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PETRIE, B., PROCTOR, K., YOUDAN, J., BARDEN, R. and KASPRZYK-HORDERN, B.

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Critical evaluation of monitoring strategy for the multi-residue determination of 90 chiral and achiral micropollutants in effluent wastewater

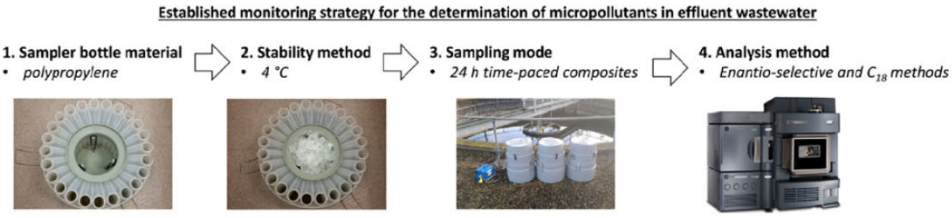
Bruce Petrie [a,b], Kathryn Proctor [a,b], Jane Youdan [c], Ruth Barden [c], Barbara Kasprzyk-Hordern [a,b,*]

[a] Department of Chemistry, University of Bath, Bath BA2 7AY, UK
[b] Water Innovation & Research Centre (WIRC), University of Bath, Bath, BA2 7AY Bath, UK
[c] Wessex Water, Bath BA2 7WW, UK

HIGHLIGHTS

- Polypropylene suitable as sampler bottle material for 89 of 90 micropollutants.
- Cooling composite samples to 4 °C stabilised ≥81 compounds in studied effluents.
- Time composites gave similar concentration data to volume composites in effluent.
- Little diurnal variability in enantiomeric distribution of chiral micropollutants.

GRAPHICAL ABSTRACT



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ABSTRACT

It is essential to monitor the release of organic micropollutants from wastewater treatment plants (WWTPs) for developing environmental risk assessment and assessing compliance with legislative regulation. In this study the impact of sampling strategy on the quantitative determination of micropollutants in effluent wastewater was investigated. An extended list of 90 chiral and achiral micropollutants representing a broad range of biological and physico-chemical properties were studied simultaneously for the first time. During composite sample collection micropollutants can degrade resulting in the under-estimation of concentration. Cooling collected sub-samples to 4 °C stabilised ≥81 of 90 micropollutants to acceptable levels (±20% of the initial concentration) in the studied effluents. However, achieving stability for all micropollutants will require an integrated approach to sample collection (i.e., multi-bottle sampling with more than one stabilisation method applied). Full-scale monitoring of effluent revealed time-paced composites attained similar information to volume-paced composites (influent wastewater requires a sampling mode responsive to flow variation). The option of monitoring effluent using time-paced composite samplers is advantageous as not all WWTPs have flow controlled samplers or suitable sites for deploying portable flow meters. There has been little research to date on the impact of monitoring strategy on the determination of chiral micropollutants at the enantiomeric level. Variability in wastewater flow results in a dynamic hydraulic retention time within the WWTP (and upstream sewerage system). Despite chiral micropollutants being susceptible to stereo-selective degradation, no diurnal variability in their enantiomeric distribution was observed. However, unused medication can be directly disposed into the sewer network creating short-term (e.g., daily) changes to their enantiomeric distribution. As enantio-specific toxicity is observed in the environment, similar resolution of enantio-selective analysis to more routinely applied achiral methods is needed throughout the monitoring period for accurate risk assessment.

* Corresponding author at: Department of Chemistry, University of Bath, Bath BA2 7AY, UK.
E-mail address: b.kasprzyk-hordern@bath.ac.uk (B. Kasprzyk-Hordern).

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1. Introduction

The presence and possible impact of municipally derived organic micropollutants in the environment is of increasing concern. Several micropollutants have been recommended for inclusion in a watch list under the Water Framework Directive (2000/60/EC) (Carvalho et al., 2015). This includes diclofenac, estrone, 17β-estradiol, 17α-ethinylestradiol, erythromycin, clarithromycin, and azithromycin. Diclofenac, 17β-estradiol and 17α-ethinylestradiol have proposed Environmental Quality Standards (EQS, expressed as annual average) of 100, 0.4 and 0.035 ng L^{-1}, respectively (European Commission, 2012). Consequently, it is expected that legislation will be implemented to govern the discharge of these types of micropollutants from wastewater treatment plants (WWTPs) into the environment. Developing environmental legislation is underpinned by robust monitoring data-sets and accurate risk assessment. However, such data-sets (previously limited by analytical capabilities) are currently lacking due to inadequate sampling protocols.

Composite sampling is usually applied to obtain average micropollutant concentrations over 24 h. An uncertainty associated with this approach is the loss of micropollutants during sample collection (McCall et al., 2016). Micropollutants could be lost due to sorption onto sampler bottles. Polypropylene is considered the most widely used sampler bottle material, yet there is a paucity of information published in the literature on the loss of micropollutants from water to its surface. Micropollutants can also be degraded by bacteria present within the wastewater matrix (Hillebrand et al., 2013). Cooling sub-samples to 4 °C, adjusting to pH 2 and adding sodium azide have all been suggested to improve stability (Baker and Kasprzyk-Hordern, 2011; Vanderford et al., 2011; Hillebrand et al., 2013). To date these different stabilisation methods have not been challenged with a high number of micropollutants (>50), representing a broad range of biological and physico-chemical properties. Ideally, a generic stabilisation method could be established for the multi-residue determination of micropollutants in wastewaters.

Ort et al. (2010) showed that collecting a time proportional composite sample with a sampling frequency of ≤20 min can give inaccurate/biased results in influent wastewater for some micropollutants. This was established through a modelling study which found a composite sampling approach that is responsive to variations in wastewater flow (flow or volume proportional) is needed to give unbiased information (depending on the sampling frequency and number of toilet flushes or 'pulses' (p) expected per micropollutant in the catchment each day) (Ort et al., 2010). It is currently unknown whether these observations are applicable to effluent wastewater. Mixing within the WWTP will provide a more uniform flow and concentration profile. On the other hand this may be counteracted by variability in micropollutant degradation due to dynamic wastewater flow and secondary treatment hydraulic retention time (HRT) (Majewsky et al., 2011). This is essential to investigate to ensure current sampling practices of effluent wastewater obtain accurate concentration information. Not all WWTPs have permanently deployed flow dependent samplers (particularly at smaller sites serving a population of ≤100,000), and rely on portable time dependent samplers for monitoring micropollutants. To date, there is a paucity of information on the impact of active sampling mode to the quantitative determination of micropollutants in effluent wastewater.

Obtaining accurate information on the enantiomeric distribution of chiral micropollutants is essential for accurate environmental risk assessment and needs incorporated into monitoring strategies (Petrie et al., 2014). Enantiomers of the same chiral micropollutant can exert different toxicological responses to exposed aquatic species (Stanley et al., 2007; De Andrés et al., 2009). However, little is known of the temporal variability in enantiomeric distribution of chiral micropollutants in effluent during a typical one-week monitoring period. As many chiral micropollutants undergo stereo-selective degradation, enantiomeric distribution could change with varying in-sewer and WWTP HRT. Such influences are expected to be compound specific as different chiral micropollutants undergo varying degrees of stereo-selectivity when exposed to environmental conditions (Kasprzyk-Hordern and Baker, 2012).

The aim of this study was to evaluate the impact of monitoring strategy on the quantitative determination of micropollutants in effluent wastewater. This will help inform the design of future environmental monitoring studies for improved data quality to improve risk assessment and assess compliance to environmental regulation. The objectives of the study were to:

i. Assess the behaviour of 90 micropollutants during composite sample collection using a range of stabilisation methods
ii. Compare grab sampling, and volume- and time- paced composite sampling for the determination of micropollutants in effluent with a wide range of expected pulses
iii. Evaluate diurnal changes in enantiomeric distribution of chiral micropollutants in effluent wastewater

A total of 90 micropollutants representing a broad range of biological and physico-chemical properties were studied (Table S1), and both concentration and EF (where possible) were determined. This is the first study which has investigated the impact of sampling strategy on such a high number of diverse micropollutants (including enantiomerism) simultaneously in effluent. Equivalent studies were also conducted in influent wastewater for comparison purposes and full findings of these can be found in Supplementary Material.

2. Materials and methods

2.1. Materials

Information on studied micropollutants are detailed in Table S1. 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, MDMA-D5, 3,4-methylenedioxy-amphetamine-D5 (MDA-D5), heroin-D9, codeine-D6, ketamine-D4, cocaine-D3, benzoylecgonine-D8, 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine-D3 (EDDP-D3), morphine-D3, cotinine-D3, cocaethylene-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 was HPLC grade and purchased from Sigma-Aldrich. Water (H_2O) was of 18.2 MΩ quality (Elga, Marlow, UK). All glassware was deactivated using 5% dimethylchlorosilane (DMDCS) in toluene (Sigma–Aldrich). Ammonium acetate (NH_4OAc), ammonium fluoride, sodium azide (NaN_3), ammonium hydroxide (NH_4OH), hydrochloric acid (HCl), formic acid (HCOOH) and acetic acid (1.0 M) were purchased from Sigma-Aldrich (Gillingham, UK). Oasis HLB (60 mg, 3 mL) solid phase extraction (SPE) cartridges were purchased from Waters (Manchester, UK).

2.2. Analytical methods

Briefly, samples for SPE were brought to room temperature, filtered (GF/F 0.7 μm glass fibre) and 50 mL aliquots spiked with 50 ng of all internal standards. These were loaded onto pre-conditioned Oasis HLB cartridges, dried and eluted using 4 mL MeOH. If SPE cartridges were frozen prior to elution, they were eluted and analysed within one

week. Methanolic extracts were dried under nitrogen and reconstituted in 500 μL 80:20 H_2O:MeOH. Samples for analysis by direct injection were filtered, spiked with the internal standard mix and adjusted with MeOH to achieve 80:20 H_2O:MeOH. Prepared samples were then analysed for 90 micropollutants using a fully validated ultra-high-performance liquid chromatography tandem mass spectrometry methodology using a Waters Acquity UPLC system (Manchester, UK) coupled to a Xevo TQD Triple Quadrupole Mass Spectrometer (Waters, Manchester, UK). Two separate chromatography runs were applied to achieve maximum sensitivity of both acidic and basic micropollutants. A full description of the method is available in Petrie et al. (2016b) (Table S2). Method recoveries in wastewaters ranged from 40 to 152% and method precision was <10% for the majority of studied compounds.

Samples for enantio-selective analysis were filtered, spiked with racemic mixtures of selected internal standards and subject to SPE as described above. Dried extracts were then reconstituted in 500 μL of the appropriate mobile phase. For enantiomeric separation of beta-blockers and anti-depressants, a Chirobiotic V column (100 × 2 mm; 5 μm internal diameter) with a mobile phase consisting of 4 mM NH_4OAc in MeOH containing 0.005% HCOOH was used. The method is described in detail in Evans et al. (2015) (Table S2). For separation of amphetamine-like compounds a Cellobiohydrolase column (100 × 2 mm, 5 μm internal diameter) and a mobile phase consisting 1 mM NH_4OAc in 85:15 H_2O:MeOH. A full description of the method is available in Castrignanò et al. (2016) (Table S2).

EFs were calculated according to Eq. (1):

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

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.

Total and dissolved organic carbon were measured using TOC-V_{CPN} Total Organic Carbon Analyser TOC-$V_{CPH/CPN}$ (Shimadzu, Milton Keynes, UK). Suspended solids were measured according to standard methods (APHA, 1998).

2.3. Wastewater treatment works

The WWTP under investigation (WWTP A) is located in South-West England with a population equivalent (PE) of 105,847. The process consisted of primary screens and grit removal, followed by conventional primary sedimentation, trickling filters and final sedimentation in humus tanks. The majority of receiving wastewater is pumped from a sewage pumping station located 8 km from the WWTP. Sub-catchments are pumped from the station intermittently with separate pumps operating for an hour at a time. Typically, a single pump is in operation all the time except in the early hours of the morning during periods of low flow. Under normal flow conditions, wastewater takes from <30 min to 6 h to reach the WWTP from the point of entry in the wastewater system. Wastewater was also collected from a second WWTP (WWTP B) located in South-West England to investigate micropollutant stability. This has a PE of 909,617 and differed from WWTP A in the biological treatment utilised. Here, sequencing batch reactors (activated sludge) were used.

2.4. Laboratory stability studies

Hourly composite samples (100 mL every 5 min to help account for short-term variability in wastewater composition) of wastewater were collected from WWTP A and B in polypropylene bottles to assess the stability of micropollutants in collected samples. Wastewater was transported to the laboratory on ice and within 1 h of collection. The applied methodology to test micropollutant stability was similar to that described by Hillebrand et al. (2013). One litre samples were spiked at room temperature with an additional 1000 ng L^{-1} of all micropollutants and mixed continuously for 30 min using a magnetic stirrer. 10 mL aliquots were then collected for SPE extraction (time 0) and the remaining sample separated equally into six polypropylene 1 L bottles. Two bottles were adjusted to pH 2 using HCl, two had NaN_3 added to achieve a concentration of 1 g L^{-1} and two were left untreated. Bottles were then stored in the dark at 18 °C and 4 °C and left unmixed for 24 h. Duplicate samples (10 mL aliquots used for SPE in this case) were then prepared for analysis as described in Section 2.2. Samples previously adjusted to pH 2 were re-adjusted to pH 7.5 with NH_4OH and mixed for an additional 30 min prior to SPE. To assess the loss of micropollutants to polypropylene sampler containers, deionised water was spiked with all micropollutants (1000 ng L^{-1}). These were then subject to SPE as described above at time 0 and following 24 h storage at 18 °C and 4 °C.

2.5. WWTP sampling

WWTP A was selected for monitoring as it has open channels for easy sampling of both influent and effluent wastewater in a time- and volume proportional manner. It was also of sufficient size (PE 105,847) such that the daily number of pulses of the studied micropollutants enabled a fair comparison of the two composite sampling modes. Influent wastewater was sampled after primary screens and grit removal, but before primary sedimentation. Effluent wastewater was collected after humus tank sedimentation. Sampling campaigns were conducted during December 2014 (influent) and January 2015 (effluent). These campaigns consisted of 8 d composite sampling (Monday to Monday). Time paced and volume paced composites were collected using ISCO 3700 portable samplers (RS Hydro, Worcestershire, UK). For time paced composites, a 10 mL (±9% RSD - Table S3) aliquot of wastewater was collected and deposited into 1 L polypropylene bottles every 15 min (10 samples per bottle). For volume paced composites 10 mL aliquots were collected once a pre-set of volume of wastewater had passed. This volume was estimated such that the same number of sub-samples as the time composite sampler (96) were collected throughout a 24 h period (average collection frequency = 15 min). For example, an expected daily flow of 40,000 m^3 would result in a 10 mL sample collected every 416.7 m^3. The frequency of collection here would therefore change in response to variations in wastewater flow (range = 8.9–23.8 min). Flow/volume measurements were made using an ISCO 2150 flow meter (RS Hydro, Worcestershire, UK; error = ±2%) coupled to the composite sampler. The flow sensor was mounted onto a stainless steel slab (35 × 57 cm), lowered and aligned in the centre of the wastewater stream. Daily flows determined by the portable flowmeter were within ±9% of that determined by the onsite flow meter (Table S4). The 24 h period of sampling each day ran from 08:00 h to 08:00 h the following day. On day one of each sampling campaign (Monday) a further sampler was used to collect hourly grab samples (500 mL). The cavity of all samplers were packed with ice to ensure collected samples were cooled and stored <4 °C until collection. Samples were then transferred to the laboratory on ice to maintain a temperature of 4 °C and processed immediately.

3. Results and discussion

3.1. Loss of micropollutants to polypropylene sampler bottles

Micropollutants can be lost during sample collection due to sorption onto the surface of sampler containers within composite samplers. Polypropylene was investigated as it is considered the most widely used sampler bottle material as it is the standard configuration when composite samplers are purchased. Furthermore, it is typically the sampler bottle material of on-site samplers whose primary focus is not for monitoring micropollutants. These on-site samplers are essential for many researchers who do not have their own equipment or direct access to

WWTPs to carry out their own sampling. Initially, the loss of 90 micropollutants representing a broad range of physico-chemical behaviours to polypropylene bottles was investigated in deionised water. This was conducted at both 18 and 4 °C as temperature is known to influence the sorption behaviour of all organic micropollutants (Ren et al., 2007). To determine the significance of findings, those outside a tolerance limit of ±20% of the starting concentration (time 0) were considered significant. This approach has been used previously by other authors studying the stability of micropollutants (Hillebrand et al., 2013; Llorca et al., 2014), and it outweighs the variability of the analytical method which is typically <10% (Petrie et al., 2016b).

No significant changes were found to the concentration of the majority of studied micropollutants in deionised water following storage in polypropylene bottles for 24 h at both 18 and 4 °C (Table 1; Table S5). This supports findings by Palmgrén et al. (2006) who noted no significant losses (>20%) of naproxen, atenolol, metoprolol and propranolol in water stored at 37 or 3 °C for 270 min. Of the 90 micropollutants investigated, only tamoxifen showed a significant change in concentration. Following 24 h storage in deionised water, tamoxifen reduced to 31 and 34% of the initial concentration at 18 and 4 °C, respectively. This is could be a result of its comparatively high hydrophobicity (log K_{ow} = 6.3 – US EPA, 2015). However, other micropollutants with a greater log K_{OW} (e.g., atorvastatin) were studied and did not behave similarly. This suggests the mechanisms which govern uptake are complex and cannot be described using individual chemical properties independently. Other bottle materials such as polytetrafluoroethylene or glass may need to be considered to avoid its loss and other similarly behaving compounds during sample collection. For example, polytetrafluoroethylene liners could be applied to existing polypropylene sampler bottles (Lapen et al., 2008).

3.2. Micropollutant stability in collected effluent wastewaters

The stability of micropollutants in collected effluent wastewater was assessed from two WWTPs utilising different treatment technologies. In effluent wastewater, several micropollutants were found to change concentration by more than ±20% over 24 h at 18 °C. A total of 23 (26%) and 20 (22%) of 90 studied micropollutants were outside this range for effluent from WWTP A and B, respectively (Table S6). Cooling the sample to 4 °C reduced degradation such that only the concentrations of 6 micropollutants were considered to have changed substantially in both effluents after 24 h (WWTP A – benzophenone-3, methylparaben, acetaminophen, cetirizine, fluoxetine, norfluoxetine and WWTP B – benzophenone-3, methylparaben, ethylparaben, propylparaben, 17β-estradiol, acetaminophen). Improved stability of micropollutants in effluent wastewater at 4 °C over short time periods (i.e., 24 h) is in agreement with findings by Hillebrand et al. (2013). However, it should be noted that some micropollutants considered not to be stable in effluent were different to those found not to be stable in influent wastewater (despite having similar pH 7.4–7.7) (Table S6). Therefore the stability of target micropollutants in the specific matrix to be monitored should be investigated prior to any sampling campaign.

