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## Persistent contaminants of emerging concern in a great lakes urban-dominant watershed



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### ABSTRACT

Within the Great Lakes, contaminants of emerging concern (CECs) have been detected in urban surface waters. Understanding the human and ecological health consequences of environmentally-relevant exposures to persistent CECs, particularly as complex mixtures, is essential. Surface water and a limited number of sediment samples were collected over two years (Spring and Fall 2018–2019) at multiple locations in the Lake Huron to Lake Erie corridor to investigate more than 150 CECs. Surface water was analyzed for pharmaceutical and personal care products (PPCPs), pesticides, and per- and polyfluoroalkyl substances (PFAS). Sediment was analyzed for PFAS. Fifty compounds were detected at ng/L or ng/kg levels. Synthetic sweeteners accounted for 55.7% of the cumulative concentration of all compounds detected across sampling events, followed by pesticides (27.5%), pharmaceuticals (11.7%), and stimulants (3.5%), with 14 compounds consistently detected: acesulfame-potassium, sucralose, sulfamethoxazole, acetaminophen, lidocaine, atenolol, gemfibrozil, iohexol, atrazine, diaminochlorotriazine, deethyl-atrazine, deisopropylatrazine, 2,4-Dichlorophenoxyacetic acid, and caffeine. Compound mixtures became increasingly complex downstream and indicated that the downstream Lake Huron to Erie corridor is wastewater effluent-dominated, whereas the aquatic environment associated with Lake St. Clair is influenced by a mixed urban, suburban, and agricultural landscape. These results will inform follow-up studies on persistent contaminant mixtures and multiple stressors, and offer science-based priorities and evaluation objectives for natural resource and public health agencies/initiatives.

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### Introduction

The Laurentian Great Lakes basin contains approximately 20% of the world's and 84% of North America's surface freshwater, supporting >30 million people and 9 major metropolitan centers in the United States (US) and Canada (CA) (US EPA Great Lakes, 2021). These metropolitan centers are heavily developed and/or industrialized with urban watersheds that are profoundly influenced by human activity. Throughout the Great Lakes ecoregion, contaminants of emerging concern (CECs) and their degradation products have been detected in urban surface waters used for recreation, sustenance/subsistence, transportation, wildlife habitat, and/or as sources for drinking water, typically at low levels

ranging from ug/L (parts per billion) to ng/L (parts per trillion) (Baldwin et al., 2016; Barber et al., 2015; Blair et al., 2013; Boulanger et al., 2004; Boyd et al., 2003; Deere et al., 2020; Elliott et al., 2017; Ferguson et al., 2013; Fogarty, 2007; Kolpin et al., 2002; Lee et al., 2012; Metcalfe et al., 2003; Remucal et al., 2019). CECs are a diverse group of chemicals, such as pharmaceutical and personal care products (PPCPs), pesticides, and per- and polyfluoroalkyl substances (PFAS), that were not previously or only recently detected, have unknown health or ecological impacts based on the levels detected in the environment, and/or remain unregulated.

CECs primarily enter the environment via the effluent of wastewater treatment plants (WWTPs), which are not optimized to remove these organic compounds, combined sewer overflows (CSOs); and non-point sources, e.g. groundwater infiltration or runoff from residential, agricultural, industrial, or military sites (Barber et al., 2015; Baldwin et al., 2013; Daughton and Ternes, 1999; Fogarty, 2007; Fraley et al., 2020; Glassmeyer et al., 2017; Heberer 2002; Hu et al., 2016; Kingsbury et al., 2008; Kolpin

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et al., 2002; Petrie et al., 2015; Schultz et al., 2006; Rahman et al., 2009; Rosi-Marshall and Royer 2012; Veach and Bernot 2011; Yan et al., 2010). In fact, many CECs are considered anthropogenic waste indicators in the aquatic environment. PFAS are a large group of synthetic compounds that are used in a variety of household and industrial products and have characteristic carbon-fluorine bonds, rendering them resistant to degradation and thus persistent in the environment, hence the term “forever chemicals”. The persistence of bioactive PPCPs and pesticides in the freshwater environment depends on multiple factors, including the amount used and/or prescribed, land use, water flow rate, and susceptibility to metabolism, biotransformation, wastewater treatment processes, sorption, microbial degradation, and other degradation processes (e.g. volatilization, phyto- or hydrolysis) (Baldwin et al., 2016; Blair et al., 2013; Daughton and Ternes, 1999; Hua et al., 2006; Petrie et al., 2015; Sprague and Nowell, 2009; Veach and Bernot, 2011; Yamamoto et al., 2009). Due to their near-constant release into the environment, some of these compounds are considered pseudo-persistent.

