

In Situ Calibration of a New Chemcatcher Configuration for the Determination of Polar Organic Micropollutants in Wastewater Effluent

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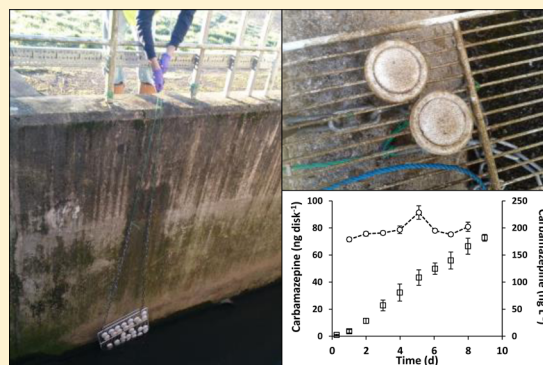
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S Supporting Information

ABSTRACT: Passive sampling is proposed as an alternative to traditional grab- and composite-sampling modes. Investigated here is a novel passive sampler configuration, the Chemcatcher containing an Atlantic HLB disk covered by a 0.2 μm poly(ether sulfone) membrane, for monitoring polar organic micropollutants (personal care products, pharmaceuticals, and illicit drugs) in wastewater effluent. In situ calibration showed linear uptake for the majority of detected micropollutants over 9 days of deployment. Sampling rates (R_S) were determined for 59 compounds and were generally in the range of 0.01–0.10 L day^{-1} . The Chemcatcher was also suitable for collecting chiral micropollutants and maintaining their enantiomeric distribution during deployment. This is essential for their future use in developing more accurate environmental risk assessments at the enantiomeric level. Application of calibration data in a subsequent monitoring study showed that the concentration estimated for 92% of micropollutants was within a factor of 2 of the known concentration. However, their application in a legislative context will require further understanding of the properties and mechanisms controlling micropollutant uptake to improve the accuracy of reported concentrations.



1. INTRODUCTION

The presence of polar organic micropollutants (e.g., personal care products, pharmaceuticals, and illicit drugs) in the aquatic environment is of concern due to their unknown long-term effects on aquatic life and on human health. Their concentrations have been reported in U.K. surface waters ranging from low ng L^{-1} levels up to $\sim 10 \mu\text{g L}^{-1}$.¹ The main route of entry into the environment for these micropollutants is from the discharge of effluent from wastewater treatment works (WWTWs). Consequently, monitoring wastewater effluent for micropollutants is essential to assess the possible risk to the receiving environment.

Traditionally, active sampling has been used to monitor polar organic micropollutants in wastewater and surface water.² This includes grab or spot sampling as well as a 24 h composite sampling (time-, volume-, or flow-proportional). However, passive samplers are proposed as a lower-cost, easy-to-use alternative.^{3–6} Passive sampling relies on the transport of micropollutant from the sampled matrix to a receiving phase within a sampling device. This is a result of the difference between chemical potentials of the micropollutant in the two types of media.⁷ Chemical potential in this case is the difference

in the physicochemical properties of the micropollutants under investigation and the resultant movement by absorption or adsorption of compounds from an unfavorable (bulk-water phase) to a more favorable medium (receiving phase). Passive samplers can be used to estimate time-weighted average concentrations for comparatively long time periods (≥ 7 days). However, for this to be successful, sampling rates (R_S) of each micropollutant must be known for the sampler applied. This has limited the use of passive sampling for quantitative analysis because R_S derived in the laboratory (typically using clean water spiked with the micropollutants under investigation) do not represent what is observed in the field.³

In situ calibration is recommended for determining representative R_S because it can be conducted in the exact location where future measurements are to be taken.⁸ Relative to laboratory calibrations, very few in situ calibrations have been

Received: May 6, 2016

Revised: July 20, 2016

Accepted: August 5, 2016

Published: August 5, 2016

performed for polar organic micropollutants in aquatic matrices,^{3–6} mainly due to the considerable amount of effort they demand. However, this approach is considered essential for quantitative purposes because it accounts for site-specific factors (e.g., matrix composition) that cannot be adequately replicated under laboratory conditions. Once calibrated in situ, the determined R_S can be applied to estimate micropollutant concentrations in future studies at the same site. In situ calibration offers other advantages as an extensive experimental laboratory setup need not be required and maintained.⁸ Moreover, it avoids the need to purchase relatively large quantities of target micropollutants for laboratory experiments, which may be cost-prohibitive.⁹

There is also debate whether or not R_S can be predicted for polar organic micropollutants using physicochemical properties. Ideally, R_S could be determined on the basis of micropollutant-specific properties such as $\log K_{OW}$ or $\log D_{OW}$.⁶ This could avoid the requirement to undertake future calibration studies. To date, this has not been possible for polar organic micropollutants, partly due to the lack of field-derived R_S available for a high-enough number of compounds using a standardized sampling approach. Nevertheless, Moschet et al.⁶ did report a weak relationship ($r^2 = 0.37$) between field R_S (river water) and $\log D_{OW}$ for 88 micropollutants.

Another emerging area of environmental research is chirality. Approximately half of all drugs are chiral and exist as two or more enantiomers.¹⁰ These tend to be dispensed as racemic mixtures (equimolar concentrations of each enantiomer). However, they are subject to stereoselective mechanisms within the human body and during wastewater treatment. Consequently, enrichment of one enantiomer is normally observed in wastewater effluent and in the environment. This is significant because enantiospecific toxicity is observed for some chiral micropollutants.^{11–13} Reporting chiral micropollutants at the enantiomeric level is essential for developing more-accurate environmental risk assessments. To date, passive samplers have not been assessed for their ability to describe the enantiomeric distribution of chiral micropollutants. Due to their length of deployment, it is possible that stereoselective changes in chiral micropollutant composition could occur.