Several authors have proposed the addition of a chemical additive (e.g., NaN_3) or acidification to pH 2 to help stabilise micropollutants by inhibiting biological activity (Vanderford et al., 2011; Hillebrand et al., 2013). Here, the addition of NaN_3 at 1 g L^{-1} resulted in numerous micropollutants failing the stability test (Table 1; Table S7). NaN_3 is thought to induce chemical changes to some micropollutants such as bezafibrate, clofibric acid, sertraline and diuron (Hillebrand et al., 2013). Chefetz et al. (2006) noted a nucleophilic aromatic substitution reaction between the Cl atom of atrazine and the azide ion. Most notably in this study, NaN_3 resulted in the loss of the deuterated surrogate of heroin (heroin-D9) in most samples. This is despite deuterated surrogates being added immediately prior to SPE. It has also been considered unsuitable for the stabilisation of atenolol, *N,N*-Diethyl-meta-toluamide and fluoxetine (Vanderford et al., 2011). It should also be noted that several micropollutants which do not have their own deuterated internal standard available had recoveries of >150% (Table 1). This could be an artefact of SPE extraction due to differences in behaviour of the micropollutant and the internal standard used for quantification. Therefore sampling strategies need consideration during the development and validation of multi-residue analytical methods. Furthermore, the use of NaN_3 in the field is controversial due to its high toxicity.

Acidification to pH 2 was hypothesised to be the best way of stabilising micropollutants in wastewater. However, it should be noted that adjustment of pH can influence the partitioning of some micropollutants between liquid and solid phases of wastewater matrices (Petrovic, 2014). Therefore prior to analysis pH was readjusted to the original pH of 7.5 (this was also the pH required for the SPE method applied here). Samples were mixed for 30 min because equilibrium following spiking environmental matrices with organic micropollutants is usually achieved within this time period (Ternes et al., 2004), and assumed to be instantaneous (Fernandez-Fontaina et al., 2013). Nevertheless, following pH adjustments several micropollutants showed an apparent concentration change of >20% (Table S8). Similar findings were found for influent wastewater and were most notable for sulfamethoxazole which was not detected in most pH adjusted samples. It is suspected that partitioning equilibrium similar to starting conditions were not re-established. This could be improved for some micropollutants if sample extraction can be performed at pH 2 (e.g., see Baker and Kasprzyk-Hordern, 2011), and internal standards used for quantification were spiked prior to sample filtration to account for changes to partitioning. However, such an approach would result in total concentration (aqueous + particulate phases) being obtained over the aqueous concentration.

Overcoming stability issues associated with composite sampling for the multi-residue determination of micropollutants may require an integrated approach to sample collection. For example, multi-bottle sampling could be applied such that more than one 24 h composite sample is collected by the same automated sampler; one stored at 4 °C, another at pH 2 (and 4 °C). Admittedly this would not be resource efficient as analysis time and costs would effectively double. Therefore trade-offs may be required when selecting an appropriate stabilisation method(s) for the multi-residue determination of micropollutants in wastewater. In future studies such decisions must be made following stability tests of the micropollutants to be studied using site specific matrix as no generic stabilisation method could be established.

3.3. Suitability of time paced composite sampling for monitoring micropollutants in effluent wastewater

The most common way of collecting a composite sample is in a time proportional manner. A number of studies adopt a default sampling frequency of 15 min (Lishman et al., 2006; Morasch et al., 2010; Nagarnaik et al., 2010; Reungoat et al., 2010; Golovko et al., 2014; Vuori et al., 2014; Mackuľak et al., 2015), which is typical for environmental applications. This is also the lowest sampling frequency which can be practically applied when using portable samplers (i.e., not connected to an external power supply). However, Ort et al. (2010) used a model to show that this sampling approach for influent wastewater is biased even at a high number of pulses per day (e.g., 10,000 p d^{-1}). Sampling errors of >20% were noted and can be attributed to the dynamic nature of wastewater flow and micropollutant concentration. This error can be reduced by sampling in a volume- or flow-proportional manner. Error distributions were unbiased and <20% for both these methods at ≥100p d^{-1} whilst at sampling frequencies of 15 min (Ort et al., 2010). For the majority of micropollutants studied and detected here, the number of pulses are estimated to be >100 p d^{-1}. However, it is unknown if time-paced composite sampling can provide similar information to volume-paced sampling for effluent wastewater.

A total of 90 micropollutants were monitored over 8 d resulting in 720 data points for comparison. Of these 720 data points, 530 were

Table 1
Loss of micropollutants in deionised water and collected effluent wastewater stored at 4 °C, 4 °C + pH 2 and 4 °C + NaN_3 in polypropylene bottles over a 24 h time period (n = 2). Underlined values show those out with ±20% significance level.

Micropollutant class	Micropollutant	Concentration relative to t = 0 after 24 h storage (%)						
		H_2O	WWTP A effluent			WWTP B effluent		
		4 °C	4 °C	4 °C + pH 2	4 °C + NaN_3	4 °C	4 °C + pH 2	4 °C + NaN_3
UV filters	Benzophenone-1	109	92	118	123	98	61	110
	Benzophenone-2	106	99	68	90	95	64	70
	Benzophenone-3	95	65	50	81	78	60	122
	Benzophenone-4	111	104	107	101	102	102	102
Parabens	Methylparaben	98	65	109	90	48	96	76
	Ethylparaben	99	80	113	90	65	93	94
	Propylparaben	106	88	90	88	75	81	95
	Butylparaben	104	80	101	100	93	102	131
Plasticizer	Bisphenol-A	95	106	171	82	116	134	91
Steroid estrogens	E1	102	101	97	107	93	94	143
	E2	91	86	90	89	35	97	35
	EE2	93	106	104	104	110	112	120
Antibacterials/antibiotics	Sulfasalazine	89	96	82	133	91	77	111
	Clarithromycin	83	86	79	91	100	74	129
	Azithromycin	87	85	41	103	89	60	256
	Trimethoprim	105	81	17	146	102	22	215
	Sulfamethoxazole	101	88	<1	90	93	3	105
	Triclosan	91	–	–	–	–	–	–
Hypertension	Valsartan	105	107	63	92	99	87	92
	Irbesartan	115	96	89	82	89	50	77
	Lisinopril	103	84	60	167	101	49	142
NSAIDs	Ketoprofen	97	106	98	101	92	92	93
	Ibuprofen	100	102	108	97	83	105	95
	Naproxen	98	100	92	86	95	100	102
	Diclofenac	92	103	45	86	89	75	91
	Acetaminophen	100	15	71	59	20	111	83
Lipid regulators	Bezafibrate	101	104	101	103	101	94	104
	Atorvastatin	100	84	32	97	89	69	86
Antihistamines	Fexofenadine	85	104	50	82	101	89	95
	Cetirizine	116	138	79	158	118	67	91
Diabetes	Metformin	100	100	91	95	98	96	93
	Gliclazide	101	98	88	68	85	72	52
Cough suppressant	Pholcodine	10	102	74	65	86	65	55
Beta-blocker	Atenolol	98	93	102	94	99	96	103
	Metoprolol	99	96	101	95	92	96	98
	Propranolol	99	94	104	103	99	104	99
H_2 receptor agonists	Ranitidine	103	86	12	99	95	54	91
	Cimetidine	92	82	110	81	91	103	71
X-ray contrast media	Iopromide	100	94	100	95	90	91	96
Drug precursor and metabolite	Ephedrine/pseudoephedrine	91	90	357	78	102	204	113
	Norephedrine	103	86	103	72	92	84	112
Anti-cancer	Azathioprine	98	93	99	77	90	84	83
	Methotrexate	99	–	–	–	–	–	–
	Ifosfamide	95	100	79	91	99	84	133
	Tamoxifen	34	–	–	–	–	–	–
Anaesthetic and metabolite	Ketamine	100	102	101	98	98	100	96
	Norketamine	98	97	100	92	97	102	104
Anti-depressants and metabolites	Venlafaxine	102	85	114	102	98	108	103
	Desvenlafaxine	101	95	92	97	95	98	100
	Fluoxetine	102	57	83	56	88	101	83
	Norfluoxetine	101	59	80	54	83	115	91
	Sertraline	94	85	110	63	87	98	85
	Mirtazapine	99	93	103	93	101	108	99
	Citalopram	95	90	105	91	108	104	104
	Desmethylcitalopram	104	98	117	79	87	131	60
Anti-epileptic and metabolites	Carbamazepine	100	96	99	96	92	95	95
	Carbamazepine10,11-epoxide	99	97	32	92	90	40	83
	10,11-Dihydro-10-hydroxycarbamazepine	97	93	93	92	93	94	93
Calcium channel blocker	Diltiazem	106	81	149	34	120	480	<1
Hypnotic	Temazepam	107	94	92	95	101	96	109
Anti-psychotic	Quetiapine	92	98	94	92	100	98	99
Veterinary	Tylosin	104	84	68	85	105	96	122
Human indicators and metabolites	Creatinine	110	112	101	44	105	141	100
	Nicotine	99	111	268	123	92	199	99
	Caffeine	98	87	93	88	87	108	110
	Cotinine	98	94	98	93	96	103	105
	1,7 dimethylxantine	105	89	99	86	94	111	105
Analgaesics and metabolites	Morphine	93	113	99	99	108	107	84
	Dihydromorphine	95	101	98	107	91	102	38

(continued on next page)

Table 1 (*continued*)

Micropollutant class	Micropollutant	Concentration relative to t = 0 after 24 h storage (%)						
		H_2O	WWTP A effluent			WWTP B effluent		
		4 °C	4 °C	4 °C + pH 2	4 °C + NaN_3	4 °C	4 °C + pH 2	4 °C + NaN_3
	Normorphine	101	95	106	101	104	130	91
	Methadone	107	93	112	91	106	117	101
	EDDP	95	98	107	101	96	104	102
	Codeine	99	98	97	99	93	103	99
	Norcodeine	103	92	108	107	97	109	103
	Dihydrocodeine	96	91	95	92	99	107	106
	Tramadol	98	103	108	103	92	96	92
	N-desmethyltramadol	100	81	119	116	99	109	136
	O-desmethyltramadol	101	91	102	87	98	101	95
Stimulants and metabolites	Amphetamine	102	94	101	112	93	103	119
	Methamphetamine	100	98	115	94	99	120	91
	MDMA	96	93	107	95	98	96	99
	MDA	105	99	105	100	102	107	101
	Cocaine	103	94	98	90	91	97	96
	Benzoylecgonine	98	102	91	102	101	89	112
	Anhydroecgonine methylester	102	120	276	115	87	157	81
	Cocaethylene	102	99	107	98	99	108	105
	Mephedrone	94	109	103	96	92	101	100
	MDPV	103	93	125	123	105	107	112
Opioid and metabolite	Heroin	99	81	104	47	84	94	<1
	6-acetylmorphine	103	105	79	102	97	57	15

Key: WWTP, wastewater treatment plant; E1, estrone; E2, 17β-estradiol; EE2, 17α-ethinylestradiol; EDDP, 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine; MDMA, 3,4-methylenedioxy-methamphetamine; MDA, 3,4-methylenedioxy-amphetamine; MDPV, methylenedioxypyrovalerone; -, the initial concentration was below the method quantitation limit for 10 mL extractions (triclosan, <81 ng L^{-1}; methotrexate, <117 ng L^{-1}; tamoxifen, <18 ng L^{-1}).

found to be >MQL. During the 8 d sampling period, no significant difference (>20%) in concentration was observed between time-paced and volume-paced composite sampling for any micropollutant in effluent wastewater (Table S9). This was in contrast to influent wastewater which saw 66 of 471 quantified micropollutants concentrations in time-paced composites to be outside a ± 20% tolerance limit of the volume-paced composite (Table S9). The HRT of the WWTP under investigation (WWTP A) is typically ~8 h considering residence times in primary sedimentation tanks, open channels, trickling filters and humus tanks providing greater mixing. Consequently, intra-day variability in concentration (calculated from all grab samples collected throughout the day) was generally lower (Table S10), resulting in similar concentration information obtained by time- and volume-paced composites. This may require further validation for different process types to ensure these observations can be extrapolated to other systems.

Interestingly, mean concentrations determined from grab sampling (n = 24, equivalent to a composite sample with a 1 h sub-sample collection frequency) were similar to those determined by composite sampling (within ±20%) (Fig. 1A). However, in practical terms if grab sampling was to be applied, only one sample would be collected per day during a monitoring study. Therefore the representativeness of grab sampling will be underpinned by the extent of diurnal concentration variation. The variation observed throughout 24 h was different between micropollutants and appeared independent of number of pulses (Fig. 1B). To demonstrate, caffeine (>10,000 p d^{-1}) varied in concentration from 1125 to 18,688 ng L^{-1} (intra-day concentration variability = 69%, n = 24). In contrast, azithromycin (200 p d^{-1}) ranged from 85 to 148 ng L^{-1} (intra-day concentration variability = 15%, n = 24). Similarly carbamazepine (2800 p d^{-1}) varied from 135 to 176 ng L^{-1} (intra-day concentration variability = 8%, n = 24). This is in agreement with Nelson et al. (2011) who noted intra-day concentration variations of 6–8% (n = 24) for carbamazepine in tertiary effluent wastewater. Consequently, of the 24 grab samples collected only three for caffeine whereas 20 and 21 for azithromycin and carbamazepine provided concentrations within ±20% of the composite sample (Fig. 1B). Therefore collecting one grab sample per day is not suitable for obtaining representative information on daily micropollutant concentrations. Nevertheless, as not all WWTPs have samplers permanently installed (particularly for smaller plants), the possibility of sampling effluent wastewater using time paced composite samplers over volume or flow composites is advantageous. This is because WWTPs are less likely to have suitable sites (e.g., easily accessible open channels) for deploying portable flow meters to measure effluent discharge and control sample collection.

3.4. Diurnal changes to the enantiomeric distribution of chiral micropollutants in effluent wastewater

Due to enantio-specific toxicity towards exposed aquatic micro-organisms, it is essential to include analysis of chiral micropollutants at the enantiomeric level in monitoring studies for accurate environmental risk assessment. However, there is a paucity of information on temporal changes to the enantiomeric distribution of chiral micropollutants in effluent wastewaters. In wastewater, enantiomeric distribution could vary both within the same day and between different days. This can be a result of (i) changing HRT (due to changes in flow) within the receiving sewer and WWTP causing varying degrees of stereo-selective transformation, or (ii) the direct disposal of non-consumed drugs which would normally undergo stereo-selective changes when consumed and metabolised (Emke et al., 2014; Petrie et al., 2016a).

Based on flow data when hourly grab samples were collected, the variability in WWTP HRT was estimated to range from 6 to 14 h. However, grab samples (n = 24) showed little change to EF of the studied chiral micropollutants (Fig. 2). Fluoxetine showed the greatest variation throughout the day with EFs ranging from 0.88 to 1.00. This EF denotes enrichment with S-(+)-fluoxetine. This enantiomer is reported to be 10 times more toxic then R-(−)-fluoxetine to both *P. promelas* (Stanley et al., 2007) and *T. thermophila* (De Andrés et al., 2009), illustrating the necessity of incorporating enantio-selective analysis into monitoring strategy for environmental risk assessment. Similarly, little change to EFs was observed between different days. Only MDMA showed temporal changes to EF, ranging from 0.24 to 0.38 over the 8 d (Fig. 3). In influent wastewater the majority of chiral micropollutants showed similar variability in their enantiomeric distribution both throughout the day and between different days (Fig. S1; Fig. S2). This suggests that the number

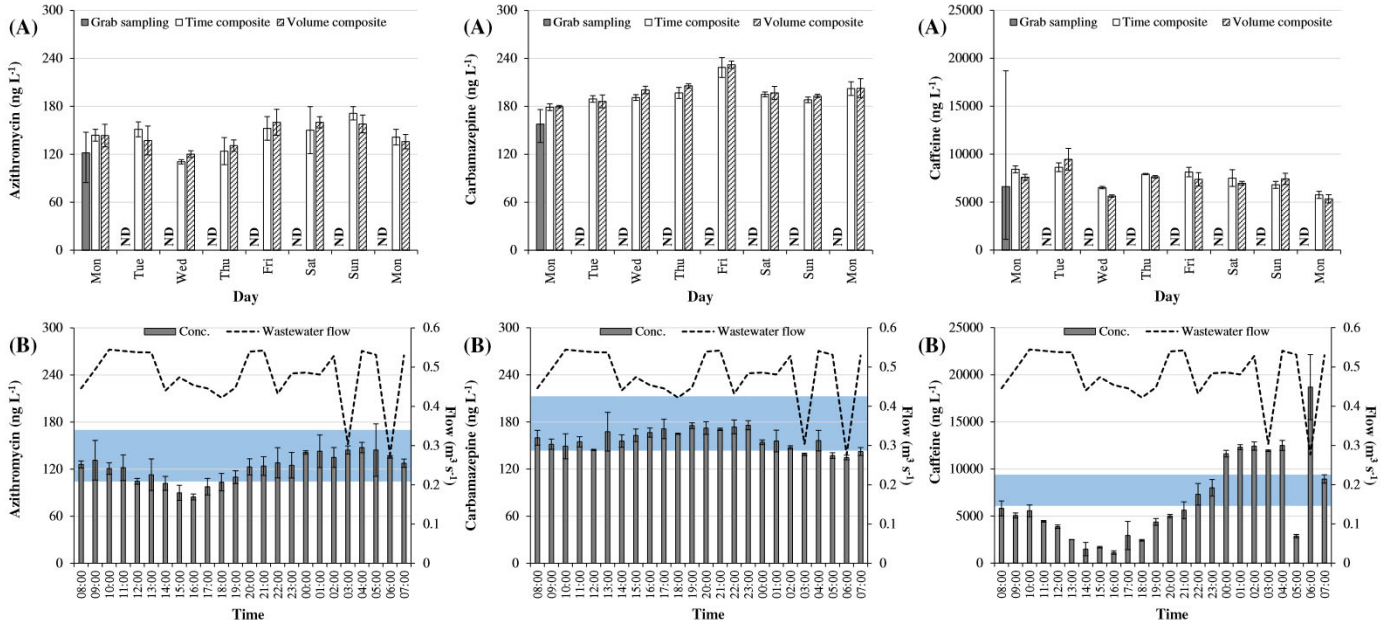

Fig. 1. Impact of sampling mode on concentration of azithromycin (200 p d^{-1}), carbamazepine (2800 p d^{-1}) and caffeine (>10,000 pd^{-1}) in effluent wastewater over 8 d (A), and hourly concentration on the first Monday of the 8 d sampling period (B) – the blue shaded area represents the average hourly concentration of the volume paced 24 h composite ±20%. Note: grab sampling in (A) is the average of n = 24 samples from (B) (equivalent to a composite sample with a 1 h sub-sample collection frequency), and error bars here represent the range of data. All other error bars represent the standard deviation of the mean. Key: p d^{-1}, pulses per day; ND, not determined.

