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Determination of uptake kinetics and sampling rates for 56 organic micropollutants using “pharmaceutical” POCIS

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Abstract

The literature increasingly reports sampling rates (R_s) for Polar Organic Chemical Integrative Samplers (POCIS) but the data obtained come from various calibration systems that are not always well-defined (agitation, temperature, measured micropollutant concentrations in water,...). In order to obtain accurate laboratory R_s for priority and emerging substances, POCIS need to be exposed in a robust and well-defined calibration system. Thus, we built a flow-through calibration system containing tap water spiked with 56 organic micropollutants (alkylphenols and phenols, hormones, pesticides, pharmaceuticals, UV filter). POCIS were immersed for up to 28 days. Tap water micropollutant concentrations and additional parameters (temperature, pH, conductivity, dissolved organic carbon, flow velocities) were kept constant and controlled throughout the calibration experiment. Based on the observed uptake kinetics, we distinguished 4 types of micropollutant accumulation patterns: curvilinear accumulation (30 molecules, group 1), accumulation with an inflexion point (13 molecules, group 2), random accumulation (8 molecules, group 3), and no or very low accumulation (5 molecules, group 4). R_s was calculated for 43 out of 56 micropollutants (groups 1 and 2). Calculated R_s values ranged from 0.030 L/d to 0.398 L/d. POCIS can supply TWA

concentrations for hormones, pesticides, several pharmaceuticals, a few alkylphenols, and the UV filter. Our R_s results are generally less than 2 fold-different (higher or lower depending on target molecule) to the literature data using the same type of calibration system or for micropollutants with $\log K_{ow} > 2.65$. We found a quadratic correlation between R_s and $\log D$ for betablockers, herbicides and hormones.

Keywords: POCIS; sampling rates; uptake kinetics; calibration system; priority and emerging substances.

Abbreviations: CF, concentration factor; DOC, dissolved organic carbon; DT, degradation time; LC, liquid chromatography; MRM, multiple reaction monitoring; MS, mass spectrometry; POCIS, polar organic chemical integrative sampler; PES, polyethersulfone; PRC, performance and reference compound; PTFE, polytetrafluoroethylene; R_s , sampling rate; RSD, relative standard deviation; SPE, solid-phase extraction; TWA, time-weighted average.

1. Introduction

Integrative samplers such as the Polar Organic Chemical Integrative Sampler (POCIS) were designed to sample hydrophilic micropollutants [1]. They are immersed for a few days to a few weeks (14 days is a common standard), and accumulate compounds by passive diffusion. They can thus be used for screening with limits of detection that are often better than classic grab sampling since they are able to directly extract micropollutants *in situ* for several days. POCIS are also claimed to give time-weighted average (TWA) micropollutant concentrations in water over the immersion duration by using accurate sampling rates (R_s). R_s are dependent on environmental parameters such as agitation, temperature or biofouling [2]. TWA concentrations can be produced with *in situ* R_s but the process entails performing an in-field calibration for each campaign, making it a heavily time-intensive method [3], and the micropollutants have to be present in the aquatic system at a relatively constant concentration. Another method to determine TWA concentrations is to calibrate the POCIS in-lab. The huge advantage of this method is that it only has to be performed once and it allows controlling micropollutant concentrations. However, the drawback is the necessity to correct the in-lab R_s that does not account for the effect of environmental conditions and can thus lead to biased *in*

situ TWA concentrations [4]. This correction is made using internal surrogates, i.e. performance and reference compounds (PRCs), which are currently difficult to identify for POCIS [5].

In order to obtain accurate laboratory R_s , it is necessary to have a reliable, robust and well-defined calibration system. Literature reports do not always detail certain aspects of calibration and calculation, giving at best only partial information on POCIS (type and mass of receiving phase, exposed surface), calibration system (zero, discrete or continuous micropollutant renewal, exposure duration, design of the exposure system, container type, agitation type, physical-chemical parameters, and analyte concentration in the water) or sampling rate calculation method. Furthermore, it is also necessary to control key parameters (temperature, flow velocity, pH, conductivity, dissolved organic carbon (DOC), tap water micropollutant concentrations) and to detail these controls [6]. Today, numerous references give laboratory R_s with POCIS for micropollutants such as alkylphenols, hormones, pesticides or pharmaceuticals [2, 4-5, 7-18]. But given that lab calibration methods are not performed in the same way nor in a well defined way, R_s could vary widely for a given micropollutant, making it difficult to select a reliable R_s as benchmark.

Here, we report results on kinetic accumulations for 56 priority and emerging micropollutants (8 alkylphenols, 9 hormones, 11 pesticides, 27 pharmaceuticals and 1 UV filter). More specifically, we identify molecules that fit or fail to fit the curvilinear model [1] and go on to discuss R_s calculation method according to molecule. We also give well-defined laboratory R_s produced with the “pharmaceutical” POCIS for 43 micropollutants. All aspects potentially influencing R_s are detailed (i.e. POCIS and calibration system used, characteristics of the exposure media and sampling rate calculation method). We also discuss the validity field of the POCIS according to target micropollutant (concentration factor, optimal exposure duration, possibility for calculating TWA concentrations). We compared our results (accumulation kinetics and R_s) with the literature and studied the influence of log D on R_s .

2. Material and methods

2.1. Chemicals, material and apparatus

Acetonitrile HiPerSolv Chromanorm, Acetonitrile LC/MS HiPerSolv Chromanorm, Dichloromethane HiPerSolv Chromanorm and Methanol HiPerSolv Chromanorm were purchased from VWR (Fontenay-sous-Bois, France). Ultrapure water was obtained on a MilliQ® Advantage A10 system equipped with an LC-Pak cartridge and a 0.22 µm filter Millipak® 40 from Merck-Millipore (Saint-Quentin-en-Yvelines, France). Acetonitrile Chromasolv grade, Acetonitrile LC/MS Chromasolv grade, methanol Chromasolv grade, ammonium acetate puriss p.a. for mass spectroscopy ≥ 99.0%, formic acid puriss p.a. eluent additive for LC-MS ≈ 98%, Ammonium formiate puriss p.a. ≥ 99.0% and acetic acid puriss p.a. ≥ 99.8% were purchased from Fluka (Saint-Quentin-Fallavier, France).

The majority of analytical standards were purchased from Sigma-Aldrich (Saint-Quentin-Fallavier, France), i.e. 7 alkylphenols and phenols (bisphenol A [BPA], t-butylphenol [t-BP], n-nonylphenol [n-NP], t-nonylphenol [t-NP], n-octylphenol [n-OP], t-octylphenol [t-OP], resorcinol [Res]), 27 pharmaceuticals including 5 antibiotics (metronidazole [Metro], ofloxacin [Oflo], roxithromycin [Roxi], sulfamethoxazole [Sulfa], trimethoprim [Trim]), 5 anti-inflammatories (diclofenac sodium salt [Diclof], ibuprofen [Ibu], ketoprofen [Keto], naproxen [Napro], salicylic acid [SalA]), 2 benzodiazepines (lorazepam [Lora], oxazepam [Oxa]), 10 betablockers (acebutolol hydrochloride [Ace], atenolol [Ate], betaxolol [Bet], bisoprolol fumarate [Bis], metoprolol tartrate [Met], nadolol [Nad], oxprenolol [Oxp], propranolol hydrochloride [Prop], sotalol hydrochloride [Sot], timolol hydrogen maleate [Tim]), 2 lipopenics (bezafibrate [Beza], fenofibrate [Feno]) and 3 other pharmaceuticals (carbamazepine [Carba], furosemide [Furo], paracetamol [Para]), 11 pesticides including 4 fungicides (carbendazim [Carb], iprodione [Ipr], prochloraz [Pro], thiram [Thi]) and 7 herbicides (2,4-dichlorophenoxyacetic acid [2.4-D], 3,4-dichloroaniline [3.4-D], acetochlore [Acet], alachlore [Ala], atrazine [Atra], diuron [Diu], linuron [Lin]), 10 hormones including 5 estrogens (estrone [E1], 17α-estradiol [α-E2], 17β-estradiol [β-E2], estriol [E3], ethinylestradiol [EE2]), 2 progestogens (megestrol acetate [MegA], progesterone [P]), 1 androgen (testosterone [T]) and 1 anticancer drugs (tamoxifen [Tamo]) and 1 UV filter (4-methylbenzylidene camphor [4-MBC]). One micropollutant (2,4-dichlorophenol-d3 [2.4-DCP]) and one internal standard (17β-estradiol acetate) were purchased from CIL (Sainte-Foy-La-Grande, France). The internal standard for betablockers (metoprolol impurity A) was purchased from LGC (Molsheim, France).