The consequences for the environmental persistence of CECs at low levels, particularly as mixtures, remains poorly understood, but evidence suggests that these chemicals have adverse impacts at all levels of biological organization (i.e. molecular to ecosystem), ranging from induction of cytochrome P450 enzymes to endocrine disruption resulting in various human diseases to altered fitness in wild fish with implications for trophic cascade (Cizmas et al., 2015; Kidd et al., 2007; Nilsen et al., 2019; Pal et al., 2014; Thomas et al., 2017). CECs associated with urban water systems, including WWTPs, exert unique selection pressure for developing antibiotic-resistant bacteria (Pruden, 2014), which shift the structure and function of microbial communities, and thus ecosystems (Martinez, 2009). Further, these changes to bacterial genomes can negatively impact human health by causing longer or more costly treatment and increased risk of death (Ashbolt et al., 2013). PFAS, specifically, have been found in biospecimens from people and wildlife (Fraleley et al., 2020; Giesy and Kannan, 2001; Remucal et al., 2019). Though a small number of PFAS, notably perfluorooctanesulfonate (PFOS) and perfluorooctanoic acid (PFOA), both of which have been phased out of production, are linked to a wide range of physiological outcomes that include cardiac, neurologic, immune, reproductive, developmental, hepatic, and renal disease, little is known about the health effects related to the thousands of other PFAS, especially the increasingly relevant shorter-chain compounds [e.g. GenX or perfluorobutane sulfonic acid (PFBS)] and PFAS mixtures (Fraleley et al., 2020; Hu et al., 2016; Rappazzo et al., 2017; Reade et al., 2019). Few studies are available on the impacts of contaminant mixtures, which have the potential to induce antagonistic, additive, or synergistic effects, particularly depending on the compounds and species involved.

Understanding the distribution and persistence of CECs in the environment is essential for informing human, animal, and ecological health outcomes and intervention strategies. This study was performed within the Lake Huron to Lake Erie corridor centered around Detroit, Michigan (US), an industrialized, urban area that is situated on the Detroit River, which serves as an international shipping route and border with Canada, the drinking water source for more than 4 million people and includes the only International Wildlife Refuge in North America which is an important habitat for over 500 native fish, wildlife, plant, and freshwater mussel species (Badra, 2006; US Fish and Wildlife, 2016, 2017). Additionally, this corridor contains 4 of 31 Great Lakes Areas of Concern (AOCs) as designated by the US Environmental Protection Agency (EPA) due to significant, anthropogenic environmental degradation (US EPA, 2021). Within this geographic area, previous studies consistently found atrazine (triazine herbicide), caffeine, carbamazepine (prescription anticonvulsant), clofibric acid (metabolite of fibrate lipid

regulators), cotinine (nicotine metabolite), and over-the-counter non-steroidal anti-inflammatories (e.g. naproxen) in surface water samples, typically at ng/L levels, but also variably detected a variety of other pharmaceuticals and pesticides, fragrances, flame retardants, and insect repellent (Aichele et al., 2005; Boyd et al., 2003; Hua et al., 2005, 2006a, 2006b; Jasim et al., 2006; Metcalfe et al., 2003; Thomas et al., 2017). However, these previous studies largely represent data collection that occurred over a decade ago, focused on a small section within the geographic area, and/or include a relatively small number of target analytes, some of which have become less relevant due to regulations or decreased use over time (e.g. triclosan). Previous research on PFAS within the study area is more limited, but one sampling event revealed PFOS, PFOA, perfluoroundecanoic acid (PFUnDA), and perfluorohexane sulfonate (PFHxS) at a maximum of 2.1 ng/L in Detroit River surface water, and up to 18 PFAS were detected in sediment samples from Lake St. Clair (Codling et al., 2018; Scott et al., 2009).

