Hydrogeochemical Fate of Pharmaceutical Chemicals Discharged into a Tidal Freshwater Estuary

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Abstract

The tidal freshwater Potomac River (TFPR) in the metropolitan Washington, DC region receives wastewater discharge from eight major wastewater treatment plants with the potential to alter water quality. A total of 90 pharmaceutical chemicals and personal care products (PPCPs) were analyzed in surface water and sediments using solid-phase extraction and QuEChERS, respectively, in conjunction with liquid-chromatography tandem mass spectrometry-multiple reaction monitoring quantitation (LC-MS/MS-MRM). There were 52 PPCPs quantified in both surface water and sediment. The most frequently quantified PPCPs in water included caffeine, fexofenadine, nicotine, sulfamethoxazole, hydrochlorothiazide, MDA, desvenlafaxine, and metoprolol ranging from 10 to 360 ng/L, and in sediment included diphenhydramine, escitalopram, desvenlafaxine, fexofenadine, sertraline and triclocarban ranging from 20 to 120 ng/g (dry weight). Comparisons of PPCP constituents in WTP discharge and adjacent surface water showed altered compositions reflecting dispersal and transformation processes acted quickly following contact of effluent with surface water. Although the PPCPs were present at their highest concentrations in surface water near the WTP discharge zones, the concentrations rapidly attenuated yielding mainstem TFPR PPCP concentrations that did not show elevated concentrations along the freshwater reach of the tidal range in the estuary. The concentrations in sediment also decreased within 1-km from the tributary shoals to the mainstem river. Two prominent seasonal trends were evident in surface water between May to September for many PPCPs correlating with use patterns and temperature.

Introduction

The presence of pharmaceutical chemicals and personal care products (PPCPs) in urban surface water has allied concern across the water quality community regarding the health effects of these micropollutants over the past two decades (Kolpin et al. 2002; Deo 2014; aus der Beek et al. 2016; Meador et al. 2016; Ebele et al. 2017; OECD 2019; Patel et al. 2019). Because of the large number of PPCPs registered in commerce in the USA, including over 4,000 pharmaceuticals alone (Boxall et al. 2012), it is exceedingly difficult to evaluate the toxicity of each chemical individually much less including the effects of relevant mixtures. Thus, defining the most relevant constituents in the aquatic environment is of upmost importance. Of most interest are prescription drugs, illicit/recreational drugs, and over the counter medications found at parts-per-trillion concentrations in natural waters and fluvial sediments that approach or exceed ecological risk factors (Cahill et al. 2004; Berset et al. 2010; González-Mariño et al. 2010; Kaplan 2013; Kolpin et al. 2013; Petrie et al. 2015; Lee et al. 2016; Wilkinson et al. 2016). Risks have been identified for PPCPs such as antibiotics (e.g., sulfamethoxazole), endocrine disrupter chemicals (e.g., 4-nonylphenol, 17β-estradiol and 17α-ethynyl estradiol) and caffeine in the aquatic environment.(Liu et al. 2020; Rogowska et al. 2020) Although the evidence of health risks from PPCPs has not been widespread, continued vigilance of the occurrence, distribution and reactions of PPCPs in the aquatic environment is vital to discovering unregulated harmful chemicals.

The primary source of pharmaceuticals in rivers and streams is linked to the high human consumption of therapeutic drugs in our society and wastewater discharge (Martin et al. 2019). In 2018, for example, 5.8 billion drug prescriptions were dispensed in the USA alone (IQVIA 2019). Loadings of pharmaceuticals to the aquatic environment is reported to be dominated by the excretion of administered therapeutic doses, with manufacturing and disposal of unused mediations comprising a small contribution (Holm et al. 2013). Consumed drugs are released into septic (Standley et al. 2008) and public sewer (Bagnis et al. 2018) systems and enter the waste treatment stream, which includes primary, secondary, and often tertiary treatment technologies. However, the extent of PPCP degradation by wastewater treatment varies considerably by chemical, season, treatment technology, and wastewater treatment plant residence time, but it is clear many PPCPs pass through water treatment only partially degraded under all conditions (Wang and Wang 2016; Li et al. 2019). Wastewater treatment plants (WTPs) are not designed specifically for removing PPCPs (and metabolites) from sewage, and there are no existing federal or state discharge regulations in the USA covering the emissions of PPCPs in the wastewater stream (Jimoh 2016; Patel et al. 2019). As such, PPCPs and associated metabolites are inadvertently released into fluvial and estuarine receiving waters at discharge rates of over one hundred thousand cubic meters per day for high-capacity WTPs. While WTP discharge and septic leaching are considered principal discharge sources of PPCPs in the aquatic environment, other sources are less well characterized. Reprocessed sewage sludge from WTP digesters may be released into the environment as biosolid fertilizers across agricultural lands, where PPCPs leach into groundwater and wash into surface water following precipitation (Topp et al. 2008). Similarly, drugs and pesticides used in veterinary health can enter the environment through outdoor pet waste and grooming (Daughton and Ruhoy 2008). Landfills have recently been identified as an underreported source of PPCPs into the hydrosphere (Yu et al. 2020). Furthermore, PPCPs can also leach into freshwater from leaky sewer pipes, (Xing et al. 2021) runoff from combined sewer outfalls (Kay et al. 2017) and loadings from the upstream segments of WTP receiving waters. Although the origin of PPCPs in surface water in most cases is WTP discharge, multiple input pathways exist in urban watersheds.

The Potomac River is the fourth largest river along the eastern coast of the USA and second largest tributary of Chesapeake Bay in terms of annual discharge (Lang 1982), highlighting its importance to local water quality in the Washington, DC region. The tidal Potomac flows through the Alluvial and Estuarine Physiographic sub-Province of the Atlantic Coastal Plain between the Fall Line and confluence with Chesapeake Bay. The Mid-Atlantic Coastal Plain is characterized as gently inclined, ranging from flat to deeply incised, with alluvial deposits that range from coarse to fine (i.e., sand to silt) in texture with abundant organic matter derived from commonly occurring marshes (Ator et al. 2005). The tidal freshwater Potomac River (TFPR) in the metropolitan Washington, D.C. region is the upstream tidal reach of the Potomac River estuary, which receives discharge from eight major (i.e., > 9,000 m^3/d discharge capacity) WTPs. Approximately 10% of the fluvial Potomac River is diverted for utility, industrial or household use and consumption, and returned as reclaimed water to the Potomac River estuary. Most diversion of Potomac River water occurs in the greater Washington, DC region. The fluvial-estuarine transition zone of the Potomac River includes a shallow estuarine system with numerous tributary

embayments that support critical spawning habitats for many freshwater and anadromous fish species (Jones 2020), along with serving as a popular recreational resource for > 5 million local residents. The fluvial-estuarine boundary has been a common geographical location for the development of large urban centers in navigable coastal regions throughout the world. Understanding the emissions, presence, and fate of PPCPs in estuaries is essential to managing sustainability at the nexus of public health, ecosystem services, water supply and reuse, and climate change in coastal urban centers. The goal of the present study was to investigate the dynamics of discharged PPCPs in the TFPR with the working hypothesis that extensive WTP discharge creates enhanced river concentrations of PPCPs carried downstream toward Chesapeake Bay. Monitoring the fate of PPCPs that are discharged into and transported out of the tidal estuaries is fundamental to assessing how urban areas impact downstream water quality in large coastal rivers.