There are two general passive sampler configurations available for monitoring polar organic micropollutants: the polar organic compound integrative sampler (POCIS) containing Oasis hydrophilic–lipophilic balance (HLB) as a loose powder, and the Chemcatcher, typically containing a styrenedivinylbenzene adsorbent bound in a PTFE matrix disk.⁶ The exposed surface of the sorbent is normally covered with a thin poly(ether sulfone) (PES) membrane. Using the HLB sorbent is an obvious choice for the receiving material because it is the preferred sorbent for analytical methods involving extracting a broad range of polar organic micropollutants in grab or composite water samples.^{14–16} This has been demonstrated in numerous previous studies using POCIS (≥ 21), with >90 individual pharmaceuticals detected.⁸ However, the Chemcatcher configuration is easier to use and handle. Using the Chemcatcher with a HLB receiving phase is desirable because it combines the proven ability of HLB as a sorbent for a broad range of polar organic micropollutants with the handling benefits of the Chemcatcher. This study investigated the use of the Chemcatcher containing an Atlantic HLB disk in wastewater effluent for the first time. To help address the suitability of this sampler configuration for monitoring polar organic micropollutants in wastewater effluent, the objectives of this study were to:

- (i) assess the Chemcatcher containing an Atlantic HLB disk for the uptake of a broad range of polar organic micropollutants and to determine their field R_S in wastewater effluent by in situ calibration;
- (ii) investigate whether $\log K_{OW}$ or $\log D_{OW}$ can be used as a reasonable predictor of field R_S in wastewater effluent;
- (iii) measure the accuracy of micropollutant concentrations determined in a future study using the field calibration data; and
- (iv) establish the suitability of the Chemcatcher for describing the enantiomeric distribution of chiral micropollutants.

This was achieved by deploying Chemcatcher samplers in effluent wastewater of a trickling filter WwTW in southwest England while simultaneously undertaking 24 h composite sampling. A total of 88 micropollutants were investigated using a fully quantitative ultraperformance liquid chromatography tandem mass spectrometry (UPLC–MS/MS) method. Enantioselective analysis was also performed to determine the enantiomeric distribution of selected chiral micropollutants.

2. MATERIALS AND METHODS

2.1. Materials. Information on 88 micropollutants studied are detailed in Table S1. These are representative of highly prescribed pharmaceuticals, over-the-counter medications, known endocrine disruptors, and illicit drugs.¹ The internal standards acetaminophen-D4, ibuprofen-D3, bisphenol A-D16, carbamazepine-13C6, ketoprofen-D3, naproxen-D3, sertraline-D3, tamoxifen-13C2–15N, propranolol-D7, atenolol-D5, and metformin (dimethyl-D6) were purchased from Sigma-Aldrich (Gillingham, UK). Bezafibrate-D6 was obtained from QMX laboratories (Thaxted, UK). Methylparaben-13C, amphetamine-D5, methamphetamine-D5, 3,4-methylenedioxy-methamphetamine-D5 (MDMA-D5), 3,4-methylenedioxy-amphetamine-D5 (MDA-D5), heroin-D9, codeine-D6, ketamine-D4, cocaine-D3, benzoylcegonine-D8, 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine-D3 (EDDP-D3), morphine-D3, cotinine-D3, cocaine-D8, temazepam-D5, 1S,2R-(+) ephedrine-D3, mephedrone-D3, methadone-D9, norketamine-D4, estrone (2,4,16,16-D4), estradiol (2,4,16,16-D4), and quetiapine-D8 hemifumurate were purchased from LGC standards (Middlesex, UK). Citalopram-D6, metoprolol-D7, fluoxetine-D5, and mirtazapine-D3 were obtained from TRC (Toronto, Canada).

Methanol (MeOH) and toluene were HPLC-grade and purchased from Sigma-Aldrich. Water (H₂O) was of 18.2 MΩ quality (Elga, Marlow, UK). Glassware was deactivated using 5% dimethylchlorosilane in toluene (Sigma-Aldrich) to mitigate the loss of basic chemicals onto –OH sites present on glass surfaces. Ammonium acetate (NH₄OAc), ammonium fluoride (NH₄F), and acetic acid (CH₃COOH, 1.0 M) used in the preparation of mobile phases were purchased from Sigma-Aldrich. Oasis HLB (60 mg, 3 mL) solid-phase extraction (SPE) cartridges were purchased from Waters (Manchester, UK). Whatman GF/F glass fiber membranes (0.7 μm) were obtained from Sigma-Aldrich. Atlantic HLB–L disks (47 mm) containing Oasis HLB sorbent were purchased from ARC Sciences (Alton, UK). Supor poly(ether sulfone) (PES) 0.2 μm membrane filters (90 mm) were obtained from Sigma-Aldrich. These were cut to 49 mm circles using a wad punch (KS Tools, Heusenstamm, Germany). The Chemcatcher samplers comprised three PTFE components; the main body, a retaining screw to hold the 47 mm receiving-phase disk in place, and a protective cover for transport (see Figure S1).

2.2. Analytical Methods. **2.2.1. Extraction of Composite Samples.** Liquid samples were filtered through 0.7 μm glass fiber membranes and 50 mL aliquots spiked with 50 ng of all surrogate and internal standards. These were loaded onto preconditioned Oasis HLB cartridges (2 mL of MeOH and 2 mL of H_2O) at 5 mL min^{-1} , dried under a vacuum, and eluted under gravity using MeOH (4 mL). Extracts were then dried under nitrogen at 40 $^\circ\text{C}$ and reconstituted in 500 μL of $\text{H}_2\text{O}/\text{MeOH}$ (80:20 v/v). Samples for analysis by direct injection (400 μL) were spiked with 50 ng of selected surrogate and internal standards and adjusted to 500 μL with MeOH.¹⁵

2.2.2. Preparation and Extraction of Atlantic HLB Disks. Atlantic HLB disks were conditioned with MeOH (50 mL) followed by H_2O (50 mL) and then dried. These were then placed on the Chemcatcher body, a pre-cleaned PES membrane was placed on top, and the retaining ring was screwed on. These were then stored at 4 $^\circ\text{C}$ for a maximum of 12 h until deployment. After deployment, collected samples were dried under vacuum and frozen until extraction. Disks were then brought to room temperature, extracted under gravity using MeOH (40 mL), and spiked with 50 ng of all surrogate and internal standards. Extracts were then evaporated to dryness using a "Rocket" centrifugal rotary evaporator (Genevac, Ipswich, UK) set at 40 $^\circ\text{C}$. Samples were then reconstituted in 500 μL of $\text{H}_2\text{O}/\text{MeOH}$ (80:20 v/v) prior to LC-MS/MS analysis.

