analyses.

3.2. Determination of binding gel capacity

The amount (µg) of each compound retained by the gel was determined (table S7) considering that the solution consisted of 1 mg L^{-1} concentration of each compound (19 ± 2 µg available in solution of each compound).

Results showed a total adsorption of 163 µg of micropollutants by the binding gel in the 4 h duration of the experiment. The fact that the binding gel did not adsorb the full amount available in the solution shows that the observed values are correct and gives an estimate of the capacity of the binding gel to adsorb these micropollutants. While the average of adsorption per compound was of 13.6 µg, with a standard deviation ranging between 0.19 −1.50 µg, benzotriazole and hydrochlorothiazide showed the lowest values, 9.05 ± 0.61 µg and 9.41 ± 0.64 µg, respectively. Analyses of pharmaceuticals using HLB-DGT gels have reported adsorption capacities of up to 9 µg per gel [33], depending on the compound. In studies focused on household and personal care products, capacities ranging from 11 to 97 µg per gel have been observed [34], values considerably higher than those typically encountered in surface waters. During field deployment, the passive sampler is exposed to various contaminants (e.g., pesticides, hormones) present in the study area, which may interact with the HLB binding phase, as well as to organic matter that may be available in the water. Nevertheless, the diffusive gel that is also part of the o-DGT device serves to limit the transport of matter, consequently reducing the risk of saturation of the binding gel.

Considering the gel capacity and the concentrations observed in the field deployment experiments, the results suggest that a longer period of deployment (> 10 days) could be considered as only 1 % of gel capacity was filled (in WWTP sampling point) by the target compounds. However, other compounds in variable concentrations are present in the water and can be captured by o-DGT. For long deployments, it is advisable to verify the saturation capacity at each experimental site, in this context, the o-DGT passive sampler show to be a suitable device for the analysis of these micropollutants.

3.3. Elution from binding gel

In this approach, after previously determining the amount of each compound retained in the gel, it was assessed the recovery percentage after elution of the analytes from the receiving gel using three sequential extractions with MeOH.

As shown in table S7, the elution results indicate a high and consistent recovery of the 12 analyzed compounds, with percentages ranging between 77–94 %. The deviation standard observed remains within acceptable limits (1–6 %), suggesting reproducibility across multiple elutions ($n = 5$). Notably, carbamazepine exhibited the highest elution efficiency, while citalopram showed the lowest recovery among

the tested compounds. These findings confirm the effectiveness of the elution procedure employed in this work.

3.4. Uptake and desorption from o-DGT materials

The concentration ratio results presented in Fig. 2 indicated varying degrees of interaction between the analyzed compounds and the different materials used in the passive sampler. Control samples (Fig. 2A), which represented the spiked solution without any material interaction, generally showed concentration ratios between 0.87 ± 0.01 and 0.99 ± 0.01, indicating minimal degradation or adsorption to the vial material. However, these slight deviations from 1, remaining under 13 %, could also be attributed to analytical variability rather than material interaction only.

On one hand, among the tested membranes (Fig. 2A), membrane AC showed the most consistent performance, with concentration ratios consistently within 0.73 ± 0.09 (diclofenac) and 1.00 ± 0.10 (clarithromycin) for all the target compounds except for carbamazepine and citalopram, this last one showing a concentration ratio of 0.55 ± 0.02. On the other hand, membrane NC and membrane PES demonstrated significantly (table S8, p-value < 0.05) lower concentration ratios, with values ranging from 0.09 ± 0.01 (citalopram) to 0.97 ± 0.04 (candesartan) for NC; and from 0.35 ± 0.03 (4&5-methylbenzotriazole) to 0.95 ± 0.05 (clarithromycin) for PES, implying strong adsorption to these membranes. Such interactions could potentially lead then to an incorrect analytical result. These results suggested that membrane AC exhibits minimum adsorption during the experiment.

Moreover, the selection of membrane AC was supported by its relatively low standard deviations, underscoring its consistent and reproducible performance with a minimal adsorption of the target compounds, preventing excessive losses and making it the most suitable choice for our study.

In addition, as shown in Fig. 2B, the diffusive gel and o-DGT holder showed moderate adsorption, with concertation ratio values ranging from 0.83 ± 0.05 (citalopram) to 0.94 ± 0.04 (irbesartan) and from 0.86 ± 0.01 (citalopram) to 0.97 ± 0.04 (hydrochlorothiazide). These values were slightly lower than the control but without significant retention (p-value > 0.05).