The goal of the current study is to determine the environmentally-relevant concentration and distribution of persistent (or pseudo-persistent) CECs in the Lake Huron to Erie corridor. The implications of investigating more than 150 CECs (including degradation products) over multiple sampling events will be broad-ranging from advising follow-up studies (e.g. on the health and ecological implications of persistent contaminant mixtures and multiple stressors) to offering specific, science-based priorities and evaluation objectives for regulatory agencies, as well as natural resource and public health initiatives.

## Materials and methods

Water samples were collected in Spring (May) and Fall (October) 2018–2019 (S18, F18, S19, F19) at 6 locations in the Lake Huron to Lake Erie corridor: Site 1: Clinton River mouth (42°35'40.7"N, 82°46'01.6"W); Site 2: Lake St. Clair Metropark (42°56'18.7"N, 82°79'66.5"W); Site 3: Northeast Belle Isle (42°35'17.1"N, 82°95'94.7"W); Site 4: Southwest Belle Isle (42°33'35.5"N, 82°98'64.2"W); Site 5: Rouge River mouth (42°27'52.1"N, 83°11'07.6"W); Site 6: Detroit River International Wildlife Refuge (DRIWR)/Trenton Channel (42°09'97.8"N, 83°18'26.0"W). The locations were chosen based on proximity to water management facilities (e.g. WWTPs, CSOs, drinking water treatment plants [DWTPs]), as well as importance for recreation and/or wildlife habitat.

Sampling kits containing high-density polyethylene (HDPE) and amber glass vials for PFAS and other compound analysis, respectively, were obtained from commercial laboratories where analysis was subsequently performed. Water samples were collected at Sites 1 – 6 from a boat using a 0.5L stainless-steel bomb sampler (DWK Life Sciences, New Jersey, US) lowered to the desired depth and deployed by stainless steel wire. Composite water samples for PPCP and pesticide analysis were collected at 1 m depth. Due to unique properties that render PFAS both hydrophobic and hydrophilic (Buck et al., 2011), composite water samples for PFAS analysis were collected from both 1 m depth and at the surface. Similarly, due to the existence of multiple isomers and resistance to typical degradation processes that affect partitioning (Buck et al., 2011), a limited number of sediment samples for PFAS analysis were collected using a stainless-steel, petite ponar grab (Wildco®, Florida, US) at Sites 2 and 5 for F18 and S19. During S19, grab water samples were additionally collected from a WWTP effluent (prior to chlorination) and DWTP influent in the study area. To prevent contamination of samples for PFAS analysis, samples for PFAS analysis were collected first at each site; one person was designated to deploy the bomb sampler or petite ponar at each site, and did not handle other sampling equipment, containers, data sheets, or related material. Sampling containers and materials were made

of high density polyethylene, amber glass, or did not have any type of waterproofing treatment. Sampling devices were disinfected between sites using a commercial detergent (Alconox<sup>®</sup>, Sigma Aldrich, Inc., St. Louis, MO), then rinsed with type 1 reagent grade water. Nitrile gloves were changed between each site. For each sampling team, blank water controls to assess sampling-based PFAS contamination were collected at the end of each day's sampling effort. All samples were kept at 4 °C for a maximum of 48 h prior to arrival at commercial laboratories for analysis. At each site, water temperature (°C) and water depth (m) were recorded using an on-board GPS system (Garmin Ltd., Olathe, KS). Conductivity (uS/cm), dissolved oxygen (DO; mg/L), and turbidity (NTU) were analyzed using a multiparameter sonde (Hydrolab Quanta Multi-Probe Meter, OTT Hydromet, Washington, D.C.). Water velocity (m/s) was determined using a flow meter (OTT MF Pro, OTT Hydromet, Washington, D.C.) that was lowered approximately 6/10 of the water column depth. Rainfall for the month preceding each sampling effort was obtained from a weather station located at Detroit Metro Airport (latitude: 42.2313; longitude: -83.3308) via the National Oceanic and Atmospheric Administration's National Centers for Environmental Information.

