Record of pharmaceutical products in river sediments: a powerful tool to assess the environmental impact of urban management?

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Abstract:

The occurrence of eight pharmaceutical products (PPs) from various therapeutic classes was studied in urban sediments collected upstream a small dam in Orleans, France. Since PPs are globally distributed contaminants since the 1950s, their spatial and historical distribution was documented in order to better understand the impact of recent urban management on the chemical quality of sediments. Concentrations of the PPs mainly ranged between 1 and 10 ng g⁻¹ within the two cores. The chronology of core LOI13-2, based on radionuclide analysis (¹³⁷Cs and ²¹⁰Pb), enabled the characterization of the changes or shift in PPs over the last 50 years, impacted by the effluent deflections i) of a large wastewater treatment plant in 1989, and ii) of 3 smaller wastewater treatment plants between 2003 and 2009. In most cases the deepest occurrence of each PP in the core matched the market authorization date of different

pharmaceuticals, indicating that some PPs can be used as chronomarkers. The study reveals that recent management of effluent discharges within the watershed improved the chemical quality of these sediments. In view of the persistence of PP pollution in trapped sediments, a total stock of 763 ± 565 g for the selected PPs was estimated at the millstream scale.. Superficial sediments therefore represent a potential source of downstream pollution in the event of the removal of a small existing dam.

Keywords: Urban Dam; Sediments; Pharmaceutical Products; Anthropogenic Management; Wastewater Treatment Plant

1. Introduction

The growing use of pharmaceutical products (PPs) for human and animal therapies since the 1950s raises concerns about the environmental fate of these products and their metabolites within the aquatic environment because of their non-negligible excretion via urine and faeces (Daughton and Ternes, 1999; Lienert et al., 2007; Farré et al., 2008). Moreover, because they are exclusively generated by human activities, PPs could provide unique stratigraphic markers to allow the assessment and dating of anthropogenic impacts on the environment in a similar manner to how microplastics, synthetic fibers or pesticides have been used (Waters et al., 2016; Zalasiewicz et al., 2016). Nevertheless, the occurrence of PPs is under reported within sedimentary archives (Bernhardt et al., 2017), despite their significant concentrations in numerous water compartments. The question about their long-term fate also represents a challenge for both an effective water resource management (Loos et al., 2009; Mompelat et al., 2009; Petrie et al., 2015) and a better tracking of the impacts of human activities on the environment.

Pharmaceutical products contain a wide variety of organic compounds (i.e. more than 3000 in France according to the French National Agency for Medicines and Health Products Safety, ANSM, 2014). These pharmaceuticals are designed to prevent and treat various diseases and to improve health in general. The main sources of PPs are domestic, hospital and industrial wastewaters (specifically pharmaceutical plants) that reach water bodies through sewage systems (Fick et al., 2009; Verlicchi et al., 2010) due to the inefficiency of classical or advanced wastewater treatment plants (WTP) to totally remove PPs (Busetti et al., 2015; Petrie et al., 2015). Accordingly, PPs enter the natural environment and potentially cause severe ecological issues and/or affect human health. Widespread contamination has been observed in surface, marine and ground waters (e.g. Heberer, 2002; McEneff et al., 2014; Lopez et al., 2015) as well as soils and sediments (e.g. Silva et al., 2011; Tamtam et al., 2011; Vazquez-Roig et al., 2012). Furthermore, the early studies related to the ecotoxicity of PPs at field-relevant concentrations have demonstrated that these pollutants are harmful to both invertebrates and vertebrates, even in low or natural concentrations (Brodin et al., 2013; De Castro-Català et al., 2016; Väitalo et al., 2017).

Beyond their hydrological impact on rivers (Hubbard et al., 2016), WTPs contribute a constant discharge of PPs in natural waters. Nevertheless, this flux is not random. For example, Klaminder et al. (2015) demonstrated a good correlation between the effluent and the downstream sediment concentrations of oxazepam (an anxiolytic drug), indicating that the impact of WTPs on the environment can be monitored (i) by the effluent concentration, and (ii) since the market authorization date of each compound.

