INVESTIGATING LEVELS AND BEHAVIOUR OF PHARMACEUTICAL AND PERSONAL CARE PRODUCTS (PPCPS) IN FRESHWATER SEDIMENT

By

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Abstract

Pharmaceuticals and personal care products (PPCPs) have received increasing scientific interest as emerging pollutants that have the potential to harm the environment and human health. While sediment has been identified as a major sink for several legacy chemical pollutants, very little is known on the concentrations and profiles of PPCPs in sediment, particularly in the freshwater environment.

In this thesis, an analytical method was optimised for determination of 30 widely used PPCPs in sediment samples using ultraperformance liquid chromatography (UPLC), coupled to high resolution mass spectrometry (HRMS). The average concentrations of Σ_{30}PPCPs in sediment samples from the River Tame, Coventry Canal, River Severn, and Birmingham & Worcester Canal, were 129, 79, 62, and 110 ng/g, respectively. Investigation into the distribution of PPCPs between sediment and water revealed a significant positive correlation between $LogK_{OW}$ of the studied compounds and their experimentally measured sediment–water distribution coefficient ($LogK_{P}$). Amoxicillin, caffeine, and 17-α-ethinylestradiol had estimated risk quotients (RQ) higher than 1 in the four study locations, raising concern over the risk of these chemicals to freshwater biota.

Over the course of a year, large seasonal variations were observed in the concentrations of target 30 PPCPs in sediment samples collected monthly from the River Sowe, River Tame, River Severn, and Worcester & Birmingham Canal (with coefficients of variation (%) of 116 %, 119 %t, 120 %, and 133 %, respectively). Highest PPCPs concentrations in all locations were recorded in summer, while the lowest concentrations were measured in winter. This could be partially explained by the lower flowrates and reduced rain fall in summer, which may facilitate the partitioning of PPCPs from water to sediment. Principle component analysis (PCA) revealed the observed variance in results may be attributed to various sources of different PPCPs to the studied waterways, including run-off from

agricultural land, sewage discharge, and veterinary applications of some PPCPs in livestock farming and aquaculture. Moreover, Σ_{30}PPCPs concentrations in sediment downstream of WWTPs in the studied rivers were significantly higher ($P < 0.05$) than those measured in upstream samples. This confirms the role of WWTPs as major input sources of PPCPs to freshwater sediments due to inefficient removal of these contaminants by traditional wastewater treatment processes.

Globally, the concentrations and profiles of 30 target PPCPs were measured and compared in sediment samples collected from rivers and freshwater lakes from 13 countries. Concentrations of Σ_{30}PPCPs in African sediment samples were significantly higher than those from other continents. The Klang River sediment in Malaysia had the highest Σ_{30}PPCPs concentration of (459 ng/g), while the Detriot River in the United States had the lowest concentration (159 ng/g). PPCPs profiles in sediment were correlated with their usage profiles in the studied countries, highlighting trends of extensive usage of antibiotics in Africa and Asia, as well as increasing consumption of anxiolytic drugs in Europe and North America to mitigate the negative impact of COVID-19 lockdown measures on mental health.

Overall, the results of this thesis provide important information on baseline concentrations of PPCPs in freshwater sediment from the UK and worldwide, as well as highlighting their potential risk to aquatic biota. While available literature focuses mainly on PPCPs in water, further research is required to fully understand the fate and risk of PPCPs in sediment.

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Abbreviations

AGC	Automated gain control
ANOVA	Analysis of Variance
AU	Arbitrary unit
BCFs	Bioconcentration factors
BUVSs	Benzotriazole ultraviolet stabilizers
CE	Collision energy
CTC	Chlortetracycline
CUR	Curtain gas
DEET	N, N-diethyltoluamide
DF	Detection frequency
DP	Declustering potential
DW	Dry weight
E1	Estrone
E2	17β-estradiol
EDCs	Endocrine-disruptive chemicals
EE2	17α-ethinylestradiol
EIC	Extracted ion chromatograms
EMA	European Medicines Agency
ESI	Electrospray ionisation
EU	European Union
FDA	Food and Drug Administration
FWHM	Full Width at Half Maximum
GC−MS	Gas Chromatography–mass spectrometry
HESI	Heated electrospray ionisation
HLB	Hydrophilic-Lipophilic Balance
HPLC-MS/MS	High Performance Liquid Chromatography Tandem Mass Spectrometry
HR	High Risk
HRMS	High Resolution Mass Spectrometry
HSD	Tukey's honestly significant difference
IDL	Instrument detection limit
IS	Internal standard
ISVF	IonSpray voltage floating
IT	Injection time
LOD	Limit of detection
LOQ	Limit of quantification
LR	Low Risk
MCX	Mixed-mode Cation- exchange
MEC	Measured Environmental Concentrations
MeOH	Methanol

MQL	Method quantification limits
MR	Medium Risk
MRL	Maximum residue limit
NSAIDs	Non-steroidal anti-inflammatory drugs
OTC	Oxytetracycline
PBT	Persistence, bioaccumulation and toxicity
PCPs	Personal Care Products
PEC	predicted environmental concentration
PLE	Pressurized liquid extraction
PNEC	Predicted No Effect Concentration
PPCPs	Pharmaceuticals and Personal Care Products
QA	Quality Assurance
QC	Quality control
QuEChERS	Quick, Easy, Cheap, Effective, Rugged, and Safe
RQs	Risk quotients
RRFs	Relative response factors
RRT	Relative retention time
RSD	Relative standard deviation
RT	Retention time
S:N	Signal to Noise
SPE	Solid Phase Extraction
SPM	Suspended particulate matte
STPs	Sewage treatment plants
TC	Tetracycline
UK	United Kingdom
UPLC	Ultra-Performance Liquid Chromatography
USEPA	United States Environmental Protection Agency
WFD	Water Framework Directive
WWTPs	Wastewater treatment plants

Chapter 1. Introduction and Literature Review

1.1. Introduction

In this era, natural resources are placed under huge stress due to several factors such as: population growth, urbanization, climate change and environmental pollution. In particular, global environmental pollution has received increasing scientific interest. This involves the study of various factors of the environmental fate and behaviour of different pollutants, their impact on the environment and biota, as well as possible methods for remediation to minimize the presence and impact of pollution.

Pharmaceutical and personal care products (PPCPs) constitute a major emerging contaminant group, currently raising concern among researchers, regulators and the general public. Pharmaceuticals comprise a large group of organic compounds widely used for the treatment of various diseases, improve the health and growth of livestock and aquaculture, personal healthcare and cosmetic purposes. This incorporates a diverse set of chemical compounds including antibiotics, hormones, antimicrobial agents, analgesics, anti-diabetics, illicit drugs, anti-depressants and anti-hypertensives (Ebele et al., 2017, Liu and Wong, 2013).

Personal care products (PCPs) are widely used by people to enhance the quality of their everyday life. For example, a study in California, found that 94-100% of people use shampoo at least monthly (Bennett et al., 2010). PCPs comprise a large and diverse series of chemicals, including disinfectants, fragrances, insect repellents, preservatives, and UV filters. These compounds are involved in a wide range of products, such as toothpastes, soaps, shampoo, cosmetics, deodorants, perfumes and sunscreens (Brausch and Rand, 2011, Jjemba, 2018). The yearly production of personal care products was estimated at about 1×10^6 tonnes worldwide (Richardson et al., 2005).

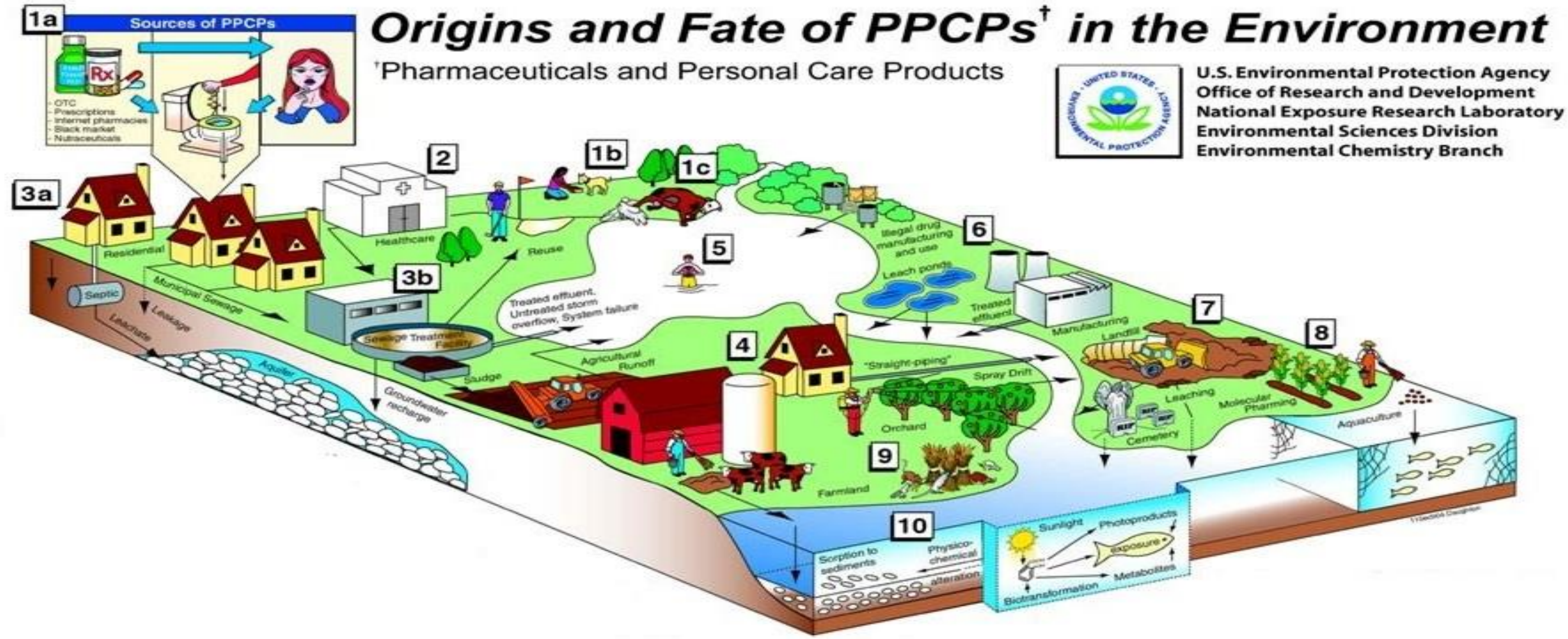
Daughton and Trenes suggested there may be as many as 6 million PPCPs commercially available worldwide with an annual increase of 3- 4% by weight per annum in 2004 (Daughton and Ternes, 1999). Nearly two million tonnes of pharmaceuticals were produced by China in 2011, estimated to represent 20% of the overall global production of PPCPs (Liu and Wong, 2013). In the UK, over 3000 active pharmaceutical substances are licensed for use, with acetaminophen (2000 tonnes/year), acetylsalicylic acid (770 tonnes/year) and metformin (106 tonnes/year) being the highest usage drugs, while a total of 170 pharmaceuticals are estimated to be used in excess of 1 tonnes per year (Ellis, 2008). Despite a large number of chemicals in this contaminant group, Alder et al. (2006)estimated that less than 50 PPCPs make up more than 95% of the total amount of active ingredient consumption in the UK. However, the pattern of PPCPs use varies substantially in different countries and overtime due to the introduction of new products in certain markets and other PPCPs may become less popular.

1.2. Sources of PPCPs to the environment

PPCPs reach the environment by multiple sources including: human and animal uses, agriculture and aquaculture applications, as well as the waste from pharmaceutical manufacturing factories. Among these sources, human and animal uses are the major sources of PPCPs to the environment because these chemicals are used considerably in medical treatment, health care and nutrition (Al-Farsi et al., 2017). For example, a report from the San Francisco Bay area, California showed that 45% of unused/expired pharmaceuticals were thrown in the toilet, whereas 28% of these pharmaceuticals were disposed of in the rubbish (Kreisberg and DC, 2007). Veterinary pharmaceuticals are applied in large doses for treatment of animals, therefor, these chemicals, or their metabolites, can be released to the environment in animal excreta or agricultural waste (Boxall et al., 2006). As reported by various studies, Sewage treatment plants (STPs) are major sources of PPCPs into the aqueous environment due to the inefficient/incomplete removal of these chemicals during the traditional water-treatment processes (Ort et al., 2010).

In general, PPCPs sources to the environment can be classified to point sources (e.g., disposal of effluents from sewer system to aquatic environment) and non-point sources (e.g., run-off from animal farming) (Richmond et al., 2017, Waghulkar, 2010). This has resulted in the ubiquitous distribution of PPCPs in all types of environmental waters, such as freshwater, seawater, wastewater, ground water, rainwater and sometimes in drinking water. They have also been detected in fish, soil, and sediments (Wilkinson et al., 2016, Yang et al., 2017). Figure 1-1 provides a summary of the sources and fate of PPCPs in the environment.

Figure 1-1: Sources and Fate of PPCPs in Environment



Available: http://www.epa.gov/nerlesd1/chemistry/pharma/image/drawing.pdf

(1a) Human usage of PPCPs for medical treatment, cosmetics and health care, these chemicals reach the sewer system through human excretion or disposal of unused/outdated drugs. (1b) Usage by animals, followed by excretion, sweat and/or vomitus. (1c) Medicated dead animal remains. (2) Throwing of treated/untreated hospital and pharmacies wastes in local sewage systems. (3a) Underground leaching from discharge system or malfunctioning infrastructure. (3b) Surplus of untreated sewage spills during storm events and runoff. (4) Agricultural applications, use of biosolids as compost in earth, nutrition of animals or spray of trees by medicine. (5) Direct release by daily use of water, washing/bathing/swimming. (6) Drainage of pharmaceutical factories' waste to the surrounding environment. (7) Leaching of hazardous and medical wastes from landfills to groundwater. (8) Usage of nutrition and medicines in aquaculture. (9) Release of drugs also used for pest control in farmlands such as warfarin used as rat poison. (10) Transformation of PPCPs in the environment via metabolism, degradation and bioaccumulation.

1.3. Ecological risk of PPCPs

1.3.1. Persistence

The occurrence, behaviour, and fate of PPCPs in the environment are related to their physicochemical properties, which varies widely across this diverse group of chemical compounds (Snyder, 2008). As a result of their large-scale production and use, PPCPs continuously enter the environment and can cause adverse effects on aquatic and terrestrial organisms due to their inherent biological activity (Suárez et al., 2008). In general, the term “persistent chemicals" is used to describe synthetic organic chemicals stable in the environment for a long time as expressed by their long half-life in one or more environmental compartments (Loganathan and Lam, 2011). Few PPCPs (e.g., oxazepam) were reported to persist in the environment over long periods of time extending to decades (Klaminder et al., 2015). High concentrations of antibiotics and barbiturates were detected in a Danish landfill over a 45-year period (Kreisberg and DC, 2007). Walters et al. (2010) monitored the fate of 72 PPCPs over three years in mesocosms containing biosolids/soil mixtures in outdoor conditions. Results revealed that the half-life for azithromycin (408-990 d) carbamazepine (462-533 d), ciprofloxacin (1155-3466 d), doxycycline (533-578 d), 4-epitetracycline (630 d), gemfibrozil (224-231 d), norfloxacin (990-1386 d), tetracycline (578 d), and triclosan (182-193 d) were longer than expected from controlled laboratory studies. Nevertheless, most PPCPs are not inherently persistent due to relatively rapid biotic and abiotic degradation. Therefore, PPCPs are widely recognized as ***pseudo persistent*** compounds as a result of stable discharge of these chemicals into the environment (Ebele et al., 2017). This continuous discharge of PPCPs to the environment is caused mainly by their incomplete removal during sewage treatment processes resulting in their continuous occurrence and ubiquitous distribution in various environmental compartments (Chen et al., 2013).

1.3.2. Bioaccumulation

Most PPCPs are readily bioavailable by design, which contributes to their rapid uptake and possible bioaccumulation in biota (Harvey, 2010). Organic pollutants can raise concern over their persistence, bioaccumlation and toxicity criteria (PBT) (Richmond et al., 2017). PPCPs namely, diclofenac, naproxen, ibuprofen, ketoprofen, and carbamazepine have been detected in the plasma of fish exposed to wastewater in aquaria (Brozinski et al., 2013). Bioconcentration factors (BCFs), defined as the ratio of compound concentration in the body of the organism to its concentration in the surrounding environment, are generally used to express bioaccumulation of chemicals in biota (DeForest et al., 2007). In China, a study on the biological effects and bioaccumulation of several steroidal and phenolic PPCPs in effluent-exposed fish reported BCFs between 17 and 59, after 141 days of exposure (Liu et al., 2012). Another study conducted in the Philippines showed that eight Benzotriazole ultraviolet stabilizers (BUVSs) used in personal care products were bioaccumulating in fish up to a concentration of 34.2 ng g^{-1} lipid weight. A significant positive correlation was established between BUVSs concentrations and fish length and weight (Kim et al., 2011). Bioaccumulation of 11 psychoactive pharmaceuticals was tested in fish living in a stream exposed to wastewater effluent. Citalopram, Mianserin, Mirtazapine and Sertraline (*anti-depressants*) had bioaccumulation factors > 500, and therefore may be categorized as bioaccumulative compounds in the environment (Grabicova et al., 2017).

1.3.3. Toxicity and risk assessments of PPCPs

1.3.3.1. Toxicity

The environment has faced many assaults due to rapid advances in technology and medicinal chemistry that numerous chemical compounds enter the ecosystem and induce toxic effects on humans and other organisms. In spite of low concentrations of PPCPs ranging from few ng/L to µg/L, these concentrations may cause unwanted physiological effects on human health and wildlife (Archer et al., 2017). Exposure of organisms to PPCPs can cause acute and chronic toxicity. In addition, present sewage treatment plants are not designed for removing pharmaceuticals as typical water pollutants. Currently, scientific and public attention has increased for endocrine disrupting chemicals, especially, steroids and phenols because of their possible hazard on breed and evolution of exposed organisms (Liu et al., 2011). In a study in Dianchi Lake, China, phenolic endocrine disrupting chemicals (EDCs), namely, 4-tertoctylphenol, 4-cumylphenol, 4-nonlyphenol, and bisphenol A were detected in various tissues of wild fish species at concentrations of 4.6, 4.4, 18.9 and 83.5 ng/g dry weight (DW), respectively. Also, steroids, such as 17b-estradiol 17a-ethynylestradiol and estriol were measured at concentrations <11.3 ng/g DW. The results of the study revealed that the liver had the highest levels of steroids and phenols compared to muscles and gills (Liu et al., 2011).

Moreover, chronic exposure to PPCPs at environmental levels has raised concern over several other adverse effects. Feminization or masculinization in fish due to endocrine disrupting chemicals (EDCs) in the aquatic environment has been reported. An experimental study compared the quality of male gametes in intersex roach (Rutilus rutilus) obtained from a river contaminated with wastewater discharges to normal male roach gathered from a control site. Results revealed that relative fecundity (number of eggs per gramme of gonad weight) was dramatically reduced in wild female roach obtained from WWTP effluent-dominated streams, and the degree of feminization in intersex fish was negatively associated with male gamete quality (Jobling et al., 2002). Another study reported on reduced male sex characteristics and fertilisation success in Fathead Minnows (*Pimephales promelas*) exposed to EE2 (17α-ethynylestradiol) concentrations of 0.32 and 0.96 ng/L (Parrott and Blunt, 2005).

Also, long exposure to antibiotics can contribute to developing anti-microbial resistance (AMR) to these chemicals (Agunbiade and Moodley, 2016). Among the various groups of pharmaceuticals in the aquatic environment, antibiotics have found special interest as an environmental hazard because of the potential emergence of resistant bacteria strains (Liu and Wong, 2013). A clear example here is that during the past few years, the resistance to third-generation cephalosporins has dramatically increased in different bacterial strains such as *Escherichia coli* and *Klebsiella pneumoniae* (Carlet et al., 2012). Antibiotic resistance was indeed an element of the modern era as early as the 1940s. In 1941, the first people were administered penicillin. In 1942, microorganisms resistant to penicillin were discovered. Then it continues: methicillin was first produced in 1960. Methicillin resistance was first reported in 1961 (Landecker, 2016).

In addition to the abovementioned toxic implications associated directly with the pharmacological actions of a certain drug or group of drugs (*e.g., endocrine disruption associated with exposure to hormones*), there remains the less characterised risk of exposure to complex mixtures of PPCPs and/or their metabolites in non-target aquatic organisms with potential additive or synergistic effects. This raises concern over potentially considerable ecotoxic effects of PPCPs mixtures, even if individual PPCPs concentrations are too low to elicit significant toxic effects. To illustrate, Cleuvers (2003) reported that carbamazepine (anti-epileptic) and clofibric acid (anti-hyperlipidemic agent) showed far greater effects on Daphnia magna than individual substances at the same dosage, despite belonging to different therapeutic groups.

Overall, risks of PPCPs in the environment extend beyond acute toxicity induced by individual therapeutic agents to include induction of aberrant biological mechanisms, reproductive impairment, higher cancer rates, the creation of antibiotic-resistant microorganisms, and the possibility for enhanced toxicities when complex PPCPs mixtures exist. (Richardson et al., 2005)

1.3.3.2. Risk assessments

The risk quotient (RQ) approach is largely adopted for assessment of the potential risks of various chemical contaminants in the environment and has widely been applied to different PPCPs chemicals and groups. The human health risk assessment and ecotoxicological risk assessment characterize possible risks to human health and the environment (Lin et al., 2016). Table 1.1 shows risk quotients (RQs) for selected PPCPs in the freshwater aquatic environment. One of the most used guidelines for risk assessment of PPCPs in recent years is the European Medicines Agency (EMA) guideline. This guideline uses the ratio between predicted environmental concentration (PEC) or measured environmental concentration (MEC) and predicted no-effect concentrations (PNEC) to estimate the risk quotient (RQ) for a single compound or a group of chemicals. If the estimated RQ is higher than one, this indicates the investigated chemicals may cause harmful ecological effects(EM, 2006).

Briefly, the RQ for individual PPCPs can be calculated as follows:

$$\boldsymbol{RQ} = \frac{\textbf{PEC (or MEC)}}{\textbf{PNEC}} \textbf{.......................(1)}$$

PNEC is usually calculated from LC_{50} values (*the concentration that kills 50% of organisms*), divided by an arbitrarily defined constant (e.g., 100 or 1000), depending on the level of uncertainty about the system: the better the system is known, the smaller the magnitude of the constant. There are two main reasons for using the uncertainty constant. First, the acute LC_{50} dose is usually much higher than the effective concentrations in ecosystems. Second, it is unlikely that all sensitive species of the ecosystem would have an experimental LC_{50} value available (Nikinmaa, 2014)

More recently, an approach using measured environmental concentrations (MEC) of pollutants (*e.g. pharmaceuticals*), and their potential adverse effects on the aquatic ecosystems through predicted no effect concentration (PNEC) values was adopted to estimate combined risk quotients (RQ_{mix}) for the measured pharmaceutical mixtures as follows (Gosset et al., 2020) :

$$\boldsymbol{RQ_x} = \frac{\textbf{MEC}_x}{\textbf{PNEC}_x} \ldots\textit{(2)}$$

where RQ_x is the risk quotient for individual pollutant x.

$$\mathbf{RQ}_{\boldsymbol{mix\ x,y}} = \sum_{\boldsymbol{y=1}}^{\boldsymbol{n}} \frac{\mathbf{MEC}_{\boldsymbol{x,y}}}{\boldsymbol{PNEC}_{\boldsymbol{x,y}}} = \sum_{\boldsymbol{y=1}}^{\boldsymbol{n}} \boldsymbol{RQ}_{\boldsymbol{x,y}} \ldots (\mathbf{3})$$

where $\boldsymbol{RQ}_{\boldsymbol{mix\ x,y}}$ is the cumulative risk quotient for the pollutant mixture x,y.

Table 1.1Risk quotients (RQs) for selected PPCPs in the freshwater aquatic environment.

PPCPs	Location	Risk Quotient (RQ)			References
		Treated wastewater	Surface water	Groundwater	
Acetaminophen	India	9.17 HR*	9.63 HR	0.643 MR*	(Sengar and Vijayanandan, 2021)
	China	0.07 LR*			(Ren et al., 2021)
	USA		2.08HR		(Deo, 2014)
Amoxicillin	India	0.00358 LR			(Sengar and Vijayanandan, 2021)
	Kenyan		6.4 HR		(Kairigo et al., 2020)
Caffeine	India	5800 HR	4350 HR	42.5 HR	(Sengar and Vijayanandan, 2021)
	China	8.27 HR			(Ren et al., 2021)
	USA		1.45HR		(Deo, 2014)
Carbamazepine	Indian	0.9 MR	1.35 HR	0.124 MR	(Sengar and Vijayanandan, 2021)
	USA		0.14MR		(Deo, 2014)
Codeine	India	0.0145 LR	0.0183 LR		(Sengar and Vijayanandan, 2021)
	USA		0.34MR		(Deo, 2014)
DEET	India		0.0792 LR	0.00286 LR	(Sengar and Vijayanandan, 2021)
	China	0.12 MR			(Ren et al., 2021)
Diazepam	India	0.0595 LR	0.0763 LR		(Sengar and Vijayanandan, 2021)
	USA		<0.01 LR		(Deo, 2014)
Diclofenac	India	3.11 HR	0.0483	1.14 HR	(Sengar and Vijayanandan, 2021)
	Bengaluru, India		0.00046191 LR		(Gopal et al., 2021)
	USA		<0.01 LR		(Deo, 2014)
	Cau River, Vietnam		0.000097		(Ngo et al., 2021)
Doxycycline	Kenya		0.7 MR		(Kairigo et al., 2020)
Erythromycin	India	0.0177 LR			(Sengar and Vijayanandan, 2021)
Gabapentin	USA		<0.01 LR		(Deo, 2014)

PPCPs	Location	Risk Quotient (RQ)			References
		Treated wastewater	Surface water	Groundwater	
Gemfibrozil	USA		0.09 LR		(Deo, 2014)
Hydrocodone	USA		<0.01 LR		(Deo, 2014)
Ibuprofen	India	0.527 MR	0.0534	0.00469	(Sengar and Vijayanandan, 2021)
	Bengaluru, India		0.000456887 LR		(Gopal et al., 2021)
	USA		0.06 LR		(Deo, 2014)
Metformin	USA		<0.01 LR		(Deo, 2014)
Metoprolol	India	128 HR	0.946 MR	0.0122	(Sengar and Vijayanandan, 2021)
	USA		<0.01 LR		(Deo, 2014)
Naproxen	India	1.1 HR	0.0275	0.00054	(Sengar and Vijayanandan, 2021)
	USA		<0.01 LR		(Deo, 2014)
	Taihu lake, China		<0.01 LR		(Li et al., 2021a)
Propranolol	India	0.0226 LR	0.00696 LR		(Sengar and Vijayanandan, 2021)
	USA		<0.01 LR		(Deo, 2014)
Sulfamethoxazole	India	4.62HR	12.9 HR	0.293 MR	(Sengar and Vijayanandan, 2021)
	China	0.02 LR			(Ren et al., 2021)
	Cau River, Vietnam		2.469		(Ngo et al., 2021)
	Kenya		3.53 HR		(Kairigo et al., 2020)
	Taihu lake, China		>1 HR		(Li et al., 2021a)
Trimethoprim	India	6.29HR	10.8HR	0.0786 LR	(Sengar and Vijayanandan, 2021)
	Cau River, Vietnam		0.00005		(Ngo et al., 2021)
	Kenya		1 HR		(Kairigo et al., 2020)
	USA		0.04 LR		(Deo, 2014)

* HR: High Risk, MR: Medium Risk, LR: Low Risk

1.4. PPCPs in the freshwater aquatic environment

Several research studies, review articles and theses have reported on the concentrations and associated risk of various PPCPs in water from freshwater lakes, rivers, boreholes, drinking water and groundwater from various parts of the world including the UK (Ebele et al., 2017, Katsikaros and Chrysikopoulos, 2021, Sengar and Vijayanandan, 2021, Mojiri et al., 2021). Therefore, the current thesis will focus mainly on PPCPs in freshwater sediment.

1.4.1. PPCPs in Sediments

Sediments are reported to receive nearly 70% of therapeutic and subtherapeutic agents used for treatment in aquacultures (Jjemba, 2018). Moreover, wastewater discharge to rivers, lakes, canals and reservoirs is considered one of the main sources of PPCPs in freshwater sediments (Clara et al., 2004). According to Yang, et al., (2015), three PPCPs abundant in sediment samples collected from nine sites along the Alafia River in Florida, USA, were carbamazepine, trimethoprim, and pseudoephedrine, with detection frequencies of 100%, 89% and 63% in the studies samples, respectively. In Scotland, some pharmaceuticals, namely, atenolol, citalopram, carbamazepine, and ibuprofen were detected in sewage sludge from 3 wastwater treatment plants located in Western , Central and Eastern Scotland , as well as freshwater sediments collected upstream and downstream of the three locations (Langford et al., 2011). In New Zealand, 21 pharmaceuticals were detected in estuarine sediments with total concentrations ranging between 0.61 and 7.66 ng/g (Stewart et al., 2014).

1.4.1.1. Personal care products

Triclocarban and triclosan (*anti-septic agents*) were frequently detected in sediment samples from different countries around the world. Triclocarban was detected at 510 ng/g in sediments from Lake Michigan, US (Blair et al., 2013). A similar study in Minnesota, the US reported average concentrations of triclocarban and triclosan in sediments collected near wastewater treatment plants at 822 and 85 ng/g, respectively. This study also reported that concentrations of triclocarban and triclosan were significantly higher downstream than upstream of the studied wastewater treatment plants (Klosterhaus et al., 2013). Others studies in China freshwater sediment reported average levels of triclocarban, 7.4, 54.3, 4330 and 400 ng/g and triclosan, 0.1, 3.67, 689 and 39 ng/g in Pearl river (Xie et al., 2019b), Yangtze river (Liu et al., 2015), urban rivers (Peng et al., 2017), and Songhua Catchment (Li et al., 2021b), respectively.

In San Francisco, CA, the maximum concentration of DEET (*insect-repellent*) in San Francisco Bay sediment was 3.4 ng/g dw (Klosterhaus et al., 2013). Nakata et al. (2009) detected UV-320 (0.3- 14 ng/g dw), UV-326 (1.5-200 ng/g dw), UV-327(1.6-190 ng/g dw) and UV328(2.6-320 ng/g dw) in sediments from the Ariake sea estuary, Japan. Table 1.2 provides an overview of PCPs concentrations reported in river sediments worldwide.

Table 1.2 Average concentrations (n/g) of personal care products in freshwater sediments worldwide.

PPCPs	Location	concentration (ng/g)	Reference
2-Ethylhexyl 4-methoxycinnamate	Songhua Catchment, Northeast China	5.2	(Li et al., 2021b)
2-Hydroxy-4-methoxybenzophenone	Songhua Catchment, Northeast China	6.2	(Li et al., 2021b)
Avobenzone	Songhua Catchment, Northeast China	3.2	(Li et al., 2021b)
Benzophenone-3	Canal of Lahore, Pakistan	44	(Ashfaq et al., 2019)
Benzyl paraben	Canal of Lahore, Pakistan	3.8	(Ashfaq et al., 2019)
DEET	San Francisco Bay, CA, USA	3.4	(Klosterhaus et al., 2013)
Ethyl paraben EtP	Songhua Catchment, Northeast China	1.2	(Li et al., 2021b)
Galaxolide	Songhua Catchment, Northeast China	23	(Li et al., 2021b)
Galaxolide (HHCB)	Urban rivers, Guangzhou, China	1480	(Peng et al., 2017)
Linear alkylbenzene sulfonate-C10	Songhua Catchment, Northeast China	250	(Li et al., 2021b)
Linear alkylbenzene sulfonate-C11	Songhua Catchment, Northeast China	660	(Li et al., 2021b)
Linear alkylbenzene sulfonate-C12	Songhua Catchment, Northeast China	700	(Li et al., 2021b)
Linear alkylbenzene sulfonate-C13	Songhua Catchment, Northeast China	1200	(Li et al., 2021b)
Methyl paraben	Canal of Lahore, Pakistan	7.4	(Ashfaq et al., 2019)
	Songhua Catchment, Northeast China	110	(Li et al., 2021b)
	Jilin Songhua River (Northeast China)	40.4	(He et al., 2018)
	Turia river and Albufera lake, Spain	19	(Sadutto et al., 2021)
Musk ketone	Urban rivers, Guangzhou, China	0.79	(Peng et al., 2017)
Musk xylene	Urban rivers, Guangzhou, China	376	(Peng et al., 2017)
Octocrylene	Canal of Lahore, Pakistan	21	(Ashfaq et al., 2019)
	Songhua Catchment, Northeast China	51	(Li et al., 2021b)
Propyl paraben	Canal of Lahore, Pakistan	5.8	(Ashfaq et al., 2019)
	Songhua Catchment, Northeast China	45	(Li et al., 2021b)
	Turia river and Albufera lake, Spain	12	(Sadutto et al., 2021)

PPCPs	Location	concentration (ng/g)	Reference
Tonalide (AHTN)	Urban rivers, Guangzhou, China	235	(Peng et al., 2017)
Triclocarban	San Francisco Bay, CA, USA	32.7	(Klosterhaus et al., 2013)
	Upstream and downstream rivers from western, central and eastern Scotland.	138.8	(Langford et al., 2011)
	Pearl river delta, China.	7.4	(Xie et al., 2019)
	Yangtze River, China.	54.3	(Liu et al., 2015)
	Turia river and Albufera lake, Spain.	15	(Sadutto et al., 2021)
	Urban rivers, Guangzhou, China.	3440	(Peng et al., 2017)
	Songhua Catchment, Northeast China.	400	(Li et al., 2021b)
	Iberian rivers, in Spain.	45	(Gorga et al., 2015)
	Rivers (Mississippi, Sauk, South Fork of the Crow, and Grindstone), creeks (Center, Okabena) and lakes (Pepin, Superior, Shagawa).	822	(Venkatesan et al., 2012)
Triclosan	13 estuarine sites around Auckland, New Zealand	Below LOQ	(Stewart et al., 2014)
	29 sites along the Kaveri, Vellar and Tamiraparani rivers and the Pichavaram mangrove, India.	85.3, 46.87 and 32.1	(Ramaswamy et al., 2011)
	Upstream and downstream rivers from western, central and eastern Scotland.	<2	(Langford et al., 2011)
	Pearl river delta, China.	0.1	(Xie et al., 2019)
	Jilin Songhua River (Northeast China).	2.1	(He et al., 2018)
	Turia river and Albufera lake, Spain.	18	(Sadutto et al., 2021)
	Yangtze River, China.	3.67	(Liu et al., 2015)
	Urban rivers, Guangzhou, China.	689	(Peng et al., 2017)
	Songhua Catchment, Northeast China.	39	(Li et al., 2021b)
	Iberian rivers, in Spain.	783	(Gorga et al., 2015)
	Rivers (Mississippi, Sauk, South Fork of the Crow, and Grindstone), creeks (Center, Okabena) and lakes (Pepin, Superior, Shagawa).	85	(Venkatesan et al., 2012)

1.4.1.2. Antibiotics

Since the last century, antibiotics have been widely applied to improve human and animal health. Table 1.3 provides a summary of the reported antibiotic concentrations in freshwater sediments worldwide. According to Chen et al., (2015) nearly 210,000 tons of antibiotics are produced annually in the world. In the United States, the production of antibiotics used for farming was 9200 tons in 2003 (Hu et al., 2010). Chen et al. (2015) studied antibiotics in the coastal environment of the Hailing Bay region, South China. The results revealed 15 antibiotics in the sediment samples, ranging from 1.95 ng/g for ciprofloxacin to 184 ng/g for chlortetracycline. In Baiyangdian Lake, China, Li et al. (2012a) analyzed 132 sediment samples for 22 antibiotics, the maximum concentrations of the four most frequently detected antibiotics were 1140, 46, 362 and 302 ng/g for norfloxacin, ciprofloxacin, ofloxacin, and roxithromycin, respectively Figure 1-2.

Additionally, in the same country, the maximum concentrations of six antibiotics detected in the Hai River sediments, namely, oxytetracycline and tetracycline, norfloxacin, ofloxacin, ciprofloxacin, and lomefloxacin, were 422, 135, 5770, 653, 1290 and 298 ng/g, respectively (Zhou et al., 2011). In the Pearl River, China, Yang et al. (2010) identified sulfadiazine (83.9ng/g), sulfamethazine (248 ng/g), oxytetracycline (99.9 ng/g), tetracycline (72.6 ng/g), norfloxacin (403 ng/g), ofloxacin (1560 ng/g), ciprofloxacin (143 ng/g), erythromycin (385 ng/g) and roxithromycin (122 ng/g) in sediments.

In studies carried out by (Xu et al., 2014) (Xie et al., 2015, Zhou et al., 2016) (Xie et al., 2017) and (Li et al., 2021a) in Taihu lake, China, roxithromycin was measured in sediments at concentration of 45.2, 42.8, 3.56, 26 and 3.96 ng/g, respectively. In the same lake, ofloxacin was reported in sediments at concentrations of 52.8, 12.2 51 and 18.27 ng/g in 2014, 2106, 2017 and 2021, respectively Figure 1-3. In the Pearl river, China, according to (Yang et al., 2010), (Liang et al., 2013) and (Xie et al., 2019), several antibiotics were detected in sediments at concentration ranges of 72.5-1560, 1.43-14 and 0.09-9.3 ng/g respectively Figure 1-4.

In Northern New Jersey, Gibs et al. (2013) reported the maximum concentration of azithromycin, ciprofloxacin, ofloxacin, and trimethoprim were 44, 10, 21 and 11 ng/g, respectively, in sediment samples from a stream receiving two wastewater treatment plant effluents. In Florida, USA, trimethoprim was also detected in the range of 0.01–0.83 ng/g in sediment samples from an urban river (Yang et al., 2015).

Figure 1-2: Concentrations (ng/g) of antibiotics: erythromycin, ofloxacin, sulfadiazine, sulfamethazine and sulfamethoxazole in Baiyangdian lake sediment, China in 2012 and 2018

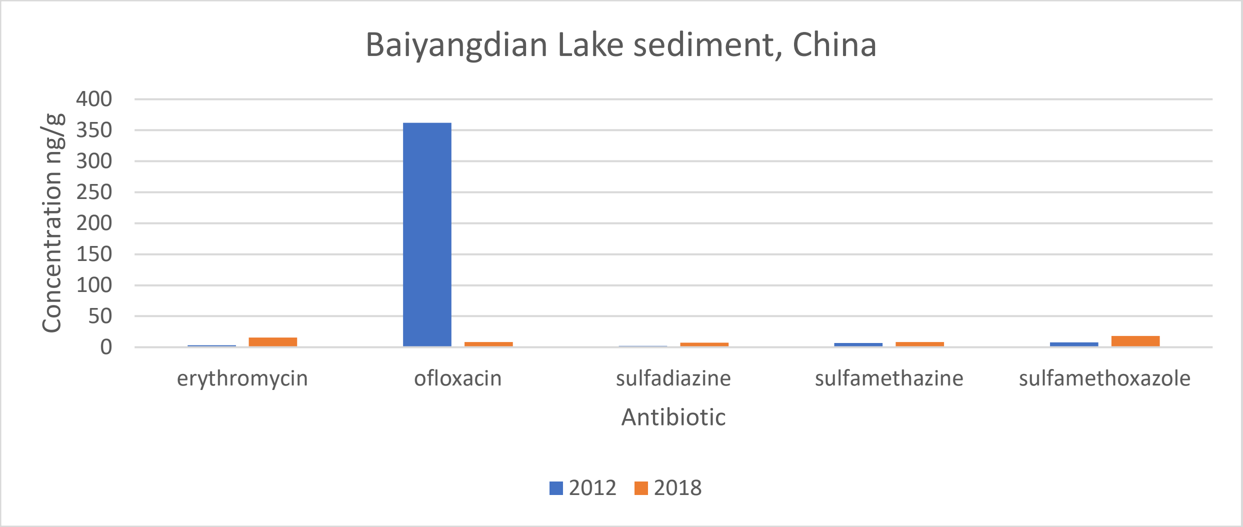


Figure 1-3: Average concentrations (ng/g) of 11 of antibiotics in Taihu lake sediment, China in 2014, 2015, 2016, 2017 and 2021.

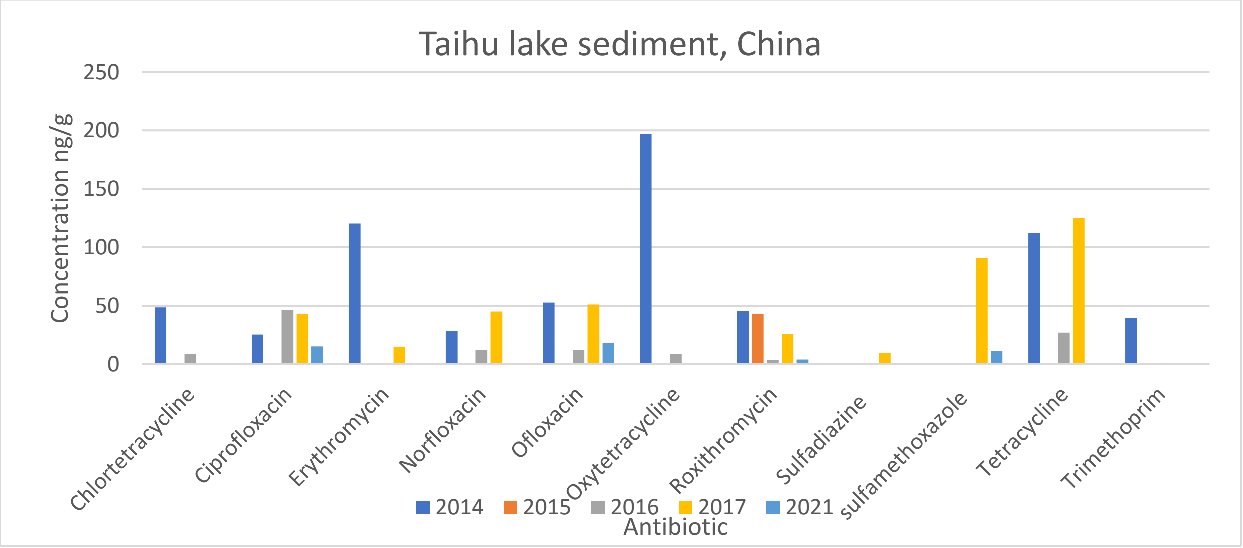


Figure 1-4: Average concentrations (ng/g) of 7 of antibiotics in Pearl River sediment, China in 2010, 2013, and 2019.

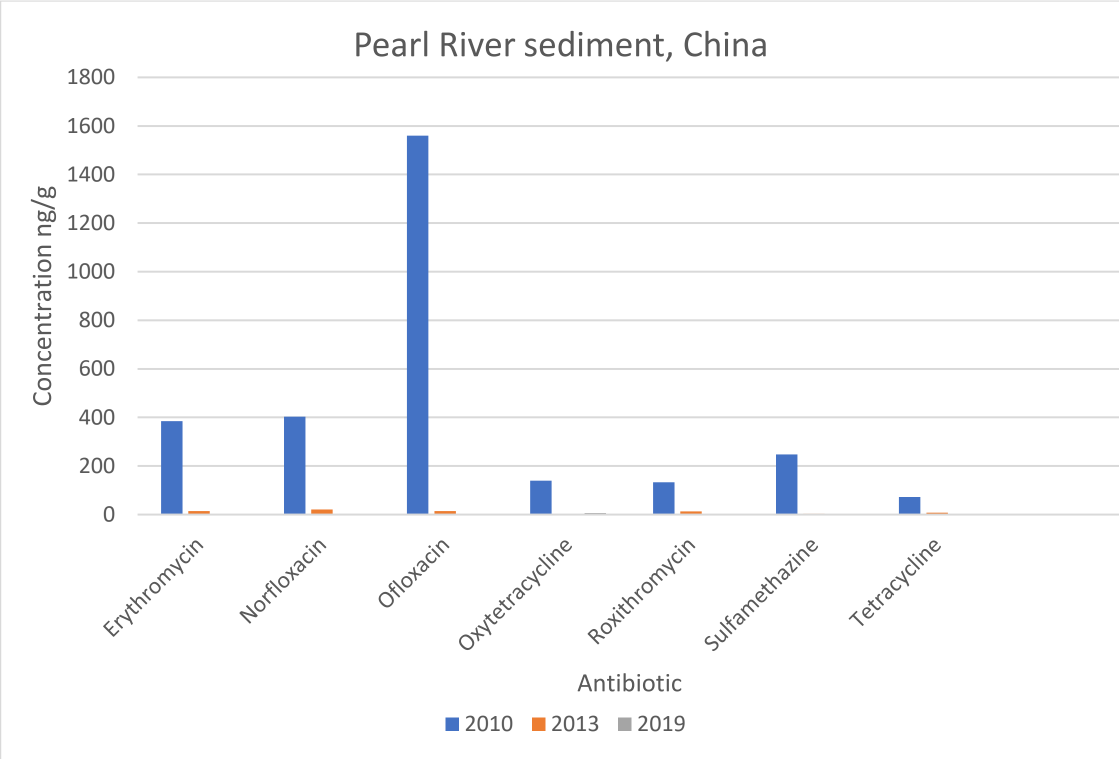


Table 1.3 Average concentrations of Antibiotics in freshwater sediments worldwide.

Antibiotics	Location	Concentration (ng/g)	Reference
Amoxicillin	Mwania river, Kenyan	4.6	(Kairigo et al., 2020)
	Chania river**,** Kenyan	43.8	
	Kanyuru river**,** Kenyan	11.7	
Ampicillin	Umgeni River, South Africa	369	(Agunbiade and Moodley, 2016)
Azithromycin	Iberian Rivers, Spain	24	(Osorio et al., 2016a)
	Northern New Jersey stream	44	(Gibs et al., 2013)
	Lake and rivers of Baiyangdian, China	38	(Zhang et al., 2018)
	Yongjiang River, china	0.79	(Xue et al., 2013)
Cefotaxime sodium	Pearl river delta, China	0.08	(Xie et al., 2019)
Chloramphenicol	Huangpu River, Shanghai, China	0.7	(Chen and Zhou, 2014)

	Turia river and Albufera lake, Spain	4	(Sadutto et al., 2021)
Chlorltetracycline	Lake and rivers of Baiyangdian, China	10	(Zhang et al., 2018)
	Huangpu River, Shanghai, China	6	(Chen and Zhou, 2014)
	Lake Taihu, China	9	(Zhou et al., 2016)
	Taihu Lake, China	48.5	(Xu et al., 2014)
Ciprofloxacin	Umgeni River, South Africa	183	(Agunbiade and Moodley, 2016)
	Northern New Jersey stream	10	(Gibs et al., 2013)
	Taihu lake, China	15	(Li et al., 2021a)
	Lake Taihu, China	46.5	(Zhou et al., 2016)
	Taihu Lake, China	25	(Xu et al., 2014)
	Jilin Songhua River (Northeast China)	53.5	(He et al., 2018)
	Mwania river, Kenyan	29	(Kairigo et al., 2020)
	Chania river, Kenyan	35	
	Canal of Lahore, Pakistan	13	(Ashfaq et al., 2019)
	Pearl river delta, China	0.2	(Xie et al., 2019)
	Baiyangdian Lake in North China	46	(Li et al., 2012)
	Taihu lake, China	43	(Xie et al., 2017)
	Yellow River Delta, China	94	(Zhao et al., 2016)
	Pearl Rivers in Guangdong Province, China.	197	(Yang et al., 2010)
Clarithromycin	Iberian Rivers, Spain	13	(Osorio et al., 2016a)
	Pearl river delta, China	0.6	(Xie et al., 2019)
	Yongjiang River, china	0.89	(Xue et al., 2013)
Danofloxacin	Lake Taihu, China	34	(Zhou et al., 2016)
Difloxacin	Lake Taihu, China	79	(Zhou et al., 2016)
Doxycycline	Lake and rivers of Baiyangdian, China	12	(Zhang et al., 2018)
	Lake Taihu, China	17	(Zhou et al., 2016)
	Jilin Songhua River (Northeast China)	9	(He et al., 2018)

	Huangpu River, Shanghai, China	21	(Chen and Zhou, 2014)
Enrofloxacin	Huangpu River, Shanghai, China	9	(Chen and Zhou, 2014)
	Lake Taihu, China	117	(Zhou et al., 2016)
	Jilin Songhua River (Northeast China)	47	(He et al., 2018)
	Pearl River Estuary, South China	1.5	(Liang et al., 2013)
	Baiyangdian Lake in North China	13	(Li et al., 2012)
	Yellow River Delta, China	29.5	(Zhao et al., 2016)
Erythromycin-H2O	Jilin Songhua River (Northeast China)	64	(He et al., 2018)
	Iberian Rivers, Spain	1	(Osorio et al., 2016a)
	Huangpu River, Shanghai, China	24.5	(Chen and Zhou, 2014)
	Lake and rivers of Baiyangdian, China	15.5	(Zhang et al., 2018)
	Pearl River Estuary, South China	14	(Liang et al., 2013)
	Taihu Lake, China	0.78	(Xie et al., 2015)
	Yellow River Delta, China	14	(Zhao et al., 2016)
	Taihu lake, China	15	(Xie et al., 2017)
	Baiyangdian Lake in North China	3	(Li et al., 2012)
	San Francisco Bay, CA, USA	3.5	(Klosterhaus et al., 2013)
	Pearl river delta, China	0.1	(Xie et al., 2019)
	Pearl Rivers in Guangdong Province, China.	385	(Yang et al., 2010)
	Taihu Lake, China	120	(Xu et al., 2014)
	Danube River and tributaries in Serbia	9	(Radović et al., 2015)
	Yongjiang River, china	2.5	(Xue et al., 2013)
Fleroxacin	Lake Taihu, China	13	(Zhou et al., 2016)
	Baiyangdian Lake in North China	7	(Li et al., 2012)
Florfenicol	Huangpu River, Shanghai, China	1	(Chen and Zhou, 2014)

	Jilin Songhua River (Northeast China)	20.5	(He et al., 2018)
Flumequine	Pearl river delta, China	0.1	(Xie et al., 2019)
Isochlortetracycline	Pearl river delta, China	0.02	(Xie et al., 2019)
Lincomycin	Lake and rivers of Baiyangdian, China	16	(Zhang et al., 2018)
Lomefloxacin	Lake Taihu, China	11	(Zhou et al., 2016)
	Baiyangdian Lake in North China	29	(Li et al., 2012)
Metronidazole	Umgeni River, South Africa	125	(Matongo et al., 2015)
Nalidixic acid	Umgeni River, South Africa	455	(Agunbiade and Moodley, 2016)
Narasin	Lake Taihu, China	9	(Zhou et al., 2016)
Norfloxacin	Pearl river delta, China	2	(Xie et al., 2019)
	Pearl Rivers in Guangdong Province, China.	403	(Yang et al., 2010)
	Lake Taihu, China	12	(Zhou et al., 2016)
	Taihu Lake, China	28.5	(Xu et al., 2014)
	Jilin Songhua River (Northeast China)	10.5	(He et al., 2018)
	Pearl River Estuary, South China	20.5	(Liang et al., 2013)
	Baiyangdian Lake in North China	1140	(Li et al., 2012)
	Taihu lake, China	45	(Xie et al., 2017)
	Yellow River Delta, China	105	(Zhao et al., 2016)
Ofloxacin	Northern New Jersey stream	9.9	(Gibs et al., 2013)
	Pearl River in Guangdong, China.	1560	(Yang et al., 2010)
	Taihu lake, China	18	(Li et al., 2021a)
	Huangpu River, Shanghai, China	12.5	(Chen and Zhou, 2014)
	Lake and rivers of Baiyangdian, China	8.5	(Zhang et al., 2018)
	Lake Taihu, China	12	(Zhou et al., 2016)
	Taihu Lake, China	53	(Xu et al., 2014)
	Jilin Songhua River (Northeast China)	17	(He et al., 2018)

	Pearl River Estuary, South China	14	(Liang et al., 2013)
	Canal of Lahore, Pakistan	4.5	(Ashfaq et al., 2019)
	Baiyangdian Lake in North China	362	(Li et al., 2012)
	Pearl river delta, China	0.5	(Xie et al., 2019)
	Taihu lake, China	51	(Xie et al., 2017)
	Yellow River Delta, China	50	(Zhao et al., 2016)
Oxytetracycline	Pearl River in Guangdong, China.	139	(Yang et al., 2010)
	Huangpu River, Shanghai, China	18.5	(Chen and Zhou, 2014)
	Lake and rivers of Baiyangdian, China	13.5	(Zhang et al., 2018)
	Lake Taihu, China	9	(Zhou et al., 2016)
	Taihu Lake, China	196.5	(Xu et al., 2014)
	Canal of Lahore, Pakistan	6.8	(Ashfaq et al., 2019)
	Pearl river delta, China	5.9	(Xie et al., 2019)
	Yellow River Delta, China	11.5	(Zhao et al., 2016)
Pefloxacin	Lake Taihu, China	9	(Zhou et al., 2016)
Roxithromycin	Pearl River in Guangdong, China.	133	(Yang et al., 2010)
	Huangpu River, Shanghai, China	4	(Chen and Zhou, 2014)
	Lake Taihu, China	3.5	(Zhou et al., 2016)
	Taihu Lake, China	45	(Xu et al., 2014)
	Pearl River Estuary, South China	13.5	(Liang et al., 2013)
	Pearl river delta, China	1	(Xie et al., 2019)
	Taihu lake, China	3.96	(Li et al., 2021a)
	Yellow River Delta, China	7.5	(Zhao et al., 2016)
	Yongjiang River, china	2	(Xue et al., 2013)
	Taihu lake, China	26	(Xie et al., 2017)
	Taihu Lake, China	43	(Xie et al., 2015)
	Baiyangdian Lake in North China	302	(Li et al., 2012)
Sarafloxacin	Lake Taihu, China	15.5	(Zhou et al., 2016)

Spectinomycin	Pearl river delta, China	9.5	(Xie et al., 2019)
Sulfacetamide	Yongjiang River, china	0.5	(Xue et al., 2013)
Sulfadiazine	Pearl Rivers in Guangdong Province, China.	84	(Yang et al., 2010)
	Huangpu River, Shanghai, China	0.7	(Chen and Zhou, 2014)
	Lake and rivers of Baiyangdian, China	7.5	(Zhang et al., 2018)
	Baiyangdian Lake in North China	2	(Li et al., 2012)
	Taihu lake, China	0.41	(Li et al., 2021a)
	Taihu lake, China	9.6	(Xie et al., 2017)
	Yongjiang River, china	0.07	(Xue et al., 2013)
Sulfadimethoxine	Canal of Lahore, Pakistan	3.5	(Ashfaq et al., 2019)
	Baiyangdian Lake in North China	0.20	(Li et al., 2012)
Sulfadimidine	Yongjiang River, china	0.81	(Xue et al., 2013)
Sulfadoxine	Lake Taihu, China	0.59	(Zhou et al., 2016)
Sulfamerazine	Huangpu River, Shanghai, China	0.8	(Chen and Zhou, 2014)
	Baiyangdian Lake in North China	2.47	(Li et al., 2012)
	Taihu lake, China	20	(Xie et al., 2017)
Sulfameter	Canal of Lahore, Pakistan	5.6	(Ashfaq et al., 2019)
Sulfamethazine	Pearl Rivers in Guangdong Province, China.	248	(Yang et al., 2010)
	Huangpu River, Shanghai, China	2.7	(Chen and Zhou, 2014)
	Lake and rivers of Baiyangdian, China	8.17	(Zhang et al., 2018)
	Pearl River Estuary, South China	3.24	(Liang et al., 2013)
	Canal of Lahore, Pakistan	3.1	(Ashfaq et al., 2019)
	Baiyangdian Lake in North China	6.92	(Li et al., 2012)
Sulfamethoxazole	Iberian Rivers, Spain	0.26	(Osorio et al., 2016a)
	San Francisco Bay, CA, USA	0.7	(Klosterhaus et al., 2013)

	Huangpu River, Shanghai, China	0.6	(Chen and Zhou, 2014)
	Lake and rivers of Baiyangdian, China	7.3	(Zhang et al., 2018)
	Canal of Lahore, Pakistan	8.9	(Ashfaq et al., 2019)
	Baiyangdian Lake in North China	7.86	(Li et al., 2012)
	Taihu lake, China	91	(Xie et al., 2017)
	Yongjiang River, china	0.2	(Xue et al., 2013)
	Taihu lake, China	11.3	(Li et al., 2021a)
Sulfamonomethoxine	Baiyangdian Lake in North China	0.50	(Li et al., 2012)
Sulfapyridine	Huangpu River, Shanghai, China	6.6	(Chen and Zhou, 2014)
Sulfapyridine SPD	Baiyangdian Lake in North China	1.40	(Li et al., 2012)
Sulfaquinoxaline	Huangpu River, Shanghai, China	0.9	(Chen and Zhou, 2014)
Sulfathiazole	Huangpu River, Shanghai, China	0.6	(Chen and Zhou, 2014)
	Baiyangdian Lake in North China	6	(Li et al., 2012)
	Baiyangdian Lake in North China	1.71	(Li et al., 2012)
Sulphachloropyridazine	Taihu Lake, China	15.8	(Xu et al., 2014)
Sulphadimethoxine	Taihu Lake, China	15.7	(Xu et al., 2014)
Sulphamethazine	Taihu Lake, China	100	(Xu et al., 2014)
Sulphamethoxazole	Taihu Lake, China	49.5	(Xu et al., 2014)
Sulphathiazole	Taihu Lake, China	51.5	(Xu et al., 2014)
	Taihu Lake, China	22.5	(Xu et al., 2014)
Tetracycline	Iberian Rivers, Spain	6	(Osorio et al., 2016a)
	Pearl river delta, China	1.5	(Xie et al., 2019)
	Pearl Rivers in Guangdong Province, China.	72.5	(Yang et al., 2010)
	Huangpu River, Shanghai, China	21.5	(Chen and Zhou, 2014)
	Lake and rivers of Baiyangdian, China	10.37	(Zhang et al., 2018)
	Lake Taihu, China	27	(Zhou et al., 2016)
	Taihu Lake, China	112.2	(Xu et al., 2014)

	Pearl River Estuary, South China	7.13	(Liang et al., 2013)
	Canal of Lahore, Pakistan	5.9	(Ashfaq et al., 2019)
	Yellow River Delta, China	26.78	(Zhao et al., 2016)
	Taihu lake, China	125	(Xie et al., 2017)
Thiamphenicol	Turia river and Albufera lake, Spain	14	(Sadutto et al., 2021)
	Huangpu River, Shanghai, China	1.3	(Chen and Zhou, 2014)
Trimethoprim	San Francisco Bay, CA, USA	18.2	(Klosterhaus et al., 2013)
	Northern New Jersey stream	11	(Gibs et al., 2013)
	Umgeni River, South Africa	87.55 ± 4.88	(Matongo et al., 2015)
	Urban river in Florida, USA	0.01–0.83	(Yang et al., 2015)
	Pearl river delta, China	0.2	(Xie et al., 2019)
	Lake and rivers of Baiyangdian, China	7.26	(Zhang et al., 2018)
	Lake Taihu, China	1.09	(Zhou et al., 2016)
	Taihu Lake, China	39.3	(Xu et al., 2014)
	Yongjiang River, china	1.07	(Xue et al., 2013)
Tylosin	Lake and rivers of Baiyangdian, China	29.09	(Zhang et al., 2018)

1.4.1.3. Steroid hormones

One of the main source of estrogens and estrogen-sulfates in the environment is animal manure used in agriculture (Goeppert et al., 2014). Nowadays, many studies have reported estrone (*E1, natural hormone*), 17β-estradiol (*E2, natural hormone*) and 17α-ethinylestradiol (*EE2, synthetic hormone*) as aquatic pollutants globally (Green et al., 2013).

A study in Auckland, New Zealand reported maximum concentrations of 17α-ethinylestradiol, 17β-estradiol and estrone in the estuarine sediment at 1.8, 1.0 and 2.2 ng/g, respectively (Stewart et al., 2014). Estrone was reported in other studies at concentrations of 71, 24.4, 492.5, 9.1, 114.8 and 181.4 ng/g in sediment from Spanish Iberian rivers (Gorga et al., 2015), Brazilian coast (Froehner et al., 2012), Jilin Songhua River, China (He et al., 2018), Three Gorges Reservoir Region, China (Wang et al., 2016), Dianchi Lake, China (Huang et al., 2013) and Erhai Lake,China (Shen et al., 2020), respectively. A summary of steroid hormones concentrations reported in freshwater sediments worldwide is provided in Table 1.4.

Table 1.4 Average concentrations of steroid hormones in freshwater sediments worldwide.

Hormones	Location	Concentration (ng/g)	Reference
17α-estradiol	Erhai Lake, a Typical Plateau Lake of China	18	(Shen et al., 2020)
	Three Gorges Reservoir Region, China	17	(Wang et al., 2016)
17α-ethinyl estradiol	Three Gorges Reservoir Region, China	17	(Wang et al., 2016)
	Brazilian coast	130	(Froehner et al., 2012)
	13 estuarine sites around Auckland, New Zealand	1.8	(Stewart et al., 2014)
	Taihu lake, China	8.3	(Xie et al., 2017)
	Dianchi Lake, the southwest of China	21.2	(Huang et al., 2013)
	Taihu Lake, China	15.1	(Xie et al., 2015)
	Luoma Lake, China	1.5	(Liu et al., 2017)
	Erhai Lake, a Typical Plateau Lake of China	26.3	(Shen et al., 2020)
	Iberian rivers, in Spain	7.1	(Gorga et al., 2015)
17-β-estradiol	Brazilian coast	49.3	(Froehner et al., 2012)
	Taihu lake, China	9.2	(Xie et al., 2017)

	13 estuarine sites around Auckland, New Zealand	0.5 to 1.0	(Stewart et al., 2014)
	Luoma Lake, China	1.21	(Liu et al., 2017)
	Taihu Lake, China	12.61	(Xie et al., 2015)
	Erhai Lake, a Typical Plateau Lake of China	79.3	(Shen et al., 2020)
	Three Gorges Reservoir Regions, China	9.5	(Wang et al., 2016)
Diethylstilbestrol	Luoma Lake, China	0.6	(Liu et al., 2017)
	Iberian rivers, in Spain	4.2	(Gorga et al., 2015)
Estradiol 17-glucuronide (E2-17G)	Iberian rivers, in Spain	14	(Gorga et al., 2015)
Estradiol	Iberian rivers, in Spain	17	(Gorga et al., 2015)
	Jilin Songhua River (Northeast China)	391	(He et al., 2018)
	Dianchi Lake, the southwest of China	37.9	(Huang et al., 2013)
Estriol	Iberian rivers, in Spain	8.3	(Gorga et al., 2015)
	Three Gorges Reservoir Regions, China	37.6	(Wang et al., 2016)
	Dianchi Lake, the southwest of China	28.5	(Huang et al., 2013)
	Erhai Lake, a Typical Plateau Lake of China	12	(Shen et al., 2020)
	Jilin Songhua River (Northeast China)	518	(He et al., 2018)
Estriol 16-glucuronide (E3-16G)	Iberian rivers, in Spain	13	(Gorga et al., 2015)

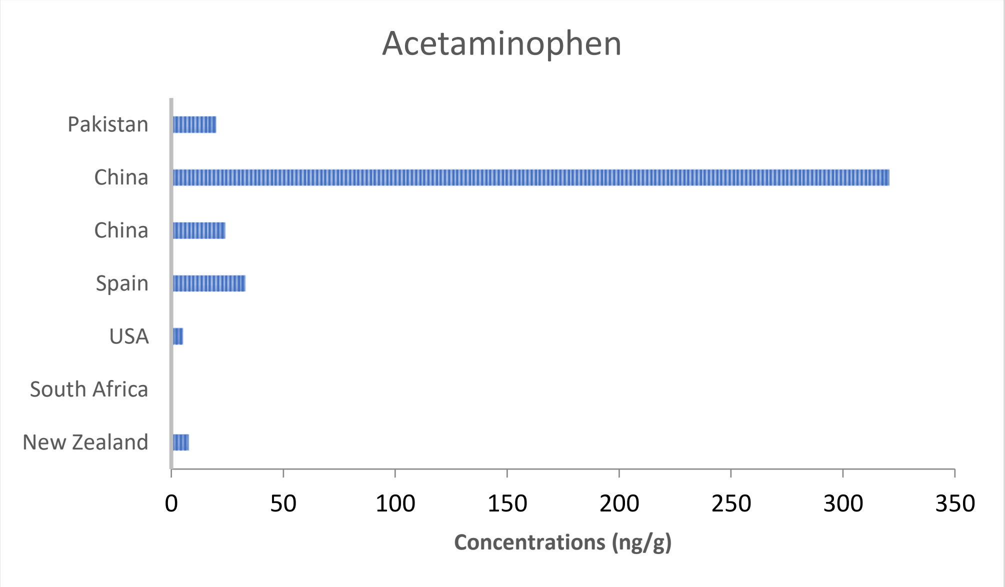
Estriol 3-sulfate (E3-3S)	Iberian rivers, in Spain	29	(Gorga et al., 2015)
Estrone 3-glucuronide (E1-3G)	Iberian rivers, in Spain	21	(Gorga et al., 2015)
Estrone	13 estuarine sites around Auckland, New Zealand	0.7 to 2.2	(Stewart et al., 2014)
	Iberian rivers, in Spain	71	(Gorga et al., 2015)
	Brazilian coast	24.4	(Froehner et al., 2012)
	Jilin Songhua River (Northeast China)	493	(He et al., 2018)
	Three Gorges Reservoir Regions, China	9.1	(Wang et al., 2016)
	Dianchi Lake, the southwest of China	115	(Huang et al., 2013)
	Erhai Lake, a Typical Plateau Lake of China	181	(Shen et al., 2020)

1.4.1.4. Analgesics and anti-inflammatories

One of the most widely used drug groups is analgesics/anti-inflammatories, which are sold freely over the counter (*OTC-without prescription*) in pharmacies and supermarkets all over the world. Analgesic/anti-inflammatory drugs are generally used to treat headaches or mild/moderate muscle pain and strains but reports have shown people tend to overuse this class of medication (Sandilands and Bateman, 2008). This extensive use has lead to several studies detecting various analgesics/anti-inflammatory drugs in freshwater sediments from all over the world. Table 1.5 presents a summary of analgesics/anti-inflammatories concentrations reported in freshwater sediments worldwide.

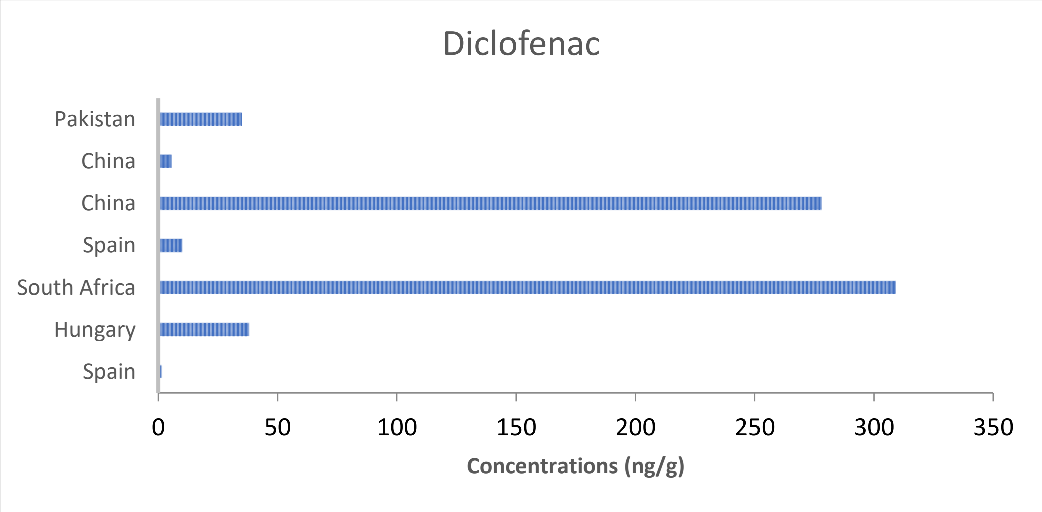
A study by He et al., (2018) reported the detection of acetaminophen (*i.e., Paracetamol)* in sediment from Jilin Songhua River, China at a concentration range of 2 - 321 ng/g, while Stewart et al., (2014) measured acetaminophen in the estuarine receiving environment around Auckland, New Zealand at concentration of 7.7 ng/g. Concentrations of acetaminophen in freshwater sediments from different parts of the world are summarised in Figure 1-5.

Figure 1-5 Average concentrations (ng/g) of acetaminophen in freshwater sediments from different parts of the world



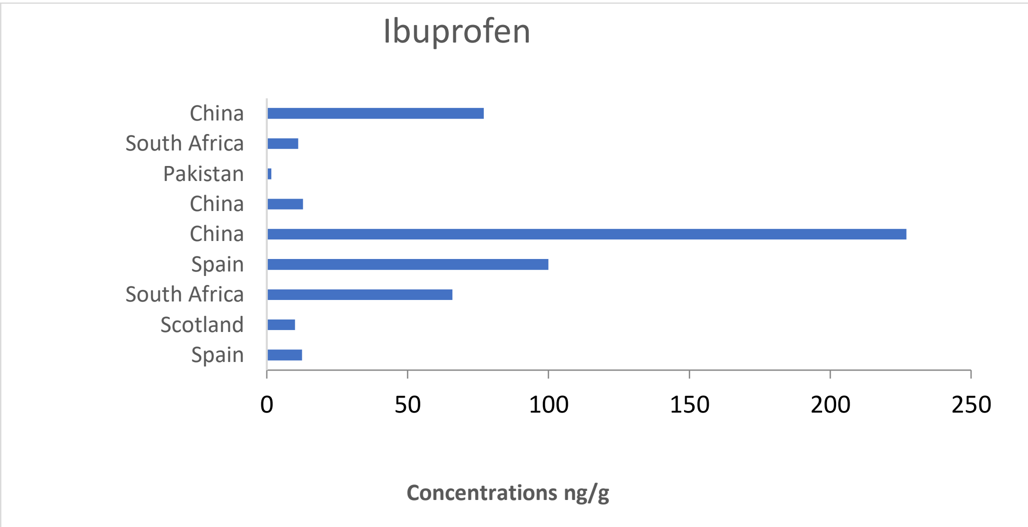
Diclofenac is another widely used non-steroidal anti-inflammatory drug (NSAID). Maximum concentrations of diclofenac in sediment of the Msunduzi river, Kwazulu-Natal, South Africa and in the Jilin Songhua River, Northeast China were reported at 309 and 278 ng/g, respectively, (Agunbiade and Moodley, 2016, He et al., 2018). However, in Iberian rivers, Spain and Pearl River delta, China, diclofenac was detected at lower concentrations of 1.29 and 0.03 ng/g, respectively. (Osorio et al., 2016a, Xie et al., 2019). Concentrations of diclofenac reported in freshwater sediments from different parts of the world are summarised in Figure 1-6.

Figure 1-6 Average concentrations (ng/g) of diclofenac in freshwater sediments from different parts of the world



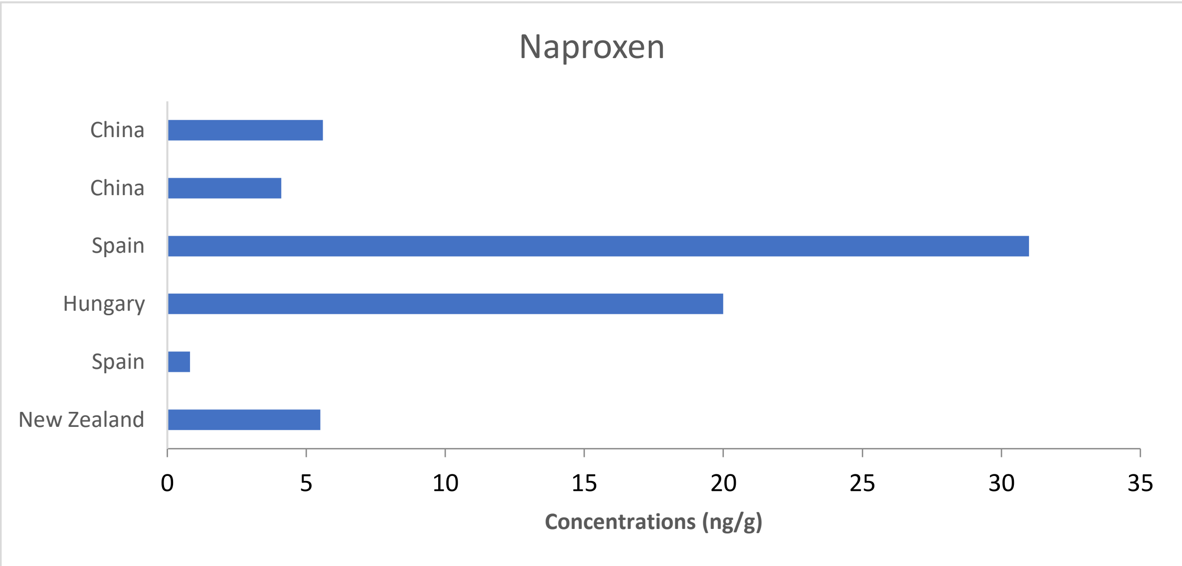
Another commonly used NSAID, ibuprofen, was detected in several studies. In China, ibuprofen was measured in Taiha lake sediment at concentrations of 13 and 77 ng/g in 2015 and 2017, respectively (Xie et al., 2015, Xie et al., 2017). Elsewhere, in the Jilin Songhua River, Northeast China, it was detected at concentrations of 227 ng/g (He et al., 2018). Concentrations of ibuprofen reported in freshwater sediments from different parts of the world are summarised in Figure 1-7.

Figure 1-7 Average concentrations (ng/g) of ibuprofen in freshwater sediments from different parts of the world.



Concentrations of naproxen in sediment of the Danube river in Budapest, Hungary ranged between 2 and 20 ng/g (Varga et al., 2010), while in Iberian Rivers, Spain it dropped in the range <0.1 -0.82 ng/g (Osorio et al., 2016a). Elsewhere, concenrtrations in Taihu lake, China ranged from not detected to 5.6 ng/g (Xie et al., 2017). Concentrations of naproxen in freshwater sediments from different parts of the world are summarised in Figure 1-8.

Figure 1-8 Average concentrations (ng/g) of naproxen in freshwater sediments from different parts of the world



Ketoprofen, a less-widely used NSAID, was detected by Agunbiade and Moodley (2016) in sediment of Msunduzi River, Kwazulu-Natal, South Africa at concentration ranges between 6.7 and 57.47 ng/g. Concentrations of ketoprofen reported in freshwater sediments from different parts of the world are summarised in Figure 1-9.

Figure 1-9): Concentrations (ng/g) of naproxen in freshwater sediments from different parts of the world.

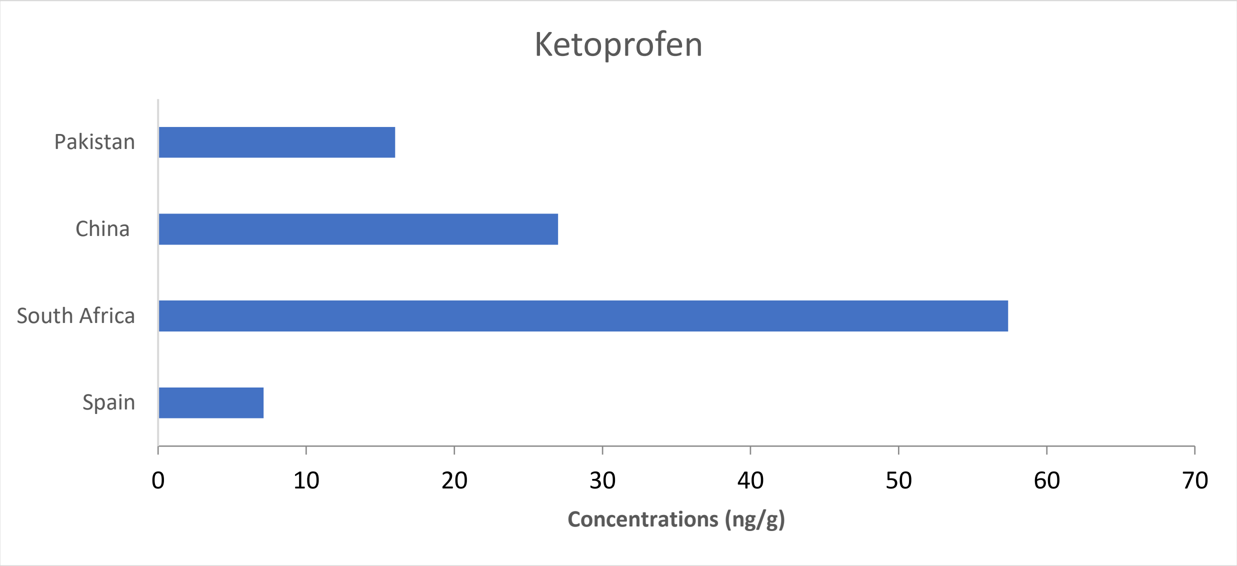


Table 1.5 Average concentrations of analgesics and anti-inflammatories in in river sediments worldwide.

Analgesics/ anti-inflammatories	Location	Concentration (ng/g)	Reference
Acetaminophen	13 estuarine sites around Auckland, New Zealand	7.7	(Stewart et al., 2014)
	Msunduzi River, South Africa	15.8	(Matongo et al., 2015)
	Urban river in Florida, USA	5.2	(Yang et al., 2015)
	Turia river and Albufera lake, Spain	33	(Sadutto et al., 2021)
	Lake and rivers of Baiyangdian, China	24	(Zhang et al., 2018)
	Jilin Songhua River (Northeast China)	321	(He et al., 2018)
	Al-Hufuf, Al-Oyun, the Al-Asfar and Al-Hubail lakes, Saudi Arabia	11.5	(Picó et al., 2020)
	Canal of Lahore, Pakistan	20	(Ashfaq et al., 2019)
Antipyrine	Canal of Lahore, Pakistan	35	(Ashfaq et al., 2019)
Aspirin	Umgeni River, South Africa	427	(Agunbiade and Moodley, 2016)

Codeine	Iberian Rivers, Spain	11.5	(Osorio et al., 2016a)
	Turia river and Albufera lake, Spain	1	(Sadutto et al., 2021)
Diclofenac	Iberian Rivers, Spain	1.3	(Osorio et al., 2016a)
	Danube river at Budapest (Hungary)	38	(Varga et al., 2010)
	Umgeni river, South Africa	309	(Agunbiade and Moodley, 2016)
	Pearl river delta, China	0.03	(Xie et al., 2019)
	Turia river and Albufera lake, Spain	10	(Sadutto et al., 2021)
	Jilin Songhua River (Northeast China)	278	(He et al., 2018)
	Taihu Lake, China	5.6	(Xie et al., 2015)
	Al-Hufuf, Al-Oyun, the Al-Asfar and Al-Hubail lakes, Saudi Arabia	22	(Picó et al., 2020)
	Canal of Lahore, Pakistan	35	(Ashfaq et al., 2019)
Diphenhydramine	Urban river in Florida, USA	0.3	(Yang et al., 2015)
	Pearl river delta, China	0.7	(Xie et al., 2019)
Ethenzamide	Canal of Lahore, Pakistan	6.5	(Ashfaq et al., 2019)
Etoricoxib	Al-Hufuf, Al-Oyun, the Al-Asfar and Al-Hubail lakes, Saudi Arabia	64	(Picó et al., 2020)
	Turia river and Albufera lake, Spain	6	(Sadutto et al., 2021)
Fenoprofen	Canal of Lahore, Pakistan	3.5	(Ashfaq et al., 2019)
Flufenamic Acid	Turia river and Albufera lake, Spain	3	(Sadutto et al., 2021)
Ibuprofen	Iberian Rivers, Spain	12.6	(Osorio et al., 2016a)
	Upstream and downstream rivers from western, central and eastern Scotland	<10	(Langford et al., 2011)
	Msunduzi River, South Africa	66	(Matongo et al., 2015)
	Pearl river delta, China	0.02	(Xie et al., 2019)

	Turia river and Albufera lake, Spain	100	(Sadutto et al., 2021)
	Jilin Songhua River (Northeast China)	227	(He et al., 2018)
	Taihu Lake, China	12.9	(Xie et al., 2015)
	Canal of Lahore, Pakistan	1.6	(Ashfaq et al., 2019)
	Umgeni River, South Africa	11.2	(Agunbiade and Moodley, 2016)
	Al-Hufuf, Al-Oyun, the Al-Asfar and Al-Hubail lakes, Saudi Arabia	23	(Picó et al., 2020)
	Taihu lake, China	77	(Xie et al., 2017)
Indomethacin	Canal of Lahore, Pakistan	3.9	(Ashfaq et al., 2019)
Ketoprofen	Iberian Rivers, Spain	7.1	(Osorio et al., 2016a)
	Umgeni River, South Africa	57	(Agunbiade and Moodley, 2016)
	Pearl river delta, China	27	(Xie et al., 2019)
	Canal of Lahore, Pakistan	16	(Ashfaq et al., 2019)
Lidocaine	Urban river in Florida, USA	0.03	(Yang et al., 2015)
Mefenamic acid	Canal of Lahore, Pakistan	8.8	(Ashfaq et al., 2019)
Naproxen	13 estuarine sites around Auckland, New Zealand	5.5	(Stewart et al., 2014)
	Iberian Rivers, Spain	0.8	(Osorio et al., 2016a)
	Danube river at Budapest (Hungary)	2-20	(Varga et al., 2010)
	Turia river and Albufera lake, Spain	31	(Sadutto et al., 2021)
	Jilin Songhua River (Northeast China)	4.1	(He et al., 2018)
	Taihu lake, China	0.06	(Li et al., 2021a)
	Taihu lake, China	5.6	(Xie et al., 2017)
Propyphenazone	Canal of Lahore, Pakistan	5.2	(Ashfaq et al., 2019)
Tramadol	Al-Hufuf, Al-Oyun, the Al-Asfar and Al-Hubail lakes, Saudi Arabia	107	(Picó et al., 2020)
	Turia river and Albufera lake, Spain	13	(Sadutto et al., 2021)

1.4.1.5. Psychiatric drugs

Psychiatric drugs are widely used on their own or in combination with NSAIDs. For example carbamazepine is one of the most often prescribed medications, with a global consumption volume of 1014 tonnes. It is also the most regularly discovered neuroactive in aquatic environments (Gasca-Pérez et al., 2019). In the US, up to 139 million prescriptions for hydrocodone combination products (with ibuprofen) were distributed in 2012(Lee, 2017). Yang et al. (2015) found carbamazepine and naproxen at average concentrations of 7.7 and 5.5 ng/g, respectively in sediment samples from Auckland, New Zealand. In Florida, USA, carbamazepine was detected in all the studied sediment samples at concentrations ranging from 0.1 to 32 ng/g (Yang et al., 2015). In Boulder Creek sediment, Colorado, fluoxetine, norfluoxetine, sertraline, norsertraline, paroxetine, citalopram, bupropion, and venlafaxine were identified at the maximum concentrations of 20, 30, 18, 11, 3, 15, 2 and 24 ng/g, respectively (Schultz et al., 2010). Table 1.6 provides a summary of average concentrations of psychiatric drugs reported in freshwa.ter sediments worldwide.

Table 1.6 Average concentrations of psychiatric drugs in freshwater sediments worldwide.

Psychiatric drugs	Location	Concentration (ng/g)	Reference
Acridone	Iberian Rivers, Spain	3.7	(Osorio et al., 2016a)
Carbamazepine	Iberian Rivers, Spain	0.1	(Osorio et al., 2016a)
	Upstream and downstream rivers from western, central and eastern Scotland	< 1	(Langford et al., 2011)
	Msunduzi River, South Africa	6.1	(Matongo et al., 2015)
	Urban river in Florida, USA	32.9	(Yang et al., 2015)
	Lake and rivers of Baiyangdian, China	54	(Zhang et al., 2018)
	Taihu Lake, China	7	(Xie et al., 2015)
	Canal of Lahore, Pakistan	4.2	(Ashfaq et al., 2019)
	Danube River and tributaries in Serbia	214	(Radović et al., 2015)
	Taihu lake, China	6.6	(Xie et al., 2017)

Citalopram	Upstream and downstream rivers from western, central and eastern Scotland	< 2	(Langford et al., 2011)
Clozapine	Msunduzi River, South Africa	17.9	(Matongo et al., 2015)
Diazepam	Iberian Rivers, Spain	0.3	(Osorio et al., 2016a)
	Danube River and tributaries in Serbia	48	(Radović et al., 2015)
Fluoxetine	Lake and rivers of Baiyangdian, China	16.2	(Zhang et al., 2018)
Norfluoxetine	Iberian Rivers, Spain	0.1	(Osorio et al., 2016a)
Sertraline	Iberian Rivers, Spain	12.1	(Osorio et al., 2016a)
	Taihu lake, China	10	(Xie et al., 2017)
Venlafaxine	Iberian Rivers, Spain	1.9	(Osorio et al., 2016a)

1.4.1.6. Other common PPCPs

Several pharmaceuticals belonging to groups of antidiabetics, antihypertensives, β-blockers, lipid regulators, stimulants, anticoagulants, antifungals, antihelmintics, fungicides, insect repellents, diuretics, proton pump inhibitors, antihyperlipedimics were occasionally reported in freshwater sediments Table 1.7. As an illustration, Metformin (*antidiabetic*) was reported in sediment at average concentration of 0.9 ng/g in Iberian Rivers, Spain, 140 ng/g in Lake Michigan, US and 56.7 ng/g in sub-arctic locations of the Faroe Islands, Iceland and Greenland (Osorio et al., 2016a, Blair et al., 2013 and Huber et al., 2016). Caffeine is one of the stimulants commonly reported in sediment. It was presented at average concentrations of 29.7 ng/g in San Francisco Bay, CA (Klosterhaus et al., 2013), 1.3 ng/g in Umgeni River, South Africa (Matongo et al., 2015), 24.4 ng/g in an urban river in Florida, USA (Yang et al., 2015), 30.5 ng/g in lake and rivers of Baiyangdian, China (Zhang et al., 2018), 63.7 ng/g in Jilin Songhua River, Northeast China (He et al., 2018), 9.0 ng/g in Lahore, Pakistan (Ashfaq et al., 2019), 19.0 ng/g in Songhua Catchment, Northeast China (Li et al., 2021b) and 10.0 ng/g in Mediterranean coastal wetland, Spain (Sadutto et al., 2021).