Materials And Methods

Study Area

The TFPR extends ~ 60 km through the first tidal segment of the Potomac River estuary ranging from Chain Bridge (Washington, D.C.) just below the river fall zone at Great Falls (MD) downstream to Quantico (VA). The estuary is broad and shallow (average depth ~ 4 m) in the freshwater region with a shoreline featuring several tributary embayments. These shoals are somewhat protected from the full force of the flow of the main body of water and are highly diverse and productive in terms of fish species and submerged aquatic vegetation (Jones 2020). The WTPs of focus in this study all discharge into streams that flow into nearby embayments. The TFPR is bordered by the densest urban areas of Washington D.C. and its suburbs supporting 84% of the Potomac basin population, with an average population density of 8,470 per km^2. The TFPR has shown historically poor water quality with eutrophication and high turbidity in this region (Jones et al. 2008).

Sampling

Surface water and surficial bottom sediment samples were collected from several locations (Table S1) throughout the mainstem TFPR along with several tributary embayments and upstream fluvial locations as reference sites (Fig. 1). Chain Bridge was selected as the most upstream TFPR site since this location is at the beginning of the estuary and a short distance downstream of the Potomac River Fall Line. The WTP discharge-receiving areas of Hunting Creek, Four Mile Run, and Gunston Cove were sampled with at least one site upstream of the WTP discharge, one site immediately downstream of the WTP discharge, and at least one additional site further downstream near entrance into the mainstem Potomac River. Quantico was selected as the most downstream site and the terminus of the tidal freshwater river before entering the oligohaline tidal zone (characterized by measurable salinity) of the Potomac River and is downstream of all WTP discharge in the sampling area. The three WTP discharge zones (Table S2, WTPs 1–3) served three different sewer-sheds in Northern Virginia with minor variations in population size. WTP 1 serves approximately 226,400 households from Arlington County, Fairfax County, and some

portions of the cities of Falls Church and Alexandria, Virginia. The population served can swell to approximately 306,500 during the daytime as commuters enter treatment zones for work and other activities. WTP 2 serves approximately 169,000 and 146,000 people from Fairfax County and the City of Alexandria, respectively, for a total of 315,000 customers. WTP 3 serves approximately 372,000 households, making up 40% of the population of Fairfax Co., Virginia.

Sampling was performed three to four times at each location on an approximate monthly basis through the period of May to September 2018 during ebb tide, employing a synoptic sampling mode within each of the sub-regions having multiple sites (e.g., Hunting Creek, Four Mile Run, Gunston Cove). Surface water samples were obtained as grabs either onboard a 6-m skiff or by wading into shallow water using a submersible pump (Typhoon submersible pump, Max Flow 11 L/min, EnviroSupply & Service, Irvine, VA). Each water sample (20 L) was collected at mid-depth. The typical water depth was 1.5 m. The water was collected in 20-L sealed stainless-steel kegs and transported to the Environmental Chemistry Laboratory at the Potomac Science Center, George Mason University. Upon return to the laboratory, the water samples were immediately filtered and stored at 10˚C prior to analytical processing within 48 hr of collection. At each sampling site two additional 1-L water samples were collected in polypropylene bottles using the same pump method for the analysis of total suspended soids (TSS) at each site. All sample containers were pre-rinsed three times with sample water prior to filling.

Riverbed sediments were obtained onboard the skiff or via shoreline sampling coincident with water sampling when available fine-grained sediment was present (i.e., primarily silt-clay in composition). Upstream sites were often rocky or coarse-sand-bottomed and sediment was not obtained. Sediment was collected using a Petite Ponar grab tethered by hemp rope. The sediment obtained in the Ponar was taken aboard the boat or shore and carefully expelled into a stainless-steel tray minimizing disturbance to sediment. Approximately 10 g of the top 2 to 4 cm of the surficial layer was removed and placed directly into a pre-cleaned amber glass jar using a stainless-steel spoon. The jar was sealed using a Teflon-lined lid and stored on ice for transportation. The samples were stored at -20˚C in the laboratory until further analytical processing.

Materials

Whatman® glass microfiber filters, GF/F and GF/D, sizes 47 mm and 150 mm, were used for water filtration for small and large volume water samples, respectively, and were purchased from Sigma Aldrich (St. Louis, MO). Oasis MAX and MCX 6 mL cartridges (500 mg Sorbent per Cartridge, 60 µm Particle Size) were used in the extraction of all water samples and were purchased from Waters Corporation (Milford, MA). QuEChERS (Agilent Technologies, Santa Clara, CA) extraction and dispersive solid phase extraction (dSPE) salts and kits, used to process all sediment samples for LC-MS/MS analysis, were purchased from Agilent Technologies (Santa Clara, CA). Acetonitrile and formic acid, used to make the LC-MS/MS mobile phases, were purchased from Thermo Fisher Scientific (Waltham, MA). Other bulk solvents used for analysis and supply preparation included methanol, acetone, and ethyl acetate were purchased from Thermo Fisher Scientific (Waltham, MA). Milli-Q Type-1 water (MQW) was used to prepare LC-MS/MS

mobile phase (Milli-Q Direct, EMD Millipore, Billerica, MA). LC-MS/MS liquid nitrogen and compressed argon and nitrogen gasses were purchased from Roberts Oxygen (Rockville, MD).

Sample Preparation

The 20-L river water samples were initially filtered through a stacked combination of GF/D overlying GF/F glass fiber filters to clear suspended particles from water (summarized in Fig. S1). The filtered water was aliquoted into 1-L glass jars for subsequent extraction. Each surface water location was analyzed in triplicate via the aliquoted 1-L bottles. The filtered water was spiked with 50 to100 ng each of the internal and surrogate standards prior to extraction. An Oasis MAX cartridge (top) was coupled to a MCX cartridge using a tube adapter and the tandem set was attached to a Supelco vacuum manifold (Sigma Aldrich, St. Louis, MO) on the outlet end and Teflon tubing (3 mm OD) to the sample bottle on the inlet end. Prior to extraction, the tandem MAX-MCX cartridge set was conditioned twice with 5 mL of 70:30 (v/v) methanol (MeOH):ethyl acetate (EtOAc), 5 mL of MeOH and 5 mL of MQW. The filtered samples were then loaded onto the cartridges via 3 mm (OD) Teflon tubing at a rate of 2 to 3 drops per second. Upon the conclusion of the extraction, the cartridges were washed twice with 95:5 (v/v) MQW:MeOH. The cartridges were aspirated on the manifold under vacuum for 30 minutes prior to elution. Following aspiration the MAX cartridges were eluted with 6 mL of 69:29:2 (v/v/v) MeOH:EtOAc:formic acid. The MCX cartridges were eluted with 6 mL of 67.5:27.5:5 (v/v/v) MeOH:EtOAc:NH_4OH. The SPE extracts were combined in a 40 mL amber vial and reduced in volume to 0.5 mL using a TurboVap (Zymark Corp., Hopkinton, MA) evaporator (employing dry N_2 gas). The evaporated extracts were filtered using 25 mm dia. PDVF syringe filters attached to a 5 mL glass syringe during transfer to 1.5 mL amber glass autosampler vials.

Thawed sediment was pre-sieved (0.5 mm) to reduce large particle heterogeneity prior to characterization. In PPCP analysis, wet sediment (corresponding to 2 g of dry sediment) was spiked with internal and surrogate standards and extracted using a QuEChERS method (Cerqueira et al. 2014; Dulaurent et al. 2016) as summarized in Fig S2. Briefly, 10 mL of acetonitrile + 10 mL of MQW were added to a 50 mL Falcon tube along with 6 g of anhydrous magnesium sulfate + 1.5 g of sodium acetate. The Falcon tubes were vortexed intermittently over 20 min while held on a shaker table. Following extraction, the tubes were centrifuged for 10 min at 2200 rpm and the acetonitrile (top) phase transferred to a 15-mL dSPE tubes containing 1.2 g of magnesium sulfate + 0.4 g of primary-secondary amine (PSA). The dSPE tubes were vortexed 4X over a 15 min period and centrifuged for 10 min at 2200 rpm, and the supernatant was transferred to a clean 40-mL amber glass vials for TurboVap (using dry N_2 gas) solvent concentration to 0.5 mL. The evaporated solvent was filtered and transferred as described for water samples above to 2 mL autosampler vials. Each location where sediment was collected was extracted and analyzed in triplicate.