The occurrence of PPs is closely related to the worldwide increase in population and the ongoing urbanization since World War II and therefore represents a major environmental issue for urban ecosystems (Heberer, 2002; Taylor and Owens, 2009). While numerous studies have been published concerning the occurrence of PPs in natural waters, there is still a

75 lack of research on the spatial and temporal trends of this widespread aquatic pollution in
76 sediments (Petrie et al., 2015). Sediments are however a relevant compartment for this type of
77 tracking thanks to their ability to record the evolution of contamination over several decades
78 and beyond (Tamtam et al., 2011; Dubois and Jacob, 2016; Lorgeoux et al., 2016).
79 Furthermore, PPs can be considered as very reactive contaminants, exhibiting some affinity
80 for both organic and inorganic surfaces (Stein et al., 2008; Zhou and Broodbank, 2014;
81 Thiebault et al., 2016a, 2016b). Moreover, several PPs have recently been added to the list of
82 priority substances in the amended Water Framework Directive of the European Union
83 (European Commission, 2013), indicating that PPs are now considered as a potential threat for
84 various organisms, including humans (De Jongh et al., 2012). Finally, an assessment of the
85 stock of contaminated sediments accumulated in small ponds and reservoirs should be
86 considered since the Water Framework Directive (European Commission, 2000) has
87 recommended the removal of dams without any practical function in order to improve the
88 ecological continuity of superficial water bodies. Such an assessment is required to prevent
89 the potential downstream propagation of PPs induced by physical modifications within the
90 reservoir such as dredging or removal, or by chemical changes in the water column.

91   In view of the potential hazards of these PPs and the need to acquire data to assess and
92 date the impact of anthropogenic activities on the environment, eight PPs were selected
93 among the most frequently detected compounds in EU waters (Tamtam et al., 2008; Loos et
94 al., 2009; Joigneaux, 2011), namely acetaminophen, atenolol, codeine, metoprolol, oxazepam,
95 ofloxacin, trimethoprim and sulfamethoxazole. In the study presented here, the presence of
96 PPs in sediments collected in a small millstream located in the urban area of Orleans, France,
97 was investigated. This work aimed to (i) quantify PPs within a sedimentary archive to assess
98 their potential as new chronomarkers; (ii) establish the long-term chronology of PP
99 contamination related to the evolution of WTPs in the catchment in order to evaluate the link

between the discharge of these contaminants and sedimentary contamination; (iii) observe the spatial variation in the occurrence of PPs in two cores to assess the contamination at a reservoir scale..

2. Environmental settings

2.1. Hydrological context

Figure 1. Aerial photograph showing the location of the Saint-Samson millstream within the urban area of Orleans (www.geoportail.gouv.fr). White lines indicate rivers. A = Les Abîmes spring; B = Le Bouillon spring. The inset illustrates the hydrographic context of the Loire karst upstream of Orleans, with groundwater circulation between infiltrations and springs. The effluent inputs from WTPs to the Dhuy River are marked by red dots: OS = Orleans-la-Source - SC = Saint-Cyr-en-Val - DS = Darvoy and Sandillon - OC = Ouvrouer-les-Champs - V = Vienne-en-Val - T = Tigy - NS = Neuvy-en-Sullias (see Table 1).

The Saint-Samson millstream is a 0.125 km² pond located in the southern part of the Orleans urban area in France (Figure 1). This area is characterized by a succession of watermills built by monks during the medieval period along the Loiret river. Among them, the upstream mill of Saint-Samson maintains an elongated pond at an elevation of 90.87 m a.s.l. with a maximum length of 1.3 km and a mean width of 80 m. Its outflow and water level are currently regulated by a small dam. It is fed by the Loiret river, whose waters come from springs connected to the fluvial-karstic system of the Loire river (Albéric and Lepiller, 1998; Albéric, 2004), and by the Dhuy river, a 30 km long tributary that flows in the agricultural lowlands of the Val d'Orléans (Figure 1). A recent report revealed that the origin of suspended sediments in the Saint-Samson millstream can be divided between the Dhuy river (216 km²), the urban catchment (34 km²) and, for a negligible fraction, the karst (Geo-hyd, 2009). This report also indicated that during winter high-flows, the Dhuy river is the main sediment supplier for the Loiret river.

At the confluence with the Loiret river, the mean annual flow of the Dhuy river is about 0.7 m³.s⁻¹ with minimum values during the end of summer (0.07 m³.s⁻¹) and maximum values during winter (1.49 m³.s⁻¹) (source: www.hydroeau.france.fr). With such weak flows, a permanent water table is maintained throughout the year due to numerous anthropogenic developments along the river banks such as small dikes, platforms, walls and wooden studs. Eutrophication has led to the proliferation of filamentous green algae (*Egeria densa* and *Elodea nuttallii*), regularly observed during summer over the last 40 years and was one of the main reasons for the deflection of effluent discharges from the millstream.