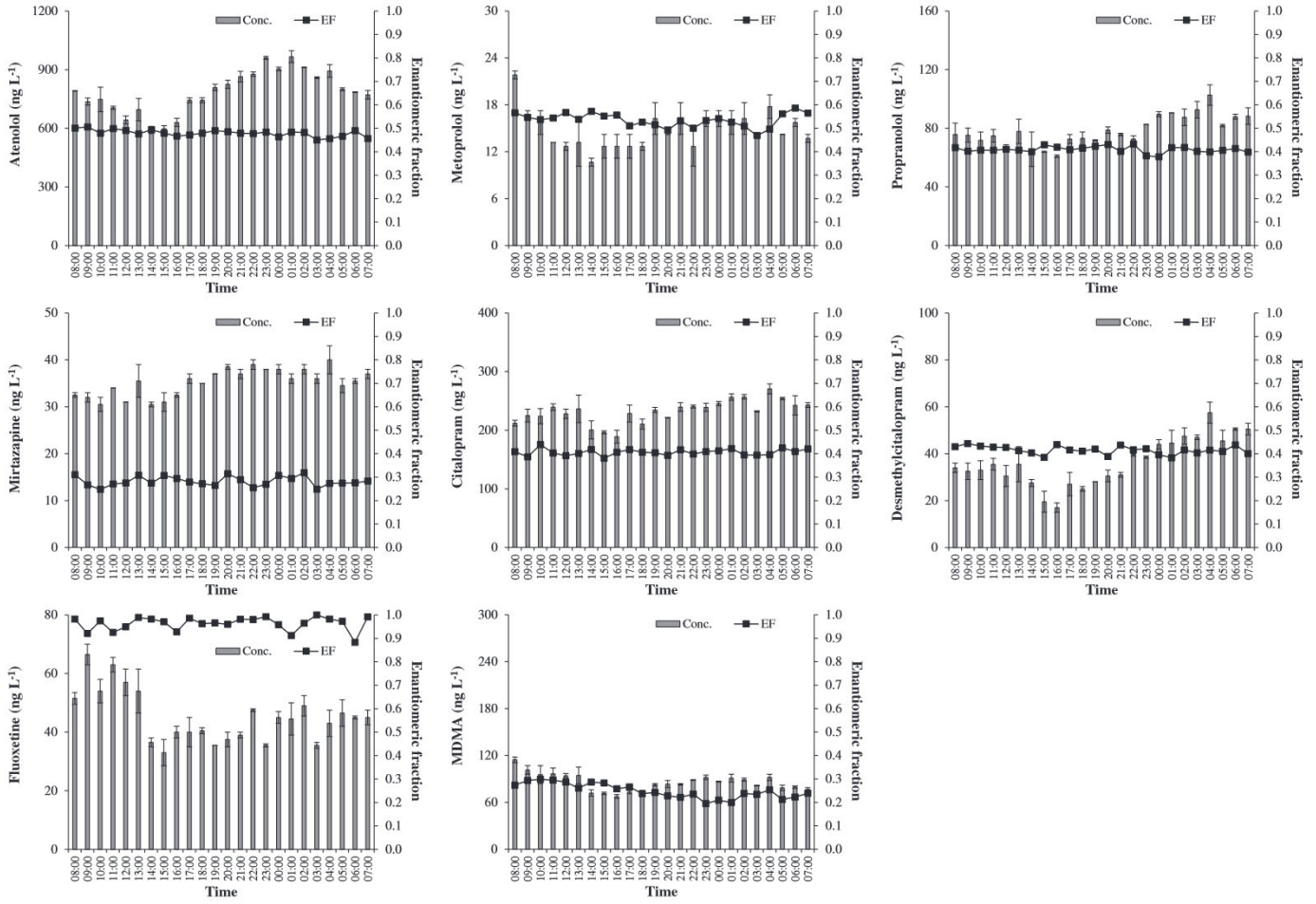

Fig. 2. Hourly concentrations and enantiomeric fraction of chiral micropollutants in effluent wastewater on the first Monday of the sampling period in January 2015. Key: EF, enantiomeric fraction; MDMA, 3,4-methylenedioxy-methamphetamine.

of enantio-selective analysis performed could be reduced during a typical week-long sampling period. Such an approach would be advantageous as several analytical methodologies are often required (including SPE protocols) to determine a range of chiral micropollutants at the enantiomeric level. However, this is not recommended as unpredictable short-term (e.g., daily) changes to enantiomeric distribution can occur by the direct disposal of unused medication (see fluoxetine - Fig. S2; Petrie et al., 2016a). Therefore the same resolution of enantio-selective analysis as more routine achiral (e.g., C_{18}) analytical methodologies is needed throughout the entire monitoring period. This will ensure accurate information for environmental risk assessment is attained.

3.5. Recommendations for monitoring micropollutants in effluent wastewater for regulatory compliance

There is likely to be legislation implemented in the future governing the discharge of trace organic micropollutants (e.g., pharmaceuticals) from WWTPs into the environment. This will put emphasis on monitoring strategies to ensure representative data are attained to accurately determine compliance with legislative discharge limits. Currently, sampling effluent wastewater quality for regulatory compliance or consent often involves the collection of low-frequency grab samples. This approach has been adopted in several national studies monitoring micropollutants in treated effluents in both the UK (Gardner et al., 2012) and across the rest of Europe (Loos et al., 2013). However, considering the diurnal variability in micropollutant concentration (Fig. 1; Table S10) and EQS are likely to applicable to annual average concentrations, collecting a sample which can provide accurate concentration information for a 24 h period or longer is recommended. Such an approach would provide representative information and be more suitable for assessing regulatory compliance. Passive sampling has been considered for providing estimated time-weighted concentrations for periods of 7 d or longer. However, this technology has yet to prove itself for providing accurate concentration information suitable for regulatory purposes (Jones et al., 2015). Therefore 24 h composite sampling will be needed for monitoring regulated micropollutants in effluent wastewater. As reported in this manuscript, ensuring the stability of micropollutants during sample collection is critical for such an approach to be successfully implemented for regulatory purposes. It is expected that chiral micropollutants will not be regulated at the enantiomeric level in the short-term. EQS are likely to apply to the sum of all enantiomers for a given micropollutant. However, the application of enantio-selective analysis as a complimentary technique where possible will help develop future legislation to ensure protection of the receiving environment.

4. Conclusions

- Polypropylene, the most common used sampler bottle material, was suitable for the determination of 89 of the 90 studied micropollutants. Only tamoxifen ($\log K_{OW} = 6.3$) showed significant losses of >20% to sample bottles.
- No generic method could be identified to stabilise all 90 micropollutants simultaneously during composite sample collection.

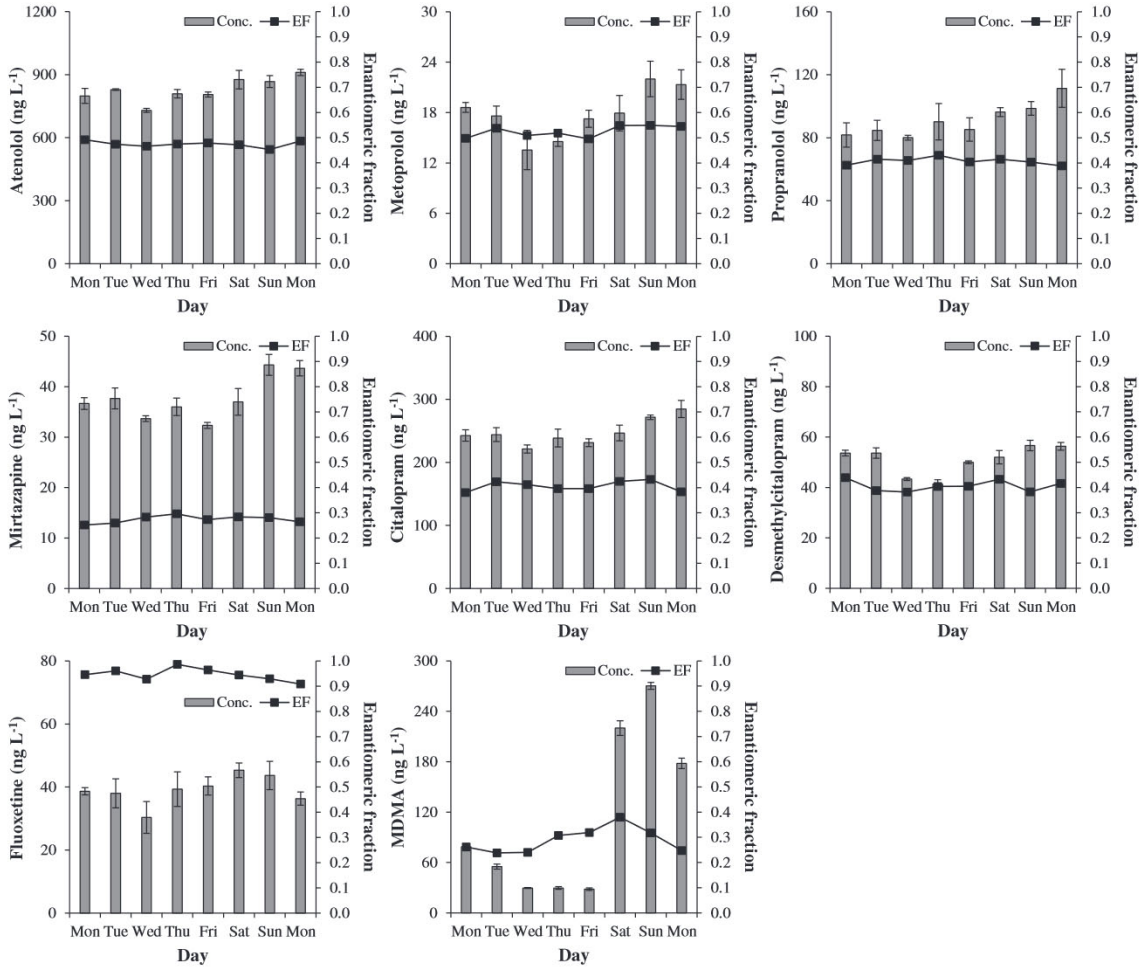

Fig. 3. Daily concentrations and enantiomeric fraction of chiral micropollutants in effluent wastewater over 8 d in January 2015 collected as 24 h volume paced composites. Key: EF, enantiomeric fraction; MDMA, 3,4-methylenedioxy-methamphetamine.

Cooling samples to 4 °C provided the best solution but to stabilise further micropollutants, multi-bottle sampling is required to provide additional storage conditions (e.g., pH 2). In any case, the stability of target micropollutants in the matrix to be monitored should be investigated prior to any sampling campaign.

- In effluent wastewater, time-paced composites provided similar concentrations (within ±20%) to volume-paced composites for the 90 micropollutants over 8 d. Reducing the need to sample effluent wastewater in a way which accounts for flow variability is advantageous as not all WWTPs have sampler compatible flow meters installed on their premises, or suitable sites for the easy deployment of portable ones.
- The enantiomeric distribution of chiral micropollutants did not change for the majority of micropollutants over 8 d. However, short-term changes may occur as a result of direct disposal. The unpredictability of such events demands similar resolution of enantio-selective analysis as more routine achiral methods throughout the sampling period.

Acknowledgements

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Appendix A. Supplementary data.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.scitotenv.2016.11.059.

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Supplementary material:

Critical evaluation of monitoring strategy for the multi-residue determination of 90 chiral and achiral micropollutants in effluent wastewater

Bruce Petrie[a,b], Kathryn Proctor[a,b], Jane Youdan[c], Ruth Barden[c] and Barbara Kasprzyk-Hordern[a,b]*

[a]Department of Chemistry, University of Bath, Bath, BA2 7AY, UK

[b]Water Innovation & Research Centre (WIRC), University of Bath, Bath BA2 7AY, Bath, UK

[c]Wessex Water, Bath, BA2 7WW, UK

Corresponding author at *b.kasprzyk-hordern@bath.ac.uk

The supplementary material contains two figures and ten tables:

Table S8. Stability (%) of micropollutants in collected influent and effluent wastewater stored at pH 2 at 18 ^{0}C and 4 ^{0}C over a 24 hour time period (n=2). Underlined values show those out with ±20 % significance level

Table S9. Difference in micropollutant concentration (%) of influent and effluent wastewater daily composites collected in a time paced versus a volume paced manner (n=3). Underlined values show those out with ±20 % significance level

Table S10. Frequency of detection, minimum, maximum and median hourly concentrations of micropollutants in grab samples of influent and effluent wastewater

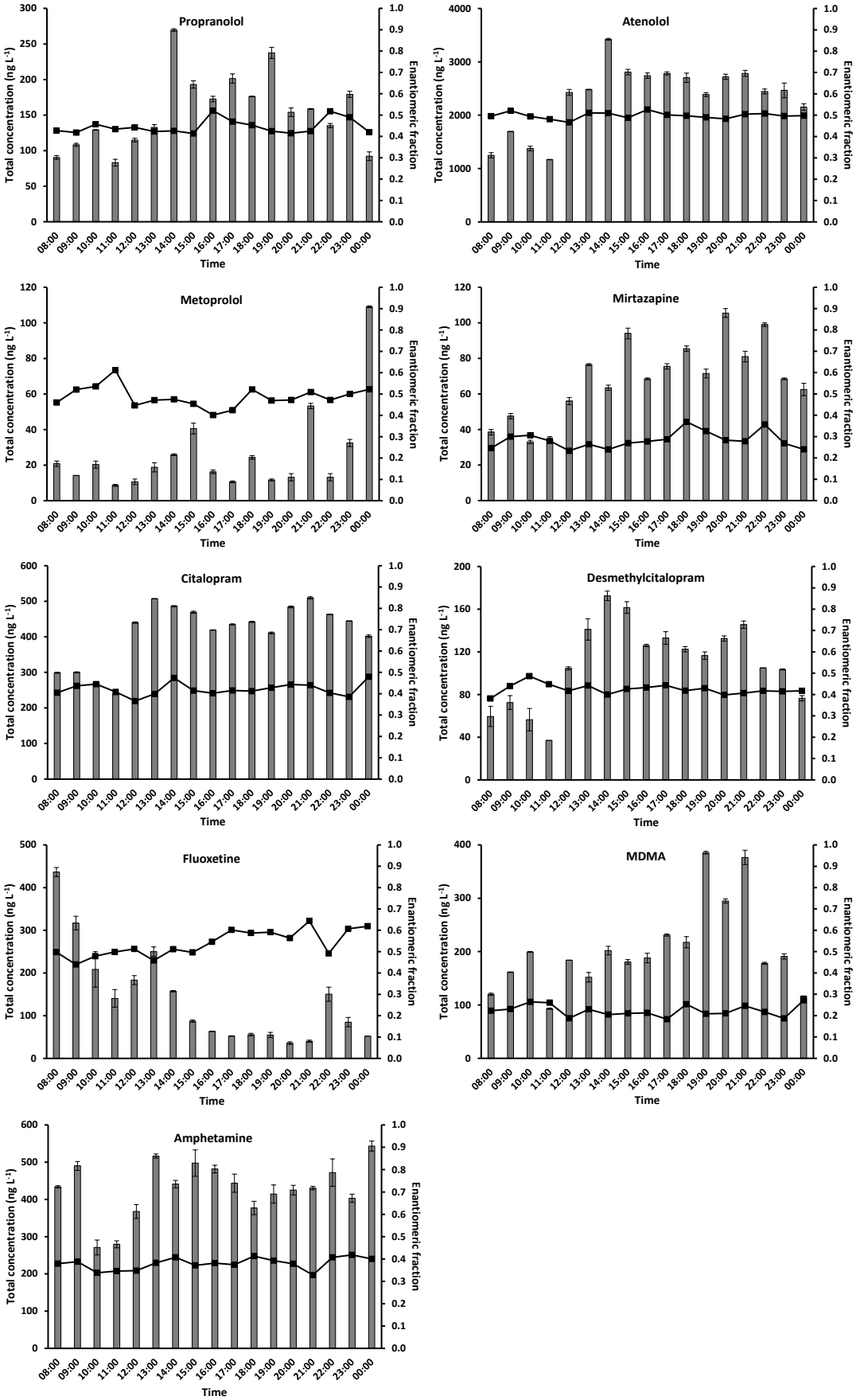

Figure S1. Hourly profile (8:00-00:00, n=17) of chiral drug concentration and enantiomeric fraction in influent wastewater grab samples. Fluoxetine graph adapted from Petrie et al [1].

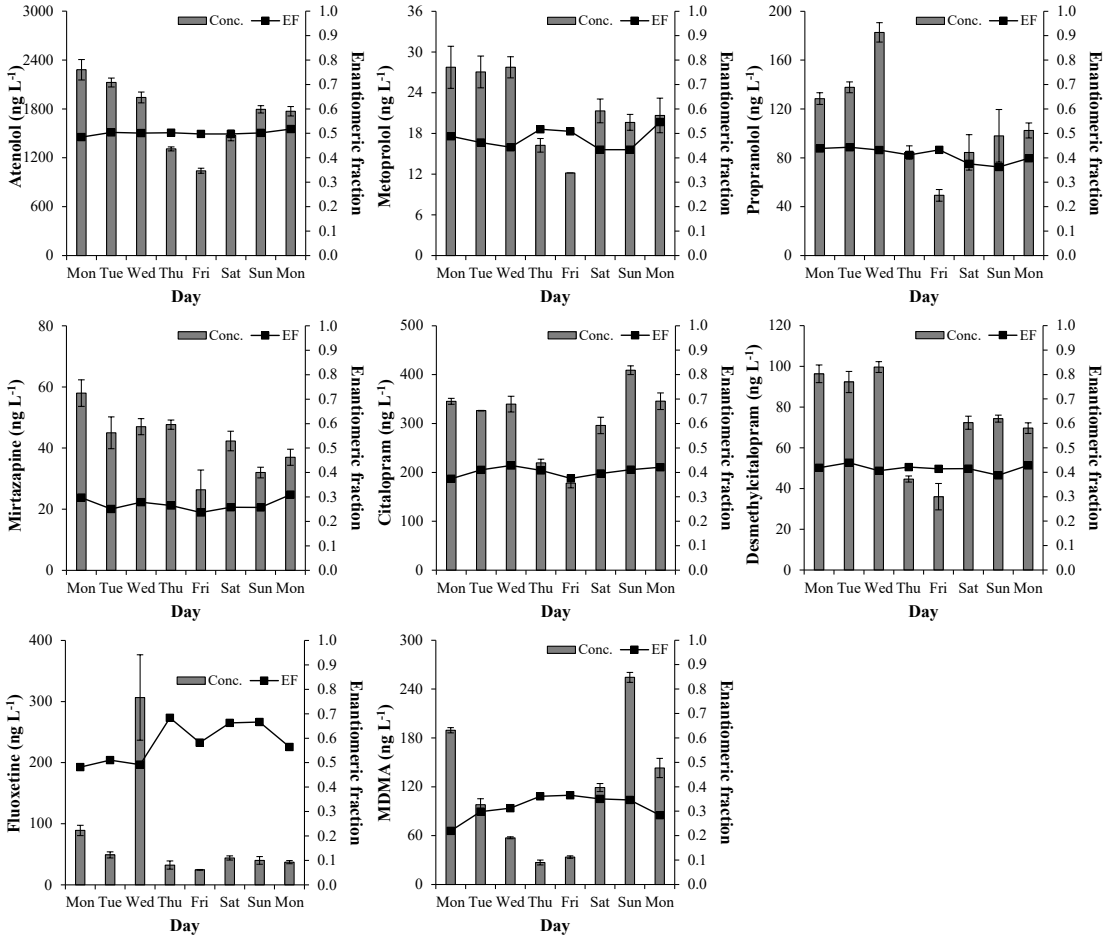

Figure S2. Daily concentrations and enantiomeric fraction of chiral micropollutants in influent wastewater over 8 d in December 2014 collected as 24 h volume paced composites. Fluoxetine graph adapted from Petrie et al [1].

