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Comparative field study on bioassay responses and micropollutant uptake of POCIS, Speedisk and SorbiCell polar passive samplers

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ABSTRACT

Routine water quality monitoring is generally performed with chemical analyses of grab samples, which has major limitations. First, snapshot samples will not give a good representation of the water quality. Second, it is not sufficient to analyze only a limited number of (priority) pollutants. These limitations can be circumvented by an alternative environmental risk assessment that combines time-integrated passive sampling (PS) with effect-based methods. This study aimed to select which of three polar PS devices was best suited for effect-based monitoring strategies.

In the first part of this study, Speedisk, SorbiCell and POCIS polar PS devices were compared by simultaneous deployment at five sites. Chemical analyses of 108 moderately polar compounds ($-1.82 < \log D < 6.28$) revealed that highest number of compounds, with the widest range of log K_{OW}, log D and pKa, were detected in extracts of POCIS, followed by Speedisk. SorbiCell samplers accumulated the lowest numbers and concentrations of compounds, so they were not further investigated. In a follow-up study, bioassay responses were compared in extracts of POCIS and Speedisk devices deployed at eight sites. The passive sampler extracts were subjected to bioassays for non-specific toxicity, endocrine disruption, and antibiotics activities. More frequent and higher responses were induced by POCIS extracts, leading to more exceedances of effect-based trigger values for environmental risks. As POCIS outperformed Speedisk, it is better suited as PS device targeting polar compounds for semi-quantitative effect-based water quality monitoring.

1. Introduction

Routine water quality monitoring is generally performed by chemically analyzing grab samples for a limited number of compounds. The European Union Water Framework Directive (WFD), for instance, aims to achieve and ensure a good chemical surface water status by implementing a regular chemical monitoring program for 45 (groups of) priority compounds. Measured concentrations are compared to environmental quality standards (EQS) for the water phase as annual average (AA) and maximum allowable (MAC) concentrations (European commission, 2013). Since regular chemical monitoring programs with conventional methods have some serious limitations, more relevant alternatives need to be developed.

In the commonly applied grab sampling, water concentrations of target contaminants are reported as the ‘snapshot’ concentrations. The monthly or yearly frequency of grab sampling does not represent the temporal variations of compounds, as concentrations of most micropollutants typically vary over time (Jones et al., 2015; Brack et al., 2017). Another disadvantage of grab sampling is that the detection limits (LOD) of some pollutants are higher than their EQS values (Harman et al., 2012). Passive sampling (PS) can overcome these limitations by applying a time-integrated measurement of bioavailable micropollutant concentrations in water, which reflects the actual exposure conditions in the water body over extended periods (Vrana et al., 2005). Moreover, with the ability to extract large volumes of water, PS techniques can lower detection limits to overcome the limitations for

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chemicals with a LOD above their EQS (Jones et al., 2015; Terzopoulou and Voutsa, 2016). A drawback of PS, particularly for adsorption-based samplers such as POCIS or Chemcatcher, is the uncertainty in calculations of accurate time-weighted average (TWA) concentrations because sampling rates (R_S) are influenced by environmental conditions such as temperature, water flow rate, salinity, and the formation of biofilms on the surface of the devices (Balaam et al., 2011; Harman et al., 2012; Jones et al., 2015; Roll and Halden, 2016). Moreover, the composition of the mixture extracted from the PS devices is not the same as the mixture in water because of compound-specific uptake rates and partitioning coefficients (Brack et al., 2016; Van der Oost et al., 2017b).

A second limitation of regular monitoring programs is that lists of target priority compounds are generally not representative of present-day contamination, and therefore provide limited information on the relationships between pollution and risks to aquatic organisms (Altenburger et al., 2019). Many priority compounds are being phased out or banned, and their emissions are decreasing (Altenburger et al., 2015; Fliedner et al., 2016) while industries have switched to alternative compounds that may have a serious impact on chemical water quality (Schwarzenbach et al., 2006; Busch et al., 2016). At present, more than 350,000 chemicals are registered for production and use on the global market (Wang et al., 2020). It can be expected that a large number of these chemicals, as well as their transformation products, will end up in the water cycle (Brack et al., 2017). In addition, environmental mixtures, with potential synergism or antagonism, may still cause adverse effects although the concentrations of individual chemicals are below the EQS values (Carvalho et al., 2014). As a result, a large portion of the toxic effects observed in surface waters cannot be explained by compounds that water authorities are required to monitor (Escher et al., 2013; Brack et al., 2016; Tousova et al., 2017). On the other hand, chemical analysis of the myriad of compounds present in the aquatic environment is practically and economically impossible. Therefore, mixture toxicity assessment should be included in water quality monitoring strategies. Bioassays integrate the combined effects of all bioactive compounds in a water sample and are thus recommended (Carvalho et al., 2014; Wernersson et al., 2015; Brack et al., 2017; Van der Oost et al., 2017a; Novák et al., 2018). For several decades, both in vivo and in vitro bioassays have been applied in water quality assessment and have been proven successful in benchmarking water quality (Escher et al., 2013; Neale et al., 2015; Di Paolo et al., 2016; Van der Oost et al., 2017b).

Given the limitations of the present chemical water quality assessment, there is an urgent need for a time-integrated effect-driven monitoring strategy that employs a combination of PS and bioassays. In recent years, the suitability of the combination of PS and subsequent effect monitoring in water quality assessment has received much attention, and accordingly, multiple monitoring strategies applying such an approach have been described (Altenburger et al., 2015; Van der Oost et al., 2017a; Hamers et al., 2018; De Baat et al., 2019, 2020). In the Dutch SIMONI strategy (Smart Integrated Monitoring), a suite of bioanalyses is exposed to the extracts of two types of passive samplers (Van der Oost et al., 2017a). Effect-based trigger values (EBT) can be subsequently used to quantify the environmental risks based on the bioassay responses, making this method suitable for routine monitoring programs (Van der Oost et al., 2017a, 2017b).

Due to passive sampler specific affinities for the wide variety of organic compounds, the adequate selection of the types of passive samplers is crucial for their successful application in water quality monitoring strategies (Ahrens et al., 2015). None of the currently known PS devices will effectively accumulate compounds from the full range of the hydrophobic (non-polar) to hydrophilic (polar) spectrum (Ahrens et al., 2015). Hence, usually a combination of passive samplers targeting non-polar and polar compounds is employed in surface water quality monitoring (Petty et al., 2004; Booij et al., 2013; Van der Oost et al., 2017a; Hamers et al., 2018; De Baat et al., 2019). Partitioning or equilibrium PS devices are generally used for the sampling of non-polar compounds and adsorptive passive samplers are generally used to collect more polar compounds (Brack et al., 2017).

Consistent results for non-polar compounds have been obtained by partitioning samplers such as silicone rubbers (SR) and semi permeable membrane devices (SPMDs) (Allan et al., 2010; Booij et al., 2016), but a selection for the most suited passive sampler for polar compounds is still under debate. Many contaminants of emerging concern, such as pharmaceuticals & personal care products (PPCPs), polar pesticides, and endocrine disruptors (EDCs), are polar substances that may exert toxic effects on aquatic organisms in the ng-μg/L range (Daughton, 2005; Fauvelle et al., 2014). This underlines the need to standardize the employment of polar passive samplers for time-integrated effect-based monitoring strategies. Therefore, the present paper is focused on adsorptive samplers targeting polar compounds. The two kinetic passive samplers most often used for polar compounds are the polar organic chemical integrative sampler (POCIS) and Chemcatcher® (Alvarez et al., 2004; Kingston et al., 2006; Mills et al., 2014). Alternatively, an increased use of Speedisk and SorbiCell devices as passive samplers for polar compounds was reported in recent years. Speedisk is a solid-phase extraction (SPE) disk that is also applied as a passive sampler for polar compounds (Hamers et al., 2018; Zwart et al., 2017). SorbiCell is a flow-through cartridge containing an adsorbent and a tracer salt that indicates the volume of water sampled during deployment (De Jonge and Rothenberg, 2005). Unlike POCIS and Speedisk, the uptake mechanism of SorbiCell is based on the advection flow of water through the sampler (Rozemeijer et al., 2010). The system does not need a pump, since this flow is produced by the hydrostatic pressure which is influenced by the depth of the sampler below the surface water (Rozemeijer et al., 2010).