2.2. Sanitation systems evolution

Land-use evolution since the 1950s resulted in the expansion of urban areas, mainly concentrated in the southern part of Orleans. Both the growing urbanization and the evolution of sanitation techniques led to the construction of several WTPs between 1966 and 2002 (Table 1 and Figure 1). The largest WTP, located close to the confluence between the two rivers in Orléans-La-Source (OS), was built in 1966 to support a population-equivalent (PE) of 60,000 (Figure 1). It discharged wastewaters into the Dhuy river until 1989. After this date a diversion via pipelines downstream to the Loire river was implemented to limit the eutrophication of the Loiret river. Meanwhile, other plants were constructed in the upstream catchment over the last 40 years to support a PE of < 15,000 (Table 1). However, several alterations were recently made to some of these plants to comply with current regulations and extend sanitation access. The WTP of Saint-Cyr-en-Val (SC) was connected to OS in 2009 while the plants in Darvoy (D) and Sandillon (S) were combined in 2003 to reach a capacity of 8,800 PE (Table 1). Since then, the effluent waters of this broad new sanitation system have flowed directly into the Loire river. Lastly, the capacity of the plant in Neuivy-en-Sullias (NS, Figure 1) was doubled in 2006 from 500 to 1,100 PE, but associated wastewater effluents still feed the Dhuy river (Table 1). It should be mentioned that all the WTPs that discharge their effluent into the millstream are conventional activated sludge treatment plants and provide only incomplete removal of PPs (Verlicchi et al., 2012; Petrie et al., 2015).

Table 1. Evolution of wastewater treatment plants along the Dhuy catchment area (sources: SAGE Loiret and <http://assainissement.developpement-durable.gouv.fr/>). TSS: Total Suspended Sediment. Data in brackets indicate the functional parameters of the WTP after renovation and/or deflection. The WTPs of Darvoy and Sandillon had the same discharge point in the Dhuy river and therefore the same distance from the Saint-Samson millstream (red dots on Figure 1). Note that these plants were upgraded and combined in 2003.

Station name	Installation date	Deflection date	Capacity (10 ³ PE)	Flow (m ³ .day ⁻¹)	TSS (kg.day ⁻¹)	Discharge-millstream distance (km)

Orleans-La-Source	1966	1989	60 (93.9)		n.d. (4050)	n.d. (1072)	4.5
Saint-Cyr-en-Val	1982	2009	2		420	86	7
Darvoy	1987	2003	1	(8.8)	300	94	11
Sandillon	1988		2		300	85	
Vienne-en-Val	1998	-	1.7		400	4	21.5
Ouvrouer-les-Champs	2002	-	0.35		52	2	25
Tigy	1999	-	2		460	9	26
Neuvy-en-Sullias	1978 (2006)	-	0.5 (1.1)		75 (205)	30	29.5

160

161 3. Materials and methods

162 3.1. Acoustic imaging and sample collection

163 The bathymetry of the millstream was assessed by combining geophysical mapping
164 techniques and handheld measures. A Knudsen® lake bottom profiler was used for seismic
165 surveys in the central part of the millstream at a frequency of 200 kHz. A P-wave velocity of
166 1500 m.s⁻¹ was used to convert the acoustic wave propagation from two-way travel time (in
167 seconds) to water-depth (in meters). A round-trip navigation was carried out with one straight
168 line in the axis of the river followed by a zigzag reaching the shores. To complete this dataset,
169 additional handheld measures of bathymetry and total sediment thickness were performed
170 using a graded stick. The bathymetric map of the millstream as well as the calculation of
171 volume and thickness of sedimentary units were performed using a GIS. Five sedimentary
172 cores were collected along a longitudinal transect using a gravity corer. The two extremes are
173 cores LOI13-2 and LOI13-6, situated at the head of the millstream, and near the outlet of the
174 Saint-Samson basin, respectively.

175 3.2. Sediment analyses and dating

176 A multi-proxy approach was adopted to characterize sediments. For each core,
177 magnetic susceptibility (MS) and spectrophotometry were performed every half-centimeter
178 using a Bartington MS2E Sensor and a Konica Minolta CM-700d, respectively. First-

derivative spectra (FDS) representative of sediment composition were then calculated for the light spectrum (400-700 nm) and values were represented by color changes within spectral maps (Debret et al., 2011). Core LOI13-2 was sampled at regular intervals (5 cm) for destructive analyses of grain size using a Mastersizer 3000 and for Total Organic Carbon (TOC) using a Rock-Eval 6 (Behar et al., 2001). Dry bulk density was also estimated every 10 cm.

