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SPATIAL DISTRIBUTION OF PHARMACEUTICALS WITHIN THE PARTICULATE PHASES OF A PERI-URBAN STREAM

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Abstract

Pharmaceutical products (PPs) are consumed worldwide and are continuously released into hydrological environments, but are not efficiently removed by sewage treatment plants. Their occurrence within the dissolved phase has been extensively studied, but only a few articles concern solid matrices. The mechanisms and extent of sorption depend on the properties of both the molecules (degradability, charge, hydrophobicity) and the matrices (clay content, organic matter content), making the spatio-temporal distribution of PPs in natural environments complex and poorly elucidated. To improve our understanding of PP distribution at a catchment scale, this study investigated different groups of molecules with varying solubility and charges, in water, suspended particulate matter, bed-load and pond sediments. The Egoutier stream, which collects the sewage effluents from two health institutions sewage effluents, is a good candidate for this investigation. Results indicate that PP occurrences in the different particulate compartments were mainly regulated by their wastewater occurrences and charges. Particulate phases all along the Egoutier stream were characterized by a limited clay content (i.e. less than 1%) and significant organic carbon content (i.e. between 0.3% and 18.0%) favouring non-specific adsorption. Therefore, neutral PPs, exhibiting higher discharge rates, persistence and hydrophobicities in comparison with cationic and anionic molecules, were the most abundant PPs in the particulate phases of this catchment. In bed-load sediments, global PP spatial distributions reflected discharge sites and sedimentary accumulation zones, mostly that of organic matter. Spatial distributions of the more hydrophobic and persistent PP in the particulate phases thus followed the stream sedimentary dynamic.

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I. Introduction

Environmental and societal concerns about the occurrence of pharmaceutical products (PPs) within aquatic systems started in the 1970s (Hignite & Azarnoff, 1977). These molecules are consumed worldwide (Jjemba, 2006; Gracia-Lor et al., 2010) and are continuously released into the environment (Loos et al., 2009) as chemical cocktails (Petrie et al., 2015; Kaushal et al., 2020). PPs can be bioaccumulated in aquatic organisms and transferred to the food chain (Sumpter et al., 1996), with negative effects on animal and human health (Gracia-Lor et al., 2010). Research efforts have therefore increased since the 1990s (Hughes et al., 2013) and PPs were qualified as an emerging class of contaminants (Boreen et al., 2003; Da Silva et al., 2011). The long-term ecotoxicological effects of these micropollutants remain unclear (Gracia-Lor et al., 2010) and thus represent a major environmental and societal issue. Understanding PP dynamics in hydrosystems is therefore needed in order to manage environmental contamination (Dobor et al., 2012; Petrie et al., 2015; Thiebault, 2020; Boulard et al., 2020).

In the European Union, about 3,000 PPs are approved for medical treatment (Da Silva et al., 2011), among which psychotropics (Calisto & Esteves, 2009), anti-inflammatory agents, β-blockers (Petrie et al., 2015) and analgesics (Verlicchi et al., 2010) are the most frequently prescribed. France has a high drug consumption; for example, in 2018 average spending per inhabitant amounted to 488 € (Leem, 2020). High releases are therefore observed in freshwater aquatic environments (Fekadu et al., 2019), but only a few studies have been conducted on French rivers (Tamtam et al., 2008; Munoz, 2009; Hughes et al., 2013). These studies evidenced the presence of PPs in both small and large basins comprising urban areas (Feitosa-Felizzola & Chiron, 2009; Mompelat et al., 2011).

Significant proportions of the consumed PPs can be excreted in an unchanged form (Baranowska & Kowalski, 2010), and therefore transferred toward wastewater treatment plants (WWTP). The presence of PPs in hydrosystems is then the consequence of the incomplete removal of PPs in domestic and hospital sewage in WWTPs (Kümmerer, 2009). These micropollutants are subject to

degradation, dilution and sorption processes but can be transported over long distances (Tamtam et al., 2008; Aminot et al., 2015). PPs are considered to be less persistent than other types of organic contaminants (such as polycyclic aromatic hydrocarbons and polychlorinated biphenyls), as they have fewer interactions with particulate phases because of their lower hydrophobicity (Svahn & Björklund, 2015; Boulard et al., 2020) and are thus less likely to be transported through sediment transport (Loos et al., 2009). This pathway is consequently often neglected, but some PPs also display significant affinities with solid organic and mineral matrices (Löffler et al., 2005; Vazquez-Roig et al., 2010; Da Silva et al., 2011; Martínez-Hernández et al., 2014; Koba et al., 2018).

In recent decades, analytical procedures that assist in distinguishing and quantifying PPs in solid matrices have been developed especially through pressurized liquid extraction (PLE, Jelić et al., 2009) followed by ultra-high performance liquid chromatography in combination with tandem mass spectrometry (UHPLC-MS^2, Gracia-Lor et al., 2010). Studies evaluating PP distribution in sediments provide useful information as they may integrate larger time scales than the dissolved ones (Zhou & Broodbank, 2014). Moreover, as the fate of PPs mainly depends on their partitioning between dissolved and particulate phases, an understanding of the sorption processes is required (Martínez-Hernández et al., 2014). Several studies conducted through batch experiments therefore evaluated the type of interactions involved in PP adsorption (Yamamoto et al., 2009), the difference in molecules' mobility (Scheytt et al., 2005), the role of solid matrix composition and the potential desorption of PPs (Stein et al., 2008). Predicting the behaviour of PPs is complex because of the variety of processes and parameters involved in their adsorption (Al-Khazrajy & Boxall, 2016) but partitioning is mainly driven by both PP (structure, charge, hydrophobicity, persistence) and particle characteristics (composition, texture; Vazquez-Roig et al., 2012; Martínez-Hernández et al., 2014; Thiebault et al., 2016).

The spatio-temporal evolution of PPs certainly depends on sources, consumption and discharge rates (Petrie et al., 2015; Wilkinson et al., 2017). In particulate phases, this evolution is also driven by

particle composition and texture as well as by the physico-chemical and hydrological conditions of the hydrosystem (Kim & Carlson, 2007; De Castro-Català et al., 2016). Consequently, PPs may show high spatial variabilities between different aquatic environments. Wastewaters from medical institutions display higher emissions than domestic ones (Kümmerer, 2009; Verlicchi et al., 2010; Huber et al., 2016) and small hydrosystems are more sensitive to these contaminations because of a lower dilution of anthropogenic inputs (Da Silva et al., 2011). At a basin scale, different spatial evolutions have already been observed. Schultz et al. (2010) measured increasing concentrations downstream of the WWTP effluent whereas Aminot et al. (2015) measured the highest accumulation near sewage discharging sites, where sediments presented a high organic carbon content. The same observations were made by Da Silva et al. (2011) and Zhou and Broodbank (2014), but variabilities according to streamflow conditions were also recorded. At the Loire Bretagne basin scale, Amalric et al. (2011) correlated observed contents with urban pressure levels. Because of the complexity of these influencing factors, the spatio-temporal evolution of PPs in solid matrices is rarely investigated (Fairbairn et al., 2015), especially when it comes to integrating different compartments of the aquatic environment (Wilkinson et al., 2017).