2.2.3. LC-MS/MS Analysis. All samples were analyzed using a fully validated UPLC-MS/MS method.¹⁵ A Waters Acquity UPLC system (Manchester, UK) coupled to a Xevo TQD Triple Quadrupole mass spectrometer (Waters) was used. A total of two chromatography methods using a reverse-phase BEH C_{18} column (150 \times 1.0 mm, 1.7 μm particle size) (Waters) with a 0.2 μm , 2.1 mm in-line column filter maintained at 25 $^\circ\text{C}$ were used. Acidic micropollutants were separated using a methanol-water gradient containing 1 mM NH_4F and basic micropollutants using 5 mM NH_4OAc and 3 mM CH_3COOH . A total of two MS/MS transitions were monitored (when possible) for quantitation and confirmation purposes (see Table S2). Standard tolerances of ion ratio and chromatographic retention time were also employed to ensure the quality of reported data (see Table S3).¹⁷ A full description of the method is available in Petrie et al.¹⁵

For the enantioselective separation of chiral micropollutants, a cellobiohydrolase (CBH) column (100 \times 2 mm, 5 μm internal diameter) and a mobile phase consisting of 1 mM NH_4OAc in $\text{H}_2\text{O}/\text{MeOH}$ (85:15 v/v) was used. A full description of the method is available in Castrignanò et al.¹⁶ (see Table S3). Enantiomeric distribution of chiral micropollutants was expressed as enantiomeric fraction (EF), which was calculated according to eq 1:

$$\text{EF} = \frac{E(+)}{[E(+)] + [E(-)]} \quad (1)$$

where EF is the enantiomeric fraction, $E(+)$ is the peak area of the (+) enantiomer corrected for the deuterated internal standard response, and $E(-)$ is the peak area of the (-) enantiomer corrected for the deuterated internal standard response. An EF of 0.5 denotes a racemic mixture.

2.3. Wastewater Properties. During all studies, wastewater properties including temperature, pH, total organic carbon (TOC), and dissolved organic carbon (DOC, filtered through 0.7 μm glass fiber membranes) content as well as suspended solids concentration were monitored. TOC and DOC were

measured using a TOC- V_{CPN} Total Organic Carbon Analyzer TOC- V_{CPN} (Shimadzu, Milton Keynes, UK). Suspended solids concentration was determined using standard methods.¹⁸

2.4. Calibration and Monitoring Studies. The WwTW used in the study was located in an area of southwest England with a population equivalent of 105 847. The process consists of primary screens and grit removal followed by conventional primary sedimentation, trickling filters, and final sedimentation in humus tanks. All sampling was conducted in a final effluent chamber that receives the whole flow of the WwTW. The effluent, on leaving this chamber, passes over a weir ensuring that it remained at the same level throughout the day, irrespective of any variation in flow. This ensured Chemcatcher samplers remained completely submerged throughout their deployment.

For the calibration study (January 19, 2015), 30 samplers were fixed onto a lightweight metal frame (54 cm \times 42 cm) using cable ties and lowered into the chamber (see Figure S2). The frame was tethered using chains, leaving the samplers submerged at a depth of approximately 1 m. Chemcatchers were removed in triplicate at times of 0.3, 1, 2, 3, 4, 5, 6, 7, 8, and 9 days. Samplers were deployed on a Monday. Upon collection, they were transported to the laboratory on ice within 30 min. These were dried and frozen at -20 $^\circ\text{C}$. During the calibration study, 24 h time composites were collected simultaneously for days 1 to 8 using an ISCO 3700 portable sampler (RS Hydro, Worcestershire, UK). Subsamples were collected every 15 min over the 24 h time period and cooled to 4 $^\circ\text{C}$.¹⁹ All subsamples were mixed on collection and transported to the laboratory on ice.

The accumulation of micropollutants in the passive sampler can be described by a first-order, one-compartment mathematical model.⁷ An initial linear uptake phase is followed by curve-linear and equilibrium phases. The overall accumulation of a micropollutant in the passive sampler can be described using eq 2:

$$C_s = C_w K_{\text{PW}} [1 - e^{-kt}] \quad (2)$$

Here, C_s is the accumulated mass of a given micropollutant in the passive sampler, C_w is concentration of the micropollutant in effluent wastewater, K_{PW} is the passive sampler-water partition coefficient of a given micropollutant, k is offload rate constant of the micropollutant from the passive sampler, and t is the deployment time.

In the linear-uptake phase, sampling rates (R_s) are derived from the slope of the regression between the mass of micropollutant accumulated on the passive disk against the concentration in effluent wastewater determined from time-composite samples versus deployment time.⁷ To calculate R_s , the average effluent concentration was used for that time period. For example, on day 5, the average effluent concentration from days 1 to 5 was used, and so on. Here, the sorbent is assumed to act as an infinite sink for micropollutants, and C_w can be calculated using eq 3:

$$C_w = \frac{C_s}{R_s t} \quad (3)$$

In the equilibrium phase, where exposure time has been sufficient to reach equilibrium with the receiving phase, C_w can be calculated according to eq 4:

$$C_w = \frac{C_s}{K_{\text{PW}} M_s} \quad (4)$$

Table 1. Mean Effluent Wastewater Concentration and Regression Information from the in Situ Calibration Study^a