Table 1.7 Average concentrations (ng/g) of PPCPs from various therapeutic groups reported in freshwater sediments worldwide.

Groups	PPCPs	Location	Concentration (ng/g)	Reference
Antidiabetic	Glibenclamide	Iberian Rivers, Spain	0.9	(Osorio et al., 2016a)
	Metformin	Lake Michigan, US	140	(Blair et al., 2013)
		Al-Hufuf, Al-Oyun, the Al-Asfar and Al-Hubail lakes, Saudi Arabia	0.6	(Picó et al., 2020)
		Sub-arctic locations of the Faroe Islands, Iceland and Greenland	56.7	(Huber et al., 2016)
Antihypertensives	Diltiazem	Pearl river delta, China	0.2	(Xie et al., 2019)
		Lake and rivers of Baiyangdian, China	15.3	(Zhang et al., 2018)
	Triamterene	San Francisco Bay, CA, USA	10.8	(Klosterhaus et al., 2013)
	Valsartan	Iberian Rivers, Spain	7.36	(Osorio et al., 2016a)
β-Blockers	Atenolol	Upstream and downstream rivers from western, central and eastern Scotland	<10	(Langford et al., 2011)

		Canal of Lahore, Pakistan	8.1	(Ashfaq et al., 2019)
		Al-Hufuf, Al-Oyun, the Al-Asfar and Al-Hubail lakes, Saudi Arabia	13.5	(Picó et al., 2020)
		Turia river and Albufera lake, Spain	16	(Sadutto et al., 2021)
	Metoprolol	Lake Haapajärvi, Finland	46	(Lahti and Oikari, 2012)
		Iberian Rivers, Spain	0.54	(Osorio et al., 2016a)
	Propranolol	Iberian Rivers, Spain	2.04	(Osorio et al., 2016a)
		Lake Haapajärvi, Finland	43	(Lahti and Oikari, 2012)
		Taihu Lake, China	18.3	(Xie et al., 2015)
		Taihu lake, China	31	(Xie et al., 2017)
Lipid regulators	Bezafibrate	Umgeni River, South Africa	80	(Agunbiade and Moodley, 2016)
	Bezafibrate	Taihu lake, China	N D	(Xie et al., 2017)
	Clofibric acid	Taihu lake, China	13	(Xie et al., 2017)
	Gemfibrozil	Iberian Rivers, Spain	1.92	(Osorio et al., 2016a)
		Taihu lake, China	N D	(Xie et al., 2017)

Stimulant	Amphetamine	San Francisco Bay, CA, USA	3.3	(Klosterhaus et al., 2013)
	Caffeine	San Francisco Bay, CA, USA	29.7	(Klosterhaus et al., 2013)
		Msunduzi River, South Africa	1.32	(Matongo et al., 2015)
		Urban river in Florida, USA	24.4	(Yang et al., 2015)
		Lake and rivers of Baiyangdian, China	30.5	(Zhang et al., 2018)
		Jilin Songhua River (Northeast China)	63.7	(He et al., 2018)
		Canal of Lahore, Pakistan	9	(Ashfaq et al., 2019)
		Songhua Catchment, Northeast China	19	(Li et al., 2021b)
		Al-Hufuf, Al-Oyun, the Al-Asfar and Al-Hubail lakes, Saudi Arabia	76	(Picó et al., 2020)
		Turia river and Albufera lake, Spain	10	(Sadutto et al., 2021)
	Cocaine	San Francisco Bay, CA, USA	0.2	(Klosterhaus et al., 2013)
	Nicotine	Urban river in Florida, USA	0.02	(Yang et al., 2015)
	Pseudoephedrine	Urban river in Florida, USA	0.2	(Yang et al., 2015)

Anticoagulant	Warfarin	Turia river and Albufera lake, Spain	9	(Sadutto et al., 2021)
Antifungal	Miconazole	Canal of Lahore, Pakistan	5.8	(Ashfaq et al., 2019)
	Thiabendazole	Canal of Lahore, Pakistan	1.7	(Ashfaq et al., 2019)
Anthelmintic	Thiabendazole	San Francisco Bay, CA, USA	9.1	(Klosterhaus et al., 2013)
Fungicides	Fluconazole	Yangtze River, China	0.3	(Liu et al., 2015)
	Climbazole	Yangtze River, China	2	(Liu et al., 2015)
	Miconazole	Yangtze River, China	5.1	(Liu et al., 2015)
	Clotrimazole	Yangtze River, China	3.4	(Liu et al., 2015)
	Thiabendazole	Yangtze River, China	0.1	(Liu et al., 2015)
	Carbendazim	Yangtze River, China	2.9	(Liu et al., 2015)
Insect repellent	DEET	Yangtze River, China	4.1	(Liu et al., 2015)
Diuretics	Furosemide	Turia river and Albufera lake, Spain	48	(Sadutto et al., 2021)

Proton pump inhibitors	Omeprazole	Turia river and Albufera lake, Spain	1	(Sadutto et al., 2021)
Statins	Atorvastatin	Turia river and Albufera lake, Spain	21	(Sadutto et al., 2021)
		Al-Hufuf, Al-Oyun, the Al-Asfar and Al-Hubail lakes, Saudi Arabia	84.49	(Picó et al., 2020)
	Simvastatin	Turia river and Albufera lake, Spain	29	(Sadutto et al., 2021)

1.4.2. PPCPs in Soil

Few studies investigated the occurrence of PPCPs in soils. Sludge land application and landfills are the principal sources of PPCPs in soil. The use of livestock wastes and reclaimed water irrigation are two practises that contribute to the direct or indirect transfer of these contaminants to the soil via runoff (Topp et al., 2008). In soil receiving wastewater in Jerez, Spain, two fragrances (Galaxolide, OTNE) and one UV filter (EHS) were detected at average concentrations of 220, 103, and 28 ng/g, respectively. As a result of the high organic matter content, the surface layer of the soil had the greatest concentrations of all target compounds in this investigation. (Biel-Maeso et al., 2019).

60-80% of antibiotics used in veterinary medical practices are estimated to be discharged into the environment (Chen et al., 2017). In soil samples from an area with intense livestock production in northern Germany, tetracycline was found at average concentrations of 82.2 (0 -10 cm) , 198.7 (10 - 20 cm) and 171.7 (20 -30 cm) ng/g. (Hamscher et al., 2002).

Acetaminophen, diclofenac, mefenamic acid and phenazone (non-steroidal anti-inflammatory drugs) were detected at average concentrations of 1.4, 1.8,0.7 and 0.4 ng/g , respectively, in soil (0-20 cm) irrigated with reclaimed wastewater from Jerez in Spain (Biel-Maeso et al., 2018). In the same area, diclofenac and carbamazepine were detected in soil at average concentrations of 0.1, 1.3 ng/g (Corada-Fernández et al., 2015).

Based on the little information available, occurrence of PPCPs in surface soil can be attributed mainly to the use of treated waste water for irrigation, sludge application and run off from livestock farms (Ebele et al., 2017).

1.4.3. PPCPs in freshwater fish

Several studies have suggested that certain PPCPs can accumulate in fish. For example, a study in the Gila River, New Mexico, USA, detected Sertraline (antidepressant) at concentrations of 19 and 545 ng/g in liver and fillet tissues of Sorona sucker fish. In addition, personal care products were detected at high concentration, for example, galaxolide and tonalide (musk fragrances) were detected at 2,100 and 290 ng/g, respectively, in the fillet. (Ramirez et al., 2009). Interestingly, another study on Tilapia fillets from the East Fork Gila River in New Mexico measured galaxolide and tonalide at 81 and 5.5 ng/g, respectively (Subedi et al., 2011).

From muscle tissues of three different fish species, collected from Manila Bay in the Philippines, triclosan, methyl paraben, propyl parben, UV-320 and UV-328 were all detected at average concentrations of 130, 2770, 311, 10 and 18 ng/g, respectively in blue tail mullet; 157, 3450, 1140, 1 and 21 ng/g, respectively in coral grouper and 123, 1000, 75, 7 and 105 in ng/g, respectively in flathead grey mullet (Kim et al., 2011).

In the US, Carbamazepine was detected at concentrations of 0.83 - 1.44 ng/g, while norfluoxetine was measured at mean concentration of 4.37 ng/g in Sunfish (Lepomis sp.) from Pecan Creek, and Clear Creek in Denton County, TX (Ramirez et al., 2007). In the Grand River watershed in southern Ontario, 1,7-dimethylxanthine has been reported in concentrations as high as 641.2 ng/g in wild freshwater mussels (Lasmigona costata) (de Solla et al., 2016).

The previous studies demonstrate the bioavailability and bioaccumulation potential of various PPCPs in edible freshwater fish upon unintentional exposure to these chemicals as emerging pollutants in the aquatic environment. However, antibiotics are intentionally used to treat and/or prevent bacterial diseases in aquaculture. This has raised concern over the potential development of anti-biotic resistance, as well as the levels of antibiotics in fish tissues intended for human consumption (Espinosa-Mansilla and de la Peña, 2009). To control the potential risk of antibiotics in fish tissues for consumers, maximum residue limit (MRL) values are applied in various countries. For instance, the European Union (EU) and China set a maximum residue limit of 100 ng/g in muscle for all fish species, whereas the U.S. Food and Drug Administration (FDA) has also set MRL of 2000 ng/g for tetracycline (TC), oxytetracycline (OTC), and chlortetracycline (CTC) in fish muscles (Wen et al., 2006).

1.5. Fate of PPCPs in the freshwater aquatic environment

Following their release to the environment, PPCPs can be degraded or depleted by a variety of mechanisms. The most prevalent mechanisms of pharmaceutical remnants degradation and depletion include hydrolysis, photolysis, biodegradation, and mineralization (Jones et al., 2001). Most studies on the fate of PPCPs in the freshwater aquatic environment were conducted on the water phase of rivers, while little is known about other phases including suspended particles, sediments, biofilms, as well as aquatic biota (Wilkinson et al., 2017).

Moreover, current knowledge on the fate of PPCPs is limited to several chemicals, and stem mainly from controlled laboratory studies attempting to mimic the natural environment. Only a few data sets are available from field studies; hence several research gaps exist in the current state-of-knowledge on the fate of PPCPs in the non-water phases of the aquatic environment (Khan et al., 2020).

Current understanding is that PPCPs degradation in non-liquid phases is affected by a variety of factors (Maldonado-Torres et al., 2018, Khan et al., 2020) including :

(a) Compound-specific properties (e.g., water solubility, K_{OW}, vapour pressure).
(b) Environmental conditions (e.g., pH, temperature, UV-radiation and redox conditions).
(c) Freshwater biota and microbial community (e.g., bacteria, algae, protozoa).
(d) sediment/soil particle composition and characteristics (e.g., organic content, mineral composition).

PPCPs released into the environment interact constantly with particles. Soil, sediments, and suspended particles in the aquatic environment play a significant role as sinks, which determines the transport of PPCPs via sorption. Maskaoui and Zhou (2010) investigated the adsorption potential of several PPCPs (propranolol, sulfamethoxazole, mebeverine, thioridazine, carbamazepine, tamoxifen, indomethacin, diclofenac, and meclofenamic acid) to aquatic colloids and suspended particulate matter (SPM) in river water, effluents from sewage treatment works (STW), and groundwater in the UK. Results revealed higher adsorption affinity in colloids than SPM, suggesting colloids can act as powerful sorbents for PPCPs in the aquatic environment. Moreover, these particles create a reactive surface on which a variety of reactions can take place. For example, soil particles, when combined with UV radiation, allows for heterogeneous photochemical reactions such hydrolysis, oxidation-reduction, polymerization, and isomerization. The pH, ionic strength, metal ions, and organic matter content of the soil had a significant effect on antibiotic degradation rate in the studied soil particles. (Wang and Wang, 2015).

Available evidence from existing literature indicates that PPCPs are generally present at lower concentrations in river sediments than suspended particulate matter or in water (Silva et al., 2011, Patrolecco et al., 2006). However, such findings cannot be generalised due to the diversity of PPCPs and the multitude of factors influencing the adsorption of these chemicals to solid particles and their subsequent degradation as outlined above.

1.6. sediment and its colloidal properties

In aquatic ecosystems, sediment is a natural component. The quantity and nature of it, can have an impact on the biological, chemical, and physical integrity of aquatic ecosystem (EPA, 2006). Particle size is frequently used to characterise sediments to: 1) Fine inorganic clay, silt, and well-decomposed organic matter particles that are generally suspended in the water column, which are less than 0.063 mm in diameter, these particles are classified as colloids. Colloids, which can function as sorbents and ion exchangers, are collections of highly dispersed or loosely cohering organic, mineral, and organo-mineral particles that are found in sediment and soil (Alemayehu and Teshome, 2021). 2) 0.063-0.250 mm: thin sands that are suspended at high water velocities, but usually sink as velocities fall 3) 0.250–2 mm: small bedload, medium to coarse sands 4) > 2 mm: coarse bedload, mainly gravels and small cobbles (EPA, 2022, Chattopadhyay and Chattopadhyay, 2003).

Sediment in rivers gets deposited as the river slows down. Larger, heavier particles like pebbles and sand are deposited first, whilst the lighter silt and clay only settle when the water slows down and is almost still. The water flow is strongest on the outside of river bends, eroding the bank, yet is slowest on the inside of the bends, allowing the deposition of gravel and sand. When a river floods, bursting its banks after heavy rainfall, the flood water spreads out across the floodplain and, as this water hardly moves, finer silt and clay are deposited. When a river reaches a lake or the sea, it quickly deposits much of its sediment. This may choke up the river channel, which then divides up into distributaries, between which swamps are formed (Wetzel, 2001).

Sediment transport is the movement of organic and inorganic particles by water. In general, the greater the flow, the more sediment that will be conveyed. Water flow can be strong enough to suspend particles in the water column as they move downstream, or simply push them along the bottom of a waterway. Transported sediment may include mineral matter, chemicals and pollutants, and organic material (EPA, 2014). This can also be expressed as sediment load. The total load includes all particles moving as bedload, suspended load, and wash load. Sediment transport is constantly subject to change. In addition to the changes in sediment load due to geology, geomorphology and organic elements, sediment transport can be altered by other external factors. The alteration to sediment transport can come from changes in water flow, water level, weather events and human influence. In general, the transportation of sediment particles in river ecosystems occurs via different ways including:

(a) Traction: large, heavy pebbles are rolled along the riverbed. This is most common near the source of a river, as the sediment load is larger.

(b) Saltation: pebbles are bounced along the riverbed, most commonly near the source.

(c) Suspension: lighter sediment particles are suspended within the water and can be carried and moved further by currents. most commonly near the mouth of the river.

(d) Solution - the transport of dissolved chemicals. This varies along the river depending on the interactions between various sediment particles, chemical contaminants, and the aqueous phase.

Between sediment and chemical contaminants, there are powerful physical, chemical, and biological interactions. There have been numerous research on the effects of surface charge characteristics on adsorption and flocculation for colloidal particles, sediment particles, and some other particles, most of which use the Derjaguin-Landau-Verwey-Overbeek (DLVO) theory in colloidal chemistry (Derjaguin et al., 1987). The DLVO theory is a theoretical model that presupposes a symmetrical sphere particle with a smooth surface and a uniform charge distribution. The architecture and pores of sediment particles, however, are incredibly complicated (Chattopadhyay and Chattopadhyay, 2003). The central problem with sediment and pollutant adsorption and desorption is surface charge distribution of the particles. An experiment was conducted on the surface charge distribution of fine silt. The findings demonstrate that quartz sand has a complex surface shape that significantly affects the charge distribution. Positive and negative charges are more evenly distributed in the groove, ridge, and flat areas of the surface as opposed to the saddle, concave, and convex regions (Huang et al., 2012). The finding that sorption often rises with soil organic carbon content and chemical hydrophobicity is significant. The degree to which an organic chemical is dispersed in equilibrium between an environmental solid (such as soil, sediment, suspended sediment, and wastewater solids) and the aqueous phase it is in contact with is quantified by the sorption coefficient. The variety of interactions between the solute chemical, the environmental solid and the aqueous phases, as well as the effects of environmental or experimental factors like organic matter quantity and type, clay mineral content and type, clay to organic matter ratio, particle size distribution and surface area of the sorbent, pH, ionic strength, suspended particulates or colloidal material, temperature, dissolved organic matter concentration, soluble organic, and inorganic matter, may all impact the sorption coefficients of chemical contaminants to sediment particles in the freshwater aquatic environment (Delle Site, 2001, Doucette, 2003, Weber et al., 2004).

Extreme rainfall events and flooding can affect sediment transport and contaminants distribution in freshwater ecosystems, as the sediments can act as a carrier of contaminants that are attached to the mobilised sediment particles. This may cause substantial short and long-term impacts on human health and influence the ecological and chemical water quality conditions (Ponting et al., 2021). Suspended particles enter fluvial systems continuously from the erosion of terrestrial surfaces and the riverbed itself. These particles are then transported along by the water current and are eventually deposited as sediment in regions of low water flow (e.g., wetlands, lowland rivers, floodplains, or estuaries). The different inorganic and organic constituents of suspended particles (e.g., clay minerals and humic substances) provide a large number of binding sites for chemicals with a broad range of physicochemical properties, including hydrophilic and lipophilic organic chemicals (Crawford et al., 2022). Consequently, these suspended sediment particles can accumulate various organic and inorganic pollutants, from the water column or other input sources to the ecosystem (e.g., industrial discharge), which are subsequently deposited in the sediment bed. With continuous deposition, older sediment layers may the contamination history of a given region and may be a source of environmental contaminants exposure during flooding events when they are eroded and transported (Heim and Schwarzbauer, 2013). However, it should be noted that research on legacy organic contaminants in historical sediment layers has, hitherto, focused mainly on persistent organic pollutants, with prolonged sediment half-life, high lipophilicity and strong binding to sedimentary organic content (e.g. DDTs, PCBs…etc), while very little is known about the suitability of sediment core archives to study the more labile, hydrophilic and more degradable PPCPs (Klaminder et al., 2015). Although the available literature on binding of PPCPs to sediment particles, their persistence and degradation rates in freshwater sediment is rather limited, compared to other chemical contaminants (e.g. POPs and heavy metals), the potential for mobilisation of contaminated sediment particles (suspended or surface sediment) by weather events like extreme rainfall and flooding has been previously reported (Ebele et al., 2017, Xu et al., 2022). Therefore, the re-suspension and consequent widespread distribution of PPCPs-contaminated sediment particles by floods and/or heavy rainfall into adjacent natural floodplains, farmland, or artificially constructed flood retention areas can pose substantial risk to the aquatic environment and wildlife and impact humans and terrestrial animals that rely on it.

1.7. Methods of PPCPs Analysis in soil and sediment.

Numerous studies have reported on various validated analytical protocols for analysis of different PPCPs in water, which is expected given the diverse nature of this contaminant group in terms of physic-chemical properties, as well as the sheer number of PPCPs. These methods have been well-covered in a couple of recent review articles summarising the main aspects of PPCPs analysis in water (Meng et al., 2021, Kachhawaha et al., 2020). However, fewer studies have reported on the quantitative determination of PPCPs in sediment and other solid matrices (e.g., soil). The next section will provide an overview of the major steps reported for analysis of PPCPs in these matrices.

1.7.1. Sampling

The sampling process can influence the quality of analytical data (Conklin Jr, 2004). Thorough cleaning of sampling tools/utensils with deionized water and acetone is one of the most widely reported steps to avoid cross-contamination between samples. (Stewart et al., 2014). To minimise potential photo-degradation of target PPCPs in the collected samples during transport to the laboratory, aluminium foil packets are recommended (Pérez-Carrera et al., 2010). Storage in a dark, cool place (López-Serna et al., 2012), as well as keeping frozen at -20 C prior to lyophilisation (Silva et al., 2011) were also reported to avoid degradation of PPCPs during sample storage.

1.7.1.1. Sample collection

Protocols for collecting sediment samples have been published by several authors Table 1.8. Sediment samples are often collected using a van Veen grab sampler or a stainless-steel grab sampler due to their practicality, availability and low cost (Ramil et al., 2010). Sediment column samplers or corers are commonly used to collect sediment core samples (Xie et al., 2019, (Siedlewicz et al., 2016), while Auger samplers are frequently reported to collect shallow sediment and soil samples (Christou et al., 2017).

The sediment samples are usually collected in amber glass bottles to avoid photodegradation. (Englert, 2007, Yang et al., 2010). Sodium aside could be used to prevent microbiological degradation over a lengthy period of storage . (Zhou et al., 2011).

1.7.1.2. Sample preparation

In the laboratory, drying is an essential step for preparation of solid environmental matrices. Commonly, lyophilisation (freeze-drying) is used for sediments, while soil samples can be air-dried. High temperatures are avoided during the drying process to minimise potential thermal degradation and/or volatilisation of target PPCPs (Vazquez-Roig et al., 2010).

The next step in sample preparation is grinding and sieving to obtain free-flowing, homogenous samples ready for extraction. However, there is no clear consensus on the particle size of the sieved samples. Sediment samples were sieved through 0.149 mm sieve (Xie et al., 2019, Díaz and Peña-Alvarez, 2017, Zhao et al., 2016, Zhang et al., 2018) or 0.5 mm sieve (Yang et al., 2010). While soil samples were sieved through 2 mm sieve (Zhang et al., 2013, Christou et al., 2017). A summary of sample preparation steps reported in literature is provided in Table 1.8.

Table 1.8 summary of sample collection and preparation steps for determination of PPCPs in solid environmental samples.

Matrix	Location	Sampling	Analytes	Storage	Sieving	Drying	Reference
Sediment	Valencia, Spain	Van veen grab sampler.	32 PPCPs	−20 °C		Lyophilized	(Sadutto et al., 2020)
Sediment	Minnesota, US	Ponar dredge or sediment siphon. (0-10 cm)	158 PPCPs	−18 °C		Air dried	(Deere et al., 2020)
Sediment	Kenyan	(0-5 cm)	6 Antibiotics			Air dried	(Kairigo et al., 2020)
Sediment	Canal of Lahore, Pakistan		52 PPCPs	−80 °C		Air dried	(Ashfaq et al., 2019)
Sediment	Pearl River Delta, China	Customized sediment column sampler. (0-10 cm)	34 PPCPs	−20 °C	0.149 mm	48 h, −50 °C	(Xie et al., 2019)
Sediment	Tula River, Hidalgo, Mexico		8 PPCPs	4°C	0.149 mm	−20°C	(Díaz and Peña-Alvarez, 2017)
Sediment	Islands, Iceland and Greenland	Van veen grab sampler.	36 PPCPs	Frozen		Air dried	(Huber et al., 2016)
Soil	China	Agricultural soil, (0 - 20 cm)	4 PPCPs		2 mm	Air-dried	(Zhang et al., 2013)
Sediment and Soil			22 PPCPs	− 20 °C		− 55 ºC under vacuum (0.05 bar) for 72 h	(Azzouz and Ballesteros, 2012)

Sediment	13 estuarine sites around Auckland, New Zealand	Corer	47 pharmaceutical s	4 °C	0.5 mm	Temperature of 20 °C	(Stewart et al., 2014)
Soil	Experiment		6 PPCPs			lyophilized	(Grossberger et al., 2014)
Sediment	Iberian Rivers, Spain		76 PPCPs	−20 °C		Lyophilized	(Osorio et al., 2016a)
Soil	Experiment			−20 °C		Lyophilized	(Papaioannou et al., 2019)
Soil	Beijing, China	Geoprobe direct-push rig	11 PPCPs	4 °C		Air dried	(Ma et al., 2018)
Soil	Experiment, US		11 PPCPs			Air dried	(Dodgen and Zheng, 2016)
Soil and Sediment		Dry-drilling method	4 estrogens	4 °C		Llyophilized	(Li et al., 2012b)
Sediment and Soil	Spain		17 PPCPs	Sediment: -20 ◦C, Soil:4 ◦C.		Air dried	(Vazquez-Roig et al., 2010)
Sediment	29 sites along the Kaveri, Vellar and Tamiraparani rivers and the Pichavaram mangrove, India		Triclosan, carbamazepine and parabens	−20 °C		Air-dried	(Ramaswamy et al., 2011)
Sediment	Hungary		4 acidic PPCPs	5°C		Air dried	(Varga et al., 2010)
Soil	Experiment	Auger sampler, (0–20 cm)	3 PPCPs	−18 °C	2 mm	Air dried	(Christou et al., 2017)

Sediment	Msunduzi River, Kwazulu-Natal, South Africa	Ekman grab sampler, (0-25cm)	8 acidic pharmaceuticals			Air dried	(Agunbiade and Moodley, 2016)
Sediment	Mackreath Creek, Scott Creek Conservation Park, South Australia.	(0-50 cm)		+4 °C for 24 h,	0.5 mm	Air dried	(Williams and Kookana, 2010)
Sediment	San Francisco Bay, CA, USA,		104 PPCPs	frozen		Air dried	(Klosterhaus et al., 2013)
Sediment and Sludge	Upstream and downstream rivers from western, central and eastern Scotland	small handheld grab, (0- 2 cm)	34 PPCPs	− 20 °C		Air dried	(Langford et al., 2011)
Agricultural soil	Experiment, Baltimore, Maryland US	(0-20 cm)	72 PPCPs			Air dried	(Walters et al., 2010)
Sediment	Iberian rivers, in Spain			− 20 °C	0.125 mm	Lyophilized	(Gorga et al., 2015)
Sediment	Baiyangdian Lake in North China		22 antibiotics	− 20 °C	0.27 mm	Lyophilized	(Li et al., 2012a)
Soil	Texas, US	(0–30 cm)	9 PPCPs	4°C		Air dried	(Karnjanapiboonwong et al., 2011)

Sediment	Rivers (Mississippi, Sauk, South Fork of the Crow, and Grindstone), creeks (Center, Okabena) and lakes (Pepin, Superior, Shagawa)	(0–10 cm)	triclosan, triclocarban	−20 ◦C		Dried at 103 ◦C	(Venkatesan et al., 2012)
Sediment	Msunduzi River, South Africa	scooping (0–10 cm)	10 PPCPs			Air dried	(Matongo et al., 2015)
Sediment	Alafia River, Florida, USA	(0–10 cm)	17 PPCPs			Air dried	(Yang et al., 2015)
Sediment	Pearl Rivers, China	(0–20 cm)	14 PPCPs	4 °C	0.5 mm	Lyophilized	(Yang et al., 2010)
Soil	Experiment	(0- 20 cm)	5 PPCPs		2 mm	Air dried	(Yu et al., 2013)
Sediment	Yellow River Delta, China		8 PPCPs		0.149 mm	Lyophilized	(Zhao et al., 2016)
Sediment	Yellow River, Hai River and Liao River in northern China		17 PPCPs			Lyophilized	(Zhou et al., 2011)
Sediment	Songhua Catchment, Northeast China	(0–20 cm)	18 PPCPs	−20 °C		Lyophilized	(Li et al., 2021b)

Sediment	Taihu Lake, China	Stainless steel grab sampler and placed in polypropylene (PP) bags	23 PPCPs	−20 °C		Lyophilized at −60 °C	(Xie et al., 2017)
Sediment	Shallow Chinese freshwater lake	Peterson grab sampler	7 PPCPs	−20 °C		Lyophilized	(Liu et al., 2017)
Sediment	Taihu Lake, China	Grab sampler (0-5 cm)	15 antibiotics	−20 °C		Air dried	(Xu et al., 2014)
Sediment	Gorges Reservoir Region, China	Stainless steel grab sampler (0–10 cm)	9 endocrine-disrupting compounds	−20 °C	0.25 mm	Air dried	(Wang et al., 2016)
Sediment	Huangpu River, Shanghai, China	Van veen grab sampler	20 antibiotics		0.1 mm	Air dried	(Chen and Zhou, 2014)
Sediment	Jilin Songhua River, Northeast China	(0–10 cm)	22 antibiotics		0.074 mm	Air dried	(He et al., 2018)
Sediment	Baiyangdian Lake, China	Stainless steel grab	18 antibiotics	−20 °C	0.149 mm	Lyophilized	(Zhang et al., 2018)
Sediment	Guanting Reservoir and its upstream rivers in north China	Stainless steel grab	18 PPCPs	−20 °C	0.074 mm	Lyophilized	(Zhang et al., 2018)
Sediment	Canal of Lahore, Pakistan.		52 PPCPs			Air dried	(Ashfaq et al., 2019)

1.7.2. Extraction

The most popular approach for extracting PPCPs from solid environmental matrices is ultrasound-assisted extraction (UAE) followed by solid phase extraction (SPE) cartridges for clean up. Table 1.9 presents a summary of the reported methods for extraction and clean up of PPCPs in sediment and soil samples. The majority of these reported methods follow the reference EPA Method-1694 (United States Environmental Protection Agency). The extraction procedure is divided into 3 main stages: (a) ultrasound-assisted extraction using a suitable solvent (e.g., methanol) or solvent mixture (e.g. methanol/acetonitrile), (b) centrifugation to separate the liquid extract from the solid particles, and (c) volume reduction under a gentle stream of Nitrogen prior to clean up using SPE. The polarity of the solvent/solvent mixture, the type and homogeneity of the sample, the ultrasonic frequency, and the sonication period have all been identified as important factors influencing the extraction efficiency of PPCPs from sediment (Albero et al., 2015).

Other methods have also been reported for extraction of PPCPs from sediment including pressurized liquid extraction (PLE) and modified QuEChERS (quick, easy, cheap, effective, rugged, and safe) methods Table 1.9. Kumirska et al. investigated two extraction methods to quantify 20 pharmaceutical pollutants in soil. According to the results, the UAE technique yielded higher extraction efficiency for all the target compounds with absolute recoveries of ≥80% with the exception of two compounds. Only ten pharmaceuticals were extracted with reasonable efficiency (≥50%) using the modified QuEChERS method (Kumirska et al., 2019).

1.7.3. Clean up

Because the sediments' solvent extracts include a significant amount of natural matrix components, clean-up processes are required to reduce chromatographic interferences and potential ion suppression in the following instrumental analysis step (Löffler and Ternes, 2003). Matrix effects can create considerable complications in pharmaceutical analysis, particularly when using LC/MS (Liquid Chromatography/ Mass spectrometry) for detection (Ternes and Joss, 2007).

According to previous studies, solid phase extraction (SPE) is the method of choice for clean-up of sediment and soil extracts prior to LC/MS analysis Table 1.9. While several C_{18}-sorbent beds have been applied, Oasis HLB (Hydrophilic-Lipophilic Balance) and similar mixed ion-exchange bonded silica gel cartridges are the most frequently used for clean-up of PPCPs in soil and sediment samples. Also, methanol: Milli-Q water (1:1) is widely used for conditioning these cartridges, while target PPCPs can be eluted using several solvent combinations including methanol, NH_4OH-methanol, acetone, and acetonitrile.

To get cleaner extracts, some studies applied a combination of two different SPE cartridges. For example, 18 antibiotics were detected in soil from two fields in Tianjin, China. The soil extracts were cleaned using two cartridges in tandem: a SAX (Strong Anion Exchange) cartridge to remove humic particles and an Oasis HLB cartridge to remove other matrix interferences (Hu et al., 2012).

Table 1.9 Summary of reported sample extraction and clean up methods for PPCPs in environmental solid samples.

Matrix	Extraction		Clean up				Reference
	Technique	Procedure	Cartridge	Conditioning	Elution	Reconstitution	
Sediment	Solid Phase Extraction	1 g of spiked with 100 µL of a mixture of internal standards at 1 µg mL-1, vortex for 5 min, sonicated for 10 min, centrifuged for 6 min at 3000 rpm.	Phenomenex Strata-X and Phenomenex Strata-X-CW were used,	6 mL of MeOH, 6 mL of Milli-Q water, and if ion pairing is form, with 6 mL of 2 mmol L-1 SDS solution	6 mL of MeOH and 3 mL of MeOH–dichloromethane (50:50 v/v) for Strata-X and with 6 mL of MeOH–NH4OH (9.5 mol L-1) (95:5 v/v) for Strata-X-CW	1 mL of 70:30 Milli-Q water–MeOH	(Sadutto et al., 2020)
Sediment	Environmental Protection Agency (EPA) Method 1694	2.5 g of wet sediment + internal standards+ phosphate buffer (for acid extraction) or (NH4OH for base extraction), extracted by sonication with acetonitrile, diluted to 200 mL in water to remove the acetonitrile, extracted using an Oasis HLB cartridge.	Oasis HLB cartridge		50 mL of methanol followed by 20 mL of 1:1 acetone: methanol		(Deere et al., 2020)
Sediment	Ultrasonic Bath	5 g of the air-dried sediment spiked with isotopically labelled internal standards	HLB cartridges	6 mL of methanol followed by 6 mL of Milli-Q ultrapure water	4 mL of 50:50 acetonitrile-methanol solution	1 mL using 20:80 ACN: H2O solvent	(Kairigo et al., 2020)

				at a flow rate of 5 mL/min^{-1}			
Sediment	Matrix Solid-Phase Dispersion (MSPD)	0.1g of freeze-dried sediment, mixed with 0.4 g C18 sorbent, spiked with surrogate standards, homogeneous mixture was put in an empty cartridge contained a polyethylene in bottom and top.			6 mL methanol followed by 10 mL acetonitrile: 5% oxalic acid (8:2, v/v)	1 mL of acetonitrile: water mixture (1:1).	(Ashfaq et al., 2019)
Sediment		2.00 ± 0.05 g of sediment + 50 ng of PPCP mixed internal standard + methanol, (5 mL citrate buffer (pH 3) and 5 mL acetonitrile), centrifuged a fume hood overnight to evaporate methanol, The mixture was vortexed for 5 s, ultrasonicated at 25 °C for 20 min, centrifuged at 4000 rpm for 5 min, diluted with 400 mL ultrapure water, and 0.2 g of Na2EDTA.	Oasis HLB cartridges	10 mL methanol and 10 mL ultrapure water	10 mL methanol	1 mL of 50% acetonitrile (acetonitrile : water = 1:1, v/v)	(Xie et al., 2019)
Sediment	Ultrasound-Assisted Extraction (UAE) combined with Solid-Phase Microextr	Ultrasound-assisted extraction–solid-phase microextraction: a 100 mg of lyophilized sediment + 7 mL of deionized water (pH 3) with 1% methanol, centrifuged for 3 min at 3,600 rpm.					(Díaz and Peña-Alvarez, 2017)

	action (SPME)						
Sediment and soil	Microwave-Assisted Extraction and continuous Solid-Phase	1 g of freeze-dried sample +10 mL of (3:2) methanol: water. the bottle was placed in a microwave oven, in front of the magnetron. then, filtered, evaporated under a gentle N2.	Sorbent Column.			10 mL of purified water (pH 7)	(Azzouz and Ballesteros, 2012)
Sediment	Accelerated Solvent Extraction.	1g of Freeze-dried sediment was extracted by Dionex Accelerated Solvent Extraction. followed by solid phase extraction (SPE).	Oasis HLB cartridges	5 mL MeOH and 5 mL H2O	2x4 mL MeOH	H_2O: MeOH (3:1, 490 µL)	(Stewart et al., 2014)
Sediment		2 g solid sample + 100 µL IS, then placed in the fume hood for 4 h, added 10 mL acetonitrile and 10 mL citric acid, vibrated, Ultrasonicated, centrifuged, evaporated and diluted to approximately 200 mL with HPLC grade water.	SAX cartridges and HLB cartridges	10 mL of methanol and then 10 mL HPLC grade water	12 mL of methanol	1 mL of methanol	(Chen et al., 2015)
Soil	Accelerated Solvent Extraction	Freeze-dried soils (5 g) were placed in a 10 mL extraction cell on top of 1 g of					(Grossberger et al., 2014)

		Florisil and covered with another 1 g of Florisil. 5 g of Freeze-dried soils were placed between 1g of Florisil in 10ml, extracted with acetonitrile: water (70:30, v/v), then evaporated, reconstituted in 1 mL acetonitrile: water (30:70), sonicated, spiked with 10 mL of a mixture of isotopically labelled internal standards in methanol, filtered using 0.22 mm then LC-MS analysis.					
Sediment	Pressurized Liquid Extraction	Pressurized liquid extraction (PLE) using Dionex. 1g dried sediments + methanol–water mixture (1:2), then diluted with water.	Oasis HLB cartridges	6 mL methanol and 6 mL HPLC grade water	6 mL pure methanol	1 mL methanol/water (10:90, v/v)	(Osorio et al., 2016a)
Soil	QuEChERS Extraction:	10g freeze-dried soil + 10 ml water, vortexed, 10 mL of 1% acetic acid in ACN were added. Then 4 g of anhydrous MgSO4, 1.0 g NaCl, and 1.0 g of trisodiumcitrate dehydrate and 0.5 g disodium hydrogen citrates were added					(Papaioannou et al., 2019
Soil	United State Environmental Protection Agency (USEPA)	2g of the vadose zone soils + IS and 8 mL methanol-water (1:2, v: v), mixed thoroughly and extracted by ultrasonication, centrifuged and extracted twice, following by solid phase extraction (SPE).	Oasis HLB cartridges	5 mL methanol and 3×5 mL ultra-pure water	5 mL methanol		(Ma et al., 2018)

	Method 1694						
Soil		8 g dw + Surrogate stock+ 30 mL of 1:1 acetone: methanol, extracted, shaken, sonicated and centrifuged, removed the solvent under nitrogen gas, followed by SPE.	Oasis HLB cartridges	10 mL each of methanol, nanopure water.	7 mL of 1:1 methanol: acetone and 7 mL of 9:1 ethyl acetate: methanol	400 µL of acetonitrile	(Dodgen and Zheng, 2016)
Soil and sediment		10 g freeze dried soil or 5 g freeze dried sediment +30 mL methanol: acetone (1:1), ultrasonicated, centrifuged, then concentrated to approximately 5 mL via rotary evaporation evaporation. followed by diluting with 1,000 mL ultrapure water.	Oasis HLB cartridges	6 ml ethyl acetate, 6 ml methanol and 10 ml ultrapure water	8 ml ethyl acetate		(Li et al., 2021a)
Sediment and soil	Pressurized Liquid Extraction (PLE)	Using ASE 200 system, 3g of freeze-dried sediment or air-dried soil + IS mixed with 25 g of Na2–EDTA. In the final method, heated to 90, then extracted using water.	SAX cartridge and Oasis HLB cartridges	5mL of methanol + 5mL of Milli-Q water	6mL of methanol	1mL methanol–water (25:75, v/v)	(Vazquez-Roig et al., 2010)
Sediment		10g air-dried sediment + 50ml acetone were extracted for 12 h in an orbital shaker. Then, the supernatant was then filtered and extracted the residue using 25mL of acetone. followed by taking the combined extracts and added 500mL	Silica Gel clean-up	15 mL of the *n*-hexane and acetone mixture	15 mL of the *n*-hexane and acetone mixture		(Ramaswamy et al., 2011)

		Milli-Q water and 5 g of NaOH and washed with 50mL of n-hexane. followed by SPE.					
Sediment		Microwave Assisted Extraction: 5 g of the air-dried sediment + 50 mL distilled water was extracted using microwave-assisted extraction (MAE) followed by dispersive matrix extraction (DME).	Oasis HLB cartridge	5 mL hexane,5 mL ethyl acetate, 10 mL methanol and 10 mL distilled water.	5 mL hexane, 5 mL ethyl acetate, and with 14 mL methanol.		(Varga et al., 2010)
Soil		5g air-dried soil with 10 mL of 1:1 MeOH:6.25 mM NaOH was vortexed, sonicated, then centrifuged. followed by SPE.	OASIS HLB column	5mL MeOH followed by 5 mL of ultrapure water	8 mL MeOH	1 mL 25% v/v MeOH/water	(Christou et al., 2017)
Sediment		50g Sediment with 45mL of acetone/acetic acid [20:1 (v/v)] was ultrasonicated, then, extracted with 45mL ethyl acetate. followed by using Buchi rotary evaporator, then, SPE.	OASIS HLB cartridges	6mL n-hexane, 2mL acetone, 10mL methanol, and 10mL double-distilled water	31mL methanol and 31mL acetone	1 ml acetone/acetic acid	(Agunbiade and Moodley, 2016)
Sediment	EPA Method 1694	1 g sediment + phosphate buffer (pH 2.0) for Acid extraction, compounds or 10 solutions of NH4OH for Base extraction compounds + add acetonitrile, then evaporated, filtered (1.6 μm), adjusted to pH 2 or to pH 10. added Na4EDTA	Oasis HLB cartridge				(Klosterhaus et al., 2013)

Sediment	Accelerated Solvent Extraction (ASE)	1–10 g mixed, + Internal standards. 100% methanol or methanol/formic acid (100[thin space (1/6-em)]: [thin space (1/6-em)]0.1, v/v) at a temperature of 70 °C					(Langford et al., 2011)
Sediment	Pressurized Liquid Extraction (PLE)	2g sediment samples + 100 ul of surrogate standard solution. Followed by a Pressurised liquid extraction (PLE): Using gentle nitrogen stream, the extract was reduced, re-dissolved in 1 mL of methanol, then centrifuged, collected 0.5 mL from the top of the centrifuge vial	HLB cartridges	5 ml of methanol followed by 5 ml of water	2× 5 ml of methanol	1 ml methanol	(Gorga et al., 2015)
Sediment		0.1 g + stainless steel extraction cell +	HLB cartridges	5 mL methanol and 5 mL DI water	6 mL of methanol containing 5% ammonium hydroxide	1 mL of a mixture of methanol/aqueous solution of 0.05% formic acid (10: 90 v/v).	(Li et al., 2012a)
Soil		Air dried sample extracted with acetonitrile, add internal standard, then centrifuged, evaporated under nitrogen until 3 ml	C18 SPE cartridge	3 mL of acetonitrile + 3 mL of Milli-Q water.	3×1 mL of acetonitrile		(Karnjanapiboonwong et al., 2011)

Sediment		Adding internal standard to 3 mL of organic solvent (50:50 mix of acetone/methanol containing 10 mM acetic acid) per g of dried sediment and Placing on a rotary shaker for 3 h at 150 rpm. then extracted to dryness, reconstituted with 1.5 mL acetonitrile, filtered, diluted to 50% (v/v) water					(Venkatesan et al., 2012)
Sediment		50g + ultrasonic bath using methanol + rotary evaporation	Oasis Hydrophobic-Lipophilic Balance (HLB) SPE cartridge	5 mL methanol and equilibrated with 5 mL water adjusted	(1 × 10 mL) of methanol	1 mL of methanol	(Matongo et al., 2015)
Sediment	Accelerated Solvent Extraction	Freeze-dried sediments were combined with Hydro matrix and poured into 34-ml stainless steel extraction cell including a glass fibre filter and 1 cm of sand. The extract solutions (60–70 ml) were diluted with nano-pure water (400 ml) until the final solution contained less than 5% organic solvent.	Strata-X (Phenomenex, Torrance) cartridge	3 × 20-ml rinses of nano-pure wate	3 ml of 1:1 methanol/water	1:9 methanol and nano-pure water	(Yang et al., 2015)
Sediment	Optimized Mixed Solution		Oasis HLB cartridges	10 mL of methanol and 10 mL of Milli-Q water	10 mL of methanol	1 mL of methanol	(Yang et al., 2010)

Soil		5 mL methanol (1 % (v/v) formic acid) and successively vortexed, ultrasonicated, and centrifuged and then the supernatant was decanted.	Oasis Hydrophilic–Lipophilic Balance HLB				(Yu et al., 2013)
Sediment		3g sediment + internal standards, adding 10 mL of acetonitrile and 10 mL of critic acid buffer (pH=3), followed by vortex, ultrasonic, centrifuged	HLB cartridges	3.0× 2mL of methanol, 3.0× 2mL of ultra-pure water and 3.0× 2mL of 10 mmol L-1 Na2EDTA buffer (pH=3.0		40% aqueous methanol	(Zhao et al., 2016)
Sediment	Ultrasonic-Assisted Extraction		SAX cartridges and HLB cartridges	10 mL methanol and 10 mL Milli-Q water	12 mL methanol with 0.1% formic acid	1 mL of methanol	(Zhou et al., 2011)
Sediment		1.0 g of freeze-dried + internal standards + 5 mL of methanol, shaken, centrifuged	Oasis HLB	6 mL of dichloromethane, 6 mL of methanol and 6 mL of purified water	7 mL methanol and 7 mL dichloromethane		(Li et al., 2021b)
Sediment			Oasis HLB	5 mL methanol and 5 mL Milli-Q water	6 mL methanol and 6 mL of acetone-methanol 50/50 (v/v)		(Xie et al., 2017)

Sediment			Oasis HLB	5 mL methanol and 5 mL ultrapure water	10 mL methanol		(Liu et al., 2017)
Sediment		51 ng IS + 2g of freeze-dried sediment + 30 mL of extraction buffer (pH = 5) (15 mL of methanol, 5 mL of 0.1 M Na2EDTA, and 10 mL of citrate buffer), then vortexed, ultrasonicated, centrifuged and evaporated	Strong Anion Exchange (SAX) and Oasis HLB cartridge	5 mL of methanol, 5 mL of water and 5 mL of 10 mM/L Na2EDTA (pH 3.0) solution	10 mL of methanol,		(Xu et al., 2014)
Sediment	Ultrasonic Assisted Solvent Extraction		Oasis HLB	5 mL of dichloromethane (DCM), 5 mL of methanol, and 5 mL of ultrapure water		100 µL of acetonitrile	(Wang et al., 2016)
Sediment	Ultrasound-Assisted Extraction		Oasis HLB	6.0 mL of methanol and 6.0 mL of Milli-Q water	6.0 mL of methanol		(He et al., 2018)
Sediment	Ultrasonic-Assisted Extraction		Oasis HLB	11 ml methanol and 10 ml DI water	10 mL of methanol and 5 mL methanol containing 5% ammonium hydroxide		(Zhang et al., 2018)

1.7.4. Instrumental analysis

Due to their diverse physico-chemical properties combined with low concentrations and the complexity of environmental solid matrices, PPCPs quantification constitutes an analytical challenge. As a result, sensitive, selective, and reproducible analytical techniques are required for tracing these compounds in various environmental matrices. For the past few years, PPCPs analysis has been conducted mainly by two hyphenated instrumentation techniques: (a) LC (liquid chromatography) with a wide range of detectors, including MS (mass spectrometry), diode array (DAD), and fluorescence detectors, or (b) GC (Gas Chromatography with various types of detectors, such as flame ionisation detectors (FID), electron capture detectors (ECD), and/or MS. (Ohoro et al., 2019). Table 1.10 provides an overview of instrumental analysis parameters, recoveries and limits of detection and quantification reported for PPCPs in sediment and soil samples.

As evident from Table 1.10, LC/MS techniques, including HPLC-MS/M, UPLC-MS/MS, UPLC-Orbitrap/MS and UPLC-Q-TOF/MS are currently the methods of choice for quantitative analysis of multiple PPCPs residues in sediment and soil samples. Consequently, the use of internal standards (preferably isotope-labelled) is required to compensate for analyte losses during sample preparation and to correct for potential ion suppression/enhancement during MS analysis (Kachhawaha et al., 2020).

Table 1.10 Summary of Instrumental analysis parameters reported for PPCPs in environmental solid samples.

Matrix	Instrumental technique	Quantification method	Recovery (%)	LOD*	LOQ**	Reference
Sediment	Ultrahigh-performance liquid chromatography–tandem mass spectrometry UHPLC–MS/MS ESI (+) and ESI (–) MPA: NH4F in MeOH, MPB: NH4F in water for negative mode MPA: MeOH, MPB: water with 0.1% formic acid in both solutions for positive mode	External standard or an internal standard	PStrata-X cartridges: 61–120%. PStrata-X-CW cartridges: 57% to 120%	PStrata-X method: 0.3- 6.7 ng/g. PStrata-X-CW method: 0.3-10 ng/g	PStrata-X method: 1-20 ng/g. PStrata-X-CW method: 1-30 ng/g	(Sadutto et al., 2020)
Sediment	Liquid chromatography with tandem mass spectrometry (LC-MS/MS) ESI (+) and ESI (–)	Isotope dilution internal standard				(Deere et al., 2020)
Sediment	Liquid chromatography electrospray ionization tandem mass spectrometer (LC-ESI-MS/MS) An Xbridge™ (3.5 µm × 2.1 mm × 100 mm) C18 reversed-phase column fitted with a Vanguard® (2.1 mm × 5 mm) pre-column	Isotopically labelled internal standards				(Kairigo et al., 2020)
Sediment	Liquid chromatography (LC-20A, Shimadzu, Japan) triple quadrupole mass spectrometry (ABI 3200Q-TRAP, US) technique (LC-QqQ-MS) ESI (+) and ESI (–), Kinetex C18 column. MPA: 0.1% formic acid in water for positive ionization mode, and 5 mmol/L ammonium acetate in water for negative ionization mode. MPB: methanol in both positive and negative ionization modes.	External standard	40 to 120%			(Ashfaq et al., 2019)

Sediment	Ultra-high-performance liquid chromatography coupled with tandem mass spectrometry (UHPLC-MS/MS), ESI (+) and ESI (–), an Agilent ZORBAX Eclipse Plus C18 column MPA: ultrapure water containing 0.1% formic acid for positive ionization mode. 100% ultrapure water for negative ionization mode. MPB: 100% acetonitrile for both positive and negative ionization mode.	Mixed internal standard	43% to 118%	0.01 to 0.6 ng/g	0.03 to 1.7 ng/g	(Xie et al., 2019)
Sediment	Hewlett-Packard Model 5890 GC with an HP 5971 mass selective detector (GC–MS). a ZB-5M (30 m × 0.32 mm ID) 0.25 μm film thickness (Zebron Phenomenex, USA) column. carrier gas:Helium		56–108%	<0.25 ng/g	<0.8 ng/g	(Díaz and Peña-Alvarez, 2017)
Sediment	Ultra-high pressure liquid chromatography triple-quadrupole mass-spectrometry (UHPLC-MS/MS)					(Huber et al., 2016)
Soil and sediment	Dionex Summit U3000 HPLC system equipped with a manual injector and a Photodiode Array Detector (PAD)		63.7-98.9 %		19.2-45 ng/g	(Zhang et al., 2013)
Sediment and soil	Gas chromatography–mass spectrometry (GC−MS), DB-5 fused silica capillary column coated with 5% phenylmethylpolysiloxane, carrier gas: helium		92 to 101%	0.8–5.1 ng/g		(Azzouz and Ballesteros, 2012)
Sediment	High Pressure Liquid Chromatography (HPLC) ESI (+) and ESI (–) quadrupole-linear ion trap mass spectrometer MPA: H2O 0.1% HCOOH (pH= 2.5) for positive ionization mod, H2O 10mM ammonium formate for negative ionization mode.	Internal Standard	43 to 116%	0.02-3.4ng/g	0.1-11.3 ng/g	(Stewart et al., 2014)

	MPB: MeCN for positive ionization mod, MeCN/MeOH (1:1, v/v) for negative ionization mode.					
Sediment	Liquid chromatography with tandem mass spectrometry (LC-MS/MS) ESI+ Agilent Zorbax Eclipse Plus-C18 column MPA: 0.2% (v/v) formic acid aqueous solution with 2 mM ammonium acetate. MPB: acetonitrile	Internal Standard	64.9 - >500	0.06–11.63 ng/g	0.20 - 38.76 ng/g	(Chen et al., 2015)
Soil	LC-MS, RP-18 column, coupled to an Agilent 6410 triple quadrupole mass spectrometer with ESI ion source. multiple reaction monitoring (MRM) mode, MPA: 1.5% acetic acid in deionized water. MPB: 0.05% acetic acid in acetonitrile.	Internal Standard	>85%	10 - 100 ug/L	50 - 500 ug/L	(Grossberger et al., 2014)
Sediment	Ultra-high-performance liquid chromatography coupled with tandem mass spectrometry (UHPLC-MS/MS), Acquity HSS T3 column for positive electrospray ionization. Acquity BEH C18 column for negative electrospray ionization. MPA: methanol for positive ionization. Acetonitrile for negative ionization. MPB: 10 mM formic acid/ammonium formate (pH 3.2) for positive ionization. 5 mM ammonium acetate/ammonia (pH = 8) for negative ionization.	Internal Standard		0.01 - 14.35 ng/g	0.05 - 25.11 ng/g	(Osorio et al., 2016a)
Soil	LC-MS/MS ESI+/ESI-MP: 0.1% formic acid/acetonitrile for positive, ultrapure water/methanol for negative.					(He et al., 2020)
Soil	Liquid chromatography with tandem mass spectrometry (LC-MS/MS)		60 and 120%		0.01 - 24.75 ng/g	(Papaioannou et al., 2019)

Soil	Shimadzu Prominence UFLC system. Agilent XDB C18 column. multiple reaction monitoring (MRM) mode. MPA: Milli-Q water containing 0.01% formic acid for positive ionization, Milli-Q water containing 2mM ammonium acetate for negative ionization. MPB: methanol for both positive and negative ionization.	Internal Standard	84 and 107 %	0.011-0.28 ng/g	0.05 - 1.2 ng/g	(Ma et al., 2018)
Soil	Liquid chromatography with tandem mass spectrometry (LC-MS/MS). Symmetry C18 column. ESI (+) and ESI (–) for estrone analysis, MPA: 10 mM ammonium hydroxide in nanopure water, MPB: acetonitrile. For all other compounds, MPA: 0.1% ammonium acetate and 0.1% acetic acid in water, MPB: 1:1 methanol:acetonitrile.		87.2% to 112.6%			(Dodgen and Zheng, 2016)
Soil, sediment	GC, VF-5 ms gas-chromatography column, Helium was used as the carrier gas	Internal Standard	82-96%	0.08-0.4ng/g		(Li et al., 2021a)
Sediment and soil	Liquid chromatography–electrospray tandem mass spectrometry (LC–ESI-MS/MS), a column Sunfire C18 for positive ion mode. a column Luna C18 for negative ion mode. MPA: formic acid 0.1% in methanol for PI mode, acetonitrile/methanol (60:40, v/v) for NI mode. MPB: formic acid 0.1% in water for PI mode, ammonium acetate 10mM in water for NI mode.	Standard mixture	≥70%,			(Vazquez-Roig et al., 2010)
Sediment	Gas chromatograph (GC-2010) interfaced with a quadrupole mass spectrometer (QP-2010)		81.1 - 102 %	0.5 - 3 ng/l		(Ramaswamy et al., 2011)

Sediment	GC–MS		95–103%			(Varga et al., 2010)
Soil	UPLC-MS/MS, (ESI), Column BEH Shield RP18. MPA: water + 0.1% formic. MPB: methanol		68-96%	5.8- 10.6 ng/l	17.6 - 32.2 ng/l	(Christou et al., 2017)
Sediment	Liquid chromatography–mass spectrometry (LC/MS). Solvent A: Water + 0.1% Formic acid, Solvent B: Acetonitrile; Flow rate – 0.4 mL/min MPA: Water + 0.1% Formic acid. MPB: Acetonitrile.	External standard pharmaceutical compounds	58.4% to 103%	0.58-14.5 ng/g	1.93 - 48.5 ng/g	(Agunbiade and Moodley, 2016)
Sediment	Liquid chromatography–tandem mass spectrometry (LC/MS/MS) operated in the ESI positive mode, the ESI negative mode	Matrix and some of the labelled standards				(Klosterhaus et al., 2013)
Sediment and sludge	Ultrahigh pressure liquid chromatography (UHPLC), methanol/water mobile phase modified with 10 mM ammonium acetate	Internal standard	56 and 128%,	1 and 50 ng g1.		(Langford et al., 2011)
Agricultural soil	Liquid chromatography with tandem mass spectrometry	Isotope-labelled internal standards	67-361 %			(Walters et al., 2010)
Sediment	TurboFlow™ column (Cyclone, 0.5 × 50 mm, silica type)		65-114%	0.006-0.21	0.021-0.69	(Gorga et al., 2015)
Sediment	Liquid chromatography-electrospray Ionization tandem mass spectrometry (HPLC-ESI MS/MS) system		63.4±10.3 - 132.2±6.4 %	0.02 - 0.5 ng/g		(Li et al., 2012a)
Soil	High-performance liquid chromatography (HPLC) with UV detection		28±7.1 - 104±1.4 %	0.3 - 3.72 ng/g		(Karnjanapiboonwong et al., 2011)

Sediment	Isotope dilution liquid chromatography negative electrospray ionization tandem mass spectrometry (LC-ESI-MS/MS).	Isotope labelled internal standards	81 - 88 %			(Venkatesan et al., 2012)
Sediment	HPLC Agilent 1200 + positive electrospray ionization ESI (+) and negative electrospray ionization ESI (−).			0.001 - 1.732	0.003-5.771	(Matongo et al., 2015)
Sediment	High-performance liquid chromatography (HPLC)			0.0013 - 0.0099 ng/g		(Yang et al., 2015)
Sediment	Rapid Resolution Liquid Chromatography–tandem mass spectrometry (RRLC–MS/MS)	Internal standard	48.2 ± 15 - 160 ± 12.1%	0.08-4.2 ng/g	0.26-14.01 ng/g	(Yang et al., 2010)
Soil	GC-MS					(Yu et al., 2013)
Sediment	Liquid chromatography–electrospray ionization tandem mass spectrometry (LC-ESI-MS/MS)	Internal standard	71-90%		0.6-1.5	(Zhao et al., 2016a)
Sediment	LC-MS/MS	Internal standard	49.4 ± 2.90 - 198 ± 46.0	0.02- 0.8 ng/g	0.24- 2.16 ng/g	(Zhou et al., 2011)
Sediment	Agilent 6430 triple quadrupole mass spectrometer with an electrospray ionization source		64.9 - 110.5%			(Li et al., 2021b)
Sediment	Agilent 1290 Ultra-high performance liquid chromatograph (UPLC) using an Eclipse Plus C18 column (150 mm × 4.6 mm, 5 µm, Agilent Technologies).	Internal standard	73 to 114%	0.02–0.44 ng/g	0.06–1.42 ng/g	(Xie et al., 2017)
Sediment	High-performance liquid chromatography–tandem mass spectrometry (HPLC–MS/MS). The mobile phase consisted of eluent A (acetonitrile) and eluent B (0.1% formic acid in ultrapure water	Internal standard	63.4% to 123.5%	0.3 ng/g to 3.9 ng/g		(Xu et al., 2014)
Sediment	Liquid chromatograph–mass spectrometry using atmospheric pressure chemical ionization (LC–MS)	Internal standard	70–105 %			(Wang et al., 2016)

Sediment	Ultrahigh performance liquid chromatography–tandem mass spectrometry (UHPLC–MS/MS)	Internal standard	53 ± 8% to 141 ± 9%	0.01 to 0.56 ng g−1	(Chen and Zhou, 2014)
Sediment	Liquid chromatography by a tandem mass spectrometry system (LC-MS/MS). ESI (+) and ESI (–)	Internal standard			(He et al., 2018)
Sediment	High-performance liquid chromatography tandem mass spectrometry (HPLC–MS/MS)		65.3 to 125.8%	0.3 - 0.9 ng/g	(Zhang et al., 2018)
Sediment	HPLC-MS/MS technique. ESI (+) and ESI (–).	External standard	30 - 107 %		(Ashfaq et al., 2019)

* LOD: limit of detection; ** LOQ: limit of quantification.

1.8. Research Aim and Objectives

Pharmaceuticals in the environment seem to become increasingly significant since these compounds differ from other common pollutants that have been widely investigated, and there is growing emphasis on their environmental monitoring. Several studies in the literature have pointed out that data and knowledge on PPCPs, particularly in sediments and soil, are lacking in comparison to water.

As a result, the overarching aim of this study was to investigate the occurrence, magnitude and profiles of Pharmaceuticals and Personal Care Products in the freshwater aquatic environment, with particular emphasis on sediments.

To address this aim, 30 PPCPCs were targeted as delegates from multiple treatment groups Table 2.2. The decision was taken in accordance with prioritized pollutant lists produced by the EU under the Water Framework Directives (WFD), as well as the USEPA priority pollutants list under the Clean Water Act. Other choosing indicators were based on reported toxicity to aquatic creatures, stability, and probability of occurrence in the ecosystem.

The selected PPCPs were investigated for their occurrences, distribution, behaviour and seasonal variation in the UK freshwater aquatic environment. Surface sediment samples were obtained from freshwater lakes and rivers from 13 countries in 5 continents to investigate the international variation in PPCPs levels and their global distribution as emerging contaminants of current concern.

In light of this, the following specific objectives were devised:

1. Investigate the occurrence, profiles and distribution of 30 PPCPs in sediment, soil and water samples collected from UK rivers and canals.
2. Investigate the seasonal and spatial variations in PPCPs concentrations in UK freshwater sediment.
3. Assess the global distribution of PPCPs as emerging contaminants in freshwater sediments and compare the contamination levels among various countries and continen

Chapter 2. Materials and Methods

This chapter provides detailed information on the methods and techniques applied for collecting the samples studied in this thesis, as well as the systemic procedures used for sample treatment, extraction and clean-up. The advanced analytical methods applied for measuring trace concentrations of PPCPs in the studied samples are discussed and the quality assurance/quality control protocols adopted throughout this work are explained.

2.1. Introduction

liquid chromatography (LC) and gas chromatography (GC) are the most common methods for detecting PPCPs in the environment. Both these techniques mostly coupled to mass spectrometry (MS). PPCPs have a large range of octanol water partition coefficients (Kow) and ionization constants (pKa), resulting in low analysis precision and efficiency. The first criterion for studies on their environmental behavior to prioritize materials is to have an adequate analytical method (Meng et al., 2021). Derivatization is frequently required for GC–MS methods, especially for acidic, polar, and nonvolatile medicinal substances. LC–MS has largely supplanted GC and HPLC–UV procedures in complex environmental matrices, with LC–tandem MS (MS/MS) and ultra-HPLC (UHPLC)–MS/MS providing greater selectivity and sensitivity (Kachhawaha et al., 2020). A complex matrix is generally present in extracts. As a result, after extraction, a clean-up step is frequently required to remove interferences. Solid phase extraction (SPE) using a wide range of sorbents has been the most popular clean-up method (Pérez-Lemus et al., 2019).

2.2. Sampling

2.2.1. Sampling locations for surface sediment and soil

In this study, surface sediment and soil samples were collected from four UK rivers (River Thames. River Medway, River Tame and River Severn), as well as two canals (Birmingham and Fazeley canal and Worcester and Birmingham canal). More details on sampling locations are provided in Figure 2-1 and Table 2.1.

Figure 2-1 sampling locations in the UK

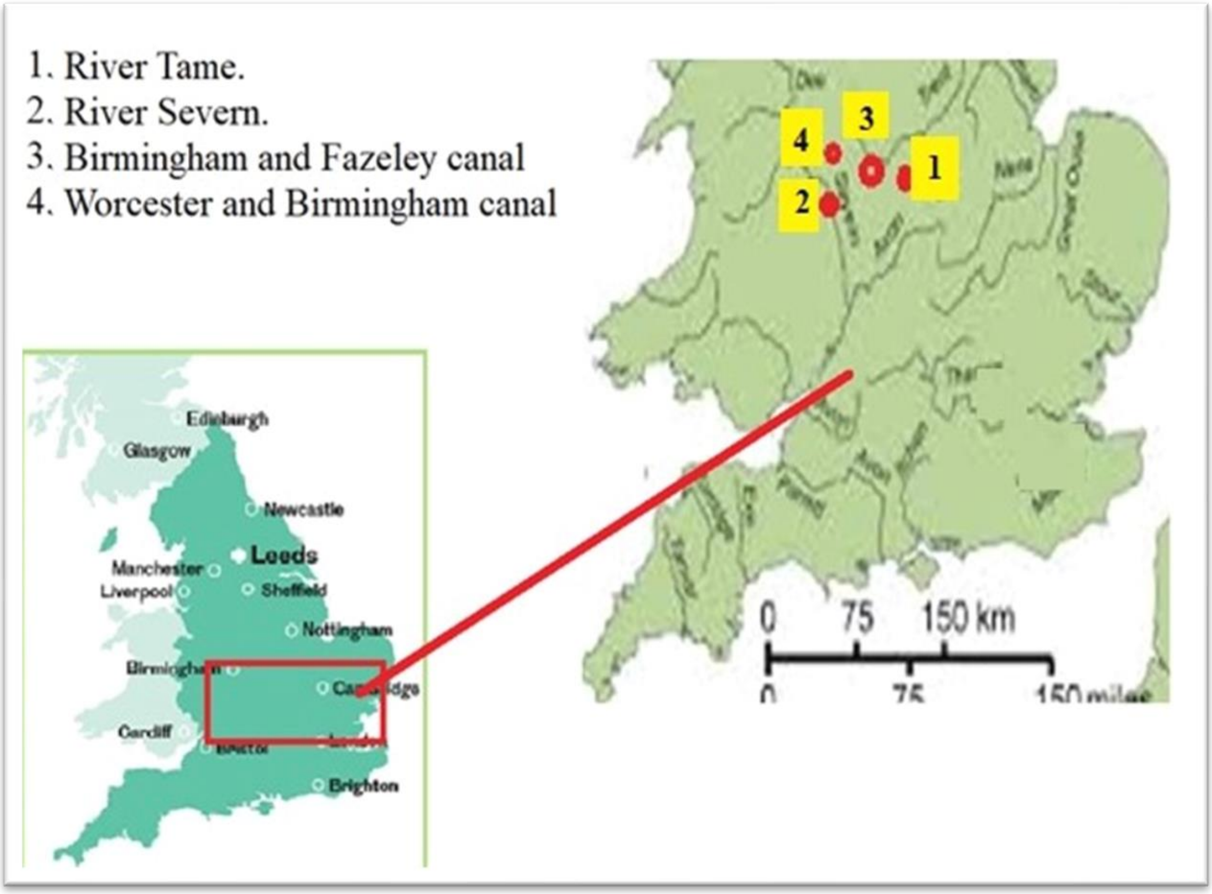


Table 2.1The GPS coordinates for sampling locations in the UK

Site name	Latitude	Longitude	length (km)
Severn River	52°10'51.31"N	2°13'28.72"W	354
Tame River	52°38'36.6"N	1°44'02.7"W	130
Birmingham and Fazeley canal	52°38'34.3"N	1°44'14.8"W	24
Worcester and Birmingham canal	52°27'3.58"N	1°56'11.91"W	47

2.2.2. Sample collection

The quality of analytical data relies on the efficiency of the sampling programme. Therefore, we aimed for decreasing the period between taking samples and chemical analysis to avoid possible degradation and/or adsorption of analytes in the samples. To avoid cross-contamination, all sampling equipment were carefully washed with water and CleanPro™ washing up liquid (UK), dried at 120°C for 2 hours and rinsed with deionized water and acetone before use.

Surface sediment samples (0-5 cm) were collected from 4 locations in the UK (2 Rivers and 2 Canals), used a stainless-steel sediment corer or a bucket auger trowel depending on the depth of the river at the sampling location. Surface soil samples (0-5 cm) were collected using a stainless-steel hand scoop, at a distance of 1 metre from the water edge of the sampled river/canal. The samples were collected in pre-cleaned amber glass bottles with quick-fit lids. These glass bottles were washed by CleanPro™ washing up liquid (UK), followed by a clean rinsing with Milli-Q water, and drying at 120°C in an electric oven (BINDER-ED 23, BINDER GmbH, Germany). The sample bottles were immediately placed in an icebox and transferred to the lab where they were stored at −20 °C in the dark until extraction.

2.3. Sample Analysis

2.3.1. Chemicals and standards

In this research, all Native compounds used (30 PPCPs) were bought from Sigma-Aldrich™ (Irvine, UK) Table 2.2 and 2.3. Five isotope-labelled internal standards (IS), namely: caffeine-D9, codeine-D3, carbamazapineD10, estone-D4 and 4-chlorophenol-2,3,5,6-D4 were purchased from QMX Laboratories Ltd (UK). Both native and internal standards were at high purity (>99%). Methanol (HPLC grade) was used for preparing all standard stock solutions. Oasis MCX (Mixed-mode Cation- exchange) cartridges used in phase solid extraction were bought from Waters™ (Hertfordshire, UK). All chemical reagents for UPLC mobile phase including: ammonium acetate for HPLC ($C_2H_7NO_2$), ammonium fluoride (H_4FN), formic acid, 99.0+%, optima™ LC/MS Grade (CH_2O_2), methanol, HPLC/GC (CH_4O), were obtained from Sigma-Aldrich™ (Gillingham, UK). Formic acid (HCOOH) and ammonium hydroxide (NH_4OH, 30 %) used in sample extraction were purchased from Sigma-Aldrich™ (Gillingham, UK).

Table 2.2 Physico-chemical properties of the studied PPCPs[a]

PPCPs	Subgroups	Log Kow	pKa	Water Solubility (mg/L) at 25 °C
Metformin	Antidiabetic	-2.64	12.4	1.06 X 10^6
Glyburide		4.79[b]	4.32[b]	0.06[b]
Nicotine	Stimulant	1.17	8.5	1 X 10^6
Caffeine		-0.07	0.7	2.16 X 10^4
Acetaminophen	Analgesics and Anti-inflammatory	-1.6	9.38	14 X 10^3
Ibuprofen		3.97	5.3	21
Naproxen		3.18	4.15	15.9
Diclofenac Na		4.02[b]	4.18[b]	4.5[b]
Codeine		1.19	8.2	1065
Tramadol		3.01	9.41	1151
Meclofenamic acid		5		30
Amoxicillin	Antibiotic	0.87	2.40[b]	3.43 X 10^3
Doxycycline		-0.02	3.09	50
Erythromycin-H_2O		3.06[b]	8.8[b]	2.01 X 10^{3}[b]
Trimethoprim		0.91	7.12	400

Sulfamethoxazole		0.89	1.6	610
Clotrimazole		0.5	4.1	0.49
17α-Ethinylestradiol	Steroid	3.67	10.24[b]	11.3
17β-estradiol		4.01	10.27[b]	3.90
Hydrocortisone		1.61	12.61[b]	320
Gabapentin	Anxiolytic drugs	-1.1	3.7	4.49 X 10^{3}
Diazepam		2.82	3.4	66
Metoprolol	Anti-hypertensive	1.88	9.7	2130
Propranolol		3.48	9.42	61.7 X 10^{-3}
Valsartan		4.00	4.73	1.4
Carbamazepine	Antipsychotics	2.45	15.96	18
DEET	Insect repellent	2.02	<2[b]	912
Mefloquine-HCl	Anti-malarial	3.85	8.6[b]	249[b]
Oxazepam	Sedative, hypnotic	2.24	1.55	20
Gemfibrozil	Anti-hyperlipidemic	4.77	4.5	11

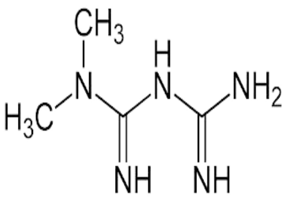
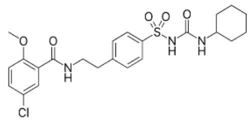
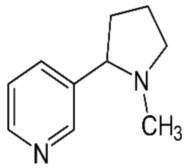
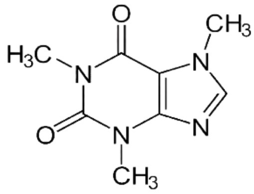
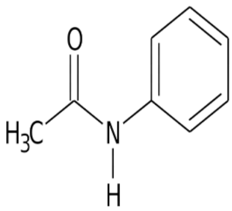
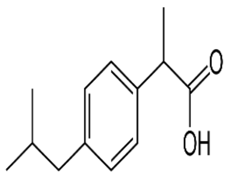
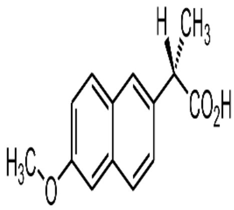
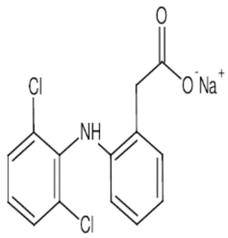
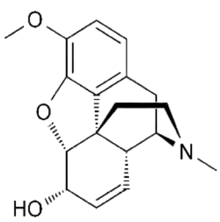
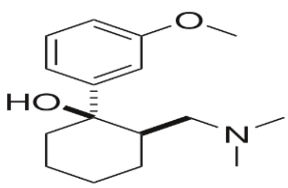
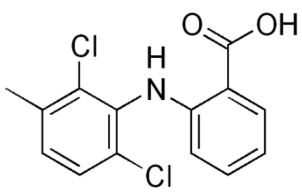
a: National Library of Medicine

National Center for Biotechnology Information

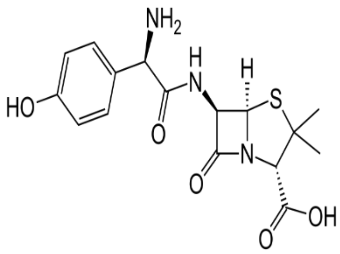
Link, https://pubchem.ncbi.nlm.nih.gov/

b: (Abdallah et al., 2019).

Table 2.3 Molecular Formula, CAS number and Structure of studied PPCPsa

Antidiabetic		**Stimulant**	
			
Metformin	Glyburide	Nicotine	Caffeine
$C_4H_{11}N_5$	$C_{23}H_{28}ClN_3O_5S$	$C_{10}H_{14}N_2$	C8H10N4 O2
CAS: 657-24-9	CAS: 10238-21-8	CAS: 54-11-5	CAS: 58-08-2
Analgesics and Anti-inflammatory			
			
Acetaminophen	Ibuprofen	Naproxen	Diclofenac Na
$C_8H_9NO_2$	$C_{13}H_{18}O_2$	$C_{14}H_{14}O_3$	$C_{14}H_{10}Cl_2NNaO_2$
CAS: 103-90-2	CAS: 15687-27-1	CAS: 22204-53-1	CAS: 15307-79-6
			
Codeine	Tramadol	Meclofenamic acid	
$C_{18}H_{21}NO_3$	$C_{16}H_{25}NO_2$	$C_{14}H_{11}Cl_2NO_2$	
CAS: 76-57-3	CAS: 27203-92-5	CAS: 644-62-2	

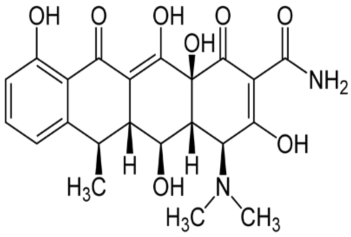
Antibiotic



Amoxicillin

$C_{16}H_{19}N_3O_5S$

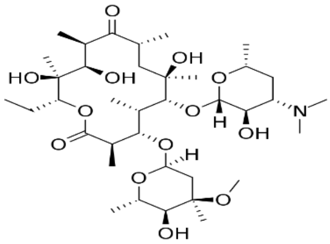
CAS: 26787-78-0



Doxycycline

$C_{22}H_{24}N_2O_8$

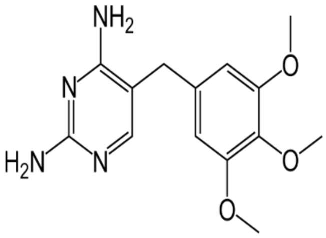
CAS: 564-25-0



Erythromycin-H_2O

$C_{37}H_{69}NO_{14}$

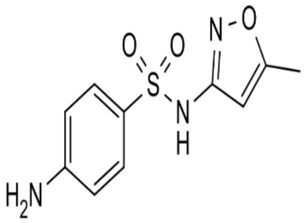
CAS: 67733-56-6



Trimethoprim

$C_{14}H_{18}N_4O_3$

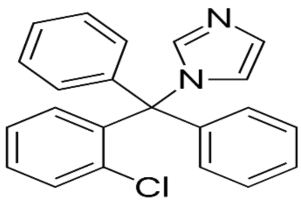
CAS: 738-70-5



Sulfamethoxazole

$C_{10}H_{11}N_3O_3S$

CAS: 723-46-6

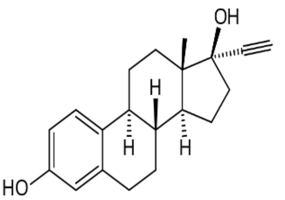


Clotrimazole

$C_{22}H_{17}ClN_2$

CAS: 23593-75-1

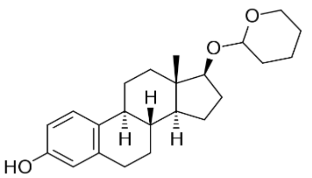
Steroid



17α-Ethinylestradiol

$C_{20}H_{24}O_2$

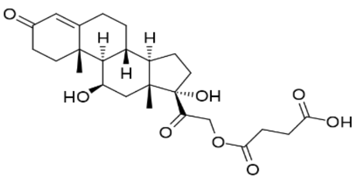
CAS: 57-63-6



17β-estradiol

$C_{18}H_{24}O_2$

CAS: 50-28-2

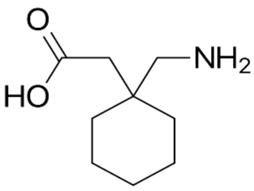


Hydrocortisone

$C_{21}H_{30}O_5$

CAS: 50-23-7

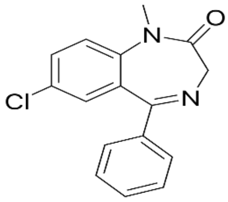
Anxiolytic drugs



Gabapentin

$C_9H_{17}NO_2$

CAS: 60142-96-3

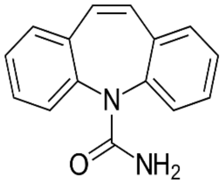


Diazepam

$C_{16}H_{13}ClN_2O$

CAS: 439-14-5

Antipsychotics

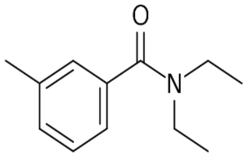


Carbamazepine

$C_{15}H_{12}N_2O$

CAS: 298-46-4

Insect repellent

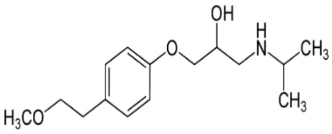


DEET

$C_{12}H_{17}NO$

CAS: 134-62-3

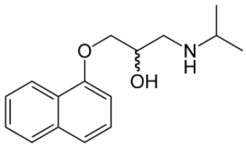
Anti-hypertensive



Metoprolol

$C_{15}H_{25}NO_3$

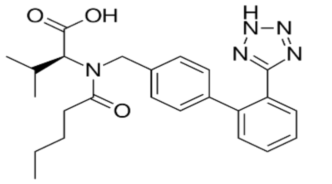
CAS: 51384-51-1



Propranolol

$C_{16}H_{21}NO_2$

CAS: 525-66-6

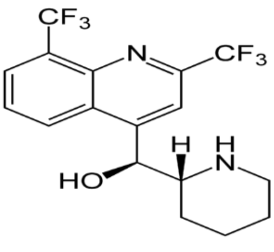


Valsartan

$C_{24}H_{29}N_5O_3$

CAS: 137862-53-4

Anti-malarial

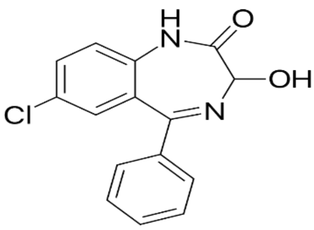


Mefloquine-HCl

$C_{17}H_{17}ClF_6N_2O$

CAS:51773-92-3

Sedative, hypnotic

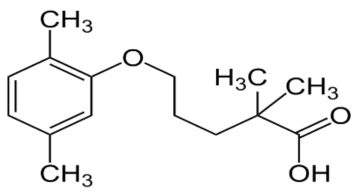


Oxazepam

$C_{15}H_{11}ClN_2O_2$

CAS:604-75-1

Anti-hyperlipidemic



Gemfibrozil

$C_{15}H_{22}O_3$

CAS: 25812-30-0

[a]US EPA, United States Environmental Protection Agency (https://www.epa.gov/)

2.3.2. Selection of target PPCPs

The great majority of pharmaceuticals used in human medicine can enter surface waters, where they may have an impact on aquatic non-target organisms biologically. Priority pollutant lists have been developed both by the European Union (EU) and the United States Environmental Protection Agency (USEPA) identifying a wide variety of chemicals present in wastewaters and storm water runoff that may pose a threat to receiving water bodies including surface water and sediment. The EU Water Framework Directive (WFD) 2000/60/EC also established a first list of 33 environmental contaminants that would be applied as a control strategy for the following years. This list should be updated every 2 years. Moreover, the 1st Watch List (WL) for substances in surface waters under the Environmental Quality Standards Directive (EQSD - Directive 2013/39/EU) was established by Commission Implementing Decision (EU) 2015/495 in March 2015. The list was first updated in June 2018 by the Commission Implementing Decision (EU) 2018/840. Consequently, the third watch list was published in 2020, and the fourth in 2022 (European Commission, 2022). While the United States Environment Protection Agency (US EPA) has been criticised for failing to take regulatory action regarding PPCPs in freshwater resources (Eckstein, 2012), EPA have since published mechanisms for assessing and regulating the presence of certain pharmaceuticals in the environment on the Management Standards for Hazardous Waste (EPA, 2019).

The selection of our target 30 PPCPs in this study was based on their widespread use and regular detection in the aquatic environment, leading to their appearance high up in various prioritisation list of active pharmaceutical ingredients (APIs), including those of regulatory interest (e.g. watch lists for EU Water Framework Directive), as well as priority lists emerging from reported rigorous research approaches applied comprehensively to prioritise PPCP chemicals of high concern/risk in the freshwater environment (Roos et al., 2012, Burns et al., 2018b). The selection of 30 widely used PPCPs, that have been frequently detected in the environment provides more opportunity for comparing our results to those previously reported from other parts of the world. This has also proven useful in conducting an international study of PPCPs in freshwater sediment (*Chapter 5*), where our target PPCPs were measured in sediment samples from various countries all over the world. Further details on the prioritisation listing of 30 target PPCPs are provided in Table 2.4.

Table 2.4 Usage and prescription rates in the UK, removal efficiency by WWTPs, priority listing and hazard classification (PBT/CMR)* for the studied PPCPs.

PPCP	Usage and prescription rates in the UK[x]	Removal efficiency by WWTPs	Priority listing	Hazard (PBT/CMR) *
Metformin	23 M number of items in 2021 in the UK.	MET was completely degraded after 15 days (Markiewicz et al., 2017)	Reported in 4th WL under the Water Framework Directive (EU)[+].	P (3/3). T (1/3). Suspected persistent in the environment. Suspected skin sensitiser. Annex III inventory (ECHA) [++]
Glyburide	6.5 M prescription in the US in 2014.	Not removed from WWTP using UV disinfection in rain season (Estrada-Arriaga et al., 2016)	Identified as priority three or more times in 76 reviewed approaches (Burns et al., 2018b).	P (1/3). B (3/3).
Nicotine	2000 items of nicotine replacement therapies in 2005 in the UK.	Chemical flocculation and activated carbon. Processes 3–73% whereas Activated sludge 57– 99% (Verovšek et al., 2022).	Identified as priority based on hazard and exposure (i.e., frequent detection) (Burns et al., 2018b).	T (3/3).

PPCP	Usage and prescription rates in the UK	Removal efficiency by WWTPs	Priority listing	Hazard (PBT/CMR)
Caffeine	Caffeine is a compound that is found in tea, coffee, cocoa, many soft drinks such as colas and some chocolates. It is also used in a wide variety of medicines especially cold remedies. On average in the UK, we drink nearly 100 million cups of tea per day, each cup containing about 40mg of caffeine. Coffee is almost as popular with 95 million cups of coffee consumed a day. About 80% of coffee drank at home is instant coffee containing around 60mg of caffeine per cup (Drugwise, 2022).	99% efficiency of removal in the secondary treatment plant and 38% efficiency of removal in the primary treatment system (aeration and filtration) (Edwards et al., 2015)	Reported as the most common emerging pollutants, widespread occurrence in the aquatic environment, suspected adverse ecological and (or) human health effects (Vieira et al., 2022).	Suspected hazardous to the aquatic environment. Suspected mutagen Suspected persistent in the environment. Suspected toxic for reproduction. Annex III inventory (ECHA)++
Acetaminophen	16 M number of items in 2021 in the UK.	Due to their high solubility and hydrophilicity, acetaminophen is easily accumulated in aquatic environments and has been found in surface waters, wastewater, and drinking water all over the world (Wu et al., 2012).	Identified as priority three or more times in 76 reviewed approaches (Burns et al., 2018b).	P (3/3). T (2/3).

PPCP	Usage and prescription rates in the UK	Removal efficiency by WWTPs	Priority listing	Hazard (PBT/CMR)
Ibuprofen	1.1 M number of items in 2021 in the UK.	The inability of microbes to effectively break down ibuprofen is one potential explanation for its existence in environmental sources (Chopra and Kumar, 2020).	Candidates for next in WL under the Water Framework Directive (EU).	Suspected hazardous to the aquatic environment. Suspected persistent in the environment. Suspected skin sensitiser. Suspected toxic for reproduction. Annex III inventory (ECHA).
Naproxen	7.2 M number of items in 2021 in the UK.	There are large differences in the removal of naproxen in wastewater treatment plants, ranging from its almost total removal to only a 40% degradation level (Wojcieszyńska and Guzik, 2020).	Identified as priority three or more times in 76 reviewed approaches (Burns et al., 2018b).	P (3/3). T (1/3)
Codeine	15 M number of items in 2021 in the UK.	From WWTP (conventional activated sludge) plant, average removal percentages of about 60% (Repice et al., 2013). After 48 h codeine was removed with 87% efficiency (Mackuľak et al., 2015).		P (3/3). T (1/3). Suspected hazardous to the aquatic environment. Suspected persistent in the environment. Suspected skin sensitiser. Suspected toxic for reproduction Annex III inventory (ECHA)

PPCP	Usage and prescription rates in the UK	Removal efficiency by WWTPs	Priority listing	Hazard (PBT/CMR)
Diclofenac Na	0.5 M number of items in 2021 in the UK.	The removal efficiencies of diclofenac from WWTPs range from 20 to 40% (Rastogi et al., 2021).	Reported in 1st WL under the Water Framework Directive (EU).	P (3/3).
Tramadol	5.8 M number of items in 2021 in the UK.	From WWTP conventional activated sludge system (nitrification, denitrification) , average removal percentages of about 17% (Rúa-Gómez and Püttmann, 2012)	Identified as priority three or more times in 76 reviewed approaches (Burns et al., 2018b).	Suspected hazardous to the aquatic environment. Suspected persistent in the environment. Suspected toxic for reproduction. Annex III inventory (ECHA)
Meclofenamic acid	N/A[¥]	Removal of Meclofenamic in activated sludge is 35% (Osorio et al., 2022).	Identified as priority three or more times in 76 reviewed approaches (Burns et al., 2018b).	Suspected bioaccumulative. Suspected hazardous to the aquatic environment. Suspected mutagen. Suspected persistent in the environment. Suspected toxic for reproduction. Annex III inventory (ECHA)
Gabapentin	7.4 M number of items in 2021 in the UK.	During activated sludge treatment, gabapentin removal was generally 84% effective (Kasprzyk-Hordern et al., 2009).	Candidates for next in WL under the Water Framework Directive (EU).	Suspected carcinogen. Suspected hazardous to the aquatic environment. Suspected skin sensitiser. Suspected toxic for reproduction. Annex III inventory (ECHA).