LC-MS/MS analysis

PPCPs in water and sediment extracts were quantified using a Shimadzu Model 8050 tandem liquid chromatograph-mass spectrometer (LC-MS/MS) configured with a SIL-20ACXR autosampler (Columbia, MD). The LC-MS/MS interface was operated in DUIS mode using both positive and negative ionization at

a scan speed of 30,000 u/s at 0.1 u step size, coupled with polarity switching of 5 ms. LC-MS/MS separation of the PPCPs was performed using a 50 mm x 2.1 mm (id), 1.8 µm (dia) particle Force Biphenyl reversed-phase UHPLC column (Restek, Bellefonte, PA) in conjunction with a raptor Biphenyl guard column, with a binary mobile phase consisting of MQW (solvent A), and acetonitrile (solvent B), both containing 0.1% formic acid as a phase modifier. Operating conditions for the LC-MS/MS are listed in Table S3.

LC-MS/MS identification and quantitation of the PPCPs was accomplished using MRM mode and included 3 MRM ions for each target chemical (with a few exceptions). The MRM ions were established for each PPCP through automated MRM optimization procedures following manual precursor ion identification using the full scan mode. The quantifier (primary) and qualifier (secondary and tertiary) product ions and the various quadrupole voltages for the PPCPs are compiled in Table S4. Quantitation was performed using a 10-point internal calibration standard (ranging from 0.05 to 250 ng/mL) based on the primary product MRM ion abundance for each PPCP relative to that of an associated internal standard. The retention times and qualifier MRM ions relative abundances were used to confirm the chemical identity of the PPCPs. Data analysis and quantitation was performed using LabSolutions software (ver. 5.91).

Quality Assurance

Surrogate spike recoveries (N = 33) for sulfamethoxazole-$^{13}C_6$, alprazolam-d_5, and benzophenone-d_{10} were 62 ± 12%, 102 ± 10% and 80 ± 15% in surface water, and 67 ± 9%, 108 ± 11% and 104 ± 17% in sediments, respectively. Matrix-spike recoveries were performed for 60 of the PPCPs in surface water (25 ng/L) and sediments (20 ng/g), including all those detected in this study, obtained from sites 6 and 7 (see Figs. S2 and S3). The quantitation limit (QL) for all the PPCPs ranged from 0.54 ng/L to 51 ng/L in water and 0.39 to 26 ng/g in sediment (Table S4) and were determined according to Eq. 1 as

$$QL = \frac{S_y \times 10}{m \times V_s\left(M_s\right)}$$

1

where S_y is the regression standard deviation at the y-intercept, m is the slope of the calibration curve and V_s is the sample volume (L) for water or M_s is sample mass (g) for sediment. All autosampler vial volumes were adjusted to 1.0 mL. Method blanks were prepared using MQW and clean sand for water and sediment, respectively. Field blanks were prepared from MQW or sand, placed in 20-L beverage kegs (water) or 200 mL glass jars (sand) and taken into the field. The water field blanks were recirculated from the pump to the beverage can for 10 min prior to sampling at the first location of each trip. The jar containing sand was opened, stirred with a steel spatula and resealed. No target chemicals were detected in the laboratory blanks. Only 6 target chemicals were found in water field blanks but at concentrations below the QL, and only caffeine was detected in water above the QL in 14% of all field blanks. The other

compounds sporadically detected below QL concentrations in water field blanks included nicotine (14% frequency), sulfamethoxazole (4%), sulfaquinoxaline (4%), fexofenadine (12%), and carbamazepine (10%). No target chemicals were detected in any of the sand field blanks. Concentrations of the PPCPs in samples are expressed as ng/L for surface water and ng/g dry weight for sediments. For PPCP compositional analysis, concentrations are expressed in terms of mole fraction-PPCPs, which is defined as mol of a single PPCP divided by total mol of all PPCPs in the sample.

All glassware used for sample storage and preparation were cleaned by washing with soap, rinsing with Type-I MQW and fired at 400°C overnight to ignite any interfering organic residues on surfaces that may have interfered with quantitative analysis. All laboratory materials were made of glass, stainless steel, or Teflon to avoid minimize contamination. The Teflon materials were cleaned the same way as glass, but without firing. All non-glass items were rinsed with methanol and air dried before use.

Ancillary Measurements

Additional measurements were conducted to determine total organic carbon (TOC), %moisture, particle size analysis (PSA), and total suspended solids (TSS). TOC content was performed by Drexel University, using a Carlo Erba Model 1112 Flash Elemental Analyzer. Approximately 1 g of sediment from each sampling location and trip was dried in an oven at approximately 60^{o}C for 1 week, and then ground to a fine powder using a mortar and pestle. The samples were placed in a ceramic crucible and fumigated with concentrated HCl for 24 hours to degas carbon dioxide derived from inorganic carbon (primarily as carbonates) following the method of (Ramnarine et al. 2011). The treated sediment was re-dried in a 60°C oven for one week to ensure that no excess HCl was present. The sample was then placed into a tin boat, weighed, and combusted at 1000°C for total C and N content.

Sediment moisture was determined by difference gravimetrically using 1 to 2 g of wet sediment with drying at 60°C for 48 to 72 hr until a constant mass. Sediment grain size was measured using a Beckman-Coulter (Brea, CA) laser diffraction (LS 13320) particle size analyzer in the GMU Coastal Geology Lab at the Potomac Science Center. Pre-sieved sediment was disaggregated with 5% aqueous hexametaphosphate prior to analysis. Grain size results were provided by the Excel program GRADISTAT for ternary diagrams. Total suspended matter (TSM) in river was determined by vacuum filtration of a 1-L river water samples through stacked, pre-weighed 47 mm (diameter) GF/D and GF/F glass fiber filters. The filters were dried at 60°C and analyzed gravimetrically to derive TSM.

Flow for each of the tributaries and Potomac River on sampling days were obtained from the USGS WATSTOR database (https://www.USGS.gov).

Results And Discussion

Ancillary Parameters

In hydrologic environments, physical and geochemical variables such as TSS, sediment grain size, sediment %moisture and sediment total organic carbon (%TOC) are all important parameters to consider when evaluating the presence, dispersal and distribution of micropollutants. Sediment %moisture varied from 30% (site 6) to 67% (site 4), with an overall average of 52% (Fig. S4). Sediment %moisture showed a weak inverse correlation (Spearman's Rho 0.44, $p<0.05$) with sediment grain size. TSS was measured at all sites where surface water was collected (Fig. S5). The detection limit for TSS was determined to be 0.1 mg/L. TSS values ranged from 0.11–261 mg/L with an overall median average of 26.3 mg/L. There was no significant difference in TSS among all sampling sites (Kruskal-Wallis, $p>0.05$). Sediment texture varied both spatially and temporally in the TFPR (Fig S6). The sediments were predominantly classified as sandy-silt for Hunting Creek (sites 6-10) and as silty for Four Mile Run (sites 3 and 4) and Gunston Cove locations (sites 12 and 13). However, there was a significant difference in grain size among the sediments across all sites (Kruskal-Wallis, $p<0.05$); for upstream Hunting Creek (site 5), a greater percentage of sand composition relative to the other downstream sites was observed. %TOC in sediment (Fig. S7) varied minimally both spatially and temporally in the TFPR, ranging from 1.2 - 2.0% (wt/wt) with a mean value of 1.6% across all the sediment sites. There was no statistical difference in %TOC among the sites (Kruskal-Wallis, $p>0.05$).