micropollutant class	micropollutant	effluent wastewater ($n = 8$, ng L ⁻¹)	linearity		comments	R_s (L d ⁻¹)	log K_{pw}
			range (day)	r^2			
UV filters	benzophenone-1	<MQL	–	–	<MQL in composites	–	–
	benzophenone-2	<MQL	–	–	<MQL in composites and passive disks	–	–
	benzophenone-3	157 ± 20.7	2–8	0.957	linear	0.011	–
	benzophenone-4	2419 ± 251	1–8	0.970	linear	0.049	–
parabens	methylparaben	23.7 ± 6.0	1–8	0.954	linear	0.055	–
	ethylparaben	6.8 ± 1.2	–	–	nonlinear	–	3.03
	propylparaben	11.1 ± 5.7	2–8	0.947	linear	0.068	–
	butylparaben	<MQL	–	–	<MQL in composites and passive disks	–	–
plasticizer steroid estrogens	bisphenol-A	120 ± 27.3	1–8	0.995	linear	0.031	–
	E1	24.4 ± 2.4	2–8	0.996	linear	0.071	–
	E2	<MQL	–	–	<MQL in composites and passive disks	–	–
antibacterials and antibiotics	EE2	<MQL	–	–	<MQL in composites and passive disks	–	–
	sulfasalazine	68.3 ± 6.1	1–8	0.996	linear	0.154	–
	clarithromycin	1962 ± 452	1–8	0.939	linear	0.024	–
	azithromycin	143 ± 18.6	1–8	0.987	linear	0.024	–
hypertension	trimethoprim	1041 ± 123	1–8	0.992	linear	0.028	–
	sulfamethoxazole	147 ± 68.4	1–8	0.946	linear	0.058	–
	valsartan	266 ± 34.8	1–8	0.992	linear	0.060	–
	irbesartan	77.0 ± 19.9	1–8	0.994	linear	0.087	–
	lisinopril	198 ± 22.2	1–8	0.976	linear	0.059	–
	NSAIDs	ketoprofen	51.3 ± 10.0	1–8	0.991	linear	0.037
lipid regulators	ibuprofen	2838 ± 347	1–8	0.988	linear	0.048	–
	naproxen	5202 ± 515	1–8	0.992	linear	0.048	–
	diclofenac	411 ± 82.5	1–8	0.993	linear	0.044	–
	acetaminophen	940 ± 276	–	–	nonlinear	–	3.08
antihistamines	bezafibrate	811 ± 62.4	1–8	0.997	linear	0.042	–
	atorvastatin	115 ± 32.9	1–8	0.976	linear	0.013	–
diabetes	fexofenadine	610 ± 62.1	1–8	0.997	linear	0.059	–
	cetirizine	403 ± 39.6	1–8	0.976	linear	0.039	–
cough suppressant	metformin	25 845 ± 2255	–	–	nonlinear	–	1.94
	glucoside	61.7 ± 9.9	1–8	0.991	linear	0.045	–
β -blocker	pholcodine	<MQL	–	–	<MQL in composites and passive disks	–	–
	atenolol	830 ± 51.7	1–8	0.985	linear	0.034	–
	metoprolol	18.2 ± 2.9	1–8	0.980	linear	0.050	–
H ₂ receptor agonists	propranolol	90.2 ± 10.0	1–8	0.995	linear	0.114	–
	ranitidine	1438 ± 331	1–7	0.944	linear	0.043	–
x-ray contrast media	cimetidine	54.0 ± 10.6	1–7	0.992	linear	0.085	–
	iopromide	<MQL	–	–	<MQL in composites and passive disks	–	–
drug precursor and metabolite	ephedrine/pseudoephedrine	220 ± 27.7	1–8	0.995	linear	0.044	–
	norephedrine	<MQL	–	–	<MQL in composites and passive disks	–	–
anticancer	azathioprine	<MQL	–	–	<MQL in composites and passive disks	–	–
	methotrexate	<MQL	–	–	<MQL in composites and passive disks	–	–
	ifosfamide	<MQL	–	–	<MQL in composites and passive disks	–	–
	tamoxifen	<MQL	–	–	<MQL in composites and passive disks	–	–
anesthetic and metabolite	ketamine	<MQL	–	–	<MQL in composites	–	–
	norketamine	<MQL	–	–	<MQL in composites and passive disks	–	–
antidepressants and metabolites	venlafaxine	235.0 ± 13.9	1–8	0.993	linear	0.065	–
	fluoxetine	38.3 ± 5.9	1–8	0.978	linear	0.032	–

Table 1. continued

micropollutant class	micropollutant	effluent wastewater ($n = 8$, ng L ⁻¹)	linearity		comments	R_s (L d ⁻¹)	log K_{pw}	
			range (day)	r^2				
antiepileptic and metabolites	norfluoxetine	29.5 ± 0.9	–	–	no linearity established (concentration too low)	–	–	
	sertraline	22.0 ± 2.7	1–8	0.988	linear	0.116	–	
	mirtazapine	36.7 ± 2.9	1–8	0.997	linear	0.074	–	
	citalopram	244 ± 18.2	1–8	0.996	linear	0.069	–	
	desmethylcitalopram	47.1 ± 6.7	1–8	0.988	linear	0.149	–	
	carbamazepine	196 ± 14.8	1–8	0.995	linear	0.045	–	
	carbamazepine 10,11-epoxide	<MQL	–	–	<MQL in composites and passive disks	–	–	
calcium channel blocker	10,11-dihydro-10-hydroxycarbamazepine	55.5 ± 9.8	1–8	0.990	linear	0.077	–	
	diltiazem	24.4 ± 8.8	3–8	0.895	linear	0.185	–	
hypnotic	temazepam	21.6 ± 4.2	1–8	0.988	linear	0.326	–	
antipsychotic	quetiapine	7.9 ± 2.0	2–8	0.989	linear	0.107	–	
veterinary	tylosin	<MQL	–	–	<MQL in composites and passive disks	–	–	
human indicators and metabolites	creatinine	12 682 ± 3975	–	–	<MQL in passive disks	–	–	
	nicotine	136 ± 28.0	1–8	0.961	linear	0.234	–	
	caffeine	7453 ± 1015	1–8	0.993	linear	0.037	–	
	cotinine	551 ± 42.3	1–8	0.992	linear	0.041	–	
	1,7-dimethylxantine	10 287 ± 1180	1–8	0.997	linear	0.052	–	
analgesics and metabolites	morphine	460 ± 72.5	1–8	0.981	linear	0.031	–	
	dihydromorphine	<MQL	–	–	<MQL in composites	–	–	
	normorphine	38.9 ± 10.5	2–8	0.954	linear	0.056	–	
	methadone	9.4 ± 2.7	1–8	0.976	linear	0.226	–	
	EDDP	66.5 ± 4.5	1–8	0.985	linear	0.056	–	
	codeine	1137 ± 96.3	1–8	0.979	linear	0.056	–	
	norcodeine	117.3 ± 9.3	1–8	0.972	linear	0.052	–	
	dihydrocodeine	257.5 ± 21.8	1–8	0.979	linear	0.047	–	
	tramadol	683 ± 57.2	1–8	0.985	linear	0.047	–	
	<i>N</i> -desmethyltramadol	134 ± 14.9	1–8	0.984	linear	0.087	–	
	<i>O</i> -desmethyltramadol	572 ± 58.9	1–8	0.954	linear	0.023	–	
	amphetamine	111 ± 55.7	1–8	0.968	linear	0.028	–	
	methamphetamine	4.9 ± 0.6	1–8	0.947	linear	0.025	–	
	MDMA	109 ± 95	1–8	0.986	linear	0.074	–	
MDA	15.5 ± 14.2	–	–	no linearity established (concentration too low)	–	–		
stimulants and metabolites	cocaine	114.7 ± 43.6	1–8	0.991	linear	0.061	–	
	benzoylecgonine	518 ± 193	1–8	0.996	linear	0.031	–	
	anhydroecgonine methylester	<MQL	–	–	<MQL in composites and passive disks	–	–	
	cocaethylene	5.0 ± 2.8	–	–	<MQL in most composites	–	–	
	mephedrone	<MQL	–	–	<MQL in composites and passive disks	–	–	
	MDPV	<MQL	–	–	<MQL in composites and passive disks	–	–	
	opioid and metabolite	heroin	<MQL	–	–	<MQL in composites and passive disks	–	–
		6-acetylmorphine	<MQL	–	–	<MQL in composites and passive disks	–	–

^aKey: E1, estrone; E2, 17 β -estradiol; EE2, 17 α -ethinylestradiol; EDDP, 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine; MDMA, 3,4-methylenedioxy-methamphetamine; MDA, 3,4-methylenedioxy-amphetamine; MDPV, methylenedioxypropylvalerone.