PPCP	Usage and prescription rates in the UK	Removal efficiency by WWTPs	Priority listing	Hazard (PBT/CMR)
Amoxicillin	7.8 M number of items in 2021 in the UK.	Amoxicillin is removed using a variety of physicochemical procedures including bioremediation, but because antibiotics are hydrophobic and lipophilic, they are resistant to degradation and cannot be entirely eliminated from the environment (Sodhi et al., 2021).	Reported in 2nd WL under the Water Framework Directive (EU).	P (3/3). T (3/3).
Doxycycline	3 M number of items in 2021 in the UK.	Doxycycline was removed in FW (free-water) systems planted (65 ± 34–75 ± 40%), in a Phragmites australis-floating macrophytes system (62 ± 31%) and in conventional horizontal SSF-systems (71 ± 39%) (Hijosa-Valsero et al., 2011).		Suspected hazardous to the aquatic environment. Suspected mutagen. Suspected persistent in the environment. Suspected toxic for reproduction. Annex III inventory (ECHA).
Erythromycin-H_2O	N/A	Not removed from WWTP using UV disinfection (Estrada-Arriaga et al., 2016). Conventional horizontal subsurface flow system was able to remove erythromycin (64±30%) (Hijosa-Valsero et al., 2011).	Reported in 1st WL under the Water Framework Directive (EU).	P (3/3). T (3/3). Suspected hazardous to the aquatic environment. Suspected persistent in the environment. Annex III inventory (ECHA).

PPCP	Usage and prescription rates in the UK	Removal efficiency by WWTPs	Priority listing	Hazard (PBT/CMR)
Sulfamethoxazole	0.75 doses per 1000 inhabitants in England per day in 2020.	Not removed from WWTP using UV disinfection (Estrada-Arriaga et al., 2016).	Reported in 3rd WL under the Water Framework Directive (EU).	P (3/3). T (3/3). Suspected carcinogen. Suspected hazardous to the aquatic environment. Suspected mutagen. Suspected persistent in the environment. Suspected toxic for reproduction. Annex III inventory (ECHA).
Clotrimazole	N/A	Average removal percentages using activated sludge system of about >80% (Kahle et al., 2008).	Reported in 3rd WL under the Water Framework Directive (EU).	P (3/3). B (3/3). T (3/3). Suspected bioaccumulative. Suspected carcinogen. Suspected mutagen. Suspected persistent in the environment. Suspected skin sensitiser. Annex III inventory (ECHA).
17α-Ethinylestradiol	N/A	The activated sludge treatment efficiently removed ethinylestradiol (EE2) (85%) (Baronti et al., 2000).	Reported in 1st WL under the Water Framework Directive (EU).	P (3/3) B (3/3) T (3/3). Suspected carcinogen. Suspected hazardous to the aquatic environment. Suspected persistent in the environment. Suspected toxic for reproduction. Annex III inventory (ECHA).

PPCP	Usage and prescription rates in the UK	Removal efficiency by WWTPs	Priority listing	Hazard (PBT/CMR)
17β-estradiol	N/A	The activated sludge treatment efficiently removed 17β-estradiol E2 (87%) (Baronti et al., 2000).	Reported in 1st WL under the Water Framework Directive (EU).	P (3/3). B (3/3). T (3/3).
Hydrocortisone	N/A	From WWTP pre-treatment, primary treatment and secondary treatment (biological treatment). removal percentages of about 100% (de Jesus Gaffney et al., 2017).		Suspected carcinogen. Suspected hazardous to the aquatic environment. Suspected persistent in the environment. Suspected skin sensitiser. Suspected toxic for reproduction. Annex III inventory (ECHA).
Mefloquine-HCl	N/A	Not removed from WWTP using UV disinfection (Estrada-Arriaga et al., 2016).	Identified as priority pollutant based on hazard. (Burns et al., 2018b)	P (3/3). T (3/3). Suspected hazardous to the aquatic environment. Suspected persistent in the environment. Suspected toxic for reproduction. Annex III inventory (ECHA).
Gabapentin	7.4 M number of items in 2021 in the UK.	During activated sludge treatment, gabapentin removal was generally 84% effective (Kasprzyk-Hordern et al., 2009).	Candidates for next in WL under the Water Framework Directive (EU).	Suspected carcinogen. Suspected hazardous to the aquatic environment. Suspected skin sensitiser. Suspected toxic for reproduction. Annex III inventory (ECHA).

PPCP	Usage and prescription rates in the UK	Removal efficiency by WWTPs	Priority listing	Hazard (PBT/CMR)
Diazepam	4.5 M number of items in 2021 in the UK.	Not removed from WWTP using UV disinfection (Estrada-Arriaga et al., 2016)	Identified among the top 50 priority contaminants based on five different prioritization schemes, Exposure potential (EP), hazard potential (HP), ecotoxicological risk quotient, human health risk quotient and priority index (Zhong et al., 2022).	Suspected carcinogen. Suspected hazardous to the aquatic environment. Suspected persistent in the environment. Suspected toxic for reproduction. Annex III inventory (ECHA).
Metoprolol	0.3 M number of items in 2021 in the UK.	Not removed from WWTP using UV disinfection in rain season (Estrada-Arriaga et al., 2016)	Identified as priority three or more times in 76 reviewed approaches (Burns et al., 2018b).	P (3/3). T (1/3). Suspected hazardous to the aquatic environment. Suspected persistent in the environment. Suspected skin sensitiser. Suspected toxic for reproduction. Annex III inventory (ECHA).
Propranolol	6.5 M number of items in 2021 in the UK.	Not removed from WWTP using UV disinfection (Estrada-Arriaga et al., 2016).	Identified as priority three or more times in 76 reviewed approaches (Burns et al., 2018b).	T (3/3). Suspected hazardous to the aquatic environment. Suspected persistent in the environment. Suspected skin sensitiser. Suspected toxic for reproduction. Annex III inventory (ECHA).

PPCP	Usage and prescription rates in the UK	Removal efficiency by WWTPs	Priority listing	Hazard (PBT/CMR)
Valsartan	0.5 M number of items in 2021 in the UK.	Removal by ordinary WWTP 2ry treatment 16%, Ozone removal 61% and Powdered activated carbon treatment pilot plant 65% (Margot et al., 2013).	Identified as priority three or more times in 76 reviewed approaches (Burns et al., 2018b).	P (3/3). T (1/3).
Carbamazepine	2.1 M number of items in 2021 in the UK.	Not removed from WWTP using UV disinfection (Estrada-Arriaga et al., 2016).	Candidates for next in WL under the Water Framework Directive (EU).	P (3/3). T (1/3). Suspected hazardous to the aquatic environment. Suspected mutagen. Suspected persistent in the environment. Suspected toxic for reproduction. Annex III inventory (ECHA).
DEET	N/A	Removed from WWTP processes of ultrafiltration (UF) >50% , Ozone 50-80% (Sui et al., 2010).	Identified among the top 50 priority contaminants based on five different prioritization schemes, Exposure potential (EP), hazard potential (HP), ecotoxicological risk quotient, human health risk quotient and priority index (Zhong et al., 2022).	Suspected hazardous to the aquatic environment. Suspected skin sensitiser. Suspected toxic for reproduction. Annex III inventory (ECHA).

PPCP	Usage and prescription rates in the UK	Removal efficiency by WWTPs	Priority listing	Hazard (PBT/CMR)
Oxazepam	59535 number of items in 2021 in the UK.	Removal by ordinary WWTP 2ry treatment 13%, Ozone removal 9% and Powdered activated carbon treatment pilot plant 69% (Margot et al., 2013).	Identified as priority three or more times in 76 reviewed approaches (Burns et al., 2018b).	Suspected carcinogen. Suspected hazardous to the aquatic environment. Suspected mutagen. Suspected persistent in the environment. Suspected toxic for reproduction. Annex III inventory (ECHA).
Gemfibrozil	N/A	Not removed from WWTP using UV disinfection in rain season (Estrada-Arriaga et al., 2016).	Candidates for next WL under the Water Framework Directive (EU).	P (3/3). T (2/3). Suspected carcinogen. Suspected hazardous to the aquatic environment. Suspected persistent in the environment. Suspected skin sensitiser. Suspected toxic for reproduction. Annex III inventory (ECHA).

PPCP	Usage and prescription rates in the UK	Removal efficiency by WWTPs	Priority listing	Hazard (PBT/CMR)
Trimethoprim	1.5 M number of items in 2021 in the UK.	50 % removal from WWTP using UV disinfection in rain season (Estrada-Arriaga et al., 2016).	Reported in 3rd WL under the Water Framework Directive (EU).	P (3/3). T (1/3). Suspected carcinogen. Suspected hazardous to the aquatic environment. Suspected mutagen. Suspected persistent in the environment. Suspected toxic for reproduction. Annex III inventory (ECHA).

* Persistence, bioaccumulation and toxicity (PBT). Carcinogenic, mutagenic and reprotoxic chemicals (CMR). Data from Stockholm Convention Council available at: https://politiquedesante.fr/wp-content/uploads/2014/05/PBT-2014-2015-copie.pdf. Ranking order: 1 = Low, 2 = medium, 3 = high.

+ Watch list under the Water Framework Directive (EU), available at https://publications.jrc.ec.europa.eu/repository.

++ European Chemicals Agency, annex III inventory (ECHA), available at https://echa.europa.eu/information-on-chemicals/annex-iii-inventory.

ӿ Data from Statista.com, available at https://www.Statista.com/statistics

¥ Usage data in the UK is not available.

2.4. Sample preparation

Sediment and soil samples were freeze-dried (Martin Christ, Beta 1-8 LSC plus, Osterode am Harz, Germany) at – 60 ◦C and 1 mbar for 60h. All visible stones, shellfish and plant material were removed from the freeze-dried samples prior to sieving through 0.42 mm brass mesh sieve and ground to a fine powder using an agate ball-mill.

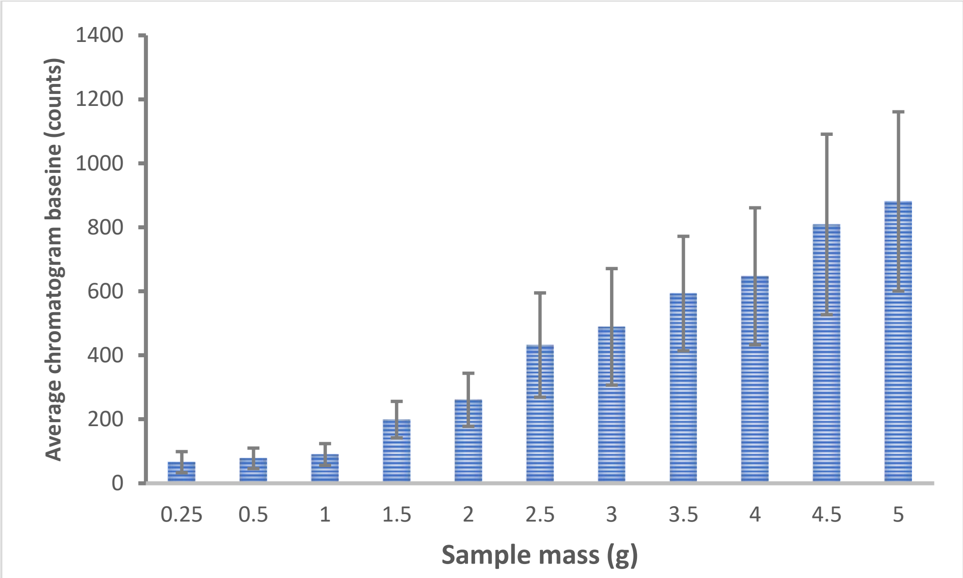
2.5. Method Optimisation

The analytical method applied for determination of target PPCPs in sediment comprises the following steps: (a) sample extraction, (b) sample clean-up, and (c) Instrumental analysis. While the instrumental analysis applied in this thesis was adopted mainly from an existing, published method by our research group for analysis of the same target compounds in surface water samples (Abou-Elwafa Abdallah et al., 2019), the extraction and clean-up steps were optimised for sediment samples.

2.5.1. Sample mass.

Previous studies on PPCPs in sediment have reported the use of dried sample mass ranging from 0.25 – 5 g Table 1.10. Sample mass optimisation was conducted using sample masses of 0.25, 0.5, 1, 1.5, 2, 2.5,3, 3.5,4, 4.5 and 5 g of a homogenised sediment samples, with the aim of selecting the optimum sample mass with low matrix effects. The matrix effects were evaluated as the average detector response of the baseline in the LC/MS chromatograms (counts). Sample masses of 0.25g, 0.5g and 1g showed no statistically significant differences on the chromatogram baseline, while higher sample masses resulted in significantly higher baseline counts Figure 2-2. A higher baseline causes a general reduction of the S/N ratio of analyte peaks resulting in an overall decrease in method sensitivity. Therefore, 1g was selected as the optimum sample mass in the present study.

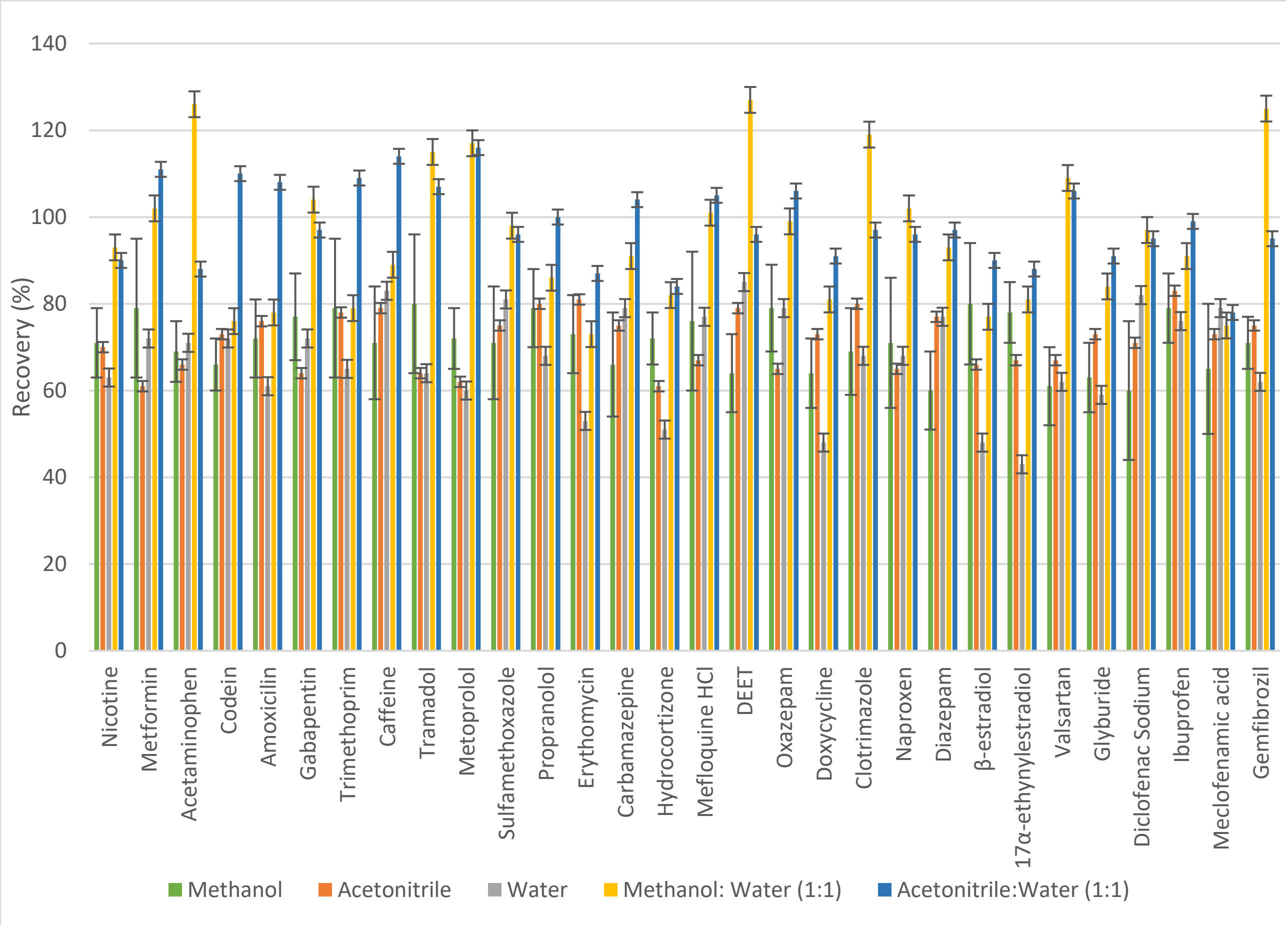
Figure 2-2 . Matrix effects expressed as average (n=3) baseline of the LC/MS chromatograms (counts) for different sediment sample masses



2.5.2. Extraction solvent

Based on the available literature on PPCPs analysis in sediment, several extraction solvents and solvent mixtures were tested. The extraction efficiency for each solvent was measured as the percent recovery of target PPCPs from a 1g aliquots of a homogenised sediment samples spiked at the 250 ng/g level. Results revealed solvent mixtures (i.e., methanol: water (1:1) and acetonitrile:water (1:1)) to have higher extraction efficiency than pure solvents (i.e., methanol, acetonitrile, water) for our target analytes Figure 2-3. This is in agreement with previous literature Table 1.9 and can be explained by the variation in structures and physicochemical properties of the target PPCPs Table 2.2. Acetonitrile: Water (1:1) was selected as the extraction solvent in the present study because it showed less variation (i.e., more precision) across the whole analyte range than Methanol: Water (1:1) Figure 2-3.

Figure 2-3Average recovery (n=3, expressed as %) of target PPCPs following extraction of spiked sediment samples (250 ng/g) using different extraction solvents.



2.5.3. Extraction parameters

Ultrasonic extraction has been reported as the method of choice for PPCPs in sediment (Ebele et al., 2017, Ohoro et al., 2019). In the present study, the parameters for ultrasonic extraction of target 30 PPCPs from sediment were adjusted by measuring the extraction efficiency (expressed as recovery %) of target analytes from 1g aliquots of a homogenised sediment sample spiked at the 250 ng/g level. The investigated parameters were (a) extraction temperature, (b) ultrasonication time, and (c) number of extraction cycles. Results revealed the optimum temperature for ultrasonic extraction was achieved at 60°C, while the optimum ultrasonic extraction time was 10 min Table 2.4. No significant differences in the extraction efficiencies of 30 target PPCPs were observed between 3 and 5 extraction cycles, therefore 3 extraction cycles were used in further sample analysis.

2.5.4. Method clean-up

Previous studies of PPCPs in sediment have reported Solid Phase Extraction (SPE) as the method of choice for sample clean-up (Ebele et al., 2017, Ohoro et al., 2019). SPE has various sorbent beds with different binding characteristics, which can provide higher affinities for certain chemical entities in the target analytes (Renita et al., 2017). The diagram below explains the different functional groups of various sorbent beds available commercially in SPE cartridges.

Figure 2-4 Functional groups in different sorbent beds available through the OASIS® SPE products.

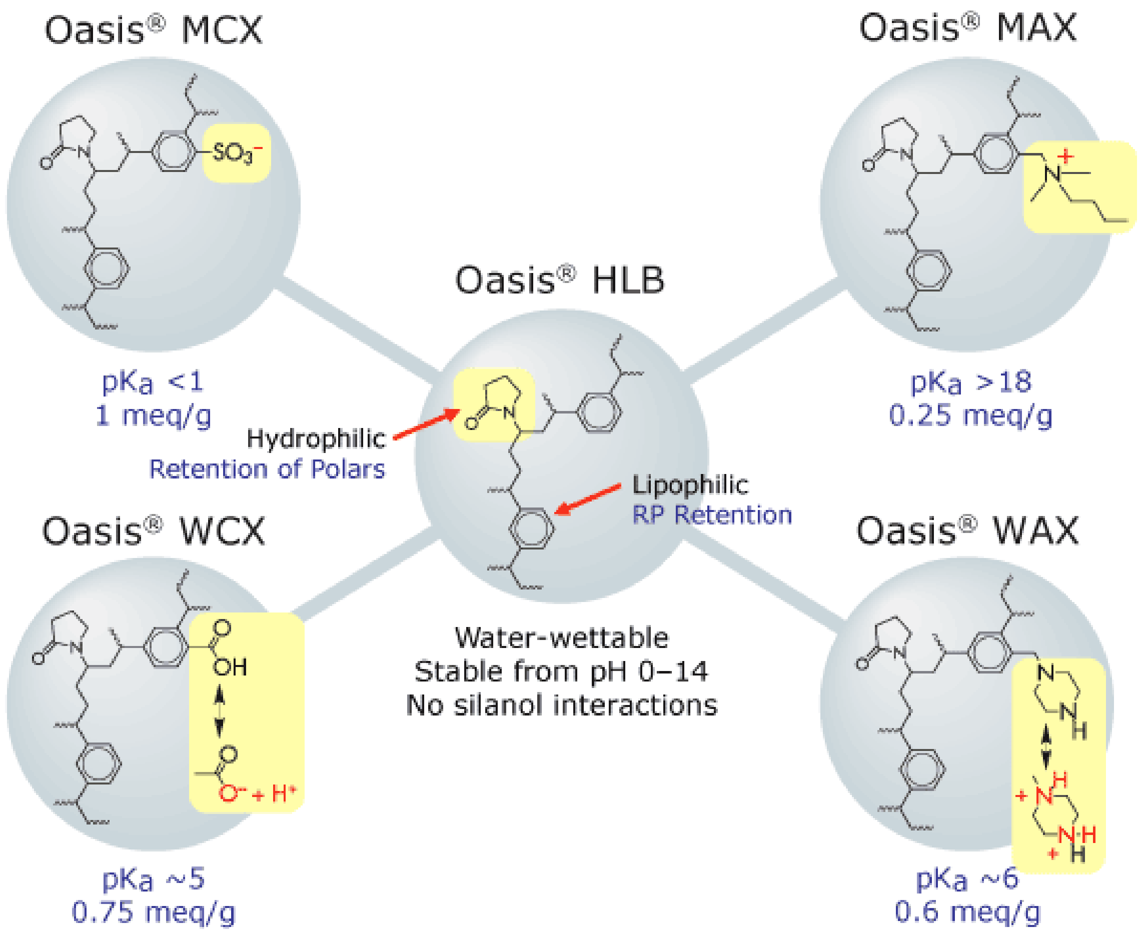


Table 2.5 Average recovery (n=3, expressed as %) of target PPCPs following extraction of spiked sediment samples (250 ng/g) using different extraction parameters.

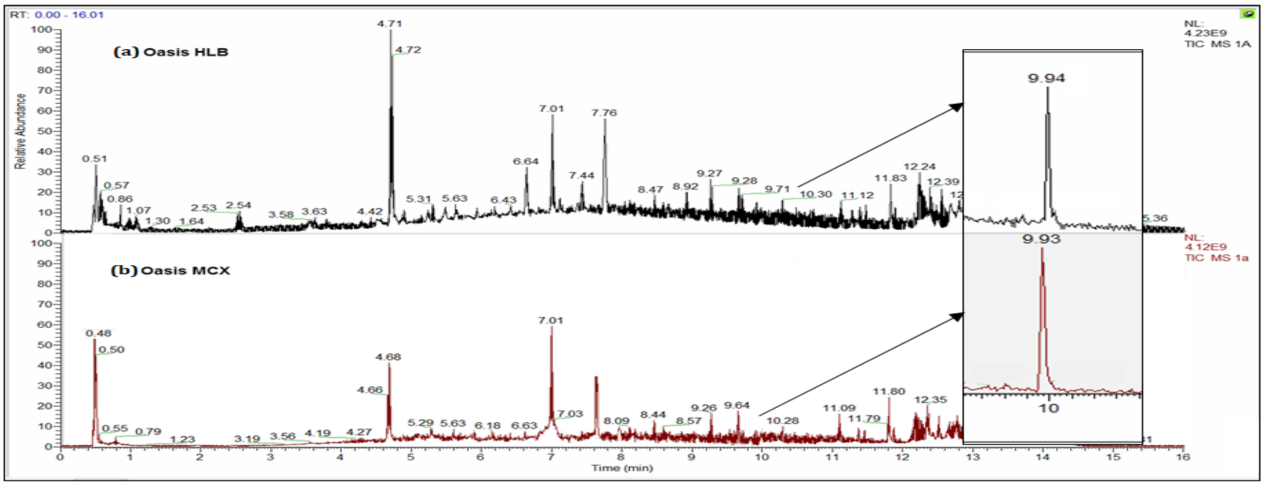
PPCPs	Temperature (°C)					Ultrasonication time (min)			Number of extraction cycles	
	30	40	50	60	70	5	10	15	3	5
Nicotine	55 ± 12	69 ± 8	86 ± 11	100 ± 12	94 ± 9	52 ± 7	104 ± 8	97 ± 12	93 ± 12	95 ± 9
Metformin	50 ± 11	44 ± 7	73 ± 12	93 ± 8	113 ± 8	78 ± 7	98 ± 8	106 ± 8	112 ± 8	108 ± 9
Acetaminophen	41 ± 10	55 ± 7	76 ± 7	99 ± 8	94 ± 7	75 ± 10	99 ± 10	94 ± 7	90 ± 11	103 ±9
Codein	64 ± 12	76 ± 10	78 ± 10	104 ± 9	101 ± 10	47 ± 10	106 ± 8	111 ± 8	98 ± 9	112 ± 9
Amoxicilin	72 ± 11	68 ± 11	90 ± 10	102 ± 8	87 ± 12	55 ± 12	102 ± 11	92 ± 11	89 ± 11	91 ± 11
Gabapentin	68 ± 11	53 ± 9	90 ± 9	104 ± 7	97 ± 11	63 ± 12	105 ± 9	97 ± 7	109 ± 7	104 ± 10
Trimethoprim	55 ± 9	60 ± 8	88 ± 8	103 ± 10	96 ± 10	71 ± 12	107 ± 9	111 ± 8	96 ± 9	104 ± 7
Caffeine	68 ± 12	72 ± 11	89 ± 8	110 ± 11	112 ± 9	47 ± 11	104 ± 8	92 ± 7	104 ± 9	109 ± 12
Tramadol	71 ± 7	76 ± 8	68 ± 11	97 ± 10	99 ± 7	72 ± 10	100 ± 11	106 ± 8	100 ± 10	99 ± 7
Metoprolol	56 ± 10	56 ± 7	90 ± 9	99 ± 7	105 ± 7	79 ± 9	93 ± 8	107 ± 8	95 ± 7	97 ± 10
Sulfamethoxazole	60 ± 8	72 ± 11	79 ± 8	103 ± 7	101 ± 12	69 ± 10	92 ± 11	91 ± 11	91 ± 7	104 ±10
Propranolol	44 ± 11	63 ± 12	75 ± 9	103 ± 9	105 ± 7	63 ± 8	106 ± 7	105 ± 8	98 ± 7	96 ± 8
Erythomycin	45 ± 12	44 ± 10	77 ± 12	89 ± 7	105 ± 7	79 ± 7	104 ± 10	102 ± 7	102 ± 9	97 ± 9
Carbamazepine	70 ± 12	67 ± 8	88 ± 10	98 ± 12	94 ± 7	79 ± 12	98 ± 9	103 ± 10	104 ± 9	99 ± 11
Hydrocortizone	63 ± 7	58 ± 7	76 ± 8	110 ± 11	89 ± 11	60 ± 7	99 ± 10	107 ± 8	95 ± 12	95 ± 8
Mefloquine HCl	69 ± 12	69 ± 10	84 ± 8	89 ± 7	92 ± 12	69 ± 10	92 ± 10	89 ± 11	88 ± 9	89 ± 9
DEET	69 ± 9	66 ± 11	67 ± 9	88 ±7	84 ± 11	54 ± 11	87 ± 8	91 ± 10	85 ± 12	89 ± 7
Oxazepam	58 ± 7	72 ± 8	74 ± 7	99 ± 10	95 ± 10	48 ± 8	97 ± 8	98 ± 8	93 ± 7	107 ± 11
Doxycycline	51 ± 9	54 ± 9	70 ± 12	103 ± 8	93 ± 9	72 ± 12	98 ± 10	97 ± 9	103 ± 9	110 ± 7
Clotrimazole	43 ± 7	47 ± 11	84 ± 10	90 ± 7	109 ± 12	79 ± 7	96 ± 11	94 ± 10	102 ± 7	111 ± 9
Naproxen	53 ± 12	58 ± 7	73 ± 11	86 ± 10	87 ± 11	45 ± 11	91 ± 11	87 ± 8	88 ± 10	86 ± 11
Diazepam	57 ± 11	63 ±12	92 ± 7	97 ± 7	108 ± 9	45 ± 7	98 ± 8	95 ± 7	105 ± 10	102 ±11

PPCPs	Temperature (°C)					Ultrasonication time (min)			Number of extraction cycles	
	30	40	50	60	70	5	10	15	3	5
β-estradiol	51 ± 12	52 ± 12	83 ± 10	99 ± 9	94 ± 10	49 ± 7	80 ± 10	78 ± 8	88 ± 8	109 ± 7
17α-ethynylestradiol	45 ± 10	44 ± 10	70 ± 11	95 ± 12	101 ± 9	62 ± 9	99 ± 9	94 ± 9	102 ± 10	107 ± 11
Valsartan	46 ± 10	54 ± 11	69 ± 10	93 ± 7	111 ± 7	73 ± 7	101 ± 9	103 ± 8	109 ± 10	100 ± 7
Glyburide	69 ± 9	72 ± 8	68 ± 12	90 ± 11	112 ± 12	63 ± 10	104 ± 9	98 ± 8	96 ± 8	102 ± 10
Diclofenac Sodium	71 ± 12	69 ± 11	78 ± 12	95 ± 7	84 ± 10	47 ± 11	97 ± 9	89 ± 9	101 ± 7	96 ± 11
Ibuprofen	55 ± 11	64 ± 10	83 ± 9	106 ± 7	91 ± 10	70 ± 10	94 ± 10	97 ± 8	110 ± 8	104 ± 8
Meclofenamic acid	45 ± 9	48 ± 8	88 ± 11	88 ± 12	91 ± 8	77 ± 12	95 ± 8	93 ± 10	100 ± 8	96 ± 7
Gemfibrozil	51 ± 8	58 ± 9	79 ± 10	105 ± 7	103 ± 12	48 ± 9	97 ± 8	95 ± 12	95 ± 10	101 ± 9

Two of the most widely reported sorbent beds for extraction of a broad range of PPCPs were tested for application in this thesis, namely: Oasis MCX and Oasis HLB. Oasis HLB is made specifically from a ratio of two monomers; hydrophilic N-vinylpyrrolidone and lipophilic divinylbenzene, which provides superior reversed-phase capacity with neutral polar hook for enhanced retention of polar analytes. However, Oasis MCX provides dual modes of retention; cation exchange and reversed phase on a single, clean, stable, high-surface-area, organic co-polymer that is stable from pH 0-14 (Waters Corporation, 2010).

While both sorbent beds provided good results in terms of sample clean-up, it was generally observed that a higher chromatographic baseline and more spectral interference occurred in extracts cleaned-up with HLB cartridges compared to MCX Figure 2.5. This is in agreement with previous results reported by Petrie et al. (Petrie et al., 2016), which was be attributed to the non-selective nature of the hydrophilic-lipophilic balance of reversed-phase HLB sorbent bed, which can cause significant matrix-related interferences when using ESI mode. Therefore, Oasis MCX was applied for the clean-up of all the samples in this thesis.

Figure 2-5 Total ion chromatogram of sample clean-up with SPE on (a) OASIS HLB cartridge (higher baseline) and (b) Oasis MCX (lower baseline). Inset shows the extracted ion chromatogram for Diazepam at m/z = 285.07928 (representative example) with a higher baseline.



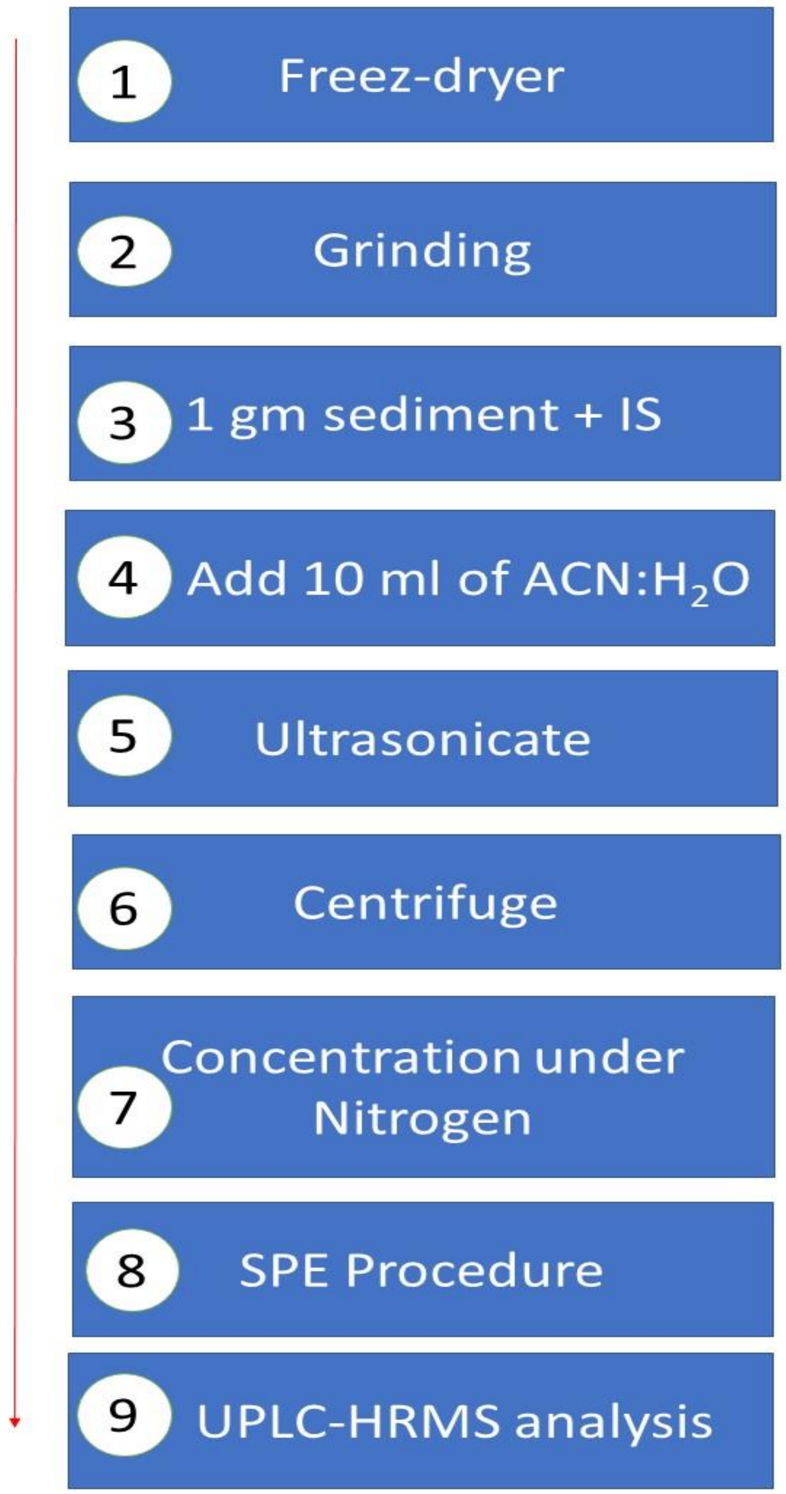
2.6. Sample extraction

One gram of freeze-dried samples was accurately weighted in a clean dry test-tube. The sample was spiked with 50 µl of the IS mixture (1 µg/ml of Caffeine-D9, Codeine-D3, CarbamazapineD10, Estone-D4 and 4-Chlorophenol-2,3,5,6-D4 in methanol) prior to extraction with 10mL of Acetonitrile/deionized water (1:1). The extraction cycle involves vortex-mixing for 1 min, followed by ultrasound-assisted extraction in ultrasonic bath (Grant, Cambridge, UK) at 60°C for 10 min, prior to centrifugation (Sigma Zentrifugen, Osterode am Harz, Germany) at 3500 rpm for 5min. The clear supernatant was transferred into a clean dry 50-ml TurboVap® vial. The extraction cycle was repeated twice using a fresh solvent mixture every time and the clear supernatants were pooled in the TurboVap® vial. The crude extract was concentrated to ~ 1 ml under a gentle stream of N2 using a Biotage Turbovap® II (Charlotte, NC, USA). Figure 2-2 shows a diagram of the extraction and clean up procedure.

2.7. Sample clean up

The crude extracts were subject to clean up using solid phase extraction (SPE). SPE was conducted using Oasis MCX, 6 ml cartridges and Waters™ 20-port controlled pressure vacuum manifold equipped with 50 Hz vacuum pump (Waters, Hertfordshire, UK). The SPE cartridges were pre-conditioned with 3 ml of methanol and equilibrated with 3 ml of Milli-Q water. The crude extracts were loaded onto the pre-conditioned cartridges at a flow rate of 5 ml/min. The cartridges were washed with 3 ml of 0.5 % HCOOH in Milli-Q water (3 ml/min). After drying, PPCPs were eluted with 5 ml of methanol following by 5 ml of 5 % NH4OH in methanol (Petrie, 2016). Finally, the clean methanol extract was evaporated under a gentle stream of Nitrogen then reconstituted in 250 µL of 8:2 water/methanol mixture and transferred into a UPLC vial.

Figure 2-6 Flow diagram of the extraction and clean up procedure.

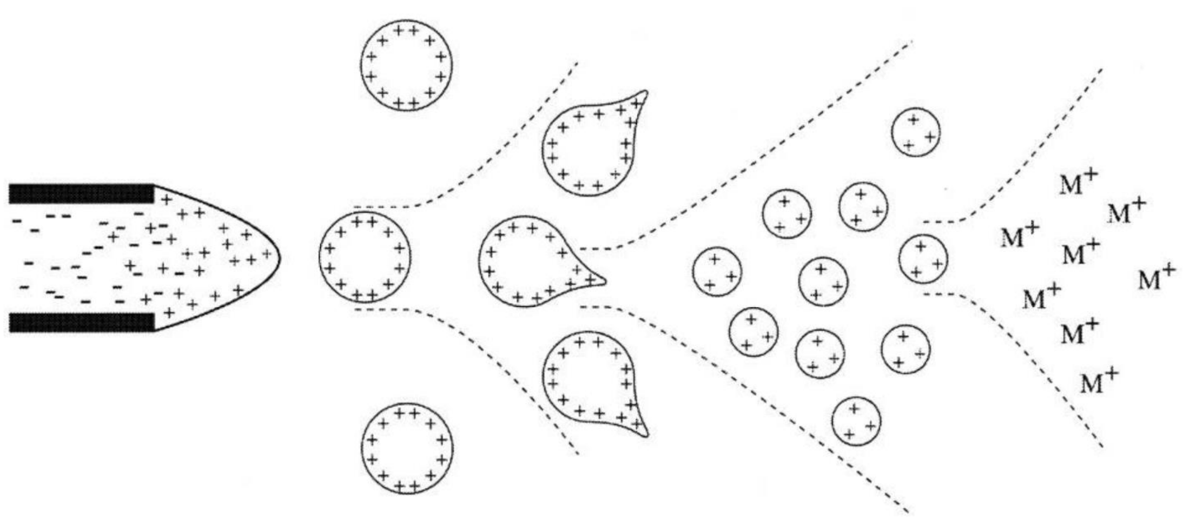


2.8. Instrumental Analysis

Instrumental analysis of samples generated throughout this thesis was conducted on two high-resolution mass spectrometry instruments depending on availability at the time of analysis. Method details for each of the applied instruments is provided below.

Ionisation is the process by which ions are produced when an electron is gained or lost from an atom or molecule. An anion is created when an atom or molecule picks up an electron; a cation is created when they lose an electron. In Mass Spectrometry, Electrospray ionisation (ESI) uses electrical energy to assist the transfer of ions from solution into the gaseous phase before they are subjected to mass spectrometric analysis. Ionic species in solution can thus be analysed by ESI-MS with increased sensitivity. Neutral compounds can also be converted to ionic form in solution or in gaseous phase by protonation (of bases) or cationisation (of acids), and hence can be studied by ESI-MS (Ho et al., 2003). The transfer of ionic species from solution into the gas phase within an ESI source involves three main steps: (a) nebulization to generate a fine spray of charged droplets, followed by (b) solvent evaporation and (3) ion transfer from the highly charged droplets into the vacuum of the mass analyser Figure 2-7. The sample solution is introduced through a highly charged capillary tube. The strong electric field at the tip of the capillary pulls positive charge towards the liquid front. When electrostatic repulsion becomes stronger than the surface tension, small electrically charged droplets leave the surface and pass through the surrounding nebuliser gas to the counter-electrode (Bruins, 1998). Under common experimental LC-MS conditions, positive charge on droplets is generated by the removal of negative charge from via electrochemical discharge of negative ions against the metal wall of the spray capillary. However, the ESI source can be set up for the detection of negative ions, where all power supplies are at reversed polarity. The supply of negative charge to the solution may also take place; electrons released from the spray capillary can be captured by sample molecules having high electron affinity (i.e., Lewis acids or electrophiles). Upon solvent evaporation in the heated ESI source, droplet size continuously decreases and the charge density at the surface of the droplet increases. When the electric field at the surface of a droplet has become sufficiently high, ions are emitted from the droplet surface into the surrounding gas and are sampled by the mass analyser (Bruins, 1998).

Figure 2-7 Mechanism of electrospray ionisation (Ho et al., 2003)



Since ESI makes use of sample ions present in solution, the sample analytes are ionised in solution. For PPCPs, they are mostly ionisable compounds that exist as ions in solution (i.e. weak organic acids, quaternary ammonium salts, sulfonates, carboxylates….etc) or can be easily ionised by mobile phase modifiers (e.g. ammonium acetate, citrates, formats…etc), which are sufficient at low enough concentrations (usually 1-5 μM) to protonate a base (positive ionisation) or deprotonate an acid (negative ionisation) according to the general equation (Liigand et al., 2017, Loos et al., 2016):

$GH^{+} + M \longrightarrow MH^{+} + G$, or

$GH^{-} + M \longrightarrow MH^{-} + G$.

Polar samples that do not contain basic or acidic functional groups aren't directly ionised by protonation or deprotonation. Alternatively, these molecules are "ionised" via association with another ion in solution, commonly known as "adducts". Commonly in ESI, ammonium and sodium ions form positive ion adducts of a sample molecule (i.e., $M.NH_4^+$ or $M.Na^+$), while chloride, acetate and formate ions form negative ion adducts as $M.X^-$ ions (Loos et al., 2016, Klont and Hopfgartner, 2021).

In this thesis, the 30 target analytes represent a broad suite of PPCPs with different physicochemical properties including weak acidic, basic and neutral polar compounds. Therefore, both positive and negative ESI ionisation modes, as well as mobile phase modifiers (ammonium acetates and ammonium fluoride) were required to ionise all analyte molecules in the studied samples. As role of thumb, acidic compounds ionise in ESI negative ion mode, while basic analytes are measured in positive ion mode. Therefore, for analysis of the studied samples, either alternating positive and negative ESI mode was applied when using the Q-Exactive Orbitrap™, or each sample was analysed in two runs (one positive and one negative ESI mode) on the SCIEX™ 5600+ Triple TOF MS, which doesn't have the alternating ESI ion source mode. It is worth noting that some target compounds contain both acidic and basic function groups (e.g., Valsartan) and can ionise in both modes. In such case, ionisation was investigated in both modes during method development and the ionisation mode with highest sensitivity (i.e., ion intensity) was selected. Moreover, for quantification, positively ionised isotope-labelled internal (surrogate) standards were used for positively ionised analytes, while negatively ionised internal standards were applied for quantification of negative ionised target compounds Table 2.5.

2.8.1. Thermo UPLC Orbitrap MS

Samples were analyzed using a UPLC system (*Thermo Fisher Scientific, Bremen, Germany*) comprising a ***Dionex Ultimate 3000*** liquid chromatograph, equipped with a HPG-3400RS dual pump, a TCC-3000 column oven and a WPS-3000 auto sampler. The UPLC system is connected to a ***Q-Exactive Plus Orbitrap*** high resolution mass spectrometer (HRMS) equipped with a heated electrospray ionisation (HESI) ion source. The UPLC system is controlled via Chromeleon™ 7.2

CDS Software, while the Orbitrap HRMS is operated via Xcalibur™ Software. This method was applied for analysis of sediment, water and soil samples in chapter 3 of this thesis.

Target analytes were separated on an ***Accucore RP-MS column (100 x 2.1 mm, 2.6 µm)*** using a mbile phase system of 2 mM NH4COOH/2 mM NH4F in water (mobile phase A) and 0.5 % formic acid in methanol (mobile phase B). A gradient elution programme at 400 µL/min flow rate was applied as follows: start at 2 % B, stay for 1 min; increase to 98 % B over 11 min, held for 1 min; then decrease to 2 % B over 0.1 min; maintained constant for a total run time of 16 min. Injection volume was 5 µL.

The Orbitrap parameters were set as follows: alternate switching (-)/(+) ESI, sheath gas flow rate 50 AU (arbitrary unit), auxiliary gas flow rate 15 AU, spray voltage ± 4.5 kV, capillary temperature 300°C, probe heater temperature 300°C. The optimal MS parameters were: S-lens RF-level 50, resolution 35,000 FWHM (Full Width at Half Maximum) and scan range 125 to 750 m/z. In each scan, the automated gain control (AGC) target in the C-traps was set at 1 x 106 ions and the maximum injection time (IT) was 50 ms.

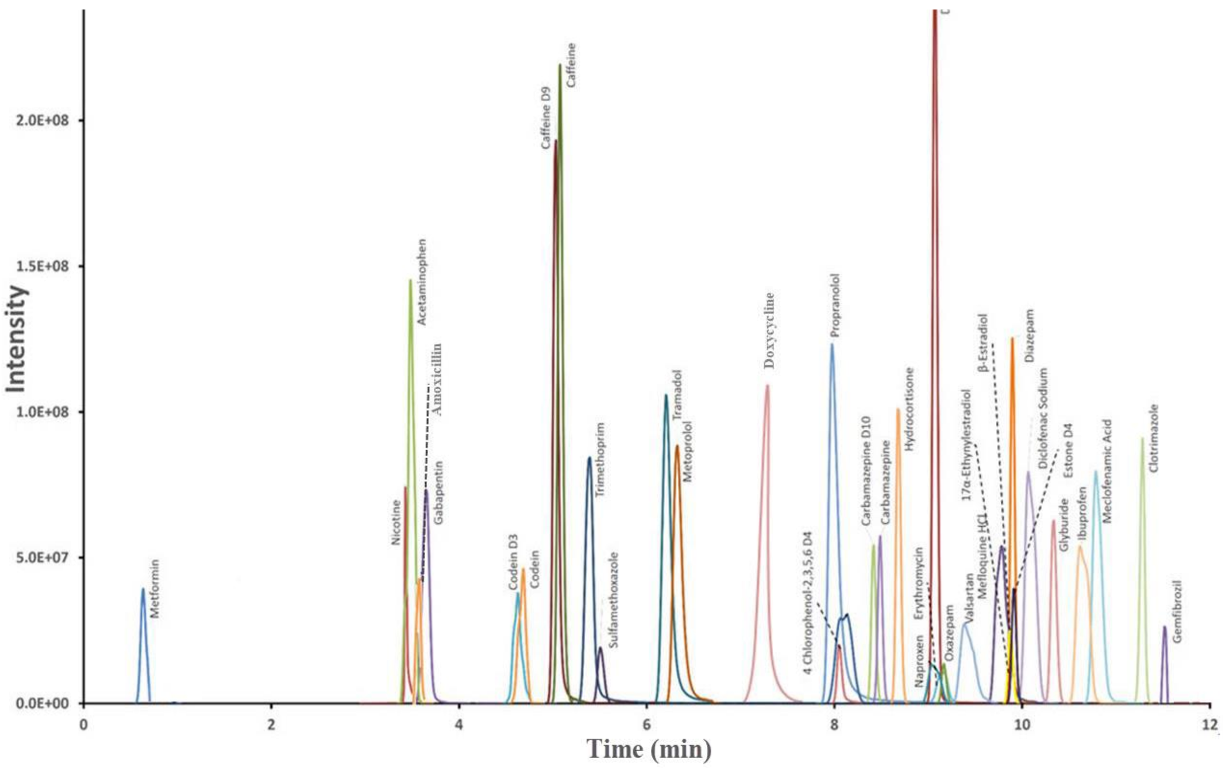
The use of Q-Exactive Orbitrap high resolution mass spectrometer Figure 2-3 provided several advantages due to its high mass resolution offered at quick scan time. The Q-Exactive MS applies accurate mass analysis for detection and quantification of chemical compounds at high scanning speed and rapid polarity switching of the heated electrospray ionisation source. This enables the simultaneous targeted analysis of 30 different week acidic, basic and neutral PPCPs in the current study. The Q-Exactive provides unique low mass error (<1 ppm), as well as highly stable accurate mass calibration over a broad mass range. The Orbitrap mass analyser has the ability to resolve analytes of interest from interferences by high resolution, accurate mass discrimination between ions of interest and interfering ions in the very low and low mass-to-charge (m/z) ranging from m/z 50-300 and m/z 300-1000, respectively (Bromirski, 2018).

Table 2.6 Analytical Method Parameters for UPLC Orbitrap MS

UPLC parameters		
Column	Accucore RP-MS column (100 x 2.1 mm, 2.6 µm)	
Injection volume	5 µL	
Mobile phase	Solvent A: 2 mM NH4COOH/2 mM NH4F in water Solvent B: .5% acetic acid in methanol	
Gradient	Time	Buffer B (%)
	1	2
	11	98
	13	98
	13.2	2
	16	2
Flow rate	0.4 mL/min	
<u>Orbitrap parameters</u>		
ESI mode	alternate switching (-)/(+)	
Sheath gas flow rate	50 AU	
Discharge volage	4.5 kV	
Capillary temperature	300 °C	
Resolution	35,000 FWHM	
AGC target	1E6	
Maximum injection time	50 ms	
Scan range	125–750 m/z	

Figure 2-8 Thermo Q-Exactive Plus Orbitrap MS platform used for analysis of samples.

Figure 2-9 Chromatographic separation of target PPCPs (500 ng/ml in methanol)



Out of 30 target PPCPs, 7 chemicals produced stable ions in negative mode, while 17 compounds were positively ionized. Interestingly, 7 target compounds, namely: valsartan, meclofenamic acid, glyburide, diclofenac sodium, naproxen, sulfamethoxazole and oxazepam produced stable ions in both positive and negative ionisation modes. However, higher intensity was observed for the positive ions, which were used for quantification of all 7 PPCPs Table 2.5.

Optimisation of mass spectrometric parameters was conducted to achieve maximum method sensitivity indicated by the highest signal/noise (S/N) ratio for the studied compounds. Although the Q-Exactive Orbitrap™ enables ultra-high mass resolution (up to 280,000 FWHM), the scan (dwell) time increases with increasing mass resolution. Long scan cycle times result in broad chromatographic peaks and few data points acquired per each peak. This ultimately results in low reproducibility of the analytical method. Therefore, a minimum of 10 data points per peak is required to define its shape and enable reproducible quantification based on area under the peak, while an optimum of 15-20 points are required to expose subtle peak-shape features (NIESSEN, 1998). Another unique feature of the Orbitrap MS is the automatic gain control (AGC), defined as the maximum number of ions (between 2×10^4 - 4×10^6) to be injected into the orbitrap mass analyser within a specified injection time (IT). A systemic approach was adopted to optimise these parameters for each target analyte. This involved gradual ramping and recording the simultaneous impacts of mass resolution (up to 280,000 FWHM) and AGC (up to 4×10^6) on the peak area of the studied compound at constant IT of 50 milliseconds with a preset minimum of 15 data points per peak. Despite few non-significant variations for a few compounds, results revealed the optimum MS parameters for the overall method as: resolution = 35000 FWHM, AGC target = 1×10^6 ions and IT = 50 ms Figure 2-5.

Figure 2-10 the impact of mass resolution (FWHM) and automatic gain control target (AGC-ions) at injection time of 50 ms, on the peak area of nicotine (500 ng/mL in methanol) and the number of data points per selected peak.

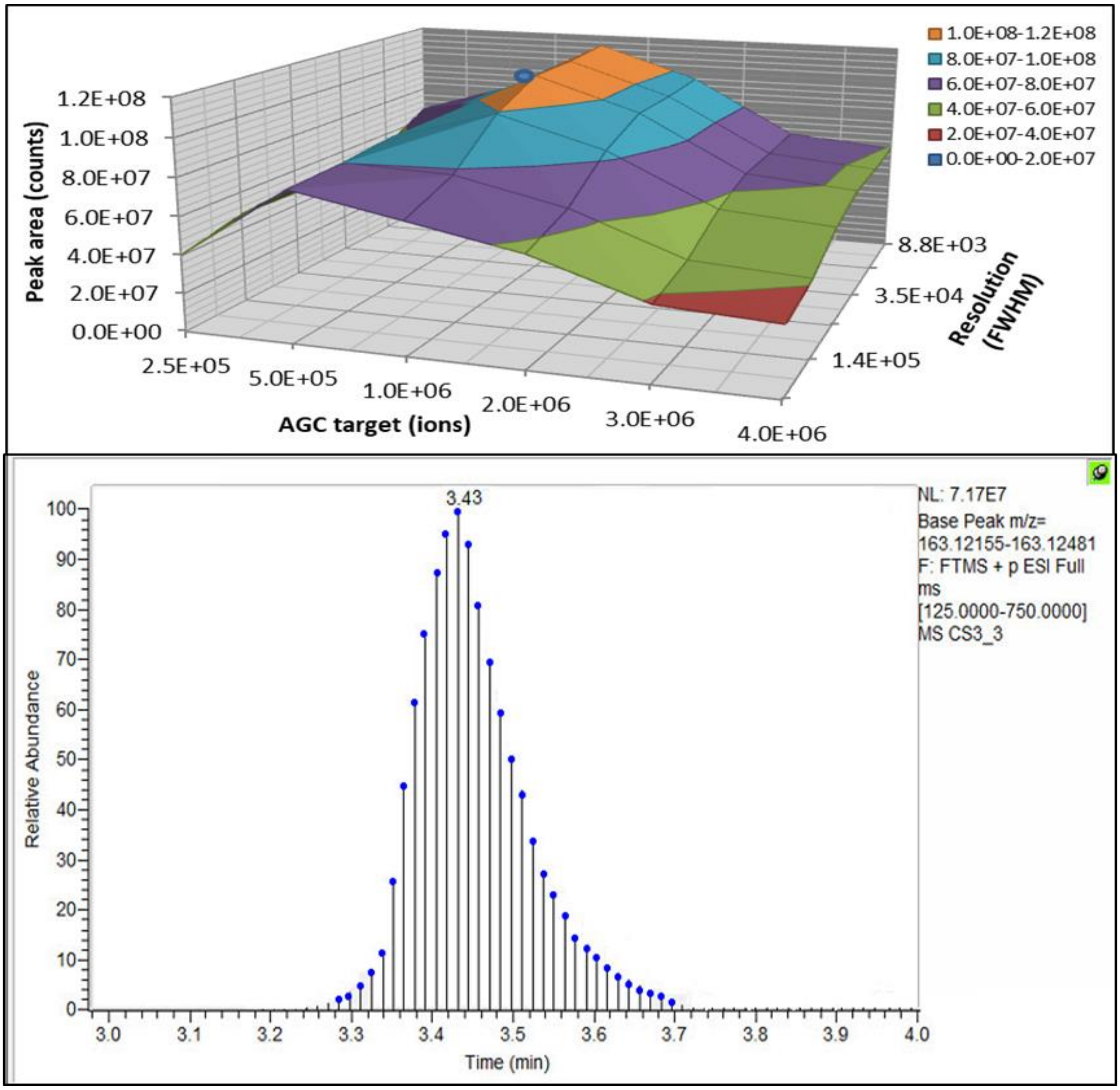


Table 2.7 Target PPCPs and their chemical formula, accurate mass, ESI mode, retention time (tR), as well as the internal (surrogate) standards used for quantification using UPLC Orbitrap MS

Name	Therapeutic group	Chemical formula	Ionisation	Accurate Mass (Da)	t_R (min)	Internal standard
Metformin	Antidiabetic	$C_4H_{11}N_5$	+ve	130.10884	0.64	Codeine-D3 (t_R= 4.63 min)
Nicotine	Stimulant	$C_{10}H_{14}N_2$	+ve	163.12318	3.43	Codeine-D3
Acetaminophen	Analgesic	$C_8H_9NO_2$	+ve	152.07143	3.46	Codeine-D3
Amoxicillin	Antibiotic	$C_{16}H_{19}N_3O_5S$	+ve	366.09687	3.53	Codeine-D3
Gabapentin	Anti-convulsant	$C_9H_{17}NO_2$	+ve	172.13417	3.65	Codeine-D3
Codeine	Narcotic analgesic	$C_{18}H_{21}NO_3$	+ve	300.16089	4.69	Codeine-D3
Caffeine	Stimulant	$C_8H_{10}N_4O_2$	+ve	195.08862	5.17	Caffeine-D9 (t_R= 5.13 min)
Trimethoprim	Anti-bacterial	$C_{14}H_{18}N_4O_3$	+ve	291.14540	5.40	Codeine-D3
Sulfamethoxazole	Anti-bacterial	$C_{10}H_{11}N_3O_3S$	+ve	254.05949	5.50	Caffeine-D9
Tramadol	Narcotic analgesic	$C_{16}H_{25}NO_2$	+ve	264.19584	6.20	Codeine-D3
Metoprolol	Beta-blocker	$C_{15}H_{25}NO_3$	+ve	268.19076	6.33	Codeine-D3
Doxycycline	Antibiotic	$C_{22}H_{24}N_2O_8$	+ve	445.14963	7.47	Codeine-D3
Propranolol	Beta-blocker	$C_{16}H_{21}NO_2$	+ve	260.16433	7.97	Codeine-D3
Carbamazepine	Anti-convulsant	$C_{15}H_{12}N_2O$	+ve	237.10333	8.49	Carbamazepine-D10 (t_R= 8.49 min)

Hydrocortisone	Steroid	$C_{21}H_{30}O_5$	+ve	363.21686	8.67	Carbamazepine-D10
Naproxen	NSAID	$C_{14}H_{14}O_3$	-ve	229.08824	9.05	4 Chlorophenol-D4 (t_R= 8.05 min)
N, N-diethyltoluamide (DEET)	Insect repellant	$C_{12}H_{17}NO$	+ve	192.13931	9.07	Carbamazepine-D10
Erythromycin	Antibiotic	$C_{37}H_{67}NO_{13}$	+ve	734.47192	9.14	Carbamazepine-D10
Oxazepam	Sedative, hypnotic	$C_{15}H_{11}ClN_2O_2$	+ve	287.05860	9.17	Carbamazepine-D10
Valsartan	Anti-hypertensive	$C_{24}H_{29}N_5O_3$	-ve	434.22117	9.56	4 Chlorophenol-D4
Mefloquine	Anti-malarial	$C_{17}H_{16}F_6N_2O$	+ve	379.12231	9.78	Carbamazepine-D10
17α-ethynylestradiol	Steroid	$C_{20}H_{24}O_2$	-ve	295.17047	9.87	Estone-D4 (t_R= 9.91 min)
β-estradiol	Steroid	$C_{18}H_{24}O_2$	-ve	271.16998	9.88	Estone-D4
Diazepam	Sedative, hypnotic	$C_{16}H_{13}ClN_2O$	+ve	285.07928	9.89	Carbamazepine-D10
Diclofenac Na	NSAID	$C_{14}H_{10}Cl_2NNaO_2$	-ve	294.01031	10.06	4 Chlorophenol-D4
Glyburide	Antidiabetic	$C_{23}H_{28}ClN_3O_5S$	-ve	492.13818	10.34	4 Chlorophenol-D4
Ibuprofen	NSAID	$C_{13}H_{18}O_2$	-ve	205.12297	10.61	4 Chlorophenol-D4
Meclofenamic acid	NSAID	$C_{14}H_{11}Cl_2NO_2$	-ve	294.01031	10.78	4 Chlorophenol-D4
Clotrimazole	Anti-fungal	$C_{22}H_{17}ClN_2$	+ve	345.11676	11.28	Carbamazepine D10
Gemfibrozil	Anti-hyperlipidemic	$C_{15}H_{22}O_3$	-ve	249.15001	11.54	4 Chlorophenol-D4

2.8.2. SCIEX UHPLC Triple TOF MS/MS

The ultrahigh-performance liquid chromatography (UHPLC) comprised of 2 Exion LC AD pumps, an Exion LC degasser, an Exion LC AD autosampler, an Exion LC AC column oven, an Exion LC controller and an Exion LC Reservoir Tray (AB Sciex LLC, USA) linked to an AB SCIEX triple TOF 5600+ MS/MS system (AB Sciex LLC, USA) equipped with Duo-Spray ion source. Electrospray ionisation (ESI) mode was applied for all sample analysis within this thesis. This method was applied for analysis of sediment samples in chapters 4 and 5 of this thesis.

The compound separation was carried out using an Accucore C_{18} (100 mm × 2.1mm x 2.6 µm) chromatographic column (Thermo Scientific, USA) kept at 40 °C. The gradient elution procedure was designed using the mobile phases A (2 mM NH4COOH/2 mM NH4F in water) and mobile phases B (0.5 % formic acid in methanol).

Table 2.8 Analytical Method Parameters for UHPLC Triple TOF MS/MS

UPLC parameters		
Column	Accucore RP-MS column (100 x 2.1 mm, 2.6 µm)	
Injection volume	5 µL	
Mobile phase	Solvent A: 2 mM NH4COOH/2 mM NH4F in water Solvent B: .5% acetic acid in methanol	
Gradient	Time	Buffer B (%)
	1	2
	11	98
	13	98
	13.2	2
	16	2
Flow rate	0.4 ml/min	
TripleTOF parameters	Positive	Negative
Ion source temperature (°C)	300 °C	300 °C

IonSpray voltage floating (ISVF)	5500	-4500
Ion source gas 1 (GS1)	35	35
Ion source gas 2 (GS2)	35	35
Curtain gas (CUR)	25	25
Collision energy (CE)	35	-45
Declustering potential (DP)	89	-89
Ion release delay (ms)	50	50
Scan range (m/z)	100 - 750	200 - 500

Figure 2-11 : Chromatographic separation of positive target PPCPs (500 ng/ml in methanol using UHPLC Triple TOF MS/MS).

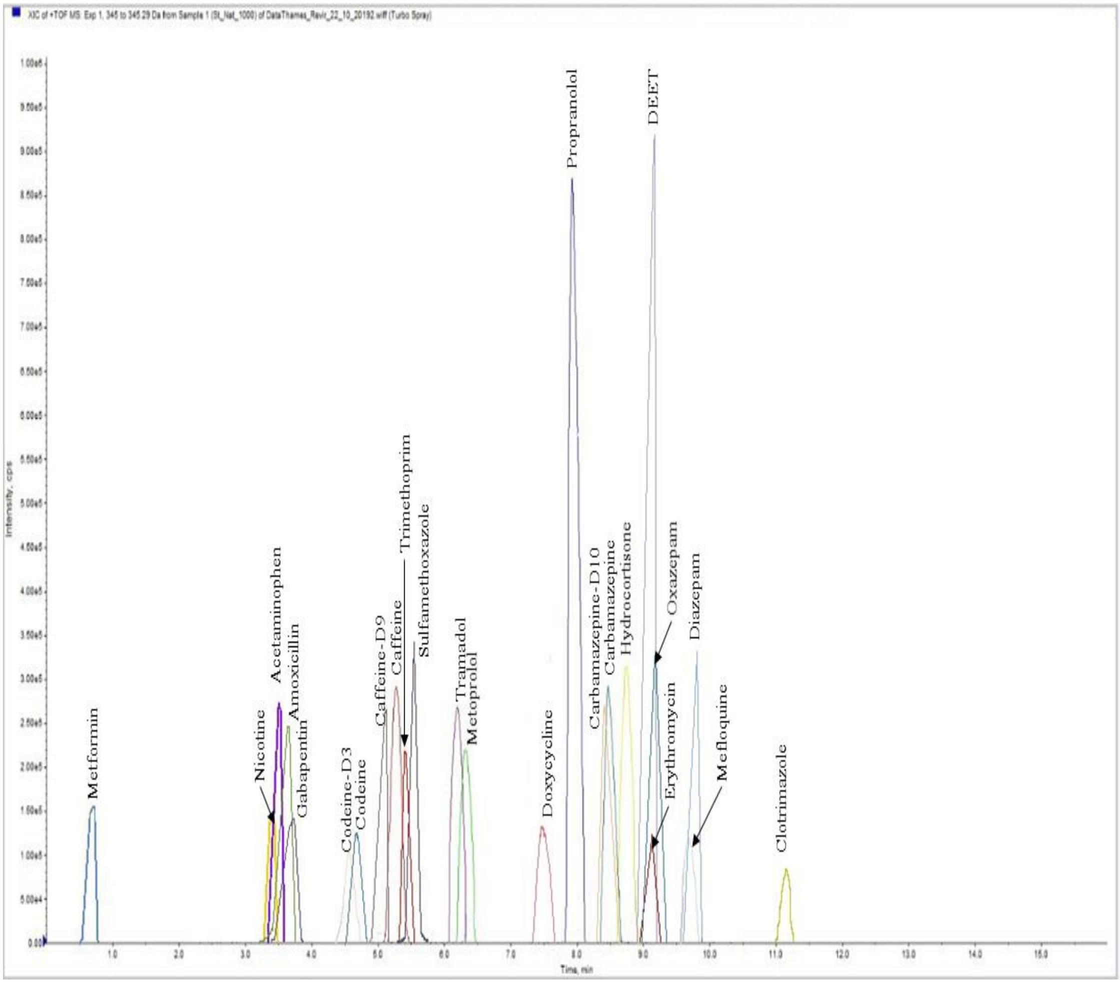


Figure 2-12 : Chromatographic separation of negative target PPCPs (500 ng/ml in methanol) using UHPLC Triple TOF MS/MS)

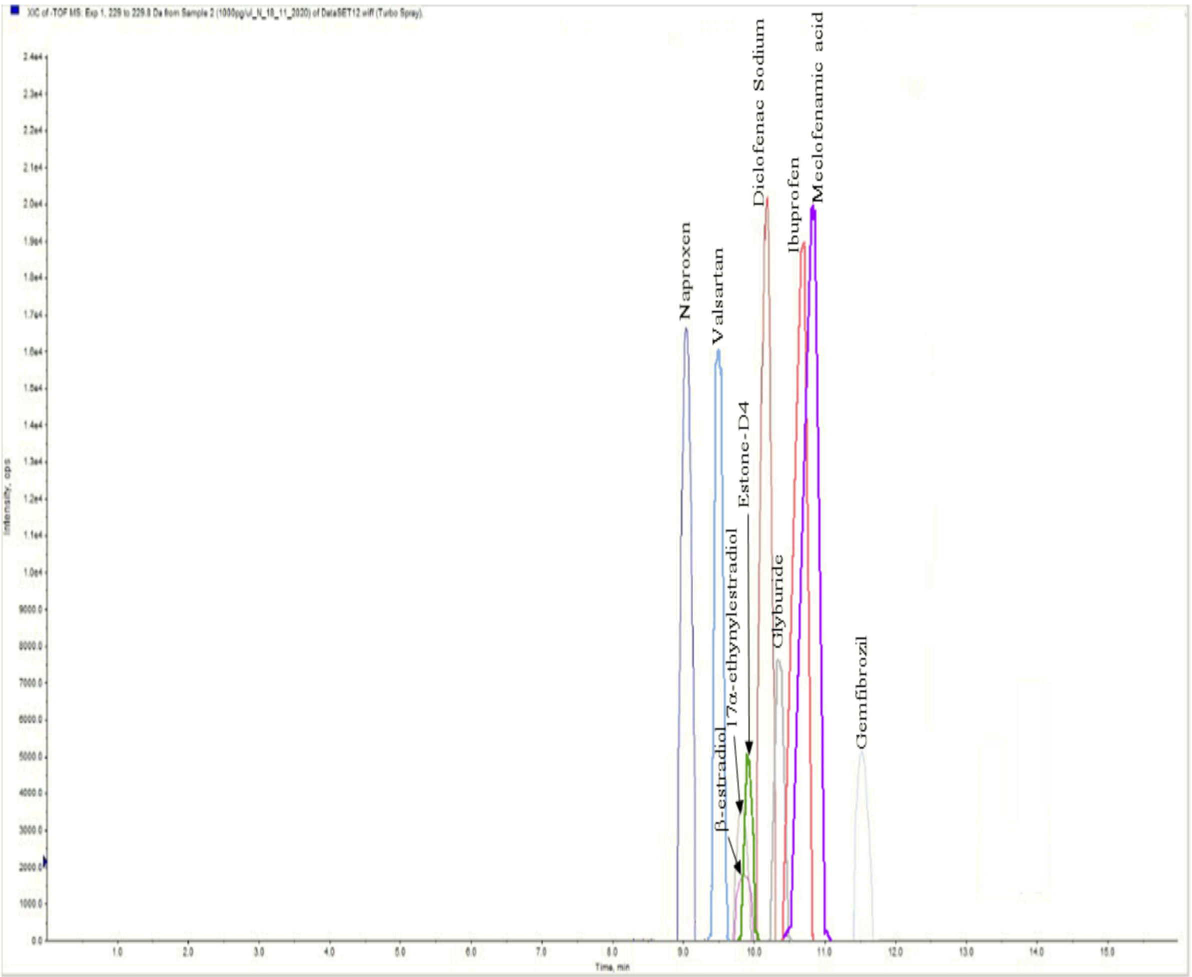


Table 2.9 Target PPCPs and their chemical formula, accurate mass, ESI mode, Retention Time (RT), as well as the internal (surrogate) standards used for quantification using UHPLC Triple TOF MS/MS).

Name	Therapeutic group	Chemical formula	Ionisation	Accurate Mass (Da)	t_R (min)	Internal standard
Metformin	Antidiabetic	$C_4H_{11}N_5$	+ve	130.1084	0.67	Codeine-D3 (t_R= 4.63 min)
Nicotine	Stimulant	$C_{10}H_{14}N_2$	+ve	163.1213	3.35	Codeine-D3
Acetaminophen	Analgesic	$C_8H_9NO_2$	+ve	152.0705	3.44	Codeine-D3
Amoxicillin	Antibiotic	$C_{16}H_{19}N_3O_5S$	+ve	366.0968	3.59	Codeine-D3
Gabapentin	Anti-convulsant	$C_9H_{17}NO_2$	+ve	172.133	3.80	Codeine-D3
Codeine	Narcotic analgesic	$C_{18}H_{21}NO_3$	+ve	300.1598	4.75	Codeine-D3
Caffeine	Stimulant	$C_8H_{10}N_4O_2$	+ve	195.0878	5.27	Caffeine-D9 (t_R= 5.13 min)
Trimethoprim	Anti-bacterial	$C_{14}H_{18}N_4O_3$	+ve	291.1456	5.49	Caffeine-D9
Sulfamethoxazole	Anti-bacterial	$C_{10}H_{11}N_3O_3S$	+ve	254.0596	5.62	Caffeine-D9

Tramadol	Narcotic analgesic	$C_{16}H_{25}NO_2$	+ve	264.1947	6.21	Caffeine-D9
Metoprolol	Beta-blocker	$C_{15}H_{25}NO_3$	+ve	268.1913	6.35	Caffeine-D9
Doxycycline	Antibiotic	$C_{22}H_{24}N_2O_8$	+ve	445.1496	7.50	Codeine-D3
Propranolol	Beta-blocker	$C_{16}H_{21}NO_2$	+ve	260.1448	7.98	Caffeine-D9
Carbamazepine	Anti-convulsant	$C_{15}H_{12}N_2O$	+ve	237.1026	8.42	Carbamazepine-D10 (t_R= 8.49 min)
Hydrocortisone	Steroid	$C_{21}H_{30}O_5$	+ve	363.2171	8.65	Carbamazepine-D10
Naproxen	NSAID	$C_{14}H_{14}O_3$	-ve	294.0144	9.03	4 Chlorophenol-D4 (t_R= 8.05 min)
DEET	Insect repellant	$C_{12}H_{17}NO$	+ve	192.1385	9.10	Carbamazepine-D10
Erythromycin	Antibiotic	$C_{37}H_{67}NO_{13}$	+ve	734.4686	9.21	Carbamazepine-D10
Oxazepam	Sedative, hypnotic	$C_{15}H_{11}ClN_2O_2$	+ve	287.0761	9.29	Carbamazepine-D10
Valsartan	Anti-hypertensive	$C_{24}H_{29}N_5O_3$	-ve	434.2276	9.71	4 Chlorophenol-D4

Mefloquine	Anti-malarial	$C_{17}H_{16}F_6N_2O$	+ve	379.1241	9.71	Carbamazepine-D10
17α-ethynylestradiol	Steroid	$C_{20}H_{24}O_2$	-ve	295.1705	9.84	Estone-D4 (t_R= 9.91 min)
β-estradiol	Steroid	$C_{18}H_{24}O_2$	-ve	271.1607	8.86	Estone-D4
Diazepam	Sedative, hypnotic	$C_{16}H_{13}ClN_2O$	+ve	285.0791	9.82	Carbamazepine-D10
Diclofenac Na	NSAID	$C_{14}H_{10}Cl_2NNaO_2$	-ve	294.0115	10.12	4 Chlorophenol-D4
Glyburide	Antidiabetic	$C_{23}H_{28}ClN_3O_5S$	-ve	492.1309	10.27	4 Chlorophenol-D4
Ibuprofen	NSAID	$C_{13}H_{18}O_2$	-ve	205.1237	10.60	4 Chlorophenol-D4
Meclofenamic acid	NSAID	$C_{14}H_{11}Cl_2NO_2$	-ve	294.0124	10.76	4 Chlorophenol-D4
Clotrimazole	Anti-fungal	$C_{22}H_{17}ClN_2$	+ve	345.1010	11.19	Carbamazepine D10
Gemfibrozil	Anti-hyperlipidemic	$C_{15}H_{22}O_3$	-ve	249.1519	11.58	4 Chlorophenol-D4

2.9. Quantification, Validation, Quality Assurance and Quality Control

In general, the method validation and QA/QC measurements were conducted according to the International Conference on Harmonisation guidelines (ICH, 1996) and the Persistent Organic Pollutants/Emerging Contaminants Group in-house QA guidelines (HARRAD, 2014).

2.9.1. Method linearity

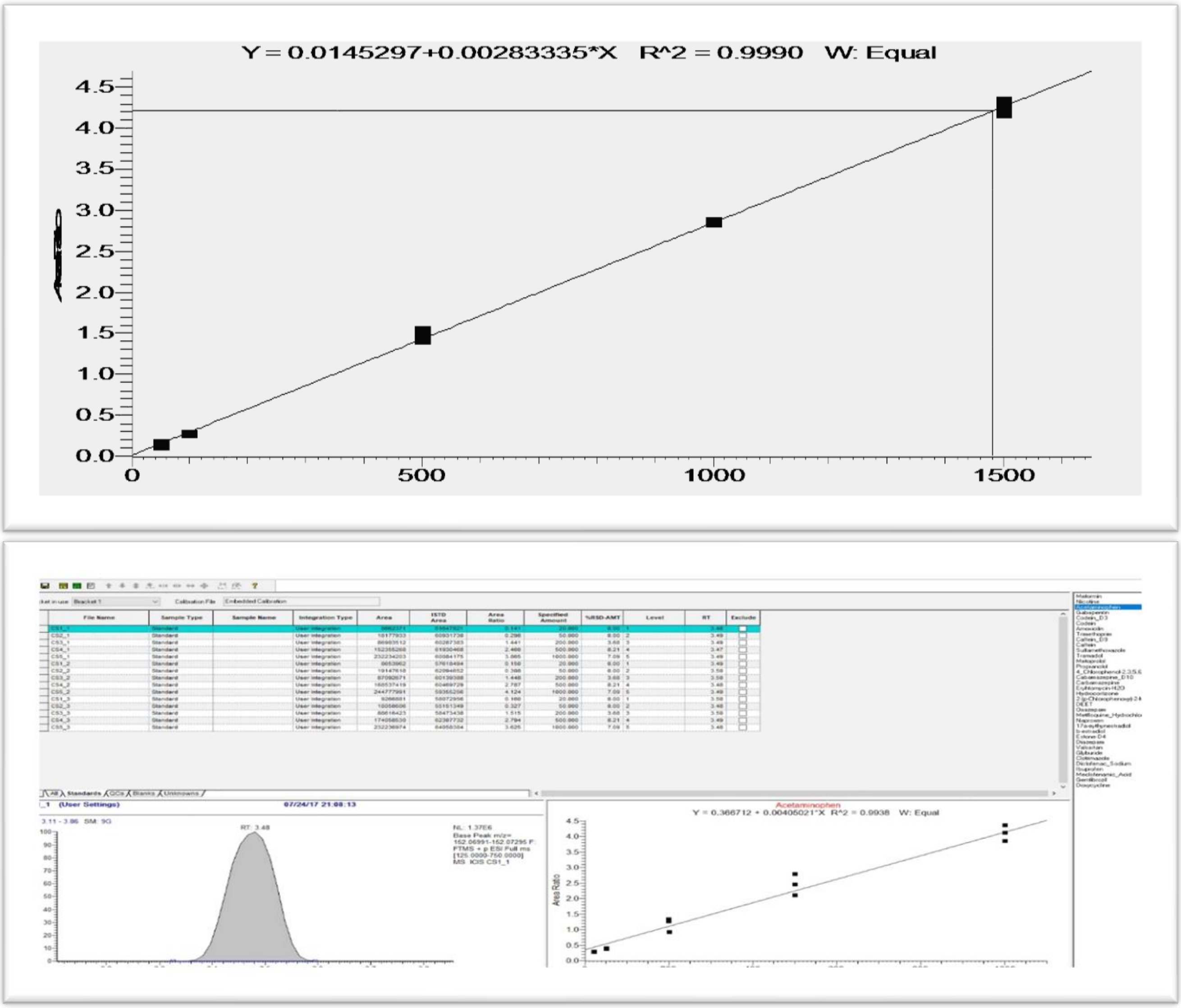
Linearity was evaluated via conducting a full 5-point calibration for each target compound in the range 100 -1000 ng/ml, with a fixed internal standard concentration of 100 ng/ml. Calibration plots of the studied PPCPs were constructed by Xcalibur™ software Figure 2-8 representing the concentration of analyte versus the peak area ratio (native compound to its corresponding internal standard). R2 (linearity coefficient) values for the studied PPCP excedded 0.9, showing very good linearity over the calibration range where the majority of Table 2.8.

Table 2.10 Linear equations and linearity coefficients for the target PPCPs using UPLC Orbitrap MS.

Name	R2	Equation
Metformin	0.993	Y = 0.0108 + 0.0019*X
Nicotine	0.999	Y = 0.0145 + 0.0028*X
Acetaminophen	0.994	Y = 0.367 + 0.0041*X
Gabapentin	0.985	Y = 0.0098 + 0.0021*X
Codeine	0.991	Y = 0.0343 + 0.002*X
Caffeine	0.996	Y = 0.0385 + 0.0018*X
Trimethoprim	0.988	Y = 0.0494 + 0.0027*X
Sulfamethoxazole	0.986	Y = 0.0825 + 0.0026*X
Tramadol	0.976	Y = 0.3368 + 0.0226*X
Metoprolol	0.989	Y = 0.1824 + 0.0201*X
Propranolol	0.992	Y = 0.5527 + 0.0284*X
Doxycycline	0.995	Y = 0.0095 + 0.0092*X
Carbamazepine	0.975	Y = 0.1566 + 0.0014*X
Hydrocortisone	0.982	Y = 0.0149 + 0.00023*X
Naproxen	0.961	Y = 0.0079 + 9E-5*X
DEET	0.958	Y = 0.8109 + 0.0055*X
Erythromycin	0.986	Y = 0.009 + 0.0009*X
Oxazepam	0.990	Y = 0.0157 + 0.0004*X

Valsartan	0.975	Y = 0.0009 + 0.0002*X
Mefloquine hydrochloride	0.984	Y = -0.0025 + 0.0002*X
17α-ethynylestradiol	0.963	Y = 0.0290 + 0.0009*X
β-estradiol	0.959	Y = 0.0483 + 0.0011*X
Diazepam	0.991	Y = 0.1909 + 0.0033*X
Diclofenac Sodium	0.974	Y = 0.0012 + 0.0002*X
Glyburide	0.985	Y = 0.00162 + 0.0002*X
Ibuprofen	0.983	Y = -0.0014 + 0.0004*X
Meclofenamic acid	0.999	Y = -0.0017 + 0.0001*X
Clotrimazole	0.958	Y = 0.0105 + 0.0002*X
Gemfibrozil	0.971	Y = -0.0007 + 3E-5*X

Figure 2-13 representative examples of the extracted calibration plot for nicotine and the Xcalibur™ software calibration window for Acetaminophen.



These calibration standards were also used to calculate relative response factors (RRFs) for each target compound. RRF is defined as the instrument response for a unit amount of target pollutant relative to the instrument response obtained for the same amount of the internal standard (IS), which can be calculated from equation 1.

$$\boldsymbol{RRF} = \frac{A_{NAT}}{A_{IS}} \times \frac{C_{IS}}{C_{NAT}} \ldots \text{(1)}$$

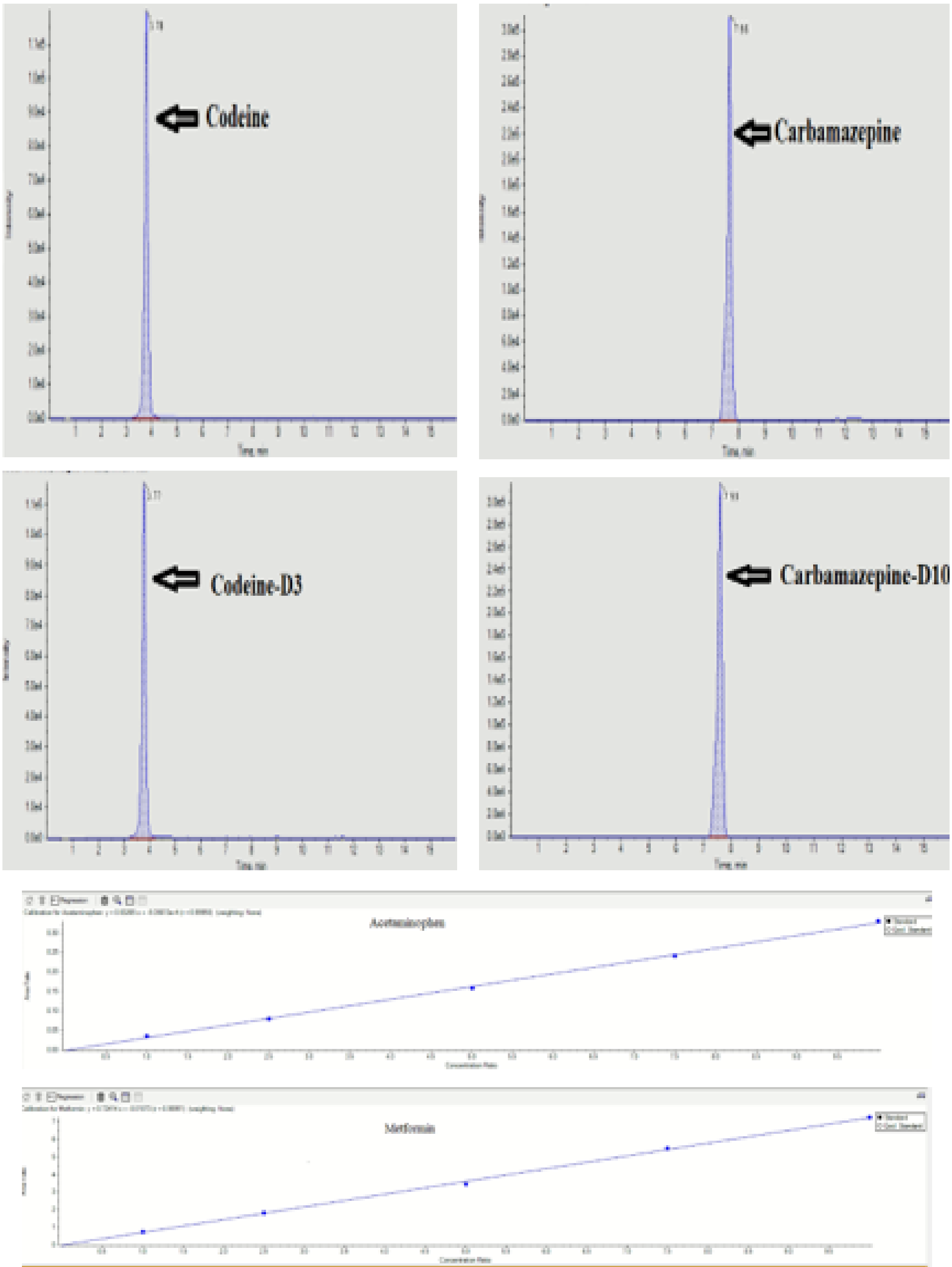
Where $\boldsymbol{A_{NAT}}$ *is the peak area for the "native" compound in the standard;* $\boldsymbol{A_{IS}}$ *is the peak area of the internal standard in the standard;* $\boldsymbol{C_{NAT}}$ *is the concentration of the "native" compound in the standard; and* $\boldsymbol{C_{IS}}$ *is the concentration of the internal standard in the standard.*

RRFs were calculated for each target compound at each of the 5 concentration levels. The relative standard deviation (*i.e.* (σ_{n-1}/average) x 100%) of RRFs for a given target compound did not exceed 10% over the whole calibration range indicating good reproducibility and linear response of the instrument over the studied range.