For S18 and F18, PFAS analysis was performed by a commercial laboratory (Pace Analytical Services<sup>®</sup>, Minneapolis, MN) that employed EPA 537 Revision 1.1 Modified method that tested for 21 compounds. For S19 and F19, PFAS analysis was performed by a different commercial laboratory (Merit Laboratories, Inc, East Lansing, MI) that employed ASTM D7979 method with isotopic dilution for water matrix and ASTM D7968-17 method for sediment matrix. These methods both detected up to 28 PFAS compounds. PPCP and pesticide analysis was exclusively performed by a third commercial laboratory (Eurofins Scientific <sup>®</sup>, Luxembourg) via solid phase extraction (SPE) followed by liquid chromatography and tandem mass spectrometry (LC-MS-MS) in positive and negative ion mode. The primary purpose of S18 was to collect initial data to inform feasibility and target compounds for subsequent sampling events, thus a total of 54 PPCPs were analyzed (Electronic Supplementary Material (ESM) Table S1), whereas 133 PPCPs and pesticides were analyzed for subsequent sampling events. In F19 at Site 5 only, an additional 59 PPCPs were analyzed by a fourth commercial laboratory (SGS AXYS Analytical Services Ltd., Sidney, British Columbia). Laboratory control samples (LCS) and LCS duplicates were also analyzed with each sample to evaluate the precision and accuracy of the analytical procedure. A compound was considered detected (i.e. quantified) if above the minimum reporting limit (for PPCPs and pesticides) or minimum detection limit (for PFAS) combined with an LCS recovery <150% and relative percent difference <40%. A list of all compounds analyzed and detected for F18 – F19 is available in ESM Table S2; all quality control results are available ESM Appendix S1

Summary statistics were used to summarize PPCPs and pesticides (mean, range) that were detected across three sampling events (F18 – F19, not including results from SGS AXYS), as well as PFAS (mean) and environmental parameters (mean ± standard deviation, range) for all sampling events (S18 – F19). PFAS results were excluded if associated with any level of PFAS quantification in the respective field blank. For additional analysis, PPCPs were divided into compound classes: synthetic sweeteners, stimulants, pharmaceuticals, and miscellaneous commercial/industrial chemicals. Statistical significance between sites for cumulative concentration of compounds and each compound class (F18 – F19) and PFAS (S18 – F19) detected was determined using a Kruskal-Wallis test with multiple comparisons using a Dunn's test. The same tests were used to evaluate for significant differences in environmental parameters between sites and rainfall between seasons. Significance was set at  $p < 0.05$ . Due to the single sampling effort from the WWTP effluent and DWTP influent, this data was

excluded from analysis and graphical representation and used solely for understanding spatial gradients and impact of water infrastructure on CECs in the study area.

