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1 **Determination of uptake kinetics and sampling rates for 56** 2 **organic micropollutants using “pharmaceutical” POCIS**

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14 15 **Abstract**

16
17 The literature increasingly reports sampling rates (R_s) for Polar Organic Chemical Integrative
18 Samplers (POCIS) but the data obtained come from various calibration systems that are not
19 always well-defined (agitation, temperature, measured micropollutant concentrations in
20 water,...). In order to obtain accurate laboratory R_s for priority and emerging substances,
21 POCIS need to be exposed in a robust and well-defined calibration system. Thus, we built a
22 flow-through calibration system containing tap water spiked with 56 organic micropollutants
23 (alkylphenols and phenols, hormones, pesticides, pharmaceuticals, UV filter). POCIS were
24 immersed for up to 28 days. Tap water micropollutant concentrations and additional
25 parameters (temperature, pH, conductivity, dissolved organic carbon, flow velocities) were
26 kept constant and controlled throughout the calibration experiment. Based on the observed
27 uptake kinetics, we distinguished 4 types of micropollutant accumulation patterns: curvilinear
28 accumulation (30 molecules, group 1), accumulation with an inflexion point (13 molecules,
29 group 2), random accumulation (8 molecules, group 3), and no or very low accumulation (5
30 molecules, group 4). R_s was calculated for 43 out of 56 micropollutants (groups 1 and 2).
31 Calculated R_s values ranged from 0.030 L/d to 0.398 L/d. POCIS can supply TWA

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

37

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

40

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

47

48 **1. Introduction**

49

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

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

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

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

91

92 **2. Material and methods**

93

94 *2.1. Chemicals, material and apparatus*

95

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

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

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

130 Germain-en-Laye, France), respectively. Empty glass solid phase extraction (SPE) tubes (6
131 mL) and polytetrafluoroethylene (PTFE) frits (20 μm porosity) were purchased from Sodipro
132 (Echirolles, France). The calibration system was composed of a Harvard Type 22 syringe
133 pump from Harvard Apparatus (Les Ulis, France) and a Ismatec model Ecoline VC-MS/CA8-
134 6 peristaltic pump from Thermofisher (Illkirch, France).

135 The chromatographic separation of 10 betablockers and 5 estrogens ([E1], [α -E2], [β -
136 E2], [E3], [EE2]) was performed with Xbridge C18 end-capped columns (150 x 2.1 mm, 3.5
137 μm) from Waters (Guyancourt, France) equipped with guard columns. The separations of the
138 41 remaining molecules were performed with a Kinetex XB-C18 Core Shell (100 x 2.1 mm,
139 1.7 μm) equipped with a KrudKatcher (0.2 μm) filter from Phenomenex (Le Pecq, France).

140 The liquid chromatography-mass spectrometry (LC-MS) system used for the analysis of
141 10 betablockers and 5 estrogens was composed of an Agilent 1100 chromatographic system
142 from Agilent (Massy, France) coupled with an API 4000 triple-quadrupole mass spectrometer
143 from AB Sciex (Les Ulis, France). The LC-MS system used for the analysis of the 41
144 remaining molecules was an Agilent 1200 chromatographic system from Agilent (Massy,
145 France) coupled with a triple-quadrupole 3200 Qtrap from AB Sciex (Les Ulis, France).

146

147 2.2. *Calibration design and POCIS exposure*

148 The calibration system is schematized in Figure 1. It consisted of 2 aquaria (up to 50 L)
149 filled by tap water freshly spiked at a nominal value of 3 $\mu\text{g/L}$ for each analyte. This
150 concentration permitted to analyze grab samples by direct injections in LC-MS and thus to
151 easily control this parameter throughout the calibration phase. Triplicates of “pharmaceutical”
152 POCIS (45.8 cm^2 of exposed surface, 200 mg of receiving phase) were immersed for $t = 1, 3,$
153 6 and 12 hours and for $t = 1, 3, 7, 14, 21$ and 28 days. Given that we worked with 2 aquaria
154 with a limited number of POCIS per aquarium and that each exposure duration was tested in
155 triplicate, the total experiment duration was 42 days. In order to closely mimic the agitation
156 conditions found in aquatic rivers, each POCIS was exposed to a current of around 10 cm/s
157 delivered perpendicularly to their surface by a diffusion ramp linked to a submersible pump.
158 This set-up was inspired by the system developed by Mazzella et al. [10]. Tap water was
159 thermostated at around 20°C by thermostated water-bath using an external thermostated tank.
160 The system was kept in the dark to prevent any photolysis of analytes.
161

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

175

176 Insert Figure 1

177

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

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

189

190 2.3. *POCIS and water sample pre-treatment and analysis*

191

192 2.3.1. POCIS preparation, deployment, retrieval and blank

193

194 The POCIS were home-made, with 200 mg (\pm 5 mg) of receiving Oasis® HLB phase
195 sandwiched between 2 PES membranes. This device set-up was kept between 2 stainless steel
196 rings linked together by screws and nuts. The home-made POCIS were then stored at 5°C (\pm
197 1°C) until immersion in the aquaria. During exposure, the POCIS were placed facing the flow
198 coming from the diffusion ramp. After retrieval, the POCIS membranes were rinsed with a
199 few mL of unspiked tap water, and the POCIS were then stored at -23°C (\pm 3°C) until
200 extraction. An additional blank POCIS, consisting in a POCIS not immersed in the exposure
201 media was produced in order to check for any contamination of the receiving phase. This
202 blank POCIS was stored at -23°C (\pm 3°C) until processing.