In this context, the present study attempts to provide new insights into PP occurrences within particulate phases of a small peri-urban stream as these sites are often neglected while represent hotspots of contamination. Their occurrences were also used to study the spatio-temporal accumulation and/or transportation of this kind of contaminants at catchment scale, in both suspended particulate matter and sediments (bed-load and pond sediments). The catchment of the peri-urban Egoutier stream, a tributary of the Loire River, which collects the wastewaters from two medical institutions, was chosen as the study site. These point sources represent a good opportunity to improve our understanding of PPs spatio-temporal distribution as well as the impact of these effluents on stream quality.

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106 10 PPs were investigated, based on their consumption in the European Union (e.g. psychotropics,
107 anti-inflammatory agents, β-blockers and analgesics; Calisto & Esteves, 2009; Verlicchi et al., 2010;
108 Petrie et al., 2015) as well as their detection frequency in aquatic environments (e.g. anticonvulsants
109 and opioids; Clara et al., 2004; Campos-Mañas et al., 2018). The occurrence of these PPs was
110 investigated in the particulate phases at the catchment scale and in the dissolved phase of WWTP
111 effluents. Environmental physico-chemical conditions, composition and textures of solid matrices
112 were also characterized. Lastly, based on the analysis of PPs emissions and properties (persistence,
113 charge state and lipophilicity), different factors driving the accumulation and spatial distribution of
114 the molecules were identified.

115

116 **II. Material and Methods**

117 1. Study site and sampling method

118 The Egoutier catchment is located east of Orléans, in the Loire River basin (Fig. 1). Characterized by a
119 temperate climate with an average annual rainfall of 650 mm (Soucémarianadin & Verbèque, 2007),
120 this small lowland catchment (27 km²) is drained by the Egoutier stream. The mean slope gradient is
121 0.5% and the geological substrate is composed of Sologne sands and clays, Orleanais sands and
122 Beauce limestone from upstream to downstream (Berger & Desprez, 1969).

123 To study the spatial evolution of PPs following a source-to-sink logic, the area investigated in
124 this work was restricted to the upstream part of the catchment, covering 8 km² and including the
125 Beulie pond in its central part (Fig. 1). In this part, the catchment is composed by solely of
126 hydromorphic soils with clay-rich subsoil layers (Soucémarianadin & Verbèque, 2007). The Egoutier
127 stream is thus supplied by stormwater runoff, but also by effluents from two WWTPs and two
128 stormwater point sources from urban areas. The two WWTPs treat effluents from a central army
129 pharmacy (CAP) and a psychiatric hospital (PH, Fig. 1), respectively. CAP effluents are continuously
130 discharged at a flow rate of 7 m^3/h, whereas PH effluents, with a treatment capacity of 400 beds, are

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not continuous and not monitored. Urban storm waters come from runoff processes on both CAP surfaces and urban areas in the eastern part of the catchment. The latter are collected in a network and released into a tributary of the stream (BLS-13b, Fig. 1).

[Figure 1]

Figure 1 : Description of the upstream part of the Egoutier catchment area studied here with land covers (Inglada et al., 2017). Locations of the two sewage water effluents from the central army pharmacy (CAP) and the psychiatric hospital (PH) and of the samples collected in the dissolved phase (W), in suspended particulate matter (SPM), bed-load (BLS) and Beulie pond sediments (EG).

In order to observe PP transportation by suspended particulate matter (SPM) at the catchment scale, SPM (grey dots, Fig. 1) were sampled at three locations. The first samples were taken downstream the CAP WWTP effluent (SPM-1, Fig. 1) to characterize the SPM geochemical fingerprint of this medical institution. The second samples were collected downstream the Beulie pond (SPM-2, Fig. 1) to integrate the PH fingerprint and quantify PP transportation despite the strong accumulation zone constituted by the pond. Finally, the third samples were taken at the outlet of the catchment (SPM-3, Fig. 1) to measure the total export of PPs. To collect enough material, SPM were collected by using GEACOS (GranulomEtric pAssive Capture of dissolved matter & Sediment, Simonneau et al., 2020) placed in the watercourse during about two months. Four campaigns were realized: between November 2018 and January 2019; March and June 2019; June and August 2019; and August and October 2019 (Table S1).

In 2018 and 2019, 15 bed-load sediment samples (BLS, brown dots, Fig. 1) were collected all along the watercourse to assess the PPs' spatial distribution and the impact level of WWTP effluents. BLS were sampled at each storm- and sewage water discharge, and upstream to downstream depending on confluence and accumulation zones, during both winters and summers (April 2018 and 2019; August 2018 and 2019, Table S1), using 50 mL polypropylene Falcon tubes. Because of some dry areas during summer, some replicates were not always sampled in summer (Table S1).

Three Beulie pond interface sediments (water/sediment limit) were also collected in April 2018, along a north-south transect using an Ekman Grab (EG, green dots, Fig. 1). All solid samples were then split into two parts; one was stored wet at 5 °C and the other was dried at 50 °C during 48 h.

Finally, two water samples (W, water drops, Fig. 1) were collected at each WWTP discharge to verify the consistency of the PPs detected in solid matrices. The PH effluent (W-PH, Fig. 1) was collected in April 2017 and the CAP effluent (W-CAP, Fig. 1) in August 2018 (Table S1), using 10 L polyethylene bottles that were stored at 5 °C before analysis.

2. Environmental parameters and sample characteristics

Stream pH conditions were measured during each BLS sampling campaign. This parameter was determined with a portable pH meter MultiLine Multi 3630 IDS.

Particle size distributions for SPM samples were already given by the GEACOS technology (Simonneau et al., 2020). They were quantified by drying each GEACOS sieve from 1 mm to 250, 60, 20 and 5 µm. The grain sizes of all the other sediment samples (moistened fractions sieved under 1.8 mm) were determined using a laser particle sizer Mastersizer 3000 (Malvern) at the GEHCO laboratory. Results obtained are the relative percentages of four grain-size classes: 0 - 2 µm for clay grain sizes, 2 - 63 µm for silt grain sizes, 63 - 250 µm for fine sand grain sizes and 250 – 1800 µm for medium to coarse sand grain sizes.

Total organic carbon (TOC) contents were estimated by Rock-Eval pyrolysis (Behar et al., 2001) using a Rock Eval 6 turbo at the ISTO laboratory. Standards provided by Vinci Technologies were used to check the reproducibility of the measures. The mean error and mean correction factor of TOC measurements were 0.14% and 1%, respectively.