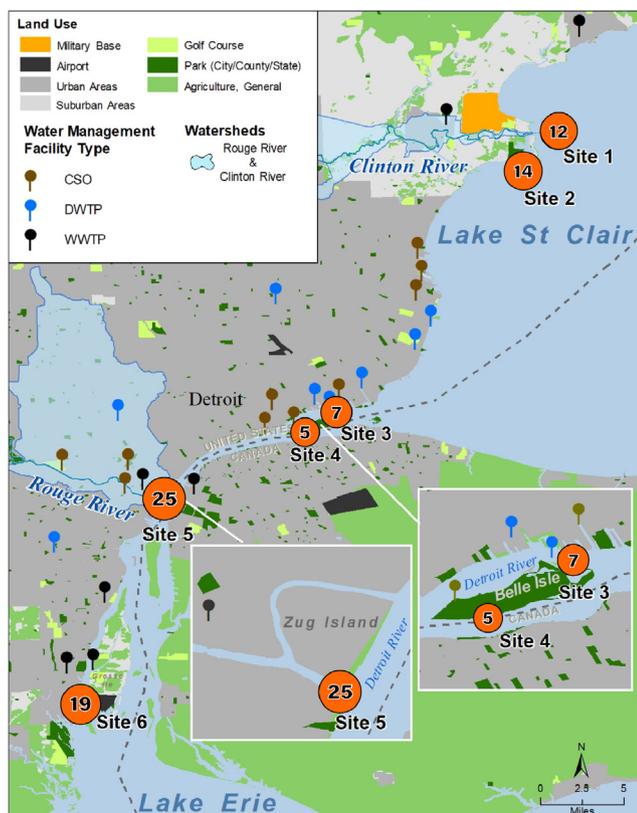
## Results and discussion

A total of 50 compounds were detected (i.e. quantified) at ng/L or ng/kg levels across Sites 1 – 6 in surface water and sediment samples collected in the Lake Huron to Erie corridor (ESM Table S2). Fig. 1 and Table 1 shows the pesticides and PPCPs (F18 – F19) and PFAS (S18 – F19) detected in surface water and the resulting potential contaminant mixtures at each site. The number of detected compounds was highest downstream in the Detroit River with 25 and 19 compounds found at Sites 5 and 6, respectively (Fig. 1 and Table 1). Sites 5 and 6 also had >10-fold higher cumulative concentration of compounds detected in surface water across sampling events compared to Sites 3 and 4, and >6-fold higher than Site 1 ( $p < 0.05$ ; Fig. 2). Sites 5 and 6 had significantly higher cumulative concentration of synthetic sweeteners compared to Sites 1 – 4 ( $p < 0.05$ ; Fig. 2), specifically >60-fold higher than Site 1, > 8-fold higher than Site 2, and >1600-fold higher than Sites 3 and 4. For pharmaceuticals, Sites 5 and 6 also had >55-fold higher cumulative concentration of detected compounds compared to Sites 1, 3, and 4 ( $p < 0.05$ ; Fig. 2), and >6-fold higher compared to Site 2, but this was only significant compared to Site 6 ( $p < 0.05$ ; Fig. 2). Though cumulative concentration of detected compounds was not significantly different between Sites 2, 5, and 6, pesticides comprised 59.2% of the cumulative concentration of detected compounds across sampling events at Site 2, whereas PPCPs were dominant at Sites 5 and 6 with pesticides accounting for only 14.7% and 10.8% of cumulative concentration, respectively (Fig. 2). Combined, these results indicate that the downstream Lake Huron to Erie corridor is wastewater effluent-dominated, whereas the aquatic environment associated with Lake St. Clair is influenced by a mixed urban, suburban, and agricultural landscape (Fig. 1) (Bai et al., 2018; Baldwin et al., 2016; Pal et al., 2014).

Cumulative PPCP and pesticide concentration across sites was higher in S19 (2983.3 ng/L) compared to F18 (1605.8 ng/L) and F19 (1887.9 ng/L; Fig. 2), coinciding with significantly higher mean rainfall for the month preceding spring sampling events (0.21 in. = 0.5 cm) compared to fall sampling events (0.12 in.;  $p = 0.02$ ). Though increased pesticide detection during spring is expected due to higher mean rainfall concurrent with the application season, PPCPs may be expected to decrease due to increased dilution and decreased residence time in surface waters (Bai et al., 2018; Kolpin et al., 2004; Pal et al., 2014). However, previous studies have shown that wet weather conditions can increase PPCP concentrations in surface waters due to increased runoff or contaminant discharges from CSOs with simultaneous increases in flow rates in WWTPs, leading to shorter retention time during the treatment process, and thus decreased PPCP removal efficiency (Bai et al., 2018; Benotti and Brownawell, 2007; Ellis, 2006; Ferguson et al., 2013; Kasprzyk-Hordern et al., 2009; Río et al., 2013). In the current study, the most consistently detected compounds in surface water samples were synthetic sweeteners, accounting for 55.7% of the cumulative concentration of all compounds detected across sampling events, followed by pesticides (27.5%) and pharmaceuticals (11.7%; Figs. 2 and 3).