203

204 2.3.2. Treatment of POCIS before analysis

205

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

216 - 500 μ L of a H₂O/ACN mixture (99/1, v/v) and 50 μ g/L of an internal standard (i.e.
217 metoprolol impurity A) for betablocker analysis,

218 - 500 μ L of a H₂O/ACN mixture (60/40, v/v) and 50 μ g/L of an internal standard (i.e.
219 estradiol acetate) for estrogen analysis,

220 - 2 mL of a H₂O/ACN mixture (80/20, v/v) for the 2 multiresidue analyses.

221 Before analysis, extracts were diluted 100 to 500 times in order to be within the
222 concentration range of each method and to guard against matrix effects. For betablocker and
223 hormone analyses, dilutions were done in their respective mobile phase mixtures. For
224 multiresidue analyses, extracts were diluted in ultrapure water. All extracts were stored at -
225 23°C (\pm 3°C) until analysis.

226

227 2.3.3. Treatment of water samples before analysis

228

229 The relatively high concentrations of micropollutants in spiked tap water (i.e. around 3
230 $\mu\text{g/L}$) made it possible to analyze water samples by direct injection in the chromatographic
231 system after moderate dilution to obtain the adequate mobile phase mixture (i.e. $\text{H}_2\text{O}/\text{ACN}$
232 (99/1, v/v) for betablockers, $\text{H}_2\text{O}/\text{ACN}$ (60/40, v/v) for estrogens, and ultrapure water only for
233 multiresidue analyses) and after adding possible internal standards (metoprolol impurity A
234 and estradiol acetate at 50 $\mu\text{g/L}$ for betablocker and estrogen analyses, respectively). Water
235 samples were kept at -23°C ($\pm 3^\circ\text{C}$) until analysis.

236

237 2.3.4. LC-MS/MS analysis

238

239 The methods used for betablockers and estrogens are detailed elsewhere [19-20].
240 Briefly, chromatographic separation was performed with Xbridge C18 end-capped columns
241 (150 x 2.1 mm, 3.5 μm) equipped with guard columns. Vials were kept at 4°C during
242 analysis. Injected volumes were 10 μL . Column oven temperature was set at 28°C for
243 betablockers and 30°C for estrogens. Gradients with LC-MS-grade water (buffered with
244 ammonium formiate for betablockers) and acetonitrile were applied at a flow rate of 0.2
245 mL/min : from 1% ACN at 0 to 5 min ramped up to 100% ACN at 21 min until 29 min for
246 betablockers, and 40% ACN from 0 to 2 min ramped up to 80% ACN at 4.5 min until 7 min
247 and up to 100% ACN at 8.25 min until 15 min for estrogens. Separations were achieved in
248 less than 20 min and 12 min for betablockers and estrogens, respectively.

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

255

256 The multiresidue methods used for the 41 other micropollutants are detailed elsewhere
257 [21]. Briefly, the chromatographic column used for separation was a Kinetex XB-C18 Core
258 Shell (100 x 2.1mm, 1.7 μm) equipped with a KrudKatcher (0.2 μm) filter. Vials were kept at
259 ambient temperature until analysis and injection volumes were 100 μL . Column oven

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

264 The mass spectrometer source was an electrospray in positive mode for 29 molecules:
265 the UV filter, the hormones (other than estrogens), all the pesticides except 2,4-
266 dichlorophenoxyacetic acid and almost all pharmaceuticals except furosemide, ibuprofen and
267 salicylic acid. The source was in negative mode for 12 molecules: all alkylphenols and
268 phenols, 1 pesticide (2,4-dichlorophenoxyacetic acid) and 3 pharmaceuticals (furosemide,
269 ibuprofen and salicylic acid). Acquisitions were performed in scheduled MRM and MRM
270 mode for positive and negative modes, respectively. Two ionization transitions were used for
271 each analyte (except for linear alkylphenols and 2,4-dichlorophenoxyacetic acid for which
272 only one transition was possible) – one for quantification and one for confirmation. The
273 instrumental limits of quantification (direct injection) varied from 1 ng/L for carbendazim to
274 579 ng/L for 2,4-dichlorophenol.

275

276 2.4. Sampling rate calculation methods

277

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

283

$$284 \quad (1) \quad C_s = C_w \frac{k_u}{k_e} (1 - e^{-k_e t})$$

285

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

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

293 POCIS to its concentration in the sampling medium via the sampling rate, using equation (2)
294 [2]:

295
296 (2)
$$C_s = \frac{C_w R_s t}{M_s}$$

297
298 where R_s is the sampling rate (L/d), and M_s the mass of sorbent in the POCIS (g).

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

303
304 (3)
$$t_{1/2} = \frac{\ln 2}{k_e}$$

305
306 Rewriting equation (2), it is possible to tease out the concentration factor, as indicated in
307 equation (4):

308
309 (4)
$$CF = \frac{C_s}{C_w} = \frac{R_s t}{M_s}$$

310
311 where CF is the concentration factor (L/g). The concentration factor makes it possible to
312 neutralize the effect of C_w variations.

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

320

321 **3. Results and discussion**

322

323 *3.1. A reliable calibration system*

324

325 Additional parameters and flow velocities were followed and kept constant during the
326 42 days experiment duration, as reported in Table 1. Indeed, the RSDs for these parameters
327 never exceeded 27%. During the whole period of the calibration phase, temperature was
328 around 21°C, pH was around 7.6, conductivity was around 430 $\mu\text{S}/\text{cm}$, DOC was around 10
329 mg/L , and the flow velocities had a mean value of 11 cm/s .