Here, M_s is mass of sorbent per sampler, and K_{PW} can be calculated by rearranging eq 4.

To determine the robustness of the derived calibration data, a monitoring study was undertaken during June of 2015. Here, seven Chemcatchers were deployed for 7 days. Over these 7 days,

24 h time composite water samples were also collected in the same way as that described above. In this case, sampling ran from Wednesday to Tuesday. Field blanks were also analyzed during the calibration and monitoring studies, with no micropollutants found to be quantifiable.

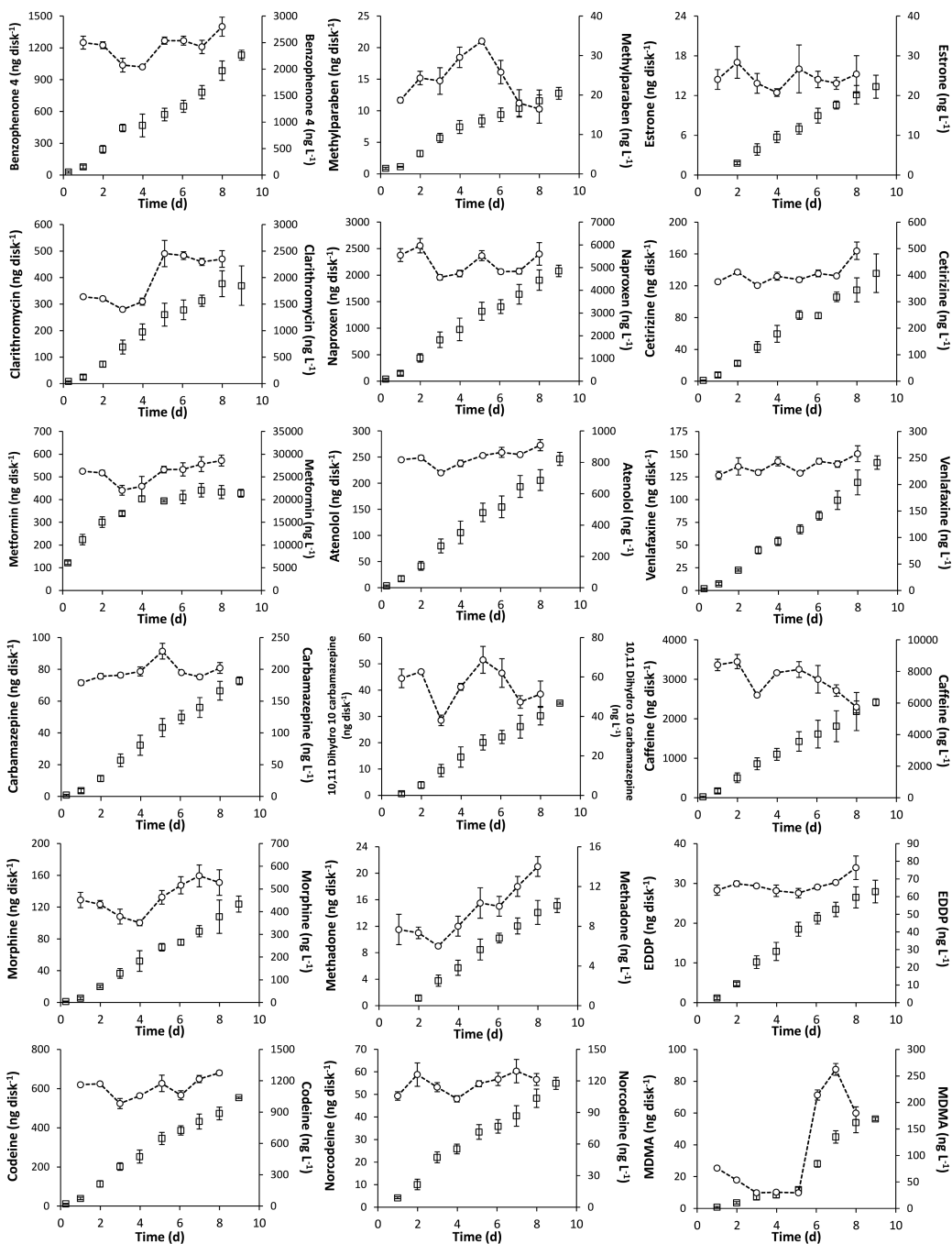


Figure 1. Representative micropollutant uptake in passive samples (□, primary axis, $n = 3$) and corresponding effluent wastewater concentration (○, secondary axis, $n = 3$) over 9 days. For all micropollutants, see [Figures S3–6](#).

3. RESULTS AND DISCUSSION

3.1. Method Performance. The UPLC–MS/MS methodology applied achieved instrumental detection limits (IDLs) ranging from 0.01 to 1.16 ng mL⁻¹ for the 88 targeted micropollutants (see [Table S3](#)).¹⁵ This corresponded to instrument quantitation limits (IQLs) between 0.03 and 5.79 ng mL⁻¹. These IDLs and IQLs are typical for similar multiresidue methods reported in the literature.^{14,20} For further information and discussion on the instrument performance and its validation, please refer to Petrie et al.¹⁵ (see [Table S3](#)).