3.5. Diffusion coefficient

Using a cell diffusion method (2.6. Diffusion coefficient), the diffusion coefficients of the 12 target compounds in agarose diffusive gel were determined. For each compound, the temporal evolution of the mass diffused into the receptive compartment was modelled using a linear regression (figure S5). Gel composition (1.5 % agarose (m/v)) and ionic strength (10^{-2} M $NaNO_3$), which can slightly influence D by affecting gel tortuosity and molecular mobility [35], were kept constant across all experiments. pH effects were considered negligible, as the pKa values of the target compounds were different to the experimental pH, maintaining a stable ionization state. Moreover, temperature corrections were theoretically applied using the Stokes-Einstein relationship and NIST water viscosity data, with no empirical adjustment required due to the well-controlled thermal conditions. Shown in Table 2, experimental diffusion values (D_{exp}) obtained values ranged from 2.46 ± 0.03×10^{-6} to 5.81 ± 0.23×10^{-6} cm^2 s^{-1} with relative standard deviations (RSD)

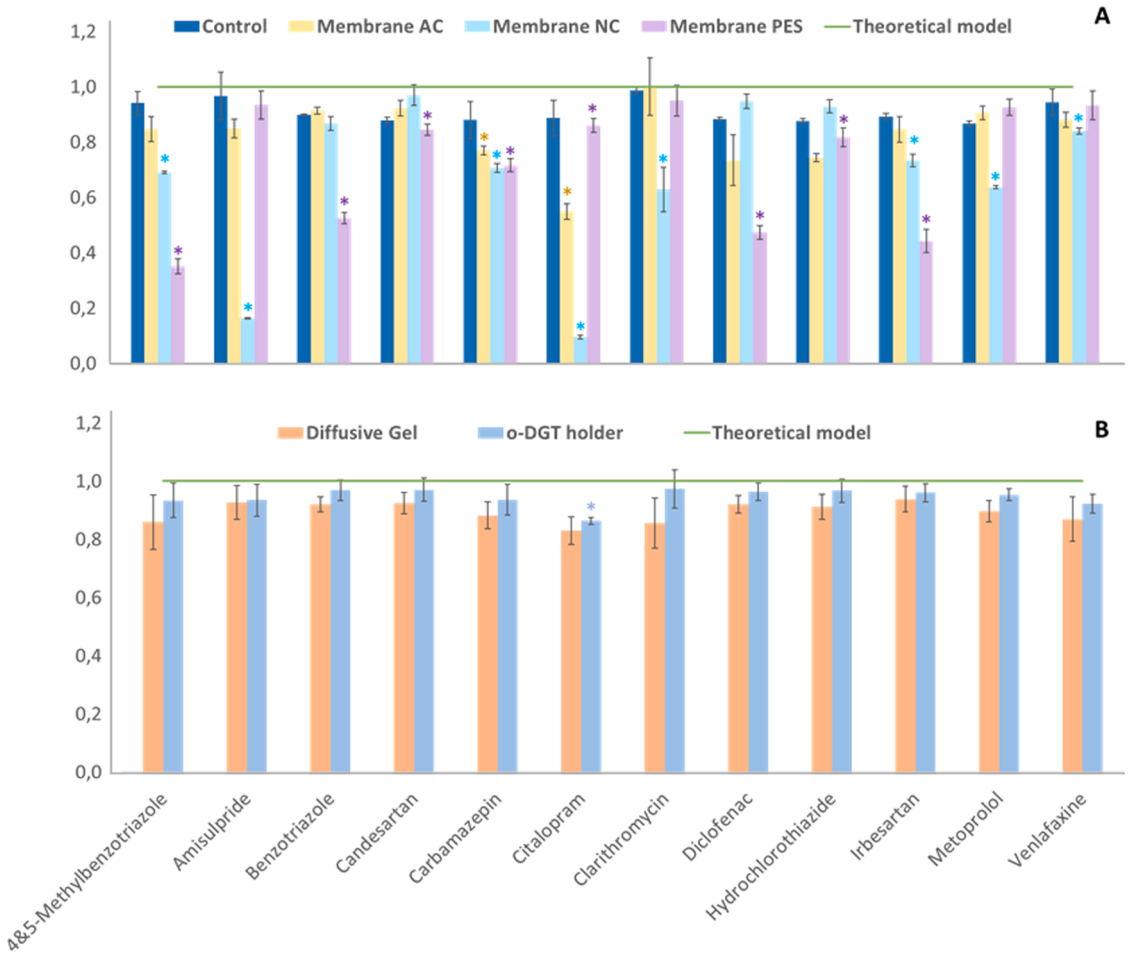

Fig. 2. 12 target compounds concentration ratios after and before exposure to A) different protective membranes, B) o-DGT holder and diffusive gel. The star (*) over bars indicates significant adsorption (p < 0.05).