Table 2.11 Linear equations and linearity coefficients for the target PPCPs using UHPLC Triple TOF MS/MS)

Name	R2	Equation
Metformin	0.9977	y = 0.0291x + 0.0049
Nicotine	0.9932	y = 0.0295x + 0.0046
Acetaminophen	0.9907	y = 0.0295x + 0.0024
Gabapentin	0.9934	y = 0.0278x + 0.0034
Codeine	0.9933	y = 0.0289x - 0.008
Caffeine	0.9888	y = 0.0289x - 0.0102
Trimethoprim	0.9836	y = 0.0279x - 0.001
Sulfamethoxazole	0.9889	y = 0.0282x - 0.0032
Tramadol	0.9904	y = 0.0277x + 0.0015
Metoprolol	0.9886	y = 0.0286x + 0.001
Propranolol	0.9974	y = 0.0297x - 0.0013
Doxycycline	0.9964	y = 0.0294x + 0.0005
Carbamazepine	0.9886	y = 0.0286x + 0.001
Hydrocortisone	0.9944	y = 0.0301x - 0.0044
Naproxen	0.9965	y = 0.031x - 0.0071
DEET	0.9994	y = 0.03x + 0.0022
Erythromycin	0.9961	y = 0.0308x - 0.0061
Oxazepam	0.989	y = 0.0295x - 0.0054
Valsartan	0.9929	y = 0.0312x - 0.0063
Mefloquine hydrochloride	0.994	y = 0.0277x
17α-ethynylestradiol	0.9908	y = 0.029x - 0.0007
β-estradiol	0.991	y = 0.0266x + 0.0176
Diazepam	0.9938	y = 0.0265x + 0.022
Diclofenac Sodium	0.9952	y = 0.0255x + 0.0312
Glyburide	0.9952	y = 0.0247x + 0.0317
Ibuprofen	0.9969	y = 0.0231x + 0.0439
Meclofenamic acid	0.9975	y = 0.0239x + 0.0378
Clotrimazole	0.9984	y = 0.0273x + 0.0054
Gemfibrozil	0.9953	y = 0.0268x + 0.0079

Figure 2-14 : Representative examples of peak integration and linear calibration plots obtained from the MultiQuant™ software following analysis by AB Sciex UHPLC Triple TOF MS/MS.



2.9.2. Accuracy and precision

The method accuracy was assessed by estimating the percent recovery of target analytes spiked onto a homogenized sediment sample at 3 concentration levels: 50 ng/mL, 250 ng/mL and 750 ng/mL. A blank comprising a non-spiked sediment sample was run along each sample batch. The percent recovery for each target compound was calculated as:

$$\text{Recovery (\%)} = \frac{\text{concentration in spiked sample} - \text{concentration in blank}}{\textit{spiked concentration}}\ x\ 100$$

For each spiking concentration level, three injections of triplicate samples (total 9 injections) were made and the results are presented in Table 2.10.

Table 2.12 : Method accuracy expressed as % recovery (average ± relative standard deviation) at 3 spiked concentration levels.

Name	50 ng/g	250ng/g	750 ng/g
Metformin	74 ± 9	81 ± 5	82 ± 6
Nicotine	80 ± 8	93 ± 9	99 ± 6
Acetaminophen	103 ± 4	100 ± 7	98 ± 7
Amoxicillin	89 ± 9	105 ± 4	101 ± 4
Gabapentin	104 ± 7	97 ± 3	103 ± 3
Codeine	107 ± 9	91 ± 8	97 ± 9
Caffeine	108 ± 3	94 ± 4	88 ± 8
Trimethoprim	95 ± 9	86 ± 3	95 ± 8
Sulfamethoxazole	108 ± 3	98 ± 4	86 ± 4
Tramadol	99 ± 3	100 ± 4	91 ± 6
Metoprolol	107 ± 3	102 ± 9	105 ± 7
Propranolol	86 ± 4	97 ± 5	88 ± 4
Doxycycline	91 ± 7	100 ± 4	106 ± 6
Carbamazepine	92 ± 3	94 ± 3	96 ± 8
Hydrocortisone	107 ± 8	90 ± 9	103 ± 7
Naproxen	110 ± 6	102 ± 7	105 ± 7
DEET	105 ± 4	91 ± 8	91 ± 9
Erythromycin	100 ± 8	86 ± 7	89 ± 3
Oxazepam	103 ± 4	97 ± 6	105 ± 6
Valsartan	101 ± 9	107 ± 7	104 ± 9
Mefloquine HCl	105 ± 3	91 ± 3	97 ± 3
17α-ethynylestradiol	87 ± 7	79 ± 5	78 ± 7

β-estradiol	82 ± 8	84 ± 5	75 ± 8
Diazepam	107 ± 8	107 ± 6	104 ± 3
Diclofenac Sodium	110 ± 6	113 ± 9	106 ± 5
Glyburide	99 ± 4	102 ± 4	97 ± 7
Ibuprofen	109 ± 3	108 ± 9	107 ± 5
Meclofenamic acid	88 ± 4	87 ± 3	105 ± 9
Clotrimazole	94 ± 4	99 ± 3	92 ± 8
Gemfibrozil	103 ± 8	95 ± 3	103 ± 6

Over a concentration range of 50-750 ng/ml, the method displayed very good accuracy ranging from 75 to 108 % recovery for all targeted compounds. The relative standard deviations (RSD) of all the recoveries were below 10 %. These results are similar to those previously reported for PPCPs analysis by (-)/(+)APCI-UPLC-Orbitrap HRMS (Huysman et al., 2017) and in line with those reported for some LC-MS/MS methods for analysis of PPCPs in sediment (Celano et al., 2014, Petrie et al., 2016, Wilkinson et al., 2018).

Precision was evaluated as RSD of 5 replicate measurements of a homogenized sediment sample, spiked at 3 concentration levels, conducted on the same day to assess repeatability (intra-day precision) and on different days to assess reproducibility (inter-day precision). RSD values for repeatability and reproducibility ranged between 3.6 to 10.3% and 4.2 to 12.7%, respectively Table 2.11.

Table 2.13 Method precision expressed as relative standard deviation (RSD %) of triplicate analyses at 3 concentration levels.

Name	Intra-day precision			Inter-day precision		
	50 ng/g	250 ng/g	750 ng/g	50 ng/g	250 ng/g	750 ng/g
Metformin	7.7	9.1	3.9	7.0	9.2	7.8
Nicotine	5.5	6.8	6.9	9.5	8.8	3.1
Acetaminophen	4.0	3.1	7.8	8.2	6.8	5.9
Amoxicillin	3.6	3.7	9.6	12.7	8.8	7.1
Gabapentin	5.0	6.0	8.6	7.6	4.2	6.5
Codeine	5.7	3.7	6.1	8.9	6.1	8.7
Caffeine	9.2	4.8	5.4	5.6	4.6	4.5
Trimethoprim	9.4	4.1	7.2	11.4	10.7	8.2
Sulfamethoxazole	6.1	5.5	7.6	6.7	5.3	5.1
Tramadol	7.2	2.8	8.2	5.4	4.7	4.8
Metoprolol	8.2	7.4	6.8	7.8	8.3	6.6
Propranolol	5.2	5.6	8.0	9.1	7.9	5.6
Doxycycline	5.1	4.1	9.7	8.5	4.7	6.8
Carbamazepine	9.2	5.6	2.6	9.1	5.0	6.8
Hydrocortisone	6.5	4.8	7.4	11.5	6.8	5.3
Naproxen	4.5	3.9	4.4	9.2	4.6	6.3
DEET	7.1	3.6	8.5	7.2	6.1	5.2
Erythromycin	6.6	4.8	5.7	10.8	7.4	6.9
Oxazepam	5.1	6.3	5.6	10.0	6.8	5.0
Valsartan	5.4	8.0	6.1	7.2	8.7	4.6
Mefloquine HCl	7.7	9.7	7.9	9.1	5.9	5.8
17α-ethynylestradiol	9.4	8.9	9.9	10.8	8.4	9.9
β-estradiol	10.3	7.8	6.2	11.7	8.2	8.8
Diazepam	4.5	6.7	8.1	6.3	7.6	6.6
Diclofenac Sodium	5.5	6.5	4.1	8.8	5.9	5.3
Glyburide	9.5	3.9	5.6	9.3	7.4	5.2
Ibuprofen	8.4	5.8	6.1	10.4	8.9	7.8
Meclofenamic acid	6.7	6.1	5.7	9.2	5.3	6.6
Clotrimazole	9.2	5.3	4.4	5.8	5.5	4.7
Gemfibrozil	9.3	4.6	5.8	7.6	8.3	6.3

2.9.3. Method Detection and quantification limits

The instrument detection and quantification limits were determined by analysis of pure standards. Instrument detection limits (IDL) were calculated as 3:1 S/N ration, while Instrument quantification limits (IQL) were calculated as 10:1 S/N ratio Table 2.12. The IDLs ranged from 0.02 to 1.21 ng/ml while IQLs ranged from 0.07 to 4.05 ng/ml. The wide variation in IDL and IQL values of targeted chemicals is possibly attributed to: (a) variable ionization efficiency for different analytes and/or polarity mode; and (b) matrix effects or co-elution at a particular retention time, which may affect the sensitivity of the instrument by increasing the background noise signal.

The Method quantification limit (MQL) values were obtained by analysis of spiked QA sediment samples containing target PPCPs at concentrations that ranged from 0.5 to 14.5 ng/g Table 2.12. The spiking concentration levels for each target compound were estimated initially based on a 10:1 S/N ratio in the spiked sediment samples at 50 ng/g. The use of signals from spiked sediment samples includes matrix effects, which is absent from chemical standard mixtures used for determination of IDLs and IQLs. The steroid hormones β-estradiol and 17α-ethynylestradiol showed the highest MQLs at 12.5 and 14.5 ng/g, respectively. This is likely attributed to the poor ionization of these high molecular weight, neutral organic compounds in the ESI source (Han and Liu, 2019).

Table 2.14 : IDLs, IQLs and MQLs of the analytical method.

Compounds	IDL (ng/g)	IQL (ng/g)	MQL (ng/g)
Metformin	0.50	1.67	3.5
Nicotine	0.10	0.33	1.5
Acetaminophen	0.10	0.33	2.0
Amoxicillin	1.10	3.67	8.5
Gabapentin	0.28	0.93	3.0
Codeine	0.23	0.77	2.0
Caffeine	0.80	2.80	4.5
Trimethoprim	0.04	0.12	0.5
Sulfamethoxazole	0.06	0.20	1.0
Tramadol	0.17	0.56	2.0
Metoprolol	0.02	0.07	0.5
Propranolol	0.04	0.14	1.0
Doxycycline	0.24	0.79	9.0
Carbamazepine	0.02	0.07	2.5
Hydrocortisone	0.34	1.13	6.5
Naproxen	0.09	0.30	4.5
DEET	0.11	0.37	3.5
Erythromycin	0.25	0.84	11.0
Oxazepam	0.15	0.49	5.5
Valsartan	0.32	1.05	6.0
Mefloquine HCl	0.30	0.99	8.0
17α-ethynylestradiol	1.21	4.05	14.5
β-estradiol	1.16	3.87	12.5
Diazepam	0.13	0.43	4.5
Diclofenac Sodium	0.15	0.50	4.0
Glyburide	0.30	0.99	5.5
Ibuprofen	0.12	0.41	4.5
Meclofenamic acid	0.17	0.57	5.5
Clotrimazole	0.36	1.19	5.5
Gemfibrozil	0.31	1.05	4.5

2.9.4. Quantification of PPCPs concentrations in sediment/soil samples

Concentrations of PPCPs in samples were calculated using the respective IS for each compound *via* the equation below (HARRAD, 2014):

$$Concentration\ (ng/g) = \frac{A_{NAT}}{A_{IS}} \times \frac{1}{RRF} \times \frac{M_{IS}}{SS} \; .....(2)$$

Where A_{IS} *= peak area of internal standard in sample;* A_{NAT} *= peak area of target compound in sample; RRF = relative response factor for the target compound (see equation 1);* M_{IS} *= mass of internal standard added to sample (ng) and SS = sample size (g).*

A calibration standard containing all the target compounds and IS (500 ng/ml) was injected before and after each sample batch Figure 2-4. For a given peak to be identified as a target analyte in a sample; the following filters were applied: maximum mass tolerance of 5 ppm, retention time window of ± 10 seconds from the calibration standard and relative retention time (RRT) window of ± 0.1 min (to the designated labelled IS). The extracted ion chromatograms (EIC) according to these filters showed well-defined correctly identified and appropriately integrated peaks in the studied real samples.

2.10. Statistical Analysis

Statistical analysis was performed using MS Excel (Microsoft Office 2017) and IBM SPSS Statistics for Windows, version 23 (IBM Corp., Armonk, N.Y., USA). Statistical summaries, average values, RRF and concentration calculations were conducted in Excel. Statistical distribution of generated datasets was determined using the Kolmogorov-Smirnov test combined with visual inspection of the Q-Q plot for data distribution in SPSS. Results revealed the generated datasets to be normally or log-normally distributed. Consequently, the differences in means among study factors (e.g., PPCPs concentrations in soil vs sediment or in sediment from various locations, etc.) were statically evaluated using the appropriate test conducted on the original or log-transformed data, according to the sample distribution. Student t-test was applied to compare between two datasets, while Analysis of Variance (ANOVA) in combination with Tukey HSD *posthoc* test were applied to compare the means among more than 2 datasets. Principal component analysis (PCA) was conducted using IBM SPSS Statistics for Windows, version 23 (IBM Corp., Armonk, N.Y., USA).

For statistical analysis purposes, concentrations below the method detection limit (MDL; Appendix II Table SI-1) were assigned a value of 0.5 MDL, except in cases of a detection frequency (DF) below 50% where a value of MDL multiplied by the detection frequency was assigned to minimize statistical bias (e.g. 0.35 MDL for compound-X with a detection frequency of 35%) (Helsel and Hirsch, 1992, Hewett and Ganser, 2007, Roosens et al., 2009). P values < 0.05 were considered significant.

Chapter 3. Spatial Distribution of PPCPs in UK Freshwater Sediment.

3.1. Synopsis

Pharmaceuticals and Personal care products (PPCPs) are chemicals, such as antibiotics and analgesics, given to living organisms for treatment of diseases or enhancing the quality of life. PPCPs, their metabolites and transformation products, are then excreted from the body in faeces and urine and discharged from wastewater treatment plants (WWTPs), clinics, healthcare facilities, manufacturing plants' effluents, and fish farming facilities to the surrounding aquatic environment. The occurrence, distribution and fate of PPCPS in the aquatic environment have become a worldwide concern (Sharma et al., 2021, Ouda et al., 2021, Wang et al., 2021). However, little is known about the occurrence and distribution of PPCPs in UK freshwater sediments. The purpose of this chapter is to examine the presence and concentrations of PPCPs in sediments from two rivers and two canals in the West Midlands, United Kingdom. The measured PPCPs concentrations in sediment are then compared to the respective levels of target chemicals in water to assess the partitioning between the two phases. Finally, the ecotoxic risk arising from such hazardous chemicals is assessed and evaluated.

3.2. Sampling and analysis

Sediment, soil, and water samples were collected from (a) River Tame, (b) River Severn, (c) Coventry Canal, and (d) Birmingham and Worcester Canal on 20th of May 2019 Figure 3.1. These four sampling sites were previously studied for the concentrations of the same target 30 PPCPs in water (Anekwe, 2020). A sample from each location was taken on the specified day, and 5 aliquots were sub-sampled for chemical analysis in order to determine the mean concentrations of target PPCPs in the studied locations. Grab samples were collected from each location according to the methods described under sections 1.6.1 in the methods chapter. Depending on the depth of the river at the sampling location, stainless-steel sediment corers or bucket auger trowels were employed to collect surface sediment samples (0–5 cm) from 4 locations in the UK (2 Rivers and 2 Canals).

A stainless-steel hand scoop was used to collect surface soil samples (0–5 cm) one metre from the river or canal being studied. All samples were transferred to the lab in cooled iceboxes and stored in the dark stored at −20 °C until analysis. The analytical methodology (extraction and clean up) in chapter 2 of this thesis was successfully applied for the determination of 30 studied PPCPs in water, sediment and soil samples. All extracted samples were analysed using a Dionex Ultimate 3000 UPLC coupled to a Q-Exactive Orbitrap^{TM}-HRMS system as described under section 2.8.1 of this thesis.

(a) <u>River Tame</u>

The River Tame originates in Oldbury and flows east through Dudley before turning north near Hams Hall and heading for Tamworth. The river meets the Trent at Arlewas, Staffordshire, after over 100 kilometres. The Tame's catchment area is over 1500 km2, with a population of approximately 1.7 million people. The Tame basin is the most densely populated river basin in the United Kingdom, accounting for 42 percent of its area. Tame was a rural river during its history. It was a fertile fishery and popular with fishermen until the nineteenth century. This began to change as Birmingham's catchment area grew significantly. The historic industries of Birmingham and the Black Country, which were centred on coal, iron, and steel, were highly toxic, then by the 1950s, the Tame was one of Britain's highly polluted rivers. Water quality has improved dramatically as a result of legislative changes and the decline of heavy industry. Improvements have been boosted even further by the creation of three massive settlement lakes. These lakes were established in 1980 to assist in the removal of heavy metals and other impurities from the water (Tamevalleywetlands.com).

(b) <u>River Severn</u>

River Severn is the longest river in the UK, measuring around 180 miles. It stretches through 220 miles from the Welsh mountains to the flatlands of the Severn Estuary, passing through stunning Shropshire and Worcestershire landscapes (CanalandRiverTrust).

(c) <u>Coventry Canal</u>

The Coventry Canal is a waterway that connects urban and rural areas. It starts at Gas Street Basin and travels into the Midlands countryside, measuring around 15 miles. (CanalandRiverTrust).

(d) <u>Birmingham & Worcester Canal</u>

The Worcester & Birmingham Canal runs from Birmingham's city centre to Worcester's cathedral city, measuring around 30 miles. It is a popular boating path for active crews (CanalandRiverTrust).

Figure 3-1 Water, sediment and soil samples collected from (a) River Tame, (b) River Severn, (c) Coventry Canal and (d) Birmingham & Worcester Canal

** a, b, c and d denote sampling locations.*

3.3. PPCPs concentration in sediments

Several chemical pollutants that were discharged into water would likely adsorb to sediment particles to varying degrees due to their hydrophobic/lipophilic properties (Fernandes et al., 2020). The concentrations of PPCPs in sediment samples from 4 studied locations are summarized in Table 3.1. Our findings showed that the Σ30 PPCPs concentrations detected in sediments were 129, 79, 62 and 110 ng/g Dry Weight (DW) in River Tame, Coventry Canal, River Severn and Birmingham & Worcester Canal, respectively Figure 3-2. 9 PPCPs were detected in 100% of samples analysed from the four studied locations, namely: Amoxicillin, gabapentin, caffeine, propranolol, DEET, naproxen, diclofenac Na, meclofenamic acid, and β-estradiol. Conversely, 15 PPCPs were not detected in any of the analysed samples, namely, metformin, nicotine, codeine, sulfamethoxazole, metoprolol, doxycycline, carbamazepine, erythromycin-H2O, clotrimazole, mefloquine-HCl, oxazepam, diazepam, valsartan, iIbuprofen and glyburide. Acetaminophen, hydrocortisone and 17-α-ethinylestradiole were measured at the detection frequency of 75%, whereas trimethoprim and tramadol occurred in 50% of the analysed samples.

Figure 3-2 shows the concentrations of target PPCPs detected in each of the studied 4 locations. The sediment samples of the Worcester & Birmingham Canal were the most polluted, with the highest number of target analytes recorded (∑PPCPs = 110 ng/g). Among the six antibiotics investigated, two compounds (amoxicillin and trimethoprim) had a detection frequency greater than 50%, whereas the other four antibiotics (doxycycline, erythromycin-H2O, sulfamethoxazole and clotrimazole) were not detected. Amoxicillin was detected in 100% of the sediment samples at concentrations of 14.9, 6.0, 7.3 and 8.8 ng/g in River Tame, Coventry Canal, River Severn and Birmingham & Worcester Canal, respectively. There are no available data on amoxicillin in UK freshwater sediment but these concentrations are generally similar to those reported in the Kenyan rivers of Mwania (4.6 ng/g), Chania (43.8 ng/g) and Kanyuru (11.7 ng/g) (Kairigo et al., 2020). Lower concentrations of amoxicillin (0.40–0.97 ng/g) were detected in sediment samples collected from Klang River estuary, Malaysia (Omar et al., 2018). Amoxicillin is not a persistent chemical (with a half-life of 0.43–0.57 days) (Braschi et al., 2013) and can be subject to degradation via hydrolysis and/or direct photolysis in aquatic ecosystems (Andreozzi et al., 2004).

Trimethoprim was measured at the detection frequency of 50% at concentration of 17.2 and 2.7 ng/g in River Tame and Birmingham & Worcester Canal, respectively. Comparing to earlier investigations, its concentrations were at an intermediate level. In Umgeni River, South Africa, trimethoprim was detected in sediment at concentration of 88 ng/g (Matongo et al., 2015), while its concentration was detected at 0.83 ng/g in Urban River in Florida, USA (Yang et al., 2015).

Five of the six analgesics and non-steroidal anti-inflammatory drugs (NSAIDs) studied had a detection frequency more than 50%. Naproxen, diclofenac Na and meclofenamic acid had high detection rates, with a 100% detection frequency. Naproxen was detected at concentration of 3.3, 1.1, 1.1 and 9.7 ng/g in River Tame, Coventry Canal, River Severn and Birmingham & Worcester Canal, respectively. In comparison to previous studies, naproxen was reported at concentration of 31 ng/g in Turia river and Albufera lake, Spain (Sadutto et al., 2021). Although naproxen was the most used drug in the treatment of rheumatic diseases gout in England in 2020 (Statista.com, 2021c). The present study is the first to report on concentrations of naproxen in UK freshwater sediment.

Diclofenac Na was investigated at concentration of 23.7, 43.6,19.5 and 38.9 ng/g in River Tame, Coventry Canal, River Severn and Birmingham & Worcester Canal, respectively. Compared with previously reported concentrations, diclofenac in all locations analysed was present at intermediate concentrations. The concentration of diclofenac was higher than reported in Iberian Rivers, Spain (Osorio et al., 2016a), with a concentration of 1.3 ng/g and lower than that reported in River Medway, Kent, UK (Zhou and Broodbank, 2014), Jilin Songhua River, China (He et al., 2018) and Umgeni river, South Africa (Agunbiade and Moodley, 2016), with concentrations of 59, 278 and 309 ng/g, respectively.

Meclofenamic acid was detected in sediment at concentrations of 10.0, 8.4, 2.6 and 10.2 ng/g in River Tame, Coventry Canal, River Severn and Birmingham & Worcester Canal, respectively. These concentrations were lower than those reported in River Medway, Kent, UK (Zhou and Broodbank, 2014), with an average concentration of 37 ng/g and similar to that reported in Canal of Lahore, Pakistan, with concentration of 8.8 ng/g (Ashfaq et al., 2019).

Acetaminophen (Paracetamol) had detection frequency of 75%, with concentrations of 0.03, 0.03 and 0.15 ng/g in River Tame, Coventry Canal and Birmingham & Worcester Canal, respectively. The concentrations of acetaminophen were much lower than the level reported in Jilin Songhua River, China (He et al., 2018), Urban River in Florida, USA (Yang et al., 2015) and Msunduzi River, South Africa (Matongo et al., 2015), with concentration of 321, 5.2 and 15.8 ng/g, respectively.

Although ibuprofen is the world's third most popular medicine, used to treat pain, fever, and rheumatic illnesses (Ali et al., 2009), its concentrations in all locations were below detection limit. In a study explaining the fate of ibuprofen in the water-sediment system, researchers assessed ibuprofen sorption onto sediment under variety of environmental variables, including pH change, dissolved organic matter, salinity, and competitive sorption. The results indicated that at pH 7, ibuprofen desorption from sediment was high, while at pH 4, it remained well-sorbed onto sediment particles (Oh et al., 2016). This may help explain our results with the average pH in the 4 studied locations at 7.6 implying preferential desorption of ibuprofen from sediment to water.

Tramadol had detection frequency of 50%, with concentration of 13.2 and 0.2 ng/g, in River Tame and River Severn, respectively. These concentrations were similar to those reported in sediments from Turia river and Albufera lake, Spain, with the mean concentrations <10 ng/g (Sadutto et al., 2021).

The frequency of detection was 100, 75 and 75% for β-estradiol, 17-α-ethinyl estradiole and Hydrocortisone, respectively. The maximum concentration of β-estradiol and 17-α-ethinyl estradiole were 2.5 and 2.1 ng/g in River Severn and River Tame, respectively. In comparison to previous studies, these concentrations are similar to those reported in Luoma Lake, China (Liu et al., 2017), with concentration of 1.2 ng/g (β-estradiol) and 1.5 ng/g (17-α-ethinyl estradiole). while it is much lower than reported in Erhai Lake of China (Shen et al., 2020), with concentration of 79.0 ng/g (β-estradiol) and 26.3 ng/g (17-α-ethinylestradiole). Hydrocortisone had the maximum concentration of 3.7 ng/g in River Severn.

Three anti-hypertensive drugs were investigated in 4 locations selected. Only propranolol was measured, with a 100% detection frequency. Its maximum concentration was 25.6 ng/g in River Tame. Propranolol was present in sediment at intermediate levels in all the areas tested, compared to previously reported concentrations. Average concentrations of propranolol in UK freshwater sediment were lower than that reported in Lake Haapajärvi, Finland (Lahti and Oikari, 2012), with mean concentration of 43 ng/g and higher than those reported in sediment from Iberian Rivers, Spain (Osorio et al., 2016a), with mean concentration of 2 ng/g.

Two stimulant drugs, caffeine and nicotine were measured in four locations studied. Caffeine was detected at maximum concentration of 2.6 ng/g in River Tame, with a 100% detection frequency whereas nicotine was not detected in any sediment sample. This may be attributable to nicotine's rapid degradation ($t_{1/2}$ = 0.7 - 9.7 days) (Benotti and Brownawell, 2009) and/or its efficient removal (up to 87%) by WWTPs (Benotti and Brownawell, 2007).

Caffeine was measured at varying concentrations in freshwater sediments around the world. Caffeine levels reported in the present study are similar to those reported in Lake Simcoe sediment, Canada, with a maximum concentration of 7ng/g (Kurissery et al., 2012). However, the maximum caffeine concentration of 3 ng/g in our UK sediment samples is lower than those reported from Saudi Arabia lakes (76 ng/g) (Picó et al., 2020), Jilin Songhua River, China (64 ng/g) (He et al., 2018) and Urban river in Florida, USA (25 ng/g) (Yang et al., 2015). The large variation in caffeine concentrations reported in freshwater sediment worldwide may be attributed to various factors including cultural variations in the consumption of coffee/tea, as well as different drugs containing caffeine as stimulant (Lin et al., 2010a). This may also be compounded by the population density in the sampled location and the efficiency of caffeine removal by the locally operating WWTP (44–75%) (Santos et al., 2009). Moreover, caffeine has relatively high water solubility (21.7 g/L), which suggests its preferential distribution to the dissolved water phase than settled sediment particles (Kurissery et al., 2012).

DEET (N,N-diethyl-meta-toluamide) is commonly used on human and livestock skin as an insect repellent and it is one of the most prevalent organic chemical contaminants discovered in environmental sediment samples (Sharma and Hanigan, 2021, Hajj-Mohamad et al., 2014, Golovko et al., 2020). In our investigation, DEET was detected at concentration of 5.6, 7.4, 6.1, 9.8 ng/g in in River Tame, Coventry Canal, River Severn and Birmingham & Worcester Canal, respectively, with a 100% detection frequency. These concentrations are slightly higher than those reported in San Francisco Bay, CA, USA at 3.5 ng/g (Klosterhaus et al., 2013) and in Yangtze River, China at 4 ng/g (Liu et al., 2015).

In 2019, the most commonly prescribed anxiolytic drug in the UK was gabapentin with 12500 prescriptions (Statista.com, 2021b). In the current study, concentrations of gabapentin were 14.9. 6.0, 7.3 and 8.8 ng/g in in River Tame, Coventry Canal, River Severn and Birmingham & Worcester Canal, respectively. To our knowledge, this is the first study to report this anxiolytic medication in freshwater sediment samples.

Gemfibrozil, a lipid regulating drug, is commonly found in freshwater environments and has been regularly prescribed to treat dyslipidemia (Henriques et al., 2016). According to our findings, the highest concentration of gemfibrozil was 23.5 ng/g in Birmingham & Worcester Canal. This concentration is higher than that reported in Iberian Rivers, Spain (1.92 ng/g) (Osorio et al., 2016a).

Table 3.1 Concentrations (ng/g) of target PPCPs in sediment samples collected from River Tame, Coventry Canal, River Severn and Birmingham & Worcester Canal

PPCPs	Sediment ng/g					Detection frequency %
	Minimum	Maximum	Mean	Std. deviation	Median	
Metformin	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Nicotine	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Acetaminophen	<LOQ	0.1	0.05	0.07	0.03	75
Amoxicillin	5.96	14.9	9.2	3.9	8.05	100
Gabapentin	0.3	13.8	4.3	6.4	1.6	100
Codeine	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Caffeine	1	2.6	1.6	0.7	1.43	100
Trimethoprim	<LOQ	17.2	5	8.2	1.36	50
Sulfamethoxazole	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Tramadol	<LOQ	13.2	3.3	6.6	0.1	50
Metoprolol	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Doxycycline	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Propranolol	0.08	25.6	6.6	12.6	0.4	100
Carbamazepine	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Hydrocortisone	<LOQ	3.7	1	1.8	0.2	75
Erythromycin-H2O	<LOQ	<LOQ	<LOQ	-	<LOQ	-
DEET	5.6	9.8	7.2	1.9	6.7	100
Clotrimazole	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Mefloquine-HCl	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Oxazepam	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Diazepam	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Valsartan	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Ibuprofen	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Naproxen	1.1	9.6	3.8	4	2.2	100
Diclofenac Na	19.5	43.6	31.4	11.6	31.2	100
Meclofenamic acid	2.6	10.2	7.8	3.5	9.2	100
Glyburide	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Gemfibrozil	2.34	23.6	11.8	8.8	10.7	100
17-α-ethinyl estradiole	1.1	2.06	1.5	0.5	1.4	75
β-estradiol	0.2	2.4	0.9	1	0.6	100

An assessment of the distribution profiles of target PPCPs in the studied sediment samples Figure 3-3 showed that propranolol (19.6%), diclofenac Na (18%), trimethoprim (13.2%), amoxicillin (11.4%) and tramadol (10 %) had the highest relative contribution to ∑PPCPs in the River Tame. Three pharmaceuticals, diclofenac Na (54.8%), gemfibrozil (12.5%) and meclofenamic acid (10.5%), accounted for 78% of $\sum_{30}$PPCPs investigated in Coventry Canal, while 77% of $\sum_{30}$PPCPs studied in River Severn were diclofenac Na (31.4%), gabapentin (22.2%), amoxicillin (11.7%) and DEET (9.8%). 66% of $\sum_{30}$PPCPs investigated in Birmingham & Worcester Canal were diclofenac Na (35.4%), gemfibrozil (21.5%) and meclofenamic acid (9.3%).

With an average of 40.5 %, diclofenac Na was the most frequent PPCP in three of the four locations studied: Birmingham and Fazeley canal, River Severn, and Worcester and Birmingham Canal. This may be attributed to the wide use of diclofenac for the past 50 years, with ~75% of the prescribed diclofenac reported to reach the water and soil ecosystems. Moreover, because of its relative stability, it is more likely to persist in the aquatic system (Sathishkumar et al., 2020).

In the four locations studied, amoxicillin and gemfibrozil contributed considerably to $\sum_{30}$PPCPs concentrations Figures 3-3 and 3-4. Interestingly, the latest UK prescription data from 2020 (Statista.com, 2021a) reveal that both are top of their respective therapeutic groups with 7,255,451and 7,392,270 prescription for amoxicillin and gemfibrozil, respectively. Notwithstanding the impact of compound-specific physicochemical properties and removal efficiencies by WWTP, this may also indicate the potential impact of human consumption on the concentrations of PPCPs in freshwater sediment.

Figure 3-2 Concentrations of pharmaceutical and personal care products (PPCPs) in sediment samples in River Tame, Coventry Canal, River Severn and Birmingham & Worcester Canal.

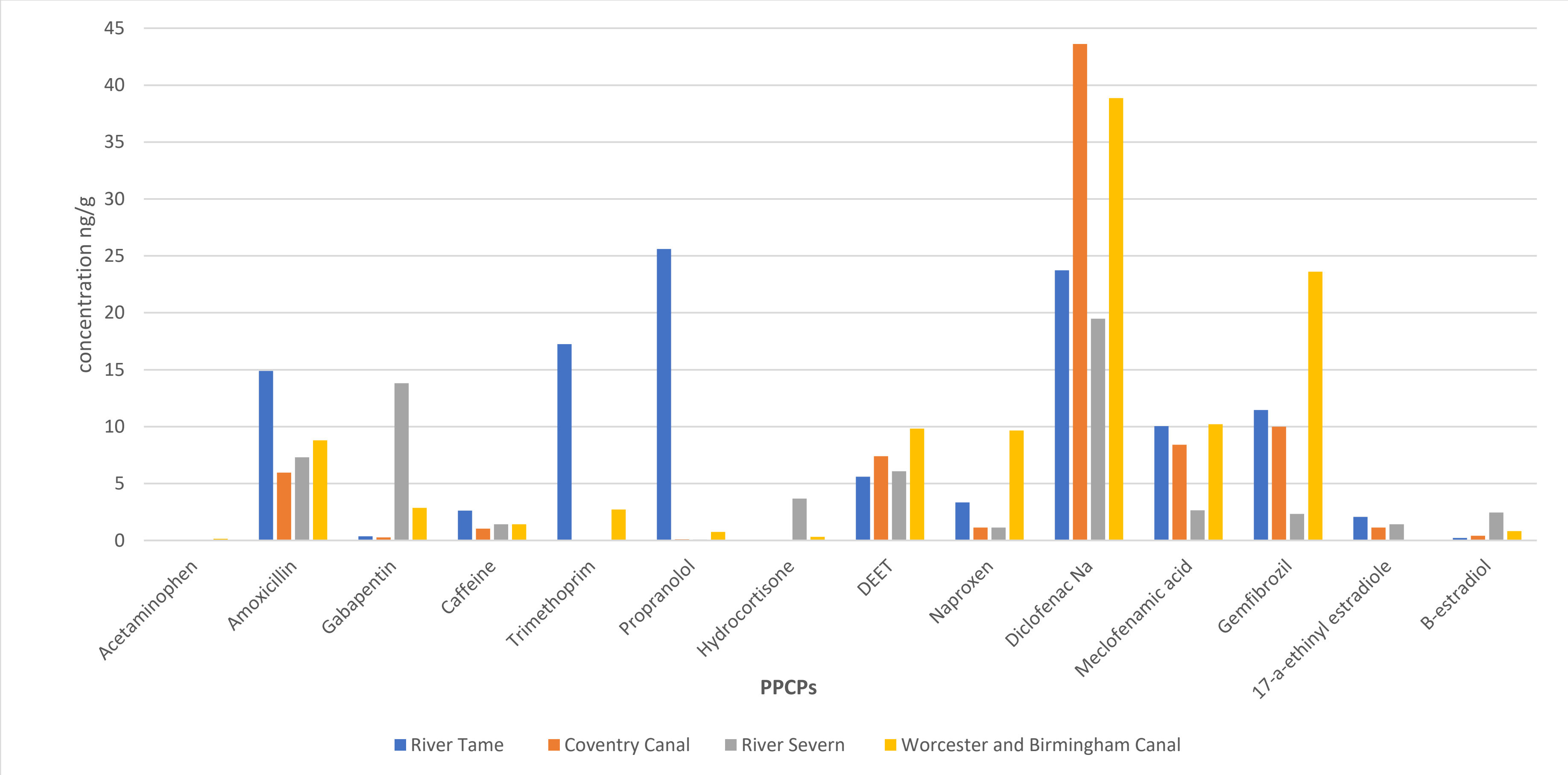


Figure 3-3 Distribution profiles (expressed as % of total ∑PPCPs) in sediments of River Tame, Coventry Canal, River Severn and Birmingham & Worcester Canal.

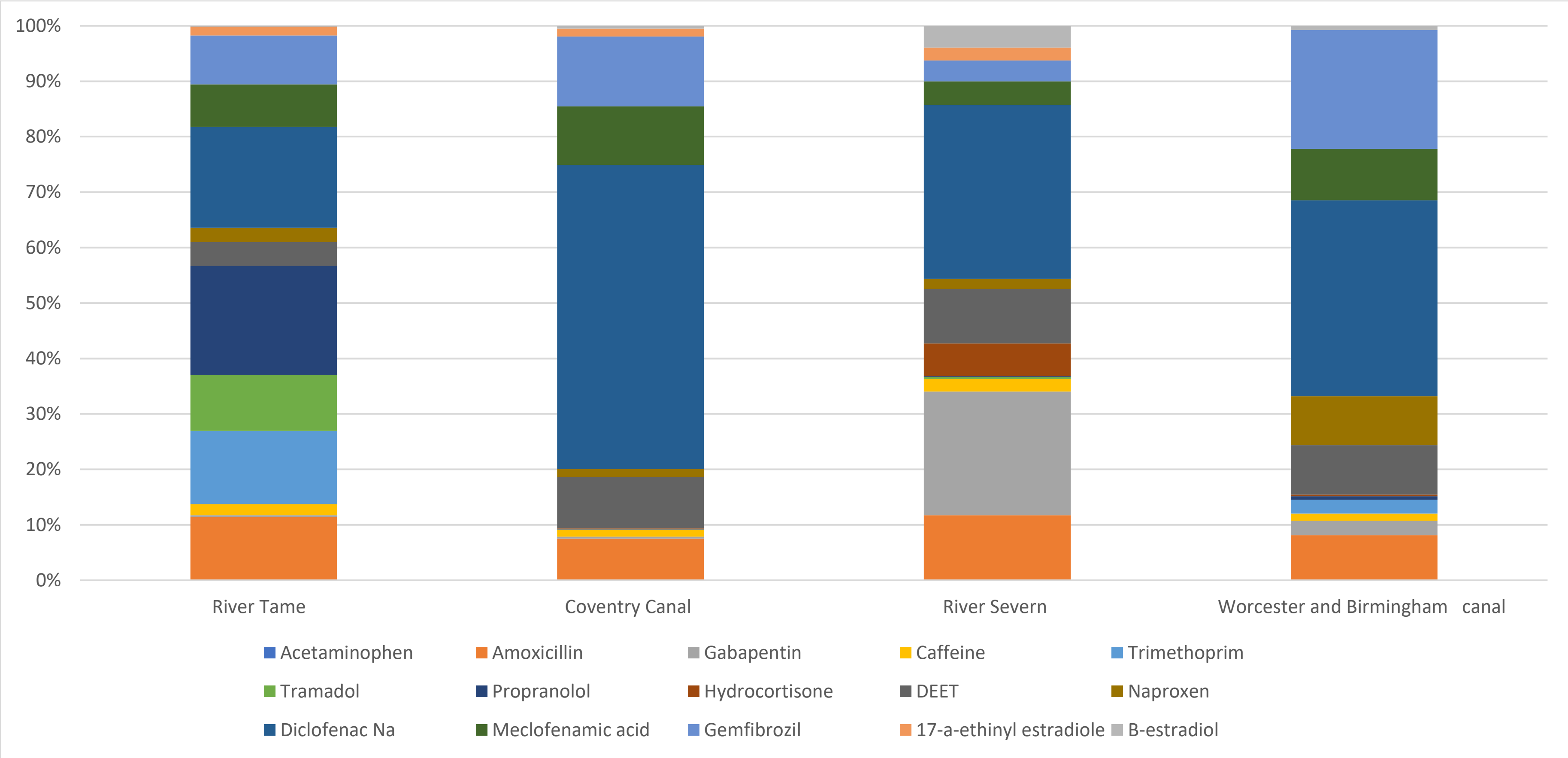


Figure 3-4 concentrations of PPCPs in studied sites.

Fig 3.4a Concentrations of PPCPs in sediment samples from River Tame.

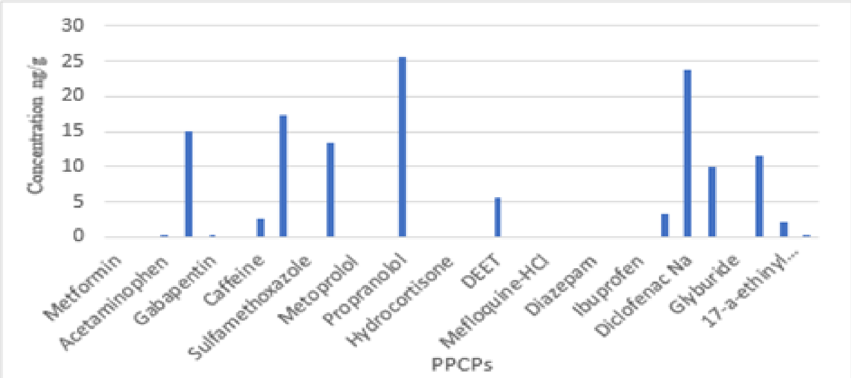


Fig 3.4b Concentrations of PPCPs in sediment samples from Coventry Canal

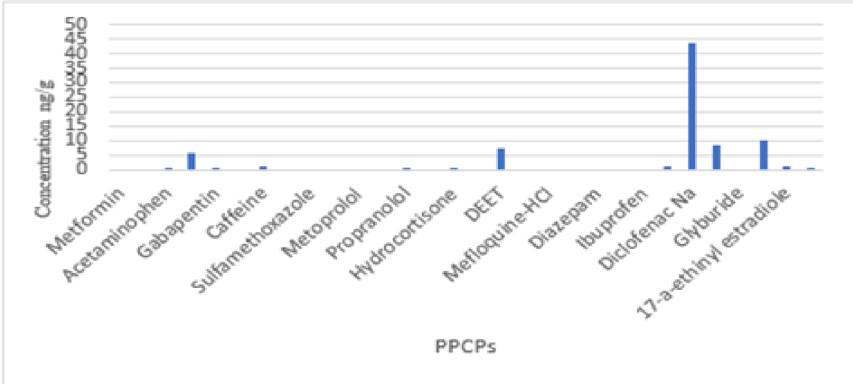


Fig 3.4c Concentrations of PPCPs in sediment samples from River Severn.

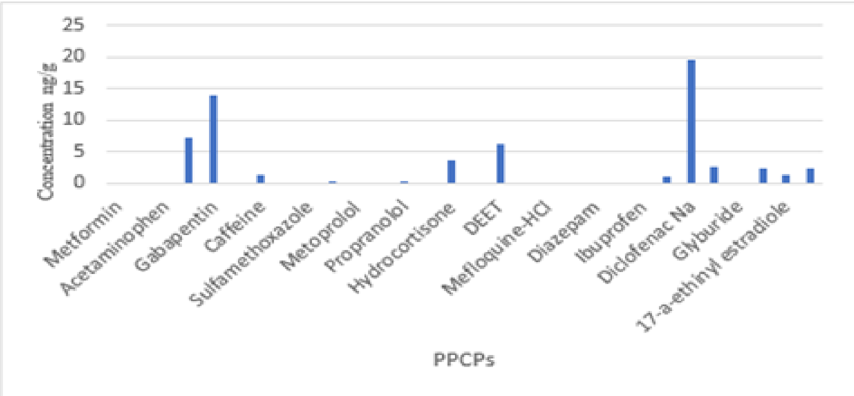
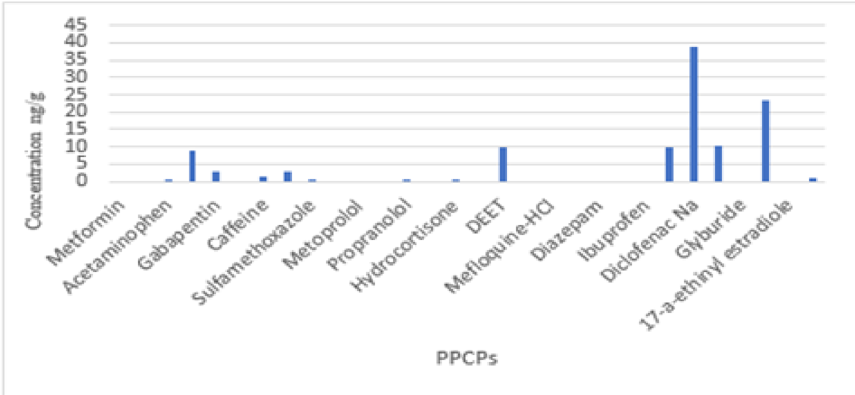


Fig 3.4d Concentrations of PPCPs in sediment samples from Birmingham & Worcester Canal.



3.3.1. Potential sources of PPCPs

The primary entry points for PPCPs into freshwater systems are wastewater treatment plants (Golovko et al., 2021, Ort et al., 2010, Hedgespeth et al., 2012), due to the limited removal efficiency of PPCPs by conventional wastewater treatment processes (Castiglioni et al., 2006, Santos et al., 2007, Jiang et al., 2019). Sewage sludge (treated sludge and biosolids) has been used in several regions of the world, as fertilizers and conditioners for agricultural land, which may represent a substantial source of PPCPs to treated soils (Hornick et al., 1984, Wong and Henry, 1985, Pöykiö et al., 2018, Tambone et al., 2010). Other sources of PPCPs to agricultural lands include direct irrigation with treated wastewater from WWTPs, as well as contamination with veterinary drugs when animal waste, either in solid or liquid states, is spread on agricultural fields as fertilizers. Consequently, run-off from agricultural land can become a source of PPCPs to receiving waters via soil erosion and/or release of sorbed PPCPs to the water discharge (Ebele et al., 2017, Fick et al., 2009, Farré et al., 2008).

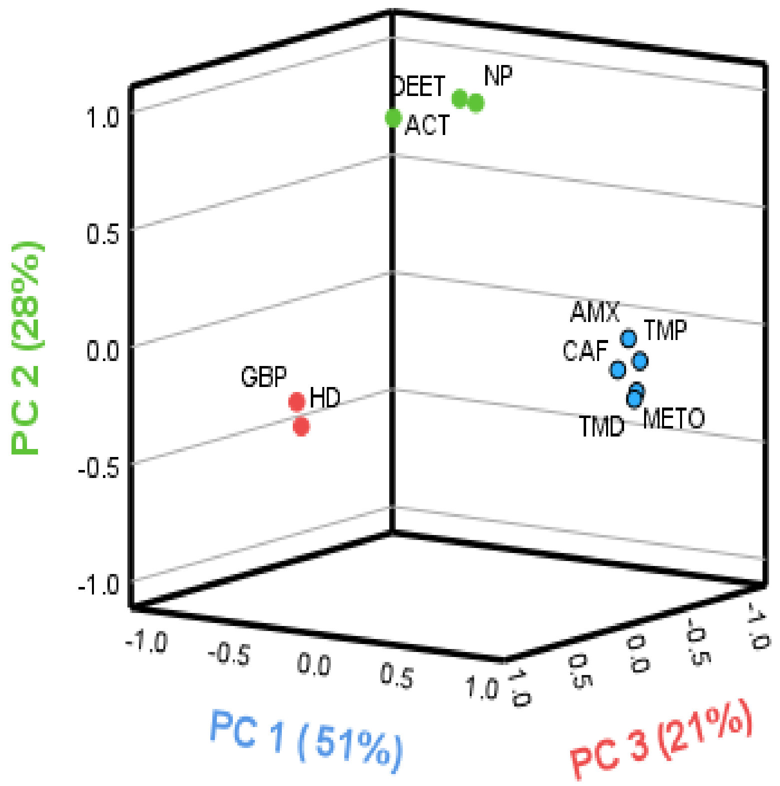
Principal component analysis (PCA) was conducted on the obtained data for 10 PPCPs that were detected in sediments from the River Tame, River Severn, Coventry Canal, and Birmingham and Worcester Canal, to investigate into potential common sources of these PPCPs and explain the variance observed in their concentrations. The PCA findings divided pharmaceuticals into three groups Table 3.2 and Figure 3-5. The first principal component (PC1) explains 51 % of the total variance in the data. this Principal component 1 was characterized by caffeine (CAF), amoxicillin (AMX), trimethoprim (TMP), metoprolol (METO) and tramadol. This component incorporates some of the most frequently detected PPCPs globally. In two wastewater treatment plants (WWTPs) in Leiria Town, Portugal, high frequencies and levels of caffeine were measured, ranging from 112 to 1927 ng/L in the WWTP effluents and from 9478 to 83,901 ng/L in the WWTP influents (Paíga et al., 2019). One of the most significant subgroups of drugs used in veterinary medicine and medicine is the antibiotics. In a study on the presence of antibiotics in the effluent and influent from three of Finland's major wastewater treatment plants, trimethoprim had the highest mean concentration in the effluent samples (532 ng/L) (Kortesmäki et al., 2020). In an Italian study, Amoxicillin (AMX) was detected in 3 out of 8 wastewater treatment plants (WWTPs) effluents at concentrations of 120 ng/L, 15 ng/L, and 25 ng/L in the WWTPs in Palermo, Latina, and Varese-Olona, respectively, (Castiglioni et al., 2005). Amoxicillin is prescribed to prevent and treat animal infections, as well as to encourage growth in a variety of animals, such as cattle, sheep and fish (Van et al., 2020). Veterinarian antibiotics such as, amoxicillin, trimethoprim, are frequently found in both livestock manure and soil that has been impacted by manure (Harms and Bauer, 2011, Martínez-Carballo et al., 2007, An et al., 2015, Wohde et al., 2016). Metoprolol was found in wastewater effluents and sludge samples from Germany at levels between 160 and 2000 ng/L (Scheurer et al., 2010, Maurer et al., 2007, Souchier et al., 2016). Tramadol (TMD) was found in untreated German wastewater at concentrations of 1,129 ng/L (Rúa-Gómez and Püttmann, 2012). PC1 may be associated with sources linked to wastewater effluents and livestock (i.e., veterinary use, and/or runoff from agriculture and aquaculture farming activities). PC2 accounts for 28% of the total data variance, represented by naproxen (NP), acetaminophen (ACT) and DEET. Detection of naproxen at a maximum concentration of 1133 ng/L was reported in the influents and effluents of two wastewater treatment plants in Portugal (Paíga et al., 2016). Frequently, acetaminophen is detected in wastewater treatment plants influents and effluents from different parts of the world (De Gusseme et al., 2011, Li et al., 2012b, Sim et al., 2010). DEET is possibly the most widely used topical insect repellent and its presence in treated wastewater was recorded in various monitoring studies (Bartelt-Hunt et al., 2009, Qian et al., 2010, Margot et al., 2015, Xing et al., 2018). PC2 might have its origins in input sources from WWTP depending on the frequent use and disposal of its components. PC3 explains 21% of the total variance in the data, contributed by gabapentin (GBP) and hydrocortisone (HD), both of these substances have been reported in effluent and downstream of wastewater treatment plants from various countries (Oliveira et al., 2015, Perazzolo et al., 2010, Reungoat et al., 2011, Li and McLachlan, 2019). Interestingly, GBP and HD have a common medicinal application for postoperative pain control, particularly after breast and spinal surgeries, and to control postoperative laparoscopic cholecystectomy pain (Ghadami et al., 2019). While PC3 may be linked to WWTP sources, the grouping of GBP and HD under this PC may be attributed to their common medicinal application.

Table 3.2 Varimax rotated factor loadings of PPCPs in sediment of the River Tame, River Severn, Coventry Canal, and Birmingham and Worcester Canal based on the principal component analysis.

PPCPs	**Rotated Component Matrix**		
	Component		
	1	2	3
CAF	.999	-.046	-.016
AMX	.990	.072	-.118
TMP	.968	-.045	-.248
METO	.955	-.175	-.238
TMD	.953	-.205	-.221
NP	.103	.991	-.088
ACT	-.090	.970	-.227
DEET	-.480	.850	-.219
GBP	-.229	-.167	.959
HD	-.218	-.272	.937
Eigenvalues	5.51	3.35	1.12
Component	**Total Variance Explained** **Rotation Sums of Squared Loadings**		

	Total	% of Variance	Cumulative %
1	5.086	50.857	50.857
2	2.828	28.279	79.136
3	2.086	20.864	100.000

Figure 3-5 Score plots of the PCA of sediment from the River Tame, River Severn, Coventry Canal, and Birmingham and Worcester Canal.



3.4. Distribution of PPCPs between sediment and water

To investigate the distribution of PPCPs between sediment and water, samples of water were collected from the 4 studied rivers at the same location and time of collecting the sediment samples.

3.4.1. Concentrations of PPCPs in water

The concentrations of PPCPs in water samples from 4 studied locations are summarized in Table 3.3. Our data indicate that the Σ_{30} PPCPs concentrations detected in water were 17120, 4507, 8355 and 8176 ng/L in River Tame, Coventry Canal, River Severn and Birmingham & Worcester Canal, respectively. Metformin, nicotine, amoxicillin, gabapentin, codeine, hydrocortisone, erythromycin-H2O, DEET, glyburide and 17-α-ethinyl estradiole were detected in 100% of water samples in four locations. While acetaminophen, doxycycline, clotrimazole, mefloquine-HCl, diazepam, valsartan and β-estradiol were below the limit of quantification in all samples. Among four locations studied, River Tame was the highest polluted, with $\sum_{30}$ PPCPs of 17120 ng/L.

Both antidiabetic drugs, metformin and glyburide, were detected in water in four locations, with maximum concentration of 11304 and 26 ng/L, respectively Figure 3-6. Metformin was the most abundant PPCP, with the highest mean concentration of 4685.3 ng/L, followed by amoxicillin, with a mean concentration of 2005.8 ng/L. In light of previous research, metformin was investigated in water samples at concentration of 2595 ng/L in Rivers Foss in the city of York, UK (Burns et al., 2018a).

Caffeine, a stimulant drug, can be found in a variety of prescription and over-the-counter medications (such as cold remedies, analgesics, stimulants, and illegal narcotics), as well as caffeinated foods and beverages (e.g. chocolate, coffee, cocoa, tea, dairy desserts, soft drinks) (Li et al., 2020a). Our result shows that caffeine was only detected in River Tame at the maximum concentration of 968 ng/L. while nicotine was present in all locations studied, with the maximum concentration of 1802 ng/L in Birmingham & Worcester Canal. In a study of pharmaceuticals and illicit drugs in the freshwater aquatic environment, six locations along 87 km of a major UK river (Avon), caffeine and nicotine were detected at maximum concentration of 1716 and 148 ng/L, respectively (Baker and Kasprzyk-

Hordern, 2013). In another UK study, caffeine was reported at the maximum concentration of 6310 ng/L in the River Thames catchment (Nakada et al., 2017).

Antibiotics have been identified as one of the medications that present the greatest risk to the aquatic environment (Ashbolt et al., 2013, Ben et al., 2019, Mutiyar and Mittal, 2014, Boonsaner and Hawker, 2013, O'Flaherty and Cummins, 2017). Our data shows that amoxicillin, erythromycin, sulfamethoxazole and trimethoprim were detected at the maximum concentrations of 2573, 124, 8 and 157 ng/L, with 100%, 100%, 75% and 50% detection frequency, respectively. In comparison to previous UK studies, amoxicillin, erythromycin, sulfamethoxazole and trimethoprim were reported at the maximum concentrations of 622, 351, 2 and 126 ng/L in surface water samples from the River Taff, UK (Kasprzyk-Hordern et al., 2008).

Among 7 analgesics and NSAIDs, codeine was detected in all locations studied at concentration of 324, 549, 592 and 560 ng/L in River Tame, Coventry Canal, River Severn and Birmingham & Worcester Canal, respectively. These concentrations are similar to those reported in surface water from the River Taff, UK, with concentration of 403 ng/L (Kasprzyk-Hordern et al., 2008). These high concentrations of codeine in UK rivers was attributed to its use, in combination with nonopioid analgesics, without a prescription, which may lead to overuse and misuse of this drug (Fleming et al., 2003).

The natural oestrogen 17-estradiol (E2) is the most administered oestrogen in the United Kingdom. Only ~ 23 Kg of the highly strong synthetic oestrogen ethinyl estradiol (EE2) is used per year, compared to 320 kg of E2 (Runnalls et al., 2010). In the present study, 17-α-ethinylestradiole and hydrocortisone were detected at the mean concentration of 61.3 and 22.8 ng/L, respectively.

An investigation into the PPCPs profiles in the studied surface water samples from different locations Figures 3-6 and 3-7 indicated that metformin (66%) and amoxicillin (10.5%) were the most frequent PPCPs in River Tame. Four pharmaceuticals, amoxicillin (38.5%), nicotine (23%), metformin (21%)

and codeine (12%), accounted for 94% of $\sum_{30}$PPCPs investigated in Coventry Canal. 81.5% of $\sum_{30}$PPCPs studied in River Severn was metformin (35%), amoxicillin (31%) and nicotine (15.5%) while 89% of $\sum_{30}$PPCPs detected in Birmingham & Worcester Canal were metformin (43.5%), amoxicillin (23.5%) and nicotine (22%). Generally, metformin, amoxicillin and nicotine had the highest relative contribution to $\sum_{30}$PPCPs in the four studied locations, with an overall average of 41%, 25% and 16%, respectively. According to the UK Department of Health's statistics section, metformin (205,795 Kg/Year) and amoxycillin (71,466 Kg/Year) were the most commonly used medications in England in 2000 (Jones et al., 2002). It's also worth mentioning that metformin is excreted 100% unchanged in humans (Straub et al., 2019, Maćerak et al., 2018). While nicotine has both therapeutic and recreational uses, both metformin and amoxicillin were in the top 50 prescribed drugs in the UK in 2020 with 22,997,556 and 7,255,451 prescriptions, respectively. This may contribute to their relative abundance in the studied UK water samples.

It's worth noting that several studies have reported on various PPCPs concentrations in environmental freshwater samples from the UK and worldwide (Singh and Suthar, 2021, Ngo et al., 2021, Kasprzyk-Hordern et al., 2008, Ellis, 2006, Archer et al., 2017, Kim et al., 2009), including a recent PhD thesis and review article by our research group (Anekwe, 2020, Ebele et al., 2017). Therefore, investigating PPCPs in water is not one of the objectives of the present thesis and was only conducted, simultaneously with sediment samples, to study the distribution of target PPCPs between water and sediment in the sampled locations.

Table 3.3 Concentrations (ng/g) of target PPCPs in water samples collected from River Tame, Coventry Canal, River Severn and Birmingham & Worcester Canal.

PPCPs	water ng/L					Detection frequency %
	Minimum	Maximum	Mean	Std. deviation	Median	
Metformin	929	5860	3324	2031	3254	100
Nicotine	834	1802	1242	419	1166	100
Acetaminophen	<LOQ	<LOQ	<LOQ	-	<LOQ	0
Amoxicillin	1733	2573	2005	387	1858	100
Gabapentin	61	221	126	67	111	100
Codeine	324	592	506	122.86	554	100
Caffeine	<LOQ	968	242	484	<LOQ	25
Trimethoprim	<LOQ	157	49	74	21	50
Sulfamethoxazole	<LOQ	8	5.7	3.8	7.5	75
Tramadol	<LOQ	494	144	234	41	75
Metoprolol	<LOQ	16	4	8	<LOQ	25
Doxycycline	<LOQ	<LOQ	<LOQ	-	<LOQ	0
Propranolol	<LOQ	30	7.5	15	<LOQ	25
Carbamazepine	<LOQ	314	104	144	51	75
Hydrocortisone	19	27	22.7	3.8	22.5	100
Erythromycin-H2O	11	124	45.2	53.7	23	100
DEET	25	61	44	15.1	45	100
Clotrimazole	<LOQ	<LOQ	<LOQ	-	<LOQ	0
Mefloquine-HCl	<LOQ	<LOQ	<LOQ	-	<LOQ	0
Oxazepam	<LOQ	8	2	4	<LOQ	25
Diazepam	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Valsartan	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Ibuprofen	<LOQ	256	115	135	103	25
Naproxen	<LOQ	65	39.2	28	46	75
Diclofenac Na	<LOQ	48	13.7	23	3.5	50
Meclofenamic acid	<LOQ	65	20.7	30.7	9	50
Glyburide	17	26	21.7	4.92	22	100
Gemfibrozil	<LOQ	79	30.7	34.1	22	75
17-α-ethinyl estradiole	42	116	61.2	36.5	43.5	100
β-estradiol	<LOQ	<LOQ	<LOQ	-	<LOQ	-

Figure 3-6 Concentrations (ng/L) of PPCPs in water samples from River Tame Coventry Canal, River Severn and Birmingham & Worcester Canal.

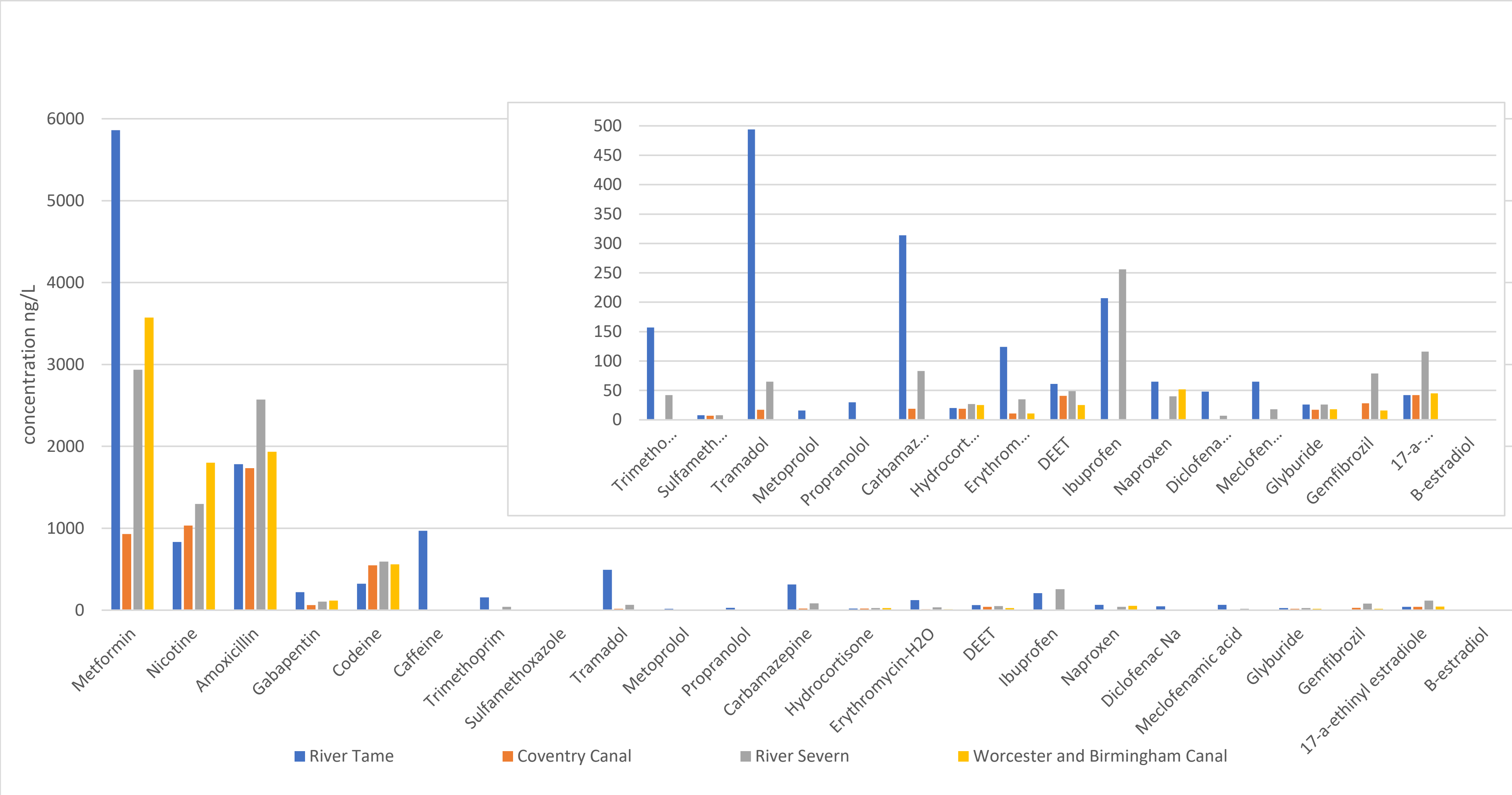


Figure 3-7 Distribution profiles (expressed as percent of ∑PPCPs) in water samples from River Tame, Coventry Canal, River Severn and Birmingham & Worcester Canal.

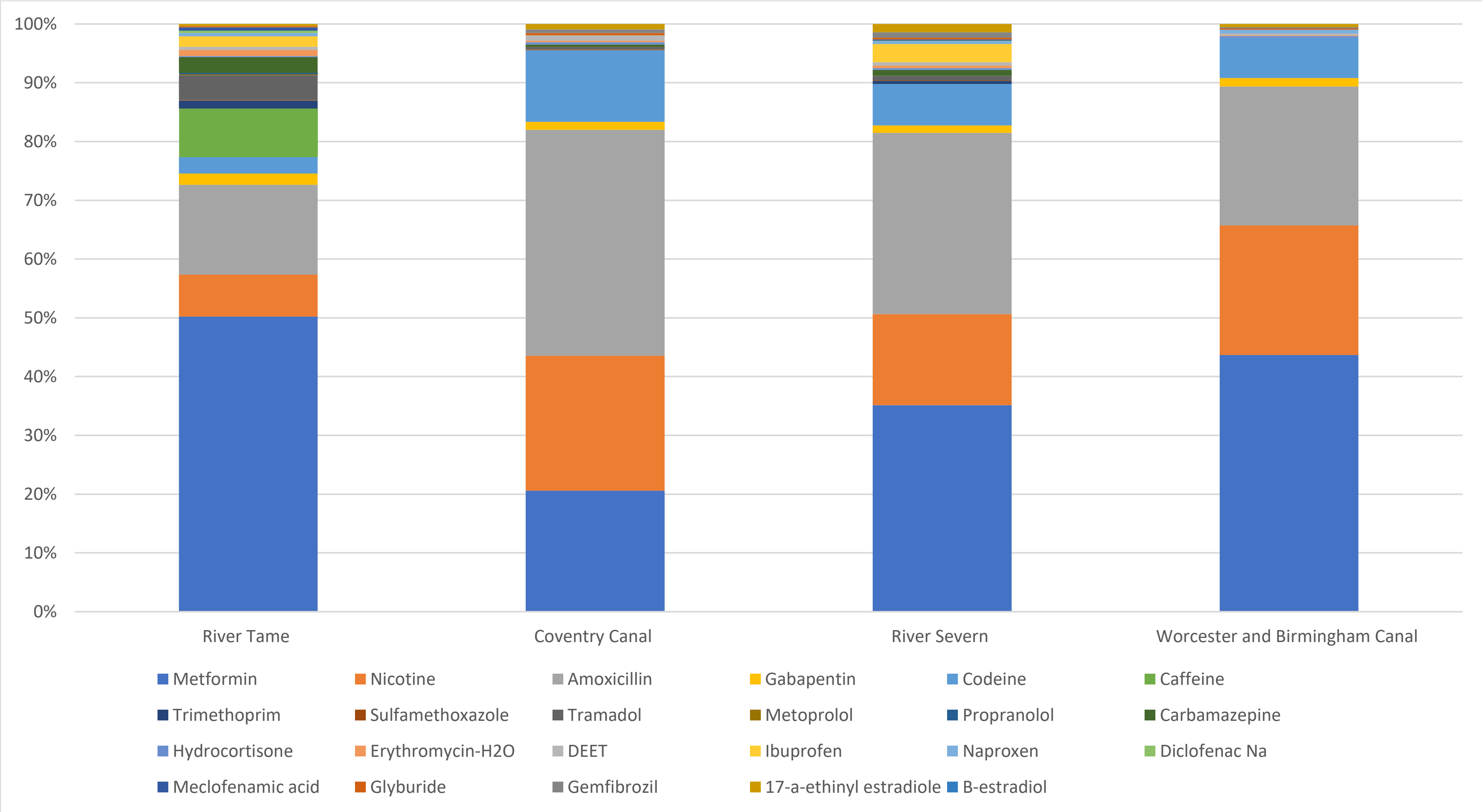


Figure 3-8 Concentrations of PPCPs in water in studied sites.

Fig 3.7a Concentrations of PPCPs in surface water from River Tame.

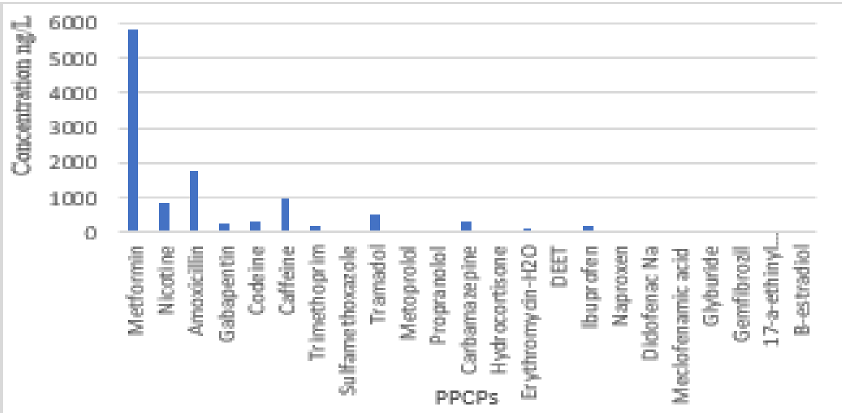


Fig 3.7b Concentrations of PPCPs in surface water from Coventry Canal.

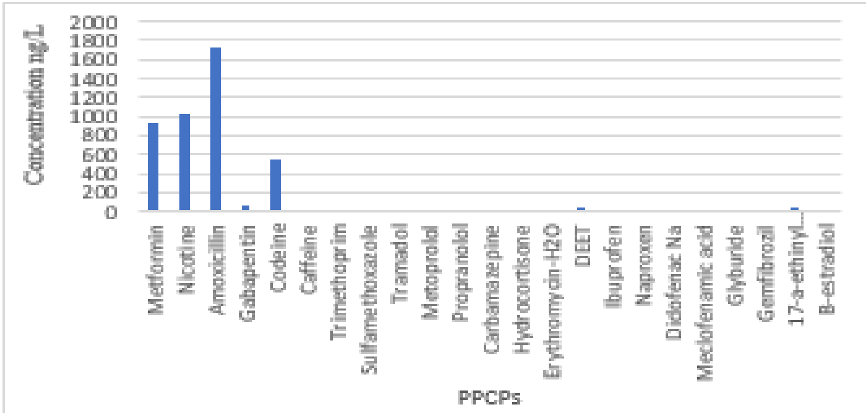


Fig 3.7c Concentrations of PPCPs in surface water from River Severn.

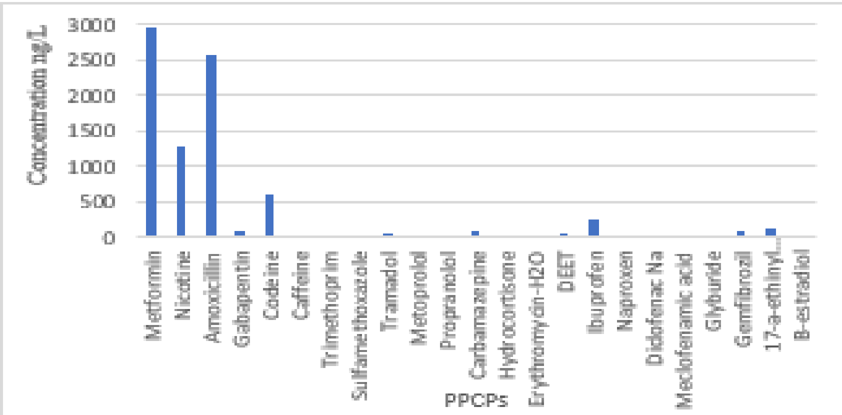
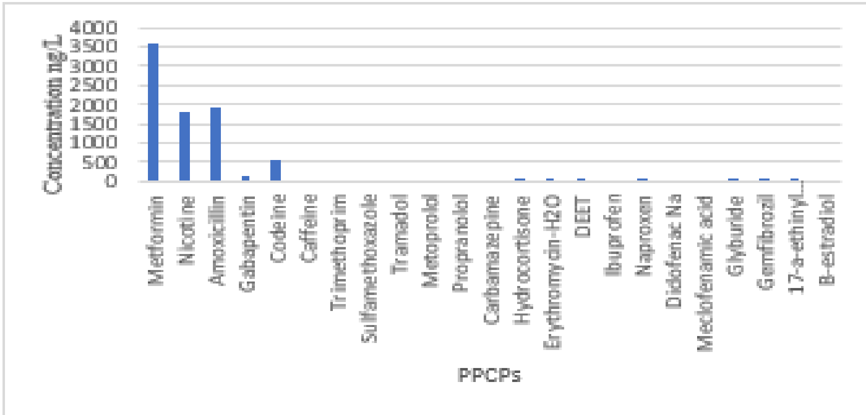


Fig 3.7d Concentrations of PPCPs in surface water from Birmingham & Worcester Canal.



3.4.2. Sediment/water distribution of target PPCPs

The partitioning of chemicals between sediment and water is an important determinant of the fate of pollutants in the freshwater aquatic environment. The distribution of a chemical between octanol and water at equilibrium is represented by log K_{ow}. This coefficient (log K_{ow}) can be used to estimate the fate of organic compounds in the environment with octanol representing the organic phase. The higher the log Kow, the more likely the chemical partition into the organic phase (i.e. representing sediment particles in this binary system) (Lei et al., 2009).

The experimentally measured sediment–water distribution coefficient (Kp, L/Kg) of PPCPs is described by the following equation (Lei et al., 2009):

$\mathbf{K_p = C_s/C_w}$ ……(*equation 3.1*)

Where, K_p is the sediment-water distribution coefficient, C_s and C_w are the concentrations of PPCPs in sediment (ng/Kg) and water phase (ng/L), respectively.

In the current study, among 30 PPCPs investigated, 9 compounds were found in paired water and sediment samples from the same location. The estimated log K_p values for target PPCPs that were detected in both water and sediment samples from the 4 studied locations are provided in Table 3.4.

The log K_p values for DEET were 1.92, 2.26, 2.09 and 2.59 in River Tam, Coventry Canal, River Severn and Birmingham & Worcester Canal, respectively. Log K_p for caffeine was 0.43 in River Tame. Comparing to a study of organic micropollutants in water and sediment from Lake Mälaren, Sweden, log K_p of DEET and Caffeine were reported at 2.3 and 0.5 (Golovko et al., 2020).

The estimated log K_p values for Gemfibrozil and Diclofenac in the present study ranged from 1.48 – 3.17 and 2.69 – 3.44, respectively. In Laboratory studies to characterise the sorption-desorption behaviour of Gemfibrozil and Diclofenac Na using aqueous solution on river sediment from the city of Šaľa, western Slovakia, The log K_p values for Gemfibrozil and Diclofenac were 1.05 and 1.62, respectively (Krascsenits et al., 2008).

The log K_p values for 17-α-ethinyl estradiole were 1.69, 1.43 and 1.08 in River Tame, Coventry Canal and River Severn, respectively. According to Lei et al. (2009), estrogenic steroids are hydrophobic organic molecules that preferentially adsorb to organic carbon-rich sediments leading to theoretical log K_p >1.

The distribution of PPCPs between sediment–water in a freshwater systems is not only influenced by compound-specific physico-chemical characteristics like K_{ow} and molecular weight, but also by water and sediment characteristics like TOC (total organic carbon), pH, and salinity, as well as texture, and cation exchange capability (Jiang et al., 2021). The organic carbon normalized partition coefficient (Koc) was determined using the following formula (Zhou and Broodbank, 2014):

$K_{oc} = K_p/f_{oc}$…….(*equation 3.2*)

Where f_{oc} is fraction organic carbon content in sediments.

In all studied locations, a positive relationship was observed between the octanol-water partition coefficient (log K_{OW}) of target PPCPs measured in water and sediment from the same location, and their experimentally measured sediment–water distribution coefficient (log K_P). A similar positive relationship was observed between log K_{OW} of these PPCPs and their estimated organic carbon normalized partition coefficient (K_{oc}). Statistical analysis revealed the correlations between log K_{OW} and Log K_P to be significant at 95% confidence level in the Tame and Severn rivers ($P < 0.05$), while the correlation was only significant at 90% confidence level ($P < 0.1$) in Coventry and Birmingham&Worcester canals Figure 3-9. A similar trend was observed for the correlation between log K_{OW} and log K_{OC} in the four studied locations Figure 3-10.

The target 30 PPCPs were ranked according to their Log K_{OW} and water solubility to investigate potential associations with their detection frequencies (%) and/or their average recorded concentrations in the studied sediment, water, and soil samples Table 3.5. Interestingly, no statistically significant correlations were observed between the investigated physicochemical properties of target analytes and their average concentrations or detection frequencies in the studied environmental matrices (correlation coefficient (r) = 0.08 – 0.2980, with $P > 0.2$).

Our combined results indicate that while the physicochemical properties (Log K_{OW} and Log K_{OC}) play a significant role in the distribution of target PPCPs between water and sediment within the same location, the impact of Log K_{OW} and water solubility on the presence (i.e., detection) and concentration of the studied PPCPs in the sampled locations and matrices is less clear. This may be attributed, at least partly, to the impact of other, more prominent factors, including the input sources and concentrations, the degradation rates, and weather/hydrological conditions, on the presence and concentrations of PPCPs at the sampled locations. It is worth noting that spot sampling applied in this chapter (i.e., one sample from each location at a given point in time) may not be sufficient to reflect the overall impact of various factors likely to influence the presence, concentrations, and profiles of a broad range of PPCPs. More detailed field and laboratory studies with specific, dedicated experimental design are required to fully understand the relative impact of various environmental and compound-specific factors that affect the concentrations and distribution of PPCPs in the various compartments of the freshwater aquatic environment."

Similar positive correlations were previously reported for various PPCPs, including some of our target compounds, in both controlled laboratory set-up (Maskaoui et al. (2007) and the river Medway, UK (Zhou and Broodbank (2014). This study indicates that the distribution of PPCPs in between water and sediment in the freshwater aquatic environment is, at least to some extent, controlled by their lipophilicity. It should be emphasized though that the behaviour of PPCPs and other endocrine-disruptive chemicals (EDCs) in the freshwater aquatic environment cannot simply be predicted based solely on lipophilicity. Sediments can act as both sources and sinks of contaminants and are crucial in transferring chemical pollutants between different environmental compartments in terrestrial and aquatic ecosystems. Depending on their chemical characteristics, organic and inorganic pollutants in surface waters are either dissolved or sorbed onto suspended matter and sediment particles. Strong sorption causes the scavenging of contaminants out of the aqueous phase, and suspended particles settling leads to the settlement of contaminants onto the beds of rivers and lakes (Chiaia-Hernández et al., 2022). However, Sediments are complex dynamic systems influenced by hydrodynamic factors (e.g., storms, flooding, subaquatic slumps), physicochemical processes (e.g., redox reactions), and microbial activity. Therefore, correct evaluation of these processes is of fundamental importance for environmental risk assessment and the prediction of the long-term fate of chemical pollution in sediments. While persistent organic pollutants (POPs) inputs to sediments at trace levels occur very widely from regional to global scales by means of riverine, run-off, industrial activities, and atmospheric deposition, understanding and modelling sediment contamination with more labile (i.e., less persistent) chemicals released into the environment directly (e.g., contaminated effluents from WWTPs) or indirectly (e.g., the runoff of pesticides applied on agricultural land) is more complex (Chiaia-Hernández et al., 2022). This was further explained by Hong et al. (2022) who investigated the sedimentary spectrum of 86 PPCPs in relation to sediment-water distribution and land use in a Chinese watershed. The study concluded that sedimentary concentrations and profiles of PPCPs are not solely reliant on the physicochemical properties of the contaminants and their sediment-water distribution, but are also impacted by multiple processes including photolysis, hydrolysis, biodegradation, adsorption, bioaccumulation, and sedimentation, within the course of the studied waterway, resulting in dramatical fate complexity of pharmaceutical residues for source-sink relationships (Hong et al., 2022). More detailed laboratory studies revealed that sorption behaviour of pharmaceuticals and EDCs is also correlated to sediment properties including particle size, cation exchange capacity (CEC), texture and organic content (OC) ((Zhou and Broodbank, 2014, Al-Khazrajy and Boxall, 2016).

Al-Khazrajy and Boxall (2016) concluded that while the use of single parameters (e.g., Log K_{OW}) may reasonably predict the distribution of some PPCPs in some rivers and lakes, the complex processes involved in the sorption of this diverse class of chemicals to sediment particles require more sophisticated, multi-parametric models for full prediction of PPCPs behaviour in the freshwater aquatic environment.

Table 3.4 Experimentally measured sediment–water distribution coefficient (Log KP) of target PPCPs in the studied locations compared to their Octanol-Water partition coefficient (Log KOW) and the estimated organic carbon normalized partition coefficient (Koc).

PPCPs	Log K_{ow}	River Tame			Coventry Canal			River Severn			Birmingham & Worcester Canal		
		Log K_p	Log K_{oc}	f_{oc}*	Log K_p	Log K_{oc}	f_{oc}	Log K_p	Log K_{oc}	f_{oc}	Log K_p	Log K_{oc}	f_{oc}
Amoxicillin	0.87	0.92	0.84	1.2	0.54	-0.07	4	0.45	0.09	2.3	0.66	-0.12	6
Gabapentin	-1.1	0.22	0.14		0.65	0.04		0.88	0.53		1.39	0.61	
Caffeine	-0.07	0.43	0.35		N.C.	N.C.		N.C.	N.C.		N.C.	N.C.	
Hydrocortisone	1.61	N.C.**	N.C.		1.02	0.26		1.25	0.89		1.09	0.32	
DEET	2.02	1.96	1.88		2.26	1.65		2.09	1.73		2.59	1.82	
Naproxen	3.18	1.71	1.63		N.C.	N.C.		1.90	1.53		2.27	1.49	
Diclofenac Na	4.51	2.69	2.61		N.C.	N.C.		3.44	3.08		N.C.	N.C.	
Gemfibrozil	4.77	N.C.	N.C.		2.55	1.95		2.60	2.14		3.17	2.39	
17-α-ethinyl estradiole	4.15	1.69	1.61		1.43	0.83		1.50	1.13		N.C.	N.C.	

* f_{oc} is fraction organic carbon content in sediments.

** N.C. not calculated - compound was not detected in the water or sediment sample.

Figure 3-9 Correlation between Experimentally measured sediment–water distribution coefficient (Log KP) of target PPCPs in the four studied locations and their Octanol-Water partition coefficient (Log KOW).

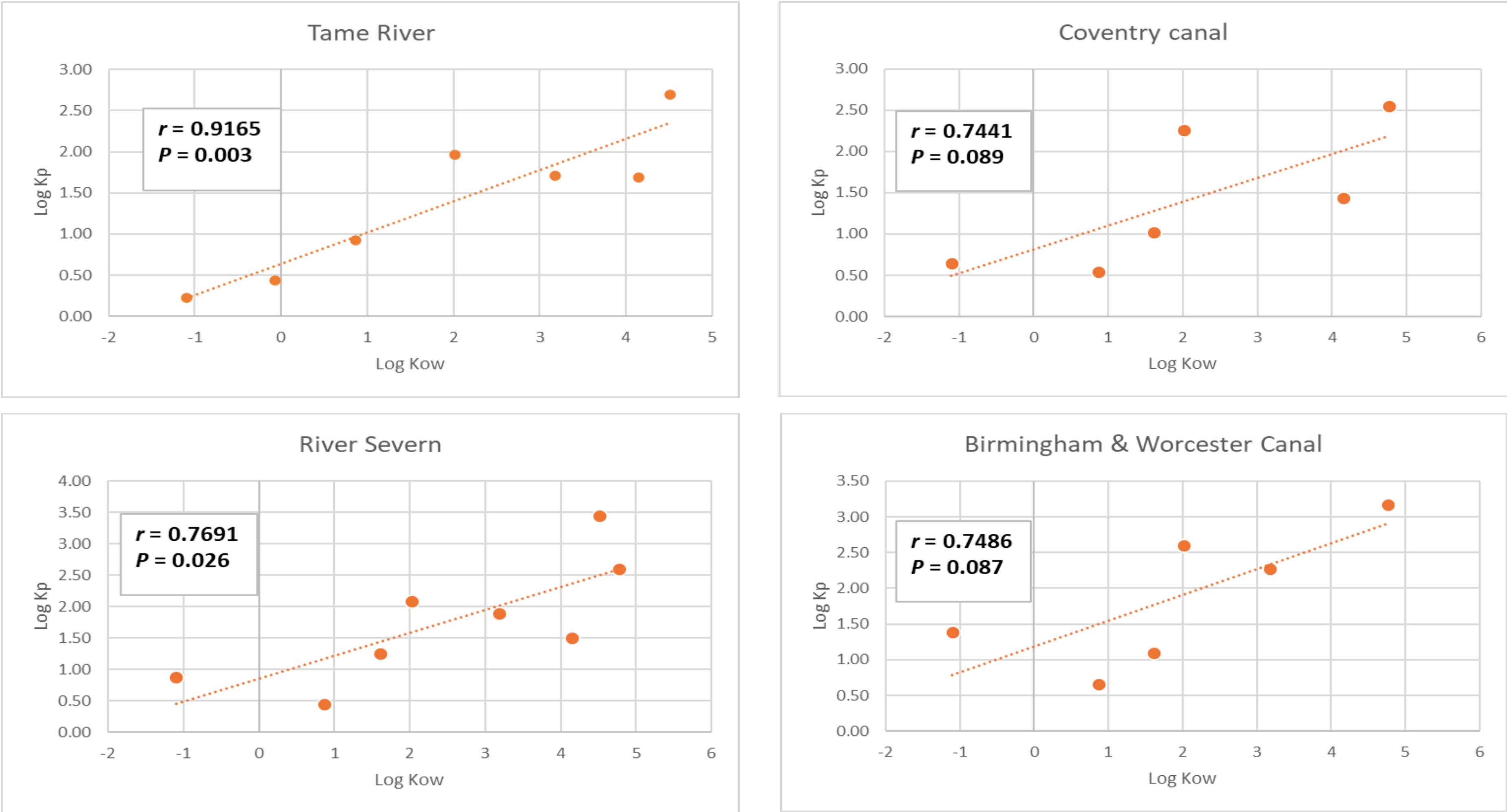


Figure 3-10 : Correlation between the estimated organic carbon normalized partition coefficient (Koc) of target PPCPs in the four studied locations and their Octanol-Water partition coefficient (Log KOW).