### Synthetic sweeteners

The synthetic sweeteners, acesulfame potassium (ACE-K) and sucralose, were detected in the highest concentrations of any compound class. These two compounds were found consistently at Sites 5 (mean: 85 ng/L and 500 ng/L, respectively; range:



**Fig. 1.** Pesticides and PPCPs (F18 - F19) and PFAS (S18 - F19) detected in surface water at each sampling site. Red circles indicate the number of compounds detected at each site across sampling events. CSO: combined sewer overflow. DWTP: drinking water treatment plant. WWTP: wastewater treatment plant. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

39 – 150 ng/L and 330 – 630 ng/L, respectively) and 6 (mean: 233 ng/L and 320 ng/L, respectively; range: 180 – 300 ng/L and 280 – 380 ng/L, respectively; Fig. 3). The mean cumulative concentration of ACE-K detected at Sites 5 and 6 was 477.5 ng/L, compared to 57 ng/L at Sites 1 and 2 (no detections at Sites 3 and 4). For sucralose, the mean cumulative concentration detected at Sites 5 and 6 was 1230 ng/L with one detection at Site 2 only (120 ng/L). The highest levels detected were in the WWTP effluent with 16,000 ng/L (16 ug/L) ACE-K and 12,000 ng/L (12 ug/L) sucralose. These compounds are common in WWTP effluent and surface waters due to their physicochemical properties, specifically high water solubility and low sorption, as well as resistance to human metabolism, abiotic degradation, and bioaccumulation (Belton et al., 2020; Tollefsen et al., 2012). For these reasons along with their exclusive production for human consumption, they are considered reliable wastewater tracers (Belton et al., 2020; Oppenheimer et al., 2011), further indicating that the downstream Lake Huron to Erie corridor is wastewater effluent-dominated, likely due to cumulative inputs from the numerous upstream WWTPs and CSOs (Fig. 1). Beyond indicating anthropogenic influence in the environment, ACE-K and sucralose have no reported adverse health effects based on long-term mammalian studies (Belton et al., 2020; Tollefsen et al., 2012). Some research in non-target, aquatic species has revealed changes in transcriptome, oxidative stress markers, microbiome, or behaviors, but no studies have shown physiological- or population-level consequences for survival, growth, or reproduction, even at exposures that far exceed environmentally-relevant levels (e.g. > 1000 mg/L) (Belton et al., 2020; Stoddard and Huggett, 2014; Tollefsen et al., 2012). Thus, ACE-K and sucralose appear to pose minimal risk to aquatic species, however ecotoxicological endpoints based on chronic (e.g. multi-year) exposures have not been assessed. Additionally, transformation products of synthetic sweeteners resulting from degradation processes in the environment or water treatment methods (e.g. photo- or biodegradation, ozonation),

**Table 1**  
Pesticides and PPCPs (F18 - F19) and PFAS (S18 - F19) detected in surface water at each sampling site. Compounds detected consistently across sampling events are bolded.

Site 1	Site 2	Site 3	Site 4	Site 5	Site 6
<b>Compounds detected at all sites</b>					
<b>Atrazine</b>	<b>Atrazine</b>	<b>Atrazine</b>	<b>Atrazine</b>	<b>Atrazine</b>	<b>Atrazine</b>
<b>DACT</b>	<b>DACT</b>	<b>DACT</b>	<b>DACT</b>	<b>DACT</b>	<b>DACT</b>
<b>DEA</b>	<b>DEA</b>	<b>DEA</b>	<b>DEA</b>	<b>DEA</b>	<b>DEA</b>
<b>DIA</b>	<b>DIA</b>	<b>DIA</b>	<b>DIA</b>	<b>DIA</b>	<b>DIA</b>
<b>Differentially detected compounds</b>					
<b>2,4-D</b>	<b>2,4-D</b>	Metformin	Metformin	<b>2,4-D</b>	<b>2,4-D</b>
<b>Acesulfame K</b>	<b>Acesulfame K</b>	PFBA		<b>1,7-dimethylxanthine</b>	<b>Acesulfame K</b>
<b>Caffeine</b>	<b>Caffeine</b>	PFBS		<b>Acetaminophen</b>	<b>Acetaminophen</b>
Diuron	DEET			<b>Caffeine</b>	<b>Atenolol</b>
6:2 FTSA	Diuron			Carbamazepine	<b>Caffeine</b>
PFBA	<b>Iohexol</b>			Cotinine	DEET
PFOA	<b>Sucralose</b>			DEET	Diltiazem
PFOS	6:2 FTSA			<b>Gemfibrozil</b>	<b>Gemfibrozil</b>
	PFOA			<b>Iohexol</b>	<b>Iohexol</b>
	PFOS			<b>Lidocaine</b>	<b>Lidocaine</b>
				Naproxen	Metformin
				<b>Sucralose</b>	<b>Sucralose</b>
				<b>Sulfamethoxazole</b>	<b>Sulfamethoxazole</b>
				Sulfameturon methyl	PFBA
				PFBA	PFOS
				PFHxA	
				PFPeA	
				PFBS	
				PFOA	
				PFOS	