Table 2
Experimentally calculated diffusion coefficient values at 25 °C ($n = 2$) together with values observed in literature for the studied 12 compounds in agarose diffusive gel.

	Diffusion coefficient, D ($cm^2\ s^{-1}$) 10^{-6} (25 °C)	
	This work (D_{exp})	Literature (D_{lit})
4&5-Methylbenzotriazole	5.68 ± 0.42	-
Amisulpride	3.21 ± 0.05	-
Benzotriazole	5.81 ± 0.23	-
Candesartan	2.46 ± 0.03	-
Carbamazepin	3.41 ± 0.08	5.01[I, a] , 5.54 ± 0.79[I, d] , 4.55 ± 0.79[II, d]
Citalopram	3.13 ± 0.01	4.20 ± 0.51[I, d] , 4.34 ± 5.50[II, d]
Clarithromycin	3.24 ± 0.11	3.16[I,b]
Diclofenac	3.30 ± 0.01	5.75 ± 0.21[I, c]
Hydrochlorothiazide	3.81 ± 0.13	6.78 ± 0.22[I, c] , 5.20 ± 0.09[II,c]
irbesartan (Avapro)	2.67 ± 0.05	-
Metoprolol	2.98 ± 0.04	4.38[I,a]
Venlafaxine	3.39 ± 0.03	3.63 ± 0.49[I,d]

[I] Cell method.
[II] Film-stacking method.
[a] Liu S. et al., 2020 [36].
[b] Liu X. et al., 2021 [37].
[c] Urík J. et al., 2020 [38].
[d] Ji., et al., 2022 [39].

below 7 % after applying the correction to a temperature of 25 °C by the Eq. 4.

Table 2 also provides the literature diffusion coefficient (D_{lit}) for seven of the target compounds, missing this information for the rest of compounds for which, to our best knowledge, no diffusion coefficient in agarose gel have been reported. Except for clarithromycin and venlafaxine, which showed similar *D* value to that observed in literature, the diffusion coefficients obtained for the rest of the compounds were slightly lower compared to literature. This level of difference can be also observed when a different technique is employed for the diffusion coefficient determination. As example, in the study by Urik et al. (2020) [38], the diffusion coefficient of, among others, hydrochlorothiazide was determined by different techniques, such as cell method or Film-stacking method. The results showed that different *D* values were obtained depending on the employed technique for its determination, with 6.78 ± 0.22 by cell method and 5.20 ± 0.09 by Film-stacking method. Generally, diffusion coefficients obtained using the film-stacking method are lower than those determined by the diffusion cell method, due to the higher resistance to mass transfer introduced by the multiple gel interfaces and potential contact imperfections between layers [40]. However, results obtained in this study and those observed in literature for diffusion coefficient were of the same order of magnitude with a deviation less than a factor 2. Previously, Guibal et al., 2017 [27] demonstrated the reliability for determining diffusion coefficients of organic and inorganic compounds in agarose gels using cell diffusion approach. Nevertheless, regarding the work of Poulier et al. (2014) [41], which compare passive and grab sampling approach for micropollutant monitoring in freshwater, a such factor (less 2) of variation for passive sampling conversion constant is suitable for a reliable micropollutant concentration monitoring in real conditions. Indeed, sample extraction and preconcentration steps in grab sampling induce the largest error on micropollutant concentration determination, step that is not present when employing passive samplers.

3.6. Analysis of field samples by the developed UHPLC-Q-ToF MS method

12 micropollutant concentrations at each sampling point were calculated using both conventional grab sampling (Grb) and the deployment of o-DGT devices (C_w). Tables 3 and 4 provides valuable insights into the occurrence of 12 micropollutants in the river system before and below the WWTP and as well as in the WWTP discharge channel, determined after grab sampling and o-DGT based passive sampling, respectively.