330

331 Insert Table 1

332

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

335

336 Insert Figure 2

337

338 Out of the 56 molecules tested, 44 had a mean of spiked tap water concentration close to
339 the nominal value ($3 \pm 2 \mu\text{g}/\text{L}$). Among the 12 remaining molecules, 8 are known to degrade
340 in water under our renewal conditions (as proved in a previous experiment), which explains
341 why their concentrations were too low (i.e. n-octylphenol, n-nonylphenol, salicylic acid,
342 fenofibrate, iprodione, thiram with concentrations $< 1 \mu\text{g}/\text{L}$) or dispersed (i.e. tamoxifen: 5.1
343 $\pm 3.4 \mu\text{g}/\text{L}$). The eighth molecule, t-octylphenol, should also be degraded (according to the
344 degradation test) but in this experiment, its concentration was higher than expected (17.0
345 $\mu\text{g}/\text{L}$). Among the final 4 remaining molecules, 3 had higher mean concentrations than
346 expected (2,4-dichlorophenol: $7.1 \mu\text{g}/\text{L}$, ofloxacin: $8 \mu\text{g}/\text{L}$ and roxithromycin: $18.5 \mu\text{g}/\text{L}$) and
347 1 had a lower mean concentration than expected (resorcinol: $0.4 \mu\text{g}/\text{L}$). This may be due to
348 biodegradation process for resorcinol [22] and possible matrix effects in water concentrations
349 for t-octylphenol, 2,4-dichlorophenol, ofloxacin and roxithromycin. Either way, ruling out
350 molecules degraded in tap water and resorcinol due of its very low mean water concentration
351 ($0.4 \mu\text{g}/\text{L}$), the relative standard deviation (RSD) never exceeded 47% (t-butylphenol and
352 progesterone) and was lower than 35% for all the other molecules, which is very satisfying
353 considering the long 42-day duration of the calibration experiment.

354 R_s were not calculated for micropollutants with tap water concentrations far from the
355 nominal value (lower than $1 \mu\text{g}/\text{L}$ or higher than $5 \mu\text{g}/\text{L}$) or with high RSD (above 35%),
356 except for 2,4-dichlorophenol and t-octylphenol (water concentrations of $7.1 \mu\text{g}/\text{L}$ and 17.0
357 $\mu\text{g}/\text{L}$ respectively; detailed data shown in supplementary material), and for t-butylphenol,
358 progesterone, 4-methylbenzylidene camphor (random water concentration variations leading

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

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

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

370

371 3.2. *Accumulation kinetics*

372

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

377 We distinguished 4 different groups:

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

385 Given that the accumulation of micropollutants from groups 2, 3 and 4 diverged from
386 the theory, it was not possible to determine k_e and then $t_{1/2}$ with XLStat software. For group 2
387 molecules, we calculated R_s from the triplicate at day 14 and according to equation (4). Figure
388 3 illustrates the 4 different types of accumulation with two examples from each group.
389 Detailed accumulation curves for the 56 micropollutants can be found in the supplementary
390 material.

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

393

394 Insert Figure 3

395

396 Insert Table 2

397

398 3.2.1. Group 1: micropollutants with a curvilinear accumulation kinetics curve

399

400 There were 30 micropollutants presenting a curvilinear accumulation kinetics curve and
401 for which the POCIS can supply TWA concentrations as explained in equation (2). Group-1
402 micropollutants had $t_{1/2}$ from 5 to 693 days. They can be ionized or neutral, with log K_{ow} from
403 1.34 to 5.12. Their molecular weights vary from 150.1 to 376.7 g/mol.

404 POCIS are generally exposed in the field for 14 days [2, 4, 16]. According to table 2, we
405 found a $t_{1/2}$ higher than or equal to 14 days with neutral micropollutants (20 over 21) and
406 lower than 14 days for ionized micropollutants (8 of 9). Moreover, micropollutants with $t_{1/2} \geq$
407 14 days have a mean log K_{ow} of 3.5 (± 0.8) whereas molecules with $t_{1/2} < 14$ days have a mean
408 log K_{ow} of 2.3 (± 0.6). Molecular weight did not seem to have any influence on $t_{1/2}$ duration.
409 Indeed, molecules with $t_{1/2} \geq 14$ days have a mean molecular weight of 272 g/mol (± 52) while
410 molecules with $t_{1/2} < 14$ days have a mean molecular weight of 267 g/mol (± 68).

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

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

424 PES membranes [21]. These effects had no impact on calculated R_s (except for 2,4-
425 dichlorophenol where R_s is possibly underestimated) since $t_{1/2}$ micropollutants were 11 to
426 2772 times higher than the lag time duration for t-octylphenol and progesterone, respectively.
427

428 3.2.2. Group 2: micropollutants with an inflexion point

429
430 This group encompassed 13 micropollutants based on their higher accumulation rate in
431 the POCIS during the first week of exposure leading to an inflexion point (generally at day
432 14) and their coefficients determined as lower than 0.99 compared to the curvilinear model
433 (e.g. ketoprofen, figure 3.d. with $R^2=0.98$). For these compounds, XLStat software
434 miscalculated $t_{1/2}$ since the model was not curvilinear over 28 days. We thus recalculated R_s
435 with POCIS immersed at day 14. We assumed that these R_s were as accurate as those of group
436 1, since there was an integrative phase after the inflexion point. As was the case for group 1,
437 POCIS can produce TWA concentrations for these micropollutants.