Finally, the bulk mineralogy of four samples (three BLS samples from the first campaign in 2018 and one EG sample) was analysed by X-Ray Diffraction spectrometry (XRD) at the ISTO

laboratory with an INEL diffractometer adjusted with a Debye-Scherrer configuration. ICDD (International Centre for Diffraction Data) PDF (Powder Diffraction File) characteristic diagrams were used to identify the minerals (Fig. S1).

3. Pharmaceutical contents

3.1. Chemical reagents

Standards for acetaminophen (ACM), atenolol (ATE), carbamazepine (CBZ), codeine (COD), diazepam (DIA), diclofenac (DIC), oxazepam (OXA), salicylic acid (SCA), tramadol (TRA) and trimethoprim (TRI) were purchased from Sigma-Aldrich with a purity >98%. The solvents used for PP extraction and separation, methanol (MeOH), acetonitrile (AcN) and formic acid (HCOOH), were purchased from Fisher-Scientific, assuming an analytical grade (purity up to 99.95%).

3.2. Extraction procedure

Extraction procedures were carried out at the ISTO laboratory. For water samples solid phase extraction (SPE) using a Chromabond HR-X cartridge (6 mL x 500 mg, Macherey-Nagel) was performed. The cartridge was conditioned with 5 mL of MeOH and 5 mL of ultra-pure water (H_2O). The cartridge was then filled with 250 mL of sample before being washed with 5 mL of H_2O and dried for 30 minutes. The analytes were finally eluted with 3 x 5 mL of MeOH. Complementarily, between 1 and 7 g of bulk sediments, depending on their composition, were extracted by pressurized liquid extraction (PLE) using an ASE-200 (Dionex, 100 °C and 1000 psi) and a mixture of MeOH/ H_2O (1:1, v/v). For both methods, eluates were then dried under nitrogen flow and reconstituted in 3 mL of H_2O. Solutions were filtered with a glass-fiber filter (GF/F, Whatman) prior to being stored at 5 °C before analysis. The recovery ratios of the investigated PPs (Table 1) during SPE and ASE were taken as those presented in Thiebault et al. (2017a, b), using the same protocol (Table S2).

Table 1 : For each therapeutic molecule, abbreviation (Abb.), CAS-Number, formula, molecular weight (MW), charge state at pH = 7 (Charge), pKa, solubility and logD are specified. [a]: https://pubchem.ncbi.nlm.nih.gov; [b]: www.drugbank.ca, [c]: www.chemspider.com.

[Table 1]

3.3. Quantification procedure

Chromatographic separation was performed using an Ultimate 3000 RSLC (Rapid Separation Liquid Chromatography, Thermo Fisher Scientific) equipped with a Nucleodur C_{18} Gravity Column (150 mm x 2 mm; 3 µm, Macherey-Nagel) at the ICOA laboratory. Separation was carried out at 30 °C with two mobile phases: H_2O (solvent A) and AcN (solvent B), both acidified with 0.1% of HCOOH. The total analysis time was 29 min with the elution gradient as follows: 95% to 5% of solvent A during 16 min, then 100% of B during 3 min, followed by a return to initial conditions (95% of A) during 10 min. The mass spectrometer was a TSQ Endura triple quadrupole equipment fitted with a heated electrospray ionization (H-ESI) interface (Thermo Fisher Scientific). The analytical performances of this method were developed in Thiebault et al. (2017a). For this work, only results with a signal-to-noise ratio higher than the limit of quantification (S/N > 10, Gracia-Lor et al., 2010; LOQ, Table S2) were used for interpretation. The sample analysis was systematically validated by a quality procedure comprising a calibration curve (6 standards), triplicates of 4 samples followed by one standard control and one blank (pure water), and a final calibration curve. For each PP, the identification parameters and quantification accuracy are detailed in Table S2. To ensure reproducibility of the quantification, mean variation coefficients were calculated by analysing triplicates of the standard solutions (Table S2).

III. Results and discussion

1. PPs occurrence and accumulation in the particulate phases

Among the 10 PPs investigated in the dissolved phase, 5 were quantified in W-CAP, whereas all the 10 were quantified in W-PH. The PP diversity found in W-PH was therefore greater than in W-CAP, as were the PP concentrations (Fig. S2). In the W-CAP sample, SCA was the most abundant PP,

exhibiting a concentration of 2170 ng.L^{-1}. TRI and CBZ exhibited medium contents with 290 and 120 ng.L^{-1}, respectively, and OXA and DIC were the least abundant with concentrations reaching 20 ng.L^{-1} (Fig. S2). In the W-PH sample, TRA and ACM exhibited the highest concentrations, with 7.97 and 6.33 µg.L^{-1}, respectively (Fig. S2) and DIC, DIA and TRI were the least concentrated PPs, with 70, 80 and 10 ng.L^{-1}, respectively (Fig. S2).

The 10 PPs were also quantified at least once in the particulate phases. Quantified in two solid samples, TRA was the least frequently detected but also the most concentrated PP, ranging from 41.9 to 5811.9 ng.g^{-1} (Fig. 2 and Table S4). Nevertheless, this high concentration appears surprising and should be considered with caution in view of the mean variations in its standard solutions (Table S2). ATE and COD exhibited low occurrences and concentrations in solid matrices, ranging from the limit of detection to 6.6 and 20.3 ng.g^{-1}, respectively (Fig. 2 and Table S4). DIC and ACM were more frequently detected but their concentrations did not exceed 6.7 and 16.9 ng.g^{-1}, respectively (Fig. 2 and Table S4). With high abundance and medium to high contents, TRI, DIA and OXA ranged from the limit of detection to 27.5, 39.6 and 141.4 ng.g^{-1}, respectively (Fig. 2 and Table S4). CBZ and SCA were detected ubiquitously in the particulate phases, ranging from the limit of detection to 130.5 and 176.2 ng.g^{-1}, respectively (Fig. 2 and Table S4).

The different PPs presented various occurrences and accumulation rates depending on their sensitivity to degradation processes, their solubility and their discharge rates. Consistently with its high degradability (Table 2) and solubility (Table 1), ACM exhibited low concentrations and was seldom detected (Fig. 2 and Table S4). Conversely, the low solubility of DIC and DIA (Table 1) allows their frequent detection in solid matrices (Table S4) in spite of their low concentrations measured in the dissolved phase (Fig. S2). The high detection frequencies and contents of OXA, TRI and CBZ in solid matrices were consistent with their moderate to high emissions (Fig. S2) and persistence (Table 2). Moreover, OXA is the main metabolite of DIA (Baker et al., 2014). The ubiquity of SCA may be explained by its presence in all anthropogenic effluents at high levels, a behaviour already observed

in other hydrosystems (Togola et al., 2008; Huber et al., 2016). Nevertheless, despite their moderate to high concentrations in the sewage effluents (Fig. S2) and persistence (Table 2), ATE, COD and TRA were the least frequently detected PPs (Fig. 2 and Table S4), suggesting that other parameters regulate their adsorption.