As previously mentioned, the analyses by Q-ToF MS were performed in MS^e mode. In this mode, all precursor ions undergo fragmentation, providing crucial information for the accurate identification of

Table 4
Calculated time-weighted average concentrations (μg L^{-1}) in the studied three sampling points by o-DGT passive samplers (Cw) exposed for 10 days ($n = 3$). Exposure in WWTP was divided in 2 series of devices exposure, 6 and 4 days.

Units: μg L^{-1}	*Cw (Up)* ($n = 3$)	*Cw (Dw)* ($n = 3$)	*Cw (WWTP 6 days)* ($n = 4$)	*Cw (WWTP 4 days)* ($n = 3$)
4 & 5-Methylbenzotriazole	0.023 ± 0.005	0.055 ± 0.016	0.657 ± 0.010	0.355 ± 0.101
Amisulpride	0.002 ± 0.001	0.042 ± 0.007	0.532 ± 0.010	0.436 ± 0.071
Benzotriazole	0.025 ± 0.010	0.169 ± 0.022	2.455 ± 0.307	2.220 ± 0.508
Candesartan	0.007 ± 0.002	0.032 ± 0.003	0.412 ± 0.001	0.257 ± 0.062
Carbamazepine	0.001 ± 0.001	0.020 ± 0.002	0.342 ± 0.002	0.152 ± 0.036
Citalopram	0.002 ± 0.001	0.005 ± 0.001	0.130 ± 0.011	0.032 ± 0.005
Clarithromycin	0.011 ± 0.001	0.012 ± 0.001	0.107 ± 0.002	0.030 ± 0.003
Diclofenac	0.013 ± 0.001	0.044 ± 0.004	0.693 ± 0.005	0.446 ± 0.072
Hydrochlorothiazide	< LOD	0.111 ± 0.014	1.441 ± 0.007	1.195 ± 0.163
irbesartan (Avapro)	0.008 ± 0.002	0.265 ± 0.058	8.916 ± 0.049	2.856 ± 0.395
Metoprolol	< LOD	0.007 ± 0.001	0.145 ± 0.002	0.060 ± 0.014
Venlafaxine	0.004 ± 0.002	0.078 ± 0.017	1.531 ± 0.204	0.742 ± 0.231

Table 3
Calculated concentrations (μg L^{-1}) in the studied three sampling points by grab sampling (Grb).

Units: μg L^{-1}	*Grb_1_Up*	*Grb_1_Dw*	*Grb_1_WWTP*	*Grb_Bis_WWTP*	*Grb_2_Up*	*Grb_2_Dw*	*Grb_2_WWTP*
4 & 5-Methylbenzotriazole	0.002	0.135	0.851	0.372	< LOD	0.026	0.411
Amisulpride	0.002	0.233	1.586	0.769	0.001	0.077	1.565
Benzotriazole	< LOD	0.817	3.614	1.024	< LOD	0.314	2.757
Candesartan	0.009	0.110	0.633	0.157	0.005	0.036	0.424
Carbamazepine	0.001	0.058	0.330	0.100	0.000	0.016	0.176
Citalopram	< LOD	0.016	0.065	0.046	< LOD	0.009	0.065
Clarithromycin	< LOD	< LOD	0.039	0.038	< LOD	< LOD	0.061
Diclofenac	< LOD	0.212	1.193	0.512	< LOD	0.069	0.928
Hydrochlorothiazide	0.029	0.333	1.264	0.645	< LOD	0.132	0.948
irbesartan (Avapro)	0.118	0.420	0.812	0.558	0.007	0.258	0.749
Metoprolol	< LOD	0.022	0.112	0.058	< LOD	0.009	0.099
Venlafaxine	0.002	0.199	1.088	0.546	< LOD	0.074	1.057

micropollutants. In fact, the number of unknown signals (features) revealed the presence of potential unidentified compounds that were not included in the list of the 12 micropollutants targeted in this study (figure S6). This finding highlights the high sensitivity of LC-Q-ToF MS in performing targeted analysis of the 12 compounds of interest in a complex matrix. However, it also enables the possibility to carry out both suspect and non-target analysis for further monitoring of unexpected micropollutants and allows the correlation of these features within the different sampling points for better understanding of the occurrence of new micropollutants in water systems. In contrast, this approach is less efficient in low-resolution techniques such as triple quadrupole (QqQ) or ion trap (IT), primarily designed for targeted analysis due to their demonstrated quantitation performance. In fact, non-target analysis requires an instrument capable of recording the entire mass spectrum to generate a sufficient number of data points, a requirement that is effectively fulfilled by modern time-of-flight mass spectrometry instruments [42].