For the Chemcatchers, Atlantic HLB disks were chosen as the receiving phase. This configuration was preferred over POCIS, which contains the equivalent mass of sorbent as a powder. This

is because loose sorbent within POCIS can sag toward the base of the device during deployment in the vertical plane, potentially reducing the active sampling surface area and increasing variability in uptake rate.⁹ In the disks, the sorbent is immobilized. Using disks over powder will help minimize variability of field data while improving ease of use. The Atlantic HLB disks achieved recoveries ranging from 21% for creatinine to 144% for *N*-desmethyltramadol. The majority of micropollutants exhibited recoveries in the range of 80–110% (see [Table S3](#)) with RSDs ($n = 3$), generally <20%. Spiked environmental extracts showed matrix suppressions ranging from -241% (signal enhancement) for atorvastatin to 96% for creatinine (see [Table S3](#)). This level of matrix suppression is

typical for environmental applications using HLB as a SPE sorbent (and electrospray ionization).^{14,15} Method detection limits were <17 ng disk⁻¹ for all micropollutants, with several reaching ≤ 0.01 ng disk⁻¹. The method quantitation limits (MQLs) achieved were in the range 0.02–55.4 ng disk⁻¹ (see Table S3). The majority of micropollutants exhibited MQLs < 1 ng disk⁻¹, demonstrating the sensitivity of the methodology applied.

3.2. Effluent Concentrations and in Situ Calibration. To ensure that accurate field R_S values could be determined, a robust composite sampling protocol was applied. Subsample collection frequencies of 15 min were used to ensure that representative samples were collected. These were cooled to 4 °C until collection and subsequent analysis to limit micropollutant degradation were completed. For further information, please refer to Petrie et al.¹⁹

From the 88 micropollutants studied, 66 were detected in composite samples during the 8 day calibration study (Table 1). Of the 66 detected compounds, 65 were found in every composite sample. Furthermore, the majority exhibited interday concentration variations of $<20\%$ ($n = 8$) except those that are used by the human population recreationally. For example, the illicit stimulants MDMA and MDA had interday concentration variations of $>50\%$ due to their high weekend usage. Nevertheless, the high detection frequency and, in general, the low concentration variation of studied micropollutants was ideal for in situ calibration.

In passive sampler extracts, a total of 68 micropollutants were quantified at least once. The majority of micropollutants showed linear uptake over the 9 day study period (Figures 1 and S3–6). R_S are reported for those micropollutants exhibiting correlation coefficients of ≥ 0.9 with at least six data points (and were quantifiable in all composite samples throughout the passive sampler deployment). A total of 59 micropollutants satisfied these criteria, with the majority being linear between 1 and 8 days (Table 1). The broad range of micropollutants accumulated in the Chemcatcher and the good linearity observed for deriving R_S demonstrates the potential of this passive sampler configuration for quantitative measurements.

The Chemcatcher was also shown to be very responsive to changes in micropollutant concentration. The best example of this is MDMA, the concentration of which in the receiving-phase disks responded to the increased concentration found in effluent from day 6 (due to recreational usage on the weekends) (Figure 1). Due to the Chemcatcher's responsiveness in relatively short-term concentration changes, the R_S of MDMA could be determined with good linearity ($r^2 = 0.986$).

Field R_S values ranged from 0.011 L day⁻¹ for benzophenone-3 to 0.326 L day⁻¹ for temazepam (Table 1). The majority of micropollutants (85%) had R_S values ranging from 0.01 to 0.10 L day⁻¹. It is difficult to directly compare the R_S values derived here with those in previous studies due to differences in the passive sampler deployed (design, exposed surfaced area, and sorbent) as well as the matrix investigated. Furthermore, this sampler configuration using the Atlantic HLB disk has not been previously reported. For three micropollutants (metformin, acetaminophen, and ethylparaben), curve-linear uptake was observed, and R_S could not be determined (Figures 1, S3, and S4). Here, equilibrium was reached within 4 days and log K_{PW} values were 1.94, 3.08, and 3.03, respectively (Table 1). Metformin had the lowest log K_{PW} due to its high hydrophilicity (log K_{OW} of -2.6).²¹

3.3. Can log K_{OW} and log D_{OW} Predict Micropollutant Uptake? Ideally, if R_S could be estimated from physicochemical properties such as log K_{OW} or log D_{OW} , less-rigorous calibration studies may be needed in the future.⁶ The majority of previous studies have attempted to relate chemical properties with the R_S values of only a few compounds (typically <25 pesticides or herbicides).^{22,23} However, Moschet et al.⁶ has reported a weak linear regression (r^2) of 0.37 with field R_S values (river water) of 88 micropollutants (onto styrenedivinylbenzene disks) and log D_{OW} values. However, no previous study has investigated the uptake of polar micropollutants to the receiving phase used here. In our study, it was attempted to relate the 59 field R_S values with compound-specific physicochemical properties.

Initially, log K_{OW} and log D_{OW} was plotted against R_S with no relationship found. Therefore, to investigate this further, studied micropollutants were separated into neutral, positively charged, negatively charged, and zwitterionic species at the pH of wastewater effluent during the calibration study (pH 7.2) (see Table S1). Field R_S for each group of micropollutants were then plotted against log K_{OW} or log D_{OW} to establish whether or not a relationship exists. For neutral micropollutants ($<50\%$ ionised), a poor linear regression was noted between R_S and log K_{OW} ($r^2 = 0.11$, $n = 9$) (see Figure S7). Linear regressions (r^2) of 0.15 ($n = 28$), 0.02 ($n = 14$), and 0.93 ($n = 4$) were found between the log D_{OW} and R_S values of positively charged, negatively charged and zwitterionic micropollutants, respectively (see Figure S7). Therefore, no clear relationship could be established using the dominant charged states of studied micropollutants with log K_{OW} or log D_{OW} for a sufficient number of data points. It is likely that other interactions govern the uptake of polar micropollutants onto the HLB sorbent, and this requires more detailed investigation in the future.

A better understanding on the role of external factors (e.g., temperature and pH) on micropollutant uptake in the field is also needed. These investigations would ideally be performed ex situ using real matrix under laboratory-style conditions (e.g., see Vermeirssen et al.).²⁴ This approach would combine the necessity of using the relevant environmental matrix for representative micropollutant uptake with the advantages of laboratory conditions, in which external factors can be closely controlled. Investigating such factors individually may help understand the underpinning properties or mechanisms controlling micropollutant uptake. However, care must be taken if this approach is to be adopted to ensure the stability of micropollutants in the test matrix if a continuous fresh supply of the matrix is not available for the duration of the study. Ideally, this would lead to the development of a theoretical model to predict R_S on the basis of physicochemical properties and specific field conditions at the site of deployment. This would also be aided if there was a standardized approach to passive sampling, such that field R_S could be collated. The Chemcatcher containing an Atlantic HLB disk provides this opportunity due to its ease of use and suitability for a broad range of micropollutants.