The present study aimed to examine which of three devices (POCIS, Speedisk and SorbiCell) is recommended to be applied as a PS device for a semi-quantitative (using average extracted water volumes for all compounds) effect-based risk assessment of a wide range of moderately polar compounds, by i) comparing the amounts, numbers, and ranges of target micropollutants that accumulated in the three types of PS devices, and ii) comparing the responses of a bioassay battery to extracts of the two types of PS devices that appeared to be most suited based on the accumulation of target compounds (POCIS and Speedisk). PS devices were simultaneously deployed in two separate sampling campaigns at sites likely to be contaminated with polar compounds. For the chemical survey, POCIS, Speedisk, and SorbiCell extracts were analyzed for 108 compounds with log K_{OW} values ranging from -0.8 to 6.6. For the biological survey, POCIS and Speedisk extracts were subjected to a suite of bioassays responsive to polar organic compounds, thus generating toxicity profiles. Ideally, the two approaches should be combined, but unfortunately the two studies for chemical and bioassay data were disconnected from each other, performed in different campaigns at different sites. Therefore, no direct comparisons could be made between chemical concentrations and bioassay responses. Establishing exact time-weighted average chemical concentrations and their relationships with bioassay responses, however, are not the primary aims of the present paper. The main objective is to provide recommendations, based on the chemical and biological results, on the preferred type of polar passive sampler for semi-quantitative effect-based monitoring strategies.

2. Materials & methods

2.1. Sampling sites

Different types of passive samplers were deployed at various surface water sites in two separate sampling campaigns, a chemical campaign performed in 2015, and an effect-based campaign performed in 2016. The selected sampling sites listed in Table 1 were located within the management areas of the Waternet and Rijnland water boards, near the city of Amsterdam. Sites were selected for their known contamination

Table 1
Sampling sites, codes and sources of micropollutants. Additional information and a site map are given in the Supportinng Information Figure S1.

Sites	Code	Potential sources of micropollutants
1. Chemical campaign		
Bethunepolder	GBP	Reference site
Gooiergracht Hilversum	HIL	Undiluted WWTP effluent
Lake Eemmeer	EEM	Diluted WWTP effluent
River Amstel Amstelveen	AVE	Diluted WWTP effluent
River Amstel Ronde Venen	ROV	Diluted WWTP effluent
2. Effect-based campaign		
Westeinderplassen	WEP	Reference site
Amstelveense Poel	AVP	Unknown urban pollution
Gooiergracht Hilversum	HIL	Undiluted WWTP effluent
River Vecht Utrecht	RVU	Diluted WWTP effluent
Zuider Legmeerpolder	ZLP	Greenhouses
Noorder Legmeerpolder	NLP	Greenhouses
Buitenwesterpolder	WOB	Greenhouses
Polder Derde Bedijking	PDB	Greenhouses

with polar compounds, originating from urban land use, agricultural activity, or WWTP effluent discharges. Reference sites were also included.

2.2. Properties, field deployment and extraction of passive samplers

2.2.1. POCIS

POCIS, with an uptake surface area of 46 cm^2, containing 0.2 g Oasis® HLB sorbent retained between two PES membranes (0.1 µm pore size), were obtained from Exposmeter (Tavelsjö, Sweden). No sampler pre-treatment was required, and samplers were transported to the study sites in their original airtight packaging.

2.2.2. Speedisk

BAKERBOND Speedisk® type no. 8072-06, with an uptake surface area of 20 cm^2, containing 0.3 g divinylbenzene (DVB) sorbent retained within two glass-fiber filters, were obtained from Avantor performance materials (Deventer, The Netherlands). Before field deployment, Speedisks were pre-treated in order to render them suitable for application as a passive sampler. The plastic tops of the Speedisks were trimmed and four holes were made to allow attachment of the sampler to the field setup. Subsequently, Speedisks were conditioned by sequential elutions over a vacuum manifold: 15 mL of dichloromethane, 15 mL of acetone, 15 mL of methanol (MeOH) and 30 mL of ultrapure water. After the final elution, the undersides of the Speedisks were closed with syringe caps and samplers were stored in ultrapure water until deployment at the study sites.

2.2.3. SorbiCell

In the present study, modified SorbiCell samplers, with lower flow resistance, were used to sample larger water volumes. Custom made SorbiCell 3 mL cartridges with the cell type 100−0142-998, containing 1 g of styrene resin (SorbiCell VOC sorbent, no information on exact type of polymer available), were obtained from Sorbisense (Galten, Denmark). The cartridges were closed and preserved in tubes filled with demineralized water. No sampler pre-treatment was required.

2.2.4. Field deployment of passive samplers

POCIS, Speedisk and SorbiCell samplers were deployed simultaneously at each sampling site in the chemical campaign. Passive samplers were deployed in cages to attach and protect samplers during the exposure period. Cages were secured to the bottom or embankment to avoid loss of samplers and to ensure permanent inundation. SorbiCell were deployed by connecting each cartridge to an empty 10 L reservoir made of high-density polymer ethane (HDPE) to collect the water passed through the cartridge. The reservoir was connected to an air hose leading above the water surface, allowing a flow of water through the cartridge due to hydraulic pressure. It was attached to a 30 kg weight in order to keep it submerged. At most sites, four POCIS and four Speedisk were exposed for a period of six weeks. At the WWTP sites of the second campaign, one POCIS and one Speedisk were exposed for four weeks. Although some compounds may equilibrate after the deployment times of 4–6 weeks (Morin et al., 2013; Ahrens et al., 2018), other compounds appeared to be linear even after 8 weeks (Alvarez et al., 2004). A 4–6 week-deployment time was chosen to ensure the maximum uptake of all targeted compounds into POCIS (Van der Oost et al., 2017a; De Baat et al., 2019) and Speedisk (Hamers et al., 2018). After exposure, the samplers were cleaned with water from the sampling site to remove attached particulates and biofilm. The cleaned samplers were transported to the laboratory and stored at −20 °C until extraction.

2.2.5. Extraction of passive samplers

The sorbents between the POCIS membranes and in the SorbiCell cartridges were transferred quantitatively into empty polypropylene SPE columns with 2 polytetrafluoroethylene (PTFE) frits. PES membranes of POCIS were not included in the extraction procedure. The columns were dried under vacuum extraction, followed by centrifugation (2000 rpm, 15 min) and nitrogen flow. The Speedisks were dried under vacuum extraction before elution. Dry SPE columns and Speedisks were eluted with 3 × 3 mL of acetone, with 5 min equilibration time between elutions. SorbiCell were eluted with 3 × 3 mL of MeOH:acetone (1:1, v/v). All eluates were collected in 10 mL conical tubes, and the extracts were filled up to exactly 10 mL.

2.2.6. Estimation of sampled water volume

The water volumes sampled by SorbiCell (modification without tracer salt) were determined as the amount collected in the reservoirs. Reported POCIS R_S rates are specific per compound and differ in the range of 30–300 mL/day (Vrana et al., 2009; Morin et al., 2013; Ahrens et al., 2018). Because of this, no specific R_S values can be applied for the compound mixtures that are detected by bioassays, and semi-quantitative estimations of the extracted water volumes had to be made. For the extracted water volumes by the POCIS samplers, the estimations proposed by Van der Oost et al. (2017b) were used, i.e. an assumed average of 100 mL/sampler/day. Since the uptake surface area of Speedisk is approximately half that of POCIS, this will lead to lower uptake rates. We therefore applied estimated extracted water volumes for Speedisk half of those for POCIS, that is 50 mL/sampler/day.

2.3. Chemical analysis

Prior to analysis, eluted extracts were transferred to analytical solvents as described by Van der Oost et al., (2017b) with slight modifications. One mL of the acetone extracts of POCIS and Speedisk, and the MeOH-acetone fractions of SorbiCell were transferred to MeOH (1 mL) by carefully evaporating the aliquot to dryness under nitrogen flow at 30 °C and dissolving the residues in MeOH. The MeOH extracts were analyzed for 92 compounds with positive ionization (POS) by a Bruker Maxis Impact TOF and a Dionex UPLC system. One mL of the acetone extracts of POCIS and Speedisk, and the MeOH-acetone fractions of SorbiCell were transferred to 40 % MeOH in HPLC water (2 mL) using the same method. These extracts were used for the analysis of 16 compounds with negative ionization (NEG) by Thermo TSQ Quantum Discovery LC–MS/MS.