^{210}Pb and ^{137}Cs activities were determined in core LOI13-2 to determine the sedimentation rate in the core that we used to provide the time frame for the sedimentary record. Between 6.1 and 11.2 g of dry sample (equivalent to 3-cm thick sections) were placed in counting boxes that were sealed to prevent any loss of ^{222}Rn . The quantification of ^{210}Pb , ^{226}Ra and ^{137}Cs activities in the sediment samples was performed at the LAFARA underground laboratory (van Beek et al., 2013) using a semi-planar germanium detector (183 cm^3 ; PROFILE-FX series; ORTEC/AMETEK). The detector is protected from cosmic radiation by 85 m of rock, ensuring a very low background to the facility. ^{137}Cs and ^{210}Pb activities were determined using the 662 keV line and the 46.5 keV line, respectively. The ^{226}Ra activity was determined using the lines of ^{214}Pb (295 keV and 352 keV) and ^{214}Bi (609 keV). Excess ^{210}Pb activities ($^{210}\text{Pb}_{\text{ex}}$) were then determined by correcting the ^{210}Pb activities for the ^{210}Pb supported by ^{226}Ra . The detector is calibrated for natural radionuclides using RGU-1 and RGTh-1 standards. The IAEA Standard #375 was used to determine the detection efficiency for ^{137}Cs .

3.3. Quantification of pharmaceuticals

The standards for the eight investigated PPs, namely acetaminophen, atenolol, codeine, metoprolol, ofloxacin, oxazepam, sulfamethoxazole and trimethoprim were purchased from Sigma-Aldrich assuming a purity of up to 98%. Extraction and separation

solvents, dichloromethane (DCM), methanol (MeOH) and acetonitrile (AcN) were purchased from Fisher-Scientific, assuming an analytical grade (purity up to 99.95 %)

Sediments were sampled on cores LOI13-2 and LOI13-6 following a regular sampling step (5 cm). They were then dried at 60°C during 48 h before being crushed in a mortar. Around 2 ± 0.1 g of material was afterward extracted by pressurized liquid extraction, using ASE-200 (Dionex). The extraction mixture was MeOH/H₂O (1:1 v/v) and the operating temperature and pressure were 100°C and 1000 psi respectively. Extracts were then dried at 60°C and stored at 3°C before liquid chromatography analysis. Samples, standards and controls were prepared with surface waters sampled in the Loiret river (filtered at 0.22 µm), which after analysis were found to be deprived of PPs. The analytical and quantification procedure is further detailed in the supplementary data.

4. Results

4.1. Bathymetry and sediment geometry.

The water-sediment interface can be seen on acoustic images with an uppermost continuous thick reflector throughout the millstream (Figure 2). In the center part, the water level had an overall flat geometry between 2 and 3 m. A circular depression in the water level reaching 4.5 m can also be seen and is likely related to a stream in this karstic context. The acoustic images also displayed a second thick reflector roughly parallel to the river bed (Figure 2). This reflector, labeled R1, was mapped to later calculate the thickness of this top-most acoustic unit U1 across the millstream (Figure S1). Results showed a plate geometry with maximum values fluctuating between 0.3 and 0.5 m thick on the longitudinal axis for an estimated volume of $21,000 \pm 100 \text{ m}^3$. This value represents almost a fifth of the total sediment stock (estimated to $102,000 \pm 6,600 \text{ m}^3$) trapped in the Saint-Samson millstream

according to the handheld measures and volume calculations performed by a design office in 2006 (Geo-hyd, 2009).

Figure 2. Navigation grid (grey lines), core locations (red dots), punctual sediment thickness measures (green dots) and acoustic images (200 kHz) of sedimentary infills within the Saint-Samson millstream. Grey letters refer to angles in the navigation grid. The dashed green line is an estimation of the karst-sediment interface depth based on measures of total sediment thickness.

4.2. Description of the sediment

Within the five collected cores (maximum length: 90 cm), the sediment is made of a greyish to brownish mud rich in water and in small leaf remains. Three sedimentary units

have been distinguished and correlated core-to-core on the basis of visual observations, spectral maps and MS values (Figures 3 and S2). The topmost brownish unit, labeled U1a, 10 cm thick, was characterized by elevated values between d675 and d695 (yellow to orange strips on the right side of the spectral map in Figure 3). The second unit, labeled U1b, was made of a greyish sediment with a thickness ranging from 20 cm in cores LOI13-2 and LOI13-6 to 41 cm in core LOI13-3. The left side of the spectral map indicates low values fluctuating from d405 to d545 across this unit. However, this spectral signature was less obvious within cores LOI13-3 and LOI13-4. Finally, the bottom of all the cores displayed a faintly laminated unit labeled U2 in which dark lamina showed fluctuating MS values. The interface between U1b and U2 across the core transect is very likely related to the reflector R1 considering the reflector depth (approximately 40 cm at the site of core LOI13-5) and the geometry of the acoustic unit U1 that can be seen both in the axis of the river and in the zigzag transect (Figure 2 and Figure 3).