Table S1. Chemical information of micropollutants studied

Micropollutant class	Micropollutant	Molecular Formula	Prescription 2012 (kg)	Water Solubility (mg L^{-1})[i]	Log Kow[ii]	Log Koc[iii]	Log Dow[iv]	Henry's Law Constant (atm m^3mol^{-1})[v]	Vapour Pressure (Torr)[vi]	pKa (Most acidic)[vii]	pKa (Most basic)[viii]
UV filters	Benzophenone-1	$C_{13}H_{10}O_3$	-	413.4	2.96	2.65E-11	2.90	2.65E-11	2.84E-07	7.72±0.35	-
	Benzophenone-2	$C_{13}H_{10}O_5$	-	398.5	2.78	3.61E-16	2.35	3.61E-16	6.69E-12	6.98±0.35	-
	Benzophenone-3	$C_{14}H_{12}O_3$	-	68.6	3.52	1.50E-08	3.06	1.50E-08	5.26E-06	7.56±0.35	-
	Benzophenone-4	$C_{14}H_{12}O_6S$	-	2.03E+04	0.37	7.03E-15	-0.53	7.06E-15	-	-0.70±0.50	-
Parabens	Methylparaben	$C_8H_8O_3$	-	5.98E+03	2.00	2.23E-09	1.63	3.61E-09	5.55E-03	8.31±0.13	-
	Ethylparaben	$C_9H_{10}O_3$	-	1.89E+03	2.49	3.01E-09	1.99	4.79E-09	7.59E-04	8.31±0.13	-
	Propylparaben	$C_{10}H_{12}O_3$	-	529.3	2.98	4.25E-09	2.51	4.25E-12	9.30E-04	8.23±0.15	-
	Butylparaben	$C_{11}H_{14}O_3$	-	159.0	3.47	6.00E-009	2.96	6.00E-09	3.56E-04	8.22±0.15	-
Plasticizer	Bisphenol-A	$C_{15}H_{16}O_2$	-	172.7	3.64	9.16E-12	4.04	9.16E-12	5.34E-07	10.29±0.10	-
Steroid estrogens	E1	$C_{18}H_{22}O_2$	-	146.8	3.43	3.80E-10	4.31	3.80E-10	1.54E-08	10.25±0.40	-
	E2	$C_{18}H_{24}O_2$	84	82.0	3.94	1.41E-12	3.74	1.41E-12	9.82E-09	10.27±0.60	-
	EE2	$C_{20}H_{24}O_2$	12	116.4	4.12	7.94E-12	3.90	7.94E-12	3.74E-09	10.24±0.60	-
Antibacterials/ antibiotics	Sulfasalazine	$C_{18}H_{14}N_4O_5S$	54,039	2.4	3.81	2.19E-18	-1.76	2.19E-18	5.95E-20	2.70±0.10	0.90±0.10
	Clarithromycin	$C_{38}H_{69}NO_{13}$	16,508	0.3	3.18	1.73E-29	2.31	1.73E-29	5.06E-30	13.08±0.70	8.16±0.70
	Azithromycin	$C_{38}H_{72}N_2O_{12}$	1,965	6.20E-02	3.24	5.30E-29	-2.48	5.30E-29	2.51E-31	13.28±0.70	8.59±0.70
	Trimethoprim	$C_{14}H_{18}N_4O_3$	10,998	2.33E+03	0.73	2.39E-14	1.13	2.39E-14	3.74E-11	-	7.04±0.10
	Sulfamethoxazole	$C_{10}H_{11}N_3O_3S$	-	3.94E+03	0.48	9.56E-13	-0.03	9.56E-13	1.87E-09	5.81±0.50	1.39±0.10
	Triclosan	$C_{12}H_7Cl_3O_2$	-	4.6	4.66	2.13E-08	4.76	2.13E-08	3.26E-05	7.80±0.35	-
Hypertension	Valsartan	$C_{24}H_{29}N_5O_3$	6,484	1.4	3.65	1.82E-18	1.15	1.82E-18	1.06E-19	3.56±0.10	0.60±0.10
	Irbesartan	$C_{25}H_{28}N_6O$	8,353	-	-	-	4.97	-	1.05E-16	4.16±0.10	2.60+0.20
	Lisinopril	$C_{21}H_{31}N_3O_5$	4,799	8.6	-0.94	1.89E-22	-3.23	1.89E-22	1.14E-18	2.18±0.10	10.50±0.10
NSAIDS	Ketoprofen	$C_{16}H_{14}O_3$	243	120.4	3.00	2.12E-11	0.08	2.12E-11	3.32E-08	4.23±0.10	-
	Ibuprofen	$C_{13}H_{18}O_2$	108,435	41.1	3.79	1.52E-07	1.25	1.52E-07	1.39E-04	4.41±0.10	-
	Naproxen	$C_{14}H_{14}O_3$	126,258	144.9	3.10	3.39E-10	-0.54	3.39E-10	3.01E-07	4.84±0.30	-
	Diclofenac	$C_{14}H_{11}Cl_2NO_2$	10,652	4.5	4.02	4.73E-12	0.73	4.73E-12	1.59E-07	4.18±0.10	-2.26±0.50
	Acetaminophen	$C_8H_9NO_2$	>2,000,000	3.04E+04	0.27	6.42E-13	0.90	6.42E-13	1.43E-06	9.86±0.13	1.72±0.50
Lipid regulators	Bezafibrate	$C_{19}H_{20}ClNO_4$	7,966	1.2	4.25	2.12E-15	0.46	2.12E-15	6.29E-14	3.29±0.10	-2.06±0.70
	Atorvostatin	$C_{33}H_{35}FN_2O_5$	13,937	1.12E-03	6.36	2.41E-23	1.86	2.41E-23	6.84E-22	4.29±0.10	0.38±0.50
Antihistamines	Fexofenadine	$C_{32}H_{39}NO_4$	8,715	2.36E-02	2.81	1.19E-18	2.93	1.19E-18	2.08E-20	4.43±0.10	9.42±0.10
	Cetirizine	$C_{21}H_{25}ClN_2O_3$	1,612	1.1	-0.61	4.19E-17	0.69	4.19E-17	1.39E-12	3.46±0.10	6.71±0.10

Diabetes	Metformin	$C_4H_{11}N_5$	-	1.00E+06	-2.64	7.64E-16	-6.45	7.64E-16	1.33	-	12.27±0.10
	Gliclazide	$C_{15}H_{21}N_3O_3S$	35,194	138.4	2.12	7.95E-13	0.79	7.95E-13	-	6.07±0.10	3.89±0.20
Cough suppressant	Pholcodine	$C_{23}H_{30}N_2O_4$	600	1.01E+04	0.59	3.42E-19	-0.48	3.42E-19	3.44E-14	13.40±0.20	8.22±0.40
Beta-blocker	Atenolol	$C_{14}H_{22}N_2O_3$	20,725	685.2	-0.03	1.37E-18	-1.71	1.37E-18	3.82E-11	13.88±0.20	9.43±0.10
	Metoprolol	$C_{15}H_{25}NO_3$	2,311	4.77E+03	1.69	1.40E-13	-0.38	1.40E-13	4.52E-07	13.89±0.20	9.43±0.10
	Propranolol	$C_{16}H_{21}NO_2$	9,076	228.0	2.60	7.98E-13	0.45	7.98E-13	2.48E-08	13.84±0.20	9.50±0.30
H_2 receptor agonists	Ranitidine	$C_{13}H_{22}N_4O_3S$	35,665	2.47E+04	0.29	3.42E-15	-1.56	3.42E-15	7.66E-08	-	8.35±0.28
	Cimetidine	$C_{10}H_{16}N_6S$	3,195	1.05E+04	0.57	9.55E-16	-0.30	9.55E-16	3.13E-09	14.13±0.10	7.07±0.61
X-ray contrast media	Iopromide	$C_{18}H_{24}I_3N_3O_8$	-	23.8	-2.49	1.00E-028	-0.44	1.00E-28	5.00E-30	10.62±0.70	-2.60±0.70
Drug precursor and metabolite	Ephedrine/ pseudoephedrine	$C_{10}H_{15}NO$	622	7.15E+04	0.68	8.65E-11	-1.13	8.65E-11	8.65E-03	13.96±0.20	9.38±0.10
	Norephedrine	$C_9H_{13}NO$	-	1.49E+05	0.22	3.94E-11	-1.40	3.94E-11	1.10E-03	12.07±0.45	8.47±0.10
Anti-cancer	Azathioprine	$C_9H_7N_7O_2S$	2,768	272.3	-0.09	2.64E-15	1.21	2.64E-15	5.94E-11	-	7.47±0.20
	Methotrexate	$C_{20}H_{22}N_8O_5$	126	2.60E+03	-1.28	1.54E-31	-7.06	1.54E-31	-	3.47±0.10	5.56±0.10
	Ifosfamide	$C_7H_{15}Cl_2N_2O_2P$	-	3.78E+03	0.97	1.36E-11	0.10	1.36E-11	1.15E-04	-	1.44±0.20
	Tamoxifen	$C_{26}H_{29}NO$	453	0.2	6.30	4.49E-10	5.07	4.49E-10	1.85E-09	-	8.69±0.28
Anaesthetic and metabolite	Ketamine	$C_{13}H_{16}ClNO$	64	3.87E+03	3.12	1.38E-08	3.18	1.38E-08	1.76E-05	-	6.46±0.20
	Norketamine	$C_{15}H_{11}ClN_2O$	-	-	-	-	2.71	1.78E-10	1.26E-05	-	6.25±0.20
Anti-depressants and metabolites	Venlafaxine	$C_{17}H_{27}N_1O_2$	16,211	266.7	3.28	2.87E-11	1.32	2.87E-11	4.92E-07	14.84±0.20	9.26±0.28
	Desmethylvenlafaxine	$C_{16}H_{25}NO_2$	-	-	-	-	1.17	-	3.03E-07	10.04±0.26	9.33±0.28
	Fluoxetine	$C_{17}H_{18}F_3NO$	5,319	60.3	4.65	8.90E-08	1.92	8.90E-08	1.88E-06	-	10.05±0.10
	Norfluoxetine	$C_{16}H_{16}F_3NO$	-	-	-	-	1.54	-	5.21E-06	-	9.05±0.13
	Sertraline	$C_{17}H_{17}Cl_2N$	11,429	3.5	5.29	5.10E-08	3.11	5.10E-08	3.85E-07	-	9.47±0.40
	Mirtazapine	$C_{17}H_{19}N_3$	3,239	-	-	-	3.15	-	1.11E-07	-	8.10±0.20
	Citalopram	$C_{20}H_{21}FN_2O$	8,878	31.1	3.74	2.69E-11	1.50	2.69E-11	1.53E-07	-	9.57±0.28
	Desmethylcitalopram	$C_{19}H_{19}FN_2O$	-	-	-	-	0.14	-	1.40E-07	-	10.50±0.10
Anti-epileptic and metabolites	Carbamazepine	$C_{15}H_{12}N_2O$	44,498	17.7	2.25	1.08E-10	2.77	1.08E-10	5.78E-07	13.94±0.20	-0.49±0.20
	Carbamazepine10,11-epoxide	$C_{15}H_{12}N_2O_2$	-	-	-	-	1.97	-	2.69E-06	13.91±0.20	-0.50±0.20
	10,11-Dihydro-10-hydroxycarbamazepine	$C_{15}H_{14}N_2O_2$	-	-	-	-	1.73	-	3.33E-08	13.75±0.20	-0.53±0.40
Calcium channel blocker	Diltiazem	$C_{22}H_{26}N_2O_4S$	21,922	12.3	2.79	8.61E-17	1.97	8.61E-17	4.27E-14	-	8.94±0.28
Hypnotic	Temazepam	$C_{16}H_{13}ClN_2O_2$	833	163.9	2.15	1.13E-08	2.79	1.13E-08	6.33E-13	11.66±0.40	1.58±0.50
Anti-psychotic	Quetiapine	$C_{21}H_{25}N_3O_2S$	9,155	0.6	3.17	7.45E-18	2.67	7.45E-18	3.22E-13	14.41±0.10	6.74±0.10
Veterinary	Tylosin	$C_{46}H_{77}NO_{17}$	-	0.5	1.05	5.77E-38	2.14	5.77E-38	0	13.06±0.70	7.39±0.70
Human indicators and metabolites	Creatinine	$C_4H_7N_3O$	-	1.66E+05	-1.21	2.42E-12	-1.07	2.42E-12	0.313	-	6.89±0.20

	Nicotine	$C_{10}H_{14}N_2$	442	1.00E+06	1.00	3.00E-09	-2.34	3.00E-09	0.0303	-	8.00±0.50
	Caffeine	$C_8H_{10}N_4O_2$	-	2.63E+03	0.16	3.58E-11	-0.55	3.58E-11	3.72E-07	-	0.52±0.70
	Cotinine	$C_{10}H_{12}N_2O$	-	9.99E+05	0.34	3.33E-12	0.21	3.33E-12	4.21E-04	-	4.72±0.12
	1,7 dimethylxantine	$C_7H_8N_4O_2$	4	4.14E+03	-0.39	1.75E-12	0.24	1.75E-12	-	8.50±0.50	0.21±0.70
Analgesics and metabolites	Morphine	$C_{17}H_{19}NO_3$	5,684	2.64E+04	0.72	1.33E-16	-0.37	1.33E-16	7.06E-10	9.48±0.40	8.25±0.40
	Dihydromorphine	$C_{17}H_{21}NO_3$	-	2.38E+04	0.93	1.51E-16	-0.26	1.51E-16	7.65E-10	9.56±0.40	8.44±0.40
	Normorphine	$C_{16}H_{17}NO_3$	-	2.56E+05	0.50	6.07E-17	-2.05	6.07E-17	2.99E-10	9.17±0.40	9.54±0.40
	Methadone	$C_{21}H_{27}NO$	1,687	48.5	4.17	4.97E-10	3.39	4.97E-10	2.20E-07	-	9.50±0.50
	EDDP	$C_{20}H_{23}N$	-	-	-	-	2.50	-	2.06E-06	-	7.71±0.60
	Codeine	$C_{18}H_{21}NO_3$	34,626	1.22E+04	1.28	7.58E-14	-0.23	7.58E-14	2.47E-09	13.40±0.20	8.23±0.40
	Norcodeine	$C_{17}H_{19}NO_3$	-	3.92E+04	1.07	3.45E-14	-2.28	3.45E-14	1.51E-09	13.34±0.20	9.28±0.40
	Dihydrocodeine	$C_{18}H_{23}NO_3$	9,720	6.53E+03	1.49	8.61E-14	-0.11	8.61E-14	2.48E-09	14.22±0.20	8.43±0.40
	Tramadol	$C_{16}H_{25}NO_2$	41,445	1.15E+03	3.01	1.54E-11	0.72	1.54E-11	1.02E-06	14.47±0.40	9.61±0.28
	N-desmethyltramadol	$C_{15}H_{23}NO_2$	-	-	-	-	-0.27	-	9.16E-06	14.46±0.40	10.56±0.10
	O-desmethyltramadol	$C_{15}H_{23}NO_2$	-	-	-	-	0.38	-	3.14E-07	10.00±0.10	9.61±0.28
Stimulants and metabolites	Amphetamine	$C_9H_{13}N_1$	-	2.80E+04	1.76	1.08E-06	-1.23	1.08E-06	0.307	-	9.94±0.10
	Methamphetamine	$C_{10}H_{15}N$	-	1.33E+04	2.22	2.37E-06	-1.01	2.37E-06	0.147	-	10.38±0.10
	MDMA	$C_{11}H_{15}NO_2$	-	7.03E+03	2.28	2.75E-09	-1.38	2.75E-09	3.17E-03	-	10.32±0.10
	MDA	$C_{13}H_{14}N_2$	-	1.96E+03	2.18	1.58E-11	-1.61	1.58E-11	1.52E-06	-	5.32±0.25
	Cocaine	$C_{17}H_{21}NO_4$	-	1.30E+03	2.17	4.24E-11	0.92	4.24E-11	1.87E-06	-	8.97±0.60
	Benzoylecgonine	$C_{16}H_{19}NO_4$	-	1.61E+03	-1.32	1.03E-13	-0.60	1.03E-13	1.32E-08	3.35±0.40	10.83±0.40
	Anhydroecgonine methylester	$C_{10}H_{15}NO_2$	-	-	-	-	0.21	-	0.0219	-	7.97±0.40
	Cocaethylene	$C_{18}H_{23}NO_4$	-	-	-	-	1.35	-	6.80E-07	-	9.04±0.60
	Mephedrone	$C_{11}H_{15}NO$	-	-	-	-	1.47	-	3.84E-03	-	7.41±0.10
	MDPV	$C_{16}H_{21}NO_3$	-	-	-	-	2.77	-	4.09E-07	-	8.41±0.20
Opioid and metabolite	Heroin	$C_{21}H_{23}NO_5$	-	2.15E+03	1.80	6.15E-13	-0.06	6.15E-13	7.38E-10	-	7.93±0.40
	6-acetylmorphine	$C_{19}H_{21}NO_4$	-	-	-	-	-0.22	-	1.83E-09	9.41±0.40	8.03±0.40

Table S2. Method performance data for LC-MS/MS methods

Micropollutant	Internal standard	t_r (min)	EF	Influent wastewater			Effluent wastewater		
				Mean recovery (%)	MDL (ng L^{-1})	MQL (ng L^{-1})	Mean recovery (%)	MDL (ng L^{-1})	MQL (ng L^{-1})
Reverse-phased C18 – acidic compounds									
4-benzophenone	Methylparaben 13C	6.94	-	101.9	7.83	25.84	122.8	5.78	19.09
Sulfasalazine	Naproxen D3	7.06	-	62.7	12.55	41.43	58.7	9.66	31.87
Methylparaben	Methylparaben 13C	7.50	-	99.8	0.28	1.41	100.8	0.19	0.94
Valsartan	Naproxen D3	7.64	-	101.1	7.24	23.90	79.9	6.40	21.12
Ketoprofen	Ketoprofen D3	7.74	-	45.4	0.36	1.82	40.3	0.34	1.68
Bezafibrate	Bezafibrate D6	7.87	-	91.4	0.64	2.11	92.9	0.38	1.25
2-benzophenone	Bisphenol A D16	7.89	-	107.2	2.38	11.90	109.2	1.60	8.00
Naproxen	Naproxen D3	8.11	-	82.7	6.29	31.45	98.0	1.17	5.85
Ethylparaben	Naproxen D3	8.32	-	87.5	0.49	1.61	83.5	0.46	1.52
Fexofenadine	Naproxen D3	8.38	-	107.3	0.56	1.85	83.8	0.40	1.32
Irbesartan	Bisphenol A D16	8.61	-	97.6	2.50	12.49	107.4	1.88	9.38
Bisphenol A	Bisphenol A D16	8.96	-	103.9	0.67	2.22	116.0	0.44	1.44
Diclofenac	Naproxen D3	9.04	-	112.2	0.85	2.79	100.7	0.56	1.84
Propylparaben	Bisphenol A D16	9.19		112.6	0.63	2.08	125.3	0.47	1.54
Atorvastatin	Naproxen D3	9.26	-	94.0	0.17	0.85	91.9	0.17	0.84
1-benzophenone	Ibuprofen D3	9.60	-	75.6	0.23	1.15	89.2	0.14	0.71
E2	E2 (2,4,16,16 D4)	9.74	-	87.9	1.83	9.15	84.6	1.46	7.32
Ibuprofen	Ibuprofen D3	9.77	-	78.9	0.19	0.93	110.8	0.08	0.42
EE2	E2 (2,4,16,16 D4)	9.80	-	106.6	1.84	9.22	87.9	1.41	7.03
E1	E1 (2,4,16,16 D4)	9.82	-	99.1	1.96	9.78	92.7	1.54	7.69
Butylparaben	E1 (2,4,16,16 D4)	10.12	-	102.4	0.24	1.21	118.3	0.14	0.71
Triclosan	E1 (2,4,16,16 D4)	12.30	-	117.5	4.93	16.27	100.8	4.55	15.02
Reverse-phased C18 – basic compounds									
Creatinine	Metformin D6	2.73	-	46.9	945	3,118*	42.9	771*	2,544*
Metformin	Metformin D6	2.84	-	78.7	457*	1,509*	96.0	163*	460*
Dihydromorphine	Morphine D3	3.30	-	95.7	0.50	2.51	96.2	0.32	1.59
Nicotine	Atenolol D7	3.34	-	77.3	508*	2,296*	83.9	5.44	17.95
Normorphine	Morphine D3	3.41	-	109.5	9.99	32.96	106.5	7.84	25.88
Anhydroecgonine methylester	Atenolol D7	3.45	-	91.3	2.95	14.76	109.5	1.99	9.96
Morphine	Morphine D3	3.46	-	93.9	8.85	29.20	109.8	6.34	20.92
Pholcodine	Atenolol D7	3.70	-	42.0	25.25	83.32	102.0	8.02	26.45
Atenolol	Atenolol D7	4.32	-	88.6	0.71	2.35	109.7	0.56	1.84
Ranitidine	Atenolol D7	4.62	-	97.8	14.76	73.79	106.8	22.28	111.39
Iopromide	Acetaminophen D4	4.89	-	138.5	24.51	123	123.7	14.11	70.56
Acetaminophen	Acetaminophen D4	5.11	-	77.8	138*	1,017*	116.4	2.39	11.95
Cimetidine	Acetaminophen D4	5.32	-	123.7	5.06	25.32	106.2	3.12	15.59
Dihydrocodeine	Codeine D6	5.47	-	85.7	0.88	2.89	118.6	0.55	1.83
Codeine	Codeine D6	6.05	-	94.8	2.56	12.82	102.8	1.46	7.31
Norephedrine	1S,2R-(+) Ephedrine D3	6.34	-	85.4	0.37	18.60	100.9	0.35	17.28