Table 2: Solid-water partition coefficient (Kd), persistence and major degradation processes (BT: biotransformation; PY: photolysis) of the investigated analgesics, antibiotics, anti-inflammatory agents, β-blockers, opioids and psychotropics.

[Table 2]

As PPs are organic molecules, sorption can occur through different types of chemical interactions with both organic and mineral surfaces, depending on the molecular charges (Martínez-Hernández et al., 2014; Svahn & Bjorklund, 2015). This speciation therefore plays a key role in PP adsorption and depends on the molecular structure and functional groups, varying with the pH value (Kümmerer, 2009). With pH values ranging from 6.9 to 9.5 (mean value of 7.5) in the Egoutier stream, ATE, COD and TRA were cationic, ACM, CBZ, DIA and OXA were neutral, and SCA and DIC were anionic (Table 1). Only the charge state of TRI may be influenced by such a range of pH values (Table 1), but it was generally mostly found as a neutral molecule (i.e. pKa = 7.2). The mineralogical parts of the Egoutier stream solid matrices were composed of quartz, calcite, albite, orthoclase and smectite (Table S3, Fig. S1), consistently with the geology of the catchment (Berger and Desprez, 1969). Some exceptions such as the presence of aragonite in BLS collected at the CAP sewage effluent (BLS-2, Fig. S1) and the absence of smectite in BLS collected downstream the pond (BLS-13) were also observed (Table S3). All solid samples had sandy-loam textures and TOC levels ranging from 0.2 to 18.0% (Table S3). As clay minerals and organic matter are negatively charged, several studies have reported a good affinity of cationic PPs with particles (Ramil et al., 2010; Martínez-Hernández et al., 2014; Svahn & Björklund, 2015; Boulard et al., 2020). In the present study, cationic, neutral and anionic PPs exhibited a detection frequency of 10, 65 and 66%, respectively (Table S4). Their concentrations ranged from 3.8 to 20.3 $ng.g^{-1}$ (mean value of 9.9 $ng.g^{-1}$), 1.2 to 141.4 $ng.g^{-1}$

(mean value of 19.6 $ng.g^{-1}$) and 4.4 to 176.2 $ng.g^{-1}$ (mean value of 33.0 $ng.g^{-1}$), respectively (Fig. 2 and Table S4). The lower occurrences of cationic PPs in this study in comparison with others might be explained by higher TOC levels (e.g. 33% in Svahn & Björklund (2015)) or by different solid matrix grain-sizes, resulting in variations in the particles' cation exchange capacity (CEC), not characterized in Svahn and Björklund (2015) and Boulard et al. (2020). Consequently, the limited clay contents in Egoutier solid matrices (Table S3) may explain this result. Moreover, as hydrophobic interactions are known to contribute significantly to PP sorption, PP lipophilicity (logD, Table 1) therefore represents another characteristic that plays a key role in their accumulation in particulate phases (Yamamoto et al., 2009). The moderate hydrophobicity (Table 1) of the cationic PPs investigated may also contribute to their lower adsorption.

2. Distribution of PPs between the different compartments of the aquatic environment

Cocktails observed in the particulate phases collected at sewage discharging sites and downstream were consistent with those quantified in WWTP effluents. All the PPs quantified in the CAP effluent (CBZ, OXA, TRI, DIC and SCA, Fig. S2) were detected at least once in the BLS and SPM sampled downstream (Fig. 2 and Table S4). In the PH effluent, all the PPs investigated were quantified (Fig. S2) and were also detected in SPM and BLS sampled downstream its discharge (Fig. 2 and Table S4). Therefore, the particulate phases well reflect the sets of PPs released in the dissolved phase. Surprisingly, CBZ, TRI and SCA were also detected in the first BLS sample collected in the upstream part of the watercourse (BLS-1, Fig. 2 and Table S4), suggesting another source at the locality present in the upstream part of the catchment (Fig. 1). All the neutral and anionic PPs were also detected in the BLS samples collected at stormwater discharge sites (BLS-2 and BLS-13b, Fig. 2 and Table S4). This observation implies leaks in the sewage networks. Except for ACM, only detected in the CAP stormwater effluent, the cocktails of PPs observed in the BLS collected at these discharges were similar (Fig. 2 and Table S4).

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[Figure 2]

Figure 2: Detection and concentrations of atenolol (ATE), codeine (COD), tramadol (TRA), acetaminophen (ACM), carbamazepine (CBZ), diazepam (DIA), oxazepam (OXA), trimethoprim (TRI), diclofenac (DIC) and salicylic acid (SCA) in bed-load sediment samples (BLS 1 to 14, Fig. 1) along the watercourse during the different campaigns. Pharmaceutical mean contents in suspended particulate matter samples (SPM 1 to 3, Fig. 1) and Eckman grabs (EG 1 to 3, Fig. 1) according to sampling period. Dotted lines represent stormwater and sewage water effluents, as well as the Beulie pond location.

Despite the consistency between the dissolved and particulate phases, the different solid matrices demonstrated various rates of PP accumulation. SPM contents in PPs were less diversified and less concentrated than in BLS samples (Fig. 2 and Table S4). Indeed, the least frequently detected PPs, ACM, ATE, COD, TRA and DIC, were not quantified in SPM and each quantified PP presented a lower concentration in SPM than in BLS samples (Fig. 2 and Table S4). SCA was the most abundant and the most concentrated in both compartments but did not exceed 32.5 $ng.g^{-1}$ in SPM, whereas it reached 169.4 $ng.g^{-1}$ in BLS samples (Fig. 2 and Table S4). TRI was also frequently quantified in SPM, ranging from 1.2 to 12.1 $ng.g^{-1}$ while reaching 27.5 $ng.g^{-1}$ in BLS samples (Fig. 2 and Table S4). OXA, DIA and CBZ were quantified only once in SPM, in concentrations of 24.3, 24.8 and 28.0 $ng.g^{-1}$, respectively, in contrast with BLS samples where they reached 141.4, 39.6 and 130.5 $ng.g^{-1}$, respectively (Fig. 2 and Table S4). Total PP concentrations therefore did not exceed 64 $ng.g^{-1}$ in SPM, but reached 212 $ng.g^{-1}$ in BLS (without considering the exceptional levels of TRA in one sample, Table S4). This tendency is not in agreement with other studies, in which higher contents were measured in SPM than in BLS in both large and small hydrosystems (Da Silva et al., 2011; Aminot et al., 2015; Comtois-Marotte et al., 2017). These studies designated SPM as a better sorbent because of its higher levels of TOC and fine particles. However in our case, the sandy-clay soils of the Egoutier catchment (Soucémarianadin & Verbèque, 2007) lead to a coarse texture of SPM (Table S3). SPM contents in TOC (ranging from 4.2 to 6.6%, Table S3) and fine particles (2-63 µm, ranging from 0.7 to 7.9%, Table S3) were therefore far lower than those of the BLS samples collected in strong accumulation zones (reaching 11.9% of TOC and 46.4% of 2-63 µm particles, Table S3). This different

336 composition explains the limited occurrence of less hydrophobic (Table 1) and persistent PPs (ACM,
337 ATE, COD, TRA and DIC, Table 2) which were released in lower quantities (Fig. 2 and Table S4).
338 Moreover, sorption regulates PP sedimentation or transportation at the catchment scale (Lahti &
339 Oikari, 2011). This therefore suggests that lower interactions with SPM limit the transportation of
340 ACM, ATE, COD, TRA and DIC over long distances.