438 Group-2 micropollutants are generally in ionic form (9 out of 13; Table 2) in a log K_{ow}
439 range of between -0.40 and 3.99. Neutral molecules are relatively polar ($\log K_{ow} \leq 2.67$). The
440 higher accumulation rate up to 7 days may be explained by a burst effect [1, 10]. This
441 phenomenon is due to the time delay required for complete wetting of the POCIS membranes
442 and can be avoided by pre-wetting the POCIS before immersion. These molecules might also
443 accumulate in POCIS following two different sorption mechanisms, e.g. adsorption and then
444 partitioning, or a multi-layer adsorption mirroring gas adsorption on a solid: a first layer
445 directly on the sorbent and a second layer over the first layer [23].
446

447 3.2.3. Group 3: micropollutants with random accumulation kinetics curves

448
449 The 8 micropollutants forming group 3 were characterized by a random accumulation in
450 the POCIS receiving phase with a concentration factor higher than 3. For these
451 micropollutants, POCIS could not supply reliable TWA concentrations but can be used for
452 screening. We supposed that this type of accumulation is not due to degradation in HLB phase
453 because tests proved that pesticides (acetochlor, alachlor, atrazine, diuron, linuron, 2,4-
454 dichlorophenoxyacetic acid), pharmaceuticals (atenolol, carbamazepin, diclofenac, ibuprofen,
455 ketoprofen, metoprolol, naproxen, propranolol, sulfamethoxazole, trimethoprim) and

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

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

460 These unpredictable accumulations make it impossible to reliably determine $t_{1/2}$. For all
461 group-3 micropollutants, the RSDs of tap water concentrations were higher than 30%, and 5
462 molecules (iprodione, t-nonylphenol, salicylic acid, thiram, fenofibrate) are known (from
463 previous experiments) to degrade in tap water under our renewal conditions (degradation time
464 50 [DT50]: iprodione < 3 d; thiram < 3.5 d; salA < 6 h; feno < 6 h), which may explain some
465 of the random accumulation curves.

466

467 3.2.4. Group 4: micropollutants with low or no accumulation kinetics curve

468

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

471 As with group 3, these micropollutants can be polar or apolar (log K_{ow} from -0.46 to
472 6.35), and neutral or ionized in tap water at pH=7.6.

473 Four of these 5 micropollutants, RSDs of tap water concentrations were higher than
474 30%, and three (n-octylphenol, n-nonylphenol and tamoxifen, DT50 < 3 h) are known to
475 degrade in tap water under our renewal conditions, which may explain their very low or no
476 accumulation rates.

477

478 3.2.5. Accumulation kinetics compared against the literature

479

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

486

487 Insert Table 3

488

489 The 17 group-1 micropollutants studied in the literature always showed linear
490 accumulation, thus confirming our findings. Nevertheless, some of these micropollutants were
491 exposed for only 8 days (t-butylphenol, metoprolol, propranolol and linuron) and their
492 accumulations were drawn with only 4 samples, which is not enough to correctly estimate the
493 $t_{1/2}$. It is important to have a lot of datapoints, especially at the beginning of the calibration, to
494 be able to refine the line of the kinetics accumulation. MacLeod *et al.* [7], Harman *et al.* [13]
495 and Martinez-Bueno *et al.* [16] reported nonlinear accumulation curves for a few
496 micropollutants (from groups 2, 3 and 4, and including antibiotics and some alkylphenols) but
497 did not discuss potential explanations for these atypical accumulation patterns nor the
498 consequence on R_s calculation. Finally, contrary to our results, MacLeod *et al.* [7], Li *et al.*
499 [14] and Bartelt-Hunt *et al.* [11] all found linear kinetic accumulations for anti-inflammatories
500 and betablockers. This divergence may be explained by their different calculation methods
501 (measuring decreasing concentrations in water instead of increasing concentrations in POCIS)
502 and calibration systems (beaker or bottle and distilled water).

503

504 3.3. Sampling rates (R_s)

505

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

513

514 We compiled calculated R_s in Table 4 and compared them against R_s values reported in
515 the literature when obtained with the same kind of POCIS (“pharmaceutical” POCIS with
516 45.8 cm² surface and 200 mg of receiving phase) and in the same conditions (under agitation
517 and at between 15 and 25°C). Sampling rates varied from 0.025 L/d for atenolol up to 0.398
518 for t-butylphenol. Our study produced 16 laboratory R_s now published for the first time here.

518

519 Insert Table 4

520

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

530 Compared to the R_s from authors using the same kind of calibration system (i.e. aquaria
531 with a flow velocity arriving directly at the front of the POCIS; Mazzella *et al.* [10] and
532 Lissalde *et al.* [15]), our R_s values are generally less than 2-fold different. Our R_s were also
533 close (i.e. less than 2 fold-different) to reported values for hydrophobic molecules ($\log K_{ow} >$
534 2.65), except Li *et al.* [14] who obtained significantly higher R_s than ours (or than those
535 reported in the literature), including up to 11-fold higher values for sulfamethoxazole. As
536 stated earlier, this can be explained by the different calculation method and calibration system
537 used, which further underlines the critical need to define standardized protocols to obtain
538 comparable sampling rates [6].

539

540 3.4. *Is it possible to predict R_s from micropollutant physical-chemical* 541 *properties?*

542

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

548

549 Insert Figure 4

550

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

554 3.5-4.5) families. The range of R_s can be predicted as a function of log D for some but not all
555 micropollutants, which suggests that other physical-chemical properties also need to be
556 considered.