PPCP Quantitation Frequency

The quantitation frequencies observed for the PPCPs in both surface water and sediments are provided in Table S5. Overall, 33 of 91 total PPCPs were quantified in water ($S_{33\text{-}w}$PPCP) and 39 of 91 were quantified in sediments ($S_{39\text{-}s}$PPCP) collected in the TFPR. Altogether, 52 of 91 PPCPs were quantified in either water or sediments. The remaining 39 PPCPs were not quantified in either matrix. The PPCPs were grouped by quantitation frequency (QF) into high (³60%), moderate (³40%), and low (£25%) categories in any single matrix to characterize abundance (Table S5). Three PPCPs were quantified at high frequency in both matrices, including fexofenadine, metoprolol, and tramadol. Those PPCPs detected primarily in water (³60%) included sulfamethoxazole, caffeine, nicotine, and carbamazepine. Conversely, the PPCPs found extensively in sediments (³60%) included diphenhydramine, escitalopram, methadone, sertraline, and fluoxetine. High QF PPCPs were those commonly quantified in both matrices, moderate frequency PPCPs were those quantified primarily in a single matrix, but not both, matrices, and low frequency PPCPs were rarely quantified £25% in either matrix.

Spatial Distribution of SPPCPs

The $S_{33\text{-}w}$PPCP concentrations (ng/L) showed significant differences in surface water spatially along the TFPR (Kruskal-Wallis, $p<0.05$), with the greatest median concentrations observed near the WTP outfalls at sites 3 and 6 (Fig. 1a). The lowest $S_{33\text{-}w}$PPCP median concentrations occurred in the mainstem Potomac River or at fluvial sites upstream from the WTP outfalls. The five mainstem TFPR sites (1,9,10, 13 and 14) showed significant differences in surface water concentrations (Kruskal-Wallis, $p>0.05$), with site 14 being an outlier. However, when site 14 was removed the four remaining mainstem locations were not significantly different in median $S_{33\text{-}w}$PPCP concentrations (Kruskal-Wallis, $p<0.05$). Site 14 was clearly

influenced by the presence of a WTP located on the Quantico Marine Base, which discharge into Quantico Creek upstream of the sampling point. The mainstem TFPR showed the smallest median $S_{33\text{-}w}$PPCP concentrations (sites 1, 9, 10 and 13), ranging from 75-113 ng/L, with the fluvial entry point to the TFPR at Chain Bridge showing the greatest upper-end-member concentration among the mainstem locations. It appeared the median concentrations decreased slightly in the downstream direction in the mainstem TFPR, although the differences were not statistically significant. This observation was likely because of dilution arising from additional surface water contributed by nine tributaries flowing into the mainstem TFPR, adding ~4% of additional flow volume below Chain Bridge. Although the high-capacity WTPs increased surface water concentrations of PPCPs in the immediate vicinity of the outfall zones, with a downstream influence of ~1 km radius, the WTPs did not appear to alter the concentrations of $S_{33\text{-}w}$PPCP in the mainstem Potomac River along the entire length of the TFPR from Chain Bridge to Quantico. The concentrations of $S_{33\text{-}w}$PPCP in the mainstem of the TRPR were consistent along its longitudinal axis, and any net increase or decrease was undetectable.

The flow-weighted average (FWA) concentrations of the PPCPs showed good agreement with the time-weighted median (TWM) concentrations as shown in Fig. 1a. That FWA » TWM implies a flat C-Q relationship between solute concentration and stream flow (Chorover et al. 2017; Moatar et al. 2017), which is not unexpected since all sampling occurred during predominantly baseflow conditions from May through September 2018.

The $S_{39\text{-}s}$PPCP concentrations in sediment also varied spatially, with the greatest concentrations observed within a 1 km radius of WTP discharge (Fig 1b). However, the distinct feature of sediment was that concentrations maximized in the embayments and not directly adjacent to the discharge zone as shown in Fig. 1b. The sediment spatial presence is best exemplified by Hunting Creek (sites 6-8), whereby the maximum concentrations were found in the deposition zone of the Lower Hunting Creek (sites 7-8). The deposition zone occurs where Lower Hunting Creek empties into its shoal and forms a bayhead delta. This sediment deposition zone clearly traps PPCPs emerging from WTP discharge undergoing downstream transport. Such a sedimentary process creates greater ecotoxicological risk in the benthic shoal community in the TFPR from PPCPs entering through the tributaries. However, the presence of relatively large $S_{39\text{-}s}$PPCP concentrations in the Lower Hunting Creek shoal was a localized phenomenon because the mainstem TFPR sediments were much lower in concentration relative to the embayments (Fig. 1b).

Individual PPCPs in WTP Effluent and Nearby Discharge Zones

The PPCPs were evaluated individually by box plots, and in this case only those with quantitation frequencies >50% were considered in statistical analysis. Fexofenadine, an antihistamine, and caffeine had the greatest concentrations in the surface water samples followed by desvenlafaxine (antidepressant), nicotine (stimulant), MDA (illicit), hydrochlorothiazide (diuretic), metoprolol (b-blocker) and sulfamethoxazole (antibiotic), all present with median concentrations greater than 20 ng/L (Figs. 2 and 3). Carbamazepine (anticonvulsant) and bupropion (antidepressant) were observed with median

concentrations greater than 10 ng/L. The remainder of the individual PPCPs in surface water were found at concentrations less than 10 ng/L.

The PPCPs measured in the effluents of WTP 1 and WTP 2 are illustrated in Figs. S8 and S9. The individual PPCP concentrations (log transformed) were well correlated between the two effluents (Spearman's Rho = 0.861, $p<<0.05$), indicating the PPCP constituent compositions among the two waste treatment discharges were similar, which was expected given the similar sociodemographics of the two sewer-sheds in Northern Virginia. But, the total PPCP concentrations were generally greater in WTP 2 effluent. The important implication of this observation is that the PPCP chemical-specific inputs into the TFPR were seemingly consistent among the major WTPs. However, the composition of PPCPs in WTP effluents differed significantly from the PPCP compositions observed in the corresponding TFPR discharge zones (Figs. 2 and 3), which was true for WTP 1 and site 3 (Spearman's Rho = 0.15, $p>0.05$) and WTP 2 and site 6 (Spearman's Rho = 0.27, $p>0.05$). There were 43 PPCPs quantified in the WTP effluents and 33 PPCPs correspondingly quantified in the WTP discharge zones. PPCPs were detected at concentrations up 14,000 ng/L in WTP effluent, while averaging up to 400 ng/L in discharge waters, yielding a ~40-fold or greater dilution upon entering the TFPR.

The substantial change in chemical composition of the PPCPs between effluent and nearby receiving waters shows that dispersal forces and reactivity act on PPCPs rapidly following discharge. The most likely physical processes that act on PPCPs immediately are dilution and sorption in geosolids, with air-water partitioning likely occurring to a minor extent with respect to the total PPCP composition. PPCPs for the most part have negligible Henry’s law constants. However, some PPCPs are highly particle-reactive, and it has been shown previously that substantial PPCP fluxes occur into bed sediments within the discharge zone of Hunting Creek (site 6) (Foster and Leahigh 2021). Degradative pathways such as biotransformation, hydrolysis and photolysis are also likely to alter the PPCP compositions in surface waters. For example, photolysis of hydrochlorothiazide, which was a predominant PPCP in our study, occurs rapidly in water with a half-life of 0.43 hr (Baena-Nogueras et al. 2017). Diphenhydramine, fexofenadine, sertraline, and escitalopram have previously been shown to be highly sorptive in sediments as reported by other studies (Stein et al. 2008; Li et al. 2011; Yu et al. 2013; Xu et al. 2021). Atenolol, metoprolol, caffeine and carbamazepine can be rapidly degraded by residual chlorine alone or in combination with UV-light (Cheng et al. 2019). Effluent has very moderate residual chlorine concentrations, which is used as a disinfectant in tertiary treatment at WTPs. Ranitidine is rapidly transformed into a nitrosamine by-product in the presence of chlorine and UV-light (Seid et al. 2021). Bupropion undergoes rapid hydrolytic degradation in aqueous solution at pH >5 to its most prominent degradation pathway that involves a hydroxide-catalyzed catalysis of the neutral base form (O’Byrne et al. 2010). The pH of receiving waters reported for the TFPR estuary have ranged from 6.8 to 7.8 depending on the season (Jones et al. 2014) promoting hydrolysis. All these examples show how geochemical distribution and partitioning along with degradative forces act on PPCPs discharged into surface waters, contributing in many cases to rapid and extensive alterations in chemical compositions.