341 As the Beulie pond sediments are mainly supplied by SPM decantation, these two
342 compartments consequently exhibited similar fingerprints (Fig. 2 and Table S4). Despite the strong
343 accumulation of organic matter (reaching 14.3%) and fine particles (2-63 µm, reaching 72.1%, Table
344 S3), only the PPs transported by SPM were also observed in the pond sediments (Fig. 2 and Table S4).
345 ACM, ATE, COD, TRA and DIC were absent, suggesting lower transportation distances (Fig. 2 and
346 Table S4) and retention zones within the catchment area. Moreover, lower concentrations in the EG
347 samples than in BLS ones highlight particle accumulation in specific locations upstream of the pond
348 (Fig. 2 and Table S4).

349

350 3. Spatial evolution of PPs in the particulate phases at the catchment scale

351 PP contents were highly variable in space and time. In order to have a high-resolution visualization of
352 PPs' spatial evolution in particulate phases, the most persistent (Table 2) neutral and cationic PPs are
353 represented in Figure 3. CBZ, DIA, OXA, ATE and COD were selected because of their concentrations
354 in specific locations compared to ubiquitous PPs such as TRI and SCA. Moreover, they have known
355 specific sources (Fig. S2) and exhibited good affinities with sediments. Total concentrations of these
356 neutral and cationic PPs were therefore compared to TOC and fine particle levels (Fig. 3), as these
357 fractions are the best sorbents (Aminot et al., 2015).

358 Thanks to their properties (hydrophobicity and persistence, Table 1 and 2), some of these PPs
359 have already been used as tracers to qualify anthropogenic impacts on the environment (Warner et
360 al., 2019). This is mainly the case for CBZ (Clara et al., 2004; Maskaoui & Zhou, 2010) and sometimes

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OXA (Amalric et al., 2011). These more persistent PPs generally present lower spatio-temporal variabilities (Vystavna et al., 2013; Klaminder et al., 2015) but this trend was not observed in the present study (Fig. 3), as the particulate phase contents of every PP were highly variable in space and time (Fig. 2 and 3).

[Figure 3]

Figure 3: Spatial evolution of persistent neutral (carbamazepine (CBZ), diazepam (DIA) and oxazepam (OXA)) and cationic molecules (atenolol (ATE) and codeine (COD)) total concentrations (∑) compared to the spatial evolution of total organic carbon (TOC) and fine particles (0 – 63 µm) percentages in suspended particulate matter (SPM 1 to 3, Fig. 1), bed-load (BLS 1 to 14, Fig. 1) and Beulie pond sediments (mean contents of EG 1 to 3, Fig. 1).

As already observed in other studies (Da Silva et al., 2011; Zhou & Broodbank, 2014; Aminot et al., 2015), high concentrations are observed at stormwater and WWTP effluent discharge sites (BLS-2, BLS-3 and BLS-7, Fig. 3). Nevertheless, specific accumulation zones also appeared downstream the PP sources (Fig. 3). In the upstream part of the catchment, between the CAP and PH effluents, PPs were always present but sparsely accumulated (Fig. 3), consistently with the low discharges measured in the CAP sewage waters (Fig. S2). This implies PP transportation, as observed in SPM samples, but only a small deposition of sediments in this part of the watercourse (Fig. 3). Indeed, low sediment thicknesses not exceeding 3 centimetres were measured during the sampling campaigns. Given the higher discharges of the PH effluent (Fig. S2), a stronger accumulation of PPs was unsurprisingly observed at its discharge (Fig. 3). Large accumulation zones also appeared between this effluent and the Beulie pond (Fig. 3) suggesting specific deposition zones in this part of the watercourse. Indeed, the specific PPs released by the PH (ATE and COD) as well as the most abundant PPs (CBZ, DIA and OXA) exhibited local concentrations downstream the PH (BLS-9 and BLS-11, Fig. 2 and 3) where sediment layers up to 67 centimetres thick were measured. These zones stored high proportions of fine particles (more than 46% of silt, Table S3) but PP amounts mainly followed the large variations in organic matter levels (Fig. 3). This was also observed in the Beulie

388 pond where PP distribution corresponds to that of the TOC (Fig. 3). The main PP-bearing phase also
389 appeared to be organic matter. Besides, sorption processes for PPs such as CBZ were already
390 demonstrated to be dominated by organic carbon-partitioning (Fairbairn et al., 2015).

391 Surprisingly, higher concentrations were generally observed in spring (Fig. 2 and 3). This can
392 be linked to a lower efficiency of degradation processes, which may be limited by a minimal
393 residence time at higher flow rates (Amalric et al., 2011) and in colder weather (Kim & Carlson,
394 2007). However, an opposite trend was already observed as higher stormwater supplies in spring can
395 dilute anthropogenic inputs (Kolpin et al., 2004) and adsorption can be enhanced by longer
396 incubation times during low flow periods (Fairbairn et al., 2015). In our case, this tendency seems to
397 be mainly driven by higher supplies in organic matter and fine particles (Fig. 3). It also illustrates
398 seasonal variations of the sedimentary dynamic, as contaminated particles are transported and
399 deposited at greater distances from PP sources in spring (Fig. 2 and 3).

400 In BLS collected downstream of the pond, PP concentrations were under the LOQ (Fig. 3;
401 Table S4). Given the absence of WWTP effluents in the downstream part of the catchment, this
402 evidences the storage capacity of the pond, which is also demonstrated by the decreasing TRI and
403 SCA concentrations towards the outlet in SPM samples (Fig. 2, 3 and Table S4). Nevertheless, CBZ,
404 OXA and COD presented higher concentrations in SPM collected downstream the pond than at the
405 other sampling locations (Fig. 2, 3 and Table S4), illustrating the transport of some contaminated
406 particles beyond the pond. This implies that particles are preferentially transported rather than
407 deposited in this part of the watercourse. Indeed, except for those collected at the stormwater
408 effluent (BLS-13b), BLS also demonstrated lower fine grain-size particles (2 – 63 µm) and TOC levels
409 (Table S3 and Fig. 3). The catchment therefore has two distinct sedimentary dynamics with low
410 transportation and strong accumulation zones in the upstream part, in contrast to high
411 transportation and low deposition in the downstream part. At the outlet, SPM therefore represents

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412 the highest risk by spreading PPs over long distances but thanks to the pond and the absence of new
413 sewage water releases, contamination levels remained low.