557

558 **4. Conclusion**

559

560 We report a calibration experiment that is reliable and robust in terms of constant values
561 for micropollutant concentrations in tap water, flow velocities and additional parameters
562 (temperature, pH, conductivity, dissolved organic carbon concentration). This system allowed
563 us to study the accumulation of 56 organic micropollutants using the “pharmaceutical” POCIS
564 for up to 28-day exposure periods. We distinguished 4 different types of accumulation curves:
565 curvilinear (group 1), with inflexion point (group 2), random (group 3), and no or low
566 accumulation (group 4). It was possible to calculate well-defined R_s for 43 micropollutants, of
567 which 16 are new R_s published here for the first time. R_s for these 43 micropollutants varied
568 from 0.025 to 0.398 L/d. Nevertheless, the sampling rates of 2,4-dichlorophenol and t-
569 octylphenol have to be validated because of suspected matrix effects in tap water for both
570 micropollutants and high lag time (3 days) coupled to short kinetic regime ($t_{1/2} = 5$ days) for
571 2,4-dichlorophenol.

572 The POCIS is particularly suitable for sampling neutral micropollutants (included in
573 group 1) with log K_{ow} ranging from 2.5 to 5, such as hormones, pesticides or several
574 pharmaceuticals. Indeed, the kinetic regime for this type of molecule is higher than or equal to
575 14 days, which is suitable for *in situ* application of POCIS to evaluate TWA water
576 concentrations. POCIS can also produce TWA concentrations for more hydrophilic (with log
577 K_{ow} as low as -0.34) and ionized micropollutants such as antibiotics, anti-inflammatories and
578 betablockers (included in groups 1 and 2). However, POCIS is only suitable for screening for
579 micropollutants with random accumulation (e.g. thiram, roxithromycin, group 3), and is not at
580 all suitable for micropollutants with very low or no accumulation (e.g. metronidazole,
581 tamoxifen, group 4).

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

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

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

591

592

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594

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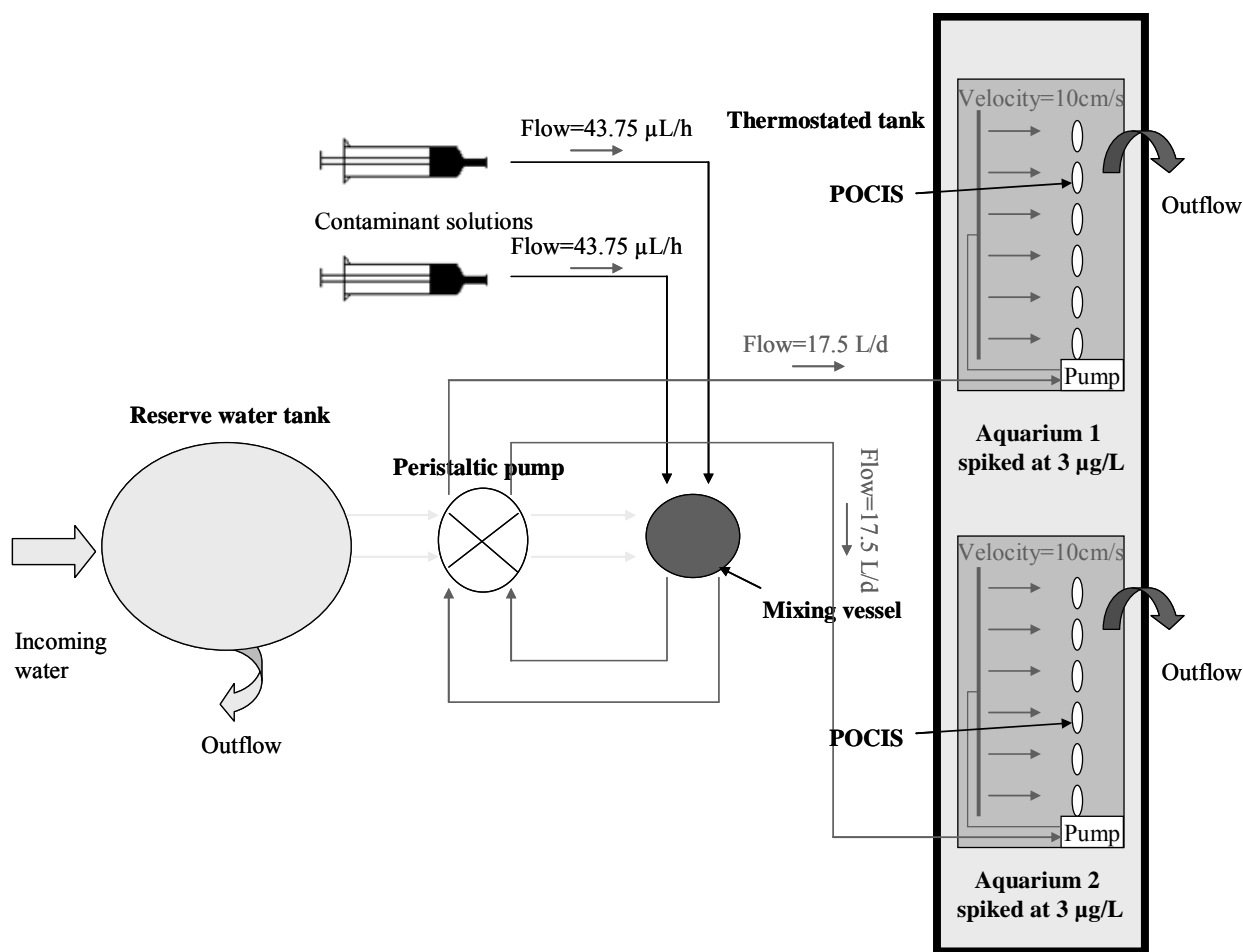
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656