PPCP Composition in Surface Water and Sediment

There were 18 individual PPCPs detected at concentrations above the QL in >50% of the samples, which included nicotine, caffeine, triamterene, metoprolol, tramadol, desvenlafaxine, bupropion, sulfamethoxazole, dextromethorphan, venlafaxine, diphenhydramine, carbamazepine epoxide, fexofenadine, carbamazepine, methadone, and celecoxib. In addition, there were several PPCPs detected in Hunting Creek (sites 5-8) and Four Mile Run (sites 2-4) that were not present at Gunston Cove (sites 11-13). These PPCPs included cotinine, atenolol, propranolol, diltiazem, hydrochlorothiazide, and furosemide. The PPCP MDA was found exclusively in surface water samples from the Four Mile Run area. There were no individual PPCPs that were unique to only the Gunston Cove area (sites 11-13).

The identity of PPCPs found at sites remote from the WTP discharge zones in the TFPR were identical to the individual PPCPs shown in Figs. 2 and 3, but with fewer of them and at lower concentrations. Along with a reduction in the concentrations of PPCPs remote from the WTP discharge zone, it was observed the compositional profile of PPCPs also changed markedly. PPCP concentrations in water were converted to mole fraction-PPCP concentrations and analyzed by principal component analysis (PCA) to visualize chemical composition trends. The compositional profiles of the PPCPs varied substantially throughout the TFPR, which is demonstrated by the PCA plot (Fig. 4) highlighting a spread of eigenvalues across a compositional arc beginning with the WTP effluents and culminating in the mainstem TFPR and upland locations (lower right quadrant of PCA). The PCA can be divided into 4 compositional segments (Fig. 4), including (i) the WTP effluent from WTPs 1 and 2 (upper left quadrant in Fig. 4), (ii) WTP discharge zone, (iii) transition mixture where the embayments flow into the mainstem TFPR and (iv) the mainstem TFPR itself in combination with the upland watersheds (lower right quadrant). The first two PCAs accounted for 87% of the compositional variability. The sites that cluster in the PCA zones are also shown in Fig. 4. The WTP effluent composition clusters in the upper left quadrant of the PCA plot, and as indicated above the two effluents were well correlated in PPCP composition. The TFPR sites nearest the WTP outfalls showed a composition on the PCA in closest proximity to the effluents (e.g., sites 3, 4, 6-9, 12 and 14), but trending down and to the right. The opposite end of the PCA in the lower right quadrant included the sites directly upstream (above the head of tide) from the WTP outfalls (e.g., sites 2, 5, and 11) and some of the mainstem TFPR sites (e.g., sites 1, 10 and 13). The mixed zone included several sites that were primarily mainstem sites (e.g., sites 9, 10, and 13) that trended upward toward the discharge zone in the PCA. The PCA was very useful in proving that site 14 was impacted by nearby WTP effluent at Quantico (site 14).

The composition of the PPCPs in surface water was distinctly different between the TFPR mainstem and the tributary discharge zones as described above. Further insight into the factors controlling the change in PPCP composition during downstream transport is further highlighted in Fig. 5. Desvenlafaxine, for example, was a major PPCP constituent in WTP effluent and was also prominent in the WTP discharge zone of Hunting Creek, but it was not detected in filtered surface water at sites 9, 10 or 13 in the mainstem TFPR. In addition, fexofenadine was replaced by caffeine as the most prominent PPCP in the mainstem TFPR. The likely explanation for this alteration in composition in the Hunting Creek region is sorption to geosolids followed by particle deposition within the Hunting Creek shoal. The sediment concentrations of PPCPs are shown in Fig. 6 with site 8, the site with the greatest PPCP observed concentrations in TFPR sediments, showing the dominant presence of desvenlafaxine and fexofenadine.

The log K_{ow} values of these PPCPs are listed in Table 1, where it is clear from inspection of the pK_a values (also in Table 1) that a significant fraction of these particular PPCPs is expected to be positively charged at ambient pH based on the observed log K_{ow} > log D_{ow} in combination with at least one pK_a > 7.6 in each case (7.6 was the average observed pH in surface water at this location). It is well known that a significant portion of PPCPs sorption occurs via mineral complexation of positively charged, protonated nitrogen species (Loeffler et al. 2005; Kiecak et al. 2019).

There were 16 PPCPs detected at concentrations above the QL in sediments at ³50% frequency. These included all the PPCPs shown in Fig. 6 for site 8. All sites showed PPCPs that were composed of subsets of these 16 constituents, except for Pohick Bay where triclocarban was quantified at <50% frequency in sediments. PPCP chemical composition in sediments diverged from that found in surface water. Further, the PPCPs detected in sediments showed no significant correlation (Spearman's Rho = 0.15, p>0.05) between log D_{ow} (n-octanol/water distribution constant at pH 7.4) and the measured conditional distribution constant, $K_{d\text{-}cond}$ ($K_{d\text{-}cond} = C_s/C_w$ for PPCP concentrations quantified in sediments (C_s) and surface water (C_w)). The dynamic interaction of PPCPs with sediments is only partially explained by log D_{ow} because sorption to sediment through electrostatic complexation mechanisms occurs in addition to organic matter partitioning (Khetan and Collins 2007; Pan et al. 2009; Martínez-Hernández et al. 2014; Yamamoto et al. 2018). The $K_{d\text{-}cond}$ estimates were often much larger than expected based upon log D_{ow}, especially for PPCPs predicted to be positively charged at ambient pH. Another possible reason for lack of correlation with log D_{ow} is because of rapid transformation that may be taking place in the environment (yielding low water concentrations). Furthermore, the sediment concentrations were not normalized to organic carbon levels because there was no observed correlation between $K_{d\text{-}cond}$ and %TOC (Spearman's Rho 0.10, p>0.05). It is generally assumed that organic micropollutants partition primarily into natural organic matter based on polarity and the (increasing) magnitude of D_{ow}. Interactions of PPCPs between water and geosolids is a mixed complexation process, and the role the organic carbon plays in geochemical fate is not dominant.