A multi-proxy characterization of the sedimentary units identified within core LOI13-2 is shown in Figure 3. Grain-size analyses revealed a sandy-silt sediment with D_{x50} ranging from a mean of 30 μm in U2 to a mean of 50 μm in U1a and U1b. At 27 cm depth, the U1-U2 interface (i.e., reflector R1) was also underlined by a slight rise in TOC content from 4 to 5%. These parameters together supported the correlation across the millstream between the acoustic unit U1 and the sedimentary units U1a and U1b. The dry bulk density displayed values ranging from 0.7 to 1 g.cm^{-3} and was unrelated to the sedimentary units.

Figure 3: Multi-proxy sediment analyses along the core LOI13-2. MS, DBD, TOC and Dx50 were magnetic susceptibility, dry bulk density, total organic carbon and mean grain-size respectively. The spectral map represents the first-derivative of spectrophotometry measures (FDS, see Figure S2 for details). The chronology is indicated with a temporal scale on the right-hand side and is based on the ^{137}Cs downcore distributions. The two clear ^{137}Cs peaks are related to the Chernobyl accident dated from 1986 and to the maximum of nuclear atmospheric tests dated from 1963, respectively. Note that the sedimentation rate is almost constant throughout the core. In this dataset, error bars varied between 4.9 and 6.3 Bq.kg^{-1} for the $^{210}\text{Pb}_{\text{ex}}$ and between 0.4 and 0.9 Bq.kg^{-1} for the ^{137}Cs .

4.3. Chronology

The down-core ^{137}Cs distribution revealed two clear peaks (Figure 3). The first peak, located in the 27-30 cm depth interval (31.9 Bq.kg^{-1}), can be related to the Chernobyl accident dated from 1986, whereas the second peak, measured in the 54-57 cm depth interval (27.6 Bq.kg^{-1}), can be related to the atmospheric testing of nuclear weapons that took place during

the 1950s and 1960s, with a maximum activity in 1963 (UNSCEAR, 2000). The use of these two chronomarkers suggests a constant accumulation rate of 1.1 cm.y^{-1} over the last 50 years. Below 7 cm, the $^{210}\text{Pb}_{\text{ex}}$ activities decrease with increasing depth (Figure 3). Whereas the top core may be affected by bioturbation, the exponential decay of the $^{210}\text{Pb}_{\text{ex}}$ activities between 7.5 and 37.5 cm indicated a sedimentation rate of 1.4 cm.y^{-1} , which is in relatively good agreement with the sedimentation rate determined from ^{137}Cs concentrations.

4.4. Pharmaceuticals

The analysis of PPs along cores LOI13-2 and LOI13-6 firstly revealed that the concentration range was the same whatever the PP investigated, varying from 1 to 30 ng.g^{-1} of dried sediments (Figure 4). The vertical distribution of PPs is guided by a first occurrence, at different depths for each PP, followed by an ongoing detection until the top of the core. In general the lowest contamination levels were in the deepest layers. The highest concentration was observed at depths varying between 35 and 10 cm followed by a progressive decrease in U1a. Secondly, concentrations exhibited significant variations all along the core profiles. For example, sulfamethoxazole was first quantifiable at 51 cm (i.e. $\text{AD}1968 \pm 1.6$) in core LOI13-2 and then continuously detected until the top of the core with a maximum concentration at 11 cm (i.e. $\text{AD}2004 \pm 1.5$).

Figure 4: Distribution of PPs along core LOI13-2 (orange circles) and core LOI13-6 (blue diamonds) according to depth and years (age-depth model performed on core LOI13-2). Concentrations are expressed in ng.g^{-1} of dried sediment. Grey markers indicate concentrations below LOQ whereas empty markers indicate concentrations below LOD. The dashed line refers to the market authorization date (found on the ANSM website, www.ansm.fr) for each compound unless otherwise specified. The evolution of WTP effluents feeding the Dhuy River is indicated on the right-hand side of the figure (Figure 1 and Table 1).