The POCIS was built using Oasis® HLB bulk sorbent (average particle diameter: 60 µm) and hydrophilic polyethersulfone (PES) SUPOR 100 membrane disc filters (0.1 µm, 90 mm membrane diameter) purchased from Waters (Guyancourt, France) and Pall (Saint-

Germain-en-Laye, France), respectively. Empty glass solid phase extraction (SPE) tubes (6 mL) and polytetrafluoroethylene (PTFE) frits (20 μ m porosity) were purchased from Sodipro (Echirolles, France). The calibration system was composed of a Harvard Type 22 syringe pump from Harvard Apparatus (Les Ulis, France) and a Ismatec model Ecoline VC-MS/CA8-6 peristaltic pump from Thermofisher (Illkirch, France).

The chromatographic separation of 10 betablockers and 5 estrogens ([E1], [α -E2], [β -E2], [E3], [EE2]) was performed with Xbridge C18 end-capped columns (150 x 2.1 mm, 3.5 μ m) from Waters (Guyancourt, France) equipped with guard columns. The separations of the 41 remaining molecules were performed with a Kinetex XB-C18 Core Shell (100 x 2.1 mm, 1.7 μ m) equipped with a KrudKatcher (0.2 μ m) filter from Phenomenex (Le Pecq, France).

The liquid chromatography-mass spectrometry (LC-MS) system used for the analysis of 10 betablockers and 5 estrogens was composed of an Agilent 1100 chromatographic system from Agilent (Massy, France) coupled with an API 4000 triple-quadrupole mass spectrometer from AB Sciex (Les Ulis, France). The LC-MS system used for the analysis of the 41 remaining molecules was an Agilent 1200 chromatographic system from Agilent (Massy, France) coupled with a triple-quadrupole 3200 Qtrap from AB Sciex (Les Ulis, France).

2.2. Calibration design and POCIS exposure

The calibration system is schematized in Figure 1. It consisted of 2 aquaria (up to 50 L) filled by tap water freshly spiked at a nominal value of 3 μ g/L for each analyte. This concentration permitted to analyze grab samples by direct injections in LC-MS and thus to easily control this parameter throughout the calibration phase. Triplicates of “pharmaceutical” POCIS (45.8 cm² of exposed surface, 200 mg of receiving phase) were immersed for t = 1, 3, 6 and 12 hours and for t = 1, 3, 7, 14, 21 and 28 days. Given that we worked with 2 aquaria with a limited number of POCIS per aquarium and that each exposure duration was tested in triplicate, the total experiment duration was 42 days. In order to closely mimic the agitation conditions found in aquatic rivers, each POCIS was exposed to a current of around 10 cm/s delivered perpendicularly to their surface by a diffusion ramp linked to a submersible pump. This set-up was inspired by the system developed by Mazzella et al. [10]. Tap water was thermostated at around 20°C by thermostated water-bath using an external thermostated tank. The system was kept in the dark to prevent any photolysis of analytes.

The whole system was a flow-through calibration system, since freshly-spiked tap water was delivered continuously into each aquarium by a peristaltic pump and the excess was evacuated via an overflow (and sent through a 10 g activated carbon column for clean-up). Unspiked tap water was contaminated with 2 contaminant solutions (around 100 mg/L each, replaced every week) syringe-pumped into a mixing vessel (which was agitated with a magnetic stirrer). The flow rate from the peristaltic pump permitted to renew 35% of each aquarium per day. Indeed, a previous experiment performed in the same calibration system revealed that 35% of aquarium capacity should be renewed per day in order to have constant concentrations for most molecules (46 out of 56). For the 10 other molecules (identified with asterisks in Figure 1), the degradation percentages were too high and would need excessively high water resources and analytical standards to keep them at a constant 3 µg/L. The flow rate of the syringe pump was set as a function of renewal percentage in order to operate at the nominal concentration.

Insert Figure 1

Before beginning the experiment, 1.5 mL of each contaminant solution was poured into each aquarium in order to obtain a concentration of around 3 µg/L in the tap water.

During the calibration experiment, physical-chemical parameters of the tap water such as temperature, pH, conductivity and DOC were controlled each week in both aquaria. The current velocities at the front of each POCIS surface were also checked every week. To enable sampling rate calculation, water concentrations of micropollutants were monitored twice a week. One sample was collected before the renewal of the contaminant solutions to check potential degradation of micropollutants. A second sample was performed a few hours after the contaminant solutions were renewed to quantify micropollutant concentrations after the system equilibration. Each sample was analyzed in duplicate or in triplicate, and contaminant solutions were analyzed every week.

2.3. *POCIS and water sample pre-treatment and analysis*

2.3.1. POCIS preparation, deployment, retrieval and blank

The POCIS were home-made, with 200 mg ($\pm$ 5 mg) of receiving Oasis® HLB phase sandwiched between 2 PES membranes. This device set-up was kept between 2 stainless steel rings linked together by screws and nuts. The home-made POCIS were then stored at 5°C ($\pm$ 1°C) until immersion in the aquaria. During exposure, the POCIS were placed facing the flow coming from the diffusion ramp. After retrieval, the POCIS membranes were rinsed with a few mL of unspiked tap water, and the POCIS were then stored at -23°C ($\pm$ 3°C) until extraction. An additional blank POCIS, consisting in a POCIS not immersed in the exposure media was produced in order to check for any contamination of the receiving phase. This blank POCIS was stored at -23°C ($\pm$ 3°C) until processing.

2.3.2. Treatment of POCIS before analysis

Exposed POCIS and blank were left at ambient temperature for 1 hr before processing. The POCIS were then disassembled and the sorbent was transferred with a few mL of ultrapure water under low vacuum in pre-weighed 6 mL glass SPE cartridges equipped with PTFE frits. The sorbent was dried under vacuum, and the micropollutants were eluted with 2 x 5 mL of methanol and then 2 x 5 mL of a methanol/dichloromethane mixture (50/50, v/v). Sorbent was dried again and weighed in order to measure the exact mass analyzed. Each eluate was separated into 3 fractions in order to quantify all micropollutants via 4 analytical methods (one fraction for betablockers analysis, one fraction for estrogen analysis, one fraction for 2 multiresidue analyses on the remaining molecules). The eluates were evaporated to dryness under a gentle stream of N₂, and the extracts were then reconstituted into:

- 500 μ L of a H₂O/ACN mixture (99/1, v/v) and 50 μ g/L of an internal standard (i.e. metoprolol impurity A) for betablocker analysis,
- 500 μ L of a H₂O/ACN mixture (60/40, v/v) and 50 μ g/L of an internal standard (i.e. estradiol acetate) for estrogen analysis,
- 2 mL of a H₂O/ACN mixture (80/20, v/v) for the 2 multiresidue analyses.