Temporal Variability

Seasonal (i.e., May through September) differences in PPCP concentrations were exemplified in the TFPR for caffeine and fexofenadine (Kruskal-Wallis, p<0.05). Two distinct seasonal profiles were apparent in our study. The examples were derived from site 6 near WTP 2 effluent because this is where the greatest concentrations of PPCPs were observed in surface waters (Fig. 7). Mole fraction-PPCP concentrations are expressed in Fig. 7 to represent compositional changes in the PPCP mixture. Caffeine displayed reduced concentrations in June and July relative to May and September (Fig. 7). The caffeine profile was negatively correlated (Spearman's rho = -0.68, p<0.05) with temperature, which was the only significantly correlated ancillary parameter identified. Other PPCPs that mirrored the caffeine seasonal profile included nicotine, metoprolol, atenolol, propranolol, celecoxib, desvenlafaxine, venlafaxine, triamterene and tramadol. Previous reports have documented the seasonal or annual variability in PPCP concentrations in surface waters (Sui et al. 2011; Sun et al. 2014; de Jesus Gaffney et al. 2017; Khasawneh and Palaniandy

2021; Singh and Suthar 2021), and suggest variables such as precipitation and stream flow, water temperature, WTP tertiary treatment technology, and dosage patterns influence seasonal variability. Another observed seasonal profile of concentration differences in surface water (Kruskal-Wallis, $p<0.05$) was demonstrated by fexofenadine (Fig. 7). Fexofenadine showed larger concentrations in May, June and July relative to September, which was a rather unique seasonal trend among this assemblage of PPCPs. Cotinine was the only other PPCP to show a similar seasonal trend to fexofenadine. The remaining PPCPs showed no significant seasonal trends. Sun et al. (2014) showed that caffeine in WTP receiving waters in China was present at the greatest concentrations in February, which was correlated with greater PPCP removal efficiencies from sewage treatment in the warmer months. Caffeine has shown a high removal efficiency (>90%) during sewage treatment indicating it is fairly labile (Kosma et al. 2014). However, even PPCPs previously reported to be recalcitrant to degradation by sewage treatment, such as metoprolol (de Jesus Gaffney et al. 2017; Khasawneh and Palaniandy 2021), showed a significantly lower composition in the summer months implying greater degradation in the WTPs during warmer temperatures.

Conclusions

Discharge from WTPs into the TFPR in the metropolitan Washington, DC region showed PPCPs concentrations are elevated within a roughly 1 km radius downstream of the discharge point. Concentrations of PPCPs in the discharge zone were also found higher in riverbed sediment. However, both water and sediment concentrations of the PPCPs were attenuated beyond ~ 1 km of the discharge points and did not lead to elevated downstream concentrations in the mainstem TFPR. It appeared that WTP discharge containing PPCPs in the tributary embayments did not yield enhanced surface water concentrations of PPCPs in the mainstem of the Potomac River, thus not leading to elevated concentrations of PPCPs carried downstream toward Chesapeake Bay. The effects of PPCPs, if any, are likely to be limited to the tributary embayments in the vicinity of WTP discharge.

Declarations

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Supplementary Information

The online version contains supplementary material available at https://

Author Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Arion Leahigh and Gregory Foster. The first draft of the manuscript was

written by Gregory Foster and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data Availability

Original data used in our study are available upon request to the corresponding author.

Declarations

The authors have no relevant financial or non-financial interests to disclose.

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Tables

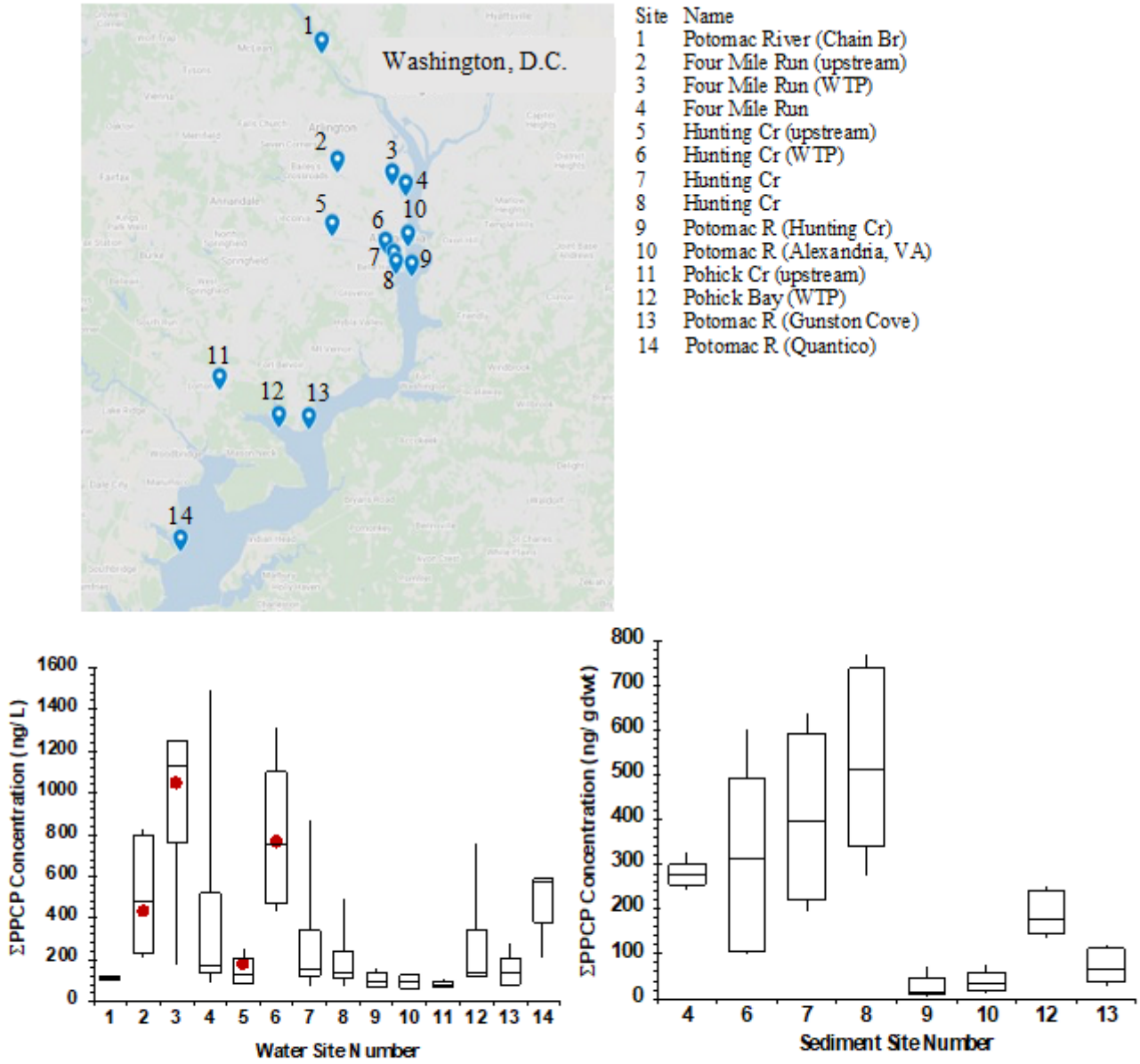
Table 1. Physical properties of selected PPCPs.

PPCP	pk_a[a]	log K_{ow}[b]	log D_{ow} (7.4)[b]
Diphenhydramine	8.98	3.27	2.34
Escitalopram	9.80	3.74	1.27
Desvenlafaxine	pK_{a1} = 9.45 pK_{a2} = 10.66	2.72	0.89
Fexofenadine	pKa1 = 8.76 (NH) pKa2 = 4.28 (COOH)	4.80	2.43

[a]pubchem.ncbi.nlm.nih.gov

[b]www.chemspider.com

Figures



Site	Name
1	Potomac River (Chain Br)
2	Four Mile Run (upstream)
3	Four Mile Run (WTP)
4	Four Mile Run
5	Hunting Cr (upstream)
6	Hunting Cr (WTP)
7	Hunting Cr
8	Hunting Cr
9	Potomac R (Hunting Cr)
10	Potomac R (Alexandria, VA)
11	Pohick Cr (upstream)
12	Pohick Bay (WTP)
13	Potomac R (Gunston Cove)
14	Potomac R (Quantico)

Figure 1. Box plots of $\Sigma_{33\text{-}w}$PPCP concentrations found in surface water (A) and $\Sigma_{39\text{-}s}$PPCP ediment (B) samples in the tidal freshwater Potomac River. The flow weighted average PPCP concentrations (red circles) in A are shown in the boxes for several sites in Hunting Creek.