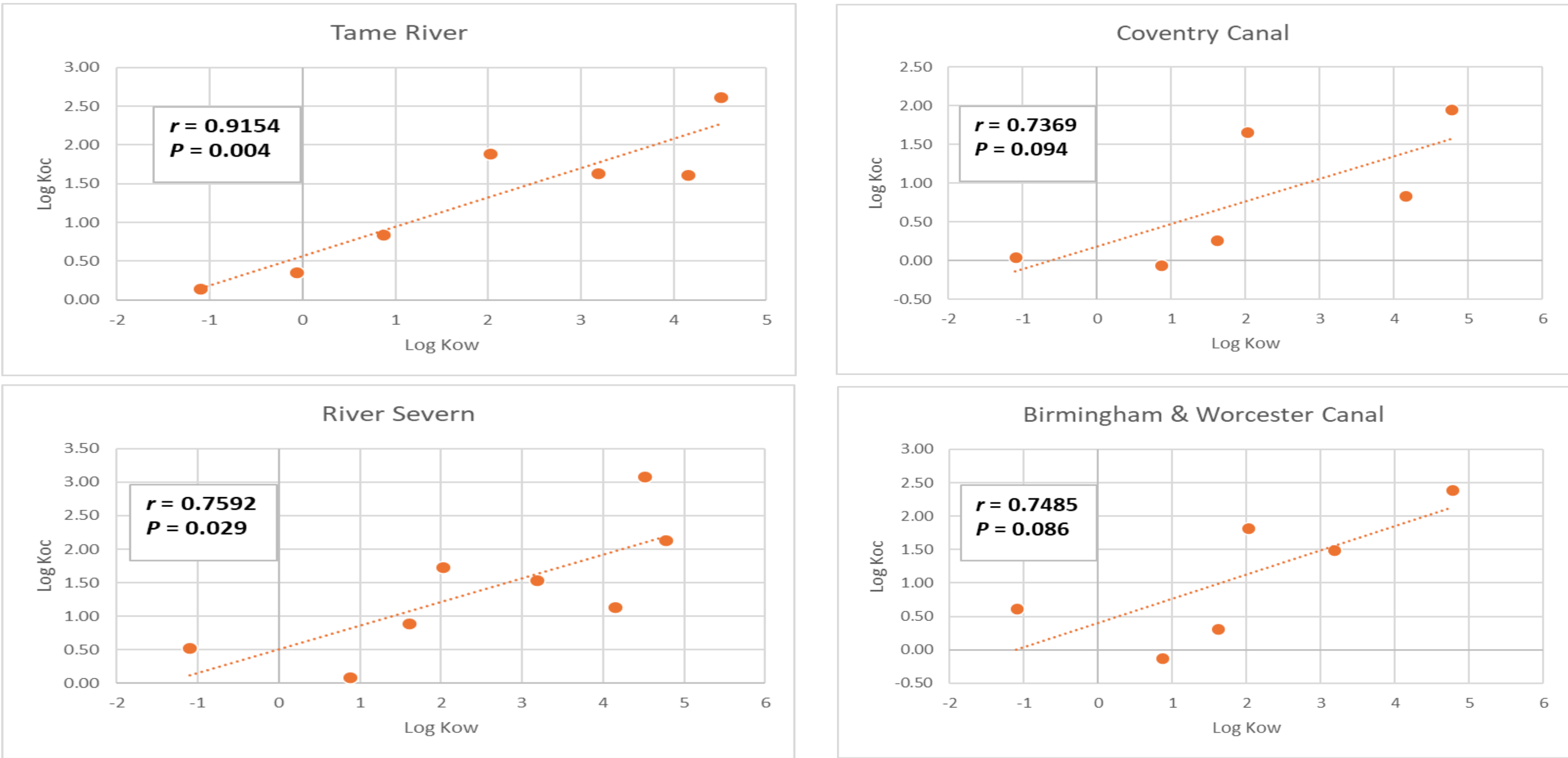


Table 3.5 Physicochemical properties, detection frequencies and average concentrations of target PPCPs in the studied sediment, water, and soil samples.

PPCPs	Average concentration			Log K_{OW}	Water Solubility (mg/L) at 25 °C	Detection frequency (%)		
	Sediment (ng/g)	water (ng/L)	Soil (ng/g)			water	Sediment	Soil
Metformin	0	3324	0	-2.64	1.06E+06	100	0	0
Nicotine	0	1242	0	1.17	1.00E+06	100	0	0
Acetaminophen	0.05	0	0	-1.6	1.40E+04	0	75	0
Amoxicillin	9.2	2005	3.88	0.87	3.43E+03	100	100	75
Gabapentin	4.3	126	0.45	-1.1	4.49E+03	100	100	25
Codeine	0	506	0	1.19	1065	100	0	0
Caffeine	1.6	242	2.45	-0.07	2.16E+04	25	100	75
Trimethoprim	5	49	0	0.91	400	50	50	0
Sulfamethoxazole	0	5.7	0	0.89	610	75	0	0
Tramadol	3.3	144	0	3.01	1151	75	50	0
Metoprolol	0	4	0	1.88	2130	25	0	0
Doxycycline	0	0	0	-0.02	50	0	0	0
Propranolol	6.6	7.5	1.7	3.48	6.17E-02	25	100	25

Carbamazepine	0	104	0	2.45	18	75	0	0
Hydrocortisone	1	22.7	0.03	1.61	320	100	75	25
Erythromycin-H2O	0	45.2	0	3.06	2.01E+03	100	0	0
DEET	7.2	44	4.35	2.02	912	100	100	100
Clotrimazole	0	0	0	0.5	0.49	0	0	0
Mefloquine-HCl	0	0	0	3.85	249	0	0	0
Oxazepam	0	2	0	2.24	20	25	0	0
Diazepam	0	0	0	2.82	66	0	0	0
Valsartan	0	0	0	4	1.4	0	0	0
Ibuprofen	0	115	0	3.97	21	25	0	0
Naproxen	3.8	39.2	0.9	3.18	15.9	75	100	50
Diclofenac Na	31.4	13.7	2.2	4.02	4.5	50	100	75
Meclofenamic acid	7.8	20.7	0	5	30	50	100	0
Glyburide	0	21.7	0	4.79	0.06	100	0	0
Gemfibrozil	11.8	30.7	1.35	4.77	11	75	100	50
17-α-ethinyl estradiole	1.5	61.2	0	3.67	11.3	100	75	0
β-estradiol	0.9	0	0	4.01	3.9	0	100	0

3.5. PPCPs in soil

To investigate the relationship between PPCPs in freshwater and the surrounding soil/run-off areas, soil samples were collected from the adjacent area of the four studied rivers. Soil samples were collected at a fixed distance of 2 metres on both sides of the waterway at the same location for collection of the sediment and water samples.

The concentrations of PPCPs in soil samples from four studied locations are summarized in Table 3.6. These data indicate that the Σ_{30} PPCPs concentrations detected in soil samples were 36.0, 22.2, 4.3 and 4.5 ng/g in River Tame, River Severn, Coventry Canal and Birmingham & Worcester Canal, respectively. As a result, soil samples of River Time were the most polluted with target PPCPs, whereas soil samples of Coventry Canal and Birmingham & Worcester Canal were the least polluted. It's likely that the higher concentrations in River Tame are attributable to the sampling site being close to an agricultural land. Previous studies have highlighted the potential for high concentrations of PPCPs in agricultural soil and run-off areas. This was attributed to a combination of factors including the use of wastewater and biosolids for irrigation and fertilisation (sludge and manure), as well as the application of large doses of PPCPs in animal husbandry and well-being (Heinonen-Tanski and van Wijk-Sijbesma, 2005, Al-Farsi et al., 2017, Gworek et al., 2021). While the application of sewage sludge on agricultural land is banned in the UK, other factors leading to higher concentrations of PPCPs in agricultural soil and run-off areas (e.g., use of incompletely treated wastewater for irrigation and application of PPCPs for animal husbandry and well-being) cannot be excluded.

Nine PPCPs, namely: DEET, amoxicillin, gabapentin, caffeine, propranolol, hydrocortisone, naproxen, diclofenac Na and gemfibrozil were frequently detected in soil samples, with 100, 75, 25, 75, 25, 25, 50, 75 and 50 % detection frequency, respectively. Amoxicillin had the highest concentrations of 8 ng/g in all the analysed soil samples, followed by DEET and propranolol at a maximum concentration of 7.1 and 6.8 ng/g, respectively, Figure 3-11.

Caffeine, was detected in soil at mean concentration of 2.5 ng/g. Among 7 Analgesics and NSAIDs, only naproxen and diclofenac Na were detected in soil samples at mean concentrations of 0.9 and 2.2 ng/g, respectively. these concentrations are lower than the levels reported in soil around the irrigation channels and lake of a Mediterranean coastal wetland, the Albufera Natural Park (Valencia, Spain), where caffeine, naproxen and diclofenac Na were reported at mean concentrations of 11, 0.18 and 1 ng/g, respectively (Sadutto et al., 2021).

In the present study, amoxicillin was detected at the mean concentration of 3.9 ng/g. Antibiotics vary in the extent of their adsorption and mobility in the soil, from highly mobile substances such as metronidazole to those that strongly adsorb such as tyrosine, depending on the specific physicochemical properties of the chemical compound, as well as the type and properties of the soil (Díaz-Cruz et al., 2003, Wang and Wang, 2015). Amoxicillin was found to be extremely mobile in soil and could therefore reach run-off areas and leach into aquatic systems (Kim et al., 2012). To our knowledge, there are no reports of amoxicillin concentrations in UK soil or elsewhere for suitable comparison with our results.

Distribution profiles of target PPCPs in the studied soil samples are summarized in Figure 3-12. Four pharmaceuticals, amoxicillin (22%), DEET (19.5%), propranolol (18.5%) and caffeine (17%), accounted for 77% of $\sum_{30}$PPCPs investigated in River Tame. 89% of target PPCPs detected in River Severn were amoxicillin (28%), DEET (26%) and diclofenac Na (25%). The same 3 PPCPs, DEET (46.5%), amoxicillin (30%) and diclofenac Na (23%) were measured in Coventry Canal, while only DEET (55.5%) and caffeine (44.5%) were detected in Birmingham & Worcester canal.

In both human and veterinary medicine, antibiotics are prescribed to treat infectious diseases (Gothwal and Shashidhar, 2015). They are also extensively employed in agriculture, aquaculture, and livestock production. Antibiotics can enter the environment in several ways and then end up in the soil. Sewage sludge and biosolids are frequently used as fertilizers for agricultural areas, and municipal wastewater containing antibiotics may be used for irrigation (KIES et al., 2020). This may explain the high detection frequency (75%) and concentrations (average = 3.88 ng/g) of amoxicillin in the soil samples analysed in the present study. A recent study from Ningbo City in eastern China revealed that soil samples taken from areas treated with sewage sludge as fertilizers had higher concentrations of 4 groups of antibiotics, compared to green spaces using chemical fertilizers (Zhao et al., 2023).

Also, the veterinary application of diclofenac sodium for treatment of cattle and pigs has been reported (Yang et al., 2019). This may partially explain the relatively high detection frequency (75%) and concentrations (average = 2.2 ng/g) of diclofenac sodium in the soil samples analysed in the present study. This is in agreement with the findings of previous study where Diclofenac sodium was detected at concentration of 2.3 ng/g in soil from the Guadalete River basin (SW Spain), where sludge is frequently used as a fertilizer and reclaimed water from a nearby wastewater treatment facility is frequently used for irrigation (Corada-Fernández et al., 2015).

Following sewage treatment, wastewater may be reused for irrigation, and sludges (treated sludge) may be used as fertiliser on farmland. Additionally, pharmaceuticals may enter waters through runoff from agricultural land that has been treated with digested sludge. Animal wastes, solid or liquid, are sprayed on agricultural fields as fertilisers, which results in the release of veterinary medications into the environment (Ebele et al., 2017). Due to its ability to fertilise soils and the minimal cost impact of this approach, the created sewage sludge is frequently used in agricultural and forestry operations (Llorens-Blanch et al., 2015). In general, few studies have reported on the occurrence, levels, distribution and fate of PPCPs in soil, compared to water and sediment. The low concentrations (or absence) of PPCPs in soil was attributed to the lack of multiple, continuous input sources of these pollutants to soil (Cf. water and sediment). Recent review articles on PPCPs in soil identified the main input sources as the application of wastewater and biosolids onto agricultural land for irrigation and fertilisation (Gworek et al., 2021, Al-Farsi et al., 2017). However, these practices are largely restricted in several countries, including the UK. Other sources include the use of veterinary medicine in animal farms and aquaculture, which can then adsorb to soil particles through excretion and run-off. However, the adsorption capacity of the soil particles and the resulting concentrations of PPCPs in soil are largely influenced by soil properties, physico-chemical characteristics of individual PPCPs, as well as environmental conditions (e.g. flow rates, temperatures and humidity) (Boxall et al., 2012, Gworek et al., 2021, Al-Farsi et al., 2017, Li et al., 2019).

Table 3.6 Concentrations (ng/g) of target PPCPs in soil samples collected from the run-off areas of River Tame, Coventry Canal, River Severn and Birmingham & Worcester Canal.

PPCPs	Soil ng/g					Detection frequency %
	Minimum	Maximum	Mean	Std. deviation	Median	
Metformin	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Nicotine	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Acetaminophen	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Amoxicillin	<LOQ	8	3.88	3.83	3.75	75
Gabapentin	<LOQ	1.8	0.45	0.9	<LOQ	25
Codeine	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Caffeine	<LOQ	6.2	2.45	2.65	1.8	75
Trimethoprim	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Sulfamethoxazole	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Tramadol	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Metoprolol	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Doxycycline	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Propranolol	<LOQ	6.8	1.7	3.4	<LOQ	25
Carbamazepine	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Hydrocortisone	<LOQ	0.12	0.03	0.06	<LOQ	25
Erythromycin-H2O	<LOQ	<LOQ	<LOQ	-	<LOQ	-
DEET	2	7.07	4.35	2.48	4.16	100
Clotrimazole	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Mefloquine-HCl	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Oxazepam	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Diazepam	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Valsartan	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Ibuprofen	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Naproxen	<LOQ	1.9	0.9	1.04	0.85	50
Diclofenac Na	<LOQ	5.6	2.2	2.99	1	75
Meclofenamic acid	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Glyburide	<LOQ	<LOQ	<LOQ	-	<LOQ	-
Gemfibrozil	<LOQ	4.1	1.35	1.93	0.65	50
17-α-ethinyl estradiole	<LOQ	<LOQ	<LOQ	0.00	<LOQ	-
β-estradiol	<LOQ	<LOQ	<LOQ	-	<LOQ	-

Figure 3-11 Concentrations (ng/g) of pharmaceutical and personal care products (PPCPs) in soil samples collected from the run-off areas of River Tame, Coventry Canal, River Severn and Birmingham & Worcester Canal.

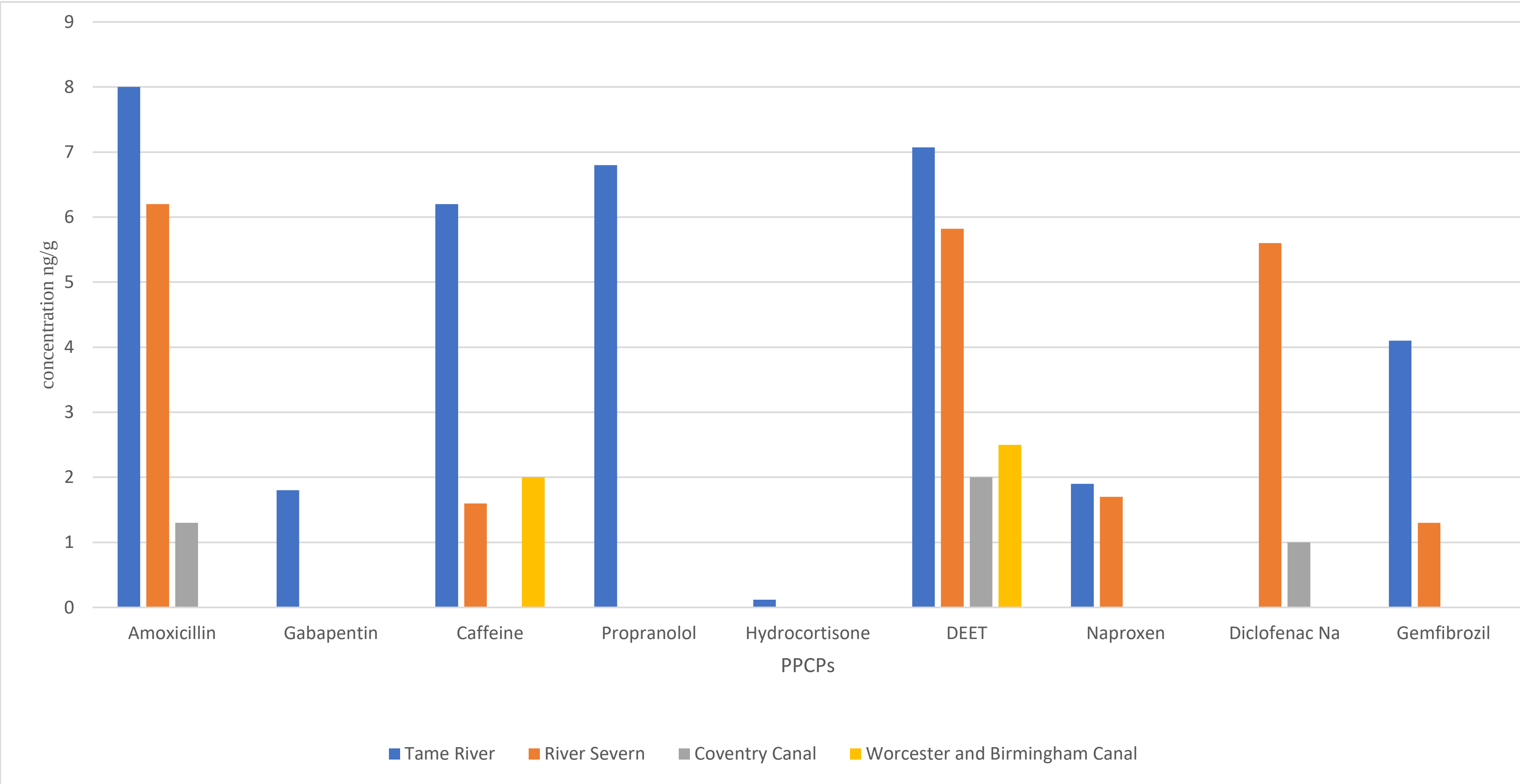


Figure 3-12 Distribution profiles (expressed as percent of ∑PPCPs) in soil samples collected from the run-off areas of River Tame, Coventry Canal, River Severn and Birmingham & Worcester Canal.

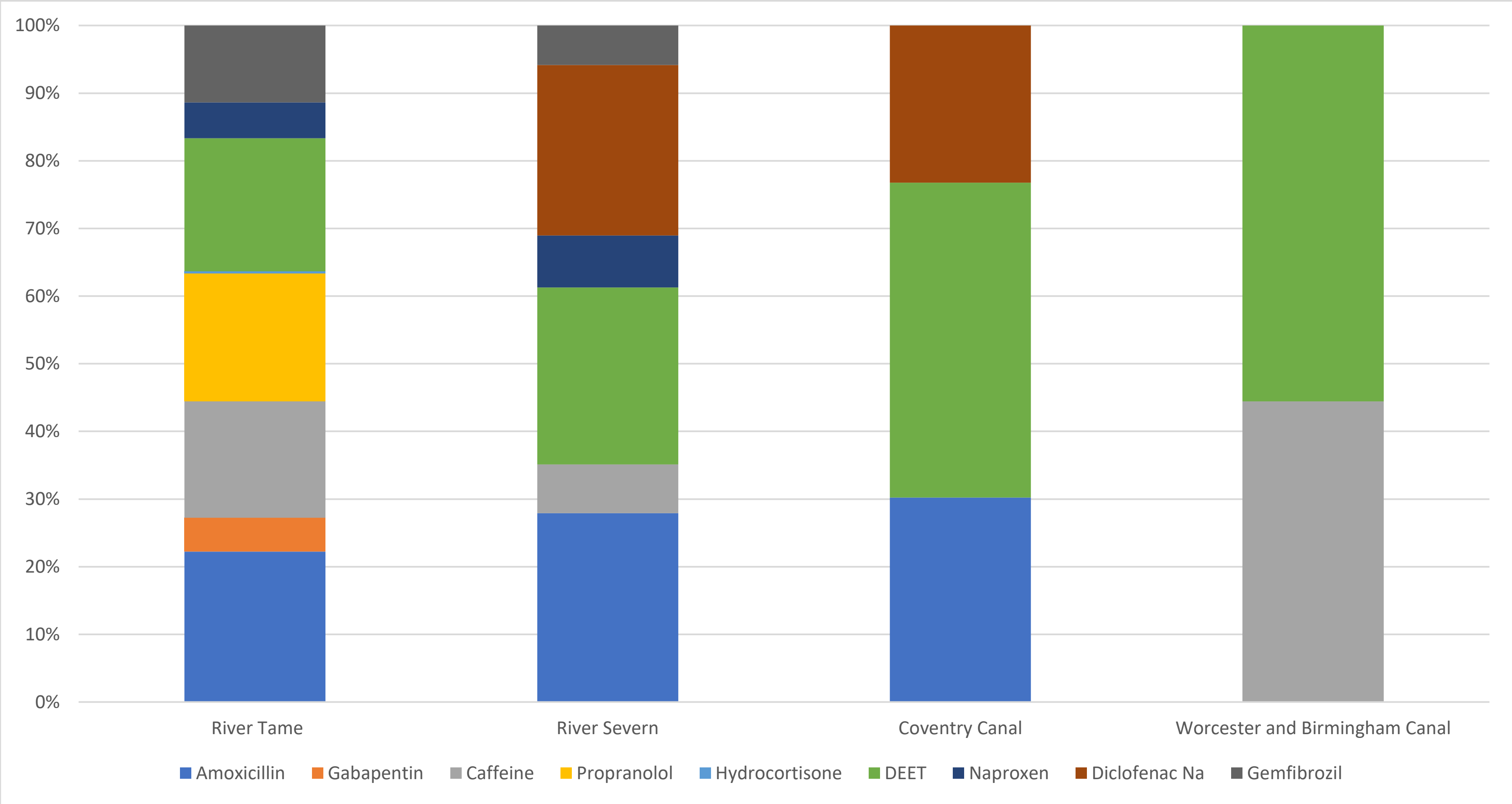


Figure 3-13 Concentrations of PPCPs in soil

Fig 3.12a Concentrations of PPCPs in soil from River Tame.

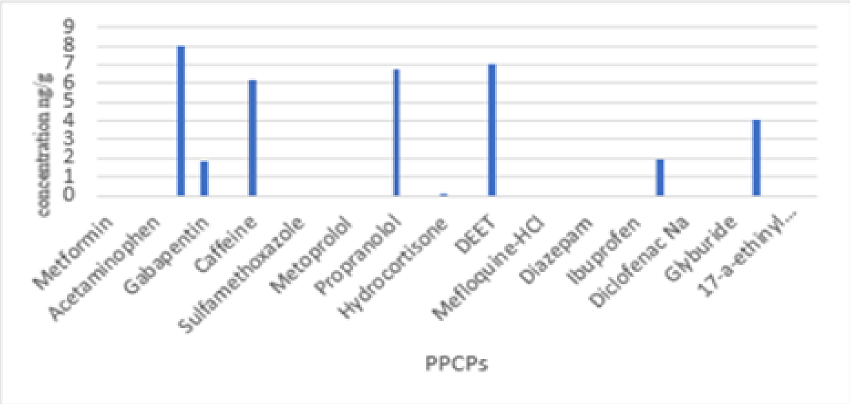


Fig 3.12b Concentrations of PPCPs in soil from Coventry Canal.

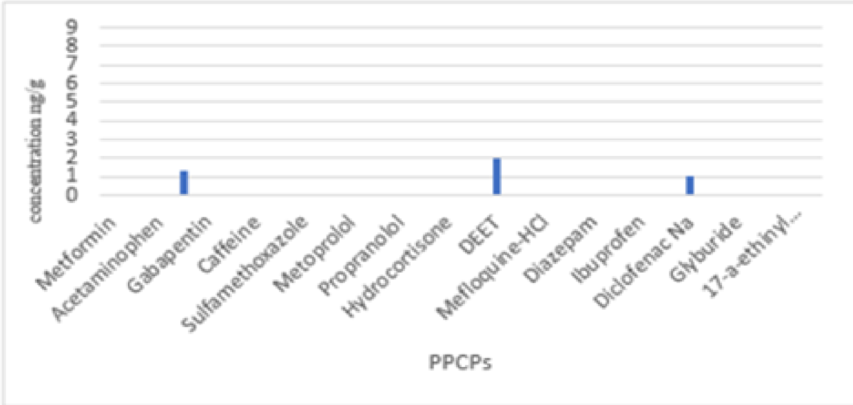


Fig 3.12c Concentrations of PPCPs in soil from River Severn

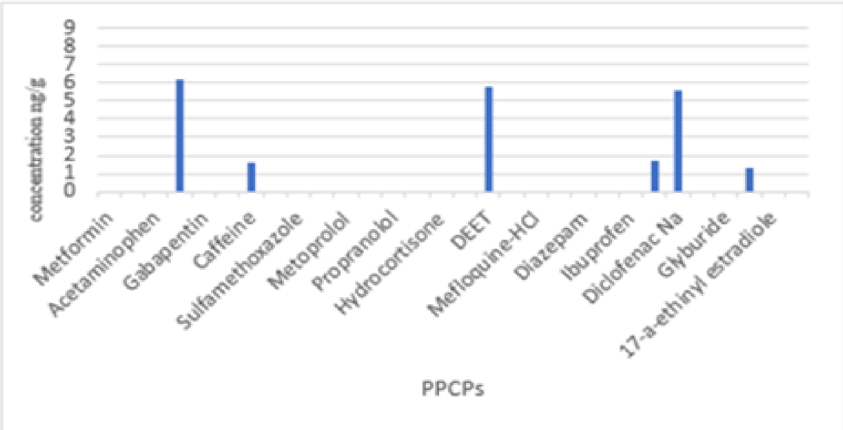
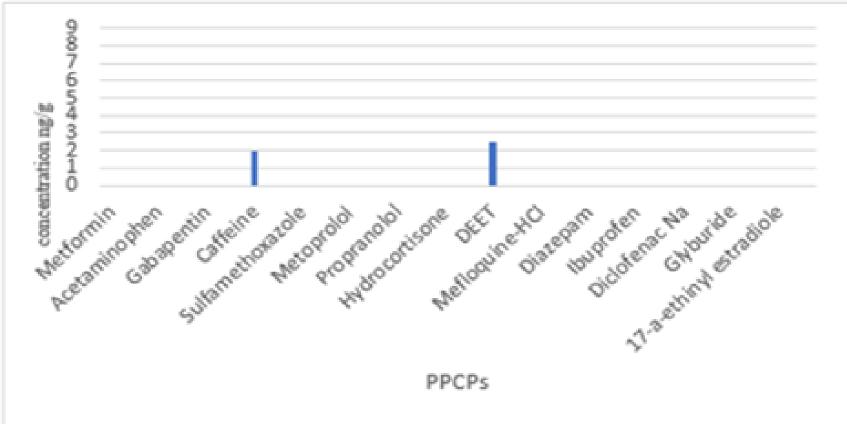


Fig 3.12d Concentrations of PPCPs in soil from Birmingham & Worcester Canal.



3.6. Ecological risk assessment

The risk quotient (RQ) approach was utilised in this thesis to assess the risk of the studied PPCPs to aquatic ecosystems. According to the guidelines issued by the European Chemicals Agency (European Chemicals Agency, 2008) and European Commission Technical Guidance Document (European Commission, 2003), the RQ is determined by comparing the observed environmental concentration (MEC) to the predicted no effect concentration (PNEC), as shown in the equation:

$$RQ = \frac{\text{measured environmental concentration (MEC)}}{\text{predicted no-effect concentration (PNEC)}_{\text{Soild}}} \text{.........}(\textit{equation 3.3})$$

While there have been various reports on the risk assessment of PPCPs in surface water, studies on their risk assessment in sediment have been limited. This is likely due to the paucity of toxicity data sets for PPCPs in sediment (such as LC_{50} and EC_{50}) in the available literature, making PNEC values difficult to estimate.

Due to the lack of toxicological endpoints for PPCPs in the sediment compartment, the method documented by Van Vlaardingen et al. (2004) was used to calculate $PNEC_{solid}$ values according to the following equations.

$PNEC_{soild} = PNEC_{water} * K_P$……………….(*equation 3.4*)

$K_P = K_{oc} * f_{oc}$ ………………..(*equation 3.5*)

Where $PNEC_{water}$ values are based on published research Table 3.7. K_P is the sediment–water distribution coefficient, K_{oc} represents the organic carbon normalized partition coefficient and f_{oc} represents the organic carbon fraction in sediment (*See Section 3.3.2 for details*). This method enabled the estimation of PNEC sediment for target PPCPs that were identified simultaneously in water and sediment samples from the same location.

The ecological risk of the studied compound can then be classified into 4 categories: "no risk" (RQ < 0.01), "low risk" (0.01 < RQ < 0.1), "medium risk" (0.1 < RQ < 1), and "high risk" (RQ > 1)(Li et al., 2021a).

The RQ of amoxicillin, gabapentin, caffeine, DEET, naproxen, diclofenac Na, gemfibrozil and 17-a-ethinylestradiole for aquatic organisms are shown in Figure 3-14. The estimated RQ values of amoxicillin, caffeine and 17-α-ethinyl estradiole in bacteria were higher than 1 and ranged from 8 to 262 in the four studied locations, indicating high risk to freshwater bacteria.

Conversely, RQ values for amoxicillin and DEET in algae, and gabapentin in fish were much lower than 0.01 (range from 10^{-4} to 10^{-5}) in the four studied locations, suggesting no risk to these aquatic organisms at the measured concentrations Table 3.8.

Few previous studies have investigated the risk of PPCPs in freshwater sediments. In a study calculating the RQ of 13 antibiotics in sediments from Hanjiang River, China, researchers reported ofloxacin, oxytetracycline, ciprofloxacin and sulfamethoxazole posed high risks (RQ > 1) to aquatic organisms (He et al., 2018). Another study investigated the risk of antibiotics in water and sediment from Yongjiang River, China. Four antibiotics, sulfamethoxazole, erythromycin-H2O, roxithromycin and clarithromycin, presented higher risks (RQ > 1) in sediment than in water (Xue et al., 2013). While none of these previous studies investigated Amoxicillin, the results are generally in line with our findings of high risk of amoxicillin (RQ > 1) in UK freshwater sediment.

According to our findings Figure 3-15, except for Birmingham & Worcester Canal, 17-α-ethinyl estradiole (EE2) posed a relatively high risk (RQ > 1) to fish. This is in agreement with previous findings reported in sediment samples from a shallow freshwater Chinese lake, where EE2 concentrations of (0.8 – 2.3 ng/g) lead to estimated RQ > 1 with the subsequent risk of feminisation in fish (Liu et al., 2017).

Diclofenac Na posed low risk (RQ < 0.1) to fish (*Oncorhynchus mykiss)* in the River Tame and River Serern, whereas it presents medium risk (0.1 < RQ < 1) to the same fish species in Coventry Canal and Birmingham & Worcester Canal. However, diclofenac Na presented no risk (RQ < 0.01) to fish (*Oryzias latipes*) at the measured concentrations in the four studied locations Table 3.8. Naproxen indicated a no risk (RQ < 0.01) level to fish and amphibians at the four studied locations. A similar no risk level (RQ < 0.01) was reported for naproxen in sediment samples collected from Taihu Lake, China (Li et al., 2021a).

Overall, it should be noted that despite the well documented occurrence of various PPCPs in freshwater sediment, very little is known about the ecotoxicological risk of these chemicals. This might be attributed to the paucity of data on toxicological endpoints for various PPCPs in sediments and solid environmental matrices in general. This is compounded by the fewer number of studies on PPCPs in sediment, compared to water, and the incomplete understanding of the sorption behaviour of different PPCPs onto sediment particles. As a conclusion, the risk assessment undertaken in the present study provides first insight into the risk of eight target PPCPs on sensitive organisms in UK freshwater sediment. However, more research is required on both the toxicological and environmental research fronts to enhance the current understanding of PPCPs risk in freshwater sediment.

Table 3.7 List of reported Predicted No-Effect Concentration values in water (PNECwater) and the corresponding estimated PNECsediment values for the studied PPCPs* using the method described by Van Vlaardingen et al. (2004).

PPCPs	Species	Class	$PNEC_{water}$ (ppb)$^{\beta}$	Reference	$PNEC_{sediment}$ (ppb)$^{+}$
Amoxicillin	*Microsystis aerugonosa*	Bacteria	3.7	(Lee et al., 2008)	0.27
	Selenastrum caprocornutum	Green algae	250000		18397
Gabapentin	*Danio rerio*	Fish	855000000	(Liu et al., 2020b)	405665093
Caffeine	*Salmo salarc*	Fish	1	(Liu et al., 2020a)	0.02
	Xenopus laevis	Amphibians	2.5	(Liu et al., 2020b)	0.04
DEET	Different Species	Algae	5210	(Guruge et al., 2019)	9419
Naproxen	*Limnodynastes peroniid*	Amphibians	1000	(Liu et al., 2020a)	645
	Different Species	Fish	1700	(Tousova et al., 2017)	1096
Diclofenac Na	*Oncorhynchus mykiss*	Fish	23	(Liu et al., 2020a)	279
	Oryzias latipes	Fish	729	(Guruge et al., 2019)	8870
Gemfibrozil	*Danio rerioc*	Fish	19	(Liu et al., 2020a)	50
	Different Species	Crustaceans	780	(Guruge et al., 2019)	2035
17-α-ethinyl estradiole	*Rutilus rutilus*	Fish	0.35	(Caldwell et al., 2008)	0.14

* Estimated for the target PPCPs that were identified simultaneously in water and sediment samples from the same location.

+ $PNEC_{sediment}$ calculated by the method described by Van Vlaardingen et al. (2004). β $PNEC_{water}$ collected from literature.

Table 3.8 : Estimated risk quotient (RQ) values of PPCPs in sediment from River Tame, Coventry Canal, River Severn and Birmingham & Worcester Canal.

PPCPs	PNEC $_{Sediment}$ (ppb)	Organism	RQ			
			River Tame	Coventry Canal	River Severn	Birmingham & Worcester Canal
Amoxicillin	0.27	Bacteria (*Microsystis aerugonosa)*	55	22	27	33
	18397	Green algae (*Selenastrum caprocornutum)*	0.00	0.00	0.00	0.00
Gabapentin	405665093	Fish (*Danio rerio)*	0.00	0.00	0.00	0.00
Caffeine	0.02	Fish (*Salmo salarc)*	262	104	143	143
	0.04	Amphibians (*Xenopus laevis)*	65	26	36	36
DEET	9419	Algae (Different Species)	0.00	0.00	0.00	0.00
Naproxen	645	Amphibians (*Limnodynastes peroniid)*	0.01	0.00	0.00	0.01
	1096	Fish (Different Species)	0.00	0.00	0.00	0.01
Diclofenac Na	279	Fish (*Oncorhynchus mykiss)*	0.08	0.16	0.07	0.14
	8870	Fish (*Oryzias latipes)*	0.00	0.00	0.00	0.00
Gemfibrozil	50	Fish (*Danio rerioc)*	0.23	0.20	0.05	0.48
	2035	Crustaceans (Different Species)	0.01	0.00	0.00	0.01
17-α-ethinyl estradiole	0.14	Fish (*Rutilus rutilus)*	15	8	10	-

PNEC=Predicted no-effect concentration

Figure 3-14 Risk quotients (RQ) of selected PPCPs for aquatic organisms in sediments from River Tame, Birmingham & Worcester Canal, River Severn and Coventry Canal.

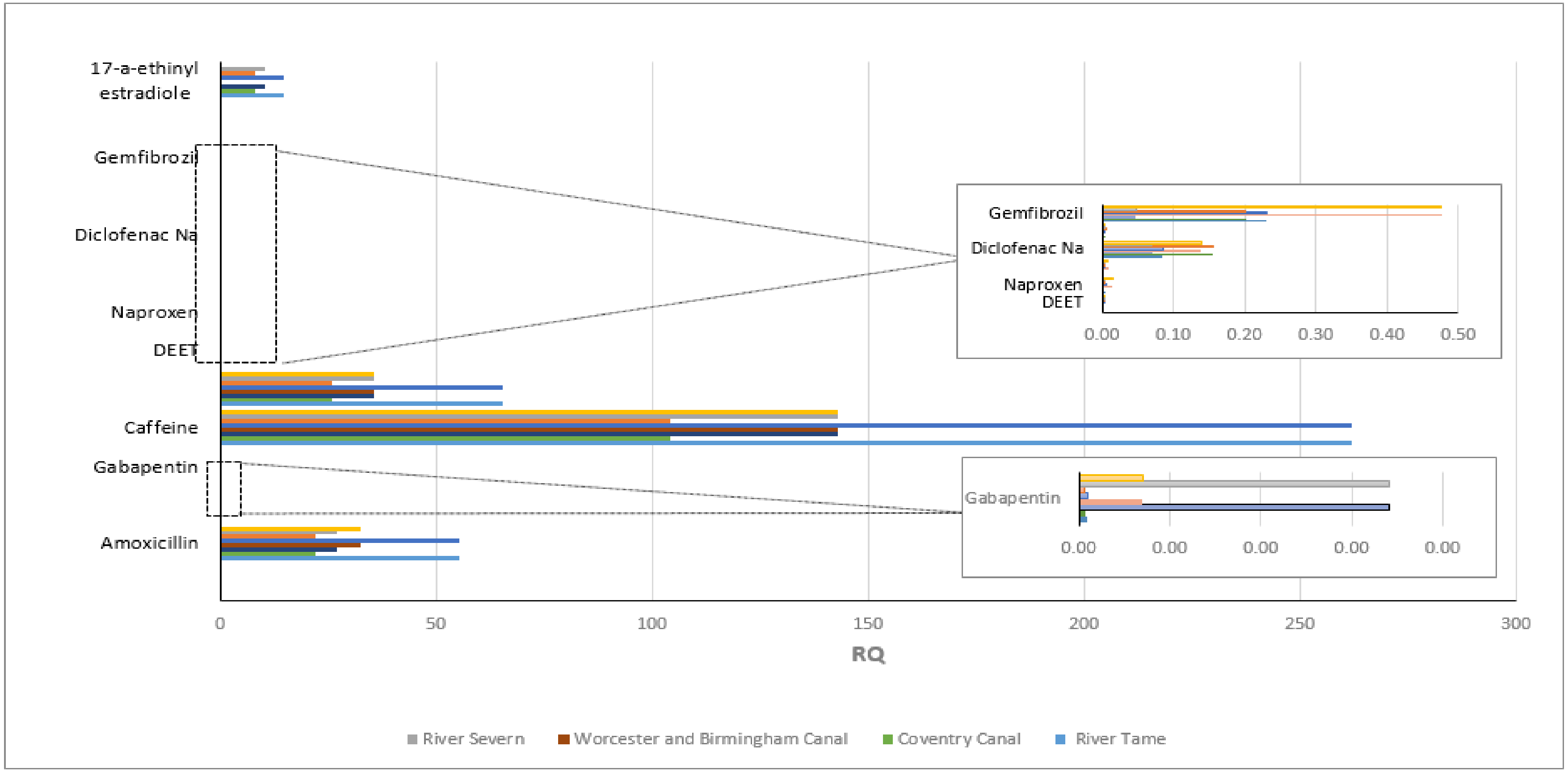
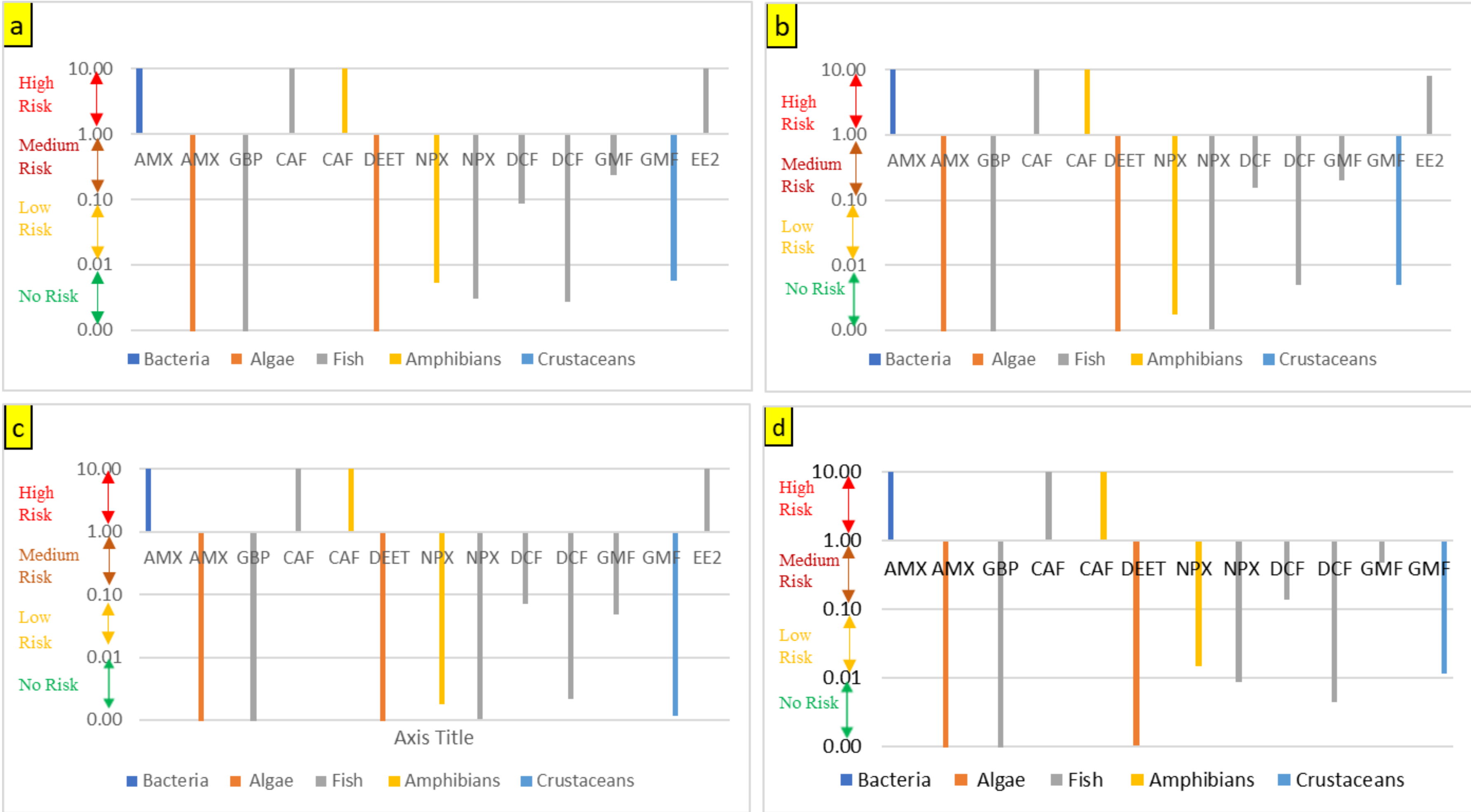


Figure 3-15 Risk quotients for PPCPs in sediments were estimated for bacteria, algae, fish, amphibians and crustaceans in River Tame (a), Coventry Canal (b), River Severn (C) and Birmingham & Worcester Canal (d).



AMX: Amoxicillin, GBP: Gabapentin, CAF: Caffeine, NPX: Naproxen, DCF: Diclofenac Na, GMF:Gemfibrozil EE2: 17-α-ethinyl estradiol

In addition to the findings of previous research on the levels and sources of PPCPs in surface water, WWTP influents, effluents, biosolids, and fish in the UK, our results address a current knowledge gap on the concentrations and profiles of PPCPs in freshwater sediment and their partitioning from water. Although our results reveal that PPCPs distribution between sediment and water may be attributed, at least partially, to the compound specific physicochemical properties (Log K_{OW}), we also highlight the need for further research to investigate other potential contributing factors, including sediment characteristics (e.g., organic carbon content, degree of mineralisation, particle size and surface area), and hydrological factors (e.g., flow rate, rainfall, redox reactions), as well as various degradation pathways (e.g. photodegradation, biodegradation) to further understand the fate of these chemicals in sediment. Moreover, our results show that concentrations of PPCPs in soil may be partly explained by the veterinary applications of some PPCPs, leading to higher concentrations in soil. These results should provide the foundation for more detailed future studies into the input sources and distribution of PPCPs in the aquatic environment. The results of our preliminary risk assessment for the measured concentrations of PPCPs in sediment highlight the need for further research into better removal efficiency of this class of emerging contaminants by WWTPs. The outcome of our research also lends support to the ban on the use of sewage sludge on agricultural lands in the UK yet calls for further development of effects-based sediment quality standards or guidelines. This knowledge will provide crucial information for environmental managers and policy makers (e.g., UK MPs) as they make important decisions regarding the disposal of raw sewage, treated sludge, and/or wastewater effluents into UK waters.

Chapter 4. Seasonal variation of pharmaceuticals and personal care products in UK Freshwater Sediment.

4.1. Synopsis

This chapter provides a study of the seasonal variation of 30 PPCPs in sediment via measuring their concentrations monthly, over one year, in 4 locations, namely: (1) River Sowe, (2) River Tame, (3) River Severn and (4) Worcester & Birmingham Canal. The individual and sum concentrations of target PPCPs are compared statistically over the 4 seasons and the factors influencing these concentrations are discussed and evaluated within the context of the available literature. The profiles of the measured PPCPs in sediment from the 4 studied locations are studied and contrasted over the study period to identify any seasonal trends associated with the usage patterns of the target chemicals. Finally, the impact of wastewater treatment plants (WWTP) on PPCPs pollution in sediment was evaluated through statistical comparison of monthly samples collected upstream and downstream of WWTPs in the 3 studied rivers.

4.1.1. Sample locations

Samples of sediment were taken at four different locations. Three rivers, River Sowe, River Tame and River Severn, and Birmingham and Worcester & Birmingham Canal Figure 4-1. “The sediment samples were collected from each location once a month for 12 months, The date of collection was the last week of each month, with River Sowe sampled on the Monday, River Tame on Tuesday, River Severn on Wednesday and Worcester and Birmingham Canal sampled on the Thursday. The sampling spots for each location were kept the same in each monthly sampling event throughout the 12-month monitoring period. In the three studied rivers, sampling was paired (i.e., ~100m distance) upstream and downstream from the respective WWTP. The exact sampling location coordinates are provided in Figure 4-1.

4.1.2. Sampling and analysis

Surface sediment samples (0-5 cm) were collected using a stainless-steel sediment corer or a bucket auger trowel depending on the depth of the river at the sampling location. Surface soil samples (0-5 cm) were collected using a stainless-steel hand scoop, at a distance of 1 metre from the water edge of the sampled river/canal. The samples were collected in pre-cleaned amber glass bottles with quick-fit lids. The sample bottles were immediately placed in an icebox and transferred to the lab where they were stored at −20 °C in the dark until extraction. To avoid cross-contamination, all sampling equipment were carefully washed with water and CleanPro™ washing up liquid, dried at 120°C for 2 hours and rinsed with deionized water and acetone before use. The determination of 30 investigated PPCPs in sediment samples was effectively accomplished using the analytical methods (extraction and clean up) in chapter 2 of this thesis. All extracted sediment samples were analysed using SCIEX™ UHPLC Triple TOF MS/MS as described under section 2.8.2 of this thesis.

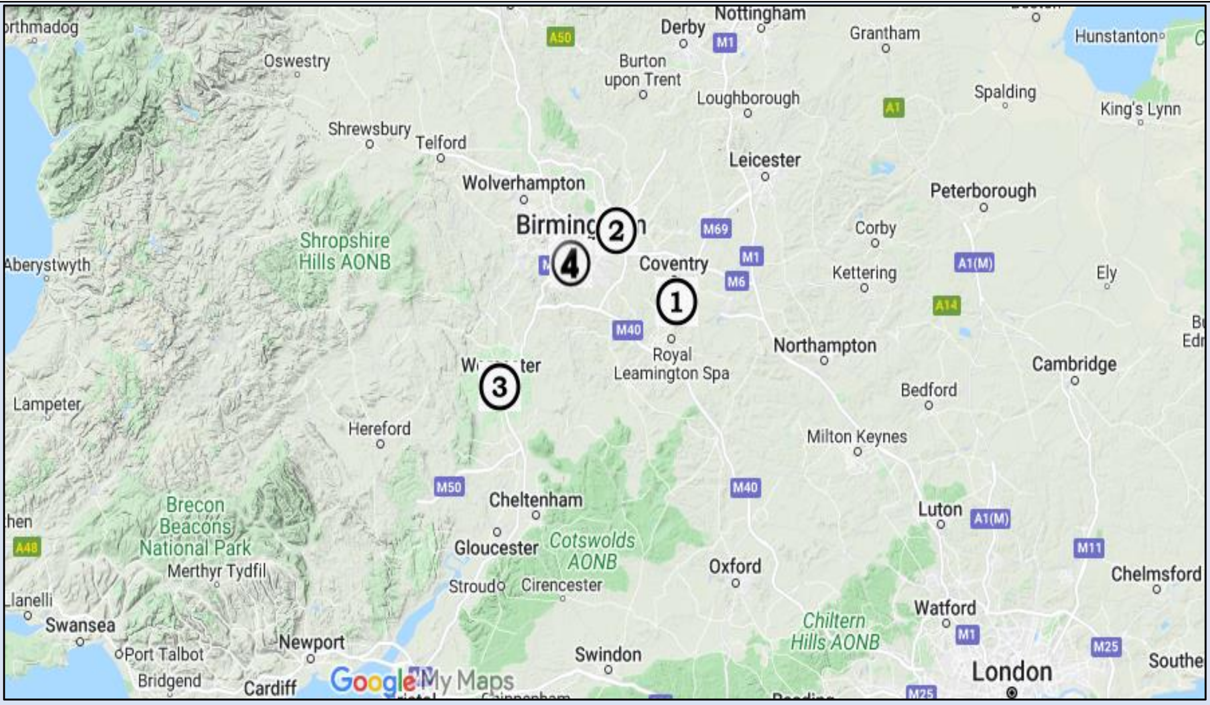
4.2. Statistical analysis

The IBM SPSS statistics 27.0 software package for Windows 10 was used to conduct the statistical analysis. Firstly, the Shapiro–Wilk test was paired with a visual evaluation of Q-Q Plot for data distribution to evaluate sample distribution. All data showed non-normal distribution transformed to a normal distribution by using $\log_{10}$ function in SSPS. Then, parametric tests were further applied on the log-transformed data for comparison of sample means (student t-test to compare between two datasets) and Analysis of Variance (ANOVA) combined with Tukey's honestly significant difference (HSD) post-hoc test. The coefficient of variation (CV%), expressed as % deviation from the mean, has been calculated according to equation 1 below, and is used to express the degree of variation (skewness of data) within the generated data sets.

$CV (\%) = \frac{S}{\dot{x}} x100$ ….(1)

Where S is the standard deviation and ẋ is the sample mean."

Figure 4-1 Sampling locations: (1) River Sowe, (2) River Tame, (3) River Severn and (4) Worcester & Birmingham Canal.



Site name	Upstream		Downstream	
	Latitude	Longitude	Latitude	Longitude
(1) Sowe river	52°22'7.95"N	1°30'46.40"W	52°21'31.34"N	1°30'50.11"W
(2) Tame River	52°31'12.57"N	1°44'45.30"W	52°31'14.60"N	1°44'35.35"W
(3) Severn River	52°10'51.32"N	2°13'29.44"W	52°10'32.13"N	2°13'28.42"W
(4) Worcester and Birmingham canal	52°27'3.58"N	1°56'11.91"W		

4.3. Seasonal variation of PPCPs in sediment

Over the period of a year, variations in concentrations of the 30 target PPCPs and Σ_{30} PPCPs at the 4 studied locations are provided in Tables 4.1 - 4.4 and Figures 4-2, 4-5.

Table 4-1 Statistical summary of PPCPs concentrations (ng/g) in sediment from the river SOWE collected monthly over a year.

PPCPS	Mean	Std. deviation	Min	Max	Coefficient of Variation (%)
Metformin	21.5	20.0	0.6	59.4	93.0
Nicotine	11.7	9.0	0.2	22.5	76.7
Acetaminophen	9.7	11.9	0.3	39.0	123.2
Amoxicillin	14.9	18.4	0.5	56.5	123.9
Gabapentin	3.6	6.8	0.2	22.7	188.5
Codeine	6.2	9.4	0.3	27.5	151.9
Caffeine	1.8	2.3	0.2	6.9	125.1
Trimethoprim	3.1	3.3	0.0	8.7	104.7
Sulfamethoxazole	1.7	2.3	0.1	8.2	139.7
Tramadol	2.1	4.0	0.2	12.7	187.4
Metoprolol	2.1	3.1	0.1	8.2	150.7
Doxycycline	8.6	18.6	0.1	58.7	217.2
Propranolol	7.2	10.1	0.2	28.4	140.8
Carbamazepine	11.8	10.1	0.4	30.7	85.2
Hydrocortisone	14.5	11.3	0.2	33.2	77.6
Erythromycin-H2O	5.6	7.0	0.1	22.4	125.7
DEET	11.5	20.3	0.0	56.1	176.7
Clotrimazole	16.2	15.8	0.4	40.2	97.5
Mefloquine-HCl	11.0	11.1	0.2	30.9	101.5
Oxazepam	17.7	20.7	0.5	67.2	117.0
Diazepam	16.4	19.0	0.4	56.9	115.8
Valsartan	16.9	21.1	0.1	59.4	125.2
Ibuprofen	26.4	15.7	10.0	52.7	59.6
Naproxen	9.2	8.4	1.7	26.2	91.2
Diclofenac Na	7.0	11.9	0.2	38.0	171.8
Meclofenamic acid	1.4	1.4	0.0	4.5	99.3
Glyburide	0.4	0.6	0.0	2.1	128.5
Gemfibrozil	14.5	11.6	1.1	34.3	79.8
17α-ethinyl estradiole	4.8	11.9	0.0	42.2	250.2
β-estradiol	16.5	14.5	1.0	47.4	88.0
Σ30 PPCPs	276.1	320.2	29.0	1029.6	115.9

Figure 4-2 Seasonal variation profile of target PPCPs in sediment from the river SOWE. (a) average concentrations (± standard deviation, n=3) of Σ30 PPCPs (ng/g), (b) relative percent contribution of each target PPCP to Σ30 PPCPs.

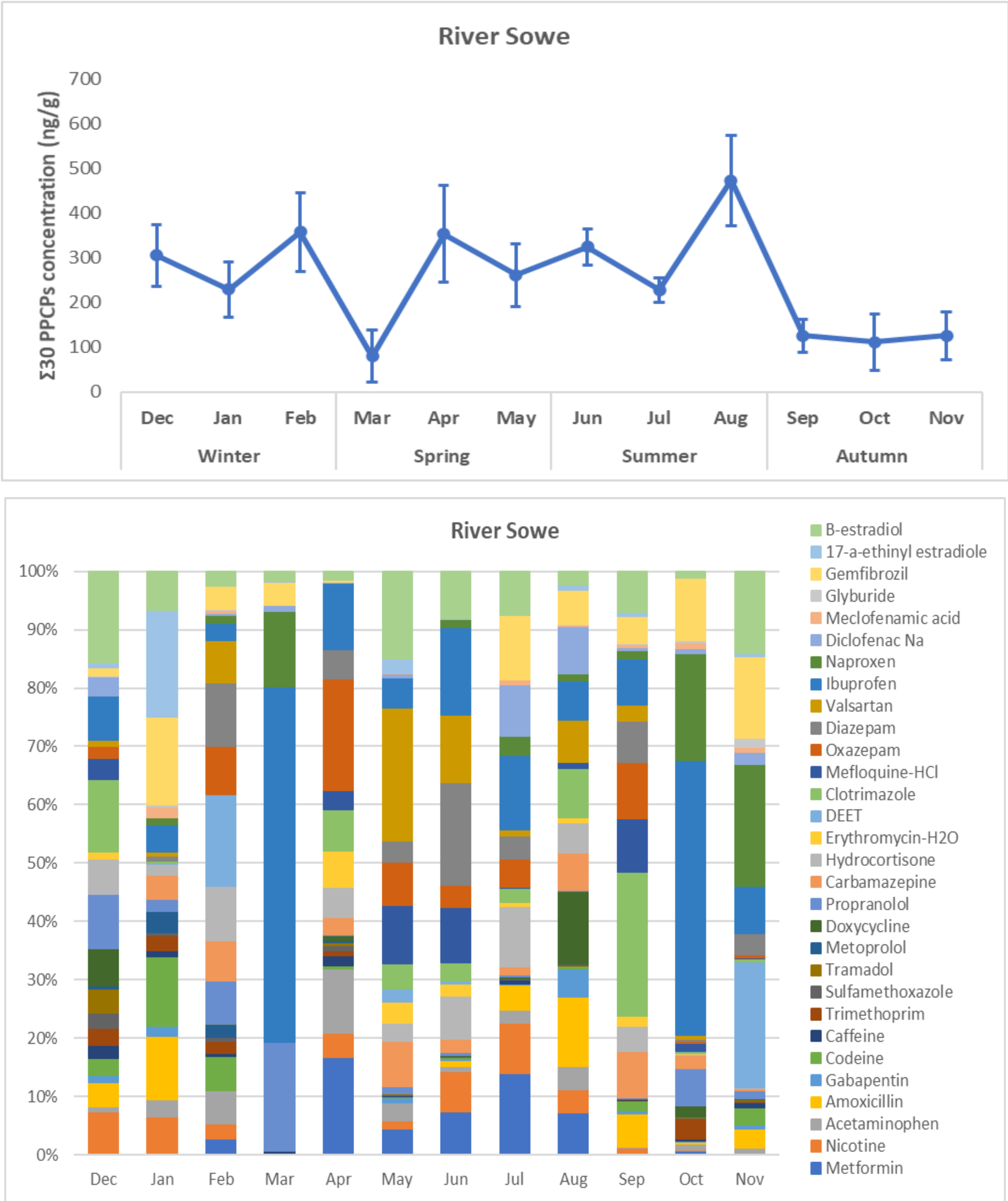


Table 4.2 Statistical summary of PPCPs concentrations (ng/g) in sediment from the river TAME collected monthly over a year.

PPCPS	Mean	SD*	Min	Max	CV (%)**
Metformin	9.6	12.0	0.1	31.0	124.7
Nicotine	15.3	12.8	0.0	34.3	84.0
Acetaminophen	13.2	16.4	0.0	50.9	124.5
Amoxicillin	12.3	12.4	2.9	37.1	100.4
Gabapentin	8.0	17.0	0.2	56.2	211.6
Codeine	7.4	6.1	0.1	18.9	83.2
Caffeine	3.3	2.5	0.1	8.6	76.3
Trimethoprim	6.4	7.7	0.1	23.7	119.4
Sulfamethoxazole	0.9	0.8	0.1	2.2	88.4
Tramadol	2.5	2.5	0.3	8.3	101.5
Metoprolol	3.6	5.1	0.3	12.8	141.8
Doxycycline	7.3	14.0	0.2	44.3	191.0
Propranolol	11.0	14.6	0.3	50.9	132.0
Carbamazepine	11.2	10.8	0.4	31.5	95.9
Hydrocortisone	15.4	19.4	0.2	57.3	126.2
Erythromycin-H2O	5.3	5.3	0.2	16.5	99.7
DEET	5.0	8.1	0.0	23.4	159.4
Clotrimazole	9.3	15.4	0.5	41.8	164.4
Mefloquine-HCl	4.6	6.8	0.0	17.8	146.8
Oxazepam	17.2	23.5	0.5	59.7	136.3
Diazepam	17.4	16.1	0.8	50.0	92.3
Valsartan	6.7	7.2	0.0	19.0	107.5
Ibuprofen	5.2	5.5	0.1	20.8	106.1
Naproxen	4.5	7.5	0.1	24.1	167.1
Diclofenac Na	1.3	1.9	0.0	5.2	148.8
Meclofenamic acid	0.4	0.3	0.1	1.0	88.0
Glyburide	0.4	0.7	0.0	1.5	174.5
Gemfibrozil	2.6	3.9	0.0	11.5	149.7
17α-ethinyl estradiole	6.3	8.6	0.1	27.1	136.0
β-estradiol	19.5	18.5	1.5	54.3	94.9
Σ_{30} PPCPs	213.0	254.3	47.4	843.4	119.4

* Standard deviation

** Coefficient of variation

Figure 4-3 Seasonal variation profile of target PPCPs in sediment from the river TAME. (a) average concentrations (± standard deviation, n=3) of Σ30 PPCPs (ng/g), (b) relative percent contribution of each target PPCP to Σ30 PPCPs.

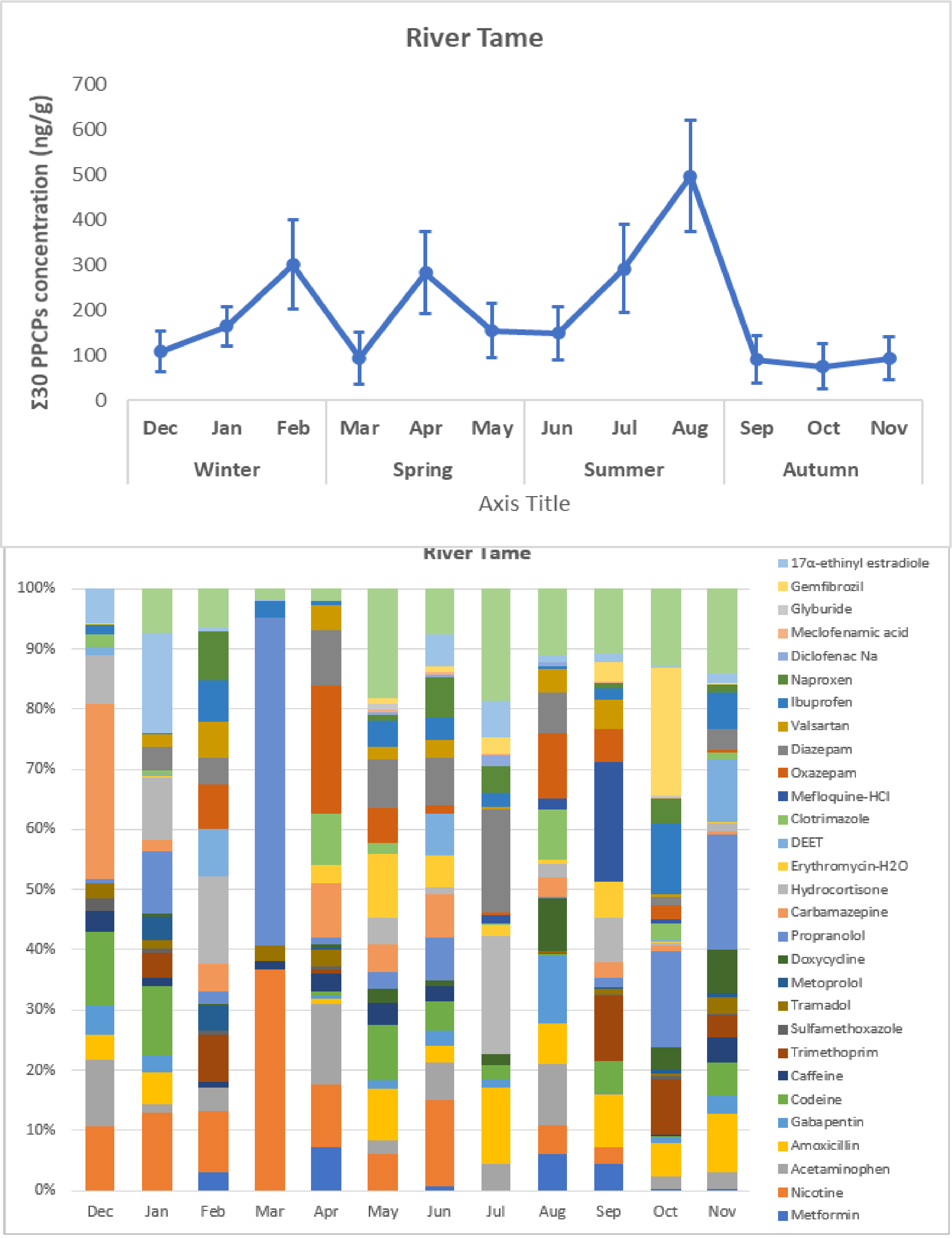


Table 4.3 Statistical summary of PPCPs concentrations (ng/g) in sediment from the river SEVERN collected monthly over a year.

PPCPS	Mean	SD*	Min	Max	CV (%)**
Metformin	19.0	17.6	0.0	42.0	92.7
Nicotine	5.5	5.2	0.0	13.6	94.7
Acetaminophen	8.3	12.5	0.0	35.1	149.5
Amoxicillin	10.9	12.8	1.4	43.3	118.2
Gabapentin	8.2	14.4	0.2	44.9	175.1
Codeine	3.0	2.6	0.1	7.1	89.4
Caffeine	2.0	1.9	0.2	5.2	94.6
Trimethoprim	3.2	5.1	0.0	13.2	158.0
Sulfamethoxazole	2.0	2.8	0.0	8.8	138.0
Tramadol	1.1	1.4	0.1	4.3	127.5
Metoprolol	0.9	1.5	0.0	4.8	174.6
Doxycycline	5.0	10.6	0.1	33.0	214.2
Propranolol	6.4	10.4	0.1	33.9	161.9
Carbamazepine	8.4	11.6	0.5	36.5	137.7
Hydrocortisone	9.5	10.2	0.1	33.4	107.6
Erythromycin-H2O	5.2	7.8	0.1	23.7	149.7
DEET	1.8	4.5	0.0	14.5	253.8
Clotrimazole	12.4	11.9	0.3	34.6	95.6
Mefloquine-HCl	12.8	18.7	0.1	48.8	146.4
Oxazepam	18.4	20.7	0.3	49.8	112.6
Diazepam	6.8	5.9	0.5	17.0	86.1
Valsartan	8.1	7.3	0.1	20.9	90.2
Ibuprofen	21.1	13.0	0.9	43.9	61.6
Naproxen	5.5	7.1	1.6	27.4	129.2
Diclofenac Na	9.3	16.5	0.1	44.1	177.4
Meclofenamic acid	1.2	1.8	0.0	5.8	155.4
Glyburide	0.4	0.4	0.0	1.0	103.5
Gemfibrozil	9.4	13.2	0.3	41.8	139.8
17α-ethinyl estradiole	8.5	17.1	0.1	50.7	200.2
β-estradiol	11.2	10.3	2.1	36.0	91.3
Σ_{30} PPCPs	210.5	251.7	37.3	821.3	119.6

* Standard deviation

** Coefficient of variation

Figure 4-4 Seasonal variation profile of target PPCPs in sediment from the river SEVERN. (a) average concentrations (± standard deviation, n=3) of Σ30 PPCPs (ng/g), (b) relative percent contribution of each target PPCP to Σ30 PPCPs

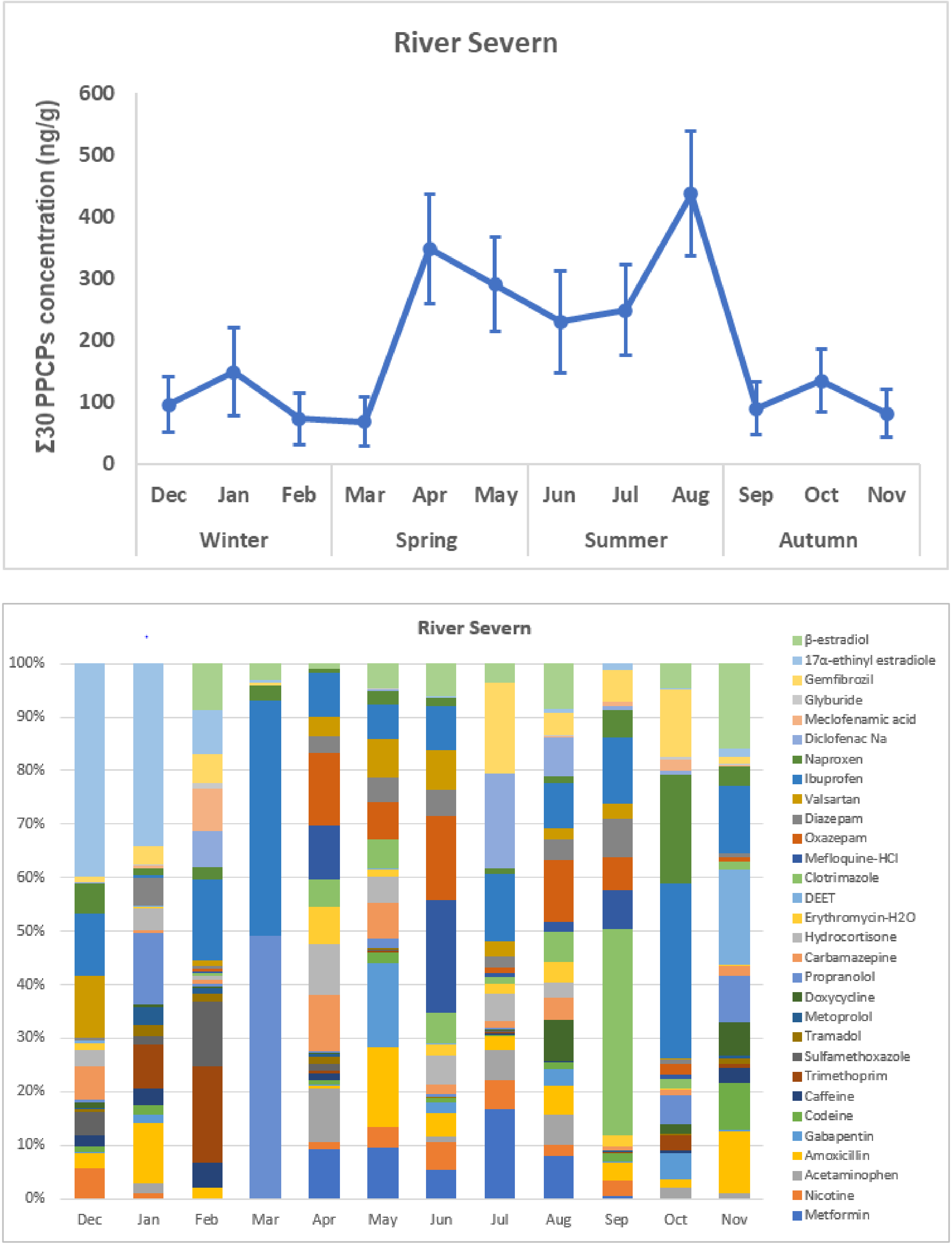


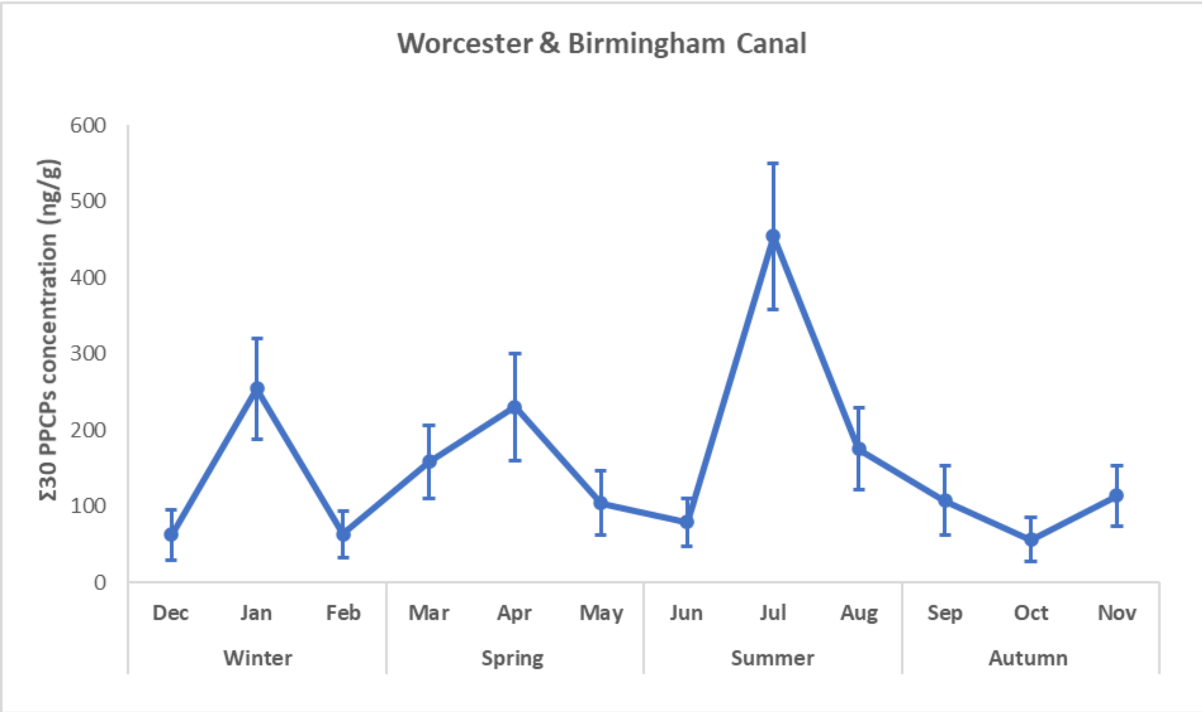
Table 4.4 Statistical summary of PPCPs concentrations (ng/g) in sediment from the Worcester & Birmingham Canal collected monthly over a year

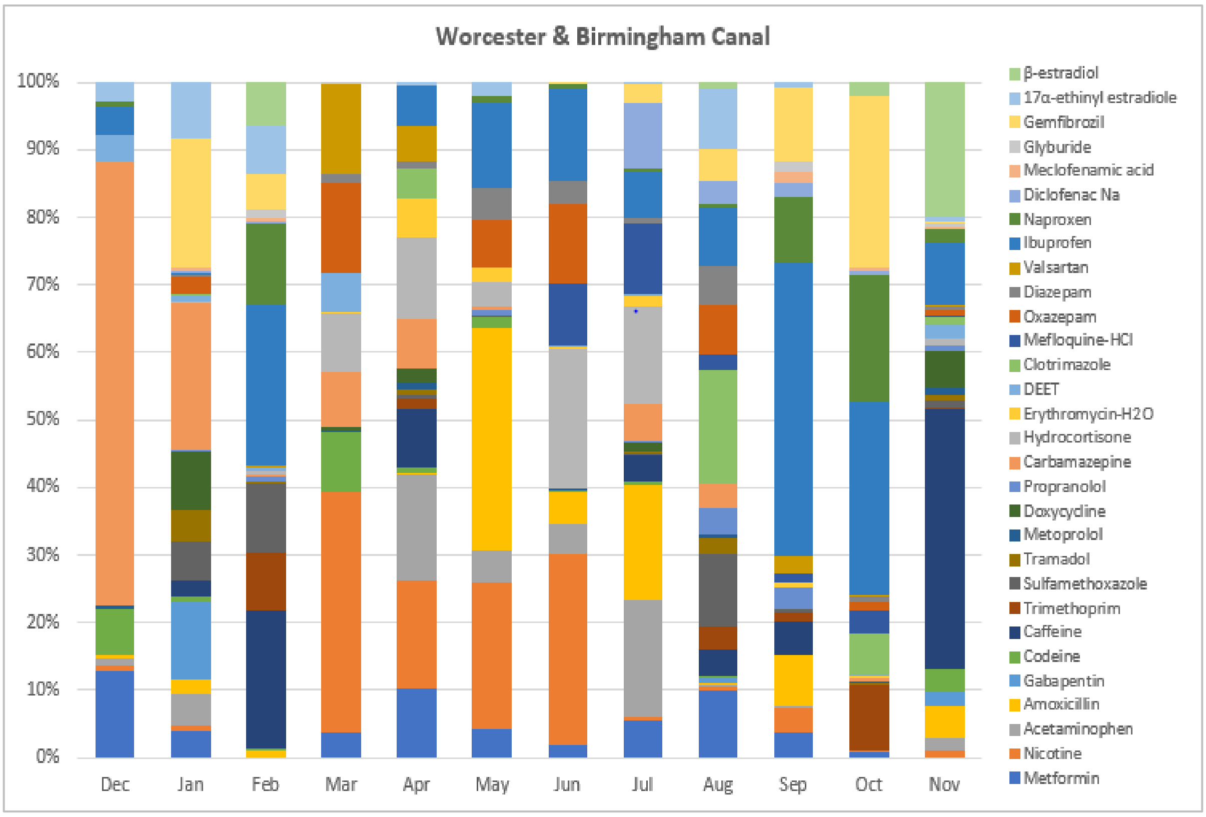
PPCPS	Mean	SD*	Min	Max	CV (%)**
Metformin	8.5	9.0	0.1	25.3	105.5
Nicotine	16.2	16.0	7.0	56.7	98.9
Acetaminophen	11.8	23.3	0.5	78.4	196.9
Amoxicillin	14.5	21.3	0.5	77.0	146.8
Gabapentin	3.5	8.1	1.0	29.2	232.8
Codeine	3.3	3.5	0.2	13.9	107.7
Caffeine	11.0	11.7	4.0	43.8	107.0
Trimethoprim	2.2	2.1	0.2	6.0	94.1
Sulfamethoxazole	4.0	6.2	0.2	18.9	153.5
Tramadol	2.3	3.3	0.2	12.1	139.9
Metoprolol	0.7	0.7	0.2	2.4	95.7
Doxycycline	4.8	5.6	0.6	21.7	117.2
Propranolol	1.6	1.8	0.2	6.5	111.5
Carbamazepine	13.3	18.0	0.3	55.6	135.7
Hydrocortisone	12.2	18.2	3.0	64.6	149.4
Erythromycin-H2O	2.7	3.9	1.0	13.4	145.0
DEET	3.4	1.8	2.2	8.9	52.2
Clotrimazole	4.3	8.3	0.9	29.2	194.2
Mefloquine-HCl	5.6	13.4	0.1	47.7	241.1
Oxazepam	5.7	6.2	0.6	21.2	108.2
Diazepam	2.6	2.8	0.4	10.0	107.0
Valsartan	3.5	6.5	0.1	21.1	185.4
Ibuprofen	15.0	12.3	4.0	46.8	82.3
Naproxen	4.5	2.7	3.0	10.4	60.9
Diclofenac Na	5.1	12.2	1.0	43.5	240.9
Meclofenamic acid	1.0	0.3	0.3	1.7	30.0
Glyburide	<0.3	<0.3	<0.3	<0.3	<0.3
Gemfibrozil	10.0	12.7	4.0	48.7	126.2
17α-ethinyl estradiole	4.5	6.6	0.4	20.9	149.0
β-estradiol	3.7	5.9	0.8	22.2	157.8
Σ_{30} PPCPs	184.3	244.3	39.0	860.7	132.6

* Standard deviation

** Coefficient of variation

Figure 4-5 Seasonal variation profile of target PPCPs in sediment from the Worcester & Birmingham Canal. (a) average concentrations (± standard deviation, n=3) of Σ30 PPCPs (ng/g), (b) relative percent contribution of each target PPCP to Σ30 PPCPs.





Averaged over the whole year, the sediment samples from the river Sowe were the most polluted with the studied PPCPs (Average $\sum_{30}$PPCPs over 12 months = 276 ng/g), whereas Worcester & Birmingham Canal was least polluted (Average $\sum_{30}$PPCPs over 12 months = 184 ng/g). This may be attributed to the lack of direct input from WWTP to the Worcester & Birmingham Canal, while all the studied rivers had WWTP effluent discharge points Table 4.5. However, statistical analysis (using ANOVA and Tukeys post-hoc test) revealed no significant differences ($P > 0.05$) in $\sum_{30}$PPCPs over 12 months in the 4 studied locations.

Table 4.5 Monthly average ∑30PPCPs concentrations (ng/g) in the studied locations from December 2019 to November 2020.

Location	Winter			Spring			Summer			Autumn			Average
	Dec	*Jan*	*Feb*	*Mar*	*Apr*	*May*	*Jun*	*Jul*	*Aug*	*Sep*	*Oct*	*Nov*	
River Sowe	305	229	357	60	353	261	324	228	473	126	112	126	276
River Tame	108	164	301	93	283	154	149	292	497	90	54	93	213
River Severn	96	149	73	69	348	290	230	249	437	90	135	82	210
Worcester & Birmingham Canal	59	254	63	159	230	104	79	454	175	107	46	114	184

Large variations in $\sum_{30}$PPCPs over 12 months monitoring programme were observed with coefficients of variation (CV%, expressed as % deviation from the mean) of 116%, 119%, 120% and 133% in river SOWE, river TAME, river SEVERN and Worcester & Birmingham Canal, respectively.

To investigate the potential contributing factors to the observed seasonal variations of target PPCPs in the studied locations, the concentrations of each analyte were plotted individually in each of the sampled locations for the studied 12-month period Figures 4-6 to 4.9. Results show large variations in concentrations of most target analytes. This likely indicates that the usage rates of the studied PPCPs and the input from direct sources (*e.g., prescription and patient usage, run-off from nearby farms for analytes with veterinary applications*) play a major role in the measured concentrations and contribute largely to the observed variations (Moreno-González et al., 2015). Other environmental factors may contribute to the observed seasonal variation including the precipitation rate and mobilisation of sediment particles by increased flowrate of rivers (Ebele et al., 2017). This may be used to explain, at least partially, the observed lower concentrations of target PPCPs in winter months, when the increased rainfall and river flowrates can result in rapid mobilisation of sediment particles with less time for partitioning of PPCPs from water to sediment, as well as the expected dilution effect of the increased rainfall on PPCPs concentrations in water (Burns et al., 2018a). It should also be noted that explaining variations in sediment concentrations of PPCPs is compounded by the low concentrations and detection frequencies of target compounds in sediment samples compared to water. Moreno-Gonzalez et al., reported on the difficulty of explaining the observed seasonal variation of 20 pharmaceuticals in marine sediments due to their heterogeneous distribution and low concentrations (lower than LOQ) (Moreno-González et al., 2015) . A more recent study applied mixed linear models to investigate various associations between compound-specific physicochemical properties, temperature, dissolved oxygen, and the concentrations of 7 antipsychotic drugs in water and sediment samples from 2 different sites in Spain. However, only the site (i.e., location) showed a statistically significant impact on the observed concentrations in sediment. The lack of associations was also attributed to the low concentrations and detection frequencies in sediment compared to water samples (Perez et al., 2022). Overall, the large seasonal variations of PPCPs concentrations in sediment may be attributed to a combination of factors including input sources (e.g., variation in prescription and usage of drugs), environmental factors (e.g., rainfall, flowrate, temperature, mobilisation of sediment particles by flooding), as well as the compound-specific physicochemical properties (e.g., Log K_{OW}) which dictate its partitioning/distribution between water and sediment.

Figure 4-6 Individual profiles for seasonal variations of target PPCPs in sediment (ng/g) from the river SOWE.

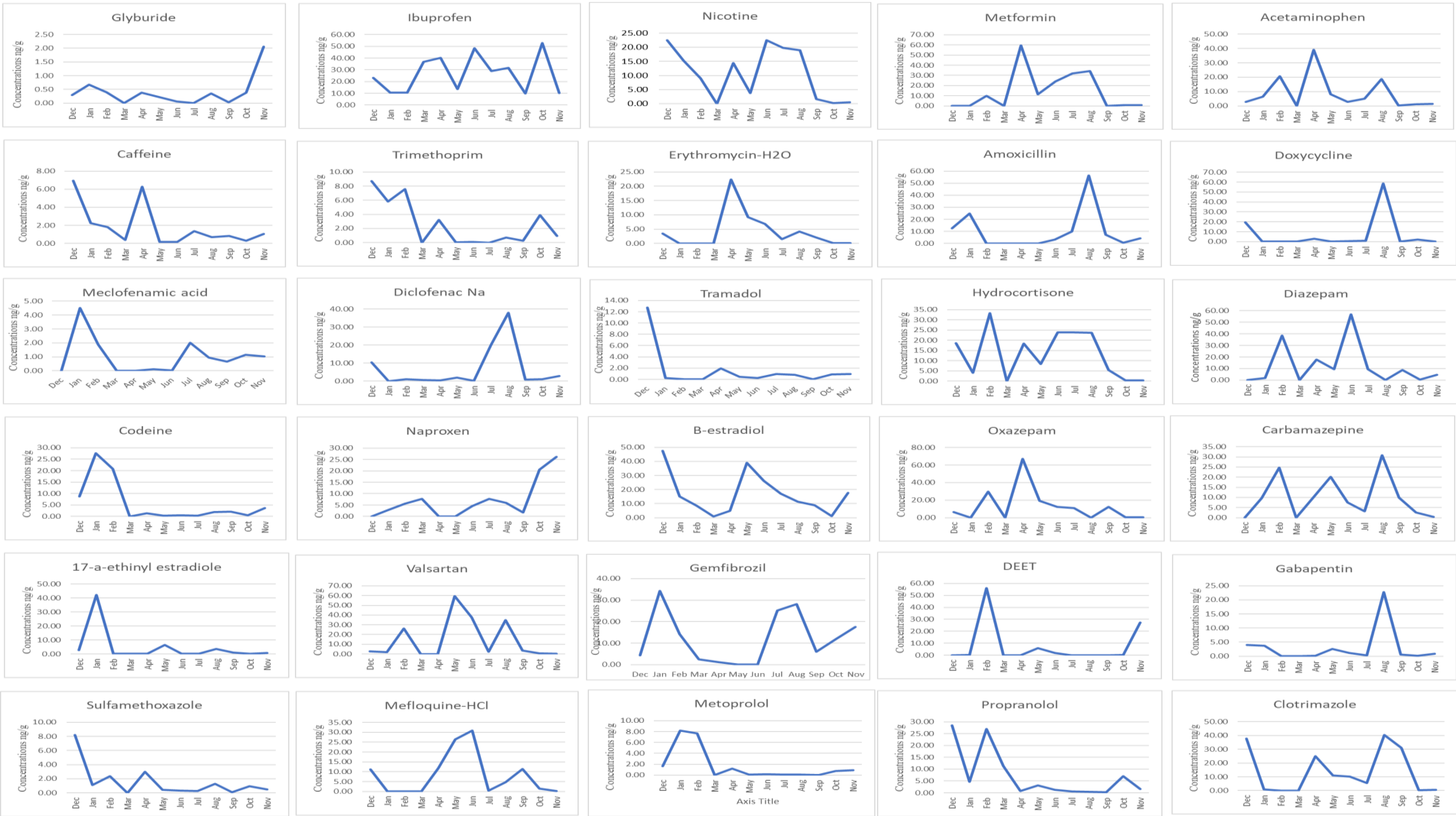


Figure 4-7 Individual profiles for seasonal variations of target PPCPs in sediment (ng/g) from the river TAME.