657

658

659

660

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

661 **Table 1**

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

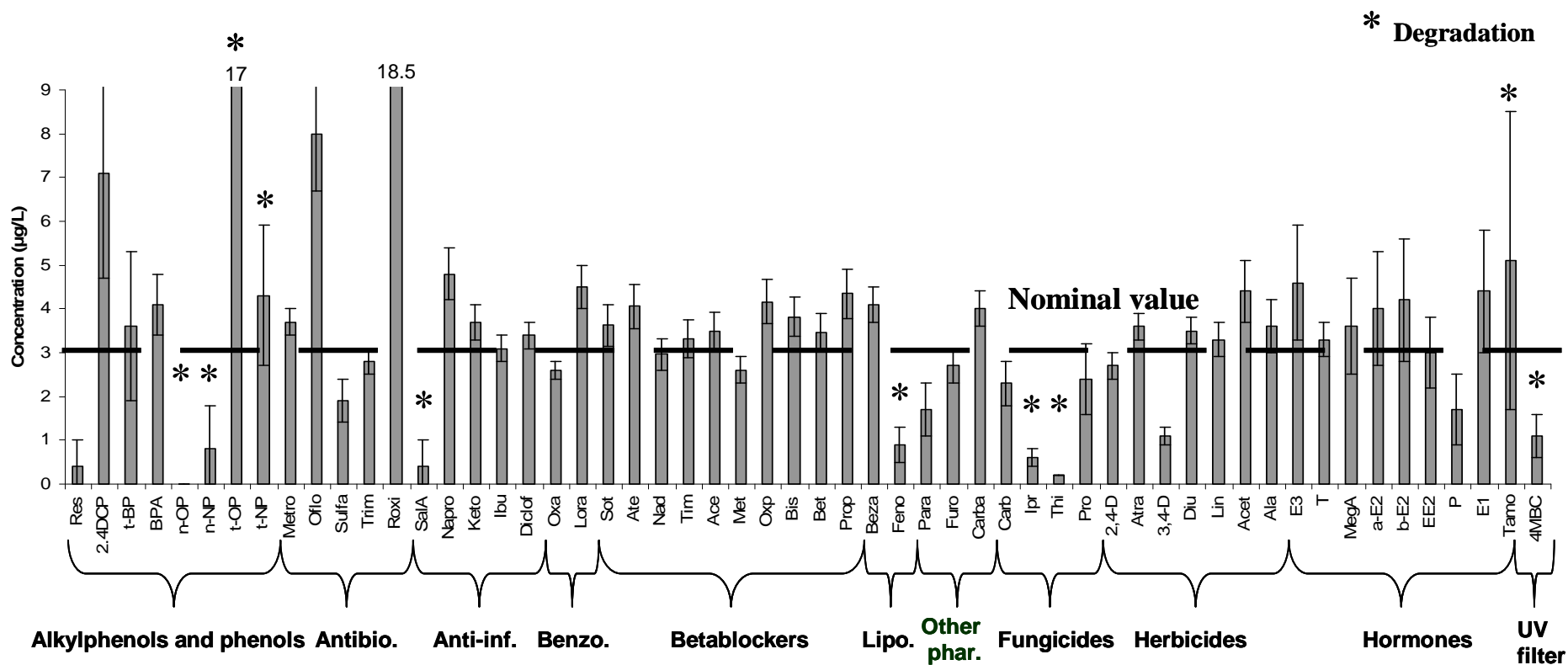
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	Temperature (°C) (n=12)	pH (n=14)	Conductivity ($\mu\text{s}/\text{cm}$) (n=14)	DOC (mg/L) (n=12)	Flow velocity (cm/s) (n=63)
Mean	20.7	7.6	429	10.1	11
RSD (%)	3	6	1	17	23

665

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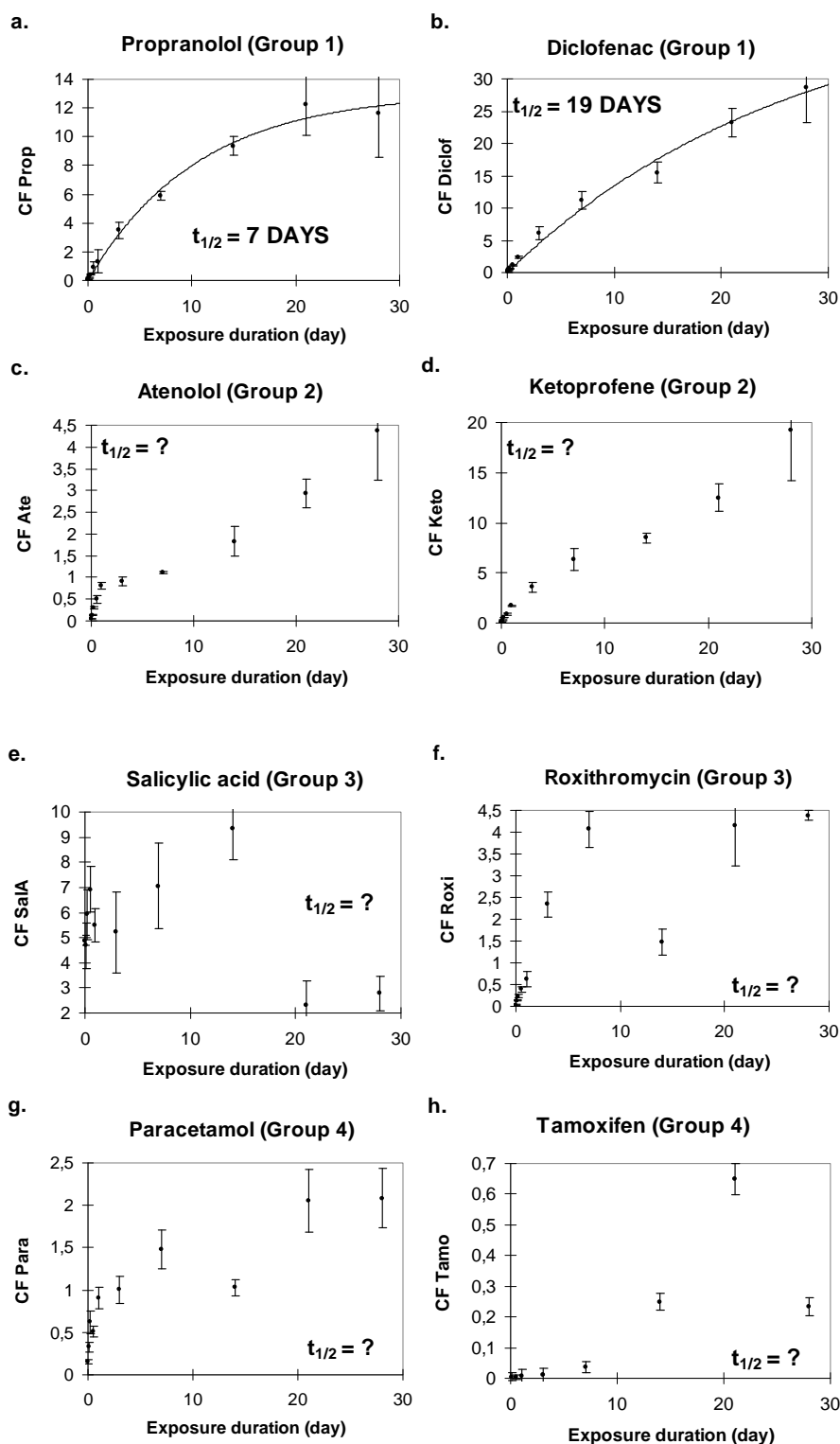
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668