Before analysis, extracts were diluted 100 to 500 times in order to be within the concentration range of each method and to guard against matrix effects. For betablocker and hormone analyses, dilutions were done in their respective mobile phase mixtures. For multiresidue analyses, extracts were diluted in ultrapure water. All extracts were stored at -23°C ($\pm$ 3°C) until analysis.

2.3.3. Treatment of water samples before analysis

The relatively high concentrations of micropollutants in spiked tap water (i.e. around 3 µg/L) made it possible to analyze water samples by direct injection in the chromatographic system after moderate dilution to obtain the adequate mobile phase mixture (i.e. H₂O/ACN (99/1, v/v) for betablockers, H₂O/ACN (60/40, v/v) for estrogens, and ultrapure water only for multiresidue analyses) and after adding possible internal standards (metoprolol impurity A and estradiol acetate at 50 µg/L for betablocker and estrogen analyses, respectively). Water samples were kept at -23°C (± 3°C) until analysis.

2.3.4. LC-MS/MS analysis

The methods used for betablockers and estrogens are detailed elsewhere [19-20]. Briefly, chromatographic separation was performed with Xbridge C18 end-capped columns (150 x 2.1 mm, 3.5 µm) equipped with guard columns. Vials were kept at 4°C during analysis. Injected volumes were 10 µL. Column oven temperature was set at 28°C for betablockers and 30°C for estrogens. Gradients with LC-MS-grade water (buffered with ammonium formate for betablockers) and acetonitrile were applied at a flow rate of 0.2 mL/min: from 1% ACN at 0 to 5 min ramped up to 100% ACN at 21 min until 29 min for betablockers, and 40% ACN from 0 to 2 min ramped up to 80% ACN at 4.5 min until 7 min and up to 100% ACN at 8.25 min until 15 min for estrogens. Separations were achieved in less than 20 min and 12 min for betablockers and estrogens, respectively.

Ionization was performed with an electrospray source in positive mode for betablockers and negative mode for estrogens. Acquisitions were performed in multiple reaction monitoring (MRM) mode. Detection included 2 ionization transitions for each analyte – one for quantification and the other for confirmation. The instrumental limits of quantification (direct injection) were 100 ng/L for betablockers and 150-700 ng/L for estrogens depending on analyte micropollutant.

The multiresidue methods used for the 41 other micropollutants are detailed elsewhere [21]. Briefly, the chromatographic column used for separation was a Kinetex XB-C18 Core Shell (100 x 2.1mm, 1.7 µm) equipped with a KrudKatcher (0.2 µm) filter. Vials were kept at ambient temperature until analysis and injection volumes were 100 µL. Column oven

temperature was 60°C for both ionization modes. In positive mode, the separation, achieved in 9 min, was performed with a multi-linear gradient with water (acidified with formic acid) and ACN. In negative mode, the separation, achieved in 7 min, was done with a multistep gradient with 0.1 mM ammonium acetate in water and ACN.

The mass spectrometer source was an electrospray in positive mode for 29 molecules: the UV filter, the hormones (other than estrogens), all the pesticides except 2,4-dichlorophenoxyacetic acid and almost all pharmaceuticals except furosemide, ibuprofen and salicylic acid. The source was in negative mode for 12 molecules: all alkylphenols and phenols, 1 pesticide (2,4-dichlorophenoxyacetic acid) and 3 pharmaceuticals (furosemide, ibuprofen and salicylic acid). Acquisitions were performed in scheduled MRM and MRM mode for positive and negative modes, respectively. Two ionization transitions were used for each analyte (except for linear alkylphenols and 2,4-dichlorophenoxyacetic acid for which only one transition was possible) – one for quantification and one for confirmation. The instrumental limits of quantification (direct injection) varied from 1 ng/L for carbendazim to 579 ng/L for 2,4-dichlorophenol.

2.4. Sampling rate calculation methods

Theoretically, it is possible to model the accumulation of micropollutants in the receiving phase of the POCIS by 3 successive accumulation regimes (as a function of time): a linear (or kinetic/integrative) regime, a pseudolinear regime, and an equilibrium regime [1]. If exchange is isotropic, this accumulation follows a first-order kinetic, which can be described by the equation (1):

$$(1) \quad C_s = C_w \frac{k_u}{k_e} (1 - e^{-k_e t})$$

where C_s is the concentration of a given micropollutant in the sorbent at time t ($\mu\text{g/g}$), C_w the TWA concentration of the same micropollutant in the water ($\mu\text{g/L}$), k_u the uptake rate constant of the micropollutant on the receiving phase (L/g/d), k_e the elimination (or exchange) rate constant of the micropollutant from the receiving phase (d^{-1}), and t the time (d).

POCIS is generally used in the linear regime to lead to TWA concentrations. In this regime, the sampler acts as an “infinite sink”, and k_e is negligible compared to k_u . It is therefore possible to simplify the equation (1) and to link the concentration quantified in the

POCIS to its concentration in the sampling medium via the sampling rate, using equation (2) [2]:

$$(2) \quad C_s = \frac{C_w R_s t}{M_s}$$

where R_s is the sampling rate (L/d), and M_s the mass of sorbent in the POCIS (g).

The frontier between the kinetic regime and the pseudolinear regime corresponds to $t_{1/2}$, i.e. the time necessary to reach half of the equilibrium concentration [5]. Thus, R_s must be calculated during a period shorter than or equal to $t_{1/2}$ in order to be accurate. $t_{1/2}$ is defined as follows:

$$(3) \quad t_{1/2} = \frac{\ln 2}{k_e}$$

Rewriting equation (2), it is possible to tease out the concentration factor, as indicated in equation (4):

$$(4) \quad CF = \frac{C_s}{C_w} = \frac{R_s t}{M_s}$$

where CF is the concentration factor (L/g). The concentration factor makes it possible to neutralize the effect of C_w variations.

In this paper, we used equation (4) until the $t_{1/2}$ of each micropollutant in order to calculate R_s . First of all, we drew CF as a function of time (using C_s and C_w quantified at each POCIS removal time). Then, the curve obtained made it possible to determine the k_e and thus the $t_{1/2}$ for each micropollutant using XLStat software. We thus obtained a line whose slope was equal to R_s/M_s . We calculated accurate R_s using this slope multiplied by the mean of POCIS masses exposed until $t_{1/2}$. The standard deviation of the slope was used to determine the standard deviation of the R_s .

3. Results and discussion

3.1. A reliable calibration system

Additional parameters and flow velocities were followed and kept constant during the 42 days experiment duration, as reported in Table 1. Indeed, the RSDs for these parameters never exceeded 27%. During the whole period of the calibration phase, temperature was around 21°C, pH was around 7.6, conductivity was around 430 µS/cm, DOC was around 10 mg/L, and the flow velocities had a mean value of 11 cm/s.

Insert Table 1

Figure 2 represents the mean of spiked tap water concentration of the 56 organic micropollutants over the course of 42-day experiment in both aquaria.