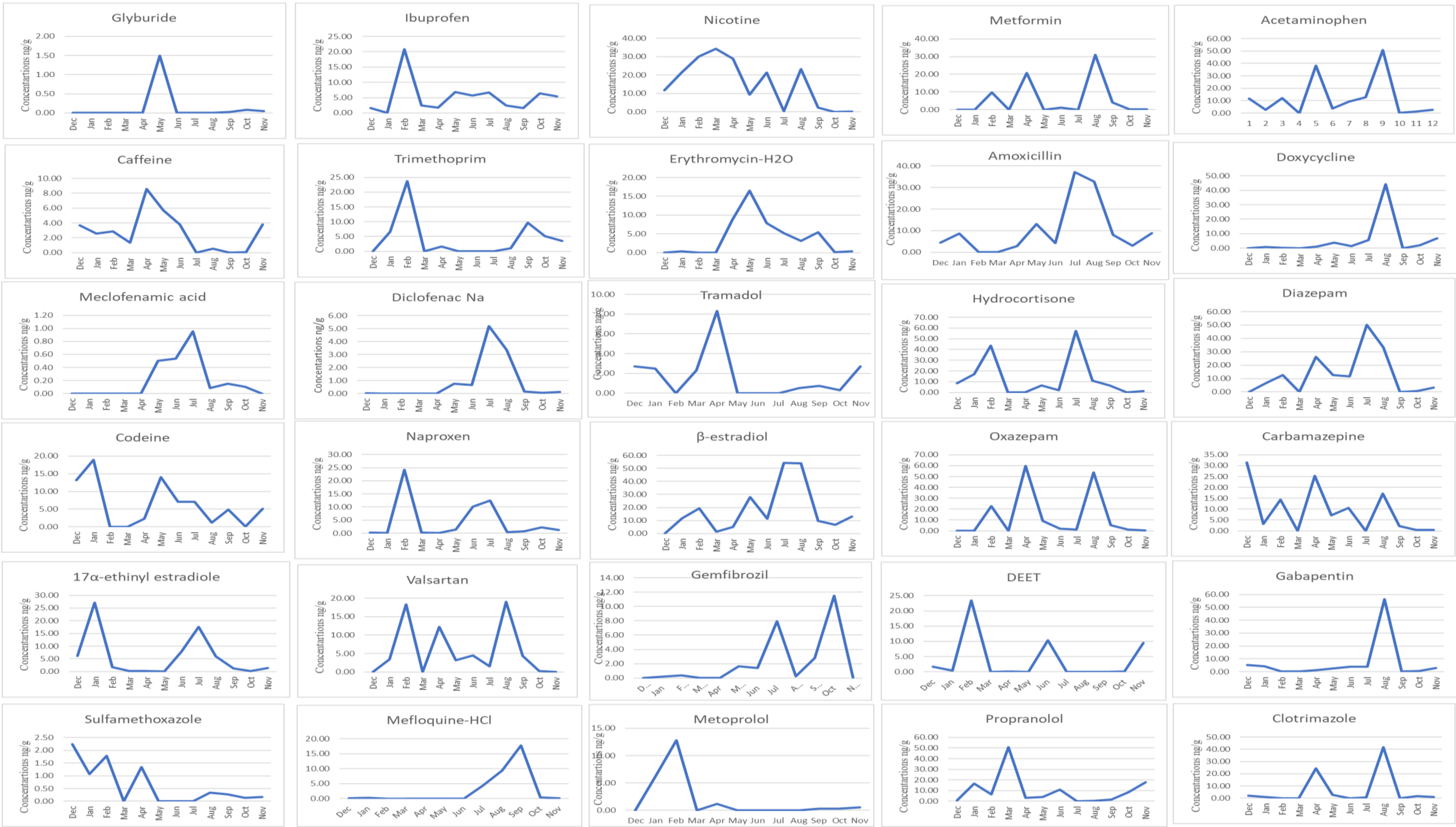


Figure 4-8 Individual profiles for seasonal variations of target PPCPs in sediment (ng/g) from the River Severn.

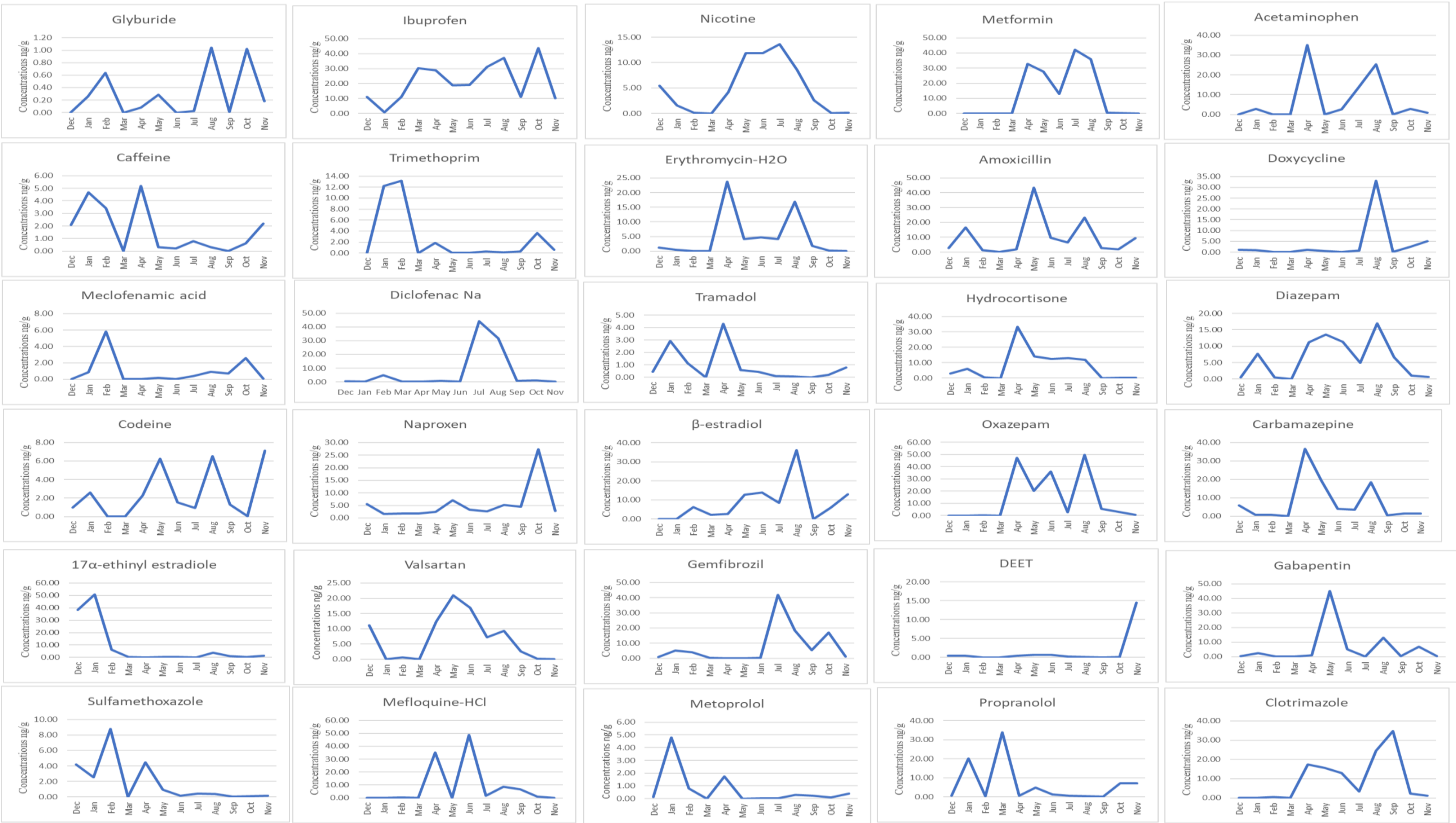
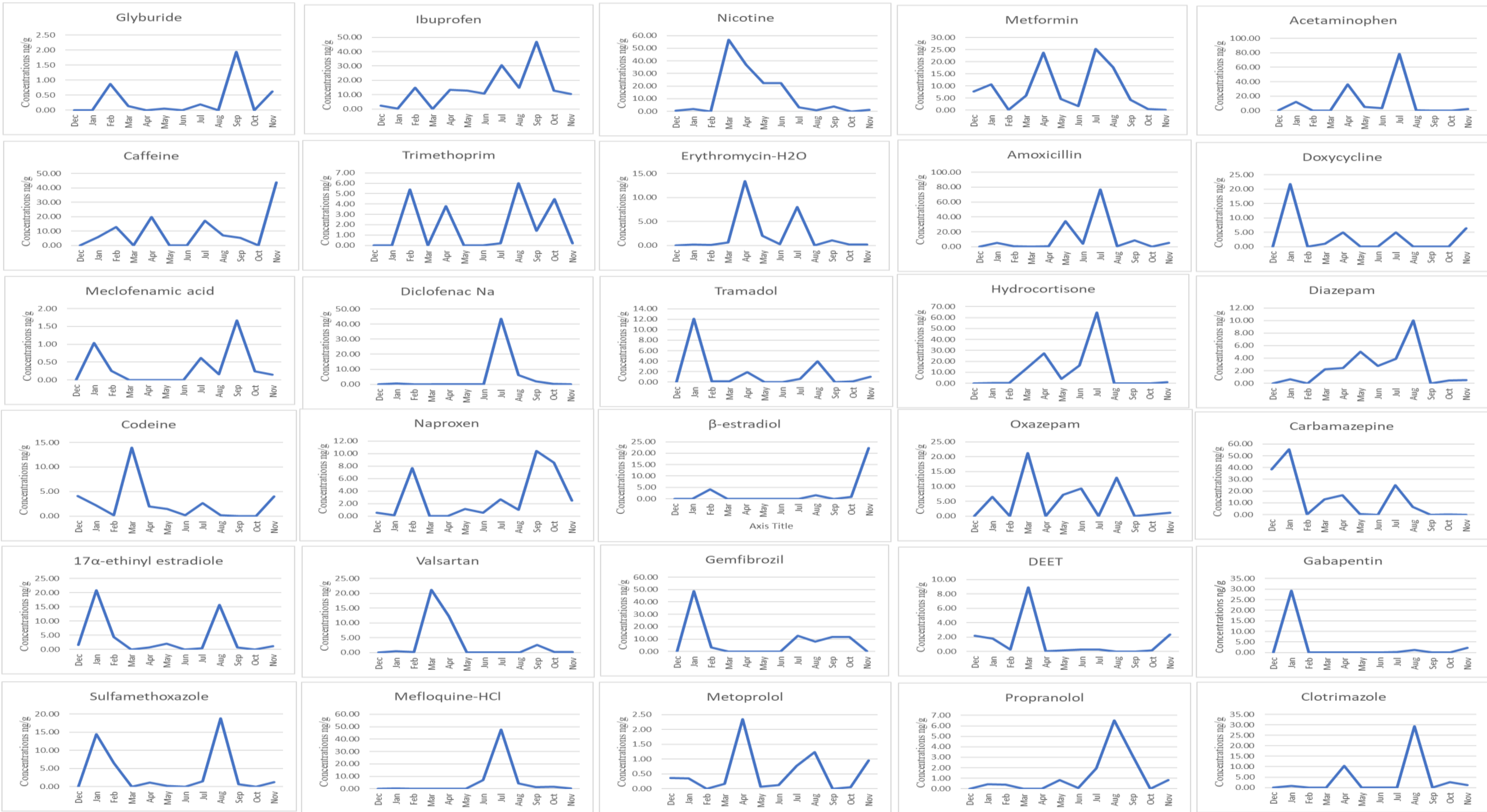


Figure 4-9 Individual profiles for seasonal variations of target PPCPs in sediment (ng/g) from the Worcester & Birmingham canal.



While only few studies exist of PPCPs seasonal variation in freshwater sediment, our results are generally in agreement with previous reports in both surface water and sediment from other countries. Zhao et al. (2016b) reported large seasonal variations of several antibiotic classes in water from Chinese rivers with CV% ranging between 73 – 188%. Similar large variations were observed in the concentrations of sulfamethoxazole (SMX) and sulfamethazine (SMZ) in the surface water of Jiulong River between August 2010 and January 2011, with concentrations ranging between 0.05 –58.3 ng/L and <0.28 – 775.5 ng/L for SMX and SMZ, respectively (Zhang et al., 2012). A recent paper by Jiang et al. (2021) reported large variations in $\sum_{61}$ PPCPs concentrations, which ranged between 400 – 1600 ng/L in water samples from the Taige Canal, China, collected over one year (2018-2019). More pertinent to the present study, large variations in Trimethoprim concentrations (CV% = 60 – 165%) were reported in sediment samples collected from Markman Canal and Swartkops River Estuary, South Africa over 3 seasons (winter, summer and spring) (Ohoro et al., 2021). This is broadly in line with the observed seasonal variation in Trimethoprim concentrations in our 4 studied locations (CV% = 119 – 158%). Such variations in individual and ∑PPCPs levels in sediment over one year should not be surprising due to the multiple factors influencing these concentrations including variation in input sources (e.g. caused by the change in human usage of different classes of PPCPs over the year), environmental conditions (e.g. precipitation rate, temperature, flow rate, organic content of sediment) and compound-specific physicochemical properties (e.g. Log K_{OW}) (Paíga et al., 2016).

Due to the complexity of the produced concentrations datasets of 30 PPCPs over 12 months in 4 locations, simplified seasonal profiles (winter, spring, summer and autumn) of $\sum_{30}$ PPCPs and individual compounds are provided in Figures 4-6 and 4-7, respectively. The full datasets are provided in the supplementary information to this chapter.

Figure 4-6 shows a clear trend of higher $\sum_{30}$ PPCPs concentrations in summer, compared to the other 3 seasons in all the studied locations. Statistical analysis revealed a significant difference ($P < 0.05$)

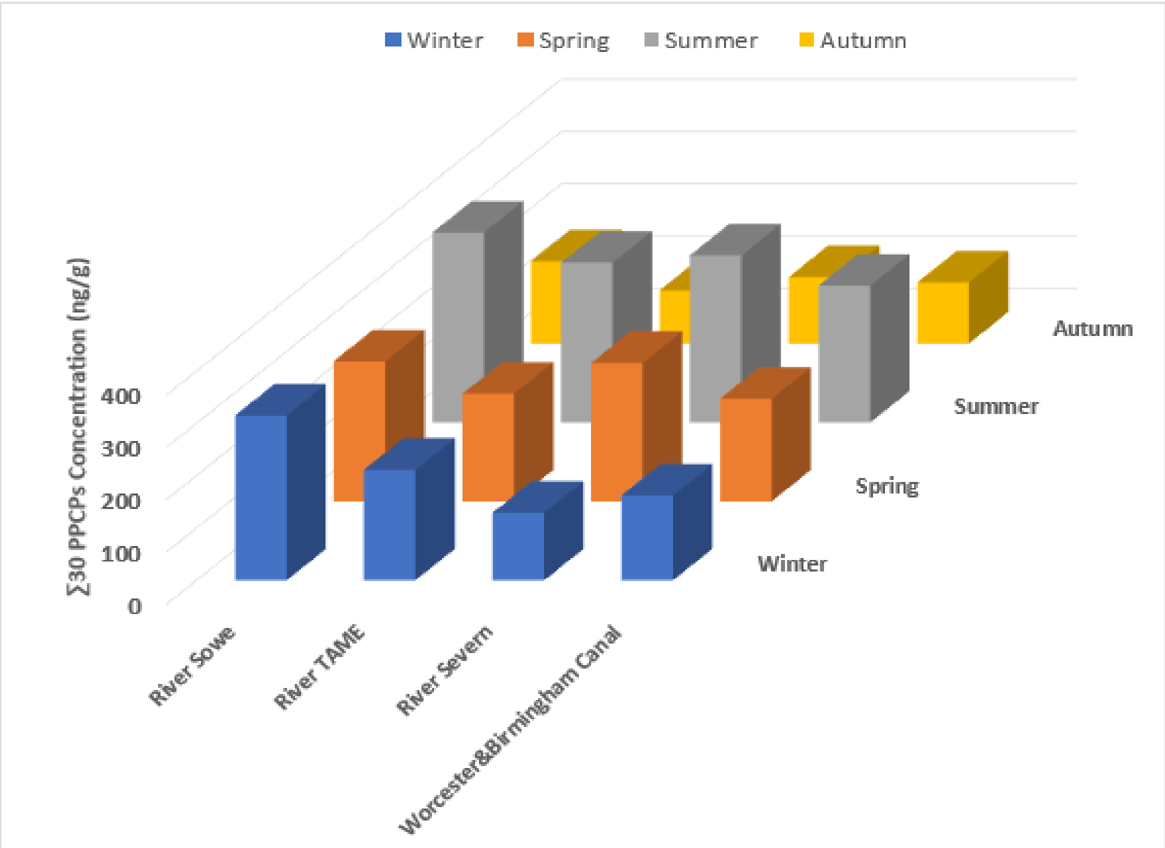
between $\sum_{30}$ PPCPs in Summer (highest) compared to Autumn (lowest) in all the studied locations, while no other significant differences were observed among the datasets for the seasons compared. A recent study of PPCPs in surface water from the river Ganges, India, revealed substantial reduction (*no statistical analysis was reported*) in the concentrations of 15 PPCPs in the monsoon season (August), compared to Summer (May) and Winter (December) seasons. This was attributed to the dilution effect by rainfall in the monsoon season with a reduced detection frequency (63.07%) of the studied compounds, as compared to winter (82.80%) and summer (75.12%) periods (Singh and Suthar, 2021). Another study of 12 PPCPs in the Huangpu River, China reported higher contamination levels in water samples collected in the dry season (December and March), compared to the wet season (August). This was mainly explained by the dilution effect of the rainfall, combined with the higher temperatures in the wet season resulting in higher evaporation and microbial degradation rates of the studied pharmaceuticals (Mei et al., 2018).

For common contaminants including nutrients, pesticides and persistent organic pollutants from diffuse sources, the impact of rainfall periods on contaminant movement and mobilisation from sediment has been widely investigated (Sherriff et al., 2016, Xie et al., 2019a, Vale and Dymond, 2020). Several studies focused on seasonal changes in occurrences and concentrations of various chemical contaminants in marine and freshwater sediments, however, only few studies investigated PPCPs occurrence in sediment and even fewer reported on their seasonal variation and the impacts of heavy rain and other weather events (Xie et al., 2022, Beretta et al., 2014, Xie et al., 2019b).

Dong et al. (2021) established a thorough monitoring plan to study how fourteen antibiotics responded to various rainfall events and inter-event low flow times. Fourteen antibiotics were measured in water and suspended particles in Chaohu Lake in China. The results showed that low flow times were shown to have pollutant-rich suspended particles with concentrations up to 1471 ng/g, while the release of antibiotics from eroded soil particles to river water was accelerated by extremely heavy rainfall events and subsequent rainfall events. As a result, these heavy rainfall events caused a drastic increase in the concentration of dissolved antibiotics up to 592 ng/L and total flux up to 25.0 g/d (Dong et al., 2021).

Another study investigated the impact of considerable rainfall events on the concentrations of 15 veterinary antibiotics, which were introduced to agricultural fields via fertilizer, in a German water system (both water and sediment) following overland transport via runoff and soil erosion (Bailey et al., 2015). Although results did not provide conclusive evidence due to low concentrations and detection frequency in sediment (lowest in winter), the presence of tetracycline in sediment samples taken from irrigation ditches in an agricultural area of high veterinary antibiotic usage offers proof that the overland transport of veterinary antibiotics is occurring. The study concluded that further research is required into the transport of veterinary antibiotics via soil erosion from agricultural fields and their presence/concentrations in sediment of receiving water systems (Bailey et al., 2015).

Figure 4-10 Seasonal variation in ∑30 PPCPs concentrations (ng/g) in the studied locations.



The climate in the United Kingdom is temperate. This means that Britain experiences cool, rainy winters and warm, rainy summers. Extremes of heat, cold, or drought are uncommon. This may reduce the dilution impact of rainy/monsoon season, and/or the concentrating effect of dry seasons on the concentrations of PPCPs in the freshwater environment, observed in other geographical locations (Paíga et al., 2016, Awad et al., 2014). Table 4.6 provide a summary of seasonal average rainfall (millimetres), flowrates ($cm^3 s^{-1}$) and temperatures (°C) in the four sampling locations during the study period (UK WATER RESOURCES PORTAL, 2022, MET OFFICE, 2022). While the mean rainfall in winter (87 mm) was significantly grearer (P <0.05) than in other seasons (53 mm, 63 mm and 56 mm in spring, summer and autumn, respectively) in the studied locations, the resulting dilution effect wasn't strong enough to induce a significant reduction of ∑30 PPCPs concentrations in winter Figures 4-10. This is in agreement with the results of Farbairn et al. (2016) who reported that association of the concentration of pharmaceuticals, such as acetaminophen and carbamazepine, in surface waters with seasonality, are frequently unclear or insignificant in the absence of extreme weather incidents (Fairbairn et al., 2016). Similar lack of association between PPCPs concentrations in the Lis River sediments, Portugal and "normal" variations in temperature and rainfall was reported (Paíga et al., 2016).

Table 4.6 Seasonal average rainfall (millimetres), flowrates ($cm^3\ s^{-1}$) and temperatures (°C) in the four sampling locations during the study period (UK WATER RESOURCES PORTAL, 2022, MET OFFICE, 2022).

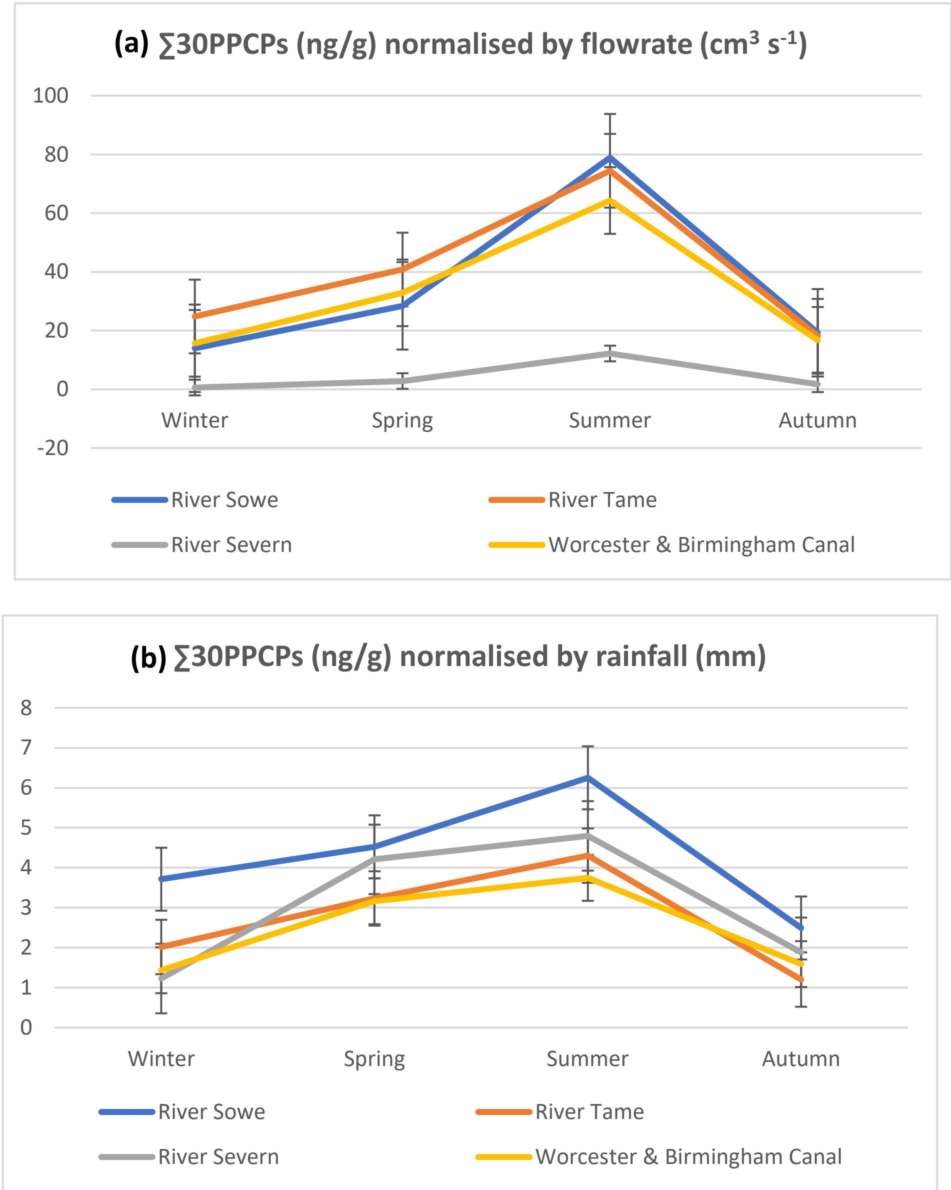
Parameter	Season	SOWE	TAME	SEVERN	W & B Canal
Rainfall (mm)	Winter	80.00	94.67	86.33	87.33
	Spring	49.67	54.67	56.00	52.00
	Summer	54.67	72.67	63.67	63.00
	Autumn	48.67	65.67	54.33	56.00
Flowrate ($cm^3\ s^{-1}$)	Winter	21.27	7.70	174.40	8.00
	Spring	7.90	4.33	83.33	5.00
	Summer	*4.33*	*4.20*	*25.03*	*3.67*
	Autumn	6.30	4.33	59.37	5.33
Temp. (°C)	Winter	4.50	4.40	4.80	4.33
	Spring	8.77	8.53	9.03	8.53
	Summer	15.87	15.50	16.07	15.53
	Autumn	10.70	10.47	10.97	10.43

Interestingly, the UK weather data in the present study showed the flowrate in the 4 studied locations to be the least in summer, compared to the other 3 seasons Table 4.6. While this difference in flowrate was not statistically significant, this may contribute to the higher concentrations of ∑30 PPCPs observed in summer as it facilitates partitioning of chemicals to sediment from water (Ebele et al., 2017). Previous research revealed that the concentrations of various organic compounds, including antibiotics, varied with flow rate; with the highest concentration and detection frequency measured during low-flow (40%), compared to high (8.7%) and medium flow (8.7%) conditions (Kolpin et al., 2004). The concentrations of 12 PPCPs in the River Taff, UK increased significantly at flowrate of 8.4 m^3/s, compared to a flowrate of 44 m^3/s (Kasprzyk-Hordern et al., 2008). Similarly, the highest concentrations of 15 antibiotics were measured at the lowest flow conditions in water and sediment samples collected between May 2003 and February 2005 at five sampling sites representing pristine, urban, and agricultural influenced areas along the Cache La Poudre River of northern Colorado (Kim and Carlson, 2007).

To further investigate the impact of the flow rate ($cm^3 s^{-1}$) and rainfall (mm) on the observed seasonal variation of target PPCPs, the average Σ_{30}PPCPs in the 4 studied locations were normalised by (a) flow rate and (b) rainfall and plotted against the 4 seasons investigated Figure 4-11.

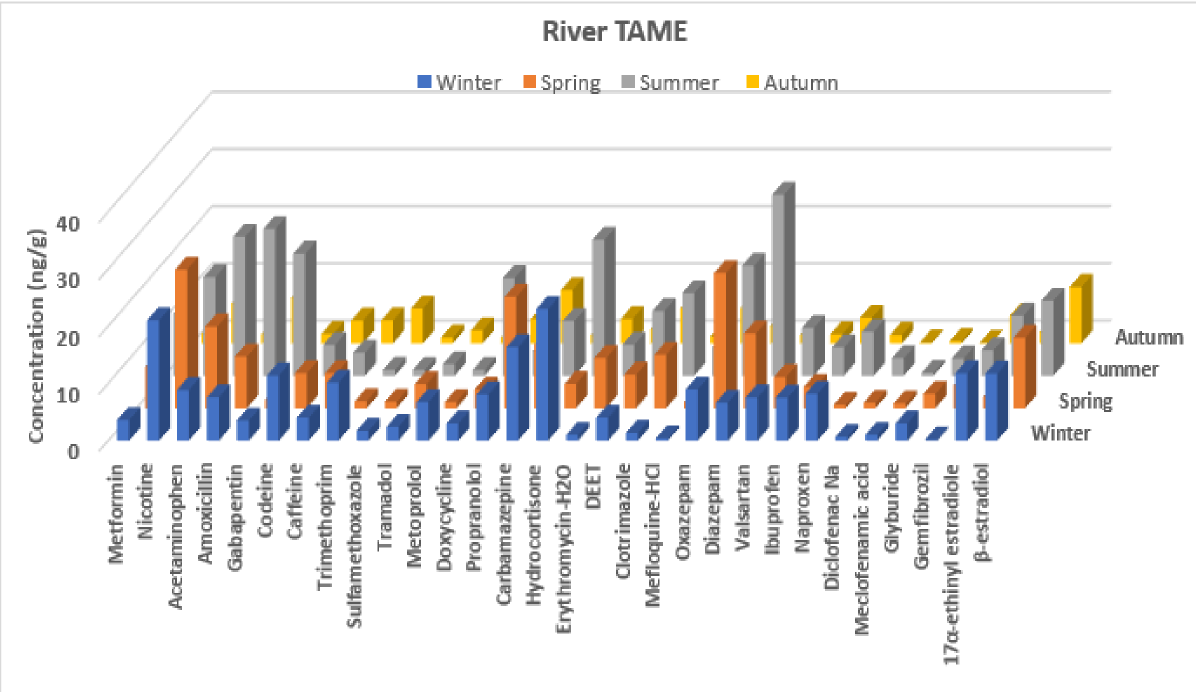
The normalised seasonal variation profiles Figures 4-2, 4-3, 4-4 and 4-5 did not show substantial difference from the original seasonal variation profile Figure 4-6. The highest concentrations in all locations remained in summer. This is understandable given that the highest Σ_{30}PPCPs and lowest flowrates measured in all 4 locations were in summer Figure 4-6 and Table 4.6. While the summer rainfall in the 4 studied locations was relatively higher than those in spring and autumn during the study period Table 4.6, such variation wasn't sufficient for this factor to account solely for the observed seasonal variation in Σ_{30}PPCPs Figure 4-11. Other factors reported to influence PPCPs concentrations in surface water and sediment are the temperatures and microbial activity. Several studies have reported that higher temperatures (e.g., in summer) can lead to increased evaporation rates, resulting in higher concentrations of PPCPs in water and sediment. On the other hand, higher temperatures are associated with increased microbial activity which may result in elevated biodegradation rates of chemicals leading to lower concentrations of PPCPs in water and sediment (Ebele et al., 2017, Ohoro et al., 2022, Sugihara, 2018, You et al., 2015, Akpotu et al., 2019, Daughton and Ruhoy, 2009, Al-Khazrajy et al., 2018). However, there exists no quantitative measurements of the impact of these opposing factors on environmental levels of PPCPs (particularly in sediment), which makes it difficult to understand their overall effect on the measured concentrations in the present study.

Figure 4-11 Seasonal variation in Concentrations of Σ30PPCPs in sediment (ng/g) normalised to (a) flowrate ($cm^3\ s^{-1}$) and (b) rainfall (mm) from the 4 sampled locations.



Other factors reported to influence PPCPs concentrations in surface water and sediment are the temperatures and microbial activity. Several studies have reported that higher temperatures (e.g., in summer) can lead to increased evaporation rates, resulting in higher concentrations of PPCPs in water and sediment. On the other hand, higher temperatures are associated with increased microbial activity resulting in higher biodegradation rates of these chemicals (Ebele et al., 2017, Ohoro et al., 2022, Sugihara, 2018, You et al., 2015, Akpotu et al., 2019, Daughton and Ruhoy, 2009, Al-Khazrajy et al., 2018). However, there exists no quantitative measurements of the impact of these opposing factors on environmental levels of PPCPs, which makes it difficult to understand their overall effect on the measured concentrations in the present study.

Figure 4-12 Seasonal profiles of target PPCPs in the studied locations



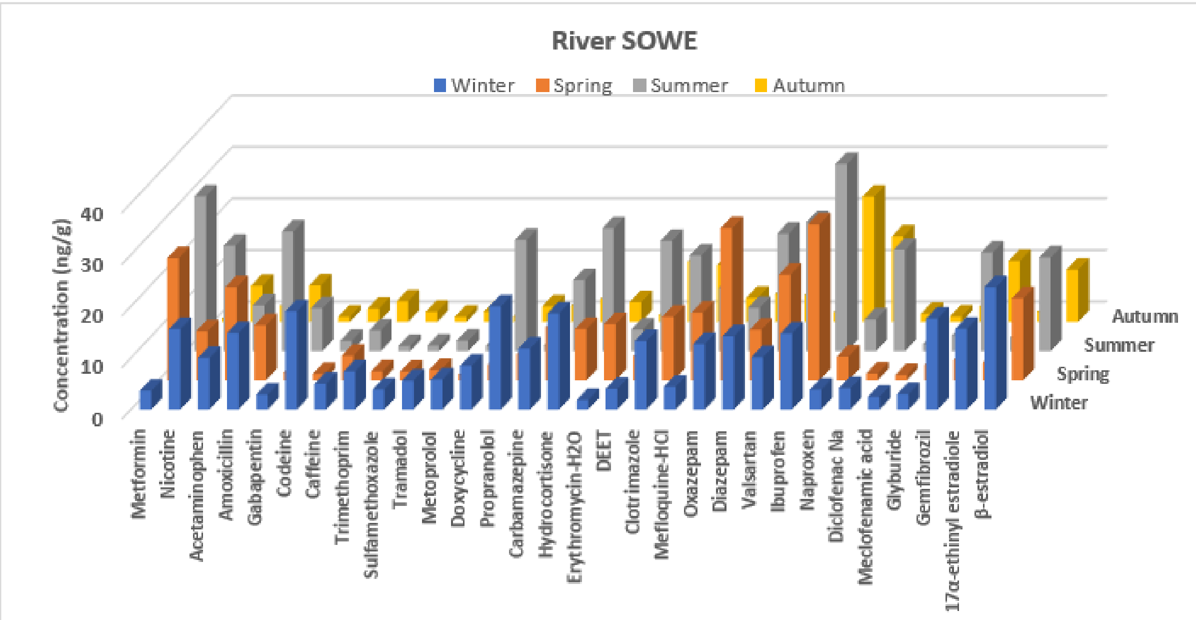
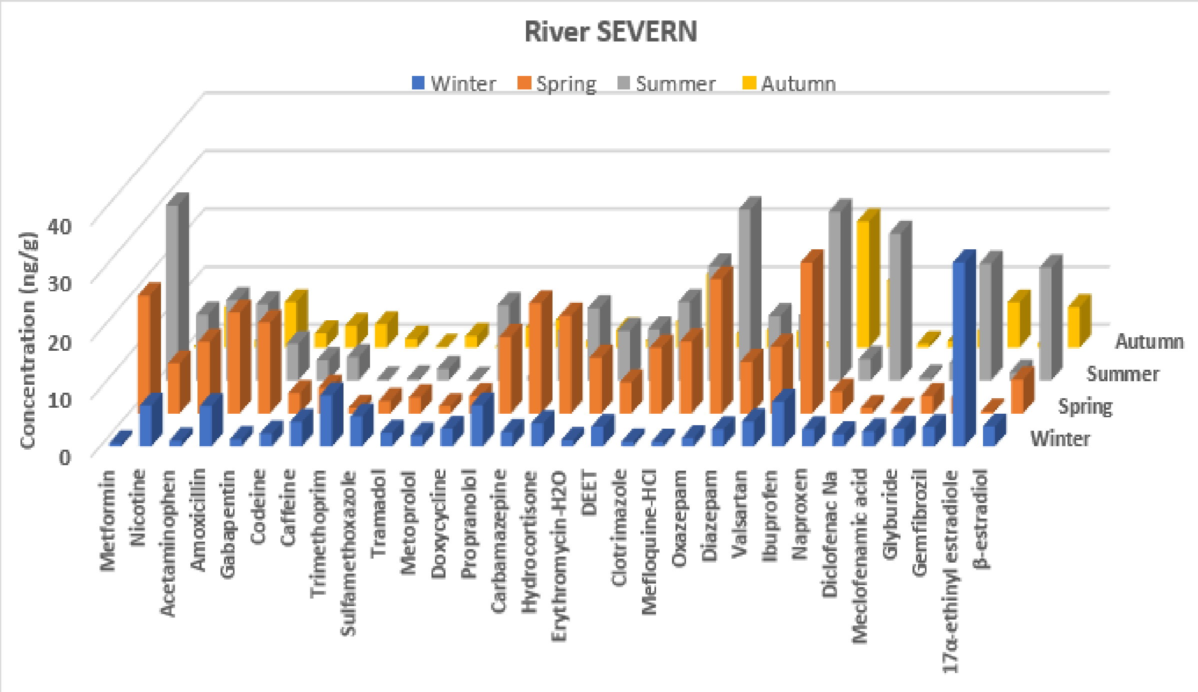
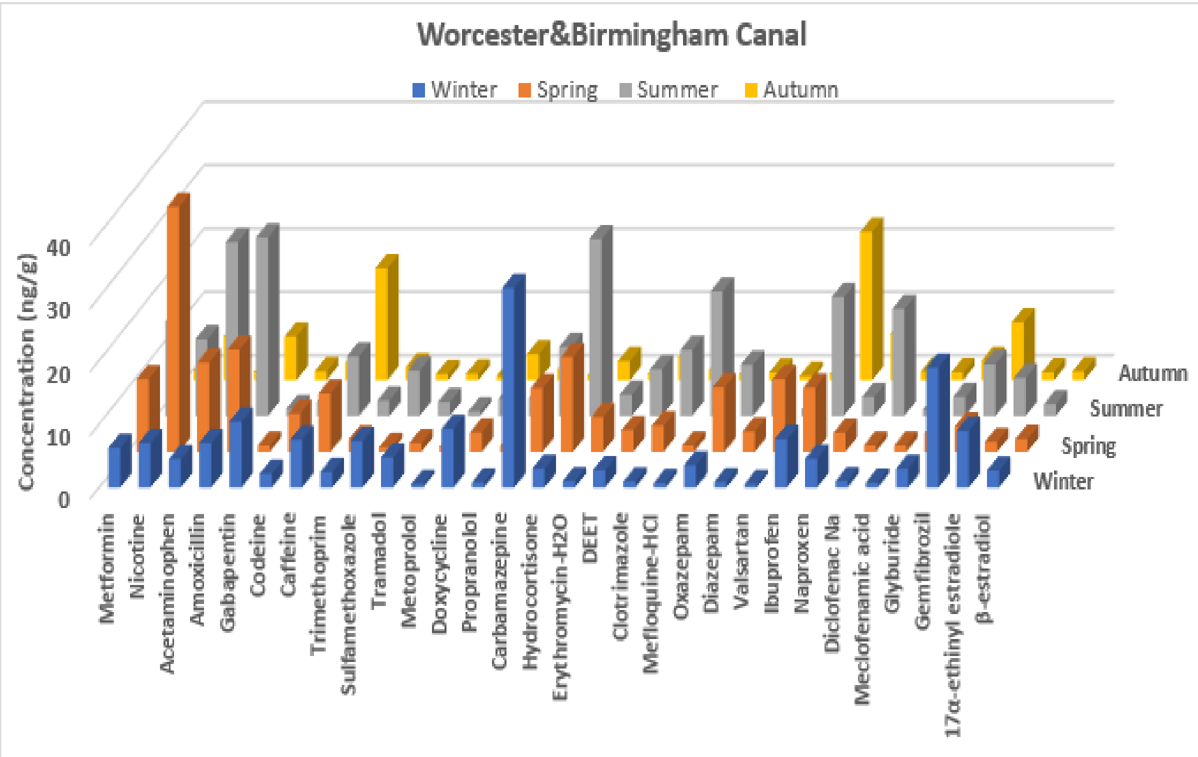


Figure 4-13 (continued): Seasonal profiles of target PPCPs in the studied locations.

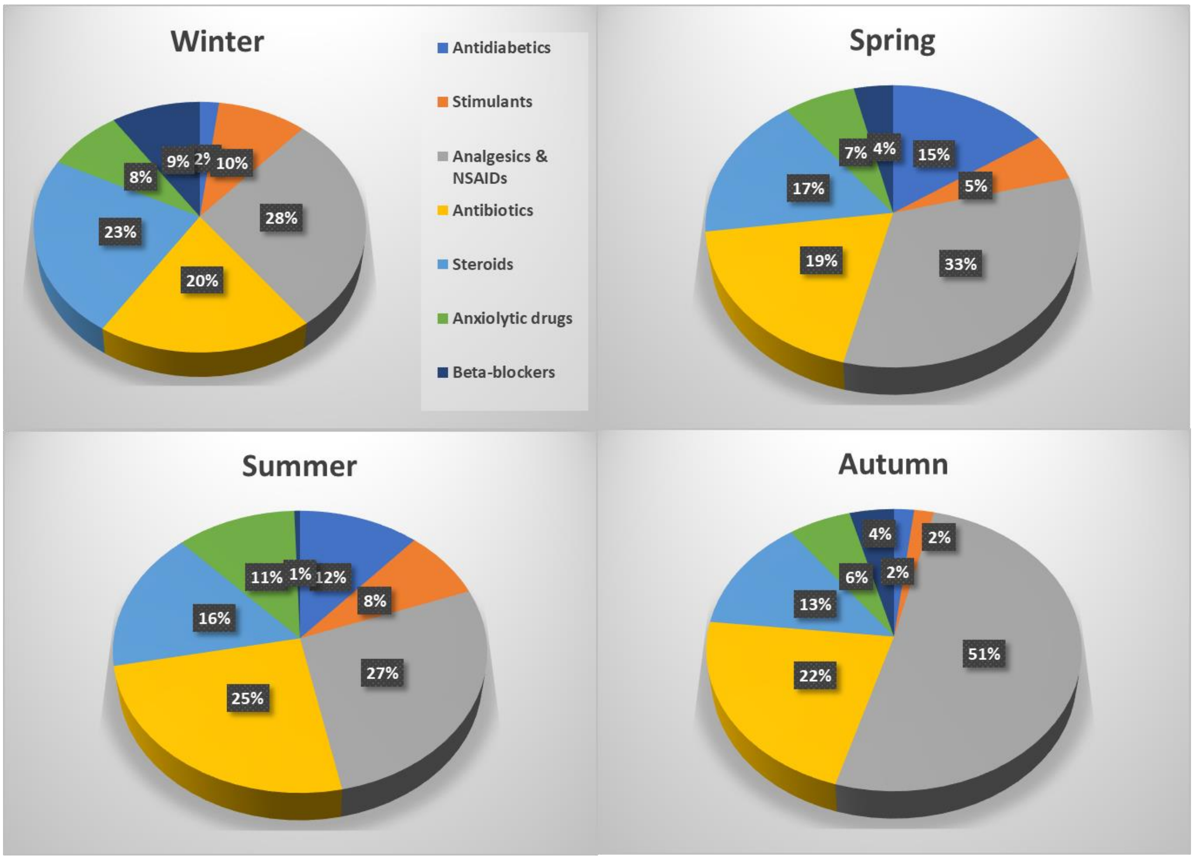




4.4. Seasonal profiles of PPCPs in sediment

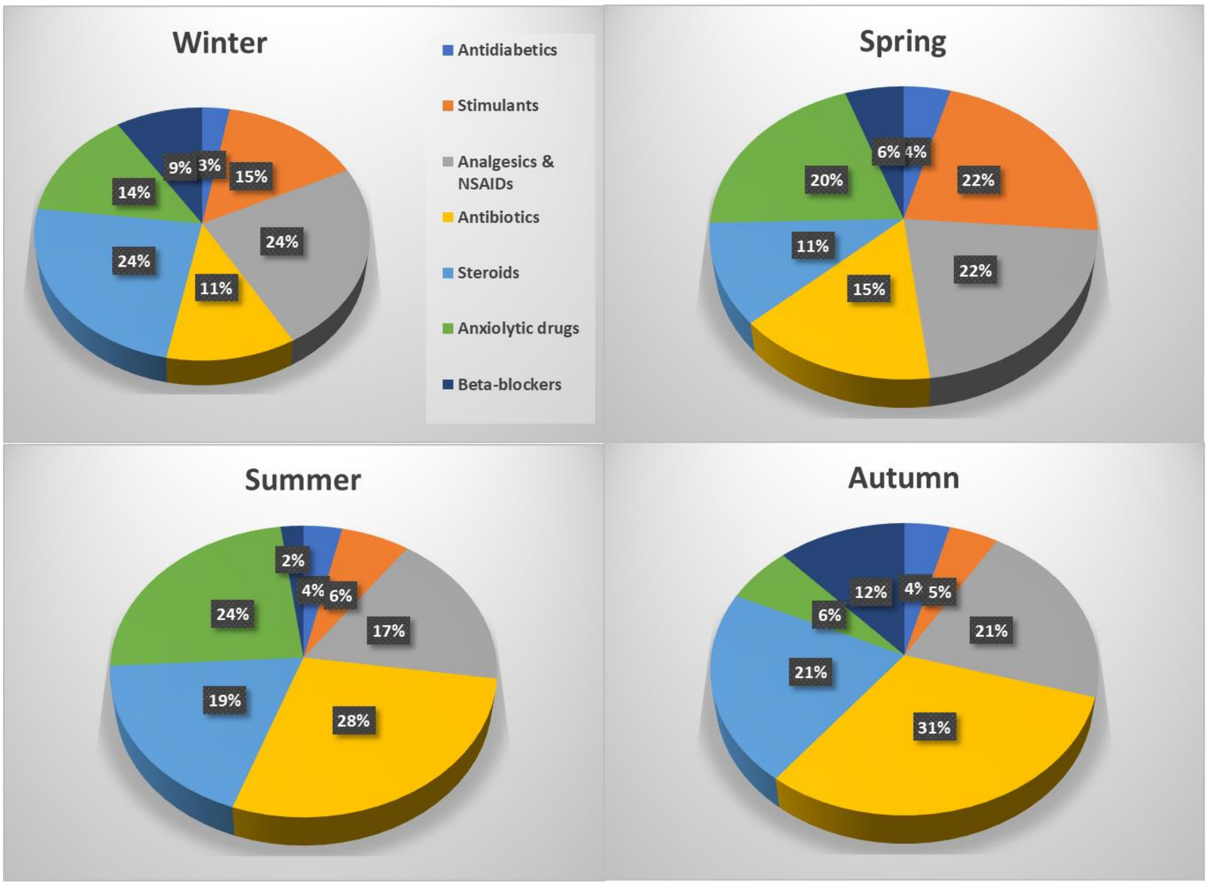
Seasonal trends of 7 PPCPs groups with the highest concentrations in the four studied locations are shown in Fig 4.14, 4.15, 4.16 and 4.17. In River Sowe, anxiolytic drugs, gabapentin, carbamazepine and diazepam, were the most abundant in sediment samples in June at mean concentration of 54 ng/g. Steroids, 17-α-ethinyl estradiole, β-estradiol and hydrocortisone were the most frequent PPCPs in January and May at mean concentration of 61 and 54 ng/g, respectively. Analgesics and NSAIDs, acetaminophen, ibuprofen, naproxen, diclofenac, codeine, tramadol and meclofenamic acid, were dominant in February, March, April, July, October and November at mean concentrations of 61, 47, 84, 65, 78 and 47 ng/g, respectively. Antibiotics, amoxicillin, doxycycline, erythromycin, trimethoprim, sulfamethoxazole and clotrimazole (anti-fungal) showed the highest concentrations in January, August and September at mean concentration of 72, 161 and 43 ng/g, respectively.

Figure 4-14 Seasonal profiles of major PPCP groups in sediment from the river SOWE.



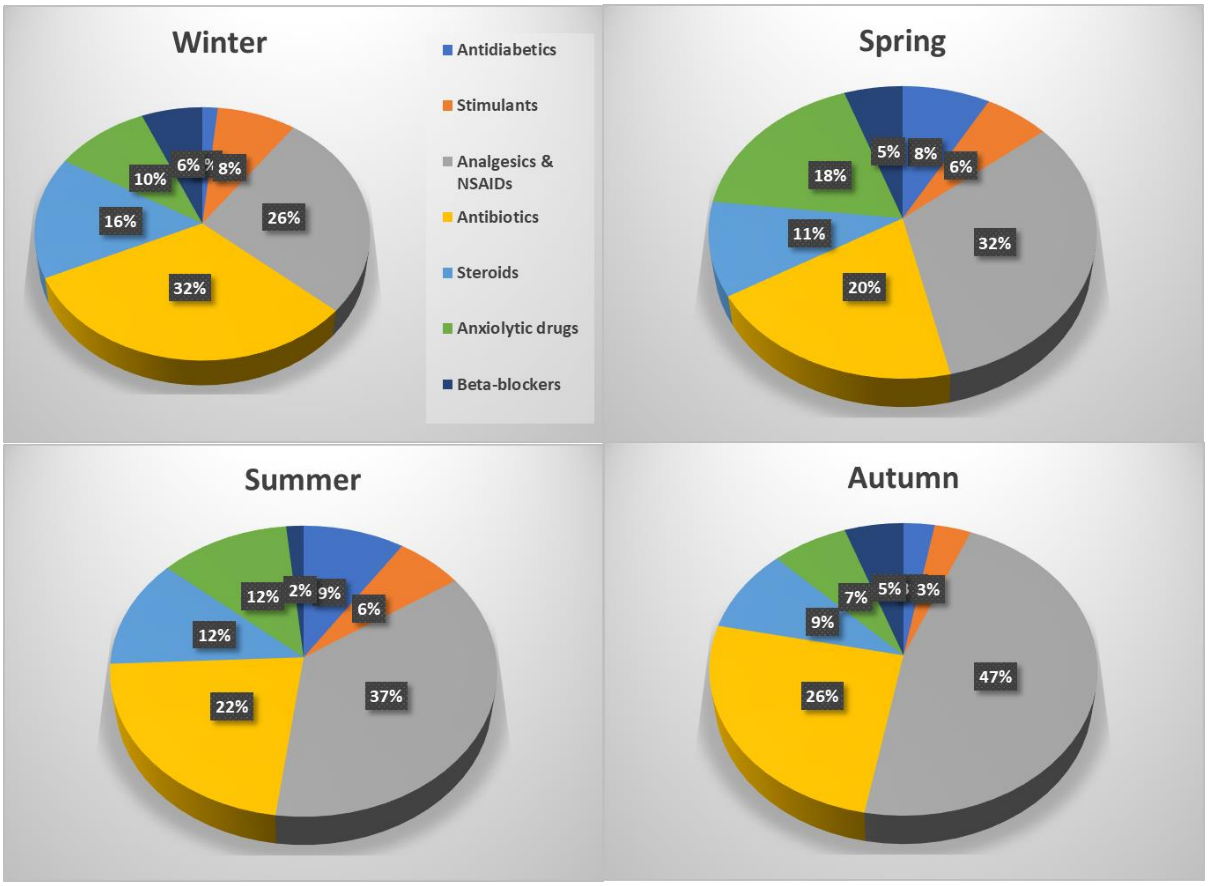
In River Tame, steroids were the dominant PPCPs in sediment samples collected in January and May and July at mean concentration of 56 and 35 ng/g, respectively, while stimulants (Caffeine and Nicotine) showed the highest concentrations in March at mean concentrations of 36 ng/g. Anxiolytic drugs (diazepam, oxazepam, gabapentin and carbamazepine) had the highest concentrations among target PPCPs in April and July at the mean concentrations of 52 and 56 ng/g. Antibiotics were the highest in TAME sediment in August and September at concentrations of 162 and 44 ng/g , while analgesics and NSAIDs dominated in December, February, June, October and November at mean concentrations of 31, 59, 34, 12 and 19 ng/g, respectively.

Figure 4-15 Seasonal profiles of major PPCP groups in sediment from the river TAME



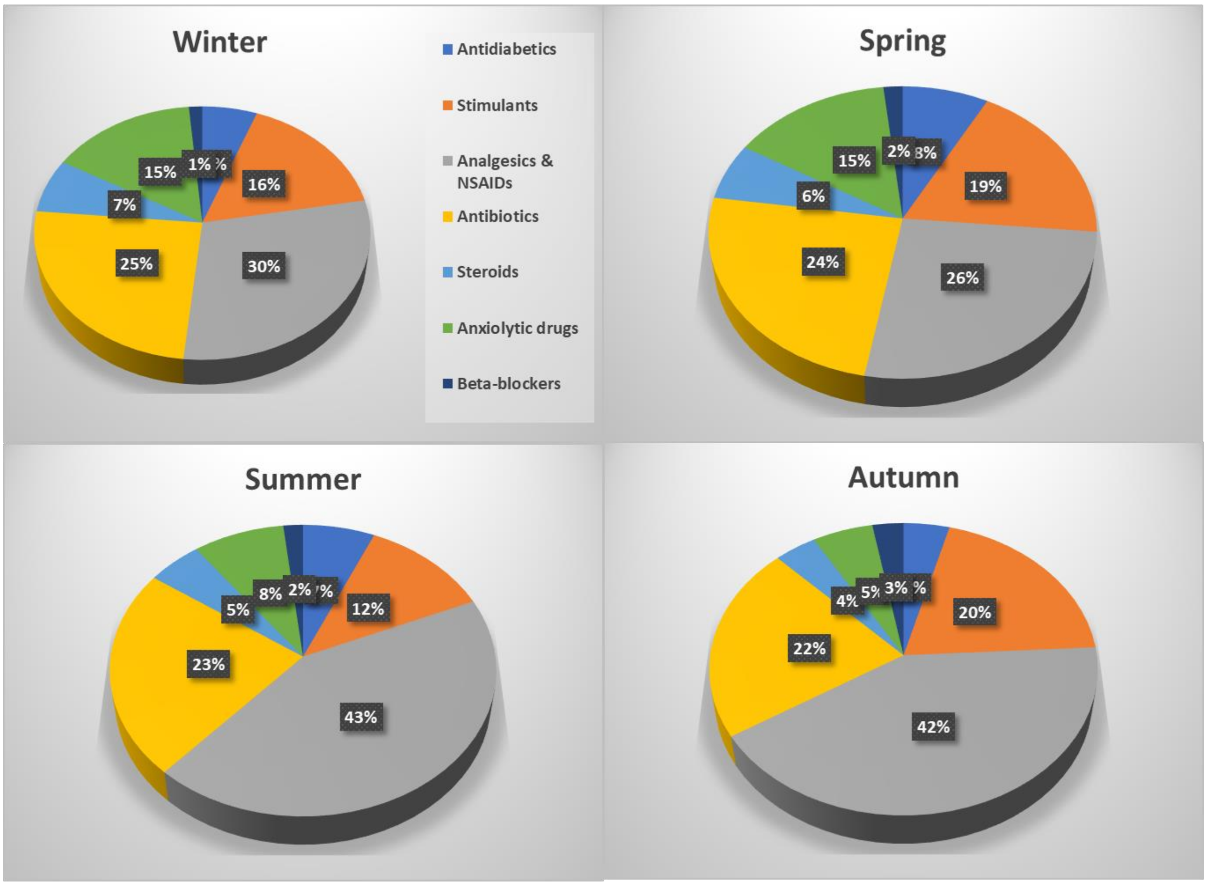
In River Severn, analgesics and NSAIDS dominated PPCPs profiles in sediment in December (20 ng/g), March (41 ng/g), April (55 ng/g), July (84 ng/g), August (107 ng/g), October (69 ng/g) and November (22 ng/g). The remaining months, January (33 ng/g), February (25 ng/g), May (57 ng/g), July (31 ng/g) and September (32 ng/g), were dominated by antibiotics.

Figure 4-16 Seasonal profiles of major PPCP groups in sediment from the river SEVERN.



In sediment samples from the Worcester & Birmingham canal, Uni canal, stimulant drugs showed the highest concentration of 25 ng/g in November. Analgesics and NSAIDs were the dominant PPCPs in sediment samples collected in January (20 ng/g), February (31 ng/g), April (35 ng/g), June (80 ng/g), July (89 ng/g), August (67 ng/g) and September (54 ng/g). The remainder of the year, sediment samples were dominated by antibiotics in December (14 ng/g), March (20 ng/g), May (39 ng/g) and October (25 ng/g).

Figure 4-17 Seasonal profiles of major PPCP groups in sediment from Worcester & Birmingham Canal.



As evident from Figures 4-12 and 4-13, the produced datasets displayed large variability among the 4 studied locations, throughout the 12 months studied. This is in agreement with previous studies in both freshwater sediment and surface water, where no clear trends, or significant variations could be identified for various PPCPs from different therapeutic groups in the absence of extreme weather conditions (e.g. monsoon or heavy rainfall) (Fairbairn et al., 2016, Ebele et al., 2017). Such large variations and lack of clear trends that enable appropriate predictions and or modelling of PPCPs concentrations in the aquatic environment have been well-documented in several recent review articles (Valdez-Carrillo et al., 2020, Patel et al., 2019, Ortúzar et al., 2022). This has been attributed to the multitude of factors influencing PPCPs concentrations in the freshwater aquatic environment in general, and particularly in sediment. These include: the input sources (e.g. raw sewage, WWTP effluents, run off from agricultural farms and aquaculture, industrial waste, landfill leachate and even direct disposal into water ways), compound-specific properties (e.g. water solubility, thermal and chemical stability, photodegradation and K_{OW}), environmental parameters (e.g. temperature, UV light, organic carbon content, flow rate and rainfall) (Ortúzar et al., 2022, Ebele et al., 2017, Patel et al., 2019, O'Flynn et al., 2021).

In the present study, concentrations of DEET (insect repellent) were consistently highest in summer, compared to the other seasons in all the studied locations Figure 4-12, 4-13. Statistical analysis revealed the summer concentrations of DEET in sediment (mean = 14.4 ng/g) were significantly higher than those measured in winter (mean = 3.4 ng/g), while the differences with spring (mean = 5.2 ng/g) and autumn (6.4 ng/g) concentrations weren't statistically significant (P > 0.05). Nevertheless, the observed profiles are generally in agreement with the usage pattern of DEET in the UK as an insect repellent used mainly during summer (UK COMMITTEE ON TOXICITY, 2012).

Similar trends of association between seasonal profiles of target individual and therapeutically grouped PPCPs and their usage patterns were not clear in the present study. For example, antibiotics and NSAIDs were the dominant groups of target PPCPs in various months of different seasons throughout the 4 studied locations Figure 4.14. While their consistent presence indicates the continuous input and frequent use of these drugs, there were no clear statistically significant patterns in their usage or seasonal occurrence. With the absence of major weather events during the study period, it's therefore thought that variation in input sources is likely a major factor influencing the concentrations of target PPCPs in sediment.

4.5. Impact of WWTP on the concentrations of PPCPs in river sediment.

Wastewater treatment plants (WWTPs) using conventional activated sludge (CAS) treatment are the most common in UK urban areas; because they provide high efficiency removal of suspended solids, nutrients and organic matter at a low cost and ease of operation (O'Flynn et al., 2021). However, most conventionally operating WWTP with primary and secondary activated sludge processes and sand filters aren't efficient in removing PPCPs, as well as most other chemicals of emerging concern (CECs, e.g. per- and poly-fluoroalkyl substances and endocrine disrupting chemicals) (Wang and Wang, 2016, Dai et al., 2014). Therefore, effluent from WWTPs has been widely identified as a primary source of PPCPs pollution to surface waters (Ebele et al., 2017, Oulton et al., 2010). The continuous release of PPCPs in WWTP effluent to receiving waters is reported to exceed their environmental degradation rates, which leads to a "pseudo-persistence" in surface waters (Ebele et al., 2017). While this is established in surface waters, very little is known about the potential impact of WWTPs on the concentrations of PPCPs in sediment. Specifically, to our knowledge, there exists no monitoring studies of PPCPs evaluating the impact of WWTP effluent on the concentrations of these pollutants in in UK freshwater sediment, which is in line with the general paucity of data on PPCPs in sediment compared to surface and ground water. This can be of particular importance to inform policy makers and regulators as PPCPs are currently moving from watch list chemicals to designation as priority substances under the EU Water Framework Directive (European Commission, 2020).

In the present study, the impact of WWTP on PPCPs concentrations in sediment was investigated by comparing the concentrations of target analytes in sediment samples collected upstream and downstream of WWTPs effluent discharge points to the rivers SOWE, TAME and SEVERN. A paired t-test comparing the means of $\sum_{30}$ PPCPs up and downstream from the WWTP over 12 months monitoring programme revealed significantly high concentrations of $\sum_{30}$ PPCPs downstream of the WWTPs in all the studied locations Table 4.7.

Table 4.7 : Comparison of means between ∑30 PPCPs (ng/g) upstream and downstream of WWTP in the studied rivers over 12-month monitoring programme.

Location	**River SOWE**		**River TAME**		**River SEVERN**	
WWTP operations	Primary treatment: ✓ Secondary treatment: ✓ N removal: ✗ P removal: ✓ UV: ✗ Ozonation: ✗ Sand filtration: ✓ Chlorination: ✗ Micro filtration: ✗ Other treatment: ✗		Primary treatment: ✓ Secondary treatment: ✓ N removal: ✗ P removal: ✗ UV: ✗ Ozonation: ✗ Sand filtration: ✗ Chlorination: ✗ Micro filtration: ✗ Other treatment: ✗		Primary treatment: ✓ Secondary treatment: ✓ N removal: ✗ P removal: ✓ UV: ✗ Ozonation: ✗ Sand filtration: ✗ Chlorination: ✗ Micro filtration: ✗ Other treatment: ✗	
population	serving over 200,000		serving over 200,000		serving 50,000 to 200,000	
$\sum_{30}$ PPCPs	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream
Dec	202.0	306.1	77.9	107.7	52.6	96.7
Jan	158.9	221.3	89.5	165.1	83.5	149.1
Feb	233.3	358.3	210.4	302.0	42.1	73.9
Mar	40.8	62.5	52.4	93.9	39.6	69.8
Apr	246.8	354.4	160.0	283.3	212.0	349.1
May	167.5	261.2	85.1	153.6	178.9	290.4
Jun	200.6	325.0	90.1	150.4	135.2	230.8
Jul	180.4	228.4	172.8	292.4	158.4	250.2
Aug	321.7	475.5	302.2	498.6	262.1	440.0
Sep	94.0	150.9	71.9	99.9	57.7	90.1
Oct	89.2	112.3	37.5	53.4	75.5	133.6
Nov	83.0	127.4	65.4	93.5	42.0	82.2
***P*-value of t-test**	**4.9 E-05**		**5.5 E-04**		**1.6 E-04**	

Interestingly, the served population by the WWTP in River Severn was less than those served by the WWTP in River SOWE and River Tame Table 4.7. This might explain the lower PPCPs concentrations detected in River Severn compared to the two other rivers, albeit not statistically significant ($P > 0.05$). While WWTP effluents have been documented as major sources of PPCPs to the freshwater aquatic environment (Ebele et al., 2017), they are other sources of PPCPs to rivers (e.g., upstream of WWTPs). The other input sources of PPCPs to rivers have been identified as: waste from hospitals, households, and manufacturing plants, runoff from agriculture and aquaculture farming using veterinary medicine, raw sewage discharge, as well as landfill leachate (Ślósarczyk et al., 2021, Okoye et al., 2022). Given the mentioned sources, combined with inefficient removal by conventional treatment methods, PPCPs enter water bodies, primarily through wastewater discharges, via different sources, and are transported further by WWTPs, with treated effluents to recipient rivers and streams.

Further investigation of the differences in target PPCPs concentrations observed each month upstream and downstream of the WWTP in each location (using a paired t-test) revealed the concentrations of 30 target analytes to be significantly higher downstream of WWTPs, apart from 3 months where the difference was NOT significant at the 95% level Table 4.8.

Table 4.8 Comparison of means between the concentrations (ng/g) of 30 target PPCPs measured upstream and downstream of WWTP in each studied location over 12-month monitoring programme.

Compared dataset pairs (n=30)	River SOWE		River TAME		River SEVERN	
	Correlation Co-efficient	Two-Sided P-value	Correlation Co-efficient	Two-Sided P-value	Correlation Co-efficient	Two-Sided P-value
Dec Upstream & Downstream	0.958	<0.001	0.583	0.173*	0.97	<0.001
Jan Upstream & Downstream	0.961	0.002	0.821	0.002	0.897	<0.001
Feb Upstream & Downstream	0.945	<0.001	0.939	<0.001	0.941	<0.001
Mar Upstream & Downstream	0.979	0.004	0.940	<0.001	0.967	<0.001
Apr Upstream & Downstream	0.940	<0.001	0.921	<0.001	0.97	<0.001
May Upstream & Downstream	0.929	<0.001	0.859	<0.001	0.952	<0.001
Jun Upstream & Downstream	0.963	0.001	0.894	<0.001	0.955	<0.001
Jul Upstream & Downstream	0.916	0.037	0.888	<0.001	0.957	<0.001
Aug Upstream & Downstream	0.970	<.001	0.882	0.002	0.946	<0.001
Sep Upstream & Downstream	0.958	0.003	0.488	0.063*	0.955	<0.001
Oct Upstream & Downstream	0.793	0.058*	0.860	0.042	0.983	<0.001
Nov Upstream & Downstream	0.951	<.001	0.947	0.003	0.964	<0.001

* Denotes not statistically significant at 95% level.

The lack of statistical significance of the higher PPCPs concentration downstream of WWTPs in these 3 months is difficult to attribute to a systemic or regular reason and is more likely down to an episodic spike in the concentration of some target PPCPs due to direct input sources (e.g. direct disposal, leaching of contaminated liquid or leakage of agricultural run-off) (O'Flynn et al., 2021). Even analytical variations cannot be excluded as a contributing factor to such irregularity among 36 pairs of datasets investigated.

Nevertheless, our results confirm the role of WWTP as important sources of PPCPs pollution in UK river sediment. This is in agreement with previous results in UK surface water (Kasprzyk-Hordern et al., 2008) and other international rivers (Singh and Suthar, 2021, Valdez-Carrillo et al., 2020, Ebele et al., 2017). Our results also confirm that conventional WWTP operations based on CAS and sand filtration are NOT sufficient for removal of PPCPs from the freshwater aquatic environment. This highlights the need for innovative approaches to enable efficient removal of chemicals of emerging concern (CECs) from our waterways.

4.5.1. Potential sources of PPCPs

Following sewage treatment, wastewater may be reused for irrigation, and sludges (treated sludge) may be used as fertiliser on farmland. Additionally, pharmaceuticals may enter waters through runoff from agricultural land that has been treated with digested sludge. Animal wastes, solid or liquid, are sprayed on agricultural fields as fertilisers, which results in the release of veterinary medications into the environment (Ebele et al., 2017).

Principal component analysis (PCA) was used to explore the potential source of PPCPs measured in sediment samples from the studied rivers (*e.g., other than the WWTPs discharge*), and explain the variance observed in the obtained datasets. The score plots of 30 PPCPs in sediment samples from River Sowe were provided in figure (4.13). The principal components 1–3 of the PCA (eigenvalues >1) explained 38.7%, 38.5% and 22.8% of the total variance, respectively. PC1 was mainly governed by PPCPs including, ethinyl estradiole (EE2), metoprolol (METO), tramadol (TMD), codeine (COD), trimethoprim (TMP), meclofenamic (MEC), carbamazepine (CBZ), acetaminophen (ACT), Clotrimazole (CMZ) and propranolol (PRO). PC1 was potentially associated with wastewater sources. For example, 17-ethinyl estradiol and metoprolol are primarily discharged into the environment through wastewater treatment plants (Laurenson et al., 2014, Cavalcante et al., 2015). The diverse nature of the grouping under PC1 precludes meaningful association with other potential sources. To explain, TMP and CMZ have been associated with veterinary application, particularly in cattle farming (Assress et al., 2020, Kortesmäki et al., 2020). While their sources maybe potentially attributed to veterinary uses and run-off from farmlands, other components of PC1 (e.g., CBZ, METO) have no known veterinary applications. PC2 showed contributions by a relatively large number of compounds including nicotine (NCT), gabapentin (GBP), ibuprofen (IB), diazepam (DZ), glyburide (GB), doxycycline (DOX), DEET, diclofenac Na (DC), hydrocortisone (HD), amoxicillin (AMX), metformin (MET), gemfibrozil (GM), β-estradiol (E2) and naproxen (NP). Therefore, PC2 might be related to livestock activity, aquaculture, and wastewater sources. For instance, Diclofenac Na, amoxicillin and doxycycline were applied to animals or used in veterinary medicine and aquaculture (Saini et al., 2012, Liu et al., 2016, Wu et al., 2022, Huff Chester et al., 2022, Ayanda et al., 2021). PC3 was mostly dominated by sulfamethoxazole (SMX), valsartan (VAL), erythromycin-H2O (ERY_H2O), caffeine (CAF), oxazepam (OX) and mefloquine-HCl (MEF). PC3 may have been related to a combination of wastewater discharges from both human (e.g., VAL, OX) and animal consumption (e.g., ERY_H2O and SMX). For example, a high detection frequency of sulfamethoxazole, mefloquine, valsartan and erythromycin-H2O were detected in wastewater discharges, where point samples were collected close to WWTPs, and were surrounded by farmland. As results, discharge from WWTP and runoff from farmland may contribute to the presence of these PPCPs in the water downstream of the sampled locations (Bhandari et al., 2008, Ofrydopoulou et al., 2022).

Figure 4-18 Score plots of the PCA of sediment from River Sowe.

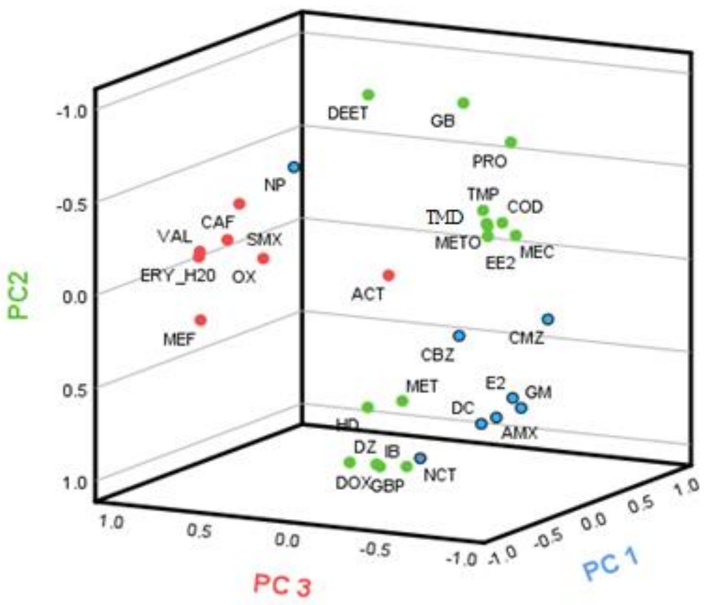


Table 4.9 Varimax rotated factor loadings of PPCPs in sediment from River Sowe based on the principal component analysis.

PPCPs	Rotated Component Matrix		
	Component		
	1	2	3
EE2	.999	-.034	-.010
METO	.996	-.089	-.011
TMD	.995	-.104	-.006
COD	.988	-.118	-.098
TMP	.985	-.174	.010
MEC	.982	-.060	-.179
CBZ	.869	.488	.085
ACT	.855	.198	.480
CMZ	.830	.338	-.443
PRO	.734	-.618	-.283

NCT	.120	.989	-.091
GBP	-.161	.973	-.163
IB	-.229	.972	-.046
DZ	-.272	.957	.103
GB	.183	-.935	-.304
DOX	-.351	.932	-.091
DEET	.328	-.890	.316
DC	.459	.850	-.260
HD	.433	.819	.375
AMX	.478	.812	-.336
MET	.556	.795	.243
GM	.462	.742	-.486
E2	.582	.722	-.374
NP	-.683	-.701	.204
SMX	.085	-.087	.993
VAL	-.283	-.096	.954
ERY_H20	-.298	-.071	.952
CAF	.136	-.275	.952
OX	.357	.059	.932
MEF	-.553	.208	.807
Eigenvalues	13.31	10.32	6.35

Component	**Total Variance Explained**		
	Rotation Sums of Squared Loadings		
	Total	**% Of Variance**	**Cumulative %**
1	11.616	38.719	38.719
2	11.555	38.516	77.235
3	6.829	22.765	100.000

PCA analysis was also conducted to assess the potential source of PPCPs in sediment samples from River Tame Table 4.10. The score plots of 30 PPCPs were shown in Figure 4-19. The principal component 1–3 of the PCA (eigenvalues >1) explained 38 %, 36% and 26% of the total variance. PC1 was mostly dominated by hydrocortisone (HD), valsartan (VAL), nicotine (NCT), gabapentin (GBP), naproxen (NP), oxazepam (OX), 17-a-ethinyl estradiole (EE2), metoprolol (METO), codeine (COD), propranolol (PRO), acetaminophen (ACT), gemfibrozil (GM), B-estradiol (E2), which points to a source from treated sewage due to their low or moderate removal efficiency by WWTPs (Velicu et al., 2007, Tixier et al., 2003, Lima et al., 2019, Lin et al., 2010b). PC2 was primarily controlled by amoxicillin (AMX), diclofenac Na (DC), doxycycline (DOX), diazepam (DZ), carbamazepine (CBZ), Clotrimazole (CMZ), mefloquine-HCl (MEF), DEET and trimethoprim (TMP). PC2 may have been attributed to aquaculture, livestock farming, and wastewater sources, due to the use of its major components in veterinary medicine/livestock husbandry practices (e.g., DOX, AMX, CMZ, TMP), aquaculture (e.g., AMX, TMP), and human medicinal treatment (e.g., CBZ) (Khadka and Mandal, 2013, Menon et al., 2020, Stadelmann et al., 2011, Sandem et al., 2006). PC3 was mainly managed by sulfamethoxazole (SMX), gemfibrozil (GB), caffeine (CAF), metformin (MET), erythromycin-H2O (ERY_H2O), meclofenamic acid (MEC), tramadol (TMD) and ibuprofen (IB). PC3 may have been associated with livestock (e.g., ERY_H2O, SMX) and wastewater sources (Zanolari et al., 2004, Selvam et al., 2017, Rauseo et al., 2019).

Figure 4-19 Score plots of the PCA of sediment from River Tame.

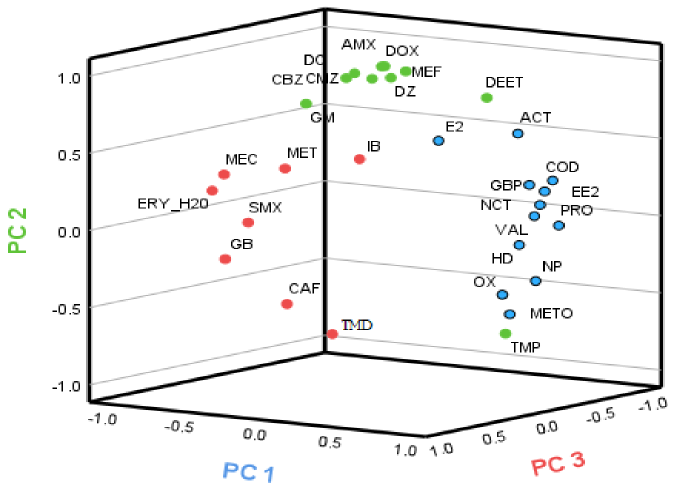


Table 4.10 Varimax rotated factor loadings of PPCPs in sediment from River Tame based on the principal component analysis.

PPCPs	Rotated Component Matrix		
	Component		
	1	2	3
HD	.997	-.032	.067
VAL	.987	.131	-.089
NCT	.967	.189	-.173
GBP	.939	.325	-.111
NP	.935	-.307	-.177
OX	.927	-.352	.126
EE2	.926	.258	-.274
METO	.859	-.510	-.041
COD	.807	.281	-.519
PRO	.747	-.037	-.664
ACT	.736	.610	-.294

GM	-.683	.656	-.322
E2	.669	.651	.358
AMX	-.033	.994	-.108
DC	-.029	.988	.154
DOX	-.058	.984	-.170
DZ	.185	.976	.118
CBZ	.116	.974	.196
CMZ	-.023	.970	.241
MEF	-.072	.918	-.391
DEET	.416	.786	-.457
TMP	.601	-.709	-.370
SMX	-.153	.129	.980
GB	-.339	-.134	.931
CAF	.062	-.385	.921
MET	.018	.481	.877
ERY_H20	-.505	.276	.818
MEC	-.427	.388	.817
TMD	.257	-.581	.772
IB	-.624	.242	-.743
Eigenvalues	12.39	10.84	6.75
Component	**Total Variance Explained** **Rotation Sums of Squared Loadings**		
	Total	**% of Variance**	**Cumulative %**
1	11.408	38.027	38.027
2	10.783	35.943	73.971
3	7.809	26.029	100

PCA analysis was employed to determine the potential source of PPCPs in sediments from River Severn Table 4.11. The score plots of 30 PPCPs were presented in Figure 4-20. The principal component 1–3 of the PCA (eigenvalues >1) explained 37 %, 36.5% and 26.5% of the total variance. PC1 was mainly governed by diazepam (DZ), valsartan (VAL), hydrocortisone (HD), erythromycin-H2O, (ERY_H2O), oxazepam (OX), acetaminophen (ACT), metformin (MET), amoxicillin (AMX), carbamazepine (CBZ), DEET, naproxen (NP), glyburide (GB), nicotine (NCT) and gemfibrozil (GM). PC1 may possibly be associated with wastewater sources and veterinary-related applications. In addition to antibiotics used in livestock farming and animal husbandry (e.g. ERY_H2O, AMX), Diazepam has a recognised place in veterinary anaesthetic protocols and is frequently used in clinical practise as a sedative, muscle relaxant, anticonvulsant, and a companion to intravenous anaesthesia in both foals and adult horses (Shini, 2000). PC2 was mostly controlled by sulfamethoxazole (SMX), 17-a-ethinyl estradiole (EE2), meclofenamic acid (MEC), metoprolol (METO), clotrimazole (CMZ), caffeine (CAF), trimethoprim (TMP), tramadol (TMD), and ibuprofen (IB). PC2 may be related to wastewater sources. For instance, both Caffeine and SMX have reported low removal efficiency by WWTPs and are frequently detected at high concentrations in effluents (Li et al., 2020b, Osorio et al., 2016b). PC3 was largely managed by diclofenac Na (DC), gabapentin (GBP), propranolol (PRO), mefloquine-HCl (MEF), B-estradiol (E2), doxycycline (DOX) and codeine (COD). PC3 might be related to livestock activity (e.g., DOX), as well as wastewater sources (Shreffler and Zuniga, 2020, Ziaaddini et al., 2015, Xu et al., 2020)

Figure 4-20 Score plots of the PCA of sediment from River Severn.

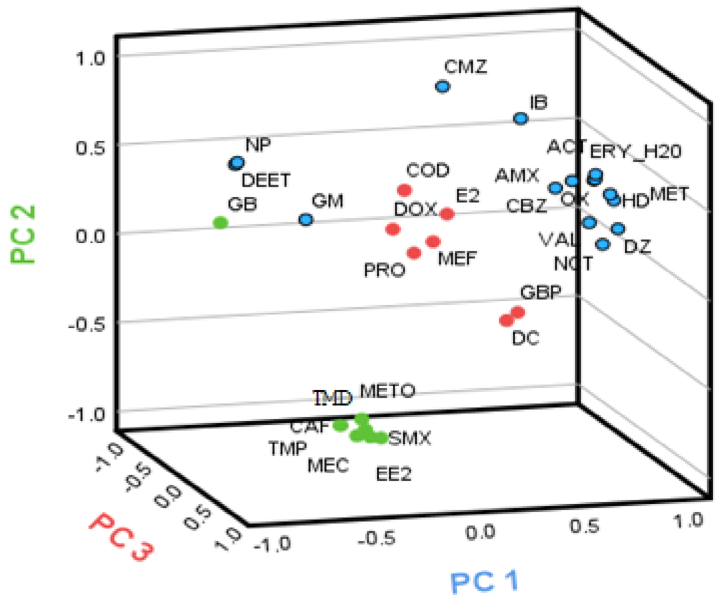


Table 4.11 Varimax rotated factor loadings of PPCPs in sediment from River Severn based on the principal component analysis.

PPCPs	Rotated Component Matrix		
	Component		
	1	2	3
DZ	.989	.145	-.017
VAL	.939	.109	-.326
HD	.936	.338	.099
ERY_H20	.908	.395	-.138
OX	.906	.409	-.112
ACT	.891	.451	-.051
MET	.873	.413	.258
AMX	.868	.340	-.362
CBZ	.825	.271	-.495
DEET	-.775	.563	-.286

NP	-.769	.578	-.274
GB	-.740	.145	-.657
NCT	.726	.235	.647
GM	-.682	.453	.574
SMX	-.119	-.984	-.133
EE2	-.169	-.976	-.138
MEC	-.234	-.963	-.132
METO	-.165	-.958	-.236
CMZ	.214	.942	-.259
CAF	-.277	-.929	-.245
TMP	-.283	-.928	-.242
TMD	-.150	-.926	-.346
IB	.450	.863	.231
DC	.166	-.075	.983
GBP	.222	-.035	.974
PRO	.273	-.165	-.948
MEF	-.168	.375	.912
E2	-.085	.511	.855
DOX	-.339	.438	.833
COD	-.255	.628	.735
Eigenvalues	14.41	9.82	5.76

Component	**Total Variance Explained**		
	Rotation Sums of Squared Loadings		
	Total	**% of Variance**	**Cumulative %**
1	11.023	36.745	36.745
2	10.968	36.559	73.303
3	8.009	26.697	100.000

This chapter provides first data on seasonal variation of PPCPs in UK freshwater sediment and investigates the impact of WWTP on concentrations of the studied chemicals in riverine sediment. Our results confirm the role of WWTP as major input sources of PPCPs to sediments, indicating the inefficient removal of these emerging contaminants by traditional primary and secondary wastewater treatment methods. This highlights the need for more research and investment into water purification and contaminant removal techniques at WWTPs to efficiently remove emerging chemical contaminants and prevent their redistribution to the receiving waterways.

Our seasonal variation results indicate that rainfall and river flowrate may influence the concentrations of PPCPs in sediment. This should provide the basis into further detailed studies on the potential impact of extended rainfall and flooding events on the mobilisation of PPCPs and other emerging contaminants sorbed onto sediment particles along rivers and the fate of these chemicals in the aquatic environment.

Moreover, our results indicate the potential contribution of veterinary applications of PPCPs towards their concentrations in freshwater sediment through run-off from agricultural land. This is of particular concern due to the extensive use of anti-biotics in livestock farming and aquaculture activities. This may lead to high concentrations of antibiotics in riverine water and sediment, with potential development of anti-microbial resistant microorganisms (e.g., bacteria, viruses, fungi and parasites). Therefore, our results raise concern and highlight the need for clear guidelines over the use of antibiotics in agricultural and aquaculture activities to protect the environment and humans from the increasing risk of anti-microbial resistance.

Chapter 5. Distribution of Pharmaceuticals and Personal Care Products in the world's Freshwater Sediments

5.1. Synopsis

Global concern over the ubiquitous distribution of pharmaceuticals and personal care products (PPCPs) in rivers has been mounting over the past few years. This is mainly due to potential adverse impacts of active pharmaceutical ingredients on aquatic biota, and consequently humans, at sub-lethal doses (e.g. endocrine disruption, anti-microbial resistance) (Su et al., 2020, Rahman et al., 2009, Overturf et al., 2015), as well as persistence (Glassmeyer et al., 2008, Baker et al., 2022) and bioaccumulation (Ebele et al., 2017, Pérez et al., 2022). Compared to water, few studies have investigated PPCPs in freshwater sediment. Moreover, direct comparison of existing results is challenging due to the different sample collection, processing and analytical techniques applied in different studies. The chapter will investigate the concentrations and profiles of 30 PPCPs in sediment samples collected from rivers and freshwater lakes in 13 countries (5 continents) around the world. The distribution of target pharmaceuticals will be examined and the most abundant PPCPs will be determined. Furthermore, the most polluted rivers will be identified to highlight the potential global risk of PPCPs contamination in freshwater sediment.

5.2. Sampling and sample locations

International sediment samples were kindly donated by the 100 Plastic Rivers project (https://www.birmingham.ac.uk/research/water-sciences/projects/plastic-rivers.aspx). This Leverhulme Trust-funded project aims to investigate micropollutants in freshwater sediment globally. The surface sediment samples investigated in this chapter were collected from 13 countries (5 continents) between 2019 – 2021 Figure 5-1, Table 5.1 using traditional methods as described under section 2.1.2. The samples were shipped in non-plastic containers to UoB, where they were stored in a cool dark place until analysis. Aliquots of ~1 g sediment were analysed for 30 PPCPs using the methods detailed in chapter 2. All extracted sediment samples were analysed using SCIEX™ UHPLC Triple TOF MS/MS as described under section 2.8.2 of this thesis.

5.3. Cumulative PPCPs Concentrations

To simplify data presentation, the sum of all PPCPs detected at each specific location was used to calculate Σ_{30} PPCPs at this sampling point. Where more than one sampling point existed for the same river (e.g., river Thur, Switzerland) or the same country (e.g., Nepal), the average concentration per river or country is used as representative. The full datasets are provided in the supplementary information to this chapter.

The highest mean Σ_{30} PPCPs in sediment was observed in Klang river, Malaysia, at 459 ng/g, while the lowest cumulative PPCPs concentration of 159 ng/g was recorded in Detriot river, USA Table 5.2. Interestingly, the sampling site in Klang river, Malaysia was linked to an increased discharge of sewage leading to high concentrations of various emerging organic pollutants from urbanized and heavy industrial activities, combined with high population density (Nazifa et al., 2020, Omar et al., 2019). This may explain the high concentrations of PPCPs in this river sediment because sewage discharge has been established as a major source of PPCPs to the aquatic environment (Ebele et al., 2017). Other sources of pharmaceutical residues to river sediments have been identified, including leaks and discharge from manufacturing industries, aquaculture and livestock farms, runoff from agricultural lands and landfill leachates (Sadutto et al., 2021, Luo et al., 2011, Sim et al., 2011, Zhou et al., 2021, Fairbairn et al., 2016, Evgenidou et al., 2015) On the other hand, Detroit river has reached record level of pollution in the 1960. However, this has triggered a multi-million-dollar large-scale conservation effort over the past 40 years to clean up the river. This included the prohibition of dumping chemicals, industrial waste, garbage, and sewage. In 2007, The Detroit river and its recovery efforts were listed as a Michigan State Historic Site (AMERICANRIVERS.ORG, 2021).