To determine the extraction efficiency, three replicates of pristine water spiked with a mixture of 108 targeted compounds were extracted with SPE columns containing OASIS-HLB (POCIS sorbent), styrene resin (SorbiCell VOC sorbent), and divinylbenzene (DVB Speedisk sorbent). The extracts were analyzed with LC–MS-TOF and LC–MS/MS. Recoveries were calculated as the ratio between the amounts found in the extracts and those spiked to the water samples. The average recoveries of the targeted compounds were 72 ± 5% for POCIS, 73 ± 5% for

Speedisk, and 43 ± 5% for SorbiCell.

For each passive sampler type, one field blank was used as the negative control. The blank concentrations of targeted compounds in the three field blanks were below the lowest calibration standards (0.03 to 0.06 μg/L). The LODs for the PS devices were calculated from the LODs of the extracts divided by the water concentration factors (1680, 840, and 112 for POCIS, Speedisk and SorbiCell, respectively). The average calculated LOD of the targeted compounds for the three samplers POCIS, Speedisk and SorbiCell were approximately 0.01 ng/L, 0.02 ng/L, and 0.16 ng/L, respectively. A more detailed description of the chemical analyses, including QA/QC aspects, is given in S2 of the supplemental data.

2.4. Bioassays

Bioassays were performed at the Waterproef Laboratory (Microtox and antibiotics SCAN) and at the BioDetection Systems BV laboratory (CALUX). Passive sampler extracts were converted to other solvents before exposure in the bioassays. Details on solvent transfer are given below. A more detailed description of QA/QC aspects of the bioassay measurements is given in S3 of the supplemental data.

2.4.1. Microtox assay

For the bacterial luminescence inhibition assay (Microtox®), passive sampler extracts were evaporated to dryness under nitrogen flow at 30 °C and residues were dissolved in freshly prepared Dutch standard water (DSW: 200 mg of $CaCl_2$-$2H_2O$, 180 mg of $MgSO_4$-$7H_2O$, 100 mg of $NaHCO_3$, and 20 mg of $KHCO_3$ per liter MilliQ water, final pH 8.2). The Microtox test was performed according to the procedure of the manufacturer (AZUR Environmental, 1998), modified for a 96 well-plate format. As the Microtox test has no specific target compound group, acute toxicity is expressed as toxic units (TU), determined with the relative enrichment factor (TU = 1/REF) at which the extract causes 50 % inhibition of luminescence (EC_{50}). Luminescence intensity was measured after 15 and 30 min of exposure. The quality of the used batch of bacteria was monitored by testing with potassium dichromate 105.9 mg/L. Microtox M500 software was used for the determination of the EC_{50} value with 95 % confidence intervals.

2.4.2. CALUX assays

Passive sampler extracts were analyzed by a panel of in vitro ERα, anti-AR and GR CALUX® bioassays. The POCIS and Speedisk extracts (2 mL in acetone) were evaporated to dryness and taken up in 100 μL of dimethyl sulfoxide (DMSO). The CALUX bioassays were carried out using previously described protocols (Murk et al., 1996; Sonneveld et al., 2004; Hamers et al., 2006; Van der Linden et al., 2008). In short, dilution series were made of all DMSO extracts. Specific CALUX cells were plated in 96-well microplates and after 24 h of pre-incubation exposed to the DMSO extracts (triplicate concentration ranges). After 24 h of exposure, cells were lysed, and the luciferase activity was determined after addition of luciferin, using a multiwell luminometer (Lucy 2, Anthos). To rule out confounding influences, cells were also monitored for cytotoxicity. Results of sample dilutions causing a cell mortality ≥20 % were not considered valid. The effects of the passive sampler extracts were expressed as bioanalytical equivalents (BEQs) of the reference compounds for each assay. To this end, concentration ranges of the reference compounds were included on each 96-well plate: ERα CALUX: estrogenic activity, expressed as 17β-estradiol (ER agonist) equivalents (EEQ); anti-AR CALUX: androgenic inhibition, expressed as flutamide (AR antagonist) equivalents (FluEQ); GR CALUX: Glucocorticoid activity, expressed as dexamethasone (GR agonist) equivalents (DexEQ).

2.4.3. RIKILT WaterSCAN assay for antibiotics activity

Activities of five classes of antibiotics were determined with the WaterSCAN assay, obtained from RIKILT (Wageningen, The Netherlands). The test system comprises five plates (details outlined in Pikkemaat et al., 2008): The T plate for tetracyclines, the Q plate for quinolones, the B&M plate for β-lactams and macrolides, the S plate for sulfonamides, and the A plate for aminoglycosides. Inoculated agar was poured as a 2.5–3.0 mm thick layer, and nine holes (14 mm diameter) were punched in each plate. Plates were stored for less than one week (4 °C) before application. POCIS and Speedisk acetone extracts (3 mL) were evaporated to dryness under nitrogen flow and dissolved in 3 mL of MeOH:water (1:1, v/v). The MeOH-water extracts (250 μL) were pipetted into the punch holes of each of the five plates, supplemented with a plate specific buffer (one drop). A plate-specific positive control (250 μL) was added to the center punch hole of each plate. Positive controls consisted of 100 μg/L oxytetracycline (T plate), 100 μg/L flumequine (Q plate), 15 μg/L penicillin G (B&M plate), 100 μg/L sulfamethoxazole (S plate), and 200 μg/L neomycin (A plate). The test plates were incubated for 16–18 h at 30 °C (T, Q and B&M plates) and 37 °C (S and A plates). After incubation, antibiotic activities were estimated by measuring the diameters (d) of the bacterial growth inhibition zones. The effect is proportional to the surface areas of the clear zones (= 0.25 x π x d^2) minus the areas of the punch holes (154 mm^2). Estimations of the antibiotic equivalents in the samples were made by comparing the inhibition zones of samples and positive controls. Antibiotic activities are expressed as BEQ concentrations of the reference antibiotics: BEQ of the T plate is expressed as oxytetracycline equivalents (OxyEQ), Q plate as flumequine equivalents (FlqEQ), B&M plate as penicillin equivalents (PenEQ), S plate as sulfamethoxazole equivalents (SulEQ) and A plate as neomycin equivalents (NeoEQ).

2.5. Data analysis

Following expression of bioassay responses as BEQs of the reference compounds or TU values, responses were compared between the sampler types and sites. The indication of an ecotoxicological risk was investigated by comparing bioassay responses to the effect-based trigger values for the applied bioassays as derived for the SIMONI strategy (SIMONI EBT) by Van der Oost et al. (2017a). Bioassay responses were considered to differ significantly between passive sampler types when the difference was at least 20 %, or when there was a response in one of the two sampler types coinciding with an absence of a response in the other type.

3. Results

3.1. Campaign 1: chemical analyses

Out of the 108 targeted compounds (Table S2), 43 compounds were detected in extracts of the three samplers (Table 2). Details on concentrations of compounds detected in each sampler per site are shown in Table S3. The overall distribution of these compounds over the samplers is shown in Fig. 1.

The highest number of compounds was detected in extracts of POCIS (n = 38), followed by Speedisk (n = 25), and SorbiCell (n = 19). Fifteen compounds were detected in extracts of all three samplers. Most unique compound identifications were found in extracts of POCIS (n = 17), and only two compounds were detected exclusively in extracts of Speedisk (n = 1) and SorbiCell (n = 1).

For non-dissociating (neutral or uncharged) compounds K_{OW} can be used to indicate their polarity, however, for the dissociating (ionic or charged) compounds the distribution coefficient (D) is a better indicator because it considers the concentrations of both the non-dissociating and the dissociating forms (Reemtsma et al., 2016). Of the 43 detected compounds, 15 are non-dissociating and 28 are dissociating (Table 2). Because pH at the sampling sites ranged from 6 to 8 (Table S1), log D values at pH 7 were selected. Fig. 2 gives an overview of the log K_{OW}, log D and pKa values for the compounds detected in the extracts of POCIS vs. Speedisk and POCIS vs. SorbiCell.