Insert Figure 2

Out of the 56 molecules tested, 44 had a mean of spiked tap water concentration close to the nominal value (3 ± 2 µg/L). Among the 12 remaining molecules, 8 are known to degrade in water under our renewal conditions (as proved in a previous experiment), which explains why their concentrations were too low (i.e. n-octylphenol, n-nonylphenol, salicylic acid, fenofibrate, iprodione, thiram with concentrations < 1 µg/L) or dispersed (i.e. tamoxifen: 5.1 ± 3.4 µg/L). The eighth molecule, t-octylphenol, should also be degraded (according to the degradation test) but in this experiment, its concentration was higher than expected (17.0 µg/L). Among the final 4 remaining molecules, 3 had higher mean concentrations than expected (2,4-dichlorophenol: 7.1 µg/L, ofloxacin: 8 µg/L and roxithromycin: 18.5 µg/L) and 1 had a lower mean concentration than expected (resorcinol: 0.4 µg/L). This may be due to biodegradation process for resorcinol [22] and possible matrix effects in water concentrations for t-octylphenol, 2,4-dichlorophenol, ofloxacin and roxithromycin. Either way, ruling out molecules degraded in tap water and resorcinol due of its very low mean water concentration (0.4 µg/L), the relative standard deviation (RSD) never exceeded 47% (t-butylphenol and progesterone) and was lower than 35% for all the other molecules, which is very satisfying considering the long 42-day duration of the calibration experiment.

R_s were not calculated for micropollutants with tap water concentrations far from the nominal value (lower than 1 µg/L or higher than 5 µg/L) or with high RSD (above 35%), except for 2,4-dichlorophenol and t-octylphenol (water concentrations of 7.1 µg/L and 17.0 µg/L respectively; detailed data shown in supplementary material), and for t-butylphenol, progesterone, 4-methylbenzylidene camphor (random water concentration variations leading

to RSDs of 46-47%; detailed data shown in supplementary material) for which the calculated CFs lead to well-defined R_s . Nonetheless, for 2,4-dichlorophenol and t-octylphenol, R_s are given for information and still need to be validated.

The supplementary material (S1) reports spiked tap water concentrations for 9 micropollutants (4 with concentrations close to the nominal value: ethinylestradiol, metoprolol, bisphenol A and linuron; 2 with concentrations far from the nominal value: 2,4-dichlorophenol and t-octylphenol; 3 with concentration variations higher than 35% over the entire experiment duration: t-butylphenol, progesterone and 4-methylbenzylidene camphor).

Allowing for small variations, our calibration system makes it possible to keep constant additional parameters, flow velocities, and waters concentrations of most of the micropollutants, thus enabling the calculation of well-defined R_s .

3.2. Accumulation kinetics

This section discusses the accumulation kinetics curves obtained for the 56 micropollutants for 28 days exposure. These curves enabled us to show the behaviour of each micropollutant in the POCIS receiving phase and, when possible, to estimate $t_{1/2}$, which is rarely if ever indicated in the literature.

We distinguished 4 different groups:

- group 1, made up of 30 micropollutants showing curvilinear accumulation kinetics as described in the model from Alvarez [1] and equation (1),
- group 2, made up of 13 micropollutants having an inflexion point in their accumulation kinetics curve,
- group 3: made up of 8 micropollutants with random accumulation kinetics curves,
- group 4: made up of 5 micropollutants, characterized by very low ($CF_{max} = 3 \text{ L/g}$) or inexistent accumulation.

Given that the accumulation of micropollutants from groups 2, 3 and 4 diverged from the theory, it was not possible to determine k_e and then $t_{1/2}$ with XLStat software. For group 2 molecules, we calculated R_s from the triplicate at day 14 and according to equation (4). Figure 3 illustrates the 4 different types of accumulation with two examples from each group. Detailed accumulation curves for the 56 micropollutants can be found in the supplementary material.

Table 2 compiles the key information on these micropollutants and indicates their physical-chemical properties, as discussed below.

Insert Figure 3

Insert Table 2

3.2.1. Group 1: micropollutants with a curvilinear accumulation kinetics curve

There were 30 micropollutants presenting a curvilinear accumulation kinetics curve and for which the POCIS can supply TWA concentrations as explained in equation (2). Group-1 micropollutants had $t_{1/2}$ from 5 to 693 days. They can be ionized or neutral, with log K_{ow} from 1.34 to 5.12. Their molecular weights vary from 150.1 to 376.7 g/mol.

POCIS are generally exposed in the field for 14 days [2, 4, 16]. According to table 2, we found a $t_{1/2}$ higher than or equal to 14 days with neutral micropollutants (20 over 21) and lower than 14 days for ionized micropollutants (8 of 9). Moreover, micropollutants with $t_{1/2} \geq 14$ days have a mean log K_{ow} of 3.5 (± 0.8) whereas molecules with $t_{1/2} < 14$ days have a mean log K_{ow} of 2.3 (± 0.6). Molecular weight did not seem to have any influence on $t_{1/2}$ duration. Indeed, molecules with $t_{1/2} \geq 14$ days have a mean molecular weight of 272 g/mol (± 52) while molecules with $t_{1/2} < 14$ days have a mean molecular weight of 267 g/mol (± 68).

The $t_{1/2}$ calculation is a fairly delicate task since $t_{1/2}$ can change dramatically with a small variation in a kinetic point, but it remains a valuable criterion for providing the optimal exposure duration of POCIS. TWA water concentrations can be easily calculated from equation (2) for micropollutants with $t_{1/2} \geq 14$ days since they are linearly accumulated during classical *in situ* 14-day exposure durations. However, for the other group-1 molecules, POCIS should not have to be immersed higher than $t_{1/2}$ for rigorous TWA concentration calculations (i.e. 5 days for 2,4-DCP).

Lag times (between 3 hours and up to 3 days) were observed for 3,4-dichloroaniline, linuron, 2,4-dichlorophenol, t-butylphenol, prochloraz, megestrol acetate, ethinylestradiol, progesterone, estrone, t-octylphenol and 4-methylbenzylidene camphor. There was no clear explanation for this phenomenon, but lag times were generally (but not systematically) observed for neutral micropollutants or for log K_{ow} higher than 2.3. Lag times have already been reported for prochloraz and 4-methylbenzylidene camphor on a C18 Chemcatcher using

PES membranes [21]. These effects had no impact on calculated R_s (except for 2,4-dichlorophenol where R_s is possibly underestimated) since $t_{1/2}$ micropollutants were 11 to 2772 times higher than the lag time duration for *t*-octylphenol and progesterone, respectively.

3.2.2. Group 2: micropollutants with an inflexion point

This group encompassed 13 micropollutants based on their higher accumulation rate in the POCIS during the first week of exposure leading to an inflexion point (generally at day 14) and their coefficients determined as lower than 0.99 compared to the curvilinear model (e.g. ketoprofen, figure 3.d. with $R^2=0.98$). For these compounds, XLStat software miscalculated $t_{1/2}$ since the model was not curvilinear over 28 days. We thus recalculated R_s with POCIS immersed at day 14. We assumed that these R_s were as accurate as those of group 1, since there was an integrative phase after the inflexion point. As was the case for group 1, POCIS can produce TWA concentrations for these micropollutants.

Group-2 micropollutants are generally in ionic form (9 out of 13; Table 2) in a log K_{ow} range of between -0.40 and 3.99. Neutral molecules are relatively polar ($\log K_{ow} \leq 2.67$). The higher accumulation rate up to 7 days may be explained by a burst effect [1, 10]. This phenomenon is due to the time delay required for complete wetting of the POCIS membranes and can be avoided by pre-wetting the POCIS before immersion. These molecules might also accumulate in POCIS following two different sorption mechanisms, e.g. adsorption and then partitioning, or a multi-layer adsorption mirroring gas adsorption on a solid: a first layer directly on the sorbent and a second layer over the first layer [23].