The 12 target compound results revealed that o-DGT calculated water concentrations, which represents the freely dissolved concentrations, were generally higher than grab sampling values. As stated earlier, no compounds were detected in the o-DGT blank analysis, thus excluding any potential interference with the actual concentrations measured by the passive sampler. Results showed that WWTP effluent (WWTP 6 and 4 days) exhibited significantly higher concentrations than river samples and confirming the WWTP as a major contributor of these contaminants to the aquatic environment. Moreover, both sampling techniques showed that compounds such as benzotriazole, hydrochlorothiazide and irbesartan (Avapro) highly present in both, river downstream and WWTP effluent samples, highlighting their incomplete removal by WWTP treatment processes. The high concentration of these micropollutants could be understand as irbesartan (Avapro) and hydrochlorothiazide are both commonly used antihypertensive drugs [43, 44] and benzotriazole is a corrosion inhibitor that showed a high stability in surface waters [45]. In addition, their Log P values indicate that irbesartan (Avapro) is highly lipophilic (Log P 5.38), hydrochlorothiazide is hydrophilic (Log P −0.58), and benzotriazole shows intermediate behaviour (Log P 1.30), resulting in limited adsorption and biodegradation efficiency by the biological treatment with activated sludge. Moreover, at the typical pH of biological treatment (7–8), their pK_a values (between 5.85 and 9.09) lead to partially or fully ionized species, which reduces sorption to activated sludge and restricts microbial uptake. Consequently, these compounds remain predominantly in the aqueous phase and are only partially removed during the WWTP process. Moreover, factors such as the high influent concentrations of micropollutants and variations between dry and wet weather conditions were shown to affect the removal efficiency [46].

Over the 10-days of monitoring a general decrease in micropollutant concentrations was observed in both the river and WWTP effluent samples. In the river, this decline (Grb_2_Dw vs. Grb_1_Dw) suggested potential natural attenuation or dilution. Considering that sampling was consistently conducted at the same time each day to minimize variability among samples, this decrease in concentrations was attributed to dilution due to natural causes. In fact, during the field deployment, 33.2 mm rain was reported in this area of southwest France for the time of the second half of the experiment. For more details, table S9 shows the flow rates ($m^3\ h^{-1}$) of river and WWTP discharge channel during the field deployment period. However, the different condition was also observed with the increase of the water current in both upstream and downstream points in the beginning and the end of the experiment (table S4). Similarly, a reduction in WWTP effluent concentrations (Grb_Bis_WWTP and Grb_2_WWTP) indicated a possible variation in wastewater composition, which is in accordance with previously mentioned rainy period during the field deployment, considering also that the monitored wastewater network collects, mainly in town centre, both wastewater and rainwater.