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

672



673

674

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

679

680 **Table 2**

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

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

	4-MBC*	693	5.12	NA	NA	Neutral	254.4
2 (accumulation with an inflexion point)	Sot	?	-0.40	-2.24	9.43	+	272.4
	Ate	?	0.43	-1.64	9.67	+	266.3
	Sulfa	?	0.79	0.52	7.66	Neutral	253.3
	Nad	?	0.87	-1.29	9.76	+	309.4
	Trim	?	1.28	1.15	7.16	Neutral	290.3
	Furo	?	1.75	-1.60	4.25	-	330.7
	Carb	?	1.80	1.80	4.28 and 9.70	Neutral	191.2
	2.4-D acid	?	2.50	-2.29	2.96	-	184.1
	E3	?	2.67	2.67	10.33	Neutral	288.4
	Napro	?	2.99	-0.42	4.19	-	230.3
	Keto	?	3.61	-0.11	3.88	-	254.3
	Ibu	?	3.84	1.09	4.85	-	206.3
	Beza	?	3.99	0.22	3.83	-	361.8
3 (random accumulation)	Oflo	?	0.65	-1.50	5.45 and 6.20	-	361.4
	Res	?	1.37	1.37	9.26 and 10.73	Neutral	110.1
	Sala	?	1.98	-2.83	2.79 and 13.23	-	138.1
	Ipr*	?	2.29	2.29	12.69 and 13.63	Neutral	330.2
	Thi	?	2.73	2.73	/	Neutral	240.4
	Roxi	?	3.00	1.51	2.29 and 9.08	+	837.0
	Feno*	?	5.28	5.28	/	Neutral	360.8
	t-NP	?	5.44	5.44	/	Neutral	220.4
4 (low or no accumulation)	Metro	?	-0.46	-0.46	3,09	Neutral	171.2
	Para	?	0.91	0.91	9.46	Neutral	151.2
	4-n-OP	?	5.30	5.30	10.31	Neutral	206.3
	4-n-NP	?	5.74	5.74	10.31	Neutral	220.4
	Tamo	?	6.35	5.16	8.76	+	371.5

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

684 *: Micropollutant with lag time

685 **Table 3**

686 Comparison of kinetic accumulation curves for “pharmaceutical” POCIS.

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

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

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

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

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

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

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

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

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

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

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

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

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

709 **Table 4**

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

Molecule (group)	Family	Log K_{ow}	R_s (L/d)	R_s from literature (L/d)	Difference (%)	Reference
Res (3)		1.37	a	b		
2,4-DCP (1)		2.88	0.068 (± 0.005)	b		
t-BP (1)	Alkylphenols and phenols	3.21	0.398 (± 0.044)	0.120	-70	[27]
BPA (1)		4.04	0.245 (± 0.006)	0.117 (± 0.019)	-57	[13]
t-OP (1)		4.69	0.065 (± 0.005)	0.835 (± 0.058)	-52	[8]
t-NP (3)		5.44	a	0.1204 (± 0.0110)	240	[14]
n-OP (4)		5.35	a	0.010 (± 0.008)	85	[8]
n-NP (4)		5.74	a	0.117 (± 0.012)		[8]
				2.459 (± 0.131)		[14]
Metro (4)	Antibiotics	-0.46	a	b		
Oflo (3)		0.65	a	b		
Sulfa (2)		0.79	0.030 (± 0.003)	0.339 (± 0.057)	1015	[14]
Trim (2)		1.28	0.162 (± 0.014)	0.118 (± 0.012)	288	[11]
Roxi (3)		3.00	a	0.436 (± 0.006)	169	[14]
				0.360 (± 0.210)	122	[7]
Sala (3)	Anti-inflammatories	1.98	a	b		
Napro (2)		2.99	0.084 (± 0.011)	0.723 (± 0.430)		[7]
Keto (2)		3.61	0.118 (± 0.007)	0.392 (± 0.024)	368	[14]
Ibu (2)		3.84	0.118 (± 0.006)	0.116 (± 0.053)	38	[7]
Diclof (1)		4.26	0.225 (± 0.009)	0.135 (± 0.035)	11	[7]
				0.348 (± 0.052)	181	[14]
			0.400 (± 0.008)	223	[11]	
Oxa (1)	Benzodiazepines	2.92	0.226 (± 0.009)	0.166 (± 0.052)	-26	[7]
Lora (1)		3.53	0.205 (± 0.006)	0.170	-24	[26]
Sot (2)	Betablockers	-0.40	0.036 (± 0.008)	b		
Ate (2)		0.43	0.025 (± 0.005)	0.151 (± 0.021)	386	[14]
Nad (2)		0.87	0.114 (± 0.009)	0.094 (± 0.015)	331	[14]
Tim (1)		1.34	0.210 (± 0.012)	0.040 (± 0.070)	84	[7]
Ace (1)		1.53	0.166 (± 0.008)	0.447 (± 0.036)	299	[14]
Met (1)		1.76	0.195 (± 0.012)	b		
			0.465 (± 0.039)	138	[14]	
			0.599 (± 0.270)	206	[7]	