5. Discussion

5.1. Mobility and persistence assessment

Mobility and persistence are both important parameters that must be taken into account when investigating the occurrence of PPs within the sedimentary archive. Mobility within sedimentary records can be assessed according to the organic carbon normalized partition coefficient values (K_{oc}) of each PP (Tamtam et al., 2011). Among the selected PPs, there is a wide chemical variety and hence different mobility. The selected PPs are classified between mobile to immobile (Table 2), which could potentially affect our reading of the results. According to literature data (Table 2), sulfamethoxazole is classified from mobile to moderately mobile whereas ofloxacin can be considered as the least mobile PP, due to its strong affinity with both organic and inorganic surfaces. Nevertheless, none of the selected PPs can be considered as highly mobile, and ofloxacin was used as a control in comparison to the other PPs.

Table 2: Relevant parameters assessing the mobility and persistence of PPs in sediments, with K_{ow} the octanol/water partition coefficient, K_d and K_{oc} respectively the solid/water partition and the normalized organic carbon partition both expressed in $L\ kg^{-1}$, mobility classification taken from ref.^h, the biodegradability based on the MITI-test (BIOWIN^{TM}, equation 6), and Removal the extreme removal (min-max) values of selected pharmaceuticals in conventional activated sludge treatment plants

^a Barron et al. (2009)

^b Al-Khazrajy and Boxall (2016)

^c Schaffer et al. (2012)

^d Stein et al. (2008)

^e Drillia et al. (2005)

^f Boxall et al. (2002)

^g Löffler et al. (2005)

^h Hollis (1991)

ⁱ Verlicchi et al., (2012)

^j Wick et al., (2009)

Compound	Log K_{ow}	K_d	Log K_{oc}	Mobility class ^h	Biodegradability	Removal ⁱ capacity
Acetaminophen	0.46	32 ^a	2.9 ^a	slightly mobile	0.51	86.4-99.9
Atenolol	0.16 /1.37	15 ^a ; 9.3 ^b	2.3 ^b ; 2.6 ^a ; 3.1 ^c	moderately-slightly mobile	0.23	10-76

Codeine	1.2	14.1 ^d	2.5 ^d	moderately mobile	0.06	82
Metoprolol	1.79	20 ^a	2.75 ^a	slightly mobile	0.14	10-31
Ofloxacin	0.84	3554 ^e	4.6 ^f ; 4.7 ^e	immobile	0.0001	13-84
Oxazepam	2.2	23.5 ^d ; 2.2 ^g	2.2 ^g ; 2.7 ^d	moderately mobile	0.03	-10-35 ^j
Sulfamethoxazole	0.9	8 ^a ; 0.9 ^d ; 37.6 ^e	1.3 ^d ; 2.3 ^a ; 2.7 ^e	mobile-moderately mobile	0.006	10-100
Trimethoprim	0.4	26 ^a	2.9 ^a ; 3.6 ^c	slightly mobile	0.16	-46-53

In contrast to mobility, persistence is usually assessed by solar and biological degradation impacts (Klaminder et al., 2015). However, the operating conditions used to determine the behavior of organic pollutants with respect to degradation are too different for these studies to be compared. We therefore estimated the degradability of each PP following the output of the same model, the MITI-test (see supplementary data for details or Tunkel et al., 2000), a component of the BIOWIN^{TM} model in the EPISuite^{TM}. According to these outputs, the only biodegradable PP (i.e. Biodegradability > 0.5) among the ones selected is acetaminophen (Blair et al., 2015; Lam et al., 2004). Moreover, the persistence of PPs should be assessed with respect to their removal rate in WTPs. In Table 2, the removal values for selected PPs concern WTPs that are similar to those present on the millstream (i.e. conventional activated sludge treatment). The literature data are very variable, except for acetaminophen, which has an extremely high removal value (i.e. mostly up to 99% in the literature). This is in accordance with the output of the MITI-test, indicating that acetaminophen is sensitive to degradation. However, due to its high consumption, acetaminophen is frequently detected in European surface waters (Loos et al., 2009). Concerning the other PPs investigated, the removal values are difficult to evaluate given the strong variations in the available literature. Nevertheless, only an incomplete removal of these PPs is achieved by WTPs.