Figure 5-1 Locations of rivers investigated in this study.

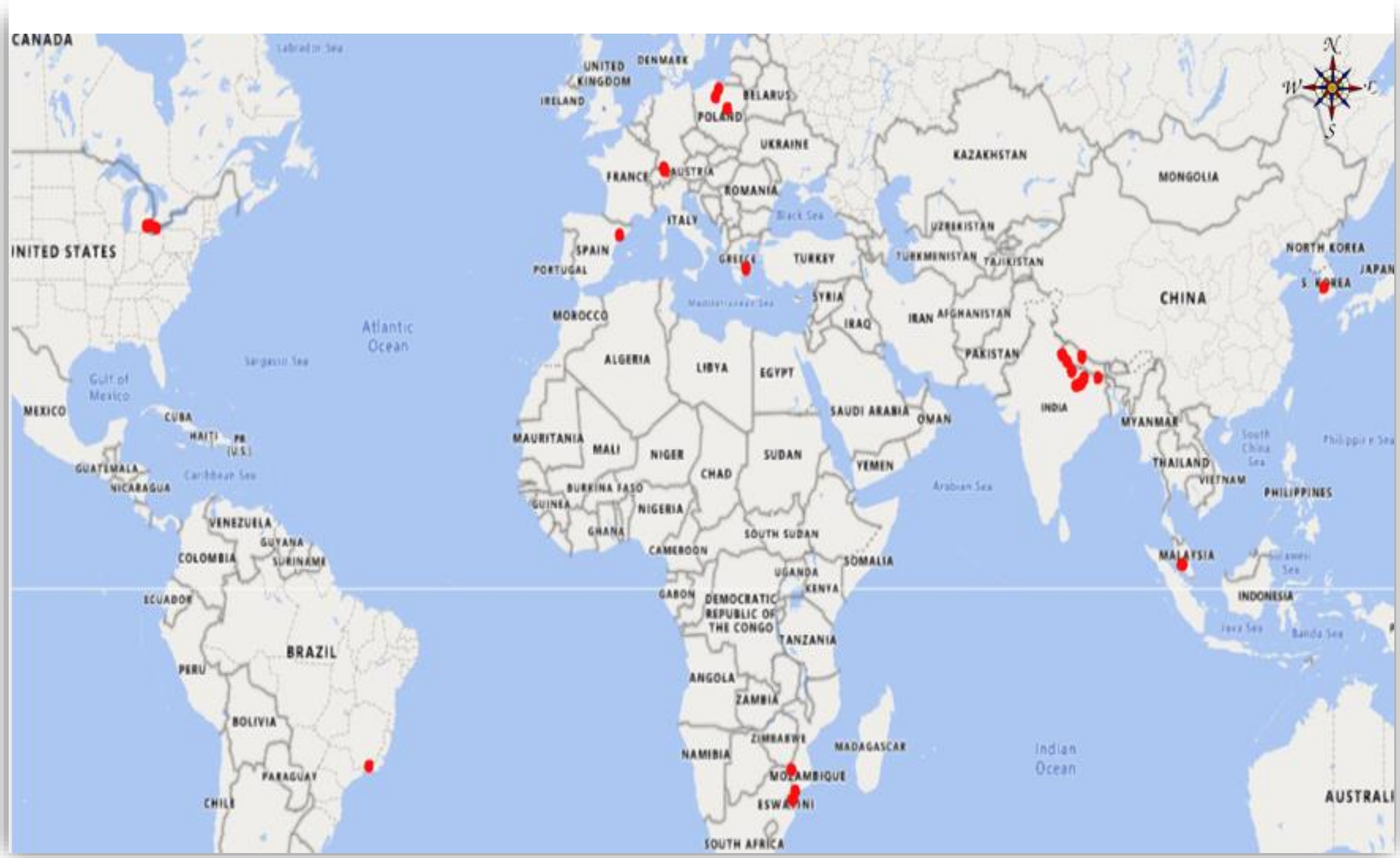


Table 5.1 List of sediment sampling locations (n = 31) from different rivers and lakes around the world.

Continent	Country	River	Date of sampling	Latitude	Longitude
Africa	Mozambique	Limpopo River	2021	22°40'37.9"S	31°49'14.9"E
		Incmati River	2021	25°11'40.2"S	32°30'20.3"E
	Eswatini	Mbuluzi River	2021	26°10'43.8"S	32°02'58.0"E
Asia	Malaysia	Klang River1	2019	3°02'41.2"N	101°36'22.0"E
		Klang River2	2019	3°02'48.4"N	01°24'42.4"E
	Nepal	Koshi River	2020	26°06'41.8"N	86°29'37.6"E
		Kali Gandaki River1	2020	28°30'09.6"N	83°39'24.8"E
		Kali Gandaki River2	2020	28°36'05.1"N	83°38'54.8"E
	South Korea	Geum River	2019	36°01'20.5"N	26°45'31.2"E
	India	Ganges river 1	2019	28°48'35.5"N	80°06'34.1"E
		Ganges river 2	2019	27°59'36.2"N	80°59'10.1"E
		Ganges river 3	2019	26°51'33.0"N	81°49'29.1"E
		Ganges river 4	2019	26°06'22.1"N	84°02'21.6"E
		Ganges river 5	2019	25°31'19.4"N	83°32'05.1"E
		Ganges river 6	2019	25°19'41.3"N	83°03'06.9"E
		Ganges river 7	2019	25°11'24.7"N	82°34'57.4"E
Europe	Switzerland	Thur river1	2020	47°11'16.1"N	9°16'09.4"E
		Thur river2	2020	47°14'42.9"N	9°10'25.1"E
		Thur river3	2020	47°17'54.3"N	9°05'22.7"E
		Thur river4	2020	47°21'28.5"N	9°05'03.3"E
		Thur river5	2020	47°26'49.4"N	9°03'50.1"E
	Poland	Vistula River1	2020	52°23'17.8"N	20°24'33.7"E
		Vistula River2	2020	53°15'17.1"N	18°17'06.9"E
		Vistula River3	2020	53°54'11.5"N	18°52'54.8"E
	Greece	Kifisos river1	2019	37°59'52.5"N	23°41'47.4"E
		Kifisos river2	2019	37°57'24.9"N	23°40'28.4"E
	Spain	Francoli River	2020	41°17'06.1"N	1°11'36.6"E
Americas	Brazil	Paraíba do Sul	2019	22°14'12.4"S	3°30'50.1"W
	USA	Detroit River	2020	42°10'39.3"N	3°09'28.4"W
	Canada	Lake Erie	2020	41°56'33.7"N	1°28'34.4"W
		Lake Saint Clair	2020	42°18'52.4"N	2°42'10.5"W

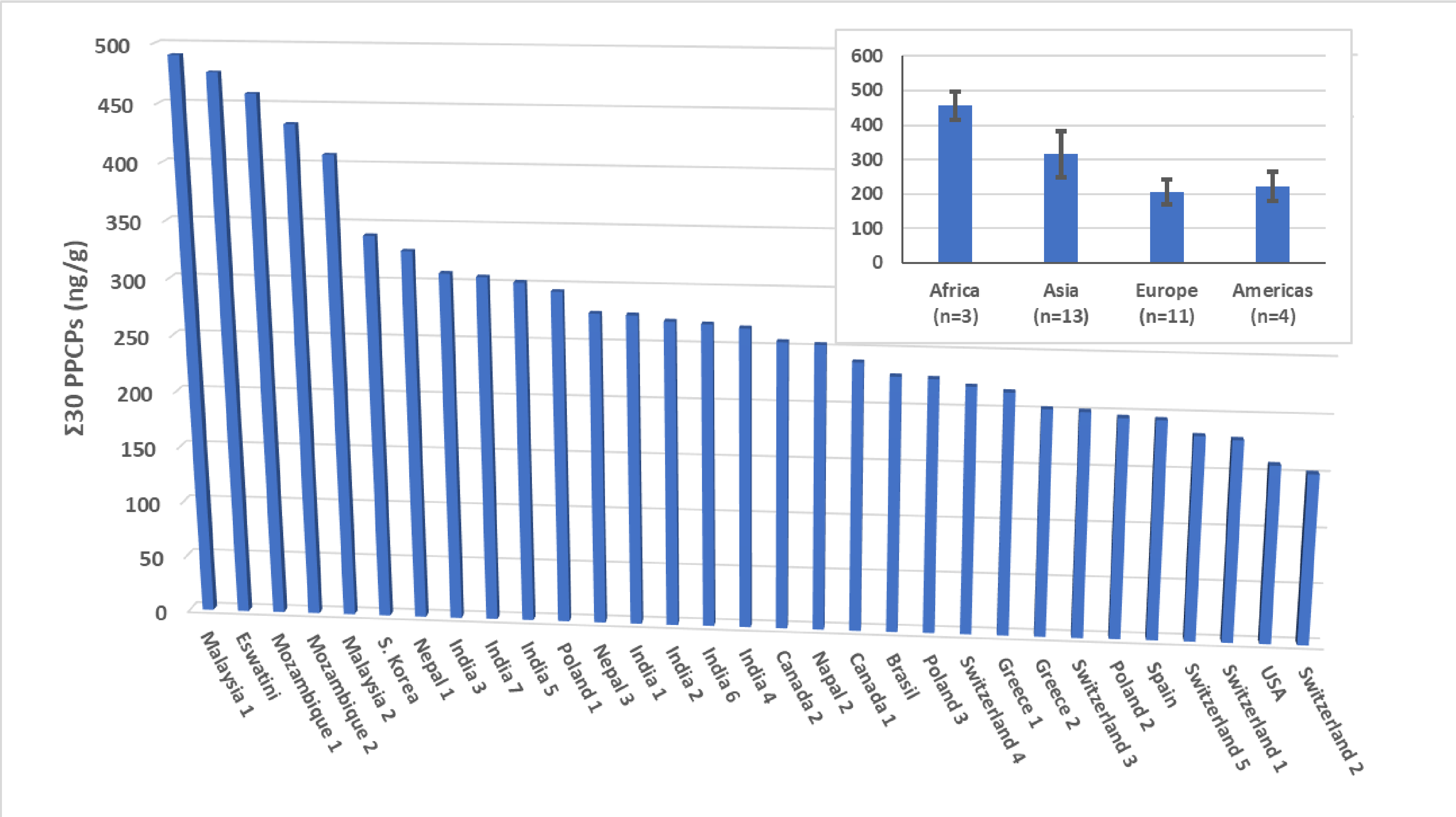
The highest PPCPs pollution levels were observed in sediment from African rivers (Mbuluzi River, Eswatini > Limpopo River, Mozambique > Incmati River, Mozambique) with a mean Σ_{30} PPCPs of 456 ng/g Figure 5-2. Asian rivers (Malaysia > S. Korea > India > Nepal) were the second most polluted with a mean continent Σ_{30} PPCPs of 315 ng/g. Europe had the least PPCPs polluted river sediments (Poland > Greece> Spain> Switzerland) with a mean Σ_{30} PPCPs of 206 ng/g Figure 5-2.

Table 5.2 Concentrations of target PPCPs (ng/g) in sediment samples from different rivers and lakes around the world.

Continent	Country	locations	Σ30 PPCPs	mean/country	mean/continent
Africa	Mozambique	Limpopo river	459	446	**456**
		Incmati river	434		
	Eswatini	Mbuluzi river	476	476	
Asia	Malaysia	Klang river 1	490	449	**315**
		Klang river 2	408		
	Nepal	Koshi river	327	285	
		Kali Gandaki River 1	254		
		Kali Gandaki River 2	277		
	South Korea	Geum River	340	340	
	India	Ganges river 1	276	286	
		Ganges river 2	271		
		Ganges river 3	309		
		Ganges river 4	267		
		Ganges river 5	302		
		Ganges river 6	270		
		Ganges river 7	306		
Europe	Switzerland	Thur river 1	180	187	**206**
		Thur river 2	152		
		Thur river 3	201		
		Thur river 4	221		

		Thur river 5	183		
	Poland	Vistula River 1	295	240	
		Vistula River 2	197		
		Vistula River 3	227		
	Greece	Kifisos river 1	217	210	
		Kifisos river 2	203		
	Spain	Francoli River	196	196	
North America	USA	Detroit River	159	159	**218**
	Canada	Lake Erie	240	248	
		Lake St Clair	256		
South America	Brazil	Paraíba do Sul, Três Rios	228	228	**228**

Figure 5-2 Concentrations of Σ30 PPCPs (ng/g) in sediment samples from the sampled rivers and lakes around the world.

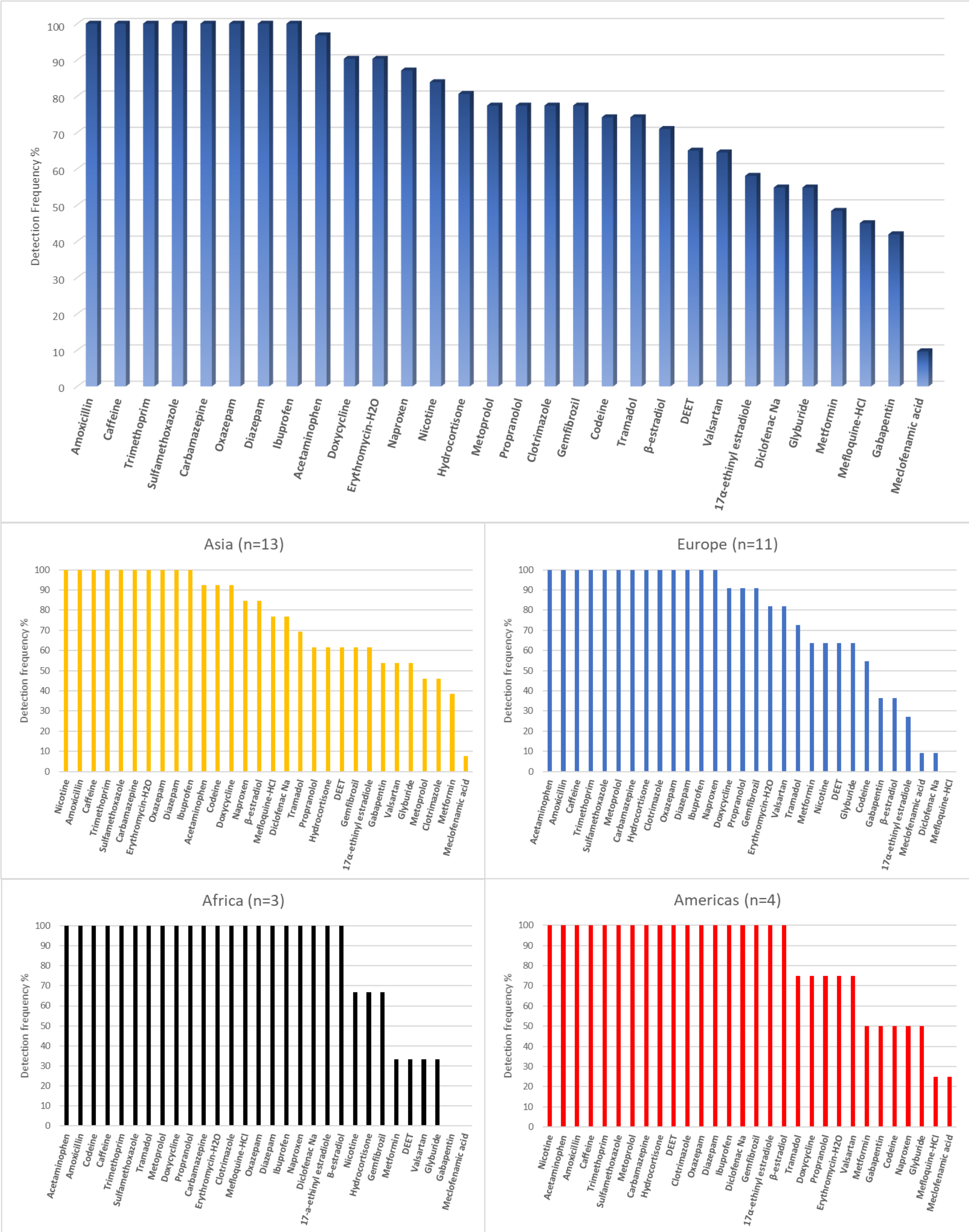


To investigate potential statistical significance of the differences in Σ_{30} PPCPs concentrations measured in sediment samples from different continents, the sample obtained from Brazil was combined with the 3 samples from North America to represent The Americas Figure 5-2, inset). While the small number of samples from Africa (n=3) and the Americas (n=4) reduce the overall confidence of the test, Analysis of Variance (with Tukey post-hoc test) revealed the measured Σ_{30} PPCPs in Africa were significantly higher than those from the other continents. Moreover, Σ_{30} PPCPs in sediment samples from Asia were significantly higher than those from Europe and the Americas, while no significant differences were observed between the latter 2 continents. It's difficult to compare these results to previous literature due to the lack of international comparison studies of PPCPs in freshwater sediment, in addition to the different types and numbers of chemicals investigated in the available studies of PPCPs in river sediments. Interestingly, an international study was published very recently, which compares the concentrations of 61 PPCPs in water from 1,052 sampling sites along 258 rivers in 104 countries of all continents (Wilkinson et al., 2022). This large study reported higher concentrations of PPCPs in river water from low- and middle-income countries (LIMIC) in sub-Saharan Africa, south Asia, and South America, compared to developed countries in Europe and North America. This is largely in agreement with our results and can be attributed to a combination of poor wastewater treatment and waste management infrastructure, extensive pharmaceutical manufacturing and/or high population density in the investigated LIMIC (Wilkinson et al., 2022). While the small sample size in the present study hampers definitive conclusions about significant differences in PPCPs contamination of freshwater sediment among different countries and continents, our results clearly highlight the ubiquitous distribution of PPCPs in river sediment worldwide. Combined with recent results on PPCPs in river water worldwide, our results raise concern over the high level of PPCPs contamination in LIMIC. This is particularly alarming due to the lack of technology, management options and infrastructure required to mitigate such pollution in LIMIC, leading to more risk to environmental and health faced by their vulnerable populations.

5.4. PPCPs profiles and detection frequencies.

High detection frequencies were generally predicted for the target analytes because they were selected from priority lists based on their extensive production and usage. Of the 30 targeted PPCPs, 8 pharmaceuticals were detected in all the studied sites. These are amoxicillin, caffeine, trimethoprim, sulfamethoxazole, carbamazepine, oxazepam, diazepam and ibuprofen Figure 5-3. Apart from caffeine which has recreational purposes, the other 7 ubiquitous chemicals belong to 3 different therapeutic groups, namely: anti-biotics, anxiolytics and NSAIDs. Interestingly, the ubiquity and risk of trimethoprim and sulfamethoxazole in European rivers have been previously highlighted using modelling approaches based on percapita consumption and excretion data from 9 European countries validated by comparison to measured concentrations of these chemicals in effluents (Johnson et al., 2015). Both antibiotics were found in all the studied rivers at a wide concentration range (70 - 438 ng/L for sulfamethoxazole and 109 - 832 ng/L for trimethoprim), raising concern over the potential impact of these pseudo-persistent antibiotics at sub-lethal dosage on increasing antibiotic resistance in the environment (Singer et al., 2019). Amoxicillin was in the top 10 prescribed pharmaceuticals in both the EU and USA from 2015-2020, and the leading anti-bacterial drug dispensed in England in 2020 (STATISTA, 2021a). A previous study of PPCPs in water samples from the Klang river estuary, Malaysia (sampled in the present study) has also reported that amoxicillin had the highest concentration (1023.1 ng/L) among the studied pharmaceuticals (Omar et al., 2019). Similarly, the extensive use of amoxicillin leading to high detection frequency and concentrations in Indian rivers (including the Ganges river sampled in the current study), and the subsequent risk of increasing antibiotic resistance has been reported (Balakrishna et al., 2017).

Figure 5-3 Detection Frequency (%) of the studied PPCPs in sediment samples from rivers and lakes around the world (n=31) and categorised by continent.



The anxiolytic drugs diazepam, oxazepam and carbamazepine have been previously identified at various concentrations (0.1 – 54 ng/g) in freshwater sediment samples from Spain, Pakistan, South Africa, USA and China (Osorio et al., 2016a, Matongo et al., 2015, Ashfaq et al., 2019, Yang et al., 2015, Zhang et al., 2018). Furthermore, both diazepam and oxazepam were reported to be persistent in freshwater sediment for prolonged durations (Thiebault et al., 2017, Klaminder et al., 2015). This may explain the ubiquitous distribution of the 3 anxiolytic drugs in the international sediments sampled in the present study.

Finally, the 100% detection frequency of ibuprofen in the present study is not surprising. Ibuprofen is one of the most widely used NSAIDs worldwide, either on its own or in combination with other drugs (STATISTA, 2021b). Ibuprofen has been previously detected at a wide range of concentrations (0.1 – 227 ng/g) in freshwater sediment all over the world (Ebele et al., 2017, Hu et al., 2018).

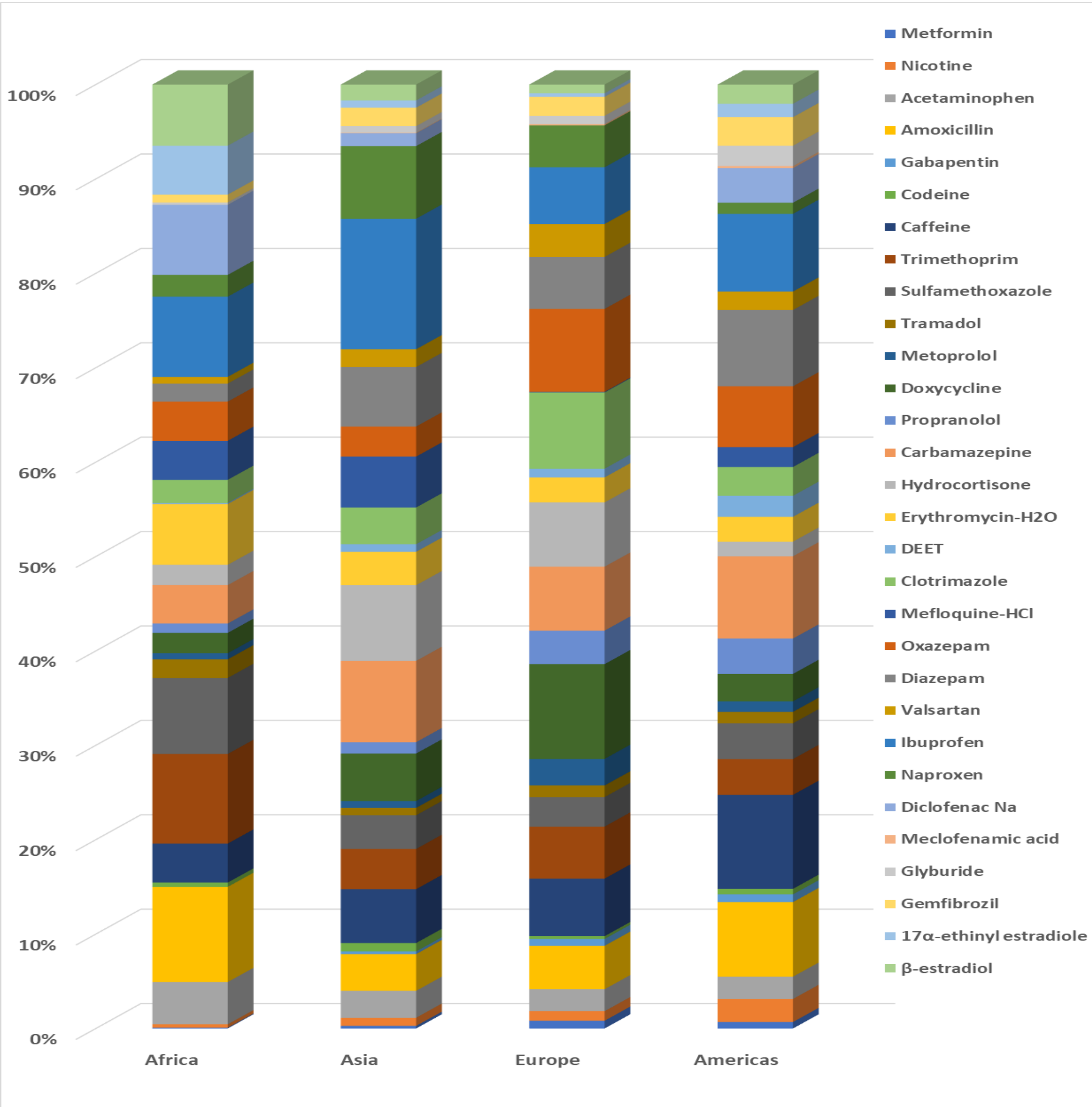
The PPCPs profile in sediment from the studied continents is provided in Figure 5-4. The observed PPCPs profiles in freshwater sediments reflect the extensive use of these chemicals worldwide and the ubiquitous distribution of various compounds from different therapeutic groups all over the world Figure 5.4. The low detection frequency of meclofenamic acid (<10% in all the studied samples) reflects the backward trend in consumption of this pain-killer drug, with a market shift towards other, more potent and efficient NSAIDs (e.g. naproxen, ibuprofen, diclofenac) (STATISTA, 2021b). Other pharmaceuticals showed some clear regional trends. For example, mefloquine HCl (antimalarial) was detected at the highest frequency (100%) and concentrations (average = 18.5 ng/g) in Africa, while it was not detected in Europe. A recent international comparison study of PPCPs in river water has also reported the detection of artemisinin (another antimalarial drug) only in Africa (Wilkinson et al., 2022). On the other hand, the detection frequency of gabapentin, a more recent upmarket anxiolytic drug, in Africa was lower than that in Asia, Europe and the Americas.

Overall detection frequencies for the discovered PPCPs ranged from 9% (meclofenamic acid) to 100 % (amoxicillin, sulfamethoxazole, trimethoprim, caffeine, diazepam, oxazepam, ibuprofen and carbamazepine) Figure 5-4. Also, acetaminophen, doxycycline and erythromycin were identified at or above 90% of all the studied samples. This highlights the ubiquitous distribution and extensive use of the two therapeutic groups of antibiotics and NSAIDs. Recent reports have attributed the increased consumption of antibiotics and NSAIDs to the COVID-19 pandemic. Anti-biotics were extensively used as prophylaxis/treatment of 2ry respiratory tract infections associated with the SARS-COV-2 virus, while NSAIDs were administered to treat the associated fever and body ache (Jampani and Chandy, 2021, Russell et al., 2021). While our results do not provide a time trend for PPCPs in sediment before and after the pandemic, the outcomes of the present study provide clear evidence on the ubiquity of Anti-biotics and NSAIDs in freshwater sediment during the COVID-19 era.

Although the observed PPCs profiles in the present study may reflect, to a certain extent, the general human usage profiles of the studied PPCP classes in different continents (*as indicated by dosage prescription statistics*), it should be noted that concentrations of PPCPs in sediment aren't solely dependent on direct input from WWTPs. Other sources of pharmaceutical residues to river sediments have been identified, including leaks and discharge from manufacturing industries, aquaculture and livestock farms, runoff from agricultural lands and landfill leachates (Sadutto et al., 2021, Luo et al., 2011, Sim et al., 2011, Zhou et al., 2021, Fairbairn et al., 2016, Evgenidou et al., 2015) Moreover, the concentrations of PPCPs in sediment can be impacted by multiple factors and processes, including adsorption, photolysis, hydrolysis, biodegradation, bioaccumulation, and sedimentation. This is further compounded by the impact of hydrological factors within the course of the river (i.e., rainfall, flowrate), as well as the sediment particle characteristics (i.e., organic content, particle size, surface area and degree of mineralisation), which have also been reported to play a major role in the sorption of chemical contaminants to sediment particles and their mobilisation along rivers.

Therefore, the fate complexity of PPCPs in river sediment should be taken into consideration upon addressing the global profiles of PPCPs in sediment, which don't rely solely on input sources from human usage (Zhu et al., 2021, Wang et al., 2021, Jaeger et al., 2019, Fairbairn et al., 2016, Hanamoto et al., 2013, Acuña et al., 2015)."

Figure 5-4 Average profiles of target 30 PPCPs presented at percent contributions to Σ30 PPCPs in the studied continents.



5.5. PPCPS Concentrations

The concentration ranges of target PPCPs in each continent are presented in Figures 5-5 to 5-14. Statistical summaries of the measured concentrations in each continent and the full concentration datasets are provide in the supplementary information to this chapter.

5.5.1. Africa

Acetaminophen had the highest concentration (59 ng/g) of all target PPCPs in analysed sediment samples from Africa, Followed by trimethoprim (49 ng/g, sulfamethoxazole (46 ng/g) and ibuprofen (46 ng/g). On the other hand, meclofenamic acid and gabapentin were not detected in African sediment samples Figure 5-5. While samples from only 3 African rivers (Limpopo River, Incmati River (Mozambique) and Mbuluzi River (Eswatini) were investigated in the present study, it should be noted that existing data on PPCPs in African freshwater sediment is scarce and come mainly from South Africa Table SI-1. Matongo et al. reported trimethoprim, ibuprofen and acetaminophen at average concentrations of 88, 66 and 51 ng/g in sediment samples from Msunduzi river (Matongo et al., 2015). Interestingly, A very high concentration of 309 ng/g of diclofenac Na was reported in Umgeni river (Agunbiade and Moodley, 2016), which is substantially higher than the average concentration (33 ng/g) of this NSAID observed in the present study. Carbamazepine was also measured in sediment samples from Msunduzi river at 6 ng/g, which is lower than the average recorded in the present study (14 ng/g).

Overall, the PPCPs profile in the studied African sediment samples was dominated by Antibiotics (38%), followed by NSAIDs (25%), which constituted on average 63% of the total ∑30 PPCPs Figure 5-6. Available data on usage of PPCPs in Africa lends support to these findings. According to the WHO, more than 50% of antibiotics market in Africa is estimated to be available without a doctor's prescription. For example, in Mozambique, out of seventeen pharmacies surveyed, fifteen admitted to distributing antibiotics without a prescription, without requesting a brief clinical history from patients, without providing a clear explanation of how to administer them properly, and/or without providing information on their negative effects (Torres et al., 2020). A study in primary care hospitals of Zambia revealed sulfamethoxazole and trimethoprim were the most frequently prescribed antibiotics (Mudenda et al., 2022). This raises concern over the extensive over the counter (OTC) use of antibiotics in Africa (Do et al., 2021) and calls for further regulation of this class of pharmaceuticals in the continent.

Two studies from South Africa and Mozambique reported acetaminophen as the most commonly used NSAID, while the South African study also ranked acetaminophen, ibuprofen, and diclofenac sodium among the top 20 most frequently prescribed drugs (Ferreira et al., 2014, Osunmakinde et al., 2013). This supports our findings of the substantial average contribution of NSAIDs (25%, including acetaminophen, ibuprofen, and diclofenac sodium) to the PPCPs profile in the analysed African sediment samples.

Figure 5-5 Concentration ranges of target PPCPs in sediment samples from Africa

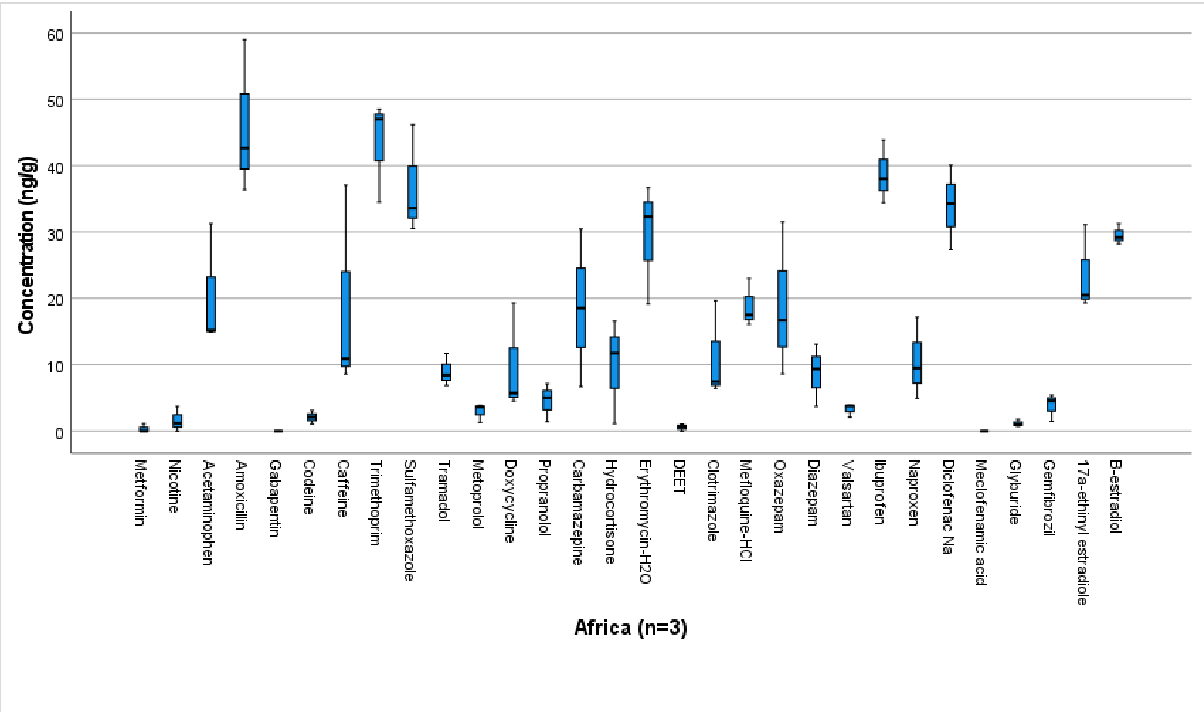
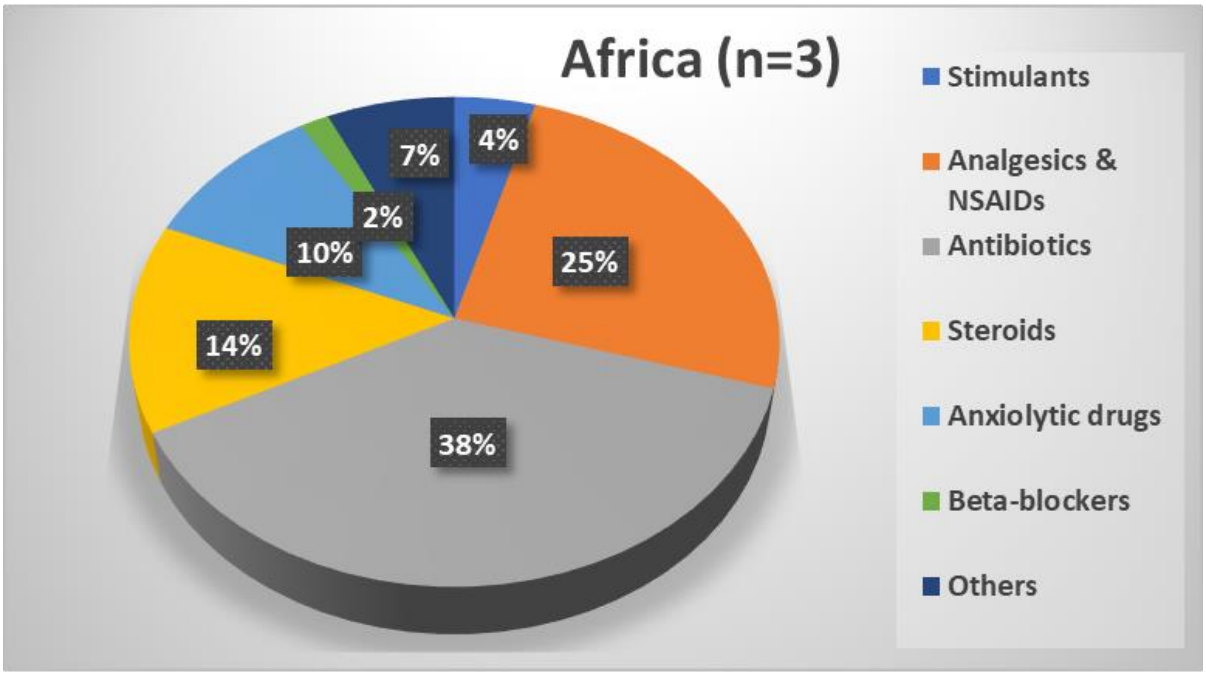


Figure 5-6 Average profile of main PPCPs groups measured in sediment samples from Africa.



5.5.2. Asia

Among the studied Asian sediment samples, Carbamazepine showed the highest concentration (87 ng/g) in Klang River, Malaysia. A previous study of PPCPs in Klang river water did not target Carbamazepine (Omar et al., 2019), but it was reported at similarly high concentration (55ng/g) in sediment from a shallow lake, south China (Zhang et al., 2018). Meclofenamic acid (analgesic) had the lowest concentration (1 ng/g) and was detected only in one sample from the Kali Gandaki River in Nepal. The overall production and use of this pharmaceutical has rapidly declined in the past few years towards more efficient NSAIDs (e.g. ibuprofen, naproxen) (STATISTA, 2021a). This is evident in the higher concentrations and detection frequencies of Ibuprofen (mean = 40 ng/g , DF = 100%), naproxen (mean = 23 ng/g , DF = 85%) and diclofenac Na (mean = 27 ng/g , DF = 77%) in the present study. Few papers have investigated PPCPs in freshwater sediment from China, while the remaining study of PPCPs in Asian sediment came from Pakistan Table SI-1. The Antibiotics, erythromycin and doxycycline, were reported at average concentrations ranging from (0.1 – 385 ng/g) and (9-21 ng/g) in freshwater sediment from different Chinese rivers and lakes including the Yellow river delta Table SI-1. Similarly, the frequently detected trimethoprim and sulfamethoxazole showed broad concentration ranges of (0.2 – 39 ng/g) and (0.2 – 50 ng/g) in Chinese sediment samples with the highest concentrations reported in Taihu lake (Xie et al., 2017, Xu et al., 2014). This is largely in agreement with the concentration ranges of these PPCPs reported in the presented study Figure 5-7.

Overall, the concentrations of target PPCPs in the current study are largely in agreement with available literature from Asia. The PPCPs profile in the studied Asian sediment was dominated by NSAIDS (32%) and antibiotics (22%). This may be partly attributed to more regulations on dispensing antibiotics in Asia compared to Africa, although the enforcement of these regulations in many Asian countries remains questionable (Do et al., 2021). Overall, the concentrations of target PPCPs in the current study are largely in agreement with available literature from Asia. The PPCPs profile in the studied Asian sediment was dominated by NSAIDS (32%) and Antibiotics (22%). Paracetamol (acetaminophen), diclophenac sodium, naproxen, and ibuprofen were ranked among the top 20 OTC drugs in Asia, with India ranked 4th in the world for consumption of these drugs (Statistia.com). Antibiotics are also applied more frequently in the investigated Asian countries. for example, a survey of the distribution patterns of antibiotics in Nepal's private pharmacies reported that one antibiotic was prescribed to 44.7% of patients at public health institutions, which is almost double the WHO-recommended amount of between 20.0 and 26.8%. (Nepal et al., 2019). In Malaysia, an antibiotic was prescribed to 30.8 % of patients in private clinics. The most frequently given antibiotics, comprising 30.7, 23.6, and 16.0% of all antibiotics, were penicillins, cephalosporins, and macrolides, respectively (Ab Rahman et al., 2016). In a study on the use of antibiotics in 517 patients in Northern India clinics, 300 of the screened individuals received antibiotic prescriptions. The two most frequently prescribed antibiotics were ceftriaxone (19.2%) and amoxicillin-clavulanic acid (16.9%) (Kaur et al., 2018). In South Korea, a statistical study revealed the increase of antibiotics use from 23.5 doses/1000 inhabitants in 2007 to 27.7 doses/1000 inhabitants in 2014. The study concluded that inappropriate antibiotic use contributes significantly to antibiotic-resistance, resulting in reduced antibiotic efficacy and increasing physical burden and cost of disease in South Korea (Park et al., 2017). Although there are more regulations on dispensing Antiobiotics in Asia compared to Africa, the enforcement of these regulations in many Asian countries remains questionable (Do et al., 2021).

Figure 5-7 Concentration ranges of target PPCPs in sediment samples from Asia.

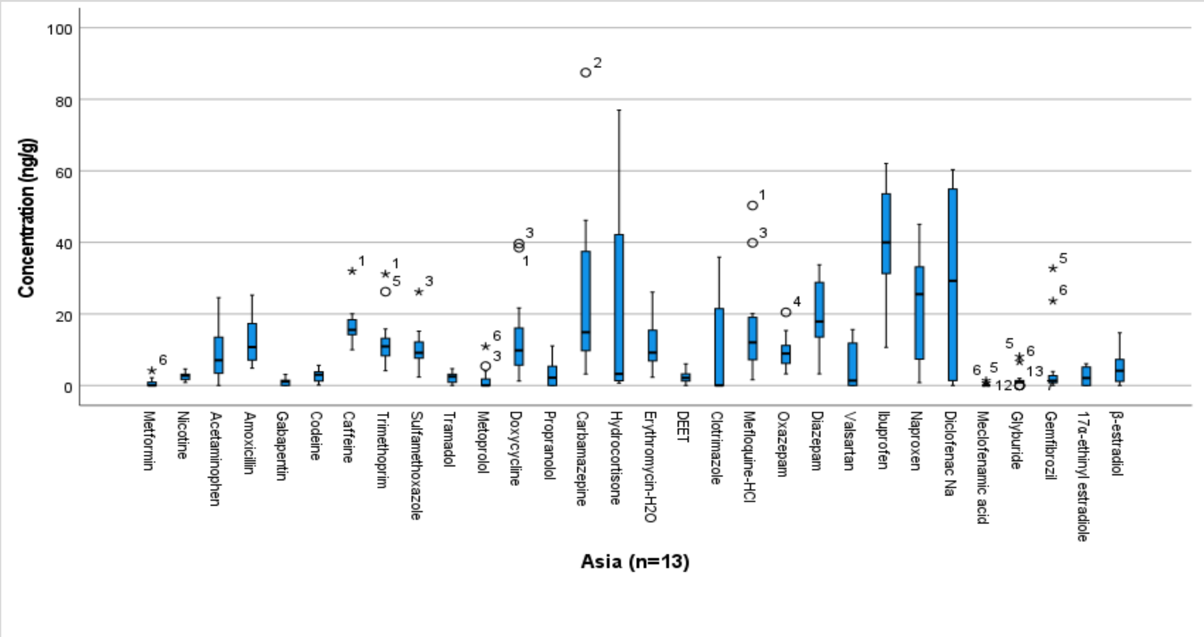
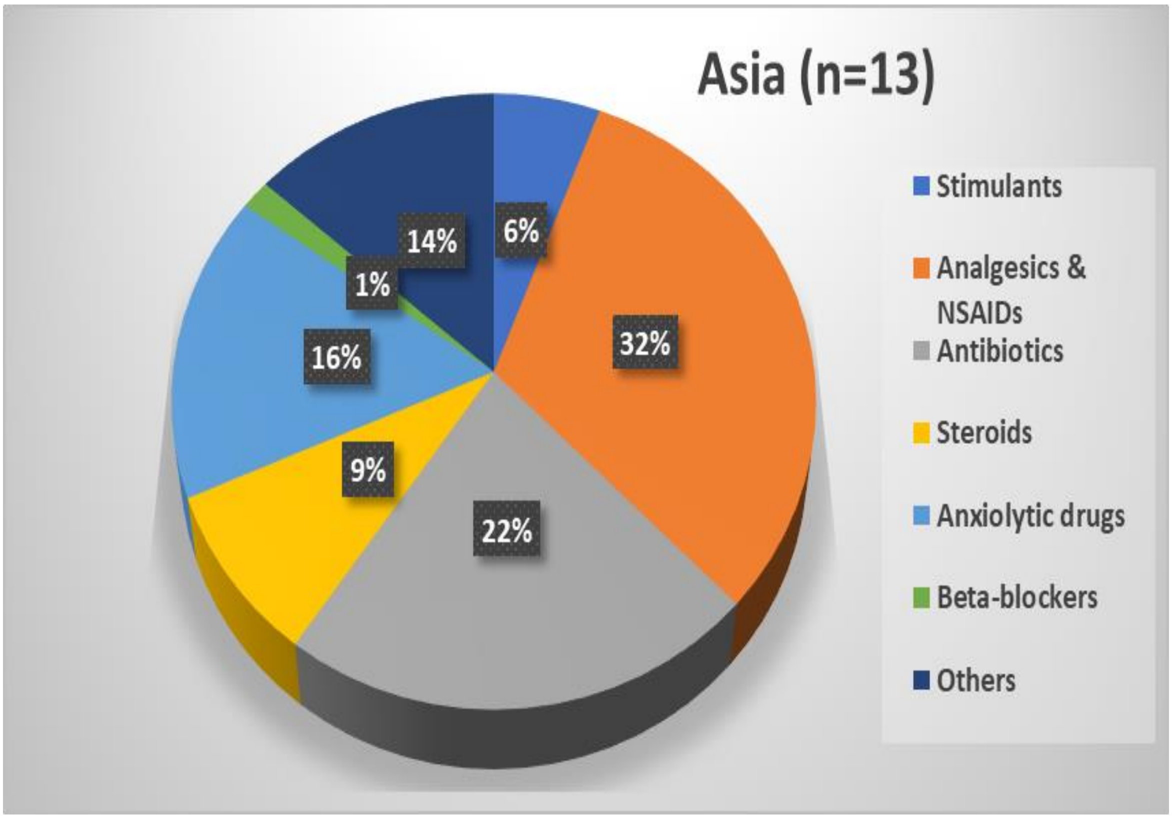


Figure 5-8 Average profile of main PPCPs groups measured in sediment samples from Asia.



5.5.3. Europe

The antibiotic, doxycycline, was measured at the highest concentration (48 ng/g) of all target PPCPs in the studied European sediment samples Figure 5-9. However, the concentrations of antibiotics in European sediment overall were significantly lower (P<0.05) than those measured in Africa and Asia, while indistinguishable from those in the Americas. This may be attributed to more awareness of antibiotic resistance issues in the developed countries, accompanied by more strict regulations over prescribing and dispensing antibiotics in Europe and North America, even in veterinary applications (ROBERTSON, 2021, EFSA, 2021, Petersen et al., 2021). Few studies have reported on PPCPs concentrations in European freshwater sediment, which were mainly from Spain and Scotland Table SI-1. In an earlier in sediment from Iberian rivers, Osario et al. (2015) reported on concentrations of some of our target PPCPs including ibuprofen, diclofenac, naproxen, carbamazepine, and diazepam at generally lower concentrations than the European average reported here, while the measured concentrations for codeine and 17α-ethinyl estradiole were higher than those reported here Table SI-1. A more recent study in sediment from a wetland in Albufera Natural Park, Spain reported similar concentrations of acetaminophen, ibuprofen, diclofenac Na, codeine and naproxen to those measured in the present study (Sadutto et al., 2021). Finally, the study from Scotland reported large variations in concentrations of ibuprofen (<10 – 385 ng/g) and carbamazepine (<1 – 87 ng/g) in sediment samples from 3 Scottish rivers (Langford et al., 2011).

Similar to Asia and Africa, PPCPs profile in European sediment is dominated by antibiotics (34%) Figure 5.10. However, a noticeable difference is the large contribution of Anxiolytic drugs (22%). The contribution of antibiotics to PPCPs profiles observed in the European sediment is in line with their continued large consumption figures. In 2020, the mean total consumption of antibiotics in humans in the EU/EEA was 16.4 daily doses per 1000 inhabitants per day (Statista.com). Interestingly, the use of anxiolytic drugs increased by nearly two and a half times from 2000 to 2020 in 18 European countries, according to data from the Organization for Economic Cooperation and Development (OECD). The average anxiolytics consumption across 18 European countries was 30.5 doses per 1,000 people per day in 2000, rising to 75.3 doses in 2020 (OECD, 2014). This may be attributed to improved awareness of mental health issues leading to increased trends in prescription of anxiolytic drugs observed recently in Europe and North America, which has been further augmented by the lockdown measures during the COVID-19 pandemic (Estrela et al., 2020, Archer et al., 2022, DEL VAYO, 2021).

Figure 5-9 Concentration ranges of target PPCPs in sediment samples from Europe.

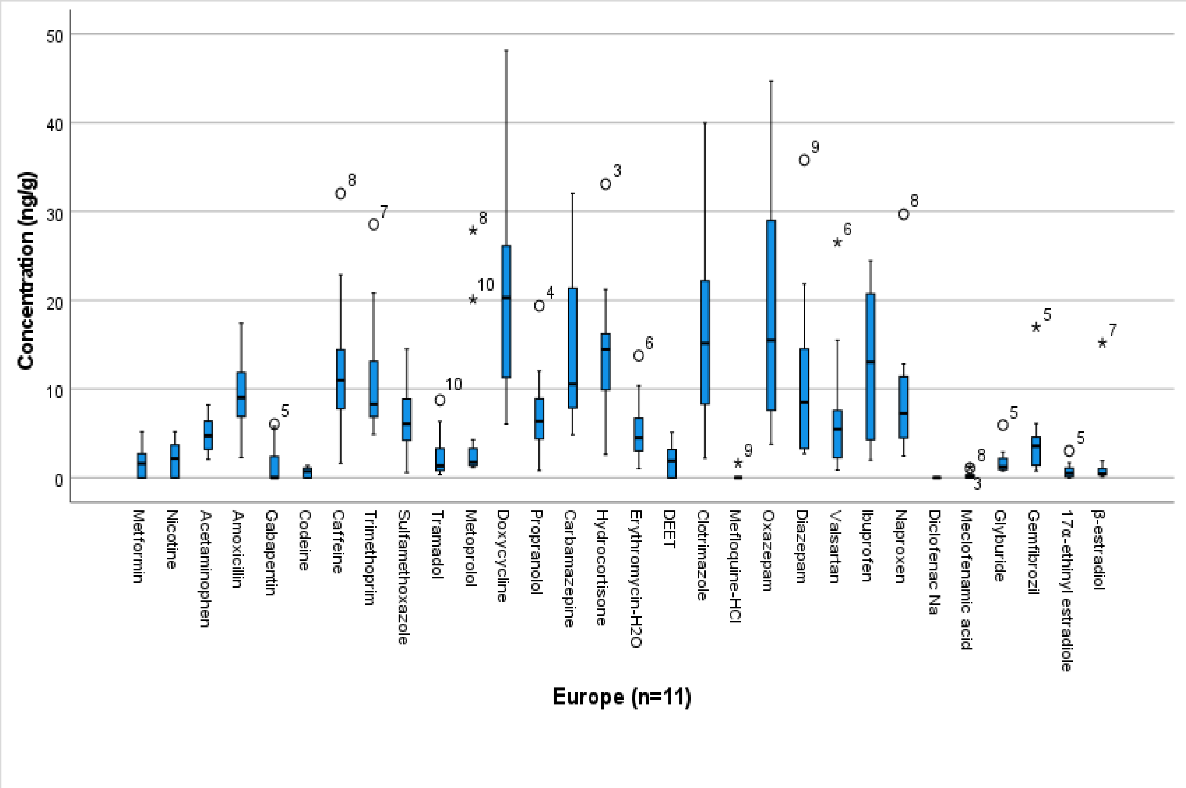
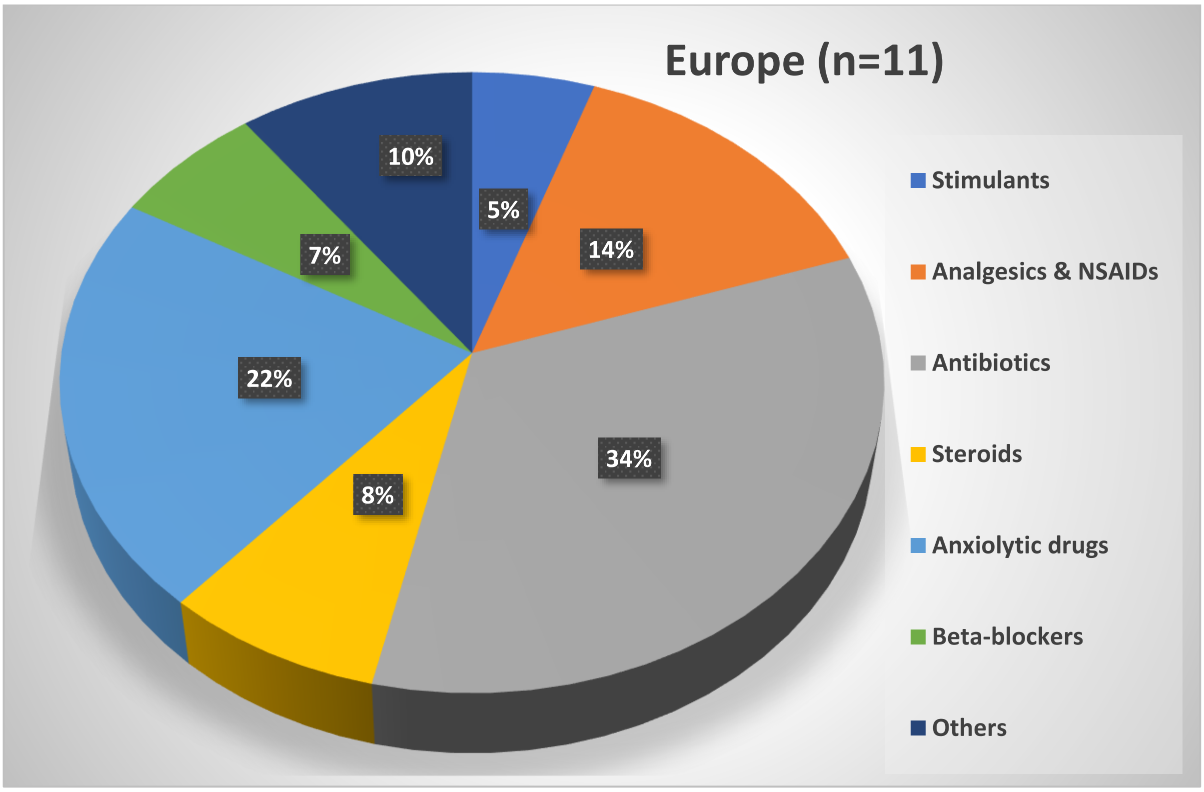


Figure 5-10 Average profile of main PPCPs groups measured in sediment samples from Europe.



5.5.4. Americas

The highest concentration measured in sediment samples from the Americas was for carbamazepine (35 ng/g), followed closely by amoxicillin (33 ng/g) Figure 5-11. Very little is known about PPCPs concentrations in freshwater sediment from North America, while the present study provides the first data from South America Table SI-1. A study of PPCPs in sediment samples from San Francisco Bay reported average concentrations of erythromycin, sulfamethoxazole and trimethoprim at 4, 1 and 18 ng/g respectively (Klosterhaus et al., 2013). Another study of sediment samples from an urban river in Florida measured trimethoprim, acetaminophen and carbamazepine at mean concentrations of 0.8, 5.2 and 33 ng/g (Yang et al., 2015). These concentrations are largely in agreement with those reported in the present study Figure 5-11. Only one sampling location from South America was available for the present study (Paraíba do Sul, Três Rios, Brasil), which precludes any meaningful statistical comparison between concentrations and profiles of PPCPs in South and North America Figure 5-12. Nevertheless, it was clear that concentrations of all 4 anxiolytic drugs (diazepam, oxazepam, carbamazepine and gabapentin) in South America ($\sum_4$ Anxiolytic drugs = 22 ng/g) were lower than in North America (mean $\sum_4$ Anxiolytic drugs = 55 ng/g). Similar to Europe, the sizeable contribution of anxiolytic drugs to $\sum_{30}$ PPCPs in sediment samples from North America may be explained by the enhanced awareness of mental health issues in USA and Canada, combined with increased prescription and usage of these drugs during the Covid-19 lockdown periods (LUHBY, 2020, Garakani et al., 2020).

Overall, PPCPs profile in American sediment was dominated by Anxiolytic drugs (23%) and Antibiotics (22%), followed by NSAIDs (17%), which is more comparable to the European PPCPs profile than those observed in Africa and Asia. In the US, oral antibiotic prescriptions reached 270.2 million in 2016, or 836 doses per 1000 inhabitants per day (King et al., 2019), while in Canada ~ 24 million antibiotic prescriptions were dispensed in 2017 (Thane, 2021). Similar to Europe, 34% rise in anti-anxiety drug prescriptions was observed in the past 2 years, which was attributed mainly to the mental health crisis caused by Covid-19 lock down measures (Express scripts, 2020).

Figure 5-11 Concentration ranges of target PPCPs in sediment samples from the Americas.

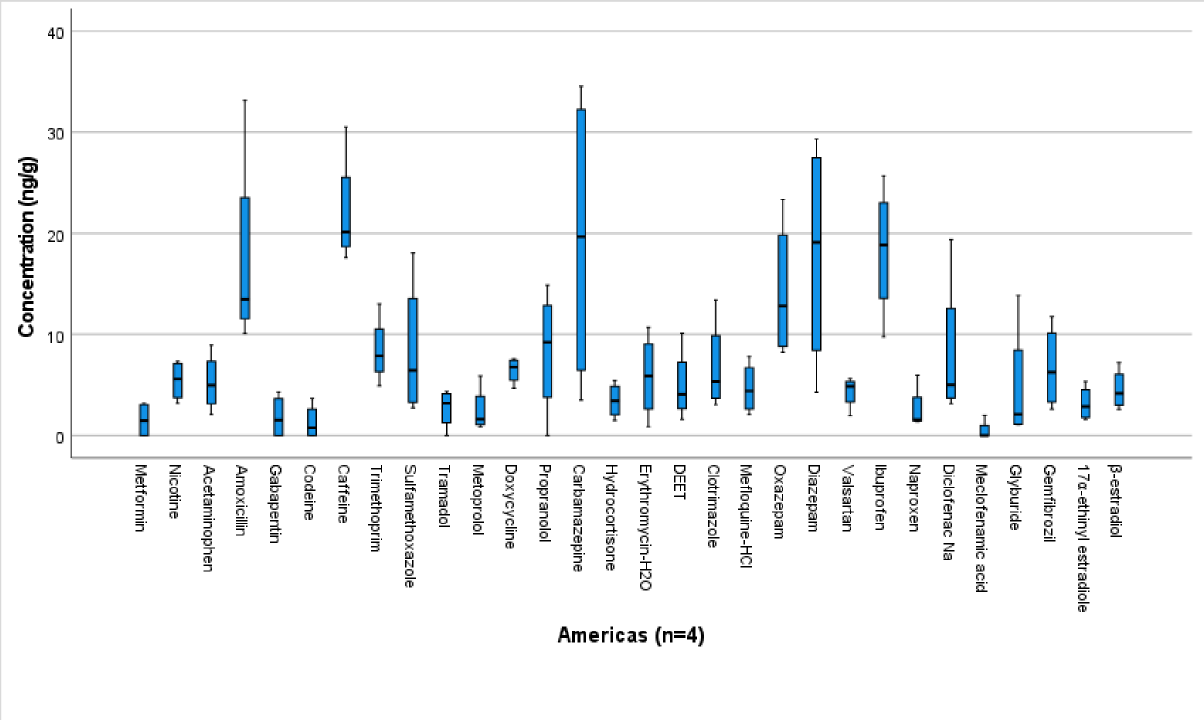


Figure 5-12 Average profile of main PPCPs groups measured in sediment samples from the Americas.

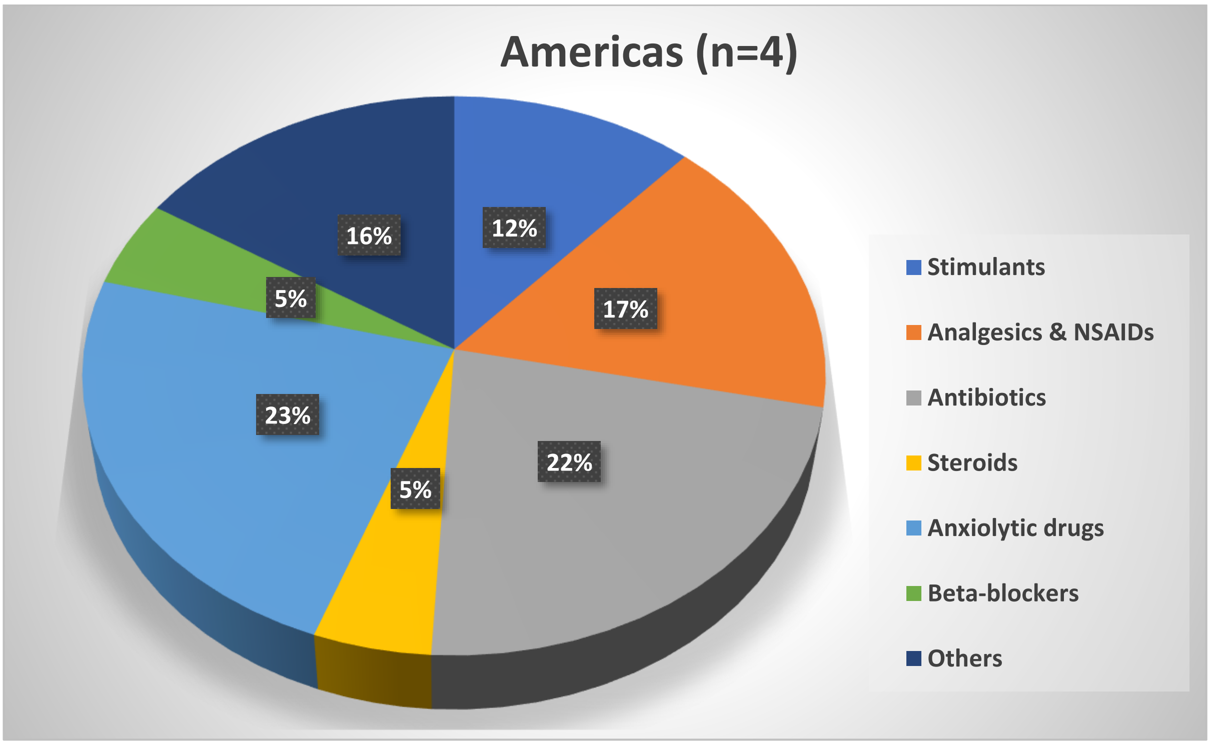
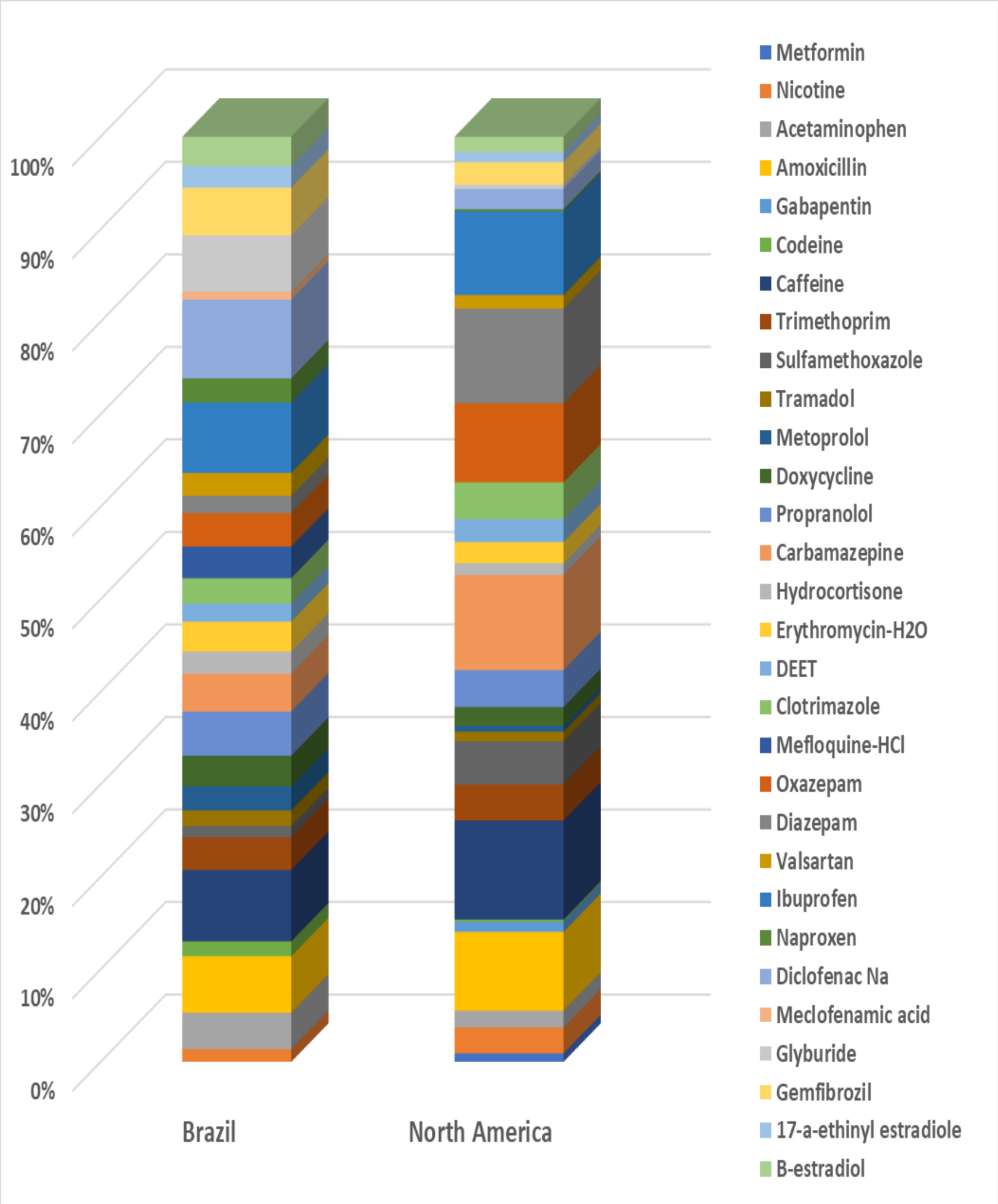


Figure 5-13 Average profiles of target PPCPs in sediment samples from South America (n=1) and North America (n=3).



5.6. Limitations

The main limitation of this study is the small sample size, particularly in Africa and Americas. Ideally a minimum of 10 samples from each continent is desired to achieve a good level of confidence in the results of statistical analysis. However, the collection of samples from different parts of the world was also hampered by the Covid-19 pandemic.

Another issue that could impact the quality of data provided here is the variable transport time from different countries to UoB laboratories. While care has been taken to minimise variation in the sample collection and packing process at source, the variation in transport time was inevitable. All samples were stored in dark containers and protected from light throughout, yet some of the target PPCPs aren't persistent (short half-lives in sediment) and may undergo some degradation during sample transport.

It should also be noted that the sediment samples collected from various rivers and freshwater water lakes from 5 continents in the present study are likely to display large variability in sediment characteristics including: organic carbon (OC), mineral content, dissolved oxygen (DO), particle size and clay/silt/sand/gravel/cobbles content (Hendrix, 2009). While there exist no studies on the impact of sediment characteristics on the concentrations of PPCPs in sediment and/or their binding/sorption to different types of sediment particles, previous studies have highlighted the potential role of sediment characteristics on the binding of other organic contaminants. To illustrate, several studies have documented statistically significant correlations between the concentrations of organic contaminants (polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyls (PCBs), and organochlorine pesticides) and sediment properties including total organic carbon (TOC), particle size distribution, particle surface area, and degree of mineralisation (Landrum et al., 1997, Barakat et al., 2011, Chiou et al., 1998, Arfaeinia et al., 2017, Hong et al., 2012, Chattopadhyay and Chattopadhyay, 2015). Furthermore, Gobas and MacLean (2003) concluded from their study in the

Great Lakes that sediment-water distribution of organic contaminants is not solely a chemical partitioning process but is to a large degree controlled by sediment organic carbon mineralisation processes (Gobas and MacLean, 2003). While sediment characteristics weren't investigated in this thesis, it is strongly recommended that future research in to PPCPs in sediment should assess various sediment characteristics and investigate their role into the sorption/binding of PPCPs to sediment particles.

Nevertheless, the present study provides the first international comparison of 30 widely used PPCPs in freshwater sediment, including the first data from several countries. Trends in concentrations and profiles have been identified and the ubiquitous distribution of 8 pharmaceuticals was confirmed. The impact of Covid-19 on the levels of certain classes of PPCPs (Antibiotics, NSAIDs and Anxiolytic drugs) was highlighted and the need for further regulation of antibiotic use in Africa and Asia has been emphasized.

The current study provides the first international comparison of 30 widely used PPCPs in freshwater sediment, including the first data from several countries. The results provide evidence on the ubiquitous distribution of this class of emerging contaminants in freshwater sediments all over the world. This calls for synchronised international effort, similar to the UNEP Stockholm Convention on Persistent Organic Pollutants, to reduce global contamination levels and mitigate the risk of PPCPs pollution to the environment and humans. Our results have revealed trends in concentrations and profiles of certain PPCPs groups that could be, at least partially, linked to global usage profiles of these compounds. For example, the high contribution of antibiotics to the overall PPCPs profiles in Africa and Asia may be attributed to the lack of regulations on their use and dispensing them as over the counter (OTC) medication without a doctor's prescription. This highlights the need for more regulations on the usage of antibiotics in developing African and Asian countries. Moreover, the impact of COVID-19 lockdown measures on mental health leading to increased used of anxiolytic drugs in Europe and North America was also reflected in higher contribution of anxiolytic drugs to the overall PPCPs profiles in sediment from these two continents. However, it should be noted that PPCPs concentrations and profiles aren't solely reliant on human usage patterns, but are also impacted by multiple processes including degradation, adsorption, bioaccumulation, and sedimentation, as well as sediment characteristics (e.g., organic carbon content, mineralisation, particle size and surface area) and hydrological factors (e.g., flooding, flowrate, rainfall). Therefore, further research is needed to fully understand the fate of PPCPs in the global environment, particularly in sediment.

Chapter 6. Summary and Conclusions.

Pharmaceuticals and personal care products (PPCPs) have received increasing attention in recent years as emerging environmental contaminants that could affect the environment and human health. Pharmaceuticals are substances that have inherent biological activity, and thereby used to treat diseases. These chemicals are frequently excreted/discharged unchanged into the environment. Personal care products are chemicals incorporated into products such as moisturisers, lipsticks, shampoos, hair colours, deodorants, and toothpastes, used to enhance the quality of daily life. PPCPs, as well as their bioactive metabolites, can be delivered directly to the aquatic environment through a variety of pathways, the most common of which is raw and treated sewage as explained in chapter 1.1. In terms of wastewater treatment, none of the widely used conventional methods is suitable for removing all these chemicals.

Through persistence, bioaccumulation, and toxicity, these substances can have an impact on aquatic life once they reach the ecosystem. Persistence refers to the ability of these PPCPs to remain in one or more environmental media for prolonged periods of time. While most PPCPs have short half-lives, monitoring studies have indicated high levels of these chemicals (e.g., antibiotics, anxiolytics) in landfill leachates and effluent-impacted surface water for years. This has been mainly attributed to continuous input of PPCPs to the receiving environmental media, which is termed “pseudo-persistence”. Bioaccumulation is the mechanism of pollutants reaching the food web via all potential exposure pathways and accumulating in the tissues of aquatic biota at higher quantities than the relevant exposure media (water, sediment and soil). PPCPs have been measured in fish and other aquatic organisms at higher concentrations than water in numerous investigations. PPCPs can induce acute and chronic toxicity in organisms. This is caused by the ability of individual and mixtures of PPCPs to react/block/induce chemical receptors in exposed organisms causing a range of adverse effects (e.g., alter homeostasis, endocrine disruption, reproductive toxicity and death). All these PPCP risks in the aquatic environment are discussed in chapter 1.2.

According to numerous studies, PPCPs have been discovered in a range of environmental media (water, sediment, soil and organisms) all over the world. PPCPs have been detected in the environment across continents as well as in various regions within the same country. The majority of research on PPCPs has concentrated on wastewater and surface water, including drinking water sources, with a far lower number of investigations on sediments and soil as explained in chapter 1.3. Even though PPCPs have been detected in relatively high amounts in the environment, some of them can be degraded or depleted through a number of mechanisms, such as, hydrolysis, photolysis, biodegradation, and mineralization as described in chapter 1.4.

Ultrasound-assisted extraction (UAE) is the most common method for extracting PPCPs from different environmental matrices, followed by solid phase extraction (SPE) for clean up as discussed in chapter 1.5. Microwave-assisted extraction accelerated solvent extraction Pressurized Liquid Extraction and QuEChERS extraction were also applied for extracting PPCPs in solid environmental matrices but to a lesser extent than UAE-SPE combination. For quantitative analysis of several PPCPs in sediment and soil samples, LC/MS techniques such as HPLC-MS/M, UPLC-MS/MS, UPLC-Orbitrap/MS, and UPLC-Q-TOF/MS are generally the methods of choice.

This thesis comprises six chapters including, introduction (chapter 1), methodology (chapter 2), followed by three experimental chapters (3,4 and 5) and finally the summary and conclusions chapter (chapter 6). Below are the key findings of this research work:

Chapter 2:

- A multi-residue analytical method for extraction, clean-up and quantification of 30 PPCPs in sediment has been optimised and validated. The extraction method is based on Ultrasonic Assisted Extraction (UAE) of target PPCPs using Acetonitrile/deionized water (1:1) solvent mixture. Clean up was conducted using bonded C_{18}-Silica Oasis MCX cartridges. Quantification was achieved using Ultraperformance Liquid Chromatography (UPLC) coupled to high resolution mass spectrometry (HRMS).
- Due to availability/accessibility reasons throughout the period of study, two UPLC-HRMS instruments were applied in this thesis. The first is a Q-Exactive Plus Orbitrap high resolution mass spectrometer (Thermo Fisher Scientific, Bremen, Germany) equipped with a heated electrospray ionisation (HESI) ion source. The second is an AB SCIEX triple TOF 5600+ MS/MS system (AB Sciex LLC, USA) equipped with Duo-Spray ion source. All instrument/compound specific parameters were optimised for each instrument. Method validation and QA/QC protocols were conducted with recoveries at 3 concentrations levels ranging between 74-113% for all 30 analytes.

Chapter 3

30 Pharmaceuticals and personal care products (PPCPs) were investigated in water, sediment and soil from River Tame, River Severn, Coventry canal and Birmingham & Worcester canal. PPCPs partitioning between the aqueous phase and sediment was investigated. Soil samples were collected from the surrounding area of the four examined waterways to evaluate the relationship between PPCPs levels in sediment/water and the surrounding soil/run-off areas.

- Amoxicillin, gabapentin, caffeine, propranolol, DEET, naproxen, diclofenac Na, meclofenamic acid and β-estradiol were detected in sediment in all studied locations, whereas metformin, nicotine, codeine, sulfamethoxazole, metoprolol, doxycycline, carbamazepine, erythromycin-H2O, clotrimazole, mefloquine-HCl, oxazepam, diazepam, valsartan, ibuprofen and glyburide were not found in any analysed sediment samples. The highest concentration in sediments was 43.6 ng/g of Diclofenac, followed by 25.6 ng/g of Propranolol, 23.6 ng/g of Gemfibrozil, and 17.2 ng/g of Trimethoprim.
- Σ_{30} PPCPs concentrations detected in sediments were 129, 79, 62 and 110 ng/g dry weight (dw) in River Tame, Coventry Canal, River Severn and Birmingham & Worcester canal, respectively.
- The distribution profiles of target PPCPs in the studied sediment samples revealed the PPCPs with highest relative contribution were in River Tame: propranolol (19.6%), diclofenac (18%); in River Severn: diclofenac Na (31.4%) and gabapentin (22.2%); in Coventry canal: diclofenac (54.8 %), gemfibrozil (12.5%); in Birmingham & Worcester canal: diclofenac Na (35.4%), gemfibrozil (21.5%).
- The octanol-water partition coefficient (Log K_{OW}) of target PPCPs detected in water and sediment from the same site, and their experimentally measured sediment–water distribution coefficient (Log K_P)., showed a positive correlation. In the Tame and Severn rivers, the correlations between Log K_{OW} and Log K_P were significant at 95% confidence level ($P < 0.05$) whereas in the Coventry and Birmingham & Worcester canals, the correlations were significant at 90% confidence level ($P < 0.1$).
- In the River Tame, River Severn, Coventry canal, and Birmingham & Worcester canal, Σ_{30} PPCPs concentrations measured in soil samples were 36.0, 22.2, 4.3, and 4.5 ng/g,

respectively. The high concentrations of PPCPs in soil from the River Tame. Run-off area may be attributed to the sampling site's proximity to a farmland.

- The risk of the measured target PPCPs in sediment on aquatic biota was assessed using a risk quotient approach. The estimated RQ values of amoxicillin, caffeine and 17α-ethinyl estradiole in bacteria were higher than 1 (ranged from 8 to 262) in the four studied locations, indicating high risk to freshwater bacteria. Conversely, RQ values for amoxicillin and DEET in algae, and Gabapentin in fish were much lower than 0.01 (range from 10 -4 to 10-5) in the four studied locations, suggesting no risk to these aquatic organisms at the measured concentrations.

Chapter 4

The seasonal variation of target PPCPs was investigated in sediments form UK rivers (River Sowe, River Severn, and River Tame) and canals (Worcester & Birmingham Canal). Over the course of a year, measurements were collected on a monthly basis. Over the four seasons, the individual and total concentrations of target PPCPs are compared. The effect of wastewater treatment plants (WWTPs) on PPCP contamination in sediment was evaluated using statistical comparisons of monthly samples obtained upstream and downstream of WWTPs in the three rivers investigated.

- The sediment samples from the river Sowe were the most polluted with target PPCPs over the studied period (average Σ_{30} PPCPs over 12 months = 276 ng/g), while the Worcester & Birmingham canal was the least polluted (average $\sum_{30}$PPCPs over 12 months = 184 ng/g). This was attributed to the lack of direct input source (WWTP) in the Worcester & Birmingham canal, while the each of the 3 sampled rivers had a WWTP.
- Large variations in $\sum_{30}$PPCPs were recorded over the course of a year with coefficients of variation (CV%) of 116 %, 119 %, 120 %, and 133 % in the river Sowe, river Tame, river Severn, and Worcester & Birmingham Canal, respectively.

- In all studied locations, statistical analysis showed significant difference ($P < 0.05$) between $\sum_{30}$PPCPs in Summer (highest) compared to Autumn (lowest). Investigation into the contributing factors to this observation revealed a combination of lower river flowrate and less rainfall during summer may contribute to the higher concentrations of PPCPs in this season.
- River Sowe
    - In June, anxiolytic medications, gabapentin, carbamazepine, and diazepam, were found the most abundance, with a mean value of 54 ng/g in sediment samples.
    - In January and May, the most common PPCPs were steroids (17-ethinyl estradiole, β-estradiol, and hydrocortisone) with mean concentrations of 61 and 54 ng/g, respectively.
    - In February, March, April, July, October, and November, analgesics and NSAIDs, such as acetaminophen, ibuprofen, naproxen, diclofenac, codeine, tramadol, and meclofenamic acid, were the most prevalent, with mean concentrations of 61, 47, 84, 65, 78, and 47 ng/g, respectively.
    - In January, August, and September, antimicrobials (amoxicillin, doxycycline, erythromycin, trimethoprim, sulfamethoxazole, and clotrimazole), had the highest mean concentrations of 72, 161, and 43 ng/g, respectively.
- River Tame
    - In January and May, steroids, like, 17α-ethinyl estradiole, β-estradiol and hydrocortisone, were the dominant PPCPs in sediment samples, with mean concentration of 56 and 35 ng/g, respectively.
    - In March, stimulant drugs (caffeine and nicotine) had the greatest quantities, with mean concentrations of 36 ng/g.

- In April and July, anxiolytic drugs, such as, Diazepam, Oxazepam, Gabapentin, and Carbamazepine, had the greatest concentrations of target PPCPs, with mean concentration of 52 and 56 ng/g, respectively.
- In August and September, antibiotics, amoxicillin, doxycycline, erythromycin-H2O, trimethoprim, sulfamethoxazole and clotrimazole, were the highest concentrations of target PPCPs, with mean concentration of 162 and 44 ng/g.
- in December, February, June, October and November, analgesics and NSAIDs dominated at 31, 59, 34, 12 and 19 ng/g, respectively.

- River Severn
  - In December (20 ng/g), March (41 ng/g), April (55 ng/g), July (84 ng/g), August (107 ng/g), October (69 ng/g) and November (22 ng/g), analgesics and NSAIDS dominated PPCPs profiles in sediment.
  - In January (33 ng/g), February (25 ng/g), May (57 ng/g), July (31 ng/g) and September (32 ng/g), antibiotics were dominated by.
- Worcester & Birmingham Canal (Uni Canal)
  - In November, stimulant drugs had the highest concentration at mean concentrations of 25 ng/g.
  - in January (20 ng/g), February (31 ng/g), April (35 ng/g), June (80 ng/g), July (89 ng/g), August (67 ng/g) and September (54 ng/g), Analgesics and NSAIDs were the dominant PPCPs in sediment samples.
  - in December (14 ng/g), March (20 ng/g), May (39 ng/g) and October (25 ng/g), antibiotics were dominated sediment samples.
- The impact of WWTP on PPCPs concentrations in sediment was investigated by comparing the concentrations of target analytes in sediment samples collected upstream and downstream

of WWTPs effluent discharge points to the rivers SOWE, TAME and SEVERN. A paired t-test comparing the means of $\sum_{30}$ PPCPs up and downstream from the WWTP over 12 months monitoring programme revealed significantly high concentrations of $\sum_{30}$ PPCPs downstream of the WWTPs in all the studied locations. Our results confirm the role of WWTP as important sources of PPCPs pollution in UK river sediment and highlight the inefficient removal of PPCPs from wastewater by conventional wastewater treatment methods.

Chapter 5

The concentrations and profiles of 30 PPCPs were examined in 31 sediment samples obtained from rivers and freshwater lakes in 13 countries (5 continents) all over the world. The level of contamination and prevalence of different PPCPs groups were evaluated using detection frequencies and relative contribution to $\sum_{30}$ PPCPs in the studied locations.

- The highest $\sum_{30}$ PPCPs concentration in sediment was reported in the Klang river in Malaysia, at 459 ng/g, while the lowest $\sum_{30}$ PPCPs concentration was detected in the Detriot River in the United States, at 159 ng/g.
- The measured average Σ_{30} PPCPs in sediment samples from Africa were significantly higher (using analysis of variance with Tukey post-hoc test) than those from the other continents. Furthermore, average Σ_{30} PPCPs in Asian sediment was significantly higher than those from European and the American sediments, while there were no significant differences between the latter two continents.
- Amoxicillin, caffeine, trimethoprim, sulfamethoxazole, carbamazepine, oxazepam, diazepam and ibuprofen were detected in all of the sites investigated.
- In Africa, antibiotics and NSAIDs dominated the PPCPs profile in the sediment samples investigated, accounting for 38% and 25% of Σ_{30}PPCPs. Acetaminophen (59 ng/g),

trimethoprim (49 ng/g), sulfamethoxazole (46 ng/g), and ibuprofen (46 ng/g) displayed the highest concentrations in sediment, while meclofenamic acid and gabapentin were not identified in any of the studied samples. The elevated concentrations and detection frequencies of Antibiotics raise concern over the extensive use of antibiotics over the counter in Africa and highlights the need for further regulation of these pharmaceuticals in the continent.

- In Asia, NSAIDS and Antibiotics dominated the PPCPs profile in the studied sediment, accounting for 32% and 22% of Σ_{30}PPCPs, respectively. Carbamazepine (87 ng/g) was determined at the highest concentration, whereas meclofenamic acid (1 ng/g) had the lowest concentration. The lower contribution of antibiotics to Σ_{30}PPCPs compared to Africa may be partly explained by more regulations on dispensing antibiotics in Asia compared to Africa, although the enforcement of these regulations in many Asian countries remains questionable.
- In Europe, antibiotics and Anxiolytic drugs dominated the PPCPs profile, accounting for 34% and 22% of Σ_{30}PPCPs, respectively. Doxycycline (48 ng/g) was measured at the highest concentration in sediment samples, while mefloquine-HCl (anti-malarial) was not detected.
- In America, anxiolytic drugs and antibiotics dominated the PPCPs profile, accounting for 23% and 22% of Σ_{30}PPCPs, respectively. Carbamazepine (35 ng/g) and amoxicillin (33 ng/g) were the highest concentration reported in America's sediment samples, while meclofenamic acid (2 ng/g) had the lowest concentration.
- The observed increase in anxiolytic drugs concentrations and detection frequencies in Europe and North America may be attributed to improved awareness of mental health issues; leading to increased trends in prescription of these drugs in Europe and North America, which has been further augmented recently by the lockdown measures during the COVID-19 pandemic.

Research gaps and future perspectives

The findings of this study revealed the ubiquitous distribution of several PPCPs in freshwater sediment. This raises concern over the potential adverse impacts of these emerging contaminants on aquatic biota and humans (via drinking). Meanwhile, the present study identified certain areas and research gaps, where more research is required to fully understand the fate and behaviour of PPCPs, as well as accurately assessing their risk to the environment and humans.

- There is a large imbalance in the volume and extent of research on PPCPs, whereas most studies are focused on water (the dissolved phase). More research is required to elucidate the occurrence, profiles, behaviour, and fate of PPCPs in other environmental media including sediment, soil and sewage sludge.
- The main point of concern regarding PPCPS is their inherent biological activity and ability to target particular metabolism, enzymatic, or cell-signalling mechanisms at low concentrations. However, very little is known about the toxicological endpoints of PPCPs in non-target organisms, particularly in the non-dissolved phase. In the present study, the lack of predicted no effect concentration (PNEC) levels of the studied PPCPs in sediment hampered accurate risk assessment of target chemicals. More research is needed into the acute and chronic toxicity of PPCPs in solid environmental matrices (sediment, soil and sludge) to enable accurate risk assessment of individual and groups of PPCPs in these environmental compartments.
- Presently, relatively little is understood about the seasonal and temporal variations of PPCPs in the aquatic environment. Most available studies, even in water, report on concentrations of different chemicals at a certain point in time. More research is required to understand the seasonal variability in concentrations and profiles of PPCPs, in addition to identifying the factors influencing such variability (e.g., rainfall, temperature, usage profiles) in different

geographical regions and climates. This is of particular importance in African countries, where very little is currently known.