3.4. Quantitative Determination of Micropollutants Using Passive Samplers. The reliability of the calibration data was tested by using the field-derived R_S (or K_{PW} for acetaminophen, ethylparaben, and metformin) to determine the average effluent concentration of the micropollutants over a 7 day trial (January 19, 2015). The use of the 7 day data point ensured being in the linear uptake phase for the majority of studied compounds (Figure 1). Considering the good linearity achieved, it is unsurprising that the effluent concentration determined using passive samples and composite samples were

similar (see Table S5). The concentration of micropollutants measured using passive samplers was generally within $\pm 20\%$ of that determined from composite samples (see Figure S8A). Only the illicit stimulant methamphetamine showed a notable difference of +52% between concentrations estimated by passive and composite samples (see Table S5). However, it should be noted that the concentrations for the majority of micropollutants determined by the passive samplers were underestimated (52 of 62), albeit not greatly (maximum = -25%) (see Figure S8A). This is due to a probable lag between deployment and the start of micropollutant uptake (Figures 1 and S3–6). Therefore, despite uptake being linear, it does not pass through the origin for all micropollutants when R_S was determined. Vermeirssen et al.²⁴ found that more-hydrophobic compounds had a tendency to accumulate on the PES membrane, resulting in a lag phase before being found in the sorbent. A further possible explanation for this is that the passive disks were deployed when dry. Although the HLB sorbent is water-wettable, deploying them wet may reduce this lag in uptake. This will be considered in future studies.

The robustness of the calibration was challenged by deploying passive samplers ($n = 7$) for 7 days in June 2015 to determine average micropollutant concentrations. Measured concentrations were compared directly to those from 24 h composite samples over the deployment period. It is assumed that the calibration can be applied to future monitoring at the same site where the calibration was performed and micropollutant uptake will not differ significantly.⁴ However, wastewater characteristics can change significantly with season, which could affect micropollutant uptake. Here, measured wastewater variables such as flow and temperature were notably different (see Table S6). Average wastewater flows were $39\,774 \pm 2492$ and $24\,875 \pm 2340$ $\text{m}^3 \text{day}^{-1}$ in January and June, respectively. Wastewater temperatures were 8.4 ± 0.5 and 14.2 ± 0.8 $^\circ\text{C}$. Such differences are typical of conditions experienced at WwTW in the United Kingdom between the winter and summer months. Of the other wastewater characteristics monitored (pH, TOC, DOC, and suspended solids), no substantial differences were observed between the studies in January and June.

Average micropollutant concentrations measured for the 7 day time period in June using passive samplers ranged from 3.5 ± 1.3 ng L^{-1} for ethylparaben to $37\,784 \pm 6435$ ng L^{-1} for metformin (see Table S5). A total of 60 micropollutants were quantified using calibration data, with 55 (92%) being within a factor of 2 of those determined in composite samples (see Figure S8B). This included micropollutants that changed significantly in their concentration between the calibration and monitoring study due to seasonal usage (e.g., the antihistamines fexofenadine and cetirizine) (see Table S5). However, generally, the percentage error of micropollutant concentrations determined by passive samples versus composite samples were greater in June than in January (when the calibration was performed) (see Table S5). This is not unexpected considering the different field conditions experienced between the two study periods. Differences in compound uptake due to variable environmental conditions can be adjusted by using performance reference compounds.^{25,26} However, they were not deemed appropriate in this study because they require further investigation for polar compounds, and conditions at the WwTW were relatively constant. Despite a lower daily flow of wastewater in June (37%), this is not expected to have had a significant impact on micropollutant uptake. This is because changes to flow velocity at the sampling site (deep chamber) is considered to be low for the changes in flow observed ($24\,875$ versus $39\,774$ $\text{m}^3 \text{day}^{-1}$). Furthermore,

previous studies have found changes in flow velocity (0.1 to 0.4 m s^{-1}) to have little impact upon field R_S in rivers.⁶

The temperature difference ($+5.8$ $^\circ\text{C}$) is more likely to contribute to the greater differences observed. Studies conducted under laboratory conditions have noted that increased water temperature generally increased R_S for test analytes.^{27,28} This is explained by a temperature increase modifying compound solubility and $\log K_{OW}$, thus facilitating the transfer of compounds from water to the sorbent.²⁷ Consideration must also be given to the competitive uptake of other organic compounds. Despite DOC (mg L^{-1}) not changing significantly between the January and June sampling periods (see Table S6), the composition of this was not further characterized. Therefore, differences in the chemical composition of wastewater, resulting in differences in micropollutant uptake between January and June conditions, cannot be excluded.

Micropollutants with a 2-fold concentration difference were amphetamine, atorvastatin, azithromycin, benzophenone-3, and fluoxetine, all of which overestimated concentration, ranging from 112 to 169% of the concentration determined in composite samples (see Table S5). Interestingly, the relationship between error and R_S showed that these five micropollutants had relatively low R_S (≤ 0.032 L day^{-1}) (see Figure S8B). It is postulated that a lower sensitivity of uptake is subject to greater interference from external factors (temperature and extent of biofouling), which can change between the time of calibration (winter) and subsequent monitoring (summer).

3.5. Passive Samplers for EF Determination of Chiral Micropollutants. Reporting concentration of chiral micropollutants at the enantiomeric level is essential for more-accurate environmental risk assessment.¹ Due to stereoselectivity within the human body and during wastewater treatment, chiral micropollutants do not enter the environment in the enantiomeric form in which they are dispensed, and stereoselective toxicity toward aquatic biota is known to occur.^{11–13} This is significant because toxicological studies are often conducted using the dispensed form of the micropollutant (typically as a racemic mixture), as stereoselectivity is not considered. Therefore, further knowledge is needed on the enantiomeric distribution of chiral micropollutants entering the environment to inform future toxicity driven studies.

To date, passive samplers have not been investigated for reporting the stereoselectivity of chiral micropollutants. Uptake of enantiomers of the same chiral micropollutant onto passive samplers will not be stereoselective in nature because it is a physicochemical process. However, stereoselective transformation may occur on the sorbent during deployment. The stability of micropollutants in passive samples is poorly understood due to the difficulty of assessing this in the field. Comparing the enantiomeric distribution of chiral micropollutants extracted from passive sampler receiving-phase disks with composite samples will help indicate micropollutant stability.