5.2. Historical distribution

The chronology was determined on core LOI13-2. Thus, only the comparison between PP concentrations and core chronology will be discussed hereafter. As noted in previous studies, the market authorization date can be confronted with the first occurrence of each PP dated in the sedimentary record (Tamtam et al., 2011; Klaminder et al., 2015). Figure 4 shows that the market authorization date was systematically older than the date of the first occurrence of a PP. Yet some exceptions can be noticed such as oxazepam, atenolol and codeine. For example, as oxazepam is both a PP and a degradation product of diazepam (Almeida et al., 2015), the degradation pattern of diazepam (sales authorized since 1953) may play a significant role in the first occurrence of oxazepam within sedimentary archives. Concerning atenolol, an occurrence before the market authorization date is unexpected due to its moderate mobility. However, mobility remains the only consistent assumption to explain occurrences older than the market authorization date (Tamtam et al., 2011). Finally, concerning codeine, the path leading to its market authorization date is very hard to follow. According to the ANSM website, the sale of codeine was authorized in 1973, but codeine is also derived from opium. It is therefore not possible to assign a precise date to the arrival of this molecule within aquatic environments.

The trend of ofloxacin, the least mobile PP (Table 2), revealed a first occurrence around 1984, consistent with its market authorization date in 1980, followed by a progressive increase until the early 2000s (Figure 4). The two most recent sample analyses (dating from 2007 and 2012, respectively) revealed a significant decrease in concentration. This trend observed on ofloxacin also applied to trimethoprim, metoprolol, atenolol and acetaminophen. However, oxazepam and codeine, which are two psychotropic drugs, exhibited a different trend, with maximum concentration before 1989.

The good agreement between market authorization date and the first occurrence of the majority of the PPs confirms that the sorption of PPs onto sediment preserves the PP from

degradation during decades, which is a well-known process in numerous environments (Keil et al., 1994; Ingerslev and Halling-Sørensen, 2001) and confirmed in other studies in analogous areas (Tamtam et al., 2011; Klaminder et al., 2015). Moreover, the oldest samples - that is to say the deepest part of the concentration profiles - are also consistent with the market authorization dates of the selected PPs, followed by a significant increase in the consumption of PPs in France, particularly between the 1950s and the 1990s (Chauveau, 2002). Nevertheless, the drop in concentrations observed in the upper part of the cores is more surprising and could be due to two developments: (i) the enhancement of WTP removal techniques, and (ii) the discharge of effluents in the rivers concerned, which has been significantly reduced over the last twenty years (Table 1).

5.3. Impact of WTP management

Despite the presence of PPs in the karstic groundwater (Joigneaux, 2011), we assume that effluents from WTPs in the Dhuy river catchment area are the main sources of PPs because the karstic springs (Figure 1) do not feed the Loiret river substantially (Geo-hyd, 2009).

Among the two above-mentioned developments, the evolution of removal techniques is difficult to assess whereas the history of effluent discharge in the selected rivers is well-known. The millstream studied here was first concerned by a major event dated from 1989 with the deflection of the effluent discharges of the WTP closest to the sampled sediments (i.e. site OS, Figure 1, Table 1). This event can be observed on the sedimentary profile, but not for all the PPs. The deflection of the discharge of effluents from OS clearly affected the trend of both codeine and oxazepam (Figure 4), the two psychotropic PPs. As this WTP also contributes to the transport of suspended sediments in the river, it is possible to link this deflection with the onset of U1 associated to a shift in sedimentological and geochemical signals (Figure 3). Concerning the other PPs, the concentration trend is more affected by the

deflection of discharge from two smaller WTPs, SC and S-D in 2009 and 2003 respectively. Overall, there is a strong impact of human management on the chemical quality of sediments because of the non-correlation between the concentrations in sediment and the global increase in the consumption of PPs. Another possibility is to characterize good markers for different sources, since psychotropic drugs seem to be more sensitive to urban effluent deflection, whereas the other PPs are more sensitive to rural WTP deflection.

5.4. Spatial Distribution

The distance between the two cores is approximately 1 km (Figure 2). This distance precluded a direct application of the dating on LOI13-6. Nevertheless, several sedimentary data (Figure 3), combined with the PP concentrations (Figure 4), give insight into the spatial distribution of PPs since vertical patterns are found and repeated within the two cores. For instance, an offset of sedimentary rate can be noticed in the lower part of the core for oxazepam and sulfamethoxazole (Figure 4). Conversely, in the upper part of the two cores, the concentrations are closer at the sampling interval used. The decrease in PP concentrations since the 2000s is visible on the two records at the same depth. More generally, the concentration range of each PP is the same between the two cores, suggesting that the contamination is potentially widespread at the millstream scale.