- Although the available literature document strong associations between sediment concentrations of legacy organic contaminants (e.g., PAHs, PCBs) and sediment characteristics, very little is known on the impact of sediment properties (e.g., organic content, particle size, particle surface area, and mineralisation) on the sorption/binding of PPCPs onto sediment particles, and ultimately on their concentrations in sediment. Therefore, it is strongly recommended that future studies on PPCPs in sediment should also investigate sediment properties and study their potential impact on the measured PPCPs levels in sediment.
- Antibiotics is a class of PPCPs that is of prime concern lately due to the increasing trend of anti-microbial resistance. Our results show the prevalence and abundance of antibiotics in freshwater sediment from 5 continents. More research is needed to investigate the toxicological impacts of this class on sediment biota, and its link to antibiotic resistance. Comprehensive studies on antibiotic groups (combined by structure similarity and mode of action such as: macrolides, tetracyclines, sulpha drugs…etc) should address the impact on antibiotic resistance, as well as the PNEC values in sediment bacteria.
- A major issue with PPCPs research, as with other emerging chemical contaminants, is that most risk assessment studies are conducted on individual chemicals. However, actual exposures in real life occur to a mixture of these chemicals. Notwithstanding the complexity of this issue, more research is required into elucidating the risk of chemical mixtures of PPCPs in the environment. Recent advances in analytical chemistry, particularly UPLC-HRMS, should assist this goal via multi-compound monitoring and non-target analysis approaches. Recommended approaches include initial studies focusing on related groups of chemicals. In

this respect, our results suggest that antibiotics and NSAIDs should be prioritised due to their abundance in freshwater sediment.

- Looking ahead, it’s important to consider potential solutions to PPCPs pollution. It’s emphasized in the present study, in agreement with previous research, that wastewater treatment plants (WWTPs) are a major source of PPCPs to the aquatic environment. Further research should be conducted to identify environmental-friendly, low cost and energy-efficient methods for efficient removal of PPCPs from wastewater.

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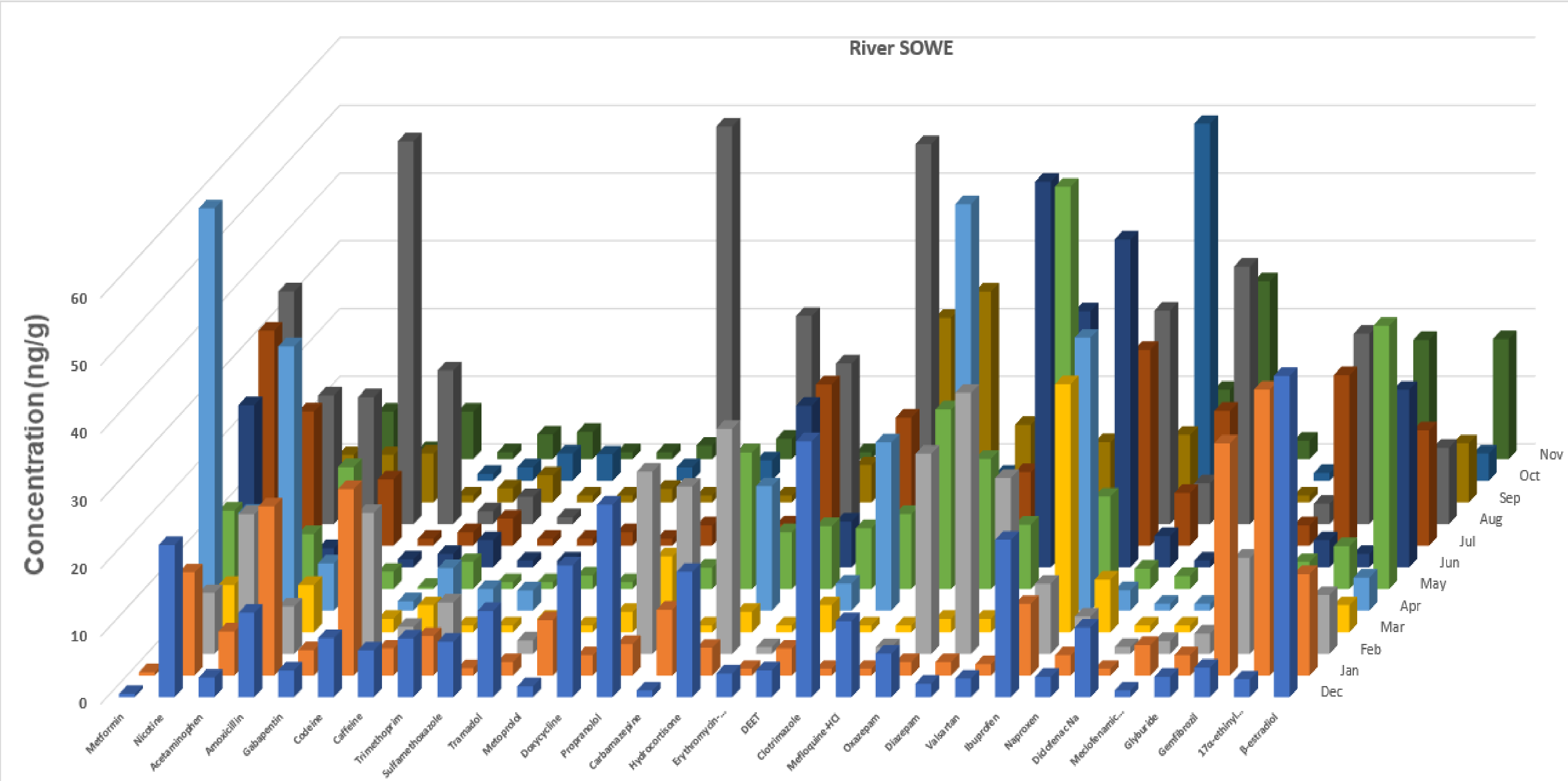
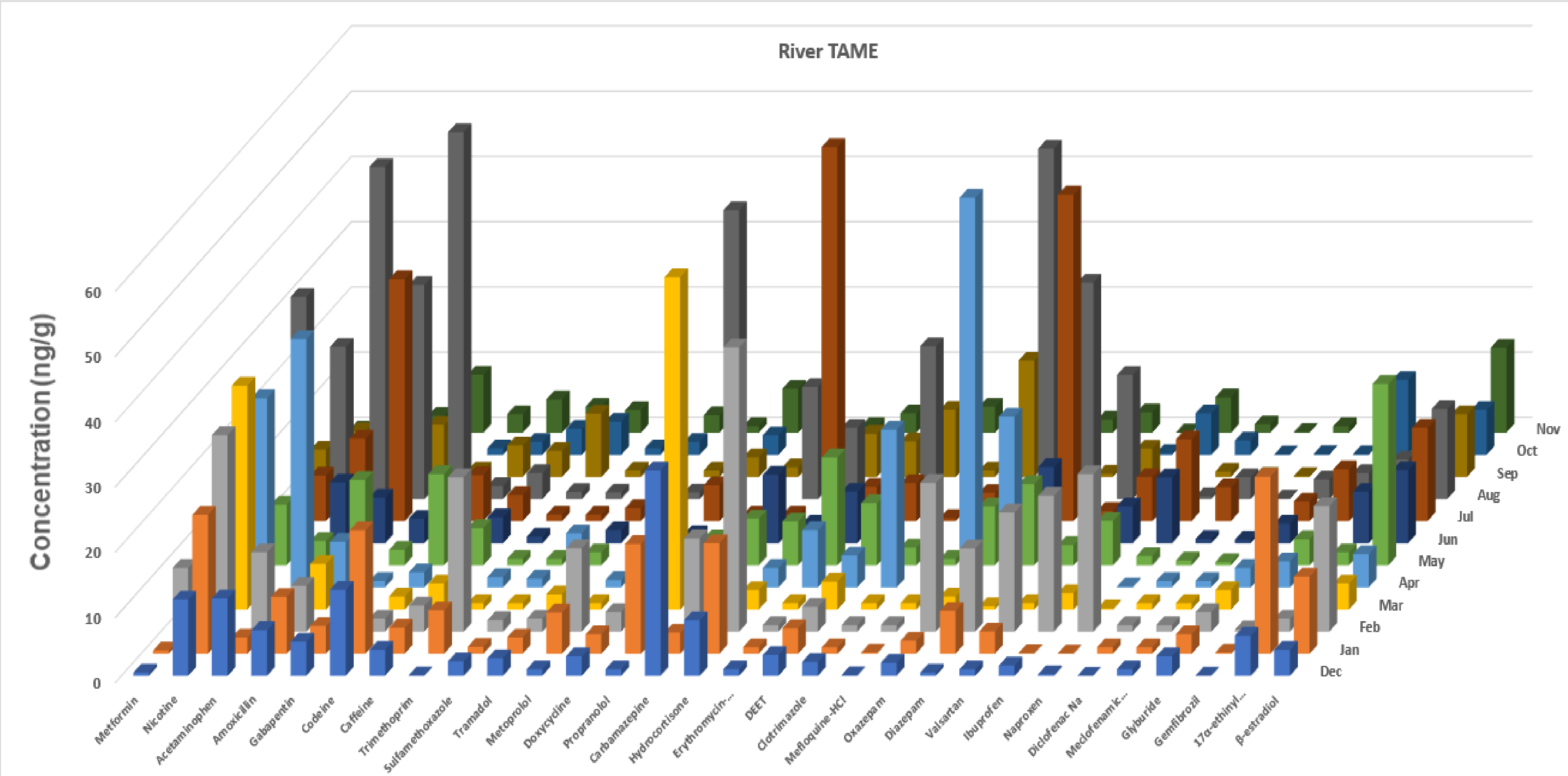
Appendix

Figure SIV-1: Profiles of target PPCPs in 4 studied locations over 12-mont monitoring programme.





River TAME
Concentration (ng/g)
0
10
20
30
40
50
60
Metformin
Nicotine
Acetaminophen
Amoxicillin
Gabapentin
Codeine
Caffeine
Trimethoprim
Sulfamethoxazole
Tramadol
Metoprolol
Doxycycline
Propranolol
Carbamazepine
Hydrocortisone
Erythromycin-...
DEET
Clotrimazole
Mefloquine-HCl
Oxazepam
Diazepam
Valsartan
Ibuprofen
Naproxen
Diclofenac Na
Meclofenamic...
Glyburide
Gemfibrozil
17α-ethinyl...
β-estradiol
Dec
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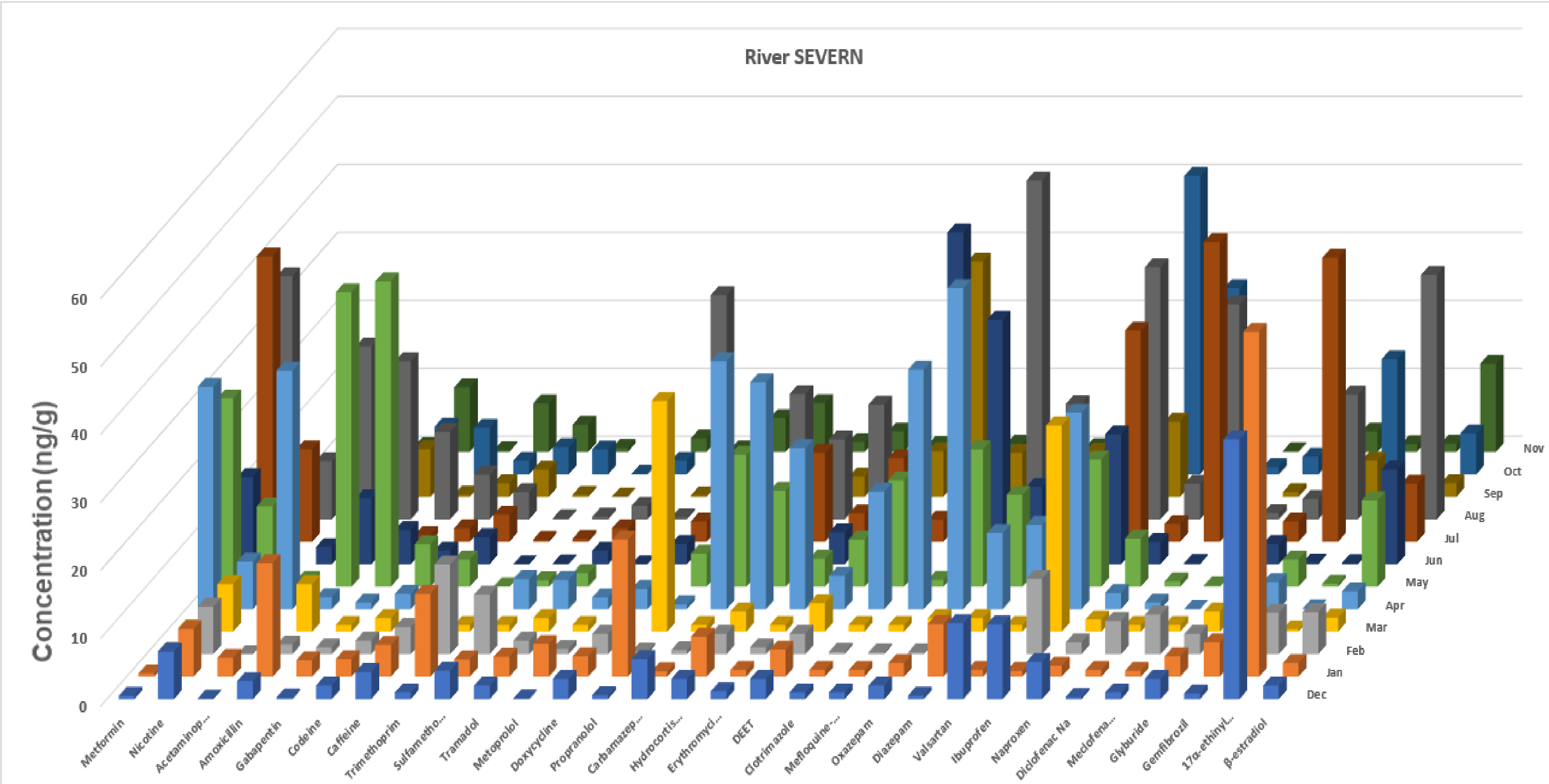
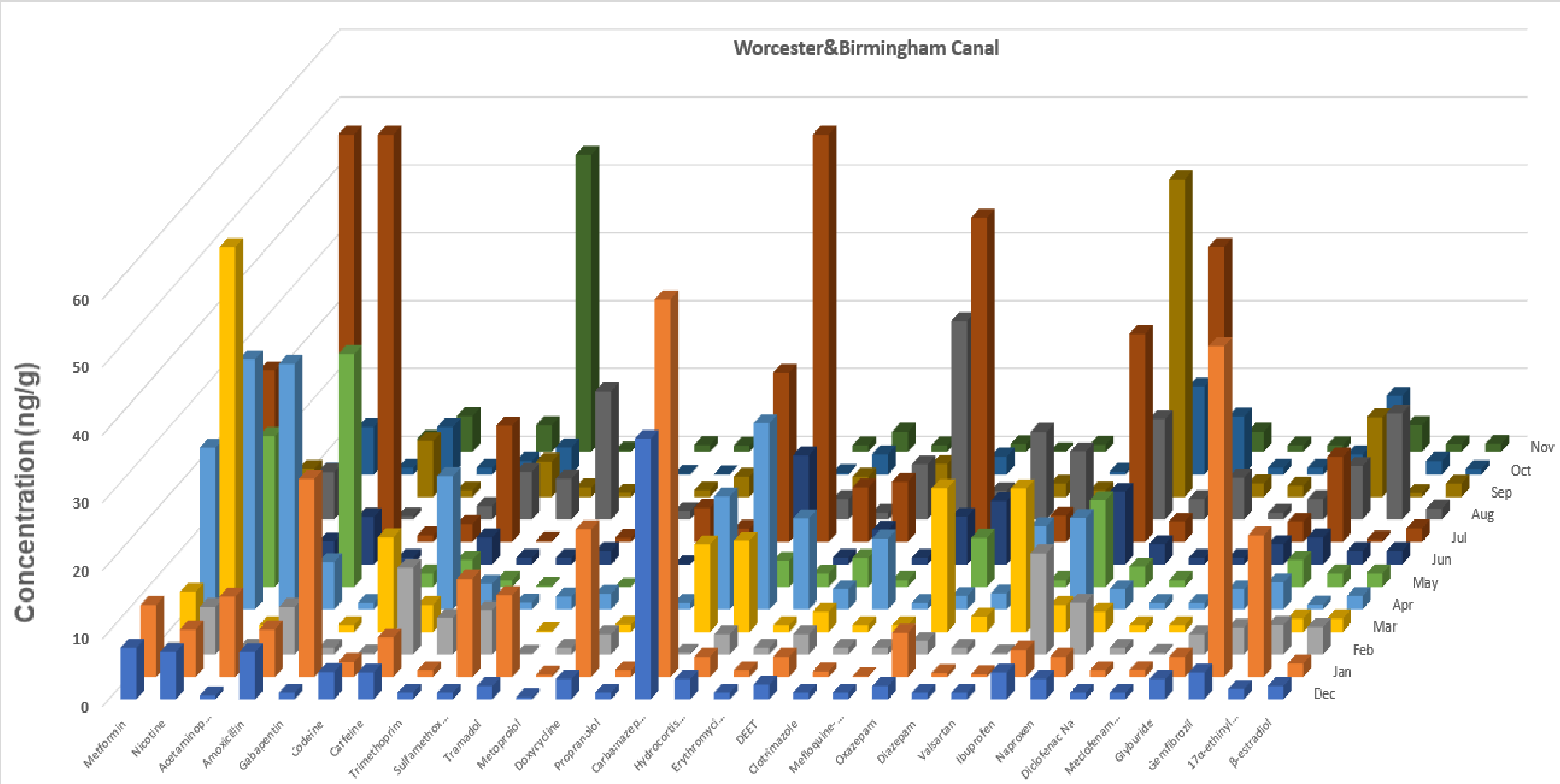


River SEVERN
Concentration (ng/g)
0
10
20
30
40
50
60
Metformin
Nicotine
Acetaminop...
Amoxicillin
Gabapentin
Codeine
Caffeine
Trimethoprim
Sulfametho...
Tramadol
Metoprolol
Doxycycline
Propranolol
Carbamazep...
Hydrocortis...
Erythromyci...
DEET
Clotrimazole
Mefloquine-...
Oxazepam
Diazepam
Valsartan
Ibuprofen
Naproxen
Diclofenac Na
Meclofena...
Glyburide
Gemfibrozil
17α-ethinyl...
β-estradiol
Dec
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov



Worcester&Birmingham Canal
Concentration (ng/g)
0
10
20
30
40
50
60
Metformin
Nicotine
Acetaminop...
Amoxicillin
Gabapentin
Codeine
Caffeine
Trimethoprim
Sulfamethox...
Tramadol
Metoprolol
Doxycycline
Propranolol
Carbamazep...
Hydrocortis...
Erythromyci...
DEET
Clotrimazole
Mefloquine-...
Oxazepam
Diazepam
Valsartan
Ibuprofen
Naproxen
Diclofenac Na
Meclofenam...
Glyburide
Gemfibrozil
17α-ethinyl...
β-estradiol
Dec
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov

Figure SIV-2: Combined Profiles of target PPCPs in 4 studied locations over 12-mont monitoring programme.

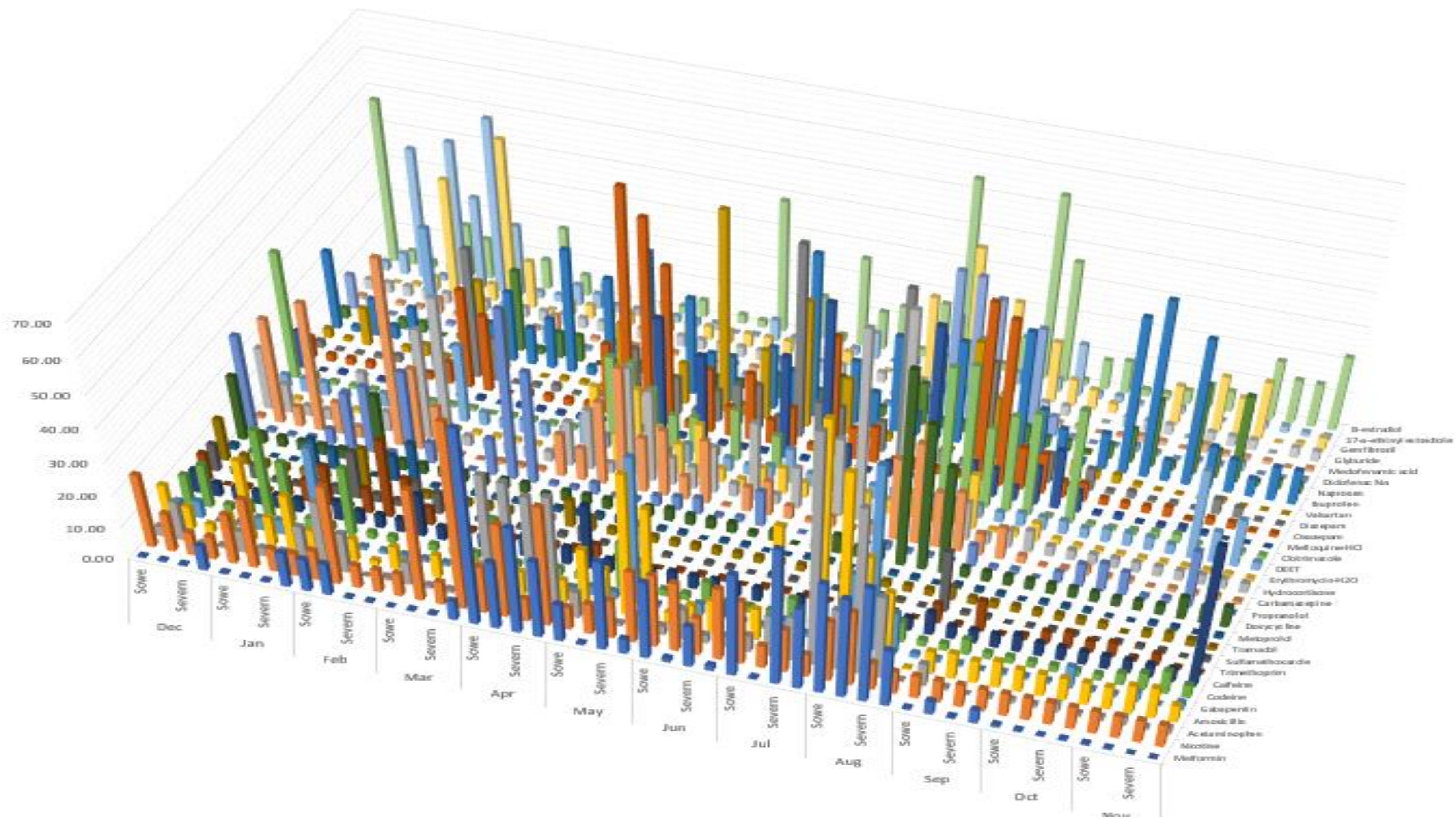


Figure SIV-3: Average monthly variation in ∑30 PPCPs concentrations in the 4 studied locations.

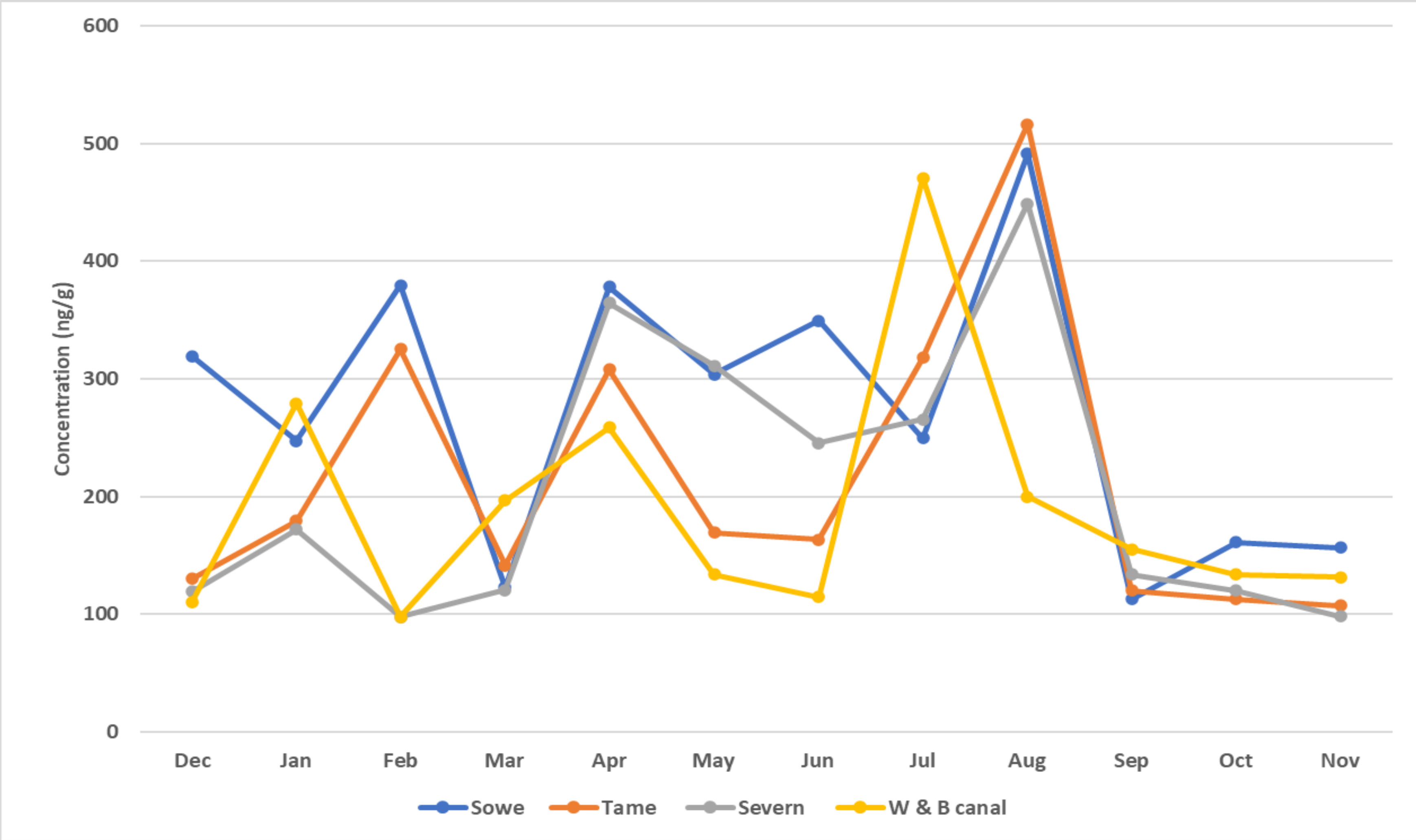


Table SIV-1: Concentrations of target PPCPs in the river SOWE.

PPCPs	Sowe River / Sediment (ng/g)																							
	Dec		Jan		Feb		Mar		Apr		May		Jun		Jul		Aug		Sep		Oct		Nov	
	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream
Metformin	1.80	2.60	<LOQ	<LOQ	4.87	5.35	<LOQ	<LOQ	11.13	24.22	11.16	15.24	15.11	21.85	6.57	9.16	9.29	11.63	<LOQ	<LOQ	0.47	2.43	5.96	14.44
Nicotine	8.53	16.43	8.23	15.24	14.82	33.86	0.93	2.05	11.44	22.27	8.37	6.62	7.88	7.25	5.88	12.26	10.98	21.81	2.88	10.27	0.61	0.08	0.12	0.30
Acetaminophen	18.29	29.89	5.95	4.09	22.04	35.48	4.91	9.28	16.19	34.55	10.54	9.96	6.08	10.17	10.06	12.11	34.39	60.38	23.54	39.26	2.41	2.58	1.85	2.41
Amoxicillin	13.50	15.44	26.28	25.65	<LOQ	4.81	0.59	0.97	6.74	10.74	1.97	4.13	4.79	6.41	17.83	16.60	36.77	53.05	6.07	8.32	3.45	2.27	5.13	8.65
Gabapentin	1.91	6.02	3.17	4.35	<LOQ	<LOQ	<LOQ	<LOQ	2.54	2.56	4.73	5.47	<LOQ	1.98	<LOQ	1.08	14.71	30.05	0.42	0.55	1.18	2.88	1.94	2.47
Codeine	6.05	11.43	7.74	14.35	7.58	7.61	<LOQ	<LOQ	2.54	3.30	0.63	3.45	<LOQ	0.71	0.27	0.57	1.14	4.28	<LOQ	1.09	<LOQ	<LOQ	5.24	6.52
Caffeine	5.12	6.92	1.87	2.61	4.86	7.50	0.41	0.33	16.07	10.44	6.69	14.81	3.51	5.29	4.41	6.90	2.70	5.59	0.58	1.42	0.83	0.31	0.73	2.72
Trimethoprim	4.37	8.69	4.86	6.78	4.96	8.93	2.98	5.18	7.51	5.98	1.68	6.08	<LOQ	1.44	<LOQ	<LOQ	2.44	2.50	<LOQ	0.54	7.38	7.70	<LOQ	0.79
Sulfamethoxazole	4.92	8.20	0.86	1.32	<LOQ	6.39	0.68	0.82	7.84	4.75	<LOQ	<LOQ	<LOQ	0.91	<LOQ	<LOQ	1.17	2.45	<LOQ	0.79	<LOQ	0.01	<LOQ	<LOQ
Tramadol	7.96	12.48	0.41	0.37	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	4.05	0.92	0.76	0.88	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	1.50	2.32	0.48	1.11
Metoprolol	1.61	<LOQ	5.79	8.57	9.95	7.20	<LOQ	<LOQ	2.29	2.92	0.74	1.76	1.85	2.00	1.05	1.22	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	1.50	1.45
Doxycycline	3.82	8.46	<LOQ	0.59	0.36	1.28	<LOQ	<LOQ	11.48	15.97	<LOQ	1.30	0.74	1.14	1.54	1.12	22.28	31.04	1.06	1.69	3.36	5.09	0.75	1.19
Propranolol	17.70	22.16	4.72	4.55	25.83	38.67	4.40	6.05	0.90	2.50	1.84	8.39	0.80	3.78	0.88	0.36	0.16	0.96	<LOQ	0.87	5.05	2.85	1.52	4.83
Carbamazepine	<LOQ	<LOQ	<LOQ	9.23	12.04	14.60	<LOQ	<LOQ	12.89	20.04	11.65	19.01	8.97	16.24	3.90	3.39	24.21	29.20	4.92	9.83	7.10	6.40	2.05	3.01
Hydrocortisone	3.05	10.51	2.28	3.92	14.10	15.96	<LOQ	<LOQ	15.89	19.47	6.25	11.40	4.31	5.30	23.68	20.10	18.72	31.84	1.95	5.04	<LOQ	<LOQ	1.81	2.19
Erythromycin	1.59	5.42	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	13.85	17.26	6.06	11.10	2.32	10.42	2.44	1.24	10.18	8.78	1.43	2.82	<LOQ	<LOQ	<LOQ	<LOQ
DEET	<LOQ	<LOQ	0.15	0.69	4.24	6.98	<LOQ	<LOQ	<LOQ	<LOQ	6.39	7.50	1.40	5.94	17.40	20.32	24.09	32.92	8.85	14.97	2.97	3.53	<LOQ	<LOQ
Clotrimazole	26.78	37.29	1.07	0.50	<LOQ	<LOQ	1.41	1.63	6.55	13.90	13.72	14.68	12.74	21.04	10.16	2.42	19.67	23.59	6.97	6.26	0.66	0.70	1.02	1.02
Mefloquine-HCl	5.28	11.12	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	3.78	<LOQ	<LOQ	1.90	6.13	<LOQ	0.57	5.18	8.48	1.73	2.20	1.67	3.98	<LOQ	<LOQ
Oxazepam	1.87	3.44	<LOQ	<LOQ	23.04	28.60	<LOQ	<LOQ	32.19	40.67	7.05	9.84	21.58	19.66	13.24	15.52	<LOQ	<LOQ	2.22	3.18	1.28	0.59	1.25	1.77
Diazepam	2.18	3.19	2.17	1.74	31.64	41.65	3.07	5.22	30.91	44.32	10.26	13.80	11.68	35.50	8.48	13.20	<LOQ	<LOQ	1.98	3.79	0.85	1.29	0.86	3.25
Valsartan	1.48	4.03	1.09	2.28	5.30	8.20	<LOQ	<LOQ	<LOQ	<LOQ	15.61	24.02	9.09	17.23	<LOQ	2.58	<LOQ	5.49	1.36	5.64	2.35	1.99	<LOQ	<LOQ
Ibuprofen	14.18	8.31	6.00	9.93	18.85	37.24	14.90	18.38	26.37	34.05	24.14	30.66	69.78	93.52	25.82	41.47	24.28	37.07	9.78	10.18	20.16	28.87	15.02	18.03

Naproxen	<LOQ	<LOQ	3.76	1.74	3.65	12.71	2.02	3.54	<LOQ	<LOQ	<LOQ	<LOQ	2.12	13.46	3.73	6.24	13.58	17.86	1.05	2.37	2.98	2.78	4.59	10.74
Diclofenac Na	7.21	12.39	4.70	9.62	1.95	2.80	0.80	0.76	0.99	1.24	1.14	6.58	5.18	7.21	12.42	22.24	23.71	27.65	1.73	2.75	1.44	2.80	5.43	6.26
Meclofenamic acid	<LOQ	<LOQ	0.46	0.53	3.71	1.16	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	2.25	<LOQ	<LOQ	1.48	4.32	2.09	2.02	0.71	0.58	1.33	3.08	<LOQ	1.65
Glyburide	3.35	2.25	1.12	1.23	2.13	2.73	<LOQ	<LOQ	1.47	4.38	1.84	1.69	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	1.03	0.03	0.05	2.48	2.86	4.40	5.50
Gemfibrozil	3.90	8.82	25.31	33.91	5.57	11.68	3.14	6.75	4.03	2.75	<LOQ	<LOQ	<LOQ	<LOQ	2.80	5.76	7.83	8.15	5.41	6.52	13.77	20.50	18.53	22.16
17-a-ethinyl estradiole	2.49	2.79	31.70	42.73	<LOQ	0.65	<LOQ	0.11	0.69	2.46	4.92	12.44	1.27	1.16	<LOQ	<LOQ	3.37	7.12	0.71	1.08	<LOQ	<LOQ	<LOQ	<LOQ
B-estradiol	33.07	47.78	9.21	14.78	11.80	16.25	0.53	1.39	4.29	5.76	9.23	18.26	6.63	9.28	6.29	7.73	8.76	10.53	8.61	8.80	3.90	4.44	2.78	4.94

Table SIV-2: Concentrations of target PPCPs in the river TAME.

PPCPs	Tame River / Sediment ng/g																							
	Dec-19		Jan-20		Feb-20		Mar-20		Apr-21		May-21		Jun-21		Jul-20		Aug-20		Sep-20		Oct-20		Nov-20	
	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream
Metformin	0.85	1.37	<LOQ	<LOQ	14.24	18.08	<LOQ	1.30	10.73	22.69	1.28	2.28	0.64	1.41	4.13	7.29	26.26	43.66	2.81	5.55	0.58	0.94	1.12	1.14
Nicotine	3.22	5.35	5.87	6.56	22.53	34.73	6.57	10.58	18.94	23.83	4.61	7.46	12.31	15.90	8.02	8.63	26.02	11.56	3.42	3.19	2.03	2.10	2.81	3.28
Acetaminophen	3.70	5.43	3.31	4.87	5.51	5.60	6.59	10.26	20.97	34.54	3.90	7.98	14.41	14.89	20.67	26.97	35.95	74.21	5.03	5.93	6.13	9.06	5.70	5.57
Amoxicillin	9.26	14.64	3.33	18.69	2.52	7.77	<LOQ	3.29	8.06	7.70	9.75	23.02	1.10	5.35	11.39	34.11	26.20	61.07	2.08	7.99	<LOQ	3.05	6.60	13.01
Gabapentin	1.98	1.87	5.81	8.21	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	5.15	1.34	2.11	1.47	2.87	4.86	10.10	2.44	7.29	0.62	0.60	<LOQ	0.79	1.62	1.94
Codeine	7.65	18.50	9.30	23.20	2.37	3.76	<LOQ	<LOQ	2.68	9.58	4.17	8.32	1.62	2.19	5.14	4.52	3.02	4.85	1.79	4.82	<LOQ	<LOQ	4.84	7.39
Caffeine	7.78	7.14	5.18	9.79	3.81	13.66	2.00	2.76	11.69	17.83	3.79	9.27	2.39	7.04	2.24	3.52	6.62	7.84	2.04	2.51	0.78	1.09	3.62	6.46
Trimethoprim	2.09	2.62	10.20	9.68	17.68	26.89	1.10	1.69	3.96	4.43	<LOQ	<LOQ	4.61	6.56	3.46	4.31	2.36	2.58	5.15	9.24	1.62	5.55	3.02	6.18
Sulfamethoxazole	18.56	3.57	1.38	2.98	<LOQ	4.58	2.69	6.45	1.83	5.29	1.04	1.21	4.61	3.67	<LOQ	<LOQ	1.79	5.16	0.68	0.80	<LOQ	<LOQ	<LOQ	<LOQ
Tramadol	2.86	4.31	1.41	1.24	<LOQ	<LOQ	1.68	1.25	3.96	5.55	1.18	1.98	<LOQ	<LOQ	1.30	1.66	<LOQ	1.53	<LOQ	0.76	<LOQ	0.62	0.99	1.42
Metoprolol	<LOQ	<LOQ	2.95	4.68	4.57	4.32	<LOQ	<LOQ	3.05	9.36	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.82	0.98	<LOQ	0.68	0.77	1.00
Doxycycline	<LOQ	<LOQ	0.85	2.05	2.28	2.39	<LOQ	<LOQ	<LOQ	3.36	3.58	3.26	<LOQ	1.75	4.87	6.47	13.12	19.72	1.69	2.89	1.94	2.18	4.02	5.93
Propranolol	<LOQ	1.23	7.13	15.29	17.77	17.39	6.73	13.92	5.64	11.95	1.74	8.58	1.49	4.25	<LOQ	3.35	<LOQ	5.54	<LOQ	1.49	6.58	10.70	7.61	12.96
Carbamazepine	3.98	10.38	5.02	7.24	8.29	16.36	2.28	5.19	8.99	19.02	2.71	4.85	2.71	3.49	<LOQ	4.35	5.98	15.16	2.47	2.09	0.79	0.75	0.75	0.99
Hydrocortisone	1.26	2.57	3.35	6.29	14.40	21.82	0.99	2.23	<LOQ	<LOQ	5.22	6.59	2.02	2.71	4.41	10.07	14.54	23.45	3.29	6.61	<LOQ	<LOQ	1.20	1.96
Erythromycin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	1.10	3.86	7.64	23.22	4.54	10.58	6.28	9.57	5.29	10.71	2.15	7.06	4.01	3.90	<LOQ	<LOQ	1.12	1.28
DEET	<LOQ	2.56	<LOQ	1.35	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	1.85	2.60	3.24	2.73	4.20	9.04	13.22	8.27	14.03	1.51	2.44	<LOQ	<LOQ	<LOQ	<LOQ
Clotrimazole	3.38	5.77	2.41	2.17	2.21	3.34	2.27	4.10	10.49	11.68	<LOQ	3.43	1.70	3.11	6.80	8.18	19.76	31.31	4.20	9.07	1.68	1.76	<LOQ	<LOQ
Mefloquine-HCl	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	9.44	12.57	11.06	15.58	<LOQ	<LOQ	<LOQ	<LOQ	0.02	<LOQ
Oxazepam	1.64	4.98	<LOQ	<LOQ	9.43	10.13	3.66	5.47	7.33	15.18	5.64	9.47	3.20	8.68	3.04	8.74	15.05	24.32	2.18	5.10	1.43	1.93	1.93	2.05
Diazepam	1.39	2.12	7.21	14.33	20.05	30.10	6.15	7.63	12.73	14.59	7.54	12.40	9.39	14.60	17.67	37.14	21.00	40.70	4.28	7.08	1.25	1.29	3.94	4.39
Valsartan	<LOQ	<LOQ	5.27	5.91	18.59	24.02	2.06	2.79	12.91	19.78	3.35	4.47	3.46	5.48	1.95	3.92	8.79	20.37	4.35	6.54	<LOQ	<LOQ	<LOQ	<LOQ
Ibuprofen	2.37	2.72	1.79	1.82	12.72	22.45	2.99	7.23	6.07	11.33	2.77	10.56	3.96	12.53	10.90	14.55	7.75	19.07	12.01	2.22	6.37	3.38	7.06	7.40
Naproxen	<LOQ	<LOQ	<LOQ	<LOQ	9.36	11.94	<LOQ	<LOQ	<LOQ	0.01	2.16	2.47	4.01	8.61	7.55	15.22	5.88	4.99	0.93	1.70	2.08	2.34	2.16	2.60

Diclofenac Na	1.66	1.61	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	1.51	1.62	0.75	1.30	7.92	11.63	11.52	17.15	1.20	1.14	<LOQ	<LOQ	<LOQ	<LOQ
Meclofenamic acid	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	1.00	1.51	1.51	2.30	1.82	1.78	2.55	2.37	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Glyburide	<LOQ	<LOQ	1.98	5.07	2.29	3.14	<LOQ	<LOQ	<LOQ	<LOQ	3.12	3.50	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Gemfibrozil	<LOQ	<LOQ	<LOQ	<LOQ	3.51	5.05	<LOQ	<LOQ	2.35	5.37	3.18	3.42	1.89	1.63	6.47	8.40	<LOQ	<LOQ	1.42	2.21	<LOQ	<LOQ	<LOQ	<LOQ
17-a-ethinyl estradiole	4.24	9.01	3.68	8.21	7.25	12.11	1.58	2.08	<LOQ	<LOQ	<LOQ	<LOQ	1.78	4.12	8.87	13.96	12.15	15.11	1.20	1.43	2.51	3.18	1.16	1.88
B-estradiol	<LOQ	<LOQ	2.07	5.53	9.04	2.43	1.97	1.81	<LOQ	<LOQ	3.40	<LOQ	<LOQ	2.22	5.54	6.99	12.03	2.89	2.69	1.62	1.76	2.00	3.28	4.68

Table SIV-3: Concentrations of target PPCPs in the river SEVERN.

PPCPs	Severn River / Sediment (ng/g)																							
	Dec-19		Jan-20		Feb-20		Mar-20		Apr-21		May-21		Jun-21		Jul-20		Aug-20		Sep-20		Oct-20		Nov-20	
	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream	Upstream	Downstream
Metformin	<LOQ	<LOQ	1.08	2.11	<LOQ	<LOQ	<LOQ	<LOQ	5.89	10.92	5.61	9.31	1.85	5.14	7.23	8.85	4.98	11.04	0.62	0.96	<LOQ	<LOQ	<LOQ	<LOQ
Nicotine	4.44	6.68	1.49	5.32	<LOQ	1.21	0.50	1.10	5.88	6.90	7.64	14.70	6.58	11.52	13.74	13.39	7.82	16.03	1.77	2.17	<LOQ	1.07	<LOQ	1.23
Acetaminophen	0.58	1.08	3.21	5.76	<LOQ	<LOQ	<LOQ	<LOQ	9.74	14.62	1.57	3.66	3.22	5.51	11.64	22.26	17.68	39.23	2.96	6.10	3.32	5.19	0.42	1.03
Amoxicillin	3.40	6.49	7.62	13.47	1.60	4.03	0.95	2.41	<LOQ	3.54	7.66	11.16	9.23	14.79	5.40	10.46	26.26	38.59	0.81	2.15	0.73	1.88	3.14	6.40
Gabapentin	<LOQ	0.51	2.62	3.99	<LOQ	<LOQ	<LOQ	<LOQ	1.64	3.68	2.53	11.35	4.19	8.34	<LOQ	<LOQ	12.35	16.59	<LOQ	<LOQ	1.22	3.46	<LOQ	<LOQ
Codeine	0.68	0.70	1.54	5.53	<LOQ	<LOQ	<LOQ	<LOQ	3.99	5.10	5.64	11.08	2.63	6.13	<LOQ	<LOQ	3.53	4.93	1.36	3.61	<LOQ	<LOQ	2.29	4.03
Caffeine	2.39	4.81	5.25	7.56	1.77	3.15	1.50	3.29	5.13	10.36	2.49	3.17	3.25	3.98	1.57	1.65	3.23	4.84	<LOQ	<LOQ	<LOQ	1.12	0.84	1.62
Trimethoprim	1.00	2.65	5.44	10.08	4.30	6.75	1.28	1.92	1.58	5.89	<LOQ	<LOQ	<LOQ	<LOQ	1.50	1.76	1.52	3.09	<LOQ	<LOQ	3.55	3.78	0.96	0.84
Sulfamethoxazole	2.21	3.00	6.25	7.54	3.59	4.69	1.45	3.62	4.69	9.05	1.54	3.45	1.27	2.64	0.89	2.03	<LOQ	<LOQ	0.67	1.75	1.47	3.11	<LOQ	<LOQ
Tramadol	0.40	1.36	1.12	2.22	0.73	0.66	<LOQ	<LOQ	1.32	4.90	1.46	2.42	0.96	1.10	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	1.04	2.39	0.47	0.52
Metoprolol	<LOQ	<LOQ	2.53	5.15	0.50	0.65	<LOQ	<LOQ	1.84	6.65	<LOQ	<LOQ	<LOQ	<LOQ	1.29	4.59	1.74	1.87	<LOQ	<LOQ	<LOQ	<LOQ	0.36	0.49
Doxycycline	0.74	0.97	2.07	2.90	<LOQ	<LOQ	1.45	3.24	2.05	4.35	1.38	1.63	<LOQ	<LOQ	<LOQ	<LOQ	11.04	20.90	2.17	4.05	1.07	2.56	2.07	3.51
Propranolol	1.60	3.47	5.65	8.48	0.98	1.02	3.39	5.69	2.16	6.65	9.67	12.97	5.30	7.55	4.41	8.03	2.90	7.84	<LOQ	0.77	<LOQ	1.15	0.68	1.74
Carbamazepine	2.15	4.09	1.21	2.32	<LOQ	0.74	1.00	2.27	17.39	30.46	9.47	23.83	6.93	13.94	6.94	15.26	8.75	20.29	1.49	2.36	1.03	2.67	1.40	1.36
Hydrocortisone	2.12	4.36	2.61	7.98	0.66	1.06	<LOQ	<LOQ	3.03	6.75	5.94	10.44	8.59	8.83	13.53	13.93	12.89	19.86	2.53	4.34	<LOQ	<LOQ	<LOQ	<LOQ
Erythromycin	0.83	2.24	<LOQ	1.00	<LOQ	<LOQ	<LOQ	<LOQ	3.02	7.80	7.11	7.53	1.52	7.58	7.41	9.12	7.50	13.76	1.11	1.62	1.82	2.33	1.22	2.85
DEET	<LOQ	<LOQ	0.90	1.24	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	1.75	5.29	1.34	3.98	4.05	5.22	8.74	12.29	1.92	3.04	<LOQ	<LOQ	<LOQ	<LOQ
Clotrimazole	2.69	3.66	<LOQ	<LOQ	1.69	3.74	1.28	2.23	7.62	14.57	10.06	13.51	5.92	12.17	2.65	6.64	13.23	24.78	6.30	8.24	2.44	5.01	2.87	6.60
Mefloquine-HCl	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	4.73	10.48	<LOQ	<LOQ	8.24	11.11	2.57	6.48	4.06	11.56	2.81	3.22	<LOQ	<LOQ	1.21	3.58
Oxazepam	1.48	3.02	2.43	5.28	2.68	5.45	1.91	4.08	11.42	15.39	15.58	18.76	2.69	8.39	1.75	4.77	10.21	17.19	2.54	4.12	2.48	5.59	1.56	2.59
Diazepam	0.84	2.49	3.74	6.49	1.60	4.14	2.36	4.14	21.21	25.49	7.42	13.84	7.81	10.44	6.24	9.72	9.13	15.85	5.35	8.46	5.07	10.96	2.44	4.38
Valsartan	2.24	3.59	2.99	6.30	1.72	2.28	<LOQ	<LOQ	12.14	19.49	21.58	34.74	12.68	24.07	8.51	14.41	7.97	12.94	2.97	5.38	3.92	6.18	2.40	4.23
Ibuprofen	3.76	8.27	9.07	9.67	5.03	10.89	7.73	10.86	37.45	57.91	27.58	38.65	18.55	28.71	32.49	44.45	43.85	51.13	7.11	9.59	19.23	28.60	5.69	11.45
Naproxen	2.07	2.83	1.66	4.12	2.26	3.13	0.87	0.79	5.13	5.41	11.96	13.17	6.33	7.94	2.07	4.42	4.49	10.06	3.79	3.72	9.17	15.59	2.49	5.20

Diclofenac Na	2.93	5.32	3.84	5.86	3.84	5.36	4.19	7.64	10.39	11.95	<LOQ	<LOQ	<LOQ	<LOQ	6.68	15.83	13.59	20.22	1.36	1.29	3.29	4.80	3.22	5.83
Meclofenamic acid	0.48	1.63	0.95	1.88	0.89	1.02	2.37	3.69	1.93	4.09	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	1.11	1.39	0.62	0.42	1.31	3.88	1.15	3.09
Glyburide	1.67	2.70	2.62	5.17	1.31	2.10	2.61	4.21	7.82	6.20	2.33	3.06	6.65	9.93	<LOQ	<LOQ	1.20	2.76	<LOQ	<LOQ	1.76	2.28	0.71	1.19
Gemfibrozil	4.79	8.13	2.95	6.92	2.62	3.13	0.59	1.54	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	5.00	8.08	10.78	18.10	4.50	8.13	9.73	13.15	0.71	2.24
17-a-ethinyl estradiole	5.83	9.99	2.69	4.79	2.66	4.38	3.16	3.71	14.34	22.50	3.70	7.89	1.43	4.06	1.46	3.30	4.29	6.47	0.79	2.16	<LOQ	2.61	0.82	2.22
B-estradiol	1.30	2.67	<LOQ	<LOQ	1.69	4.33	0.95	3.34	8.51	17.98	7.22	14.81	8.00	12.92	9.40	15.48	7.23	16.40	2.17	2.41	1.81	4.24	2.91	3.96

Table SIV-4: Concentrations of target PPCPs in Birmingham & Worcester Canal.

PPCPs	Birmingham & Worcester Canal/ sediment (ng/g)											
	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov
Metformin	7.62	10.63	<LOQ	5.92	23.83	4.60	1.64	25.28	17.73	4.17	0.47	0.12
Glyburide	<LOQ	<LOQ	0.87	0.14	<LOQ	0.05	<LOQ	0.19	<LOQ	1.94	<LOQ	0.63
Nicotine	0.42	1.76	<LOQ	56.70	36.84	22.25	22.25	3.08	0.93	3.89	0.02	1.35
Caffeine	<LOQ	5.83	12.76	<LOQ	19.65	0.13	0.03	17.15	7.05	5.21	<LOQ	43.76
Acetaminophen	0.62	11.84	<LOQ	<LOQ	36.17	4.93	3.43	78.35	0.49	0.14	<LOQ	2.00
Ibuprofen	2.40	0.52	14.92	<LOQ	13.48	12.78	10.73	30.65	14.82	46.80	12.99	10.45
Naproxen	0.53	0.17	7.66	<LOQ	<LOQ	1.14	0.55	2.67	0.99	10.40	8.54	2.44
Diclofenac Na	<LOQ	0.48	0.15	<LOQ	0.16	<LOQ	0.01	43.47	6.15	2.04	0.26	0.14
Codeine	4.07	2.24	0.20	13.94	1.94	1.42	0.17	2.66	0.16	<LOQ	<LOQ	3.96
Tramadol	<LOQ	12.07	0.15	0.14	1.91	<LOQ	<LOQ	0.61	3.96	<LOQ	0.12	1.04
Meclofenamic acid	<LOQ	1.04	0.26	<LOQ	<LOQ	<LOQ	<LOQ	0.62	0.16	1.67	0.25	0.15
Amoxicillin	0.23	5.29	0.76	<LOQ	0.73	34.31	3.79	76.95	0.50	8.27	<LOQ	5.30
Doxycycline	<LOQ	21.74	<LOQ	1.08	5.02	<LOQ	0.05	5.03	<LOQ	<LOQ	<LOQ	6.39
Erythromycin-H2O	<LOQ	0.22	0.10	0.63	13.41	1.99	0.31	8.05	<LOQ	1.06	0.16	0.15
Trimethoprim	<LOQ	<LOQ	5.40	<LOQ	3.81	0.01	<LOQ	0.22	6.00	1.43	4.49	0.23
Sulfamethoxazole	<LOQ	14.50	6.54	<LOQ	1.06	0.16	<LOQ	1.46	18.87	0.64	<LOQ	1.20
Clotrimazole	<LOQ	0.85	<LOQ	<LOQ	10.44	<LOQ	<LOQ	<LOQ	29.24	<LOQ	2.66	1.20
17α-ethinyl estradiole	1.56	20.88	4.38	<LOQ	0.74	2.00	<LOQ	0.36	15.65	0.60	<LOQ	1.17
β-estradiol	<LOQ	<LOQ	4.04	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	1.60	<LOQ	0.82	22.23
Hydrocortisone	<LOQ	0.21	0.22	13.45	27.43	3.90	16.10	64.62	<LOQ	<LOQ	<LOQ	1.14
Gabapentin	<LOQ	29.16	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.20	1.33	<LOQ	<LOQ	2.26
Diazepam	<LOQ	0.60	<LOQ	2.26	2.40	5.00	2.76	3.88	10.01	<LOQ	0.44	0.52
Metoprolol	0.36	0.35	<LOQ	0.17	2.35	0.06	0.12	0.77	1.23	<LOQ	0.05	0.95
Propranolol	<LOQ	0.42	0.38	<LOQ	<LOQ	0.83	0.06	1.95	6.51	3.24	<LOQ	0.83
Valsartan	<LOQ	0.42	0.20	21.14	12.26	<LOQ	<LOQ	<LOQ	<LOQ	2.61	0.13	0.18
Carbamazepine	38.42	55.60	0.27	12.90	16.65	0.47	<LOQ	24.92	6.71	<LOQ	0.25	<LOQ
DEET	2.21	1.80	0.28	8.89	0.04	0.18	0.26	0.30	<LOQ	<LOQ	0.15	2.37
Mefloquine-HCl	<LOQ	0.11	<LOQ	<LOQ	<LOQ	<LOQ	7.05	47.74	4.20	1.38	1.59	0.10
Oxazepam	<LOQ	6.52	<LOQ	21.18	<LOQ	7.24	9.35	<LOQ	12.91	<LOQ	0.57	1.08
Gemfibrozil	<LOQ	48.71	3.31	<LOQ	<LOQ	<LOQ	0.05	12.60	7.90	11.72	11.60	0.14

Table SV-1: Mean concentrations of target PPCPs in the available literature.

Antibiotics	Location	Concentration (ng/g)	Reference
Doxycycline	Lake and rivers of Baiyangdian, China	12	(Zhang et al., 2018)
	Lake Taihu, China	17	(Zhou et al., 2016)
	Jilin Songhua River (Northeast China)	9	(He et al., 2018)
	Huangpu River, Shanghai, China	21	(Chen and Zhou, 2014)
Erythromycin-H2O	Jilin Songhua River (Northeast China)	64	(He et al., 2018)
	Iberian Rivers, Spain	1	(Osorio et al., 2016a)
	Huangpu River, Shanghai, China	24.5	(Chen and Zhou, 2014)
	Lake and rivers of Baiyangdian, China	15.5	(Zhang et al., 2018)
	Pearl River Estuary, South China	14	(Liang et al., 2013)
	Taihu Lake, China	0.78	(Xie et al., 2015)
	Yellow River Delta, China	14	(Zhao et al., 2016)
	Taihu lake, China	15	(Xie et al., 2017)
	Baiyangdian Lake in North China	3	(Li et al., 2012)
	San Francisco Bay, CA, USA	3.5	(Klosterhaus et al., 2013)
	Pearl river delta, China	0.1	(Xie et al., 2019)
	Pearl Rivers in Guangdong Province, China.	385	(Yang et al., 2010)
	Taihu Lake, China	120	(Xu et al., 2014)
	Yongjiang River, china	2.5	(Xue et al., 2013)
Naproxen	Taihu lake, China	0.06	(Li et al., 2021)
Sulfamethoxazole	Iberian Rivers, Spain	0.26	(Osorio et al., 2016a)
	San Francisco Bay, CA, USA	0.7	(Klosterhaus et al., 2013)
	Huangpu River, Shanghai, China	0.6	(Chen and Zhou, 2014)
	Lake and rivers of Baiyangdian, China	7.33	(Zhang et al., 2018)

	Canal of Lahore, Pakistan	8.9	(Ashfaq et al., 2019)
	Baiyangdian Lake in North China	7.86	(Li et al., 2012)
	Taihu lake, China	50	(Xie et al., 2017)
	Yongjiang River, china	0.2	(Xue et al., 2013)
	Taihu lake, China	11.3	(Li et al., 2021)
Trimethoprim	San Francisco Bay, CA, USA	18.2	(Klosterhaus et al., 2013)
	Northern New Jersey stream	11	(Gibs et al., 2013)
	Umgeni River, South Africa	87.55 ± 4.88	(Matongo et al., 2015)
	Urban river in Florida, USA	0.01–0.83	(Yang et al., 2015)
	Pearl river delta, China	0.2	(Xie et al., 2019)
	Lake and rivers of Baiyangdian, China	7.26	(Zhang et al., 2018)
	Lake Taihu, China	1.09	(Zhou et al., 2016)
	Taihu Lake, China	39.3	(Xu et al., 2014)
	Yongjiang River, china	1.07	(Xue et al., 2013)
Hormones	**Location**	**Concentration (ng/g)**	**Reference**
17α-ethinyl estradiol	Three Gorges Reservoir Region, China	17	(Wang et al., 2016)
	Brazilian coast	130	(Froehner et al., 2012)
	13 estuarine sites around Auckland, New Zealand	1.8	(Stewart et al., 2014)
	Taihu lake, China	8.3	(Xie et al., 2017)
	Dianchi Lake, the southwest of China	21.2	(Huang et al., 2013)
	Taihu Lake, China	15.1	(Xie et al., 2015)
	Luoma Lake, China	1.5	(Liu et al., 2017)
	Erhai Lake, a Typical Plateau Lake of China	26.3	(Shen et al., 2020)
	Iberian rivers, in Spain	7.1	(Gorga et al., 2015)
17-β-estradiol	Brazilian coast	49.3	(Froehner et al., 2012)

	Taihu lake, China	9.2	(Xie et al., 2017)
	13 estuarine sites around Auckland, New Zealand	0.5 to 1.0	(Stewart et al., 2014)
	Luoma Lake, China	1.21	(Liu et al., 2017)
	Taihu Lake, China	12.61	(Xie et al., 2015)
	Erhai Lake, a Typical Plateau Lake of China	79.3	(Shen et al., 2020)
	Three Gorges Reservoir Regions, China	9.5	(Wang et al., 2016)
Analgesics/ anti-inflammatories	**Location**	**Concentration (ng/g)**	**Reference**
Acetaminophen	13 estuarine sites around Auckland, New Zealand	7.7	(Stewart et al., 2014)
	Msunduzi River, South Africa	15.8	(Matongo et al., 2015)
	Urban river in Florida, USA	5.2	(Yang et al., 2015)
	Mediterranean coastal wetland, Spain	33	(Sadutto et al., 2021)
	Lake and rivers of Baiyangdian, China	24	(Zhang et al., 2018)
	Jilin Songhua River (Northeast China)	321	(He et al., 2018)
	Canal of Lahore, Pakistan	20	(Ashfaq et al., 2019)
Codeine	Iberian Rivers, Spain	11.5	(Osorio et al., 2016a)
	Mediterranean coastal wetland, Spain	1	(Sadutto et al., 2021)
Diclofenac	Iberian Rivers, Spain	1.3	(Osorio et al., 2016a)
	Danube river at Budapest (Hungary)	38	(Varga et al., 2010)
	Umgeni river, South Africa	309	(Agunbiade and Moodley, 2016)
	Pearl river delta, China	0.03	(Xie et al., 2019)
	Mediterranean coastal wetland, Spain	10	(Sadutto et al., 2021)
	Jilin Songhua River (Northeast China)	278	(He et al., 2018)
	Taihu Lake, China	5.6	(Xie et al., 2015)
	Canal of Lahore, Pakistan	35	(Ashfaq et al., 2019)
Ibuprofen	Iberian Rivers, Spain	12.6	(Osorio et al., 2016a)

	Upstream and downstream rivers from western, central and eastern Scotland	<10	(Langford et al., 2011)
	Msunduzi River, South Africa	66	(Matongo et al., 2015)
	Pearl river delta, China	0.02	(Xie et al., 2019)
	Mediterranean coastal wetland, Spain	100	(Sadutto et al., 2021)
	Jilin Songhua River (Northeast China)	227	(He et al., 2018)
	Taihu Lake, China	12.9	(Xie et al., 2015)
	Canal of Lahore, Pakistan	1.6	(Ashfaq et al., 2019)
	Umgeni River, South Africa	11.2	(Agunbiade and Moodley, 2016)
	Taihu lake, China	77	(Xie et al., 2017)
Mefenamic acid	Canal of Lahore, Pakistan	8.8	(Ashfaq et al., 2019)
Naproxen	13 estuarine sites around Auckland, New Zealand	5.5	(Stewart et al., 2014)
	Iberian Rivers, Spain	0.8	(Osorio et al., 2016a)
	Danube river at Budapest (Hungary)	2.2	(Varga et al., 2010)
	Mediterranean coastal wetland, Spain	31	(Sadutto et al., 2021)
	Jilin Songhua River (Northeast China)	4.1	(He et al., 2018)
	Taihu lake, China	5.6	(Xie et al., 2017)
Tramadol	Mediterranean coastal wetland, Spain	13	(Sadutto et al., 2021)
Anxiolytic drugs	**Location**	**Concentration (ng/g)**	**Reference**
Carbamazepine	Iberian Rivers, Spain	0.1	(Osorio et al., 2016a)
	Upstream and downstream rivers from western, central and eastern Scotland	< 1	(Langford et al., 2011)
	Msunduzi River, South Africa	6.1	(Matongo et al., 2015)
	Urban river in Florida, USA	32.9	(Yang et al., 2015)
	Lake and rivers of Baiyangdian, China	54	(Zhang et al., 2018)
	Taihu Lake, China	7	(Xie et al., 2015)

	Canal of Lahore, Pakistan	4.2	(Ashfaq et al., 2019)
	Taihu lake, China	6.6	(Xie et al., 2017)
Diazepam	Iberian Rivers, Spain	0.3	(Osorio et al., 2016a)

Table SV-2: Statistical Summary of PPCPs concentrations (ng/g) in sediment samples from Africa (n=3).

PPCPs	Min	Max	Mean	Std. deviation
Metformin	<LOD	1.13	0.38	0.65
Nicotine	<LOD	3.72	1.63	1.90
Acetaminophen	14.92	31.29	20.46	9.38
Amoxicillin	36.38	59.01	46.02	11.68
Gabapentin	<LOD	<LOD	<LOD	<LOD
Codeine	1.06	3.10	2.09	1.02
Caffeine	8.58	37.09	18.86	15.83
Trimethoprim	34.51	48.51	43.35	7.69
Sulfamethoxazole	30.53	46.19	36.78	8.30
Tramadol	6.89	11.72	9.02	2.46
Metoprolol	1.29	3.87	2.93	1.42
Doxycycline	4.50	19.32	9.85	8.23
Propranolol	1.41	7.14	4.52	2.90
Carbamazepine	7.94	30.48	18.99	11.27
Hydrocortisone	<LOD	16.60	9.45	8.53
Erythromycin-H2O	19.15	36.70	29.39	9.13
DEET	<LOD	0.65	0.22	0.38
Clotrimazole	6.40	19.66	11.17	7.38
Mefloquine-HCl	16.11	22.97	18.87	3.62
Oxazepam	8.59	31.55	18.96	11.64
Diazepam	3.72	13.08	9.06	4.82
Valsartan	<LOD	3.88	1.29	2.24
Ibuprofen	34.44	45.85	40.77	5.81
Naproxen	4.90	17.20	10.53	6.21
Diclofenac Na	27.34	40.08	33.90	6.38
Meclofenamic acid	<LOD	<LOD	<LOD	<LOD
Glyburide	<LOD	1.78	0.59	1.03
Gemfibrozil	<LOD	5.42	3.32	2.91
17α-ethinyl estradiole	20.32	32.12	24.98	6.28
β-estradiol	28.25	31.28	29.58	1.55

Table SV-3: Statistical Summary of PPCPs concentrations (ng/g) in sediment samples from Asia (n=13).

PPCPs	Min	Max	Mean	Std. deviation
Metformin	<LOD	4.17	0.76	1.26
Nicotine	0.84	4.62	2.56	1.21
Acetaminophen	<LOD	24.55	9.31	7.61
Amoxicillin	4.84	25.26	12.54	6.38
Gabapentin	<LOD	3.11	0.99	1.11
Codeine	<LOD	5.65	2.70	1.76
Caffeine	10.02	31.98	16.75	5.35
Trimethoprim	4.16	31.16	12.63	7.88
Sulfamethoxazole	2.39	26.19	10.64	5.69
Tramadol	<LOD	4.72	2.06	1.64
Metoprolol	<LOD	10.91	1.97	3.21
Doxycycline	<LOD	39.68	14.24	12.76
Propranolol	<LOD	11.08	3.28	3.87
Carbamazepine	3.20	87.48	24.08	23.77
Hydrocortisone	<LOD	76.98	21.61	28.11
Erythromycin-H2O	2.34	26.12	12.32	7.58
DEET	<LOD	6.05	1.99	1.95
Clotrimazole	<LOD	35.89	10.61	13.13
Mefloquine-HCl	<LOD	50.33	16.11	14.48
Oxazepam	3.27	22.47	9.62	5.28
Diazepam	3.25	33.74	18.98	9.96
Valsartan	<LOD	15.66	4.99	6.60
Ibuprofen	11.69	62.07	40.48	15.76
Naproxen	<LOD	45.07	22.58	15.52
Diclofenac Na	<LOD	60.36	27.22	24.30
Meclofenamic acid	<LOD	1.38	0.11	0.38
Glyburide	<LOD	8.10	1.87	2.64
Gemfibrozil	<LOD	32.73	5.32	10.39
17α-ethinyl estradiole	<LOD	6.11	2.55	2.43
β-estradiol	<LOD	14.75	4.94	4.92

Table SV-4: Statistical Summary of PPCPs concentrations (ng/g) in sediment samples from Europe (n=11).

PPCPs	Min	Max	Mean	Std. deviation
Metformin	<LOD	5.2	1.7	1.8
Nicotine	<LOD	5.2	2.1	1.9
Acetaminophen	2.1	8.2	4.8	2.1
Amoxicillin	2.3	17.4	9.6	4.6
Gabapentin	<LOD	6.0	1.5	2.4
Codeine	<LOD	1.3	0.6	0.6
Caffeine	1.6	32.0	12.7	8.4
Trimethoprim	4.9	28.6	11.5	7.4
Sulfamethoxazole	0.7	14.5	6.5	4.0
Tramadol	<LOD	8.7	2.4	2.9
Metoprolol	1.2	27.9	5.9	9.2
Doxycycline	<LOD	48.1	20.4	12.6
Propranolol	<LOD	19.4	7.9	5.2
Carbamazepine	4.8	32.0	14.1	8.8
Hydrocortisone	2.6	33.1	14.2	8.4
Erythromycin-H2O	<LOD	13.8	5.2	4.3
DEET	<LOD	5.1	1.9	1.8
Clotrimazole	2.2	4<LOD	17.2	11.0
Mefloquine-HCl	<LOD	<LOD	<LOD	<LOD
Oxazepam	3.7	44.7	18.4	13.4
Diazepam	2.7	35.8	11.5	10.2
Valsartan	<LOD	26.5	7.2	7.8
Ibuprofen	3.0	24.5	12.7	8.7
Naproxen	2.5	29.7	9.6	7.5
Diclofenac Na	<LOD	1.1	0.1	0.3
Meclofenamic acid	<LOD	1.1	0.1	0.3
Glyburide	<LOD	5.9	1.7	1.9
Gemfibrozil	<LOD	17.0	4.4	4.5
17α-ethinyl estradiole	<LOD	3.0	0.5	1.0
β-estradiol	<LOD	15.2	1.7	4.5

Table SV-5: Statistical Summary of PPCPs concentrations (ng/g) in sediment samples from the Americas (n=4).

PPCPs	Min	Max	Mean	Std. deviation
Metformin	<LOD	3.19	1.52	1.76
Nicotine	3.18	7.34	5.42	2.01
Acetaminophen	2.09	8.93	5.24	2.88
Amoxicillin	10.08	33.17	17.54	10.55
Gabapentin	<LOD	4.28	1.82	2.17
Codeine	<LOD	3.66	1.30	1.73
Caffeine	17.62	30.52	22.11	5.74
Trimethoprim	4.91	13.02	8.42	3.37
Sulfamethoxazole	2.73	18.06	8.41	6.99
Tramadol	<LOD	4.37	2.68	1.95
Metoprolol	0.83	5.90	2.48	2.32
Doxycycline	<LOD	7.57	5.28	3.56
Propranolol	<LOD	14.85	9.32	6.45
Carbamazepine	3.51	34.55	19.35	15.21
Hydrocortisone	1.48	5.43	3.45	1.75
Erythromycin-H2O	<LOD	10.71	5.62	4.55
DEET	1.59	10.09	5.20	3.55
Clotrimazole	6.23	13.40	8.15	3.51
Mefloquine-HCl	<LOD	7.79	1.95	3.89
Oxazepam	8.24	23.35	16.21	7.53
Diazepam	4.26	29.33	17.95	11.62
Valsartan	<LOD	5.64	3.84	2.59
Ibuprofen	13.75	25.66	19.28	5.04
Naproxen	<LOD	5.97	1.89	2.82
Diclofenac Na	3.14	19.38	8.47	7.46
Meclofenamic acid	<LOD	2.00	0.50	1.00
Glyburide	<LOD	13.85	4.22	6.58
Gemfibrozil	2.60	11.78	6.97	4.01
17α-ethinyl estradiole	1.58	5.33	3.15	1.73
β-estradiol	2.58	7.22	4.52	2.04

Table SV-6 Concentrations of target PPCPs (ng/g) in the studied sediment samples.

Africa	Location	Metformin	Nicotine	Acetaminophen	Amoxicillin	Gabapentin	Codeine	Caffeine	Trimethoprim
1	Limpopo River, Mozambique	<LOQ	<LOQ	14.92	36.38	<LOQ	2.10	10.92	47.02
2	Mkomati River , Mozambique	<LOQ	1.18	15.16	59.01	<LOQ	1.06	8.58	48.51
3	Mbuluzi River, Swaziland	1.13	3.72	31.29	42.66	<LOQ	3.10	37.09	34.51
Asia	**Location**	**Metformin**	**Nicotine**	**Acetaminophen**	**Amoxicillin**	**Gabapentin**	**Codeine**	**Caffeine**	**Trimethoprim**
4	Klang River1, Malaysia	2.19	0.84	2.66	20.85	<LOQ	2.10	31.98	31.16
5	Klang River2, Malaysia	<LOQ	2.97	6.82	7.12	<LOQ	1.27	15.01	7.57
6	Koshi River, Nepal	<LOQ	1.68	0.00	6.92	<LOQ	0.00	20.09	5.03
7	Kali Gandaki River1, Nepal	<LOQ	1.05	1.08	4.84	<LOQ	3.05	15.70	8.44
8	Kali Gandaki River2, Nepal	<LOQ	2.16	3.42	7.33	<LOQ	4.12	12.01	26.23
9	Geum River, South Korea	4.17	3.92	3.96	6.35	<LOQ	5.05	18.85	8.33
10	Ganges river, India 1	<LOQ	1.38	9.72	10.78	1.19	3.82	14.46	4.16
11	Ganges river, India 2	0.95	3.19	11.84	13.79	2.23	0.95	13.96	9.16
12	Ganges river, India 3	<LOQ	2.78	13.53	13.50	1.11	3.08	17.48	15.82
13	Ganges river, India 4	0.83	4.15	7.09	18.66	1.12	0.79	10.02	11.98
14	Ganges river, India 5	<LOQ	4.62	16.35	10.29	3.11	1.38	18.41	12.18
15	Ganges river, India 6	1.68	1.78	24.55	17.35	1.48	5.65	14.23	10.95
16	Ganges river, India 7	<LOQ	2.76	20.04	25.26	2.60	3.81	15.57	13.21
Europe	**Location**	**Metformin**	**Nicotine**	**Acetaminophen**	**Amoxicillin**	**Gabapentin**	**Codeine**	**Caffeine**	**Trimethoprim**
17	Thur river1, Switzerland	1.78	<LOQ	2.18	9.02	<LOQ	<LOQ	13.12	17.04
18	Thur river2, Switzerland	3.29	2.19	4.71	5.14	3.72	0.77	15.77	6.65
19	Thur river3, Switzerland	5.19	<LOQ	3.56	9.86	<LOQ	<LOQ	6.27	9.19
20	Thur river4, Switzerland	2.11	1.74	7.12	6.79	5.79	1.34	11.36	4.88
21	Thur river5, Switzerland	1.58	<LOQ	2.84	9.71	6.04	<LOQ	6.67	8.01
22	Vistula River1, Poland	<LOQ	3.82	8.19	16.32	<LOQ	1.11	8.89	20.79
23	Vistula River2, Poland	<LOQ	<LOQ	5.62	6.96	<LOQ	<LOQ	10.18	28.56

24	Vistula River3, Poland	<LOQ	2.91	7.18	8.21	<LOQ	0.70	32.04	9.09
25	Kifisos river1, Greece	<LOQ	5.18	4.53	13.82	<LOQ	0.00	10.97	6.67
26	Kifisos river2, Greece	1.14	3.77	2.06	2.29	<LOQ	1.06	22.85	7.06
27	Francoli River, Spain	3.67	3.59	5.28	17.38	1.08	1.24	1.61	8.29
Americas	**Location**	**Metformin**	**Nicotine**	**Acetaminophen**	**Amoxicillin**	**Gabapentin**	**Codeine**	**Caffeine**	**Trimethoprim**
28	Paraíba do Sul, Brazil	<LOQ	3.18	8.93	13.92	<LOQ	3.66	17.62	8.06
29	Detroit River, USA	3.19	6.89	2.09	33.17	<LOQ	<LOQ	30.52	4.91
30	Lake Erie, Canada	0.00	4.28	4.18	10.08	4.28	<LOQ	19.76	7.69
31	Lake Saint Clair, Canada	2.90	7.34	5.76	13.00	3.01	1.53	20.53	13.02

Africa	Location	Sulfamethoxazole	Tramadol	Metoprolol	Doxycycline	Propranolol	Carbamazepine	Hydrocortisone
1	Limpopo River, Mozambique	33.62	8.44	3.87	5.71	7.14	30.48	11.75
2	Mkomati River , Mozambique	30.53	11.72	1.29	4.50	5.02	7.94	<LOQ
3	Mbuluzi River, Swaziland	46.19	6.89	3.63	19.32	1.41	18.55	16.60
Asia	**Location**	**Sulfamethoxazole**	**Tramadol**	**Metoprolol**	**Doxycycline**	**Propranolol**	**Carbamazepine**	**Hydrocortisone**
4	Klang River1, Malaysia	8.38	3.24	4.12	38.53	1.36	37.47	69.80
5	Klang River2, Malaysia	2.39	2.30	1.50	21.68	6.39	87.48	76.98
6	Koshi River, Nepal	26.19	2.52	5.44	39.68	10.00	7.60	46.55
7	Kali Gandaki River1, Nepal	6.76	<LOQ	1.81	16.07	5.38	43.24	15.82
8	Kali Gandaki River2, Nepal	7.64	3.63	1.85	18.43	2.37	3.20	23.23
9	Geum River, South Korea	7.87	1.11	10.91	14.56	11.08	46.19	42.17
10	Ganges river, India 1	11.23	3.18	<LOQ	9.82	0.00	16.89	<LOQ
11	Ganges river, India 2	7.17	3.16	<LOQ	8.19	2.19	9.72	<LOQ
12	Ganges river, India 3	9.18	<LOQ	<LOQ	<LOQ	<LOQ	14.89	3.26
13	Ganges river, India 4	12.19	4.72	<LOQ	3.29	<LOQ	17.33	<LOQ
14	Ganges river, India 5	15.19	2.88	<LOQ	5.91	3.91	11.28	<LOQ
15	Ganges river, India 6	12.28	<LOQ	<LOQ	3.28	<LOQ	9.77	<LOQ

16	Ganges river, India 7	11.78	<LOQ	<LOQ	5.69	<LOQ	7.92	3.15
Europe	**Location**	**Sulfamethoxazole**	**Tramadol**	**Metoprolol**	**Doxycycline**	**Propranolol**	**Carbamazepine**	**Hydrocortisone**
17	Thur river1, Switzerland	8.65	1.60	4.30	11.12	<LOQ	32.04	15.36
18	Thur river2, Switzerland	4.72	1.20	1.22	11.48	9.61	21.32	15.57
19	Thur river3, Switzerland	4.38	0.97	1.74	25.61	6.34	11.20	33.10
20	Thur river4, Switzerland	4.03	0.00	1.48	29.48	19.38	4.83	7.79
21	Thur river5, Switzerland	0.67	1.59	1.18	19.40	3.82	7.52	16.82
22	Vistula River1, Poland	9.13	1.33	1.18	48.15	7.83	5.92	4.26
23	Vistula River2, Poland	14.54	<LOQ	1.73	21.11	8.21	22.55	14.49
24	Vistula River3, Poland	7.62	5.00	27.86	0.00	10.59	10.52	12.04
25	Kifisos river1, Greece	10.22	6.33	2.28	26.61	4.35	8.24	2.60
26	Kifisos river2, Greece	6.08	8.72	20.09	10.66	4.42	9.65	21.23
27	Francoli River, Spain	1.74	0.00	1.54	20.29	12.04	21.42	12.76
Americas	**Location**	**Sulfamethoxazole**	**Tramadol**	**Metoprolol**	**Doxycycline**	**Propranolol**	**Carbamazepine**	**Hydrocortisone**
28	Paraíba do Sul, Brazil	2.73	3.86	5.90	7.57	10.90	9.38	5.43
29	Detroit River, USA	3.85	0.00	1.35	7.29	0.00	3.51	2.60
30	Lake Erie, Canada	18.06	4.37	1.84	0.00	11.55	34.55	4.28
31	Lake Saint Clair, Canada	9.01	2.51	0.83	6.25	14.85	29.95	1.48

Africa	**Location**	**Erythromycin-H2O**	**DEET**	**Clotrimazole**	**Mefloquine-HCl**	**Oxazepam**	**Diazepam**	**Valsartan**	**Ibuprofen**
1	Limpopo River, Mozambique	32.32	0.00	19.66	16.11	16.73	10.38	0.00	42.04
2	Mkomati River , Mozambique	19.15	0.65	7.45	22.97	31.55	13.08	0.00	45.85
3	Mbuluzi River, Swaziland	36.70	0.00	6.40	17.53	8.59	3.72	3.88	34.44
Asia	**Location**	**Erythromycin-H2O**	**DEET**	**Clotrimazole**	**Mefloquine-HCl**	**Oxazepam**	**Diazepam**	**Valsartan**	**Ibuprofen**
4	Klang River1, Malaysia	14.48	4.27	27.91	50.33	10.39	30.07	15.21	53.60
5	Klang River2, Malaysia	2.75	6.05	21.52	18.81	7.97	33.74	4.28	41.00
6	Koshi River, Nepal	11.82	0.00	35.89	39.89	15.39	9.47	14.23	11.69

7	Kali Gandaki River1, Nepal	2.34	3.31	22.53	0.00	22.47	4.42	15.66	41.95
8	Kali Gandaki River2, Nepal	6.89	0.00	10.42	7.22	3.27	3.25	11.88	29.00
9	Geum River, South Korea	7.87	2.39	19.61	20.11	4.53	13.57	1.39	16.56
10	Ganges river, India 1	16.79	2.11	0.00	11.50	4.17	17.92	0.00	51.51
11	Ganges river, India 2	5.56	0.00	0.00	2.02	8.93	15.28	0.00	62.07
12	Ganges river, India 3	24.67	0.00	0.00	14.61	6.18	29.84	0.00	59.31
13	Ganges river, India 4	10.70	3.28	0.00	12.07	13.41	19.05	0.00	38.78
14	Ganges river, India 5	12.08	0.00	0.00	5.89	6.92	17.62	2.19	55.02
15	Ganges river, India 6	18.06	1.79	0.00	7.96	11.19	30.11	0.00	32.33
16	Ganges river, India 7	26.12	2.61	0.00	19.04	10.16	22.35	0.00	33.42
Europe	**Location**	**Erythromycin-H2O**	**DEET**	**Clotrimazole**	**Mefloquine-HCl**	**Oxazepam**	**Diazepam**	**Valsartan**	**Ibuprofen**
17	Thur river1, Switzerland	1.05	3.33	19.56	0.00	17.81	2.71	0.00	2.98
18	Thur river2, Switzerland	6.82	1.89	5.77	0.00	4.81	3.25	1.56	13.03
19	Thur river3, Switzerland	4.04	0.00	9.40	0.00	29.44	7.99	6.06	22.52
20	Thur river4, Switzerland	4.50	0.00	39.98	0.00	15.50	18.27	2.99	15.52
21	Thur river5, Switzerland	0.00	0.00	25.07	0.00	4.31	3.35	5.81	23.79
22	Vistula River1, Poland	13.76	5.09	28.45	0.00	44.70	8.49	26.53	24.45
23	Vistula River2, Poland	0.00	2.88	10.17	0.00	10.36	3.05	6.76	5.31
24	Vistula River3, Poland	6.63	3.07	20.70	0.00	3.73	10.80	5.47	6.53
25	Kifisos river1, Greece	3.53	0.00	12.87	0.00	12.29	35.79	15.49	18.90
26	Kifisos river2, Greece	6.39	3.31	15.14	0.00	28.52	10.67	0.00	3.91
27	Francoli River, Spain	10.36	1.59	2.22	0.00	31.29	21.83	8.39	3.27
Americas	**Location**	**Erythromycin-H2O**	**DEET**	**Clotrimazole**	**Mefloquine-HCl**	**Oxazepam**	**Diazepam**	**Valsartan**	**Ibuprofen**
28	Paraíba do Sul, Brazil	7.38	4.39	6.32	7.79	8.24	4.26	5.64	17.36
29	Detroit River, USA	4.40	1.59	6.23	0.00	11.36	12.57	0.00	13.75
30	Lake Erie, Canada	0.00	4.73	6.64	0.00	23.35	25.65	5.02	25.66
31	Lake Saint Clair, Canada	10.71	10.09	13.40	0.00	21.87	29.33	4.71	20.37

Africa	Location	Naproxen	Diclofenac Na	Meclofenamic acid	Glyburide	Gemfibrozil	17α-ethinyl estradiole	β-estradiol
1	Limpopo River, Mozambique	9.51	34.28	0.00	0.00	5.42	32.12	28.25
2	Mkomati River , Mozambique	17.20	27.34	0.00	0.00	4.54	20.32	29.20
3	Mbuluzi River, Swaziland	4.90	40.08	0.00	1.78	0.00	22.50	31.28
Asia	**Location**	**Naproxen**	**Diclofenac Na**	**Meclofenamic acid**	**Glyburide**	**Gemfibrozil**	**17α-ethinyl estradiole**	**β-estradiol**
4	Klang River1, Malaysia	3.80	10.67	0.00	1.28	1.99	3.37	10.35
5	Klang River2, Malaysia	0.00	12.07	0.00	0.00	0.00	5.18	14.75
6	Koshi River, Nepal	0.00	0.00	0.00	1.95	0.00	3.10	12.45
7	Kali Gandaki River1, Nepal	7.38	0.00	0.00	2.02	3.91	2.10	2.08
8	Kali Gandaki River2, Nepal	45.07	0.00	1.38	8.10	32.73	0.95	1.18
9	Geum River, South Korea	40.74	2.59	0.00	6.67	23.67	0.00	0.00
10	Ganges river, India 1	26.07	55.81	0.00	0.00	1.34	0.00	2.27
11	Ganges river, India 2	33.18	55.76	0.00	2.31	0.00	0.00	0.00
12	Ganges river, India 3	19.78	55.94	0.00	0.00	1.31	1.04	0.00
13	Ganges river, India 4	31.47	40.56	0.00	0.00	1.49	0.00	4.71
14	Ganges river, India 5	25.56	60.36	0.00	1.96	0.00	5.28	4.15
15	Ganges river, India 6	22.73	30.87	0.00	0.00	0.00	6.11	7.30
16	Ganges river, India 7	37.81	29.26	0.00	0.00	2.77	5.96	4.92
Europe	**Location**	**Naproxen**	**Diclofenac Na**	**Meclofenamic acid**	**Glyburide**	**Gemfibrozil**	**17α-ethinyl estradiole**	**β-estradiol**
17	Thur river1, Switzerland	8.21	0.00	0.00	0.00	6.10	1.14	1.91
18	Thur river2, Switzerland	5.46	0.00	0.00	1.04	4.55	0.00	0.00
19	Thur river3, Switzerland	4.87	0.00	0.00	0.00	4.92	0.00	0.00
20	Thur river4, Switzerland	10.61	0.00	0.00	1.69	4.26	0.00	0.97
21	Thur river5, Switzerland	9.57	0.00	0.00	5.93	16.96	3.02	1.06
22	Vistula River1, Poland	2.46	0.00	0.00	3.82	0.00	0.00	0.00
23	Vistula River2, Poland	2.81	0.00	0.00	2.86	1.72	1.66	15.20
24	Vistula River3, Poland	29.70	1.08	1.06	1.60	3.72	0.00	0.00
25	Kifisos river1, Greece	12.80	0.00	0.00	0.00	2.37	0.00	0.00

26	Kifisos river2, Greece	12.18	0.00	0.00	1.36	1.27	0.00	0.00
27	Francoli River, Spain	6.88	0.00	0.00	0.00	2.49	0.00	0.00
Americas	**Location**	**Naproxen**	**Diclofenac Na**	**Meclofenamic acid**	**Glyburide**	**Gemfibrozil**	**17α-ethinyl estradiole**	**β-estradiol**
28	Paraíba do Sul, Brazil	5.97	19.38	2.00	13.85	11.78	5.33	7.22
29	Detroit River, USA	0.00	3.14	0.00	0.00	2.60	3.75	4.89
30	Lake Erie, Canada	0.00	7.07	0.00	3.04	8.46	1.94	2.58
31	Lake Saint Clair, Canada	1.59	4.28	0.00	0.00	5.05	1.58	3.39