3.2.3. Group 3: micropollutants with random accumulation kinetics curves

The 8 micropollutants forming group 3 were characterized by a random accumulation in the POCIS receiving phase with a concentration factor higher than 3. For these micropollutants, POCIS could not supply reliable TWA concentrations but can be used for screening. We supposed that this type of accumulation is not due to degradation in HLB phase because tests proved that pesticides (acetochlor, alachlor, atrazine, diuron, linuron, 2,4-dichlorophenoxyacetic acid), pharmaceuticals (atenolol, carbamazepin, diclofenac, ibuprofen, ketoprofen, metoprolol, naproxen, propranolol, sulfamethoxazole, trimethoprim) and

hormones (estrone, estriol, ethinylestradiol) adsorbed on it are well conserved during weeks to months [24-25].

These micropollutants are polar or apolar (log K_{ow} from 0.65 to 5.44), neutral or ionized in tap water at pH = 7.6. They include 6 pharmaceuticals, resorcinol, and t-nonylphenol.

These unpredictable accumulations make it impossible to reliably determine $t_{1/2}$. For all group-3 micropollutants, the RSDs of tap water concentrations were higher than 30%, and 5 molecules (iprodione, t-nonylphenol, salicylic acid, thiram, fenofibrate) are known (from previous experiments) to degrade in tap water under our renewal conditions (degradation time 50 [DT50]: iprodione < 3 d; thiram < 3.5 d; salA < 6 h; feno < 6 h), which may explain some of the random accumulation curves.

3.2.4. Group 4: micropollutants with low or no accumulation kinetics curve

Five molecules were characterized by a very low or no accumulation in the POCIS receiving phase (Table 2). The POCIS is not designed to sample such micropollutants.

As with group 3, these micropollutants can be polar or apolar (log K_{ow} from -0.46 to 6.35), and neutral or ionized in tap water at pH=7.6.

Four of these 5 micropollutants, RSDs of tap water concentrations were higher than 30%, and three (n-octylphenol, n-nonylphenol and tamoxifen, DT50 < 3 h) are known to degrade in tap water under our renewal conditions, which may explain their very low or no accumulation rates.

3.2.5. Accumulation kinetics compared against the literature

There are already literature reports of accumulation kinetics studied in-lab with “pharmaceutical” POCIS for 29 out of our 56 micropollutants of interest. However, the great majority of authors only show linear or curvilinear accumulation curves, notable exceptions being MacLeod *et al.* [7] and Harman *et al.* [13]. We cannot find any author taking time to discuss atypical accumulation (with inflexion point, random or low) and the consequences on R_s calculation. For comparison, Table 3 reports kinetic curves data studied in the literature.

Insert Table 3

The 17 group-1 micropollutants studied in the literature always showed linear accumulation, thus confirming our findings. Nevertheless, some of these micropollutants were exposed for only 8 days (t-butylphenol, metoprolol, propranolol and linuron) and their accumulations were drawn with only 4 samples, which is not enough to correctly estimate the $t_{1/2}$. It is important to have a lot of datapoints, especially at the beginning of the calibration, to be able to refine the line of the kinetics accumulation. MacLeod *et al.* [7], Harman *et al.* [13] and Martinez-Bueno *et al.* [16] reported nonlinear accumulation curves for a few micropollutants (from groups 2, 3 and 4, and including antibiotics and some alkylphenols) but did not discuss potential explanations for these atypical accumulation patterns nor the consequence on R_s calculation. Finally, contrary to our results, MacLeod *et al.* [7], Li *et al.* [14] and Bartelt-Hunt *et al.* [11] all found linear kinetic accumulations for anti-inflammatories and betablockers. This divergence may be explained by their different calculation methods (measuring decreasing concentrations in water instead of increasing concentrations in POCIS) and calibration systems (beaker or bottle and distilled water).

3.3. Sampling rates (R_s)

One essential point for accurately calculating R_s is to be in the kinetic regime of the POCIS. Thus, for group-1 molecules, we calculated R_s using the slope of the line $CF=f(t)$ until their respective $t_{1/2}$, as explained in the experimental section. For group-2 molecules, we calculated sampling rates at day 14 using equation [4], with a possible bias since the duration of the kinetic regime was not well-defined in this case. Note that it was not possible to calculate any sampling rates for group-3 or group-4 molecules because they were randomly, poorly or not at all accumulated.

We compiled calculated R_s in Table 4 and compared them against R_s values reported in the literature when obtained with the same kind of POCIS (“pharmaceutical” POCIS with 45.8 cm² surface and 200 mg of receiving phase) and in the same conditions (under agitation and at between 15 and 25°C). Sampling rates varied from 0.025 L/d for atenolol up to 0.398 for t-butylphenol. Our study produced 16 laboratory R_s now published for the first time here.

Insert Table 4

The POCIS is a useful tool for sampling herbicides, hormones, some alkylphenols, some pharmaceuticals like benzodiazepines, and the UV filter. Indeed, for these micropollutants (group 1), the kinetic regime is equal to or higher than 14 days, which is a comfortable duration for using the POCIS *in situ* to determine TWA concentrations. If the POCIS is immersed just for 7 days, it can be useful for betablockers with $\log K_{ow} > 1.34$ ($t_{1/2}$ between 7 and 14 days; group 1). We assume that POCIS are suitable for some antibiotics, anti-inflammatories, and hydrophilic betablockers with R_s calculated from the triplicate at 14 days (group 2). For group-3 micropollutants, the POCIS is only suitable for screening. For group-4 molecules, the POCIS is simply not suitable.

Compared to the R_s from authors using the same kind of calibration system (i.e. aquaria with a flow velocity arriving directly at the front of the POCIS; Mazzella *et al.* [10] and Lissalde *et al.* [15]), our R_s values are generally less than 2-fold different. Our R_s were also close (i.e. less than 2 fold-different) to reported values for hydrophobic molecules ($\log K_{ow} > 2.65$), except Li *et al.* [14] who obtained significantly higher R_s than ours (or than those reported in the literature), including up to 11-fold higher values for sulfamethoxazole. As stated earlier, this can be explained by the different calculation method and calibration system used, which further underlines the critical need to define standardized protocols to obtain comparable sampling rates [6].

3.4. Is it possible to predict R_s from micropollutant physical-chemical properties?

We found a quadratic correlation between R_s and $\log D$ for betablockers, herbicides and hormones, as illustrated in Figure 4. We used this parameter because it takes into account the hydrophobic-hydrophilic character ($\log K_{ow}$) of a micropollutant as well as its potential charge (pKa). Other studies have also attempted to find correlations to explain R_s values, but with $\log K_{ow}$ and not $\log D$ [8, 10, 26].

Insert Figure 4

Figure 4 shows increasing R_s values as a function of $\log D$ for betablockers, herbicides and hormones. However, the line of the curve is not the same for a given family, and reached a plateau for the betablockers ($\log D$ 0.0-0.5), herbicides ($\log D$ 2.5-3.5) and hormones ($\log D$

3.5-4.5) families. The range of R_s can be predicted as a function of log D for some but not all micropollutants, which suggests that other physical-chemical properties also need to be considered.

4. Conclusion

We report a calibration experiment that is reliable and robust in terms of constant values for micropollutant concentrations in tap water, flow velocities and additional parameters (temperature, pH, conductivity, dissolved organic carbon concentration). This system allowed us to study the accumulation of 56 organic micropollutants using the “pharmaceutical” POCIS for up to 28-day exposure periods. We distinguished 4 different types of accumulation curves: curvilinear (group 1), with inflexion point (group 2), random (group 3), and no or low accumulation (group 4). It was possible to calculate well-defined R_s for 43 micropollutants, of which 16 are new R_s published here for the first time. R_s for these 43 micropollutants varied from 0.025 to 0.398 L/d. Nevertheless, the sampling rates of 2,4-dichlorophenol and *t*-octylphenol have to be validated because of suspected matrix effects in tap water for both micropollutants and high lag time (3 days) coupled to short kinetic regime ($t_{1/2} = 5$ days) for 2,4-dichlorophenol.