Figure 1

See image above for figure legend.

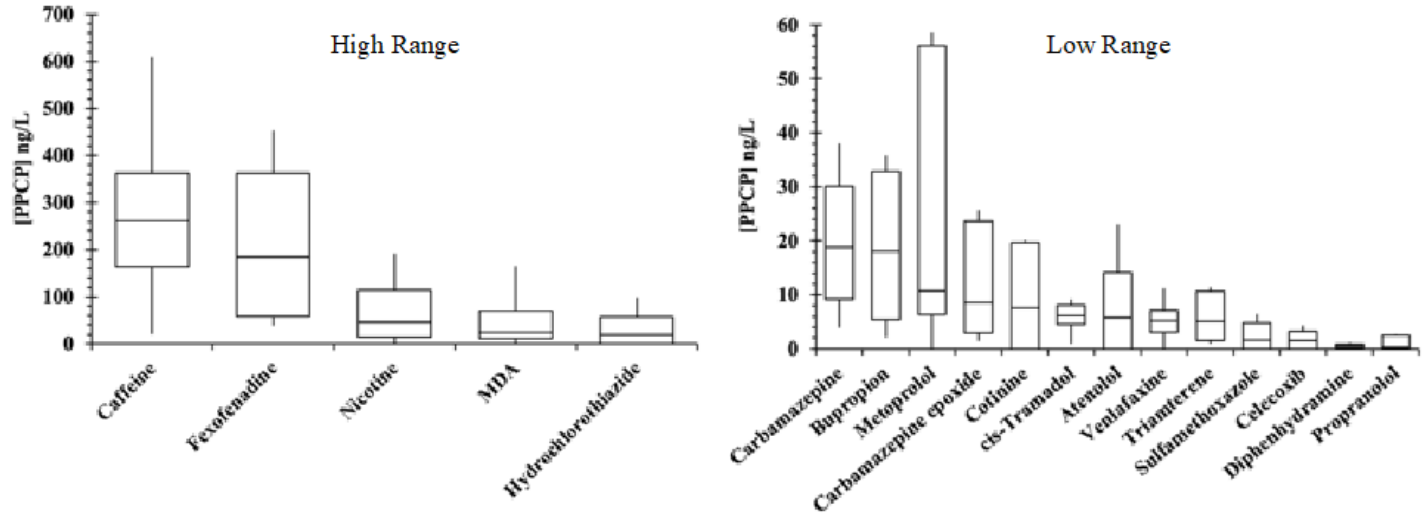


Figure 2. Box plot of individual PPCP concentrations at site 3 near WTP 1 in the TFPR. Boxes represent 25th and 75th percentiles and whiskers 5th and 95th percentiles. PPCPs at this site are separated into high range and low range concentrations.

Figure 2

See image above for figure legend.

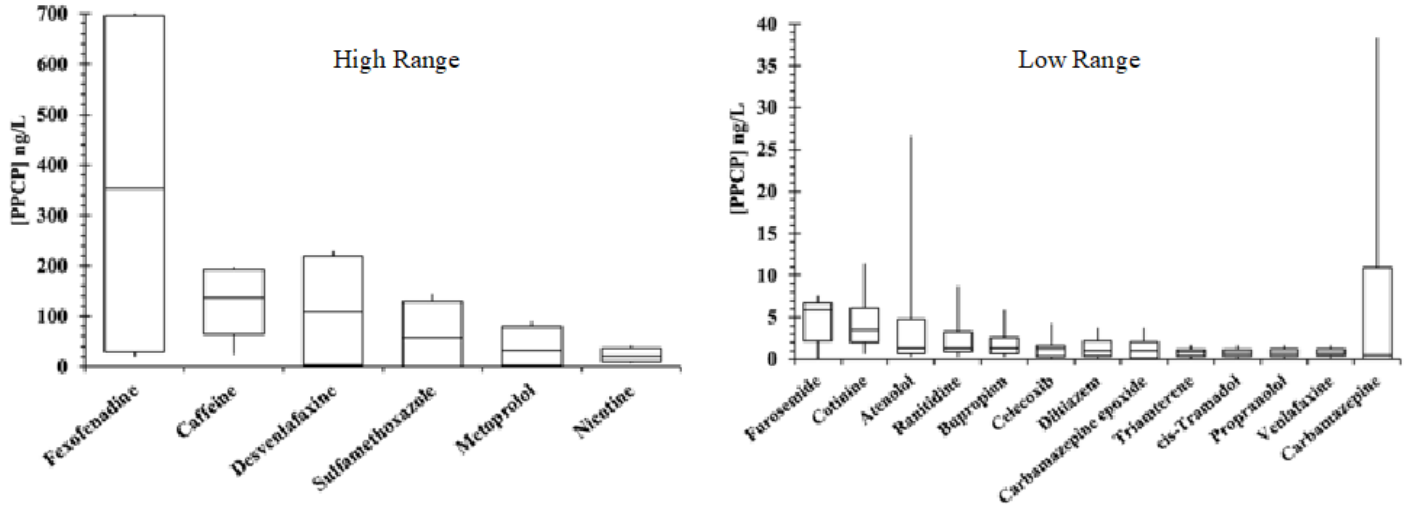


Figure 3. Box plot of individual PPCP concentrations at site 6 near WTP 2 in the TFPR. Boxes represent 25th and 75th percentiles and whiskers 5th and 95th percentiles. PPCPs at this site are separated into high range and low range concentrations.

Figure 3

See image above for figure legend.

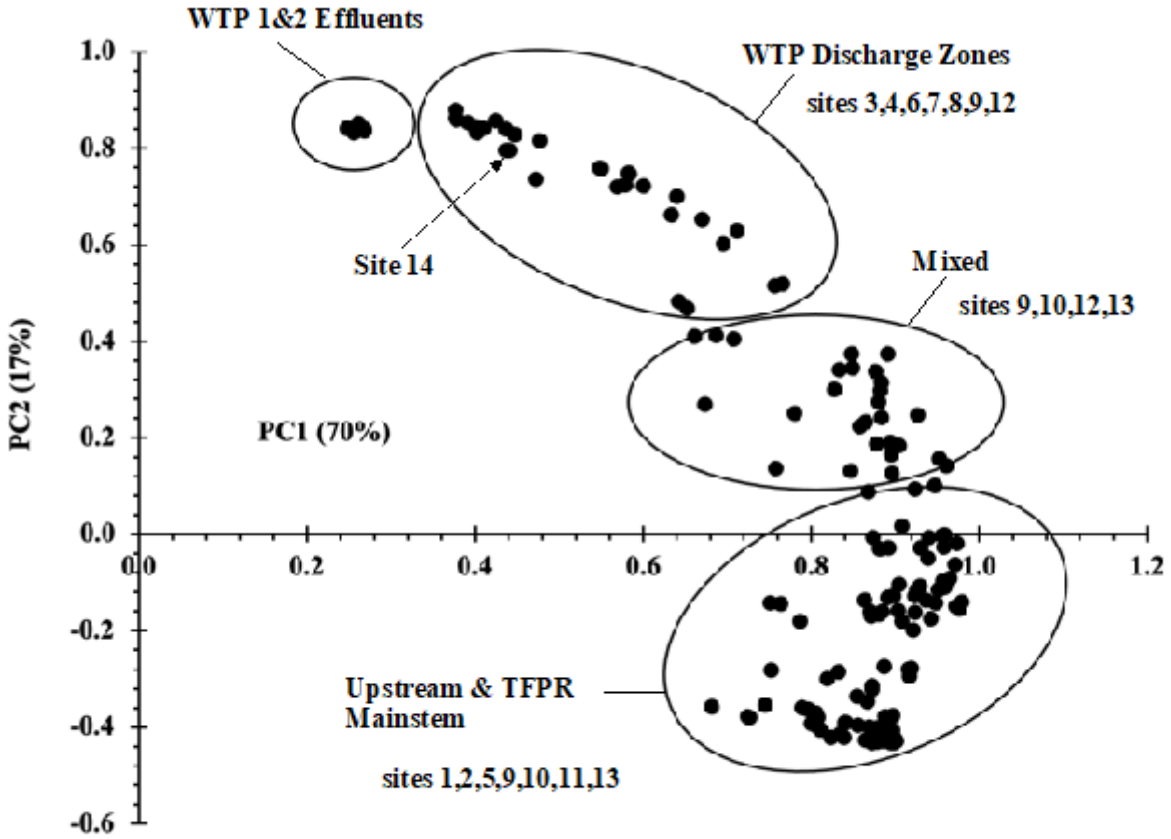


Figure 4. PCA loadings plot of PPCP composition across all surface water sites.