414

415 **IV. Conclusions**

416 All the PP investigated were quantified in the particulate phases, but in various abundances
417 and levels. PP discharges and persistence drive their occurrences and the observed concentrations
418 depend on the properties of both the released molecules (charge, persistenice and lipophilicity) and
419 the receiving environment (physico-chemical conditions, composition, and texture), as it drives the
420 processes involved in adsorption. In the Egoutier stream, the low contents in clay grain-sizes, the
421 relatively high persistence and discharges of neutral PPs led to the predominance of hydrophobic
422 interactions with organic matter.

423 Particulate phases, mostly bed-load sediments, well represent the PP cocktails released into
424 the aquatic environment. The different particulate compartments accumulate PPs in different ways.
425 Depending on the composition of the suspended particulate matter, the prevalence of neutral PPs
426 and their sorption to organic matter in the Egoutier stream, these solid matrices exhibit low
427 interaction with cationic molecules. The latter are consequently transported over smaller distances
428 and not stored in the pond sediments. In the same way, the most degradable PPs are sparsely
429 accumulated in bed-load sediments, but not in suspended solids and pond sediments.

430 In accordance with these conclusions, the spatial distribution of PPs in particulate phases at
431 the Egoutier scale mainly reflects the discharge sites. In addition, the most abundantly adsorbed and
432 persistent molecules highlight the sedimentary dynamic of the watercourse, in particular that of
433 organic matter. Sedimentary deposition areas thus strongly stored the molecules because of large
434 deposits of organic matter. These accumulation zones are mainly located upstream of the pond,
435 evidencing the strong storage capacity of the Beulie pond and a preferential transportation over
436 deposition in the downstream part of the catchment. Seasonal variations also appear to be driven by

437 limited degradation processes and/or higher supplies in organic matter. Moreover, PPs can be
438 transported over longer distances in periods of high flows.

439 To go further, with such an anthropogenic gradient and point sources of sewage and storm
440 waters, the Egoutier stream could be a favourable place to investigate the spatial distribution of
441 other types of contaminants in the different particulate compartments. Moreover, the sediments of
442 the Beulie pond, which has been in place for centuries, could represent an archive of past
443 contamination levels.

444

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SPATIAL DISTRIBUTION OF PHARMACEUTICALS WITHIN THE PARTICULATE PHASES OF A PERI-URBAN STREAM

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Table 1 : For each therapeutic molecule, abbreviation (Abb.), CAS-Number, formula, molecular weight (MW), charge state at pH = 7 (Charge), pKa, solubility and logD are specified. [a]: https://pubchem.ncbi.nlm.nih.gov; [b]: www.drugbank.ca, [c]: www.chemspider.com.

Therapeutic group	*Name*	*Abb.*	*CAS-Number*[a]	*Formula*[b]	*Mw* ($gmol^{-1}$)[b]	*Charge*[b]	*pKa*[b]	*Solubility* ($mg.mL^{-1}$)[b]	*LogD*[c]
Analgesics	Acetaminophen	ACM	103-90-2	$C_8H_9NO_2$	151.16	0	9.4	4.15	0.40
	Salicylic acid	SCA	69-72-7	$C_7H_6O_3$	138.12	-	3.5	11.3	-0.77
Antibiotics	Trimethoprim	TRI	738-70-5	$C_{14}H_{18}N_4O_3$	290.32	0/+	7.2	0.62	-1.15
Non-steroidal anti-inflammatory agents	Diclofenac	DIC	15307-86-5	$C_{14}H_{11}Cl_2NO_2$	296.15	-	4.2	0.005	1.37
ß-blockers	Atenolol	ATE	29122-68-7	$C_{14}H_{22}N_2O_3$	266.34	+	9.6	0.43	-1.85
Opioids	Codeine	COD	76-57-3	$C_{18}H_{21}NO_3$	299.36	+	8.2	0.58	0.28
	Tramadol	TRA	27203-92-5	$C_{16}H_{25}NO_2$	263.38	+	9.4	0.75	0.52
Anticonvulsants	Carbamazepine	CBZ	298-46-4	$C_{15}H_{12}N_2O$	236.27	0	13.9	0.15	0.29
Psychotropics	Diazepam	DIA	439-14-5	$C_{16}H_{13}ClN_2O$	284.74	0	3.4	0.01	2.92
	Oxazepam	OXA	604-75-1	$C_{15}H_{11}ClN_2O_2$	286.71	0	1.5	0.088	1.50

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Table 2: Solid-water partition coefficient (Kd), persistence and major degradation processes (BT: biotransformation; PY: photolysis) of the investigated analgesics, antibiotics, anti-inflammatory agents, β-blockers, opioids and psychotropics.

Therapeutic group	*Molecule*	*Kd (L/kg)*	*Persistence*	*Major degradation processes*
Analgesics	ACM	0.5 – 7.7 [p,v]	Low [l,w]	BT [l,w]
	SCA	3.6 – 28.2 [a]	Low [c]	Both [c]
Antibiotics	TRI	18.84– 104.6 [u]	High [d,l]	*Debated* [c,l]
Non-steroidal anti-inflammatory agents	DIC	0.2 – 107.1 [a,f,h]	Low [b]	PY [e,k]
β-blockers	ATE	1.3 – 24.6 [f,v]	Moderate [d,s]	BT [n,s,v]
Opioids	COD	2.1 – 14.1 [t]	High [i]	PY [m]
	TRA	23.7 – 63.1 [f,j]	Moderate [q]	PY [q]
Psychotropics	CBZ	0.1 – 23.9 [j,t,v]	High [d,l]	PY [l]
	DIA	2.3 – 12 [r]	High [o]	PY [e,g]
	OXA	2 – 38.5 [f,t]	Moderate [o]	BT [g]

References: [a]Agunbiade and Moodley, 2015 ; [b]Ashton et al., 2004 ; [c]Baena-Nogueras et al., 2017 ; [d]Bendz et al., 2005 ; [e]Boreen et al., 2003 ; [f]Boulard et al., 2020 ; [g]Calisto and Esteves, 2009 ; [h]Dobor et al., 2012 ; [i]Fekadu et al., 2019 ; [j]Koba et al. 2018 ; [k]Koumaki et al., 2015 ; [l]Lam et al., 2004 ; [m]Lin et al., 2014 ; [n]Liu et Williams, 2007 ; [o]Löffler et al., 2005 ; [p]Martínez-Hernández et al., 2014 ; [q]Müller et al., 2018 ; [r]Nunes et al., 2019 ; [s]Ramil et al., 2010 ; [t]Stein et al., 2008 ; [u]Tang et al., 2019 ; [v]Yamamoto et al., 2009 ; [w]Yu et al., 2006