Norcodeine	Codeine D6	6.45	-	95.7	8.53	28.15	87.5	8.32	27.44
1,7 dimethylxanthine	Cotinine D3	6.78	-	79.6	560*	2,165*	110.6	11.40	37.63
Lisinopril	Amphetamine D5	7.14	-	102.3	3.25	32.54	88.5	4.25	42.51
Ephedrine/pseudoephedrine	1S,2R-(+) Ephedrine D3	7.22	-	92.8	1.32	4.36	88.6	1.62	5.36
Cotinine	Cotinine D3	7.22	-	85.2	0.27	1.34	101.5	0.21	1.06
6-acetylmorphine	Cotinine D3	7.65	-	103.6	0.89	2.95	85.4	0.76	2.50
Azathioprine	Cotinine D3	7.75	-	109.5	0.41	1.36	83.8	0.36	1.20
Methotrexate	Amphetamine D5	7.89	-	98.8	7.11	23.45	114.1	9.04	29.83
Caffeine	Cotinine D3	8.29	-	96.6	121*	581*	131.7	1.11	5.57
O-desmethyltramadol	Cotinine D3	8.29	-	87.3	0.31	31.41	93.9	0.28	27.79
Amphetamine	Amphetamine D5	8.39	-	91.7	1.23	4.07	107.8	1.11	3.65
Trimethoprim	Methamphetamine D5	8.43	-	109.6	0.73	2.41	123.7	0.51	1.67
Methamphetamine	Methamphetamine D5	8.51	-	102.1	0.95	3.13	97.1	0.71	2.35
MDA	MDA D5	8.59	-	99.4	0.99	3.26	99.1	1.00	3.30
MDMA	MDMA D5	8.62	-	118.5	0.34	1.70	112.9	0.27	1.35
Sulfamethoxazole	Benzoylecgonine D8	9.56	-	102.8	0.72	2.38	111.0	0.47	1.56
Benzoylecgonine	Benzoylecgonine D8	9.68	-	106.3	0.21	1.07	116.4	0.18	0.91
Mephedrone	Mephedrone D3	9.79	-	94.8	0.55	2.75	103.7	0.44	2.19
Ketamine	Ketamine D4	10.59	-	111.6	0.24	1.20	115.6	0.19	0.93
Heroin	Heroin D9	10.85	-	105.3	4.18	20.89	103.0	3.44	17.21
Tramadol	Metoprolol D7	10.97	-	69.5	0.30	30.03	88.3	0.21	21.29
Norketamine	Norketamine D4	11.08	-	98.9	0.72	2.37	108.6	0.56	1.86
Metoprolol	Metoprolol D7	11.17	-	97.4	0.28	1.40	104.3	0.19	0.96
Cocaine	Cocaine D3	11.32	-	97.4	0.46	2.31	105.2	0.22	1.11
N-desmethyltramadol	Cocaine D3	11.88	-	81.3	0.56	27.90	98.8	0.30	14.97
MDPV	Cocaethylene D3	12.11	-	136.8	0.48	2.41	87.9	0.12	0.59
Ifosfamide	Metoprolol D7	12.69	-	89.2	0.31	1.53	80.2	0.24	1.22
Cocaethylene	Cocaethylene D3	12.91	-	109.9	1.31	6.54	107.4	0.21	1.04
Carbamazepine10,11-epoxide	Carbamazepine 13C6	13.47	-	143.7	0.53	1.76	126.9	0.55	1.82
10,11-Dihydro-10-hydroxycarbamazepine	Carbamazepine 13C6	13.49	-	152.2	0.99	9.94	120.6	0.84	8.41
Mirtazapine	Mirtazapine D3	13.52	-	84.7	0.39	1.94	97.0	0.25	1.25
Azithromycin	EDDP D3	13.95	-	100.1	0.74	2.45	87.5	1.35	4.45
Venlafaxine	Metoprolol D7	14.14	-	70.2	0.37	1.83	89.5	0.24	1.20
EDDP	EDDP D3	14.80	-	111.6	0.23	1.13	113.6	0.29	1.47
Citalopram	Citalopram D6	15.06	-	119.9	1.24	12.40	124.1	1.41	14.10
Propranolol	Propranolol D7	15.14	-	105.0	0.68	2.25	102.7	0.73	2.41
Desmethylcitalopram	Citalopram D6	15.17	-	93.1	0.31	1.54	110.9	0.36	1.82
Carbamazepine	Carbamazepine 13C6	16.15	-	88.3	0.27	1.37	102.5	0.19	0.93
Diltiazem	Carbamazepine 13C6	16.72	-	118.1	0.27	2.68	82.3	0.32	3.23
Tylosin	Methadone D9	17.25	-	98.3	3.27	16.34	110.0	2.23	11.14
Methadone	Methadone D9	17.59	-	109.0	0.20	1.01	111.7	0.21	1.04
Gliclazide	Quetiapine D8	17.80	-	80.1	0.22	1.09	108.4	0.16	0.82
Quetiapine	Quetiapine D8	17.87	-	72.6	0.26	1.32	95.1	0.21	1.07
Temazepam	Temazepam D5	18.16	-	107.3	0.18	0.92	113.9	0.14	0.69
Fluoxetine	Fluoxetine D5	18.35	-	110.7	0.50	2.52	111.1	1.42	7.08

Norfluoxetine	Fluoxetine D5	18.42	-	94.8	0.42	2.12	91.7	1.27	6.35
Cetirizine	Temazepam D5	18.68	-	77.3	0.52	1.72	114.3	0.32	1.06
Clarithromycin	Methadone D9	18.87	-	80.9	0.34	1.69	97.2	0.28	1.40
Sertraline	Sertraline D3	19.22	-	91.5	0.74	3.72	105.0	1.21	6.05
3-benzophenone	Methadone D9	21.23	-	58.5	0.37	1.87	89.4	0.19	0.97
Tamoxifen	Tamoxifen 13C2 15N	22.39	-	85.2	0.70	3.50	98.4	0.76	3.82
			Enantio-selective Chirobiotic V						
S(-)-atenolol	S(-)-atenolol-d7	44.3	0.5	21.4	17.4	58.0	55.1	32.7	109.1
R(+)-atenolol	R(+)-atenolol-d7	48.5		19.5	28.7	95.8	54.8	30.8	102.7
S(+)-citalopram	S(+)-citalopram-d7	57.8	0.5	91.9	0.24	13.1	82.3	0.21	11.2
R(-)-citalopram	R(-)-citalopram-d7	62.9		95.1	0.31	13.7	76.9	0.27	11.8
S(+)-desmethylcitalopram	S(+)-citalopram-d7	55.7	0.5	99.7	0.36	1.21	73.2	0.29	0.96
R(-)-desmethylcitalopram	R(-)-citalopram-d7	71.7		102.4	0.50	1.68	77.3	0.40	1.34
S(+)-fluoxetine	S(+)-fluoxetine-d5	39.8	0.5	120.4	0.07	0.22	108.7	0.04	0.14
R(-)-fluoxetine	R(-)-fluoxetine-d5	43.2		91.2	0.08	0.26	108.3	0.05	0.17
R(-)-mirtazapine	R(-)-mirtazapine-d7	18.5	0.6	72.5	0.40	1.32	105.8	0.40	1.32
S(+)-mirtazapine	S(+)-mirtazapine-d7	23.1		81.5	1.17	3.89	120.1	0.86	2.86
S(-)-metoprolol	S(-)-metoprolol-d7	28.4	0.5	87.2	0.06	0.18	87.2	0.04	0.12
R(+)-metoprolol	R(+)-metoprolol-d7	31.3		87.1	0.08	0.27	86.2	0.05	0.15
S(-)-propranolol	S(-)-propranolol-d7	31.2	0.5	109.4	0.09	0.30	108.8	0.05	0.17
R(+)-propranolol	R(+)-propranolol-d7	34.8		108.9	0.08	0.26	110.6	0.06	0.20
			Enantio-selective CBH						
R(-)-MDMA	R(-)-MDMA-d5	21.9	0.5	81.0	0.3	1.4	-	-	-
S(+)-MDMA	S(+)-MDMA-d5	32.9		100.0	0.3	1.3	-	-	-
R(-)-Amphetamine	R(-)-Amphetamine-d5	15.5	0.5	76.0	0.8	2.9	-	-	-
S(+)-Amphetamine	S(+)-Amphetamine-d5	22.6		99.0	0.8	2.9	-	-	-

Table S3. Repeatability of sample volume collected by automated sampler using a 5 ft suction line and a single rinse cycle (n=100)

Replicate number	Volume collected (mL)	Replicate number	Volume collected (mL)	Replicate number	Volume collected (mL)	Replicate number	Volume collected (mL)
1	13.4	26	16.3	51	15.0	76	15.4
2	13.2	27	16.8	52	14.7	77	14.0
3	16.4	28	16.7	53	16.6	78	13.5
4	15.9	29	14.0	54	14.5	79	13.5
5	16.0	30	14.5	55	17.2	80	12.9
6	16.1	31	16.6	56	16.8	81	12.6
7	17.3	32	16.7	57	16.8	82	17.0
8	16.8	33	17.4	58	15.2	83	16.7
9	17.0	34	16.6	59	16.5	84	16.5
10	16.9	35	17.8	60	16.4	85	15.9
11	12.7	36	17.8	61	17.2	86	16.9
12	17.2	37	17.3	62	17.3	87	16.0
13	13.1	38	16.9	63	18.3	88	16.3
14	17.3	39	18.3	64	16.7	89	16.4
15	17.5	40	17.6	65	17.1	90	17.5
16	17.3	41	17.3	66	17.2	91	16.4
17	17.0	42	13.3	67	17.0	92	17.2
18	18.2	43	18.0	68	15.9	93	17.6
19	17.7	44	17.0	69	18.6	94	14.3
20	17.2	45	17.6	70	17.3	95	17.7
21	17.7	46	16.5	71	17.1	96	18.1
22	15.5	47	17.5	72	18.1	97	17.7
23	15.0	48	17.2	73	12.8	98	17.2
24	17.6	49	17.5	74	17.5	99	16.8
25	17.7	50	18.4	75	17.3	100	16.1

Table S4. Measured variables during influent and effluent wastewater sampling campaigns.

Measured variable	Day of week							
	Mon	**Tues**	**Wed**	**Thurs**	**Fri**	**Sat**	**Sun**	**Mon**
Influent wastewater (December 2014)								
Total flow - portable (m^3 d^{-1})	32,444	36,843	34,363	42,651	38,857	40,247	38,266	36,369
Total flow - on-site (m^3 d^{-1})	30,408	39,954	37,327	43,683	39,564	37,391	40,963	39,068
Difference (%)	6	-8	-9	-2	-2	7	-7	-7
Rainfall (mm)	0.0	1.0	3.7	15.9	0.0	0.2	0.2	0.4
Wastewater temp. (^{0}C)	14.0	12.0	13.0	10.0	11.0	11.0	12.0	13.0
Mean ambient temp. (^{0}C)	2.3	8.1	6.2	7.5	2.5	2.2	7.1	5.4
Collected wastewater temp (^{0}C)	1.0	2.0	1.0	1.0	1.0	1.0	2.0	1.0
pH	7.7	7.5	7.5	7.2	7.4	8.0	7.8	7.2
TOC (mg L^{-1})	123.1	79.0	233.5	63.6	101.0	171.9	73.3	123.4
DOC (mg L^{-1})	53.2	53.6	103.1	23.7	45.6	39.4	42.3	29.6
Suspended solids (mg L^{-1})	392.7	295.0	395.3	329.7	302.7	348.0	294.3	282.0
Effluent wastewater (January 2015)								
Total flow - portable (m^3 d^{-1})	40,227	40,655	42,354	42,185	41,242	38,942	37,496	35,087
Rainfall (mm)	0.0	2.8	4.3	0.2	1.0	0.0	0.2	0.2
Wastewater temp. (^{0}C)	8.0	9.0	9.0	8.0	8.0	9.0	8.0	8.0
Mean ambient temp. (^{0}C)	0.6	3.2	3.9	0.3	5.2	2.7	7.9	5.1
Collected wastewater temp. (^{0}C)	1.0	1.0	1.0	-1.0	1.0	1.0	2.0	1.0
pH	7.2	7.2	7.7	7.7	7.0	6.9	6.9	6.8
TOC (mg L^{-1})	24.0	13.1	9.7	13.1	34.5	10.1	11.2	55.2
DOC (mg L^{-1})	10.1	8.8	7.3	8.2	27.6	8.5	8.7	39.0
Suspended solids (mg L^{-1})	92.2	45.6	41.4	42.0	71.6	54.6	52.4	66.4

Key: TOC, total organic carbon; DOC, dissolved organic carbon
Note: All reported data runs from 08:00 to 08:00 the following day to correspond with times of composite sampling

Table S5. Loss of micropollutants in water stored in polypropylene bottles at 18 ºC and 4 ºC over a 24 h time period (n=2). Underlined values show those out with ±20 % significance level

Micropollutant class	Micropollutant	Concentration relative to t=0 after 24 h storage (%)	
		18 ºC	4 ºC
UV filters	Benzophenone-1	111.4	108.6
	Benzophenone-2	114.4	106.4
	Benzophenone-3	98.2	94.7
	Benzophenone-4	105.2	110.7
Parabens	Methylparaben	92.3	98.0
	Ethylparaben	87.1	98.7
	Propylparaben	89.4	106.4
	Butylparaben	105.8	103.8
Plasticizer	Bisphenol-A	90.0	95.1
Steroid estrogens	E1	98.3	102.0
	E2	102.4	90.7
	EE2	104.5	93.0
Antibacterials/antibiotics	Sulfasalazine	99.6	89.3
	Clarithromycin	105.3	82.8
	Azithromycin	89.9	87.4
	Trimethoprim	112.4	105.4
	Sulfamethoxazole	102.3	101.1
	Triclosan	94.0	91.0
Hypertension	Valsartan	113.3	105.4
	Irbesartan	117.7	114.9
	Lisinopril	108.8	103.0
NSAIDs	Ketoprofen	97.8	97.2
	Ibuprofen	96.5	99.7
	Naproxen	100.2	98.0
	Diclofenac	114.7	92.1
	Acetaminophen	94.5	99.7
Lipid regulators	Bezafibrate	96.6	100.8
	Atorvastatin	110.5	99.8
Antihistamines	Fexofenadine	110.9	85.0
	Cetirizine	109.1	115.8
Diabetes	Metformin	101.0	100.4
	Gliclazide	98.7	101.4
Cough suppressant	Pholcodine	111.4	100.3
Beta-blocker	Atenolol	99.6	98.3
	Metoprolol	97.4	99.2
	Propranolol	102.3	98.5
H_2 receptor agonists	Ranitidine	111.2	102.6
	Cimetidine	90.2	92.1
X-ray contrast media	Iopromide	98.7	100.1
Drug precursor and metabolite	Ephedrine/pseudoephedrine	108.5	91.0
	Norephedrine	108.5	103.4
Anti-cancer	Azathioprine	97.6	97.9
	Methotrexate	109.2	98.8
	Ifosfamide	107.4	95.3
	Tamoxifen	<u>30.8</u>	<u>34.3</u>
Anaesthetic and metabolite	Ketamine	96.9	99.8
	Norketamine	95.8	98.1
Anti-depressants and metabolites	Venlafaxine	102.9	102.0
	Desvenlafaxine	102.9	101.0
	Fluoxetine	104.2	101.8
	Norfluoxetine	86.8	101.0
	Sertraline	85.8	93.5
	Mirtazapine	95.1	98.9
	Citalopram	102.9	95.3
	Desmethylcitalopram	82.5	104.4
Anti-epileptic and metabolites	Carbamazepine	96.7	99.5
	Carbamazepine10,11-epoxide	99.9	98.6
	10,11-Dihydro-10-hydroxycarbamazepine	96.3	97.4
Calcium channel blocker	Diltiazem	111.8	106.4
Hypnotic	Temazepam	101.5	107.0
Anti-psychotic	Quetiapine	95.6	92.3
Veterinary	Tylosin	96.6	104.1
Human indicators and metabolites	Creatinine	93.7	110.1
	Nicotine	84.1	98.5
	Caffeine	98.1	98.0
	Cotinine	96.8	98.2
	1,7 dimethylxantine	107.4	105.0
Analgaesics and metabolites	Morphine	90.3	93.1

	Dihydromorphine	94.3	94.8
	Normorphine	92.4	100.9
	Methadone	95.3	106.8
	EDDP	92.1	94.9
	Codeine	96.9	99.3
	Norcodeine	91.2	103.2
	Dihydrocodeine	90.8	96.2
	Tramadol	99.7	97.6
	N-desmethyltramadol	84.6	100.1
	O-desmethyltramadol	97.2	101.4
Stimulants and metabolites	Amphetamine	100.3	101.7
	Methamphetamine	92.9	99.5
	MDMA	94.1	96.1
	MDA	100.3	104.8
	Cocaine	91.3	102.7
	Benzoylecgonine	110.1	97.6
	Anhydroecgonine methylester	86.9	102.1
	Cocaethylene	97.2	102.4
	Mephedrone	103.2	93.5
	MDPV	95.4	102.7
Opioid and metabolite	Heroin	88.6	98.8
	6-acetylmorphine	93.4	102.9