The POCIS is particularly suitable for sampling neutral micropollutants (included in group 1) with log K_{ow} ranging from 2.5 to 5, such as hormones, pesticides or several pharmaceuticals. Indeed, the kinetic regime for this type of molecule is higher than or equal to 14 days, which is suitable for *in situ* application of POCIS to evaluate TWA water concentrations. POCIS can also produce TWA concentrations for more hydrophilic (with log K_{ow} as low as -0.34) and ionized micropollutants such as antibiotics, anti-inflammatories and betablockers (included in groups 1 and 2). However, POCIS is only suitable for screening for micropollutants with random accumulation (e.g. thiram, roxithromycin, group 3), and is not at all suitable for micropollutants with very low or no accumulation (e.g. metronidazole, tamoxifen, group 4).

To our knowledge, this is the first paper dealing with POCIS-derived accumulation curves with an inflexion point. There is a need to determine a model which better described this type of accumulation. Moreover, it would be interesting to better understand the underlying processes involved in POCIS accumulation of these micropollutants (large burst

586 effect, two biphasic accumulation phenomena, multi-layer adsorption are candidates).
587 Analysis of the POCIS membranes could give clues.

588 Finally, it is difficult to predict R_s as a function of the physical-chemical properties of
589 target molecules, except for betablockers, herbicides and hormones with log D. This point
590 should be a direction for further research.

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Fig. 1. Schematized flow-through calibration system for POCIS exposure.

Table 1

Mean values for temperature, pH, conductivity, DOC and flow velocity in the two aquaria, and their associated variability (RSD).

	Temperature (°C) (n=12)	pH (n=14)	Conductivity (μs/cm) (n=14)	DOC (mg/L) (n=12)	Flow velocity (cm/s) (n=63)
Mean	20.7	7.6	429	10.1	11
RSD (%)	3	6	1	17	23

Fig. 2. Mean spiked tap water concentrations of the 56 studied micropollutants (n=74 for betablockers and estrogens i.e. E1, α -E2, β -E2, E3, EE2; n=24 for others) across both aquaria. Micropollutants are grouped by family and by increasing log K_{ow} . The bold dashed line represents the nominal value. Asterisks flag molecules degraded in tap water with 35% renewal per day (based on data from previous experiments).

Fig. 3. The 4 types of micropollutant accumulation in the POCIS receiving phase, illustrated by a: propranolol (group 1), b: diclofenac (group 1), c: atenolol (group 2), d: ketoprofen (group 2), e: salicylic acid (group 3), f: roxithromycin (group 3), g: paracetamol (group 4), h: tamoxifen (group 4).

Table 2

Characteristics of the 56 micropollutants. Micropollutants are classified according to type of accumulation curve (groups 1-4) and by increasing $t_{1/2}$ followed by increasing $\log K_{ow}$.

Group	Micropollutant	$t_{1/2}$ (day)	$\log K_{ow}^a$	$\log D$ (pH=7.6)	pKa ^a	Ionization (pH=7.6)	Molar mass ^a (g/mol)
1 (curvilinear accumulation)	2,4-DCP*	5	2.88	2.49	7.44	-	163.0
	Prop	7	2.58	0.51	9.67	+	269.3
	Ace	8	1.53	-0.44	9.57	+	336.4
	Tim	9	1.34	-0.82	9.76	+	316.4
	Oxp	9	2.17	0.01	9.67	+	265.3
	Bet	10	2.54	0.47	9.67	+	307.4
	t-BP*	10	3.21	3.21	10.24	Neutral	150.1
	Met	11	1.76	-0.31	9.67	+	267.4
	Bis	11	2.20	0.13	9.67	+	325.4
	Lin*	14	2.68	2.68	11.94	Neutral	249.1
	Oxa	15	2.92	2.92	10.61 and 12.47	Neutral	286.7
	Diclof	19	4.26	0.66	4.0	-	296.1
	T	20	3.37	3.37	/	Neutral	288.4
	Diu	22	2.53	2.53	13.18	Neutral	233.1
	Lora	23	3.53	3.53	10.61 and 12.46	Neutral	321.2
	Atra	30	2.2	2.2	3.20	Neutral	215.7
	t-OP*	32	4.69	4.69	10.23	Neutral	206.3
	Ala	33	3.59	3.59	/	Neutral	269.8
	Acet	35	3.50	3.50	/	Neutral	269.8
	b-E2	35	3.75	3.75	10.33	Neutral	272.4
	MegA*	50	3.72	3.72	/	Neutral	384.5
	E1*	50	4.31	4.31	10.33	Neutral	270.4
	a-E2	53	3.75	3.75	10.33	Neutral	272.4
	Carba	69	2.77	2.77	/	Neutral	236.3
	EE2*	99	3.90	3.90	10.33	Neutral	296.4
	Pro*	347	3.62	3.62	2.75	Neutral	376.7
	BPA	347	4.04	4.04	9.78 and 10.39	Neutral	228.3
	3,4-D*	693	2.35	2.35	2.78	Neutral	162.0
	P*	693	4.15	4.15	/	Neutral	314.5

	4-MBC*	693	5.12	NA	NA	Neutral	254.4
2 (accumulation with an inflexion point)	Sot	?	-0.40	-2.24	9.43	+	272.4
	Ate	?	0.43	-1.64	9.67	+	266.3
	Sulfa	?	0.79	0.52	7.66	Neutral	253.3
	Nad	?	0.87	-1.29	9.76	+	309.4
	Trim	?	1.28	1.15	7.16	Neutral	290.3
	Furo	?	1.75	-1.60	4.25	-	330.7
	Carb	?	1.80	1.80	4.28 and 9.70	Neutral	191.2
	2.4-D acid	?	2.50	-2.29	2.96	-	184.1
	E3	?	2.67	2.67	10.33	Neutral	288.4
	Napro	?	2.99	-0.42	4.19	-	230.3
	Keto	?	3.61	-0.11	3.88	-	254.3
	Ibu	?	3.84	1.09	4.85	-	206.3
	Beza	?	3.99	0.22	3.83	-	361.8
3 (random accumulation)	Oflo	?	0.65	-1.50	5.45 and 6.20	-	361.4
	Res	?	1.37	1.37	9.26 and 10.73	Neutral	110.1
	Sala	?	1.98	-2.83	2.79 and 13.23	-	138.1
	Ipr*	?	2.29	2.29	12.69 and 13.63	Neutral	330.2
	Thi	?	2.73	2.73	/	Neutral	240.4
	Roxi	?	3.00	1.51	2.29 and 9.08	+	837.0
	Feno*	?	5.28	5.28	/	Neutral	360.8
	t-NP	?	5.44	5.44	/	Neutral	220.4
4 (low or no accumulation)	Metro	?	-0.46	-0.46	3.09	Neutral	171.2
	Para	?	0.91	0.91	9.46	Neutral	151.2
	4-n-OP	?	5.30	5.30	10.31	Neutral	206.3
	4-n-NP	?	5.74	5.74	10.31	Neutral	220.4
	Tamo	?	6.35	5.16	8.76	+	371.5

^a: Source: <http://www.chemicalize.org>

*: Micropollutant with lag time

Table 3

Comparison of kinetic accumulation curves for “pharmaceutical” POCIS.

Molecules are grouped by family and by increasing log K_{ow} .