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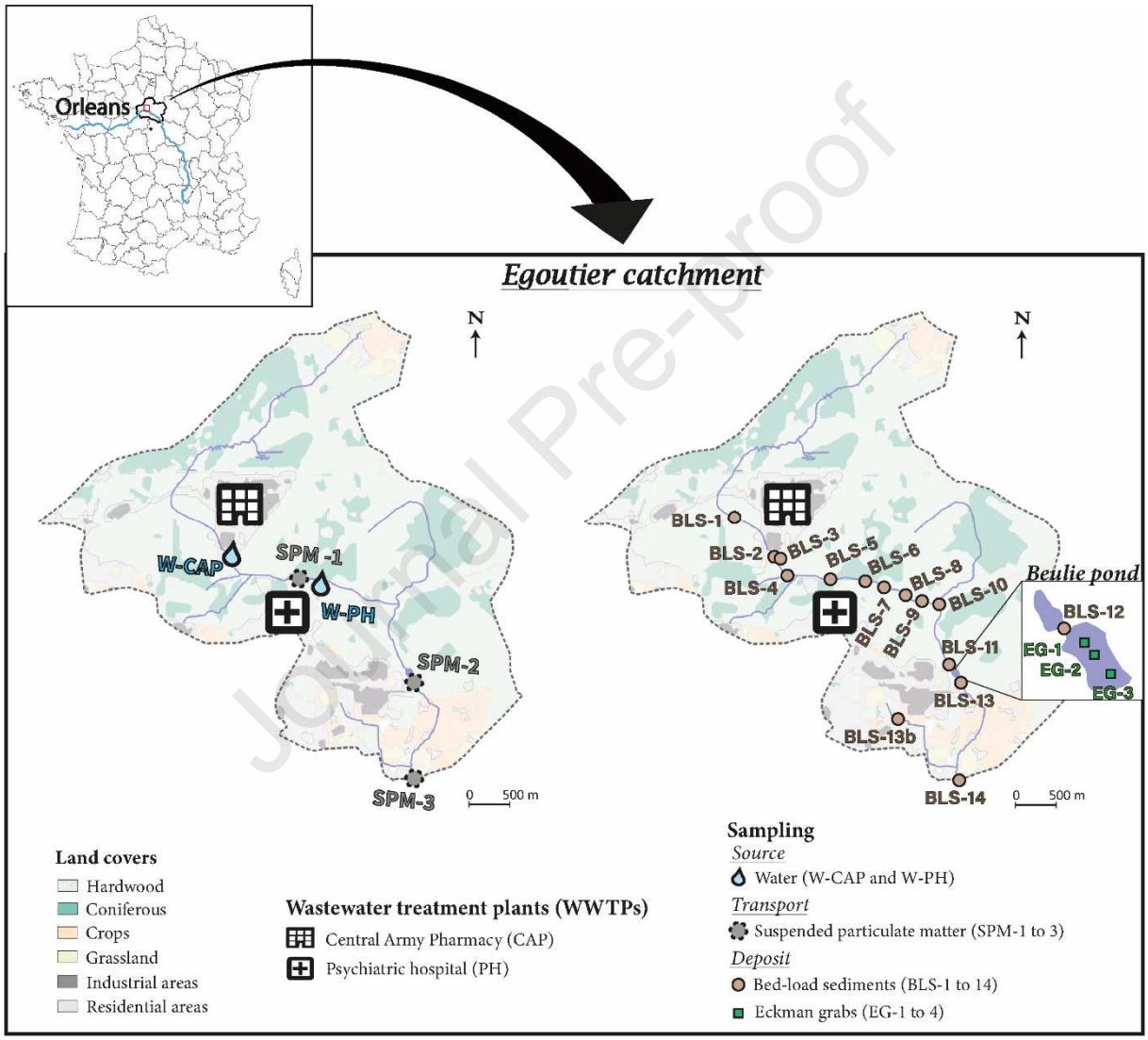


Figure 1 : Description of the upstream part of the Egoutier catchment area studied here with land covers (Inglada et al., 2017). Locations of the two sewage water effluents from the central army pharmacy (CAP) and the psychiatric hospital (PH) and of the samples collected in the dissolved phase (W), in suspended particulate matter (SPM), bed-load (BLS) and Beulie pond sediments (EG).

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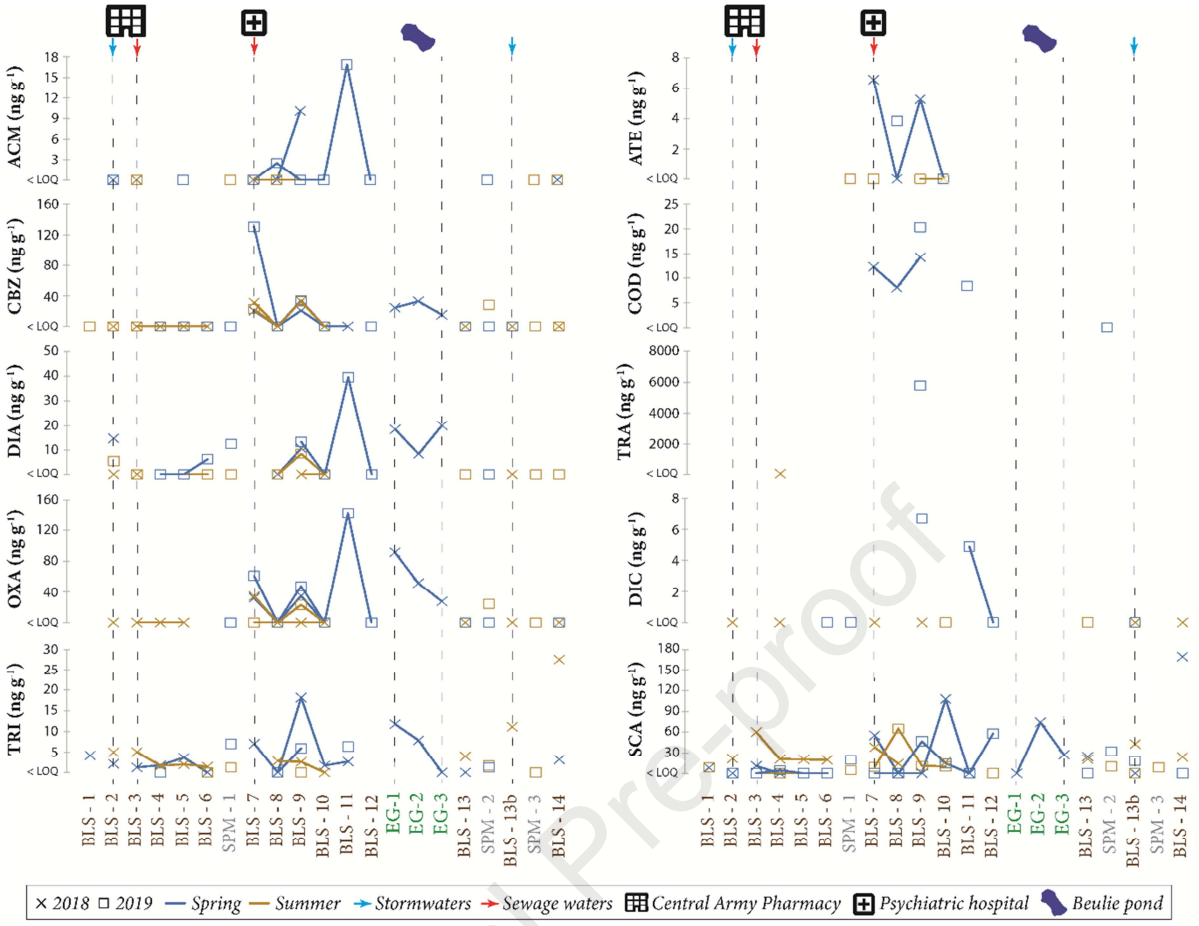