Mean EFs of atenolol, MDMA, tramadol, and venlafaxine determined from composite samples over 7 days were 0.48 ± 0.01 , 0.28 ± 0.06 , 0.53 ± 0.01 , and 0.50 ± 0.02 , respectively (Table 2). In extracts from passive samplers deployed for 7 days, EFs were 0.48 ± 0.02 , 0.31 ± 0.02 , 0.52 ± 0.01 , and 0.49 ± 0.01 , showing no significant differences with composite samples. This demonstrates there were no stereoselective changes for these micropollutants during the deployment of passive samplers. Considering bacteria tend to be 0.2 to 2.0 μm in diameter, the PES membrane (0.2 μm pores) should provide a physical barrier to their transport onto the sorbent.

Table 2. Comparison of Enantiomeric Fraction of Chiral Micropollutants Determined in Time Composite Samples and Passive Samples Using the Enantio-Selective CBH Method ($n = 7$)^a

chiral micropollutant	enantiomeric fraction	
	time composites ($n = 7$)	passive samples ($n = 7$)
atenolol	0.48 ± 0.01	0.48 ± 0.02
MDMA	0.28 ± 0.06	0.31 ± 0.02
MDA	<MQL	0.55 ± 0.03
tramadol	0.53 ± 0.01	0.52 ± 0.01
venlafaxine	0.50 ± 0.02	0.49 ± 0.01
amphetamine	<MQL	<MQL
methamphetamine	<MQL	<MQL
mephedrone	<MQL	<MQL

^aKey: MQL, method quantitation limit of CBH method; MDMA, 3,4-methylenedioxy-methamphetamine; MDA, 3,4-methylenedioxy-amphetamine.

Therefore, passive samplers were successful in describing the enantiomeric distribution of these chiral micropollutants and can be used for the development of more accurate environmental risk assessments. Also, improved sensitivity in passive samples enabled the EF of MDA to be determined (EF = 0.55 ± 0.03) (Table 2). This was not possible for composite samples using the enantioselective CBH method due to the low background concentrations found in final effluent.

3.6. Considerations for Implementing Passive Sampling for Routine Environmental Monitoring. Implementing passive sampling into routine monitoring of micropollutants offers several advantages. The approximate cost per sample (consumable and analysis costs only) for passive and active sampling was €33.57 and €22.12, respectively (see Table S7). However, the total cost of consumables and analysis for the monitoring study conducted over 7 days (June 3–9, 2015) using 24 h composite samples was €464.52 ($n = 21$, triplicate analysis). In comparison, passive sampling was ~50% cheaper at a cost of €234.99 ($n = 7$). This is due to the higher number of samples required for active sampling for a 7 day monitoring period. Yet the difference in cost between the sampling modes will be greater considering the number of site visits required. Each site visit here cost approximately €10.32 (24 km traveled at €0.43 per km). Passive sampling only required two site visits for the 7 day study, one for deployment and one for collection. This was suitable for wastewater effluent because little fouling occurred on the surface of the samplers during deployment. In contrast, 7 day composite sampling required a total of eight site visits (one for deployment and seven for collection). The number of site visits could not be reduced due to the poor stability of micropollutants in collected wastewater at 4 °C for >24 h.¹⁹ Hence, the total financial savings by applying passive sampling over composite sampling will be dependent on the proximity of the sampling site to the analysis laboratory. In this study, the total cost of monitoring wastewater effluent for a 7 day period was €255.63 for passive sampling and €547.19 for active sampling (excluding labor costs). Further savings can also be made if passive samplers are deployed for longer time periods. Samplers for quantitative analysis have been previously deployed in the field for up to 14 days.^{3,4,6}

Passive sampling also avoids problems associated with composite samplers, which can malfunction despite daily maintenance, resulting in the loss of sample continuity.¹⁹ Passive samplers can also fail (e.g., due to membrane breakage) but replicates are deployed, which helps overcome this issue.

Furthermore, several micropollutants (benzophenone-1, dihydromorphine, and ketamine) were detected in passive samples that were not found in their corresponding composite samples (Table 1). This improved sensitivity demonstrates their possible application as a qualitative tool for nontargeted screening and identifying of unknown compounds. However, passive sampling does have some limitations. For example, it cannot achieve the resolution of daily sampling, and acute variability in micropollutant concentration (e.g., from recreational use or direct disposal)²⁹ will not be fully appreciated during a weekly sampling campaign. A further disadvantage of passive sampling, particularly with in situ calibration observed during this study, is associated with temporal changes in micropollutant occurrence. For example, a calibration could not be established for benzophenone-1 and ketamine due to their concentration in composite samples being <MQL in January, 2015 (<0.71 and <0.93 ng L⁻¹, respectively). However, in the monitoring study (June, 2015), they were found at concentrations of 60.1 ± 20.4 and 4.1 ± 1.5 ng L⁻¹, respectively, in composite samples but could not be quantified using passive samples because the R_s was unknown (see Table S5). Nevertheless, in situ calibration of passive samplers has shown to be very promising for the quantitative determination of micropollutants in wastewater effluent. However, their application in a legislative context will require further understanding of the physicochemical properties controlling micropollutant uptake and the influence of external factors experienced in the field during monitoring studies (e.g., temperature). This will help improve the accuracy of micropollutant concentrations reported by passive sampling. Therefore, in the short term, it is expected that future monitoring studies using passive samplers (previously calibrated in situ) will need to be supported with some active sampling to help validate findings.

■ ASSOCIATED CONTENT

📄 Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.est.6b02216.

Additional details including photographs of Chemcatcher components and deployment (Figures S1 and S2), micropollutant uptake graphs (Figure S3–6), graphs showing the relationship between R_s and physicochemical properties (Figure S7) and percent error (Figure S8), physicochemical properties of micropollutants (Table S1), method details (Tables S2–4), micropollutant concentrations determined by passive and active sampling (Table S5), wastewater properties (Table S6), and cost analysis (Table S7). (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The support of Wessex Water and the University of Bath's EPSRC Impact Acceleration Account (project nos. EP/K503897/1 and ZR-Z0248) is greatly appreciated. The authors thank Richard Standerwick from Wessex Water for his help

throughout the project and Melanie Schumacher from Natural Resources Wales for help in the laboratory.

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