Table 2
Compounds detected in extracts of POCIS, Speedisk and SorbiCell, with CAS number, octanol-water partition coefficient (log Kow), octanol-water distribution coefficient (log D) at pH = 7, and acid dissociation constant (pKa).

No	Compounds	CAS number	Log Kow	Log D at pH 7	pKa	POCIS	Speedisk	SorbiCell
1	1H-Benzotriazole (1,2,3-benzatriazol)	95−14-7	1.4	1.5	8.4	x	x	x
2	2,4-Dichlorophenoxyacetic acid (2,4-D)	94−75-7	2.8	−0.8	2.7		x	x
3	2,6-dichlorobenzamide (BAM)	2008−58-4	0.8	1.3	NA	x	x	
4	Acetamiprid	135410−20-7	0.8	1.1	0.7	x	x	x
5	Acridine	260−94-6	3.4	3.3	5.5	x	x	x
6	Azithromycin	83905−01-5	4.0	1.4	8.7	x		
7	Azoxystrobin	131860−33-8	2.5	3.5	0.9	x		
8	Bentazon	25057−89-0	2.3	0.0	3.5		x	x
9	Boscalid	188425−85-6	3.0	4.7	10.8	x	x	
10	Bromacil	314−40-9	2.1	0.1	9.3	x		
11	Carbamazepine	298−46-4	2.4	0.3	4.3	x	x	x
12	Carbendazim	10605−21-7	1.5	1.6	4.2	x	x	
13	Carboxin	5234−68-4	2.3	2.2	0.5	x		
14	Chloridazon	1698−60-8	1.1	0.9	3.3	x		
15	Clarithromycin	81103−11-9	3.2	2.4	9.0	x	x	x
16	Cybutryne (Irgarol)	28159−98-0	4.0	3.2	4.1	x	x	
17	Cyprodinil	121552−61-2	4.0	3.6	4.4	x	x	x
18	Dimethomorph	110488−70-5	2.6	3.3	−1.3	x		
19	Diuron	330−54-1	2.7	0.2	−1.0	x		
20	Dodemorph	1593−77-7	5.7	4.5	7.8	x		
21	Erythromycin	114−07-8	3.1	1.7	8.9	x	x	x
22	Fipronil	120068−37-3	4.0	3.7	NA	x	x	x
23	Fluacrypyrim	229977−93-9	4.5	4.0	NA	x		
24	Imazalil	35554−44-0	3.8	3.9	6.5	x		
25	Imidacloprid	138261−41-3	0.6	−0.3	NA	x	x	x
26	MCPA (4-Chloro-2-methylphenoxy)acetic acid	94−74-6	3.3	−1.1	3.3		x	x
27	MCPP (Mecoprop)	93−65-2	3.1	−0.7	3.8	x	x	x
28	Metamiton	41394−05-2	0.8	0.9	NA	x		
29	Methoxyfenozide	161050−58-4	3.7	3.6	12.2	x		
30	Metolachlor	51218−45-2	3.1	3.2	NA	x		
31	Metoprolol	37350−58-6	1.9	−0.3	9.7	x	x	x
32	Metribuzin	161050−58-4	1.7	1.5	1.3	x		
33	Pentachlorophenol	21087−64-9	5.1	2.5	4.7		x	
34	Propyzamide	23950−58-5	3.4	3.4	10.4	x	x	
35	Sotalol	3930−20-9	0.2	−1.6	8.2 and 9.8	x	x	x
36	Sulfamethoxazole	723−46-6	0.9	−0.6	1.6 and 5.7	x	x	x
37	Terbutryn	886−50-0	3.7	1.4	4.3	x		
38	Thiabendazole	148−79-8	2.5	2.4	4.7	x	x	
39	Thiacloprid	111988−49-9	1.3	1.2	NA	x		
40	Thiamethoxam	153719−23-4	−0.1	−0.3	NA	x		
41	Triphenylphosphine oxide	791−28-6	2.8	3.7	NA	x	x	x
42	Triphenylphosphine sulfide	3878−45-3	4.9	4.5	NA			x
43	Tris(2-butoxyethyl) phosphate (TBEP)	78−51-3	3.8	3.5	NA	x	x	x

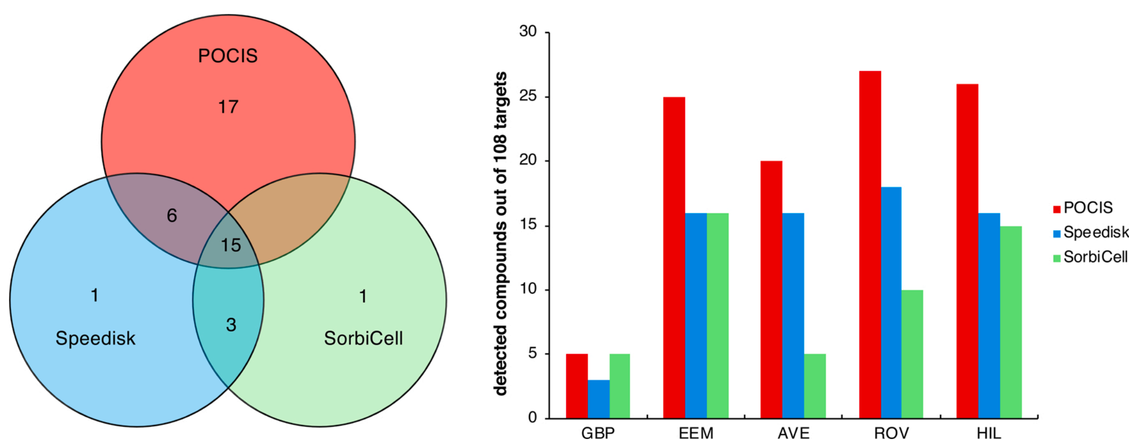

Fig. 1. Number of detected compounds in extracts of POCIS (red), Speedisk (blue), SorbiCell (green); overall distribution (left) and detected compounds per site (right).

Fig. 2 shows that compounds that were detected in all three samplers were hydrophilic to hydrophobic (log K_{OW} 0.2–4 and log D -1.6−3.7), and acidic to basic (pKa 0.7–9.7). In terms of log K_{OW} and pKa, the compounds that were only detected in the POCIS extracts exhibit larger ranges than those detected in the Speedisk and SorbiCell extracts (Fig. 2 a,c,d,f). In terms of log D, it is notable that two compounds in the lower log D range were detected in both the Speedisk and the SorbiCell extracts but not in the POCIS extracts (blue circles, Fig. 2 b,e). The other