5.5. Assessment of the stock of pollution

Despite the low concentrations and the decreasing trends observed for recent decades, sediment contamination by PPs remains a potential threat for aquatic environments. In this context, the quantification of PPs was combined with the sediment volume calculation (Figures 2 and S1) to assess sedimentary contamination at the millstream scale. The volume of U1, estimated at $21,000 \pm 100 \text{ m}^3$, was converted into a mass of $18,900 \pm 90 \text{ t}$, applying a mean density of 0.9 g.cm^3 (Figure 3). This amount of sediment was then converted into a

mass of PPs on the basis of the mean concentrations in U1a and U1b covering the 1989 - 2013 period (Figure S2). Results indicate that during this period, a total of 763 ± 565 g of the studied PPs accumulated in the sediments trapped in the millstream. These results likely represent a small part of the global pharmaceutical pollution in this millstream. Nevertheless, they constitute one of the first applications of sediment volume calculations coupled to pharmaceutical pollution to assess the contamination at the reservoir scale, and although the mass of PPs in this study represents a first approximation, it provides useful indicative information for the future management and potential decommissioning of reservoirs where the storage of contaminated sediments may be an issue for the quality of the aquatic environment. Furthermore, assessment of the uppermost sedimentary unit (U1, Figure S1) indicates the amount of contaminants discharged over the last 30 years. This assessment of PPs represents the first step toward estimating the historical concentrations in river sediments, based on solid/water partition of each PP. Moreover, the long-term consumption of each PP in the catchment could be estimated based on the PPs concentrations in sediments, compared to the existing approach of calculating catchment influent mass loads using only a limited temporal period that is subject to significant daily variations (Thiebault et al., 2017).

6. Conclusion

This work provides new insights into the contamination of urban sediments by PPs. For the first time, the occurrence of PPs from various therapeutic groups was assessed and quantified following a temporal and spatial distribution. Pharmaceutical products are differently recorded in the sediment from a chronological perspective depending on their mode of consumption and their main origin. The chronological distribution of pharmaceuticals was consistent with the global increase in drug consumption all around the world and particularly in France since World War II. In the deepest part of the core (dated

between the 1950s and 1980s), PPs concentrations increased continually following their initial market authorization date.

However, an opposite concentration trend was observed in recent decades, that can first of all be assigned to the enhancement of WTP removal techniques (i.e. addition of secondary treatment) but also to the management of the effluent discharge points during the last 30 years. The nearest and largest WTP discharge points in the studied millstream were deviated from the Dhuy river to the Loire river. As a result, the chemical quality of these sediments regarding PP concentration was significantly enhanced in more recent years, thus proving that the anthropogenic impact on river waters can be limited if appropriate management is conducted. Yet, not all the PPs are sensitive in the same way to the deviation of the discharge point of WTPs. Whereas the deflection of effluent discharges from the catchment of the urban WTP impacted the concentrations of psychotropic PPs, the effluent deflections of 3 more rural WTPs impacted antibiotic occurrences, indicating that the link between consumption and concentrations in sediments is not instinctive and should be carefully addressed depending on the investigated site. Finally, while the chemical quality of the sampled river was enhanced, the diversion of the effluents probably increased the contamination of the Loire river.

The quantification of PPs along the two cores gives similar concentrations, at least in the same order of magnitude, making it possible to estimate a stock of less than 1 kg of contaminants trapped within the sediments into the millstream. While a good ecological continuity can be achieved for many rivers by removing small dams, such management practices may damage the chemical status of superficial waters with the release of PP-contaminated sediments. Finally, as the adsorption onto organic or inorganic surfaces seems to preserve organic contaminants from degradation during several decades, the detection of some PPs in recent sediments, such as antibiotics (i.e. poorly biodegradable and poorly

mobile), has potential for use as chronomarkers for age-depth modeling to assess anthropogenic impacts on river and sediment quality.

Acknowledgments

The authors wish to thank the Agence de l'Eau Loire-Bretagne (AELB) and the Région Centre-Val de Loire for their financial support with projects EDIFIS (2012-120026501) and HARPE (2012-00073536) respectively. The authors also gratefully acknowledge Hervé Noël, Carine Biot and Stéphane Thauvin for fruitful scientific discussions and their logistical supports during field works and data interpretations, Laurent Perdereau for his contribution during seismic campaign and two graduate students (Nicolas Soudan and Adeline Rente) for their contribution to this work. We also wish to thank Hermann Zouzou (GEODE) for preparing the samples designed to the radionuclide analysis. The authors are grateful to EDF (Electricité De France) for allowing them to run our germanium detectors in the tunnel of Ferrières. Europe and Région Occitanie Pyrénées-Méditerranée are also gratefully thanked for supporting the LAFARA underground laboratory through a FEDER funding (SELECT project).

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