Figure 4

See image above for figure legend.

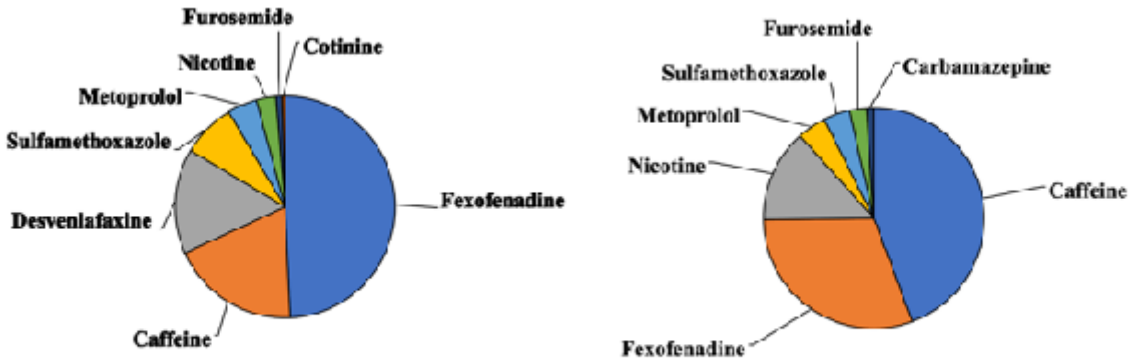


Figure 5. Major PPCP constituents in WTP discharge zone (site 6) and in the downstream TFPR mainstem (site 9).

Figure 5

See image above for figure legend.

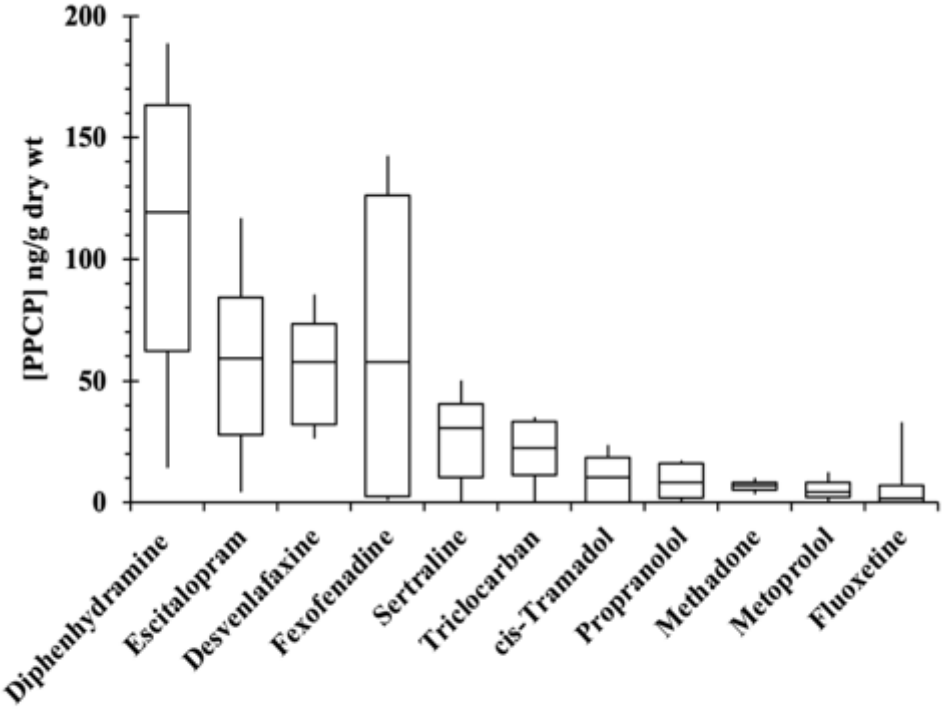


Figure 6. Box plot of sediment PPCP concentrations (ng/g dry wt) at site 8. The log Kow and Dow of the

Figure 6

See image above for figure legend.

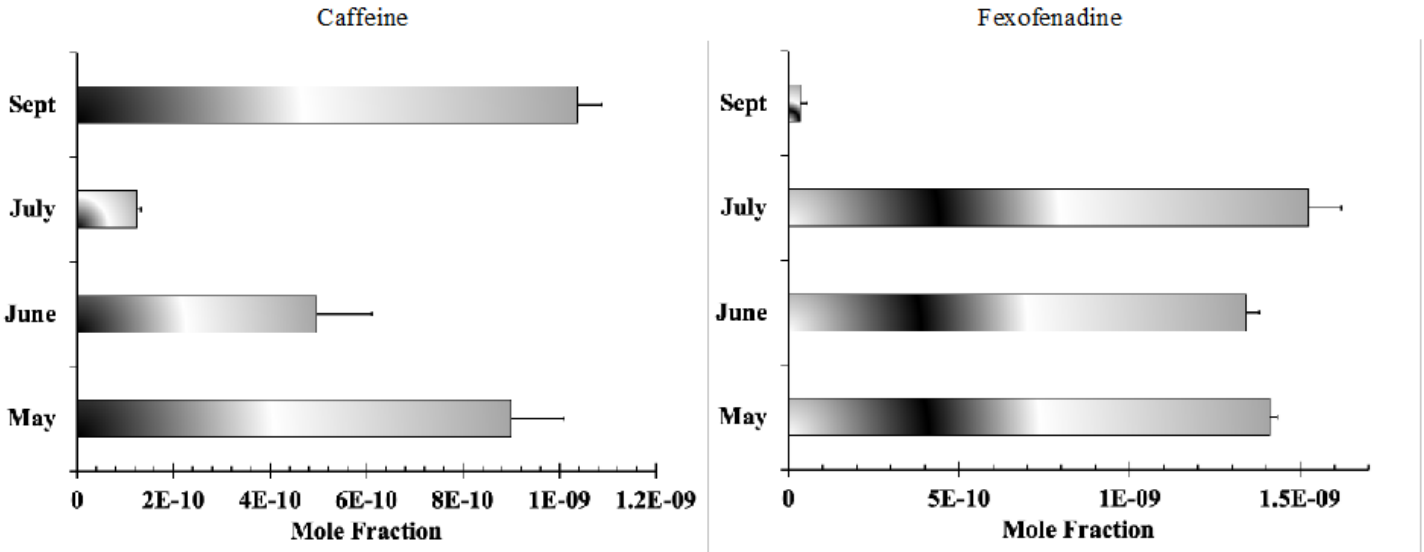


Figure 7. Comparison of the seasonal profiles of selected PPCP concentrations at site 6 near WTP 2 discharge into Hunting Creek.

Figure 7

See image above for figure legend.

Supplementary Files

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- GraphicalABstract.png
- Supplementaryinformation.docx