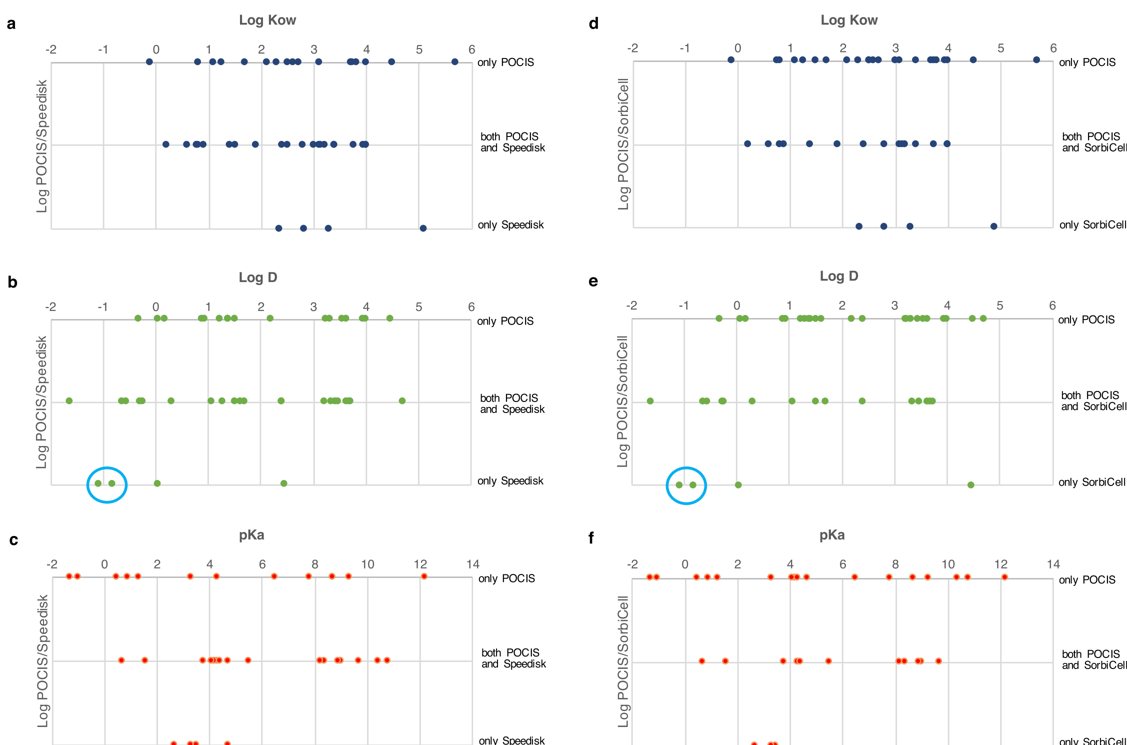

Fig. 2. Overview of log K_{ow}, log D and pKa of compounds detected in POCIS vs. Speedisk (a,b,c) and in POCIS vs. SorbiCell (d,e,f). For explanation of the blue circles see text.

three compounds that were not detected in POCIS extracts have log D values within the log D range of the other detected compounds, which suggests that their absence in POCIS extracts is not due to their polarity and acidity/alkalinity.

Overall, the results show that most compounds with the widest range of log K_{OW}, log D and pKa were detected in extracts of POCIS, followed by Speedisk. SorbiCell accumulated the lowest number of compounds. The absence of five compounds (2,4-D, bentazon, MCPA, pentachlorophenol and triphenylphosphine sulfide) in POCIS extracts, while being detected in Speedisk and/or SorbiCell, is discussed in section *4.1.1 Uptake mechanisms of PS devices*. A lack of detection of 65 target compounds in the passive sampler extracts is either due to their absence at the investigated sites in concentrations above the LOD, or the inability of the deployed passive samplers to efficiently accumulate these compounds. The highest compound concentrations were generally observed in the POCIS extracts, except pesticides in negative ionization mode that had higher concentrations in the Speedisk extracts (Table S3).

3.2. Campaign 2: bioassay responses

For a fitting comparison of bioassay data all responses of the POCIS and Speedisk extracts were recalculated as estimated responses in surface water, as described in the materials and methods section (2.2.6). If less than 20 % difference was observed, the bioassay responses were considered similar. Table 3 shows comparisons between frequency and intensity of bioassay responses to POCIS and Speedisk extracts. Details of bioassay responses to the extracts per site are shown in Figs. 3–6.

Table 3 shows that the responses of POCIS extracts to Microtox, anti-AR CALUX and most antibiotics (tetracyclines, sulfonamides and aminoglycosides) assays were more frequent and intense than those of

Table 3
Frequency and intensity of bioassays responses to POCIS and Speedisk extracts; red = highest frequency & intensity in POCIS; blue = highest frequency & intensity in Speedisk.

		Frequency		Intensity	
		Percentage POCIS extracts cause responses	Percentage Speedisk extracts cause responses	Number POCIS extracts with reponses higher than Speedisk	Number Speedisk extracts with reponses higher than POCIS
non-specific	Microtox	88%	50%	4	3
specific toxicity	ERα CALUX	88%	88%	4	2
	anti-AR CALUX	100%	50%	7	0
	GR CALUX	25%	25%	1	1
antibiotics scan	Tetracyclines	63%	25%	3	2
	Quinolones	25%	38%	0	2
	β-lactams/Macrolides	25%	25%	1	0
	Sulfonamides	25%	0%	2	0
	Aminoglycosides	63%	38%	5	2

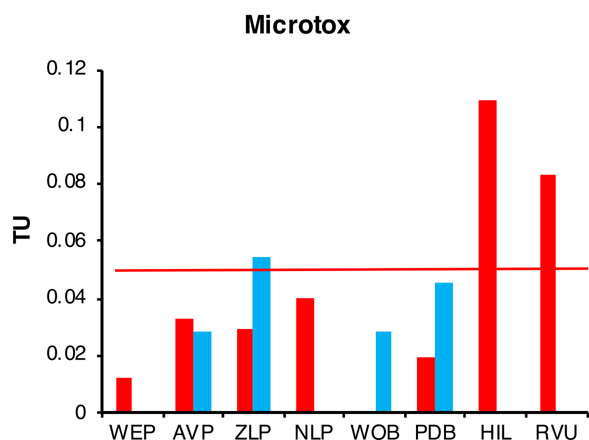

Fig. 3. Microtox responses to extracts of POCIS (red bars) and Speedisk (blue bars). Red line indicates SIMONI EBT (Van der Oost 2017a).

Speedisk extracts. More or less similar responses of ERα CALUX and β-lactams/macrolides responses were observed for POCIS and Speedisk extracts, but highest responses were observed for POCIS extracts. The responses of POCIS and Speedisk extracts to GR CALUX were similar. The extracts of Speedisk were more active in the quinolones antibiotics assay than those of POCIS. Overall, the responses of POCIS extracts to the endocrine activity bioassays were most frequent and intense.

Most Microtox responses were higher in POCIS extracts, but Speedisk responses at the greenhouse sites ZLP and PDB were higher than those of POCIS (Fig. 3). Most striking differences were observed at the sites that were impacted by WWTP effluents, with high responses in the POCIS and no response in Speedisk. In general, the POCIS extracts caused more frequent and higher Microtox responses than the Speedisk extracts.

Responses of the ERα, anti-AR and GR CALUX assays to the POCIS and Speedisk extracts are shown in Fig. 4. Both POCIS and Speedisk caused a response in the ERα CALUX assay at all eight sites (Fig. 4A). Overall, the responses of the ERα CALUX assay to POCIS extracts were more intense than those to Speedisk extracts. The POCIS extracts caused responses in the anti-AR CALUX assay at all eight sites while low responses to the Speedisk extracts were only observed at the four greenhouse sites (Fig. 4B). It is obvious that the POCIS extracts were much more active in the anti-AR CALUX assay than those of Speedisk. Similar GR CALUX responses were observed for POCIS and Speedisk extracts only at the two sites affected by WWTP effluent (Fig. 4C).

Bioassay responses were observed for all of the five antibiotics classes in the RIKILT WaterSCAN assay (Fig. 5). Most responses in the tetracyclines class antibiotics assay, expressed as oxytetracycline equivalents (OxyEQ), were observed in POCIS extracts (Fig. 5A). Clear responses to POCIS extracts at the two WWTP affected sites (HIL, RVU) were not observed in Speedisk extracts. For quinolones activity, expressed as flumequine equivalents (FlqEQ/L), Speedisk responses were more frequent and intense that those of POCIS (Fig. 5B). Results for

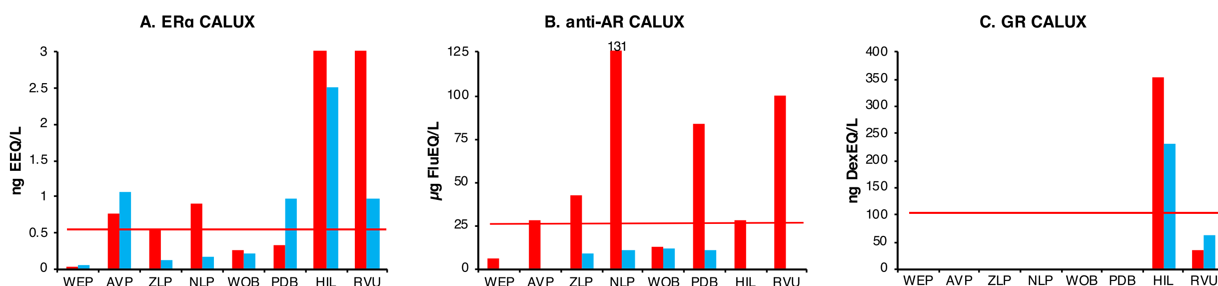

Fig. 4. Responses of CALUX bioassays to extracts of POCIS (red bars) and Speedisk (blue bars). A) ng EEQ/L: 17β-estradiol equivalents. B) µg FluEQ/L: Flutamide equivalents. C) ng DexEQ/L: Dexamethasone equivalents. Red lines indicate SIMONI EBT (Van der Oost 2017a).