Molecule (group)	Family	Type of accumulation	Reference
t-Butylphenol (1)	Alkylphenols and phenols	Linear over 10 days ($t_{1/2}=10$ d)	This study ^a
		Linear over 28 days ($r^2 = 0.88$)	[13] ^b
		Linear over 28 days ($t_{1/2}=693$ d)	This study ^a
Bisphenol A (1)		Linear over 28 days	[8] ^c
		Linear over 10 days ($r^2 > 0.97$)	[18] ^d
		No accumulation over 28 days	This study ^a
n-Octylphenol (4)		Linear over 28 days	[8] ^c
		No accumulation over 28 days	[13] ^b
n-Nonylphenol (4)		No accumulation over 28 days	This study ^a
		No accumulation over 28 days	[13] ^b
		Linear over 28 days ($t_{1/2}=32$ d)	This study ^a
t-Octylphenol (1)	Antibiotics	Linear over 28 days	[8] ^c
		Linear over 28 days ($r^2 = 0.63$)	[13] ^b
Metronidazole (4)		Low	This study ^a
		Logarithmic ($r^2 = 0.70$)	[16] ^g
		With an inflexion point	This study ^a
		Linear over 25 days	[7] ^h
Sulfamethoxazole (2)		Logarithmic ($r^2 = 1.00$)	[16] ^g
		Linear over 8 days	[14] ⁱ
		Linear over 28 days ($r^2 = 0.82$)	[11] ^j
		With an inflexion point	This study ^a
Trimethoprim (2)	Anti-inflammatory	Not linear	[7] ^h
		Logarithmic ($r^2 = 1.00$)	[16] ^g
		Linear over 8 days	[14] ⁱ
Roxithromycin (3)		Random	This study ^a
		Linear over 25 days	[7] ^h
		With an inflexion point	This study ^a
Naproxen (2)		Linear over 25 days	[7] ^h
		Linear over 8 days	[14] ⁱ
Ketoprofen (2)		With an inflexion point	This study ^a
		Linear over 25 days	[7] ^h

Ibuprofen (2)		With an inflexion point	This study ^a
		Linear over 25 days	[7] ^h
		Linear over 8 days	[14] ⁱ
		Linear over 28 days ($r^2 = 0.82$)	[11] ^j
Sotalol (2)		With an inflexion point	This study ^a
		Linear over 8 days	[14] ⁱ
Atenolol (2)		With an inflexion point	This study ^a
		Linear over 25 days	[7] ^h
		Linear over 8 days	[14] ⁱ
Nadolol (2)	Betablockers	With an inflexion point	This study ^a
		Linear over 8 days	[14] ⁱ
Metoprolol (1)		Linear over 11 days ($t_{1/2}=11$ d)	This study ^a
		Linear over 25 days	[7] ^h
		Linear over 8 days	[14] ⁱ
Propranolol (1)		Linear over 7 days ($t_{1/2}=7$ d)	This study ^a
		Linear over 25 days	[7] ^h
		Linear over 8 days	[14] ⁱ
Carbamazepine (1)		Linear over 28 days ($t_{1/2}=69$ d)	This study ^a
		Linear over 25 days	[7] ^h
		Linear over 8 days	[14] ⁱ
		Linear over 28 days ($r^2 = 0.77$)	[11] ^j
Atrazine (1)		Linear over 28 days ($t_{1/2}=30$ d)	This study ^a
		Linear over 21 days ($r^2 > 0.92$)	[10] ^e
		Linear over 7 days ($r^2 > 0.97$)	[16] ^g
		Linear over 28 days ($r^2 = 0.71$)	[11] ^j
		Linear over 24 days ($r^2 > 0.92$)	[15] ^f
Diuron (1)	Herbicides	Linear over 22 days ($t_{1/2}=22$ d)	This study ^a
		Linear over 21 days ($r^2 > 0.92$)	[10] ^e
		Linear over 7 days ($r^2 > 0.97$)	[16] ^g
Linuron (1)		Linear over 24 days ($r^2 > 0.92$)	[15] ^f
		Linear over 14 days ($t_{1/2}=14$ d)	This study ^a
		Linear over 21 days ($r^2 > 0.92$)	[10] ^e
		Linear over 24 days ($r^2 > 0.92$)	[15] ^f

Acetochlor (1)		Linear over 28 days ($t_{1/2}=35$ d)	This study ^a
		Linear over 21 days ($r^2 > 0.92$)	[10] ^c
		Linear over 24 days ($r^2 > 0.92$)	[15] ^f
Alachlor (1)		Linear over 28 days ($t_{1/2}=33$ d)	This study ^a
		Linear over 28 days ($r^2 = 0.77$)	[11] ^j
		Linear over 24 days ($r^2 > 0.92$)	[15] ^f
Estriol (2)		With an inflexion point	This study ^a
		Linear over 28 days	[8] ^c
		Linear over 28 days ($r^2 = 0.87$)	[11] ^j
α -Estradiol (1)		Linear over 28 days ($t_{1/2}=53$ d)	This study ^a
		Linear over 28 days	[8] ^c
		Linear over 28 days ($r^2 = 0.91$)	[11] ^j
β -Estradiol (1)		Linear over 28 days ($t_{1/2}=35$ d)	This study ^a
		Linear over 28 days	[8] ^c
		Linear over 10 days ($r^2 > 0.97$)	[18] ^d
Hormones		Linear over 28 days ($r^2 = 0.91$)	[11] ^j
		Linear over 28 days ($t_{1/2}=99$ d)	This study ^a
		Linear over 28 days	[8] ^c
Ethinylestradiol (1)		Linear over 10 days ($r^2 > 0.97$)	[18] ^d
		Linear over 28 days ($r^2 = 0.81$)	[11] ^j
		Linear over 28 days ($t_{1/2}=693$ d)	This study ^a
Progesterone (1)		Linear over 28 days ($r^2 = 0.91$)	[11] ^j
		Linear over 28 days ($t_{1/2}=50$ d)	This study ^a
		Linear over 28 days	[8] ^c
Estrone (1)		Linear over 10 days ($r^2 > 0.97$)	[18] ^d
		Linear over 28 days ($r^2 = 0.88$)	[11] ^j

688 ^a: Flow-through, aquarium (tap water, 50 L, 3 $\mu\text{g/L}$, 21°C, 10 cm/s), POCIS analysis at t = 1, 3, 6, 12 h and 1, 3,
689 7, 14, 21, 28 d, kinetic accumulation drawn by measurement in the POCIS receiving phase

690 ^b: Flow-through, aquarium (seawater, 200 L, 0.050-0.120 $\mu\text{g/L}$, 10°C, 100 rpm), POCIS analysis at t = 7, 14, 21,
691 28 d, kinetic accumulation drawn by measurement in the POCIS receiving phase

692 ^c: Static renewal, beaker (distilled water, 1 L, 0.5 $\mu\text{g/L}$, 23.5°C, 350 rpm), POCIS analysis at t = 7, 14, 28 d,
693 kinetic accumulation drawn by measurement in the POCIS receiving phase

694 ^d: Flow-through, aquarium (distilled water, 30 L, 0.01 to 1 $\mu\text{g/L}$, 15°C, ? cm/s), POCIS analysis at t = 1, 2, 3, 4,
695 5, 6, 7, 8, 9, 10 d, kinetic accumulation drawn by measurement in the POCIS receiving phase

696 ^e: Static, aquarium (tap water with 2 μM CuSO_4 , 80 L, 1-2 $\mu\text{g/L}$, 17°C, 2-3 cm/s), POCIS analysis at t = 5, 10,
697 15, 21 d, kinetic accumulation drawn by measurement in the POCIS receiving phase