Figure 2: Detection and concentrations of atenolol (ATE), codeine (COD), tramadol (TRA), acetaminophen (ACM), carbamazepine (CBZ), diazepam (DIA), oxazepam (OXA), trimethoprim (TRI), diclofenac (DIC) and salicylic acid (SCA) in bed-load sediment samples (BLS 1 to 14, Fig. 1) along the watercourse during the different campaigns. Pharmaceutical mean contents in suspended particulate matter samples (SPM 1 to 3, Fig. 1) and Eckman grabs (EG 1 to 3, Fig. 1) according to sampling period. Dotted lines represent stormwater and sewage water effluents, as well as the Beulie pond location.

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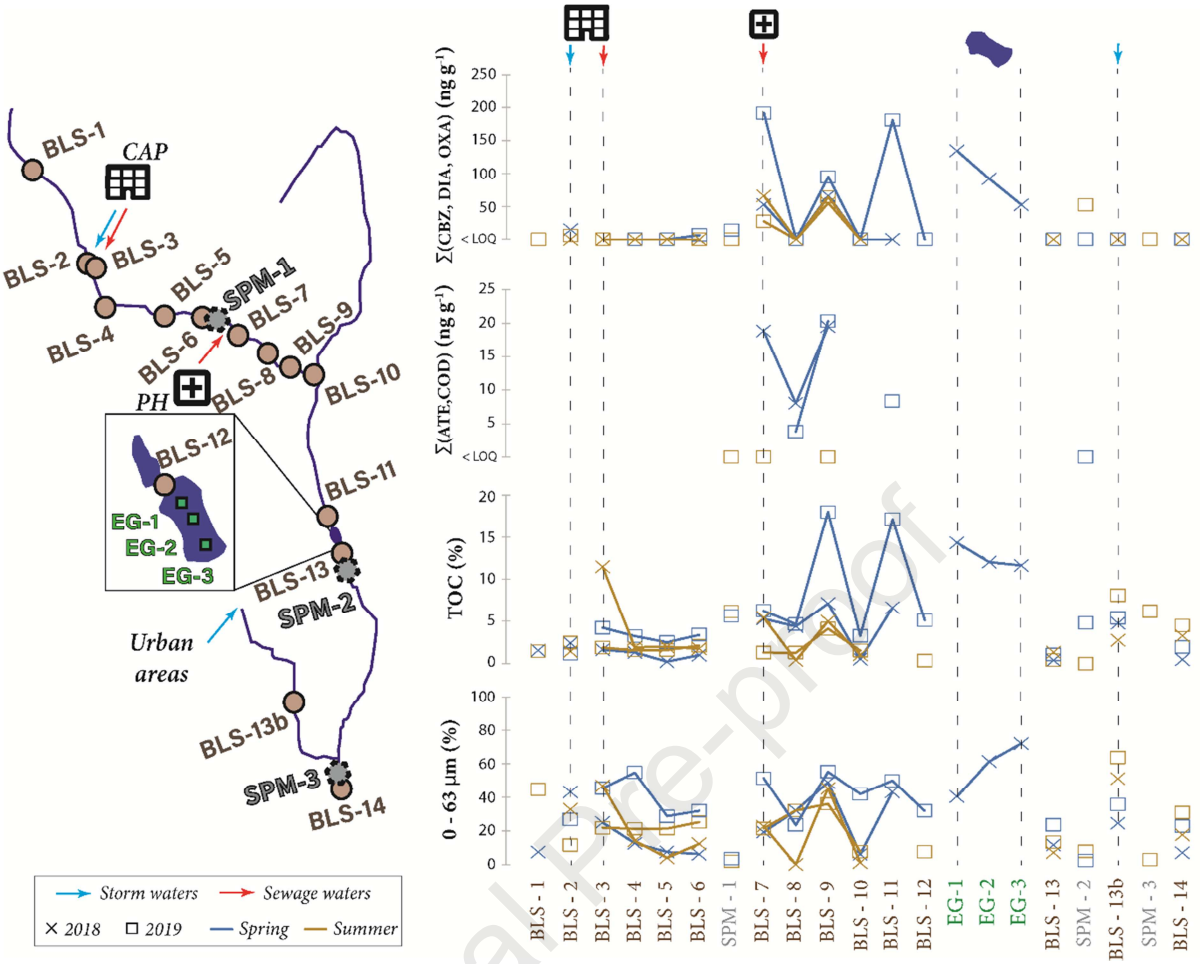


Figure 3: Spatial evolution of persistent neutral (carbamazepine (CBZ), diazepam (DIA) and oxazepam (OXA)) and cationic molecules (atenolol (ATE) and codeine (COD)) total concentrations (∑) compared to the spatial evolution of total organic carbon (TOC) and fine particles (0 – 63 µm) percentages in suspended particulate matter (SPM 1 to 3, Fig. 1), bed-load (BLS 1 to 14, Fig. 1) and Beulie pond sediments (mean contents of EG 1 to 3, Fig. 1).

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Highlights

- Particulate phases well represent the PP diversity found in the dissolved fraction
- Organic matter content is the most important driver impacting the partition of PPs
- Most contaminated areas are discharging sites and sedimentary accumulation zones
- In the urban part of the catchment, transportation of particles is enhanced
- Seasonal variations depend on degradation, bearing phases and transfer distances

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Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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