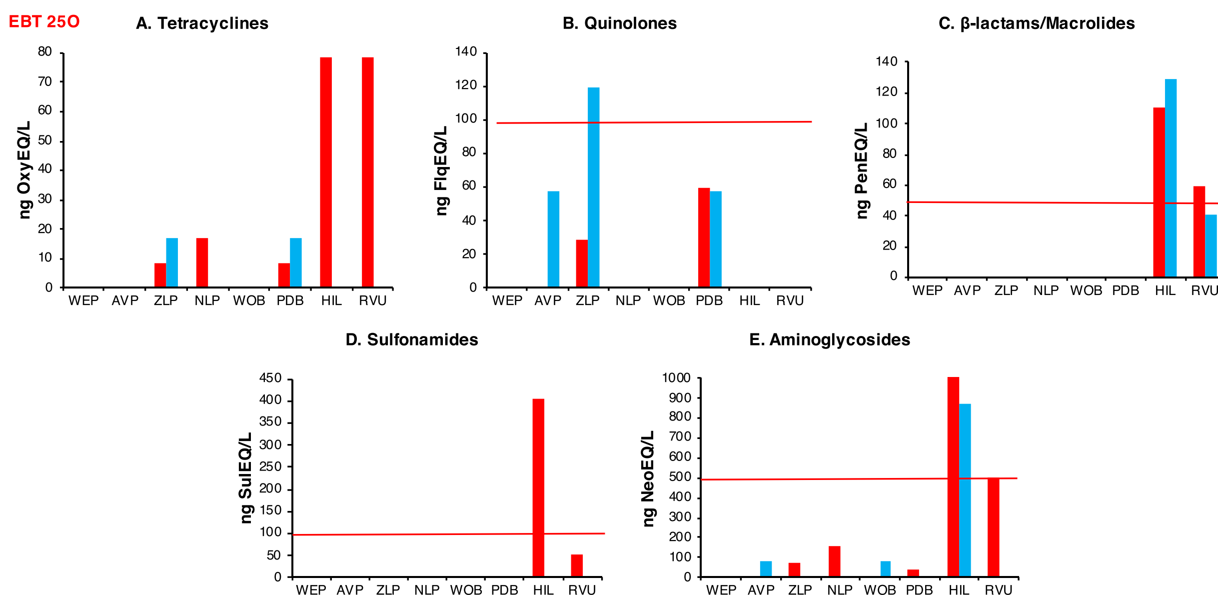

Fig. 5. Antibiotic responses to extracts of POCIS (red bars) and Speedisk (blue bars). A) ng OxyEQ/L: Oxytetracycline equivalents. B) ng FlqEQ/L: Flumequine equivalents. C) ng PenEQ/L: Penicillin equivalents. D) ng SulEQ/L: Sulfamethoxazole equivalents. E) ng NeoEQ/L: Neomycin equivalents. Red lines indicate SIMONI EBT (Van der Oost 2017a).

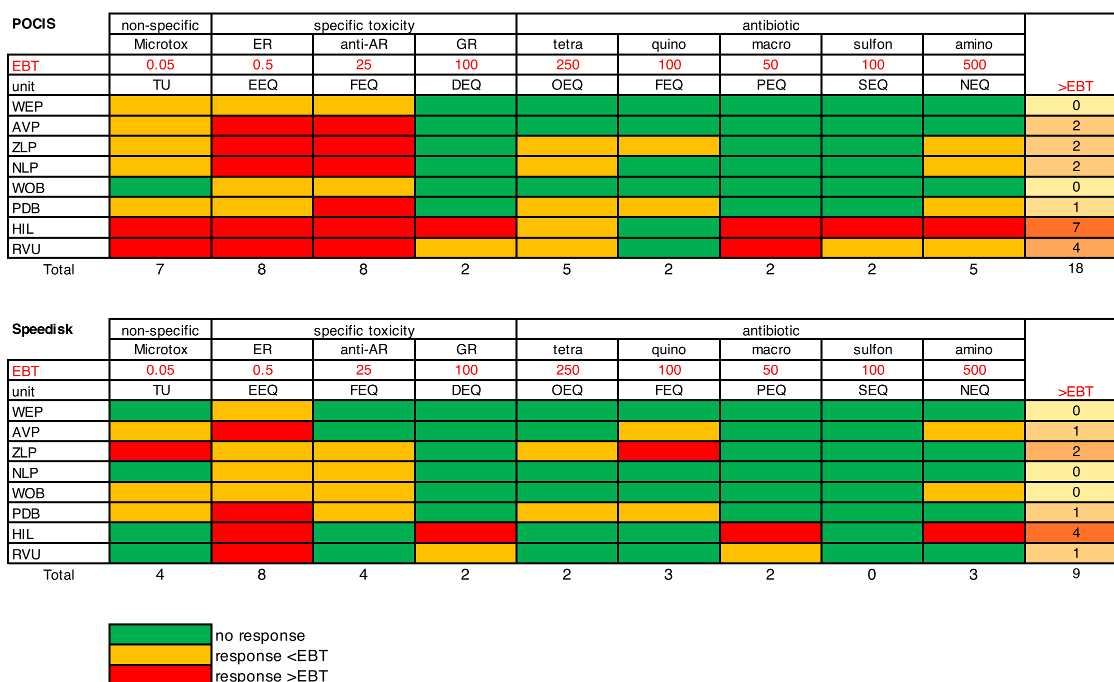

Fig. 6. Heatmaps with bioassay responses of extracts of POCIS (upper graph) and Speedisk (bottom graph) at all the studied sites. Bioassay responses exceeding the respective SIMONI EBTs are shown in red, responses below the EBTs in orange, and no response in green. 'Total' represents the total number of responses for each bioassay.

β-lactams/macrolides activity, expressed as penicillin G equivalents (PenEQ/L) were quite similar (Fig. 5C). Both POCIS and Speedisk at the two WWTP affected sites (HIL, RVU) caused clear responses. Fig. 5D shows that sulfonamides activity, expressed as sulfamethoxazole equivalents (SulEQ/L), was only observed for POCIS at the two WWTP affected sites. Aminoglycosides activities, expressed as neomycin equivalents (NeoEQ/L), were similar at the HIL WWTP site but different at most sites (Fig. 5E). At four (agricultural/WWTP) sites responses were only found for POCIS, while responses at two (urban/agricultural) sites were only observed in Speedisk extracts.

3.3. *Risk assessment using bioanalytical results*

The SIMONI risk analysis is performed by measuring the effects of the whole extractable mixture of substances with a battery of bioassays (Van der Oost et al., 2017a, 2017b). For this method the water is concentrated with PS, and their extracts are tested with a battery of bioassays to assess general and specific toxicity of the mixture. In the tier 1 screening, a risk indication is determined by comparing bioassay results to effect-based trigger values (EBT). Bioassay responses above the EBT are indications of increased ecotoxicological risks (Van der Oost et al., 2017a). Because the results of bioassays do not reveal which substances cause the effects, a further chemical-toxicological study is carried out at sites with highest ecological risks in a tier 2 risk assessment. A comparison of bioassay responses with SIMONI EBTs for both PS devices at all investigated sites is presented in the heatmaps of Fig. 6. The heatmaps clearly demonstrate the differences in toxicity profiles obtained by the different PS devices. For both samplers, no EBT exceedances were observed at the WEP reference site and the WOB greenhouse site, indicating low ecotoxicological risks at these sites. The toxicity profiles further indicated six and five sites with increased risks for the ecosystem (exceedances of one or more EBT) with POCIS and Speedisk, respectively. At urban and greenhouse sites increased environmental risks were indicated with POCIS due to EBT exceedances for the ERα CALUX (AVP, ZLP, NLP) and anti-AR CALUX (AVP, ZLP, NLP, PDB) assays. With Speedisk, some EBT exceedances were observed at three of these sites, with Microtox (ZLP), ERα CALUX (AVP and PDB) and antibiotics (ZLP), while no EBT exceedances were observed at the NLP greenhouse site. Most EBT exceedances, ranging from cytotoxicity (non-specific) to specific endocrine disruption and antibiotic activities, were observed at two sites affected by WWTP effluents (HIL, RVU). In POCIS samplers, EBT exceedances were observed for Microtox, ERα, anti-AR and GR CALUX as well as antibiotics activities. No EBT exceedances for Microtox and anti-AR were observed for Speedisk at the WWTP sites. The fact that seven of the nine EBT were exceeded in POCIS at the HIL site indicates a high risk of diverse adverse effects due to micropollutants in this virtually undiluted WWTP effluent.