Table S6. Stability (%) of micropollutants in collected influent and effluent wastewater stored at 18 °C and 4 °C over a 24 h time period (n=2). Underlined values show those out with ±20 % significance level

Micropollutant class	Micropollutant	WWTP A				WWTP B			
		Influent wastewater		Effluent wastewater		Influent wastewater		Effluent wastewater	
		18 °C	4 °C	18 °C	4 °C	18 °C	4 °C	18 °C	4 °C
UV filters	Benzophenone-1	98.9	88.8	112.6	91.5	97.7	85.6	90.9	97.9
	Benzophenone-2	97.2	88.3	87.0	99.4	115.5	103.9	80.8	95.3
	Benzophenone-3	47.7	57.8	60.7	65.1	69.5	64.8	63.8	78.2
	Benzophenone-4	105.3	100.3	102.9	104.0	116.5	106.3	100.4	102.0
Parabens	Methylparaben	55.0	91.6	31.9	65.2	72.3	89.5	21.1	47.9
	Ethylparaben	66.7	87.0	51.7	80.1	85.7	94.1	38.0	65.2
	Propylparaben	71.3	91.0	72.3	88.3	46.9	91.8	54.1	75.4
	Butylparaben	50.7	81.4	59.1	80.2	31.1	81.5	57.5	93.4
Plasticizer	Bisphenol-A	124.3	96.5	98.3	106.3	102.5	102.5	71.3	116.4
Steroid estrogens	E1	88.1	107.6	65.8	101.4	120.7	81.5	57.5	93.4
	E2	45.7	89.9	39.3	85.5	58.1	92.2	1.1	34.9
	EE2	113.1	106.8	92.1	106.1	86.5	85.7	104.0	110.4
Antibacterials/ antibiotics	Sulfasalazine	93.7	85.9	98.3	96.0	95.4	95.0	98.4	90.8
	Clarithromycin	100.6	88.1	108.3	85.6	86.6	85.4	86.4	100.0
	Azithromycin	81.6	93.2	100.1	85.2	67.6	82.5	101.4	89.0
	Trimethoprim	92.6	82.6	84.1	81.4	94.9	88.0	96.8	101.7
	Sulfamethoxazole	96.4	91.6	92.1	88.4	106.4	93.2	93.1	93.1
	Triclosan	-	-	-	-	-	-	-	-
Hypertension	Valsartan	92.0	95.0	109.0	106.5	121.2	111.4	99.5	98.6
	Irbesartan	91.5	90.2	97.1	96.1	92.9	107.4	93.2	88.7
	Lisinopril	114.1	81.9	105.5	83.6	89.1	81.5	76.3	101.1
NSAIDs	Ketoprofen	102.0	97.5	102.2	105.9	98.7	107.6	95.7	91.7
	Ibuprofen	97.5	89.1	100.2	102.3	99.2	100.3	83.2	83.2
	Naproxen	96.4	99.1	98.6	100.3	103.5	94.9	100.3	95.4
	Diclofenac	113.0	103.9	108.2	102.7	101.9	107.6	95.3	88.7
	Acetaminophen	74.1	96.5	7.3	14.5	98.0	97.3	2.0	20.4
Lipid regulators	Bezafibrate	91.4	91.9	95.8	103.5	91.8	87.0	98.4	100.9
	Atorvostatin	90.3	87.5	79.0	84.1	113.6	112.8	101.7	89.4
Antihistamines	Fexofenadine	99.4	106.6	94.0	103.9	125.5	102.1	95.3	101.0
	Cetirizine	253.0	131.8	259.2	137.5	188.7	111.0	213.5	118.0
Diabetes	Metformin	98.6	98.0	96.7	99.7	94.1	98.7	103.4	97.7
	Gliclazide	102.3	102.1	83.7	97.8	103.1	98.7	80.9	84.5
Cough suppressant	Pholcodine	119.6	101.6	106.4	102.1	96.7	99.7	95.2	86.4
Beta-blocker	Atenolol	95.6	92.4	100.3	93.2	94.0	89.0	102.2	99.1
	Metoprolol	96.0	94.1	96.7	96.2	96.4	92.5	101.7	92.3
	Propranolol	102.8	96.0	93.1	93.6	100.0	95.7	100.3	98.9
H_2 receptor agonists	Ranitidine	90.1	89.2	97.7	86.1	92.7	94.9	91.5	94.8
	Cimetidine	93.2	89.5	74.5	81.5	100.0	92.0	108.0	91.4
X-ray contrast media	Iopromide	100.0	89.5	92.8	93.6	95.5	92.8	91.0	90.2
Drug precursor and metabolite	Ephedrine/pseudoephedrine	75.9	77.6	95.0	90.0	133.2	116.2	119.7	102.1
	Norephedrine	93.4	84.9	95.9	85.6	96.4	101.5	134.6	91.6
Anti-cancer	Azathioprine	98.3	90.3	95.3	93.2	91.5	88.7	93.7	90.3
	Methotrexate	-	-	-	-	-	-	-	-
	Ifosfamide	94.3	91.0	98.1	99.5	99.7	92.4	107.4	99.1
	Tamoxifen	-	-	-	-	-	-	-	-
Anaesthetic and metabolite	Ketamine	104.1	100.2	103.7	102.2	101.8	93.2	105.4	97.7
	Norketamine	103.2	100.5	102.4	96.8	103.3	99.5	104.6	96.8
Anti-depressants and metabolites	Venlafaxine	105.2	104.6	100.1	85.2	93.8	96.2	102.0	98.3
	Fluoxetine	95.0	81.7	75.7	57.3	96.5	80.5	88.3	87.8
	Norfluoxetine	74.6	71.3	60.0	58.8	95.8	80.7	96.0	83.2
	Sertraline	62.7	81.8	81.5	84.6	111.9	119.4	82.6	87.4
	Mirtazapine	101.8	102.3	95.6	93.2	98.8	92.5	107.2	101.3
	Citalopram	106.8	98.2	110.8	90.2	92.3	91.6	106.2	108.1
	Desmethylcitalopram	63.2	89.5	100.8	98.4	108.5	91.0	95.5	86.8

Anti-epileptic and metabolites	Carbamazepine	95.9	91.6	96.2	96.0	101.3	94.1	98.2	92.2
	Carbamazepine10,11-epoxide	94.9	88.1	101.1	97.3	95.7	87.5	97.3	89.6
	10,11-Dihydro-10-hydroxycarbamazepine	94.0	91.3	95.8	93.3	97.4	86.7	101.1	92.6
Calcium channel blocker	Diltiazem	≤10.0	84.7	73.9	81.1	109.0	92.2	162.9	119.9
Hypnotic	Temazepam	105.7	97.3	103.8	93.7	97.6	96.0	112.3	100.5
Anti-psychotic	Quetiapine	99.0	95.7	99.2	97.7	93.4	92.4	100.6	100.0
Veterinary	Tylosin	98.3	98.6	91.5	84.4	106.2	89.7	104.0	105.0
Human indicators and metabolites	Creatinine	5.7	80.0	45.8	112.0	43.2	89.0	102.4	104.8
	Nicotine	113.7	94.8	113.6	111.0	115.8	111.8	82.1	91.6
	Caffeine	97.0	97.2	84.1	87.0	99.8	92.6	78.2	86.8
	Cotinine	96.1	94.2	96.0	94.4	100.6	93.9	90.7	96.3
	1,7 dimethylxantine	95.8	92.1	87.4	89.0	101.4	96.6	143.7	94.3
Analgaesics and metabolites	Morphine	126.3	114.3	142.4	113.3	175.0	117.6	138.9	108.4
	Dihydromorphine	64.7	95.8	69.0	100.8	118.3	103.1	92.4	91.3
	Normorphine	74.7	93.0	87.9	95.2	124.7	106.8	118.6	104.1
	Methadone	98.4	102.8	92.9	92.5	97.6	93.4	108.4	105.9
	EDDP	98.2	100.9	98.3	98.0	101.7	97.4	103.7	95.5
	Codeine	116.0	98.3	97.9	97.6	118.4	99.4	99.5	92.5
	Norcodeine	107.1	91.6	105.0	92.2	93.4	87.5	100.3	97.0
	Dihydrocodeine	89.7	87.1	89.0	91.1	99.4	90.4	99.8	99.1
	Tramadol	103.9	98.7	108.1	102.7	94.7	90.6	101.5	92.4
	N-desmethyltramadol	164.4	105.5	111.3	80.6	80.1	87.5	98.5	99.4
	O-desmethyltramadol	95.2	90.9	99.0	90.8	100.0	90.5	97.2	97.5
Stimulants and metabolites	Amphetamine	97.2	97.4	75.6	93.6	86.0	89.2	82.1	93.4
	Methamphetamine	96.7	97.4	93.8	97.5	104.5	101.9	102.7	98.6
	MDMA	108.6	102.1	97.8	93.0	105.0	95.3	99.5	98.1
	MDA	97.5	94.1	93.0	98.5	105.4	95.5	110.5	101.5
	Cocaine	75.2	94.3	68.8	94.0	65.5	85.6	62.5	90.8
	Benzoylecgonine	130.3	102.2	127.8	101.8	11.6	93.5	132.9	100.6
	Anhydroecgonine methylester	121.9	100.0	122.0	119.5	109.9	109.6	88.5	86.7
	Cocaethylene	95.5	95.2	87.0	98.8	79.2	87.0	83.7	99.4
	Mephedrone	90.2	95.8	80.2	108.8	73.3	89.1	79.2	91.8
	MDPV	156.9	103.0	107.3	92.7	72.5	89.4	110.3	104.8
Opioid and metabolite	Heroin	2.3	84.1	59.3	81.2	20.2	56.1	32.3	84.1
	6-acetylmorphine	62.4	93.6	126.9	105.3	99.5	89.6	101.7	96.9

Key: E1, estrone; E2, 17β-estradiol; EE2, 17α-ethinylestradiol; EDDP, 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine; MDMA, 3,4-methylenedioxy-methamphetamine; MDA, 3,4-methylenedioxy-amphetamine; MDPV, methylenedioxypyrovalerone; -, the initial concentration was below the method quantitation limit for 10 mL extractions (triclosan, <81 ng L^{-1}; methotrexate, <117 ng L^{-1}; tamoxifen, <18 ng L^{-1})

Table S7. Stability (%) of micropollutants in collected influent and effluent wastewater stored with the addition of NaN_3 (1 g L^{-1}) at 18 °C and 4 °C over a 24 hour time period (n=2). Underlined values show those out with ±20 % significance level

Micropollutant class	Micropollutant	WWTP A				WWTP B			
		Influent wastewater		Effluent wastewater		Influent wastewater		Effluent wastewater	
		18 °C	4 °C	18 °C	4 °C	18 °C	4 °C	18 °C	4 °C
UV filters	Benzophenone-1	118.7	120.9	142.5	123.3	118.7	119.9	107.7	109.9
	Benzophenone-2	120.6	118.9	103.4	90.4	123.2	111.0	39.9	69.9
	Benzophenone-3	70.8	70.6	72.3	81.0	107.8	100.6	100.8	121.8
	Benzophenone-4	101.2	97.6	97.8	101.2	95.9	95.0	97.8	101.7
Parabens	Methylparaben	92.6	92.9	62.6	90.2	88.8	92.1	48.2	75.5
	Ethylparaben	93.9	94.1	82.1	90.4	104.2	122.2	71.8	93.7
	Propylparaben	86.8	100.1	94.1	88.1	87.6	87.1	79.2	95.3
	Butylparaben	84.4	100.6	87.9	100.4	93.0	95.2	118.2	131.3
Plasticizer	Bisphenol-A	119.4	95.6	97.5	82.0	108.6	100.7	120.4	90.6
Steroid estrogens	E1	119.2	113.3	115.3	106.8	136.2	111.7	157.8	142.9
	E2	87.9	86.1	84.6	89.1	52.9	64.2	6.2	35.2
	EE2	118.9	114.6	127.6	104.2	96.8	98.4	112.4	119.9
Antibacterials/ antibiotics	Sulfasalazine	124.6	117.8	148.6	132.9	118.7	97.7	123.8	111.4
	Clarithromycin	108.5	111.9	107.8	91.0	146.7	111.8	129.3	129.3
	Azithromycin	129.1	115.2	115.7	103.3	137.7	148.5	180.0	255.5
	Trimethoprim	172.8	114.8	171.2	146.3	255.0	288.4	206.8	215.2
	Sulfamethoxazole	110.4	104.2	106.1	89.5	127.7	106.6	111.5	105.2
	Triclosan	-	-	-	-	-	-	-	-
Hypertension	Valsartan	106.9	100.0	95.3	91.9	109.2	95.7	97.0	91.5
	Irbesartan	101.0	89.7	93.7	81.5	108.3	96.3	79.1	77.0
	Lisinopril	222.4	149.2	229.9	166.5	230.7	284.6	127.0	142.4
NSAIDs	Ketoprofen	98.5	99.5	104.3	100.5	111.1	84.0	99.3	93.1
	Ibuprofen	101.7	95.0	112.9	97.2	104.3	100.0	108.6	95.2
	Naproxen	100.1	94.0	93.2	85.6	106.4	105.3	104.5	102.2
	Diclofenac	104.4	113.7	97.9	85.6	113.8	96.4	81.8	90.8
	Acetaminophen	96.4	96.1	52.2	59.4	103.3	95.8	62.1	83.1
Lipid regulators	Bezafibrate	101.7	91.6	110.0	102.9	98.7	95.6	104.9	103.5
	Atorvostatin	122.2	132.4	114.8	97.0	145.9	113.2	114.8	86.1
Antihistamines	Fexofenadine	99.7	116.3	93.7	81.5	105.9	112.5	97.5	95.0
	Cetirizine	242.0	178.8	242.5	157.8	241.0	179.3	121.6	91.2
Diabetes	Metformin	96.4	99.0	97.0	94.7	103.2	98.3	101.4	92.9
	Gliclazide	93.4	84.4	90.0	67.8	106.6	99.3	75.1	51.5
Cough suppressant	Pholcodine	89.9	69.9	83.3	65.4	56.1	45.8	63.0	55.4
Beta-blocker	Atenolol	94.6	91.4	104.9	93.8	109.9	98.5	106.0	103.1
	Metoprolol	96.9	95.2	106.0	94.8	105.0	97.2	97.7	98.3
	Propranolol	96.9	92.6	105.0	102.7	101.9	92.0	103.8	99.2
H_2 receptor agonists	Ranitidine	92.4	95.8	112.6	98.5	113.1	99.9	90.2	90.8
	Cimetidine	106.5	91.4	103.2	80.9	112.0	102.2	94.2	71.0
X-ray contrast media	Iopromide	98.6	90.9	103.3	94.7	93.9	96.6	93.8	95.8
Drug precursor and metabolite	Ephedrine/pseudoephedrine	82.9	74.7	95.0	77.5	180.2	98.8	99.3	113.4
	Norephedrine	76.7	61.0	81.2	72.0	73.1	72.4	101.9	112.2
Anti-cancer	Azathioprine	93.3	85.0	93.5	77.4	99.7	90.4	81.1	83.2
	Methotrexate	-	-	-	-	-	-	-	-
	Ifosfamide	88.1	86.9	101.2	90.6	109.2	98.9	141.3	132.6
	Tamoxifen	-	-	-	-	-	-	-	-
Anaesthetic and metabolite	Ketamine	98.9	95.9	108.1	98.3	105.3	90.0	101.8	95.9
	Norketamine	98.5	97.3	105.8	91.8	99.2	91.3	105.5	104.3
Anti-depressants and metabolites	Venlafaxine	100.6	100.6	109.1	101.9	115.2	98.1	111.6	103.2
	Desmethylvenlafaxine	97.7	93.3	105.5	96.7	114.6	98.8	105.5	100.0
	Fluoxetine	94.4	68.9	78.6	55.8	96.5	74.0	104.7	83.1
	Norfluoxetine	80.3	65.6	61.2	54.1	95.8	71.4	121.6	91.2
	Sertraline	88.2	55.5	86.2	63.1	80.6	64.2	84.7	84.7
	Mirtazapine	98.5	94.2	99.3	93.7	99.0	95.6	104.1	99.0
	Citalopram	100.7	100.0	103.5	90.8	115.4	91.8	109.4	103.5

	Desmethylcitalopram	54.5	34.0	84.8	78.7	62.3	44.2	49.8	60.1
Anti-epileptic and metabolites	Carbamazepine	94.6	91.6	104.4	96.4	102.2	93.4	98.8	94.7
	Carbamazepine10,11-epoxide	87.5	88.1	102.7	92.3	92.8	84.6	90.5	82.7
	10,11-Dihydro-10-hydroxycarbamazepine	88.3	85.7	104.7	91.9	102.8	90.2	97.7	93.0
Calcium channel blocker	Diltiazem	<1.0	<1.0	58.6	34.2	<1.0	<1.0	<1.0	<1.0
Hypnotic	Temazepam	102.1	93.4	106.3	94.8	110.0	93.8	112.8	108.5
Anti-psychotic	Quetiapine	95.9	91.9	100.8	91.8	115.7	98.3	102.8	99.4
Veterinary	Tylosin	96.8	108.4	104.0	85.4	130.9	106.7	135.6	121.8
Human indicators and metabolites	Creatinine	32.1	34.0	<1	43.8	36.7	38.0	102.4	100.0
	Nicotine	100.4	145.9	139.3	123.0	114.0	78.2	114.3	99.2
	Caffeine	100.4	95.5	95.0	88.4	102.1	91.4	101.9	110.2
	Cotinine	94.0	92.6	106.4	92.5	103.9	93.8	101.9	105.3
	1,7 dimethylxantine	96.2	89.8	94.8	85.8	107.8	97.3	103.2	104.9
Analgaesics and metabolites	Morphine	84.3	90.0	93.7	98.9	120.1	101.6	110.0	84.1
	Dihydromorphine	77.7	66.1	127.0	107.3	73.8	67.5	56.1	38.4
	Normorphine	91.4	74.3	118.3	100.7	62.2	52.1	74.0	91.1
	Methadone	95.9	86.6	102.7	90.6	122.1	99.0	113.0	101.3
	EDDP	103.3	100.0	109.4	100.9	108.5	96.3	112.7	102.3
	Codeine	110.6	99.2	109.1	99.1	112.4	107.9	101.3	99.2
	Norcodeine	94.9	98.0	115.6	107.3	81.6	71.9	92.7	102.7
	Dihydrocodeine	94.7	90.6	102.2	92.1	94.3	88.4	104.0	105.6
	Tramadol	97.8	101.3	112.9	103.2	107.0	92.5	95.2	91.7
	N-desmethyltramadol	199.8	193.5	119.7	116.3	194.5	166.9	146.3	136.2
	O-desmethyltramadol	95.9	90.9	98.8	87.2	106.4	92.1	97.0	95.4
Stimulants and metabolites	Amphetamine	116.1	106.5	114.9	112.3	182.0	182.1	117.9	119.0
	Methamphetamine	92.5	88.2	94.4	94.1	96.3	81.7	89.2	90.8
	MDMA	111.6	105.0	108.3	94.9	112.7	104.4	101.9	98.7
	MDA	90.0	91.2	99.6	100.0	106.6	98.5	108.7	100.9
	Cocaine	84.2	99.1	84.9	89.9	69.2	94.1	73.4	96.2
	Benzoylecgonine	126.8	109.7	126.6	102.0	140.3	106.4	141.6	111.9
	Anhydroecgonine methylester	96.1	129.0	124.4	115.2	91.8	70.2	85.8	80.5
	Cocaethylene	93.8	99.4	97.7	98.3	89.6	93.2	100.0	105.2
	Mephedrone	84.3	97.3	93.2	96.0	78.1	96.4	90.9	100.0
	MDPV	180.7	184.0	118.2	122.9	177.1	157.7	155.9	112.2
Opioid and metabolite	Heroin	<1.0	<1.0	23.3	47.1	<1.0	<1.0	<1.0	<1.0
	6-acetylmorphine	34.8	20.5	138.5	101.7	2.5	4.0	4.0	15.0