698 ^f: Static renewal, aquarium (tap water, 80 L, 1 $\mu\text{g/L}$, 17°C, 2-3 cm/s), POCIS analysis at t = 6, 12, 18, 24 d,
699 kinetic accumulation drawn by measurement in the POCIS receiving phase

700 ^g: Static renewal, beaker (seawater, 2 L, 0.5 $\mu\text{g/L}$, 21°C, ? rpm), POCIS analysis at t = 1, 3, 7 d, kinetic
701 accumulation draw by measurement in the POCIS receiving phase

702 ^h: Static renewal, beaker (distilled water, 3 L, 1 $\mu\text{g/L}$, 28°C, 12 cm/s), POCIS analysis at t = ? (total exposure
703 duration 25 d), kinetic accumulation drawn by measurement decreases in distilled water

704 ⁱ: Static, bottle (distilled water, 3 L, 2-10 µg/L, 25°C, 800-900 rpm), POCIS analysis at t = ? (total exposure
705 duration 8 d), kinetic accumulation drawn by measurement decreases in distilled water
706 ^j: Static, beaker (distilled water, 2 L, 5 µg/L, 25°C, 450 cm/s), POCIS analysis at t = 28 d, kinetic accumulation
707 drawn by measurement decreases in distilled water
708

Table 4

Sampling rates (R_s) calculated for the 56 studied micropollutants and comparison against literature data (micropollutants grouped by families and by increasing log K_{ow}). Comparison performed only when studies used the same POCIS configuration and the same calibration conditions as here. Micropollutants in bold characters correspond to unpublished literature R_s .

Molecule (group)	Family	Log K_{ow}	R_s (L/d)	R_s from literature (L/d)	Difference (%)	Reference
Res (3)	Alkylphenols and phenols	1.37	a	b		
2,4-DCP (1)		2.88	0.068 (± 0.005)	b		
t-BP (1)		3.21	0.398 (± 0.044)	0.120	-70	[27]
BPA (1)		4.04	0.245 (± 0.006)	0.170	-57	[13]
t-OP (1)		4.69	0.065 (± 0.005)	0.117 (± 0.019)	-52	[8]
t-NP (3)		5.44	a	0.835 (± 0.058)	240	[14]
n-OP (4)		5.35	a	0.1204 (± 0.0110)	85	[8]
n-NP (4)		5.74	a	0.117 (± 0.012)		[8]
				2.459 (± 0.131)		[14]
Metro (4)	Antibiotics	-0.46	a	b		
Oflo (3)		0.65	a	b		
Sulfa (2)		0.79	0.030 (± 0.003)	0.339 (± 0.057)	1015	[14]
Trim (2)		1.28	0.162 (± 0.014)	0.118 (± 0.012)	288	[11]
Roxi (3)		3.00	a	0.436 (± 0.006)	169	[14]
				0.360 (± 0.210)	122	[7]
Sala (3)	Anti-inflammatories	1.98	a	b		
Napro (2)		2.99	0.084 (± 0.011)	0.723 (± 0.430)		[7]
Keto (2)		3.61	0.118 (± 0.007)	0.392 (± 0.024)	368	[14]
Ibu (2)		3.84	0.118 (± 0.006)	0.116 (± 0.053)	38	[7]
Diclof (1)		4.26	0.225 (± 0.009)	0.135 (± 0.035)	11	[7]
				0.348 (± 0.052)	181	[14]
	Benzodiazepines			0.400 (± 0.008)	223	[11]
Oxa (1)		2.92	0.226 (± 0.009)	0.166 (± 0.052)	-26	[7]
Lora (1)		3.53	0.205 (± 0.006)	0.170	-24	[26]
Sot (2)		-0.40	0.036 (± 0.008)	b		
Ate (2)		0.43	0.025 (± 0.005)	0.151 (± 0.021)	386	[14]
Nad (2)		0.87	0.114 (± 0.009)	0.094 (± 0.015)	331	[14]
Tim (1)	Betablockers	1.34	0.210 (± 0.012)	0.040 (± 0.070)	84	[7]
Ace (1)		1.53	0.166 (± 0.008)	0.447 (± 0.036)	299	[14]
Met (1)		1.76	0.195 (± 0.012)	b		
				0.465 (± 0.039)	138	[14]
				0.599 (± 0.270)	206	[7]

Oxp (1)		2.17	0.185 (± 0.010)	b		
Bis (1)		2.20	0.161 (± 0.008)	b		
Bet (1)		2.54	0.217 (± 0.010)	b		
Prop (1)		2.58	0.165 (± 0.009)	0.917 (± 0.084)	455	[14]
				0.980 (± 0.345)	493	[7]
Beza (2)	Lipopenics	3.99	0.146 (± 0.034)	b		
Feno (3)		5.28	a	b		
Para (4)		0.91	a	0.020	80	[26]
Furo (2)	Other	1.75	0.129 (± 0.007)	b		
	pharmaceuticals			0.348 (± 0.116)	86	[7]
Carba (1)		2.77	0.188 (± 0.005)	0.400	113	[26]
				0.561 (± 0.024)	199	[14]
				0.288 (± 0.009)	54	[11]
Carb (2)		1.80	0.213 (± 0.004)	b		
Ipr (3)	Fongicides	2.29	a	b		
Thi (3)		2.73	a	b		
Pro (1)		3.62	0.208 (± 0.004)	0.098	-53	[5]
2,4-D (2)		2.50	0.044 (± 0.009)	0.092	111	[5]
				0.240	27	[5]
				0.042	-78	[9]
Atra (1)		2.20	0.189 (± 0.006)	0.228 (± 0.041)	21	[15]
				0.214	13	[16]
				0.239 (± 0.008)	26	[10]
3,4-D (1)	Herbicides	2.35	0.241 (± 0.038)	b		
				0.199 (± 0.038)	1	[15]
Diu (1)		2.53	0.198 (± 0.005)	0.086	-56	[16]
				0.247	25	[10]
Lin (1)		2.68	0.182 (± 0.008)	0.204 (± 0.037)	12	[15]
				0.236	30	[10]
Acet (1)		3.50	0.195 (± 0.006)	0.241 (± 0.034)	23	[15]
				0.225	15	[10]
Ala (1)		3.59	0.192 (± 0.006)	0.205 (± 0.004)	7	[15]
E3 (2)		2.67	0.185 (± 0.009)	0.157 (± 0.004)	-4	[8]
T (1)		3.37	0.280 (± 0.007)	b		
MegA (1)		3.72	0.265 (± 0.005)	b		
a-E2 (1)		3.75	0.239 (± 0.014)	0.122 (± 0.003)	-49	[8]
				0.115 (± 0.014)	-48	[8]
b-E2 (1)	Hormones	3.75	0.221 (± 0.013)	0.693 (± 0.092)	214	[14]
				0.129	-42	[28]
				0.222 (± 0.053)	-15	[8]
EE2 (1)		3.9	0.260 (± 0.013)	0.180	-31	[9]
				0.853 (± 0.143)	227	[14]
P (1)		4.15	0.346 (± 0.008)	b		
E1 (1)		4.31	0.230 (± 0.012)	0.120 (± 0.018)	-48	[8]
				0.150	-35	[9]

				0.699 (± 0.087)	204	[14]
Tamo (4)		6.35	a	b		
4-MBC (1)	UV filter	5.12	0.215 (± 0.004)	b		

714 ^a: not calculated because randomly or poorly accumulated in the POCIS (i.e. qualifying
715 as group-3 or group-4 molecules).

716 ^b: never determined with this POCIS configuration and in these conditions.

717

Fig. 4. Sampling rate (R_s) versus log D for a) betablockers, herbicides and hormones, b) betablockers only, c) herbicides only, d) hormones only.