4. Discussion

4.1. *Chemical analyses*

Summarizing the literature data on compound affinities for passive samplers, silicone rubbers and SPMDs are reported to effectively take up the hydrophobic compounds ($\log K_{OW}$ range 3–7), whereas hydrophilic compounds accumulate more effectively in Speedisk ($\log K_{OW}$ range -0.7 to 4.5) and in POCIS ($\log K_{OW}$ range -2.6 to 4.0) (Mazzella et al., 2007; Vermeirssen et al., 2012; Morin et al., 2012, 2013; Fauvelle et al., 2014; Booij et al., 2016; Silvani et al., 2017). In fact, several hydrophobic compounds ($\log K_{OW}>4$) are reported to accumulate in POCIS, but due to low sampling rates POCIS is an inefficient sampler for this group of compounds (Harman et al., 2012). No such information on this topic has been published for SorbiCell samplers.

4.1.1. *Uptake mechanisms of PS devices*

The exchange surface of the flow-through SorbiCell is unknown, but the extracted water volume is measured by collecting the water that passed through the column. Differences in the sampled water volumes of POCIS and Speedisk samplers can be partly attributed to differences in the uptake mechanisms and surface areas. POCIS are exposed to surface water from two sides, with a water → membrane → sorbent uptake pathway, while Speedisk (and SorbiCell) are exposed to the water from one side only, with a water → glass fibre→sorbent uptake pathway (Figure S2 supplemental data). Because of the two-sided water exposure,

POCIS has a larger exchange surface area than Speedisk.

According to Vrana et al. (2005), the amount of compounds accumulated in a passive sampler highly depends on its exchange surface area. The uptake rate R_S is proportional to the exchange surface area of a sampler, therefore the larger exchange surface area of POCIS contributes to a larger R_S which results in larger volumes of water sampled compared to the Speedisk and SorbiCell. An increased R_S leads to improved chemical and bioanalytical detection limits. Because POCIS and Speedisk are deployed in vertical or diagonal position against waterflow in the field, the effective sampling surface area can be smaller than assumed due to the sagging of the sorbent to the bottom of the discs.

Membranes that contain the POCIS resin will exclude particulates, biofims, and other large molecules from fouling the sorbent, and allow for longer exposure periods of PS devices (Endo and Matsuura, 2018), making them better fit for the determination of TWA concentrations over extended periods. A disadvantage of the PES membrane commonly used in POCIS is its absorption ability. Ionic and neutral polar compounds can be absorbed by PES membranes (Vermeirssen et al., 2012; Endo and Matsuura, 2018), which may result in delayed or blocked transfer through the membrane. In the present study, five compounds found in Speedisk or SorbiCell were not detected in POCIS. However, since four of these compounds showed high recoveries in OASIS-HLB receiving phase of POCIS (bentazone 110 %, MCPA 100 %, pentachlorophenol 94 % and trifephnylphosphine sulfide 103 %), the absence of these compounds could be due to the sorption capacity of the PES membrane. Since the herbicide 2,4-D was not detected in POCIS in both the recovery test and the field application, this is probably due to a lack of affinity of this compound for the sorbent. It has been recommended to extract the PES membrane along with the POCIS sorbent to optimise analyte recoveries (Vermeirssen et al., 2012; Silvani et al., 2017). However, this could also introduce contaminants from the PES membrane and (bio)fouling to sample extracts (Challis et al., 2018). The PES membrane could be extracted seperately and subsenquently analyzed for targeted compounds, but this was not done in the current study. A better alternative may be to replace the PES membranes by PTFE membranes that show little sorption if any (Endo and Matsuura, 2018).

Because the uptake mechanism of SorbiCell is based on the advection flow of water through the sampler (Rozemeijer et al., 2010), the low volumes collected at the EEM and HIL sites of the present study could be caused by the obstructed flow due to clogging in the cartridge. Nonetheless, the exact sampled volumes for the SorbiCell samplers were recorded, and the differences in volumes between the locations were corrected for.

4.1.2. Sampler specific affinities

Compound uptake is dictated by the passive sampler/water partitioning coefficient K_{PW}, which depends on the physicochemical properties of the compound and on the environmental conditions, but especially on the passive sampler material and design (Harman et al., 2012; Ahrens et al., 2015). Hence, compound uptake is partly dictated by compound affinity for the sorbent used in the PS devices (Bäuerlein et al., 2012). The Oasis HLB sorbent used in POCIS samplers is a hydrophilic-lipophilic balanced copolymer of divinylbenzene and N-vinylpyrrolidone (Alvarez et al., 2004; Mazzella et al., 2007). The divinylbenzene subunit is used to attract lipophilic compounds due to its specific interaction with aromatic groups and the N-vinylpyrrolidone subunit is used to increase sorption with hydrophilic compounds thanks to its H-bond acceptor (Mazzella et al., 2007). The sorbent H_2O-Philic DVB of Speedisk samplers is a copolymer of divinylbenzene and N-methyl-*N*-vinyl amide. The presence of the carboxyl groups in the DVB and the different amides in the Oasis HLB (Huysman et al., 2019) could explain the slightly better accumulation of negatively charged compounds in Speedisk than POCIS in the present study. Huysman et al. (2019) demonstrated a slightly stronger affinity of hydrophilic DVB, as compared to Oasis HLB, for 131 environmentally relevant organic contaminants with a broad polarity range. The similarity in sorbent structures of the two samplers, both consisting of divinylbenzene subunits, could explain that most of the detected compounds are extracted by both samplers. Therefore, differences in compound uptake between POCIS and Speedisk will be mainly due to the differences in design and surface area of the samplers. Detection of compounds in POCIS and not in Speedisk might be due to the lower sampled volume of Speedisk, leading to compound concentrations below the LOD.

The only information provided by the manufacturer of SorbiCell was that the sorbent is a styrene resin, described as SorbiCell VOC sorbent (www.eurofins.dk). The low average extraction recoveries (43 %) indicate that many compounds are either not well retained by the sorbent or are not released during the elution. In the present study, the lowest number of compounds with the smallest log K_{OW} range were detected in SorbiCell extracts. This indicates that SorbiCell is not a feasible substitute for POCIS to sample a wide range of polar compounds.

4.1.3. Conclusions on chemical analyses

It was demonstrated that both POCIS and Speedisk samplers have their advantages and disadvantages in terms of accumulation and handling. POCIS accumulated not only the widest range of compounds in term of log K_{OW}, but also the largest number of polar compounds, which are the target analyte group for these samplers. However, the PES membranes are vulnerable to damage during deployment by handling or aquatic species and may limit transfer of certain compounds to the sorbent. In contrast, Speedisk accumulated fewer compounds than POCIS. The robust design of Speedisk is an advantage for field deployment but requires disassembly to avoid elution of compounds in particulate matter attached to the sampler. In addition, pre-treatments of Speedisk are needed before deployment. It was demonstrated that the applied SorbiCell system is the least suitable for sampling a wide range of polar organic compounds in surface waters because of the lowest numbers and concentrations of detected compounds, clogging issues, and inconvenient deployment.