In this context, o-DGT results proved to be much more reliable in quantifying target micropollutants, being less affected by variability caused by unforeseen events. Moreover, passive sampler binding showed to offer better stability of target compounds compared to water samples [47]. Despite the significant dilution caused by rainfall, the passive sampler was able to provide a clear picture of the presence of the target micropollutants in the river, which grab sampling was not able to achieve. This discrepancy could be expected as o-DGT devices integrate contaminant accumulation over time, providing a time-weighted average and reduction of the LOQs, while grab sampling captures a single moment picture and may underestimate peak concentrations [8, 48]. Several micropollutants were below the LOD in grab sampling but detected and quantified using o-DGT devices, demonstrating the greater sensitivity and time-integrative capability of passive samplers, as it was already demonstrated by Ren et al. (2014) [7]. This was particularly evident in upstream samples with low-concentration contaminants such as benzotriazole, clarithromycin, citalopram and diclofenac, for which o-DGT passive sampling showed to be the suitable method for their correct monitoring. In the event of sporadic or unexpected contamination episodes in monitored areas, the use of passive samplers would therefore provide an average estimate of contamination over the selected deployment period. Consequently, if the aim is to identify such short-term events, it would be necessary either to shorten the deployment periods or to complement the monitoring with grab sampling, achieving a high-frequency sampling regime capable of determining, when required, the specific moment at which the contamination increase occurred. While the passive sampler has proven effective in monitoring the target compounds throughout the entire deployment period, implementing a high-frequency grab sampling strategy would drastically increase the time required for sample collection, processing, and analysis. For cases in which the sampling area contains low concentrations of micropollutants, Martins de Barros et al. (2023) [10] demonstrated that increasing the sampling area of the DGT device (L-DGT) enhances its sensitivity, while maintaining all the inherent advantages of using passive samplers. In addition, not only due to its significantly lower cost compared to other refrigerated automatic samplers, but the passive sampler also offered an advantage over other devices in its ability to measure the balance of input and output mass of the 12 micropollutants in WWTP without energy consumption. Indeed, as the volume of sampled water could be known during the passive sampler field deployment, determined by the flow rate, the mass of the target compounds was accurately quantified (table S10) [41]. This data demonstrated the quantity (g) of each micropollutant tracer discharged in the river per days from WWTP, showing despite different deployment time, an enrichment of micropollutants at the river level. The mass-flux results (table S10), together with the measured flow rates (table S9), show that the WWTP effluent is the main contributor to the downstream load of the studied micropollutants. Despite representing <2 % of the total river flow, the discharge notably increased downstream fluxes, especially for persistent compounds such as irbesartan (Avapro), benzotriazole, and hydrochlorothiazide. These findings confirm that even small effluent volumes can significantly influence downstream water contamination and that the o-DGT samplers provided consistent, time-integrated estimates of contaminant transport.

Interestingly, in the study carried by Wiest et al. (2021) [49], several target compounds of current study were detected and quantified in 10 raw and treated WWTP (from France) water samples. These results, together with the previously carried out study in French WWTPs [50], supports and validates those obtained in our study employing an innovative approach combining o-DGT passive sampling and the developed UHPLC-Q-ToF MS analytical method for the target analysis of the 12 compounds introduced in the new Urban Wastewater Directive (PE-CONS 85/1/24) by the European Council.

4. Conclusion and perspectives

This work proposed an innovative sampling by o-DGT and analysis

method by UHPLC-Q-ToF MS for the quantification of the 12 key micropollutants used as tracer of WWTP performances referred in the updated Urban Wastewater Directive (PE-CONS 85/1/24). A design of o-DGT was tested and proposed consisting in an agarose gel, HLB binding phase and acetate cellulose protective membrane. This work gives all the diffusion coefficient required, providing 5 new values, for the determination of time-weighted average concentration of the target 12 micropollutants. Moreover, elution and dilution method were given to minimize matrix effect after o-DGT field deployment. In low concentration sampling points, during river and WWTP discharge channel deployment, several micropollutants undetectable by grab sampling were quantified using o-DGT, highlighting its better sensitivity for the monitoring of organic micropollutants. Furthermore, the time-weight average concentration provided by passive sampler for the targeted compounds, displays the advantage to determine real mass balance of trace micropollutants at low cost and easy field implementation. Nevertheless, future work could further refine the methodology by exploring additional factors that may influence its performance in even more polluted environments. For instance, the role of dissolved organic matter in affecting diffusion and binding behaviour warrants detailed investigation, particularly in complex environmental matrices. Moreover, since the current o-DGT configuration has shown excellent performance for the 12 regulated micropollutants, it could also be evaluated for its capacity to sample other emerging contaminants that might be included in future regulatory frameworks, without the need for device modification. Testing the sampler at the inlet of wastewater treatment plant, where the matrix is especially complex, would also provide valuable insights into its robustness and allow assessment of the reduction rates of target molecules across treatment processes. Such studies would expand the applicability of the method and further support its use in ensuring compliance with upcoming WWTP performance standards.

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CRediT authorship contribution statement

Mikel Bernabeu de Maria: Writing – review & editing, Writing – original draft, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Robin Guibal:** Writing – review & editing, Validation, Supervision, Methodology, Investigation, Formal analysis, Conceptualization. **Matthias Monneron-Gyurits:** Writing – review & editing, Validation, Funding acquisition, Conceptualization. **Gilles Guibaud:** Writing – review & editing, Validation, Supervision, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Mikel Bernabeu de Maria reports financial support was provided by Nouvelle-Aquitaine Regional Council. Mikel Bernabeu de Maria reports financial support was provided by SAS Ecometrique. If there are other authors, they 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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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.talo.2025.100594.

Data availability

Data will be made available on request.

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