Key: E1, estrone; E2, 17β-estradiol; EE2, 17α-ethinylestradiol; EDDP, 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine; MDMA, 3,4-methylenedioxy-methamphetamine; MDA, 3,4-methylenedioxy-amphetamine; MDPV, methylenedioxypyrovalerone; -, the initial concentration was below the method quantitation limit for 10 mL extractions (triclosan, <81 ng L^{-1}; methotrexate, <117 ng L^{-1}; tamoxifen, <18 ng L^{-1})

Table S8. Stability (%) of micropollutants in collected influent and effluent wastewater stored at pH 2 at 18 ºC and 4 ºC over a 24 hour time period (n=2). Underlined values show those out with ±20 % significance level

Micropollutant class	Micropollutant	WWTP A				WWTP B			
		Influent wastewater		Effluent wastewater		Influent wastewater		Effluent wastewater	
		18 ºC	4 ºC	18 ºC	4 ºC	18 ºC	4 ºC	18 ºC	4 ºC
UV filters	Benzophenone-1	83.4	102.2	74.8	118.4	85.6	85.3	66.0	61.1
	Benzophenone-2	58.9	73.3	52.0	67.8	87.1	96.1	77.2	63.7
	Benzophenone-3	40.9	43.5	43.6	50.2	62.3	69.8	58.4	59.9
	Benzophenone-4	104.3	125.0	120.0	106.9	115.6	112.9	106.6	102.2
Parabens	Methylparaben	100.0	99.6	119.8	109.2	105.9	97.6	98.7	96.4
	Ethylparaben	98.9	112.0	112.2	113.3	90.6	81.0	93.5	93.2
	Propylparaben	84.8	85.2	109.2	90.4	89.0	80.8	89.5	80.9
	Butylparaben	93.6	96.8	100.9	100.6	110.2	97.4	109.4	102.0
Plasticizer	Bisphenol-A	189.8	186.1	162.3	171.1	99.1	94.3	127.9	134.2
Steroid estrogens	E1	90.8	94.6	106.0	97.3	94.4	87.8	102.8	94.4
	E2	88.4	92.2	101.2	90.2	96.2	87.0	89.3	96.6
	EE2	95.6	117.0	94.4	103.7	106.8	97.6	117.9	111.9
Antibacterials/ antibiotics	Sulfasalazine	82.7	80.6	93.6	82.1	99.1	87.7	80.0	77.3
	Clarithromycin	23.9	56.7	59.4	78.7	34.3	73.0	47.4	74.2
	Azithromycin	27.6	41.5	34.0	40.7	60.0	70.1	44.7	59.6
	Trimethoprim	13.1	13.2	19.3	16.7	69.7	57.1	23.5	22.4
	Sulfamethoxazole	<1.0	<1.0	<1.0	<1.0	<1.0	<1.0	<1.0	2.9
	Triclosan	-	-	-	-	-	-	-	-
Hypertension	Valsartan	81.2	84.6	72.9	62.5	135.6	128.5	90.6	87.1
	Irbesartan	95.1	103.9	66.9	88.6	78.3	64.7	75.9	50.3
	Lisinopril	49.2	46.3	62.1	60.4	74.8	79.1	48.9	48.5
NSAIDs	Ketoprofen	90.4	88.4	95.4	97.8	89.5	98.9	90.3	92.0
	Ibuprofen	98.3	104.4	94.5	107.8	99.2	97.1	111.7	105.4
	Naproxen	98.6	101.7	98.6	91.9	97.6	92.2	103.5	100.2
	Diclofenac	49.7	52.0	50.2	45.3	49.8	52.0	86.7	75.1
	Acetaminophen	92.5	94.4	73.7	71.2	92.7	92.1	184.5	111.4
Lipid regulators	Bezafibrate	95.6	92.4	105.6	101.0	95.6	95.2	105.8	94.4
	Atorvostatin	57.4	40.1	49.9	32.1	69.5	62.8	67.4	69.4
Antihistamines	Fexofenadine	53.2	71.7	32.1	50.4	93.8	88.4	93.0	88.5
	Cetirizine	75.1	77.0	89.0	78.6	72.8	62.9	79.3	67.3
Diabetes	Metformin	100.8	84.3	99.7	91.1	97.3	105.2	97.2	96.0
	Gliclazide	29.5	81.7	26.5	88.0	17.4	34.0	74.2	71.5
Cough suppressant	Pholcodine	79.6	84.1	79.5	74.1	102.2	85.3	74.0	64.9
Beta-blocker	Atenolol	94.5	91.0	98.5	101.8	103.2	92.9	97.8	95.8
	Metoprolol	95.2	94.4	105.2	100.5	99.4	93.6	100.6	96.3
	Propranolol	97.5	100.6	105.8	104.0	103.4	96.0	108.4	103.8
H_2 receptor agonists	Ranitidine	1.8	7.5	7.6	11.7	1.3	1.2	60.2	54.0
	Cimetidine	93.5	101.6	94.4	109.7	138.8	115.9	118.5	102.8
X-ray contrast media	Iopromide	95.7	92.3	101.7	100.0	99.5	94.4	97.5	91.0
Drug precursor and metabolite	Ephedrine/pseudoephedrine	183.5	245.3	199.5	356.5	155.7	161.3	214.8	203.5
	Norephedrine	81.1	89.4	102.4	103.4	130.5	136.7	95.8	83.7
Anti-cancer	Azathioprine	107.7	102.7	104.3	98.9	107.4	98.4	104.6	84.0
	Methotrexate	-	-	-	-	-	-	-	-
	Ifosfamide	49.9	67.5	79.9	79.1	58.8	78.3	69.1	83.5
	Tamoxifen	-	-	-	-	-	-	-	-
Anaesthetic and metabolite	Ketamine	92.5	100.0	103.2	101.0	100.8	92.7	102.8	99.5
	Norketamine	95.3	95.5	101.1	99.7	98.1	95.9	103.2	102.0
Anti-depressants and metabolites	Venlafaxine	111.2	112.1	118.4	113.5	101.1	102.4	111.6	107.8
	Desmethylvenlafaxine	87.2	87.0	91.3	92.3	93.1	89.3	97.7	97.7
	Fluoxetine	82.8	91.1	80.6	83.0	83.0	98.0	93.4	100.5
	Norfluoxetine	98.4	107.4	82.9	80.0	103.4	120.2	97.6	115.2
	Sertraline	90.9	91.8	108.5	110.0	69.4	90.3	93.2	97.9
	Mirtazapine	93.5	99.7	99.5	103.0	97.1	95.4	111.8	108.2
	Citalopram	94.6	107.9	103.5	105.1	100.2	105.2	115.9	104.3

	Desmethylcitalopram	120.6	127.8	119.7	117.2	153.8	161.8	152.3	131.3
Anti-epileptic and metabolites	Carbamazepine	91.2	93.2	100.0	98.7	100.0	96.9	102.0	94.9
	Carbamazepine10,11-epoxide	<1.0	6.8	<1.0	32.2	<1.0	4.3	<1.0	39.5
	10,11-Dihydro-10-hydroxycarbamazepine	82.8	87.4	97.2	92.6	101.5	91.0	102.3	93.9
Calcium channel blocker	Diltiazem	225.9	252.9	153.2	148.6	153.0	173.5	531.4	480.0
Hypnotic	Temazepam	69.5	86.7	91.0	91.6	77.9	85.7	94.7	96.0
Anti-psychotic	Quetiapine	88.4	91.4	96.2	94.1	102.7	90.2	105.5	97.5
Veterinary	Tylosin	17.4	48.1	50.8	67.5	24.7	59.4	55.1	96.4
Human indicators and metabolites	Creatinine	135.8	111.1	112.0	101.3	81.6	89.9	152.4	140.5
	Nicotine	387.4	378.5	292.1	268.1	203.2	180.8	217.1	199.2
	Caffeine	98.3	93.5	96.9	93.2	102.0	90.4	130.3	107.7
	Cotinine	100.3	95.4	100.6	98.3	100.4	93.6	107.2	102.7
	1,7 dimethylxantine	103.0	98.7	103.6	99.3	103.9	99.2	183.4	110.9
Analgaesics and metabolites	Morphine	84.3	90.0	93.7	98.9	82.5	88.2	109.2	107.2
	Dihydromorphine	109.2	116.3	95.8	98.3	111.0	100.0	120.9	102.0
	Normorphine	99.2	112.1	89.3	105.9	91.4	92.9	123.8	130.1
	Methadone	93.1	106.5	109.8	111.8	104.5	116.2	124.3	117.2
	EDDP	98.2	103.3	110.0	106.9	107.4	103.4	108.5	103.7
	Codeine	95.4	98.6	103.6	97.0	93.0	90.4	105.4	102.9
	Norcodeine	91.6	86.5	108.7	107.8	92.3	91.8	97.0	109.0
	Dihydrocodeine	83.9	98.4	99.8	94.7	91.6	93.7	100.7	107.0
	Tramadol	100.2	106.1	110.7	107.5	95.7	94.6	100.9	95.5
	N-desmethyltramadol	101.8	110.2	133.3	118.9	79.8	76.1	113.9	109.2
	O-desmethyltramadol	100.5	95.7	102.6	102.0	92.9	87.9	104.0	100.9
Stimulants and metabolites	Amphetamine	87.6	91.5	104.9	100.5	88.9	89.7	102.5	102.7
	Methamphetamine	110.8	115.4	116.0	115.1	112.7	105.6	131.5	120.0
	MDMA	107.4	108.0	106.1	107.0	106.4	97.5	105.3	96.3
	MDA	102.5	104.2	107.3	105.1	115.1	114.8	112.0	106.6
	Cocaine	93.2	98.6	104.3	98.2	96.7	95.2	104.6	97.3
	Benzoylecgonine	88.3	89.2	92.9	90.9	86.2	83.2	90.5	88.7
	Anhydroecgonine methylester	306.5	303.9	278.7	275.6	147.4	137.1	162.8	157.1
	Cocaethylene	94.1	94.6	109.6	107.2	95.1	95.3	110.5	107.7
	Mephedrone	100.3	99.4	106.5	103.1	99.2	97.5	108.2	100.9
	MDPV	103.7	108.6	129.8	124.7	83.8	88.1	113.5	107.4
Opioid and metabolite	Heroin	98.3	104.8	107.4	103.7	97.0	99.1	99.0	94.4
	6-acetylmorphine	78.7	78.1	77.6	79.2	62.0	48.4	64.9	56.9

Key: E1, estrone; E2, 17β-estradiol; EE2, 17α-ethinylestradiol; EDDP, 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine; MDMA, 3,4-methylenedioxy-methamphetamine; MDA, 3,4-methylenedioxy-amphetamine; MDPV, methylenedioxypyrovalerone; -, the initial concentration was below the method quantitation limit for 10 mL extractions (triclosan, <81 ng L^{-1}; methotrexate, <117 ng L^{-1}; tamoxifen, <18 ng L^{-1})

Table S9. Difference in micropollutant concentration (%) of influent and effluent wastewater daily composites collected in a time paced versus a volume paced manner (n=3). Underlined values show those out with ±20 % significance level

Micropollutant class	Micropollutant	Influent wastewater (December 2014)							Effluent wastewater (January 2015)							
		Mon	Tues	Wed	Thurs	Fri	Sat	Sun	Mon	Mon	Tues	Wed	Thurs	Fri	Sat	Sun	Mon
UV filters	Benzophenone-1	+12.4	0.0	NA	+1.4	+27.3	+16.0	+15.6	-2.1	-	-	-	-	-	-	-	-
	Benzophenone-2	-	-	NA	-	-	-	-	-	-	-	-	-	-	-	-	-
	Benzophenone-3	+3.4	+7.6	NA	+3.8	+0.7	-11.5	-7.0	-8.5	-9.4	-2.9	-19.3	-14.8	-12.7	0.0	-11.2	-17.7
	Benzophenone-4	-4.9	-3.9	NA	-5.6	-9.1	-0.6	+2.0	+4.5	+5.5	+0.4	+4.5	-6.6	+1.8	-0.3	-10.7	+6.6
Parabens	Methylparaben	+3.5	+11.1	NA	+5.7	+8.3	+38.0	+7.9	+15.5	+13.6	+18.2	+12.5	+16.2	+13.9	+13.1	-2.0	+2.3
	Ethylparaben	+22.0	+31.4	NA	+38.3	+29.6	+70.1	+33.9	+36.7	+6.7	+12.5	+15.4	+5.0	+15.8	+9.5	-5.6	+15.4
	Propylparaben	+22.3	+25.9	NA	+17.5	+20.2	+43.5	+19.5	+20.9	+4.0	-2.9	-10.7	-16.7	+1.9	+13.3	-16.7	+12.5
	Butylparaben	+21.4	+52.5	NA	+18.5	+51.1	+61.0	+31.4	+38.0	-	-	-	-	-	-	-	-
Plasticizer	Bisphenol-A	-5.7	-8.2	NA	-3.8	-15.1	-17.1	-6.4	-5.9	+3.9	+7.8	+8.4	-4.8	+8.4	-18.9	+13.6	+11.1
Steroid estrogens	E1	-7.5	-0.7	NA	-14.2	-9.2	-14.9	-25.7	-8.7	-7.6	+7.5	+4.5	-13.7	+2.5	-3.9	-14.6	+1.3
	E2	-	-	NA	-	-	-	-	-	-	-	-	-	-	-	-	-
	EE2	-	-	NA	-	-	-	-	-	-	-	-	-	-	-	-	-
Antibacterials/ antibiotics	Sulfasalazine	-3.5	+2.1	NA	-0.1	+7.7	+6.0	-8.0	+20.5	+8.7	+7.3	+14.9	+7.3	+5.7	+5.5	+2.3	+19.0
	Clarithromycin	+7.2	-5.2	NA	+13.9	+2.2	-16.2	-19.8	-6.5	-5.5	-5.4	-4.2	-0.5	-0.1	-0.6	-6.9	+0.5
	Azithromycin	+13.3	+15.4	NA	+29.6	-5.7	-8.0	-2.6	-3.8	+0.2	+10.2	-7.9	-5.3	-4.8	-6.1	+8.4	+4.1
	Trimethoprim	+12.0	-1.7	NA	+10.3	-1.4	-10.4	-10.8	-9.3	+12.8	+13.9	+6.6	-2.2	+8.4	+19.7	+17.9	+13.8
	Sulfamethoxazole	-13.8	-4.1	NA	+14.8	+4.3	+0.7	+10.3	-5.2	-0.8	-3.8	+8.6	-4.8	+3.7	-2.7	-1.0	+7.1
	Triclosan	+5.6	+3.3	NA	+0.8	-20.0	+2.7	-13.9	+4.2	-12.0	+5.9	-10.1	-6.1	-2.4	+5.1	-1.7	+5.5
Hypertension	Valsartan	+4.3	+5.0	NA	+0.6	-7.0	+18.9	-7.9	-4.9	-0.4	-5.8	+2.7	0.0	+2.4	-8.1	-3.0	+7.3
	Irbesartan	+6.7	+2.4	NA	-5.1	-9.9	+28.2	-17.0	-2.0	-2.6	0.0	+12.1	+15.6	+1.8	-1.5	+10.5	+16.3
	Lisinopril	+2.6	-3.5	NA	+9.6	-4.5	+45.6	+12.4	-9.4	+10.6	-0.5	-3.3	-14.8	+11.7	+0.9	+1.1	+14.3
NSAIDs	Ketoprofen	-	-	NA	-	-	-	-	-	+3.4	+8.9	+6.4	+4.8	-6.3	+10.8	-1.8	+8.0
	Ibuprofen	+0.7	0.0	NA	+7.1	+1.3	+0.4	+10.5	-4.9	+1.4	+2.5	+3.8	+1.4	+0.3	+2.7	-3.2	+14.4
	Naproxen	+0.5	+5.2	NA	+10.8	+14.3	+5.5	+5.5	-0.8	+2.8	-1.8	+4.2	-4.5	-4.9	-4.1	-6.3	+11.0
	Diclofenac	+2.2	+20.4	NA	-1.3	+2.0	+23.4	+1.3	+3.6	-4.3	+11.3	-1.6	+0.5	-3.1	+9.8	+1.0	+15.9
	Acetaminophen	+1.3	-0.3	NA	+6.0	+11.0	+16.8	+0.9	+8.1	+16.3	+14.3	+19.5	+13.1	+18.1	+6.8	+6.8	+17.8
Lipid regulators	Bezafibrate	-2.2	+2.8	NA	+4.2	+9.2	+10.5	+10.4	-6.7	+4.3	-2.8	+13.4	-1.1	+0.6	+0.1	-4.3	+11.1
	Atorvostatin	-5.4	-14.6	NA	-21.1	-21.1	-26.2	-11.9	-4.1	-7.1	-19.2	-2.0	-5.8	+2.0	-9.1	+16.5	+12.9
Antihistamines	Fexofenadine	-6.1	+4.8	NA	+17.5	+22.4	+36.6	-4.9	-12.2	+8.8	+17.8	+11.7	+5.9	+0.8	+7.3	-9.5	+16.6
	Cetirizine	+8.0	+1.7	NA	+6.2	+4.1	+7.3	+3.1	0.0	-4.6	+1.2	-3.5	-4.2	+3.7	+5.0	-3.8	+3.0
Diabetes	Metformin	-0.1	-1.7	NA	+1.9	+3.3	+14.0	-11.4	+0.4	+4.0	-2.2	-0.6	+0.2	+2.2	-1.6	+1.3	-0.7
	Gliclazide	+15.6	+13.7	NA	+2.7	-2.2	+14.7	+36.5	-10.4	+2.0	-1.6	-5.7	-16.8	-6.8	+3.3	-3.8	-9.3
Cough suppressant	Pholcodine	-	-	NA	-	-	-	-	-	-	-	-	-	-	-	-	-
Beta-blocker	Atenolol	+5.7	+8.3	NA	+3.7	0.0	+7.0	-7.9	+2.8	+2.3	0.0	+0.6	-1.9	+4.8	-1.5	-2.0	-0.1
	Metoprolol	+12.2	+2.5	NA	+4.2	-2.8	-12.7	+5.2	0.0	-1.8	0.0	+2.5	0.0	+9.8	+11.3	-7.7	+4.8
	Propranolol	+13.3	+2.9	NA	0.0	-12.9	-11.0	-7.7	-2.3	-3.2	+1.7	+4.0	-8.0	+3.7	-2.4	-0.9	-1.3
H_2 receptor agonists	Ranitidine	+5.1	-0.1	NA	+1.8	+1.1	-4.9	-12.2	+0.7	-11.5	-7.7	0.0	-12.9	+0.1	-2.0	-6.3	-4.6