4.2. Bioassay responses

4.2.1. Sampled water volumes

Standardized protocols for the determination of the volume sampled by passive samplers using performance reference compounds (PRCs) have been described for non-polar samplers (Booij and Smedes, 2010; Smedes and Booij, 2012) but for polar passive samplers no such consensus has yet been reached (Harman et al., 2011). Attempts were made to develop a PRC for POCIS such as deuterium-labeled atrazine--deisopropyl (DIA-d5) (Mazzella et al., 2010; Lissalde et al., 2011). However, the difference between the release of DIA-d5 and the uptake of target compounds seems to be a problem for this approach (Harman et al., 2011). The uptake rate (R_S) is unique for each compound and could be determined by calibration in the laboratory under controlled temperature and water flow rate (Terzopoulou and Voutsa, 2016; Miège et al., 2012). However, conditions in the field are different from those in the laboratory, with variable temperatures and flow rates during the deployment period. In addition, the formation of biofouling on the surface of passive samplers could affect the uptake rate (Jálová et al., 2013; Lissalde et al., 2014). In a comparative study (Ahrens et al., 2018) it was demonstrated that median R_S values for POCIS determined in the laboratory were much higher than those measured in situ (220 vs. 35 mL/day).

Sampling rates for uptake of polar compounds in POCIS have been reported ranging from 0.03 to 0.3 L/day (Vrana et al., 2009; Morin et al., 2013; Ahrens et al., 2018). Since the compounds that cause the effects in the bioassays are unknown, it is impossible to use reported sampling rates for individual compounds. To overcome this limitation of diverging sampling rates, previous studies applied a semi-quantitative approach with an average sampled volume of 0.1 L/day for POCIS

samplers in combination with bioassay-based effect monitoring (Van der Oost et al., 2017b). An approach to estimate the sampling rate of Speedisk by using 15 compounds detected in simultaneously deployed Speedisk and silicone rubber samplers was introduced by Hamers et al. (2018). This approach was not possible in the present study since no silicone rubbers were applied. The uptake surface area of Speedisk is two times smaller than that of POCIS, which results in a lower uptake rate (Vrana et al., 2005). In the present study the estimated sampled volume to determine the water concentration factor was considered to be proportional to the surface area of the devices, so 100 mL/day for POCIS and 50 mL/day for Speedisk. The Speedisk R_S used in the present study was in line with those determined by Hamers et al., 2018, ranging from 31 to 87 mL in surface waters. Although it is possible that equilibrium is reached for certain compounds during longer PS deployments, many compounds are reported to be in the linear uptake mode after six to eight weeks of POCIS exposures (4 out of 8 compounds after 8 weeks by Alvarez et al., 2004; 39 out of 62 compounds after 6 weeks by Ahrens et al., 2018). In a field study in WWTP effluents that compared the results of PS with those obtained by flow-proportional daily grab-sampling, it appeared that R_s values of both POCIS and Speedisk showed large variations for different compounds (Van der Oost et al., unpublished data). Average R_s values of 38 detected pharmaceuticals (SPE extraction) and pesticides (direct injection) were 52 mL/d (range 0.1–384) for POCIS and 33 mL/d (range 0.0–263) for Speedisk. Mean R_s for 9 compounds that were also determined in the present study were 96 and 62 mL/d for POCIS and Speedisk, respectively, which was close to our assumptions of 100 and 50 mL/d. Due to the large R_s variations, however, these assumptions can only be applied for semi-quantitative assessments.

4.2.2. Passive sampler specific responses

Responses were observed in all applied bioassays after exposure to POCIS and Speedisk extracts. Although the above-mentioned correction was made for the estimated uptake rates of the samplers, bioassay effects were observed more frequently and intensely after exposure to POCIS extracts, most probably due to the higher diversity and concentrations of micropollutants. Since the bioassay effects directly relate to the compounds accumulated in the PS device, and since both types were deployed simultaneously at all sites, these results are in line with the higher amounts and numbers of polar micropollutants that were observed in the POCIS extracts in the chemical campaign (Fig. 1 and Table S3). In the present study it was demonsterated that Speedisk more efficiently accumulates pesticides than pharmaceuticals, which could explain the less frequent and lower responses observed at the two WWTP affected sites for this sampler type.

4.2.3. Ecotoxicological implications

Bioassays responses of the POCIS and Speedisk extracts were converted to estimated responses in surface water, as described in the materials and methods section (2.2.6) and discussed above (section 4.2.1). Fig. 6 shows that bioassay responses observed in the present study frequently exceeded EBTs, indicating organic micropollutant concentrations in the field at levels that can cause ecotoxicological risks (Van der Oost et al., 2017a). Responses above the EBTs were observed in all CALUX assays, for three out of five antibiotics in the SCAN test, as well as in the Microtox assay. Although no EBT exceedances were observed at the WEP reference site, low responses of Microtox, ERα and anti-AR CALUX indicate the presence of certain bioactive compounds. For the urban lake AVP, the specific effects observed reveal the activities of micropollutants with estrogenic and anti-androgenic modes of action. Agricultural greenhouse sites generated responses above the EBT in ERα and anti-AR CALUX assays. Most EBT exceedances were observed at the WWTP sites, indicating the most diverse and intense environmental risks.

The elevated ERα CALUX responses (Fig. 6, both samplers) could be caused by a range of estrogenic compounds such as natural or synthetic estrogens, pseudo-estrogens, pesticides (e.g., alachlor, triclosan, vinclozolin), bisphenol A, phthalates, or alkyl phenols (Vethaak et al., 2005). The anti-AR EBT exceedances (Fig. 6, POCIS) could be due to pesticides, insecticides, herbicides, brominated flame retardants, [pseudo-]androgens, steroids, antibiotics, growth promoters, estrogens, or PCBs. EBT exceedances at WWTP sites are likely due to high and continuous input of a complex mixture of compounds with endocrine disrupting, antibiotic, and antibacterial activity (Van der Linden et al., 2008; Escher et al., 2014). The responses above the EBTs of in ERα and anti-AR CALUX assays at agricultural sites are possibly due to activity of natural and synthetic estrogens and pesticides or their metabolites (Kojima et al., 2004; Sun et al., 2007). Moreover, several agricultural sites exhibited activity of quinolone antibiotics, although below the EBT, which may be attributed to biocides application in the greenhouses (Martínez-Carballo et al., 2007).

The responses observed in the Microtox assay might be partly attributable to the antibiotic activity of the passive sampler extracts, as antibiotics of the indicated classes have previously been shown to cause inhibition in the Microtox assay as well (Isidori et al., 2005). Moreover, EBT exceedances of both antibiotics and Microtox assays coincided at the two WWTP sites.

4.2.4. Conclusion on effect-based analyses

The two investigated PS devices generated different response profiles in the applied bioassay battery, with several unique responses per passive sampler. Nonetheless, POCIS extracts caused bioassay responses more frequently and more intensely, leading to more frequent indications of ecotoxicological risks. Although the identity of the compounds that caused the bioassay effects was not determined, it was clear that POCIS outperformed Speedisk in accumulating compounds that cause significant bioassay responses at all investigated sites.

4.3. Overall conclusions

Unfortunately, the two studies for chemical and bioassay data were disconnected from each other, since they were performed in different campaigns at different sites. Therefore, it was impossible to reveal the substances that were (partly) responsible for the observed effects. This was, however, not the main objective of the present study that was focused on a semi-quantitative Tier 1 bioanalytical screening. If increased ecological risks are indicated in Tier 1, a Tier 2 follow-up study can be performed in order to identify and quantify the main drivers of toxicity (Van der Oost et al., 2017a). The least number of target compounds at lowest concentrations accumulated in the modified SorbiCell device. Since the performance of both POCIS and Speedisk was clearly better, SorbiCell samplers were considered the least suited to be applied for effect-based monitoring campaigns. General performance criteria, such as sampling repeatability and integrative uptake are essentially the same for POCIS and Speedisk. With the results of the present study (numbers and concentrations of accumulated target compounds and frequency and intensity of bioassay effects) it was demonstrated that POCIS is better suited than Speedisk as PS device targeting polar compounds for a semi-quantitative risk analysis in effect-based water quality monitoring strategies.

CRediT authorship contribution statement

M. Thao Nguyen: Formal analysis, Investigation, Data curation, Writing - original draft, Writing - review & editing, Visualization. **Milo L. De Baat:** Data curation, Writing - original draft, Writing - review & editing. **Ron Van Der Oost:** Conceptualization, Methodology, Validation, Writing - review & editing, Supervision, Funding acquisition. **Willie Van Den Berg:** Writing - review & editing, Funding acquisition. **Pim De Voogt:** Writing - review & editing.

Declaration of Competing Interest

The authors report no declarations of interest.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.etap.2020.103549.

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