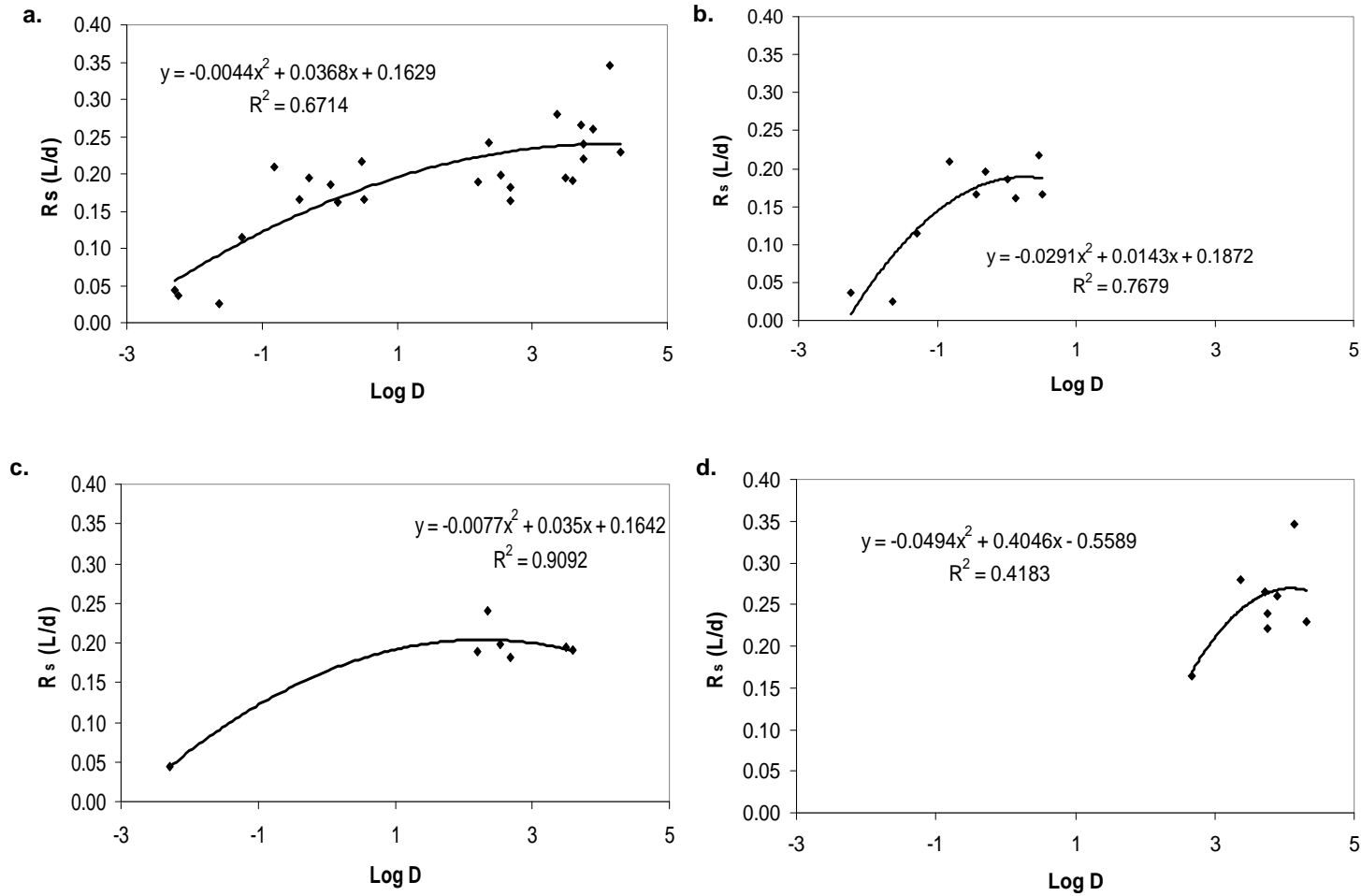
Oxp (1)		2.17	0.185 (± 0.010)	b		
Bis (1)		2.20	0.161 (± 0.008)	b		
Bet (1)		2.54	0.217 (± 0.010)	b		
Prop (1)		2.58	0.165 (± 0.009)	0.917 (± 0.084)	455	[14]
				0.980 (± 0.345)	493	[7]
Beza (2)	Lipopenics	3.99	0.146 (± 0.034)	b		
Feno (3)		5.28	a	b		
Para (4)		0.91	a	0.020	80	[26]
Furo (2)	Other pharmaceuticals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

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

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

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

717



718

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

720