	Cimetidine	-14.9	+3.9	NA	-3.6	-1.7	+37.7	-3.8	+9.8	-19.4	-19.0	+13.1	-3.8	-14.7	-15.9	-9.5	-7.4
X-ray contrast media	Iopromide	-	-	NA	-	-	-	-	-	-	-	-	-	-	-	-	-
Drug precursor and metabolite	Ephedrine/pseudoephedrine	+8.3	+5.7	NA	+17.1	+18.8	-4.9	+4.8	-5.6	+14.8	+4.5	+5.7	-0.7	+11.8	-3.7	-2.9	+4.9
	Norephedrine	-	-	NA	-	-	-	-	-	-	-	-	-	-	-	-	-
Anti-cancer	Azathioprine	-	-	NA	-	-	-	-	-	-	-	-	-	-	-	-	-
	Methotrexate	-	-	NA	-	-	-	-	-	-	-	-	-	-	-	-	-
	Ifosfamide	-	-	NA	-	-	-	-	-	-	-	-	-	-	-	-	-
	Tamoxifen	-	-	NA	-	-	-	-	-	-	-	-	-	-	-	-	-
Anaesthetic and metabolite	Ketamine	-	-	NA	-	-	-	-	-	-	-	-	-	-	-	-	-
	Norketamine	-	-	NA	-	-	-	-	-	-	-	-	-	-	-	-	-
Anti-depressants and metabolites	Venlafaxine	+9.7	-0.5	NA	-36.2	+8.8	+3.5	+0.8	-7.2	-5.2	-3.7	+5.8	+0.2	-1.5	+0.2	+0.9	+5.3
	Fluoxetine	+67.8	+49.7	NA	-1.0	-5.5	+29.5	+12.5	-3.6	-11.2	+15.8	-8.8	-10.2	+5.0	0.0	-14.5	+11.0
	Norfluoxetine	+9.6	+12.5	NA	-1.0	-5.2	+6.7	-0.9	-4.6	-3.3	-5.5	-4.4	-6.6	-1.1	+9.5	-3.2	1.1
	Sertraline	+25.8	0.0	NA	-10.7	-7.9	-6.1	-8.0	-2.7	-5.6	-5.3	-6.2	-3.0	+8.2	-8.2	-11.0	+5.2
	Mirtazapine	+8.6	+12.6	NA	+11.9	+8.9	-18.1	-1.0	-2.7	-2.7	-0.9	-1.0	-0.9	+3.1	-1.8	-7.5	-6.9
	Citalopram	+18.4	+7.5	NA	+6.4	+8.8	+5.1	-12.2	-4.5	-6.9	-0.1	-0.5	+2.2	+1.0	0.0	-4.5	-2.7
	Desmethylcitalopram	+13.5	+18.4	NA	+29.1	+13.9	+17.5	+0.9	+14.8	-12.4	-7.5	-12.3	-3.2	-16.0	-4.5	+0.6	-5.3
Anti-epileptic and metabolites	Carbamazepine	+2.8	+0.6	NA	-0.2	+7.1	+4.3	+45.4	+3.0	-0.4	+1.7	-4.8	-4.3	-1.5	-0.9	-2.5	-0.2
	Carbamazepine10,11-epoxide	-	-	NA	-	-	-	-	-	-	-	-	-	-	-	-	-
	10,11-Dihydro-10-hydroxycarbamazepine	-4.4	-18.6	NA	+14.4	+8.9	-0.5	-7.2	+17.8	+3.5	+19.0	+16.3	-9.3	+9.0	+3.3	-3.4	0.0
Calcium channel blocker	Diltiazem	+44.1	+16.5	NA	+26.8	+30.8	+3.6	+12.3	+8.2	-2.8	+5.7	0.0	-1.7	+2.0	-5.9	-11.1	0.0
Hypnotic	Temazepam	+11.5	+2.5	NA	+25.0	-10.1	-7.7	-8.7	-12.4	-9.5	+1.5	-8.9	0.0	+8.3	+11.7	-5.6	+9.6
Anti-psychotic	Quetiapine	-4.7	+18.1	NA	+8.3	-35.0	+8.3	+111	-15.9	-3.3	+6.7	-10.5	-12.5	-4.5	+3.8	-10.3	-14.8
Veterinary	Tylosin	-	-	NA	-	-	-	+81.0	-8.3	-	-	-	-	-	-	-	-
Human indicators and metabolites	Creatinine	-1.1	+3.0	NA	+16.6	+21.4	+37.3	+4.6	+17.0	+8.4	-16.9	+10.5	+14.2	+17.7	-2.5	+4.9	+14.4
	Nicotine	-5.4	-4.1	NA	-12.2	-8.6	-2.7	-3.7	+2.7	-3.2	-14.3	-0.9	+15.8	-17.3	-11.9	-12.0	-19.7
	Caffeine	-15.0	-12.0	NA	-20.9	+12.9	+10.1	-9.2	+3.2	+11.0	-8.8	+15.6	+3.8	+10.2	+7.8	-8.4	+7.8
	Cotinine	+2.0	+1.5	NA	+4.2	+10.1	-0.1	-0.3	-4.8	+2.6	+5.7	+2.7	-0.8	+4.0	-5.8	+2.8	+5.4
	1,7 dimethylxantine	+8.5	-3.6	NA	-2.5	+28.6	+21.1	-3.8	+0.6	+1.1	-6.1	+2.8	-6.0	+4.7	-7.3	-1.2	+7.4
Analgaesics and metabolites	Morphine	-4.1	-8.9	NA	+24.4	+5.4	-5.7	+1.0	-0.9	+4.2	-7.2	+5.1	-3.2	-2.5	-0.6	-0.7	+6.7
	Dihydromorphine	-	-16.7	NA	-	-	-	-	-	-	-	-	-	-	-	-	-
	Normorphine	-9.3	+8.8	NA	+37.6	-23.1	+8.9	-19.5	-11.4	+6.5	-13.5	-7.8	-17.6	+0.9	-11.0	+11.8	+4.6
	Methadone	+11.9	+8.3	NA	+10.0	+14.3	0.0	+1.9	-14.9	0.0	0.0	0.0	-4.0	+10.7	-9.1	-7.7	-4.5
	EDDP	+3.2	+6.4	NA	-1.8	+11.8	-3.3	-7.6	-3.6	-4.5	-7.3	-3.4	-5.0	-2.6	-2.5	-3.3	+2.7
	Codeine	+2.4	+1.9	NA	+9.0	+1.4	-16.9	-4.8	-2.3	+10.8	+2.4	+5.5	-5.0	+5.5	-3.4	+1.4	+1.8
	Norcodeine	+13.5	+2.0	NA	+15.2	+17.2	-19.5	-7.3	-23.7	+16.1	+9.2	+13.6	-1.0	+2.9	+5.5	+5.1	+7.7

	Dihydrocodeine	+1.0	+1.2	NA	+14.4	-4.2	-18.5	-6.4	-5.6	+5.7	+11.6	+5.7	+10.1	+9.6	+11.3	+13.3	+15.3
	Tramadol	+3.2	+2.4	NA	+15.0	+12.3	-9.3	-4.6	-3.2	-9.5	-6.4	+3.9	+2.1	-2.4	+1.4	-3.3	+3.8
	N-desmethyltramadol	+5.7	-19.1	NA	-8.5	-9.1	+9.4	-25.3	-17.7	-3.9	-2.8	+3.6	-4.0	+3.3	-1.4	-2.5	-6.2
	O-desmethyltramadol	+20.8	-0.7	NA	+6.5	+10.2	+17.4	-10.0	-1.5	+17.0	+17.7	+15.1	-0.1	+14.7	+9.4	+9.0	+5.2
Stimulants and metabolites	Amphetamine	-4.2	+3.3	NA	+9.9	+5.8	-5.5	-2.4	-0.2	+14.1	+6.2	-13.2	-17.0	+2.3	+14.7	+15.2	+9.6
	Methamphetamine	+4.5	-4.8	NA	+5.3	+6.3	0.0	-4.3	+3.8	0.0	0.0	0.0	+7.1	-18.8	0.0	0.0	0.0
	MDMA	+2.8	-8.8	NA	-6.2	+30.7	+9.8	-13.4	-1.6	-3.4	-2.4	-1.1	+3.4	+3.5	-2.7	-3.0	+0.9
	MDA	-	-	NA	-	-	-	-	-	0.0	5.3	0.0	-8.3	0.0	-5.2	-1.7	12.6
	Cocaine	+10.4	-0.9	NA	-0.8	+46.8	+1.9	-1.2	+0.6	-2.8	-0.4	0.0	+0.9	-1.6	+0.8	-1.2	+0.8
	Benzoylecgonine	-1.7	+2.1	NA	+8.9	+21.8	+8.3	-8.9	-2.8	-3.3	-4.6	-2.8	-1.6	+6.0	-0.4	+1.6	+0.3
	Anhydroecgonine methylester	-	-	NA	-	-	-	-	-	-	-	-	-	-	-	-	-
	Cocaethylene	-	-	NA	-	-	+25.4	-14.3	-	-	-	-	-	-	+12.5	+16.7	-
	Mephedrone	-21.4	+4.2	NA	-	-	+5.0	-	-	-	-	-	-	-	-	-	-
	MDPV	-	-	NA	-	-	-	-	-	-	-	-	-	-	-	-	-
Opioid and metabolite	Heroin	-	-	NA	-	-	-	-	-	-	-	-	-	-	-	-	-
	6-acetylmorphine	-36.8	-	NA	-	-	-	-	-	-	-	-	-	-	-	-	-

Key: NA, not available due to malfunction of the time composite sampler; -, concentration <MQL

Table S10. Frequency of detection, minimum, maximum and median concentration of micropollutants in grab samples of influent and effluent wastewater

Micropollutant class	Micropollutant	Influent wastewater concentration (n=17[a])					Effluent wastewater concentration (n=24)				
		Frequency (%)	Range		Median (ng L^{-1})	Intra-day variability (%)	Frequency (%)	Range		Median (ng L^{-1})	Intra-day variability (%)
			Min (ng L^{-1})	Max (ng L^{-1})				Min (ng L^{-1})	Max (ng L^{-1})		
UV filters	Benzophenone-1	100	60.4	152.8	89.5	27.3	0	-	-	-	-
	Benzophenone-2	0	-	-	-	-	0	-	-	-	-
	Benzophenone-3	100	207.1	620.6	331.8	27.1	100	118.2	205.0	166.9	16.8
	Benzophenone-4	100	1,858	9,524	4,030	46.6	100	1,682	4,739	2,239	25.9
Parabens	Methylparaben	100	958.2	6,104	2,896	45.7	100	22.4	43.2	28.3	20.7
	Ethylparaben	100	126.1	1,185	483.3	52.7	100	3.9	8.8	6.9	19.7
	Propylparaben	100	299.7	1,868	1,226	41.8	100	2.9	23.1	6.9	62.6
	Butylparaben	100	5.2	117.8	81.9	50.9	0	-	-	-	-
Plasticizer	Bisphenol-A	100	465.6	946.4	847.2	49.2	100	57.4	201.5	102.1	34.7
Steroid estrogens	E1	100	26.2	76.2	51.9	27.8	100	14.3	30.7	25.0	17.3
	E2	0	-	-	-	-	0	-	-	-	-
	EE2	0	-	-	-	-	0	-	-	-	-
Antibacterials/ antibiotics	Sulfasalazine	100	57.4	537.9	180.8	60.7	100	45.2	88.6	65.3	17.0
	Clarithromycin	100	547.0	3,234	860.6	65.3	100	1,404	2,761	2,012	22.5
	Azithromycin	100	52.0	283.5	141.2	58.4	100	84.5	147.5	124.4	14.6
	Trimethoprim	100	931.5	2,124	1,229	28.9	100	554.0	1,104	839.8	14.5
	Sulfamethoxazole	100	64.5	1,154	192.0	94.7	100	23.0	188.8	120.5	33.1
	Triclosan	100	339.0	2,359	1,579	45.2	100	96.4	461.9	297.2	31.5
Hypertension	Valsartan	100	187.4	939.1	476.9	44.3	100	151.5	380.4	270.1	20.5
	Irbesartan	100	93.1	268.1	138.8	37.0	100	14.1	98.1	71.7	30.0
	Lisinopril	100	200.2	526.9	311.9	25.8	100	120.6	228.1	166.0	15.4
NSAIDs	Ketoprofen	0	-	-	-	-	100	15.2	64.0	42.0	33.6
	Ibuprofen	100	4,016	20,215	16,266	32.5	100	1,746	3,718	2,943	20.1
	Naproxen	100	6,985	20,398	15,824	33.1	100	3,291	6,412	5,368	18.4
	Diclofenac	100	239.9	1,881	687.3	59.5	100	239.4	521.2	387.8	21.6
	Acetaminophen	100	171,875	512,813	347,250	29.6	100	692.0	2,195	1,092	30.9
Lipid regulators	Bezafibrate	100	544.6	2,032	1,336	38.7	100	511.9	874.0	734.0	14.9
	Atorvostatin	100	216.5	788.5	382.0	35.6	100	69.0	233.0	142.5	25.3
Antihistamines	Fexofenadine	100	568.3	4,555	1,686	53.9	100	341.5	632.5	525.7	16.7
	Cetirizine	100	954.4	2,333	1,868	25.8	100	302.5	470.8	402.1	12.9
Diabetes	Metformin	100	43,582	98,706	74,002	24.4	100	13,754	29,881	25,000	20.2
	Gliclazide	100	50.3	276.4	68.6	62.9	100	57.9	91.4	73.7	10.3
Cough suppressant	Pholcodine	0	-	-	-	-	0	-	-	-	-
Beta-blocker	Atenolol	100	1,168	3,423	2,466	26.6	100	591.4	966.8	788.2	13.7
	Metoprolol	100	8.6	109.1	18.8	93.6	100	10.7	21.8	14.2	15.9
	Propranolol	100	83.1	269.7	154.0	33.7	100	60.9	102.7	75.7	13.0
H_2 receptor agonists	Ranitidine	100	1,130	3,943	1,799	40.5	100	829.8	2,116	1,574	20.0
	Cimetidine	100	43.3	1,114	136.1	119.2	100	6.8	76.1	55.5	31.2

X-ray contrast media	Iopromide	12	<123	1,441	<123	-	0	-	-	-	-
Drug precursor and metabolite	Ephedrine/pseudoephedrine	100	327.5	955.5	627.5	26.9	100	141.0	227.0	178.5	11.3
	Norephedrine	0	-	-	-	-	0	-	-	-	-
Anti-cancer	Azathioprine	0	-	-	-	-	0	-	-	-	-
	Methotrexate	0	-	-	-	-	0	-	-	-	-
	Ifosfamide	0	-	-	-	-	0	-	-	-	-
	Tamoxifen	0	-	-	-	-	0	-	-	-	-
Anaesthetic and metabolite	Ketamine	6	<1.2	30.0	<1.2	-	0	-	-	-	-
	Norketamine	0	-	-	-	-	0	-	-	-	-
Anti-depressants and metabolites	Venlafaxine	100	119.2	642.9	288.4	51.0	100	170.5	251.4	215.1	9.8
	Fluoxetine	100	36.0	436.5	87.5	80.2	100	33.0	66.5	44.8	19.6
	Norfluoxetine	100	29.5	46.0	34.0	14.4	100	26.5	34.5	30.5	6.2
	Sertraline	100	35.5	104.0	42.5	33.1	100	13.5	44.5	28.0	21.8
	Mirtazapine	100	33.0	105.5	68.5	31.7	100	30.5	40.0	35.8	8.2
	Citalopram	100	239.0	509.5	440.0	20.4	100	189.0	270.5	235.5	8.6
	Desmethylcitalopram	100	37.0	172.5	166.5	35.0	100	17.0	57.5	34.8	28.5
Anti-epileptic and metabolites	Carbamazepine	100	168.6	367.0	244.7	23.1	100	134.7	175.8	156.0	8.0
	Carbamazepine10,11-epoxide	0	-	-	-	-	0	-	-	-	-
	10,11-Dihydro-10-hydroxycarbamazepine	88	<9.9	564.0	157.5	95.0	92	<8.4	84.0	47.5	53.5
Calcium channel blocker	Diltiazem	100	87.5	399.0	180.8	39.8	100	8.3	29.2	21.4	27.5
Hypnotic	Temazepam	100	49.5	205.0	99.5	38.3	100	15.4	25.9	21.0	15.9
Anti-psychotic	Quetiapine	100	9.5	57.5	30.5	47.2	100	7.0	21.0	11.0	33.1
Veterinary	Tylosin	0	-	-	-	-	0	-	-	-	-
Human indicators and metabolites	Creatinine	100	320,562	2,400,438	1,182,313	46.7	100	9,938	29,000	14,500	32.1
	Nicotine	100	7,313	9,000	8,188	6.8	100	116.0	196.0	161.3	14.4
	Caffeine	100	41,625	230,562	190,938	46.8	100	1,125	18,688	5,313	68.8
	Cotinine	100	1,153	2,191	2,029	18.7	100	367.0	562.5	487.3	12.0
	1,7 dimethylxantine	100	52,938	133,313	115,875	26.1	100	5,813	19,188	9,313	32.2
Analgaesics and metabolites	Morphine	100	640.0	1,618	1,209	22.6	100	293.0	504.0	418.0	11.3
	Dihydromorphine	0	-	-	-	-	0	-	-	-	-
	Normorphine	100	62.0	177.0	146.0	25.1	100	16.5	60.5	36.5	26.3
	Methadone	100	19.5	62.5	36.5	29.4	100	3.0	24.5	8.8	50.0
	EDDP	100	78.0	161.5	121.5	20.0	100	50.5	75.0	64.5	9.6
	Codeine	100	1,023	2,801	1,654	28.2	100	761.5	1,198.0	991.3	11.4
	Norcodeine	100	90.5	169.0	115.5	19.7	100	73.0	120.0	98.5	13.0
	Dihydrocodeine	100	151.5	384.5	224.0	29.6	100	166.0	221.0	191.0	7.6
	Tramadol	100	448.0	913.0	593.5	18.1	100	422.5	716.5	590.8	13.5

	N-desmethyltramadol	100	178.0	491.0	346.0	29.0	100	91.5	163.5	123.8	15.4
	O-desmethyltramadol	100	465.5	1,193	907.0	23.9	100	6.8	76.1	55.5	17.3
Stimulants and metabolites	Amphetamine	100	271.0	543.5	434.0	17.4	100	24.5	81.5	52.5	31.6
	Methamphetamine	100	4.5	17.5	6.5	42.4	100	5.0	6.5	6.0	9.2
	MDMA	100	93.0	385.5	188.0	39.8	100	67.5	114.5	85.0	12.8
	MDA	0	-	-	-	-	100	6.5	12.5	9.3	17.4
	Cocaine	100	189.5	367.5	264.0	20.9	100	74.5	131.5	87.3	18.8
	Benzoylecgonine	100	739.5	2,617	1,139	35.6	100	348.5	511.0	417.8	11.2
	Anhydroecgonine methylester	0	-	-	-	-	0	-	-	-	-
	Cocaethylene	47	<6.5	25.0	10.0	49.0	0	-	-	-	-
	Mephedrone	65	<2.8	136.5	17.0	174.6	0	-	-	-	-
	MDPV	0	-	-	-	-	0	-	-	-	-
Opioid and metabolite	Heroin	0	-	-	-	-	0	-	-	-	-
	6-acetylmorphine	18	<3.0	66.0	<3.0	-	0	-	-	-	-

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