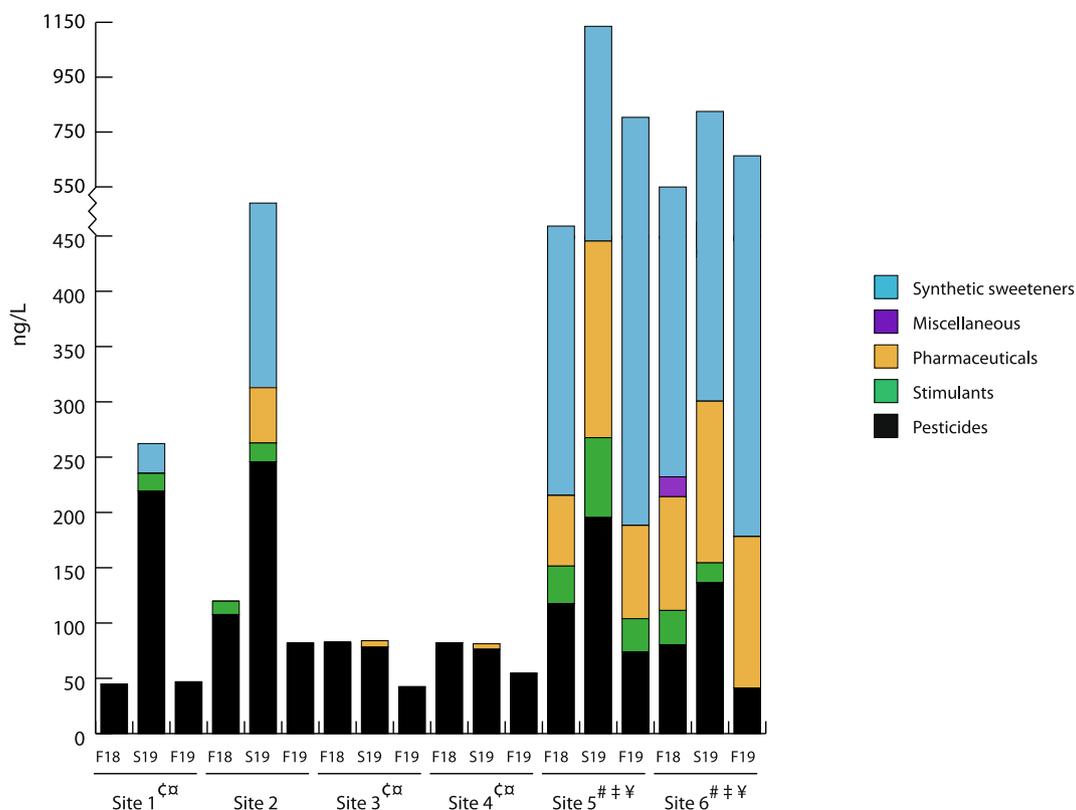


Fig. 2. Total concentration of compound detected per class (ng/L) per site per season (F18–19). # significant difference ( $p < 0.05$ ) from Site 1; † Site 3; ¥ Site 4; ¢ Site 5; □ Site 6.

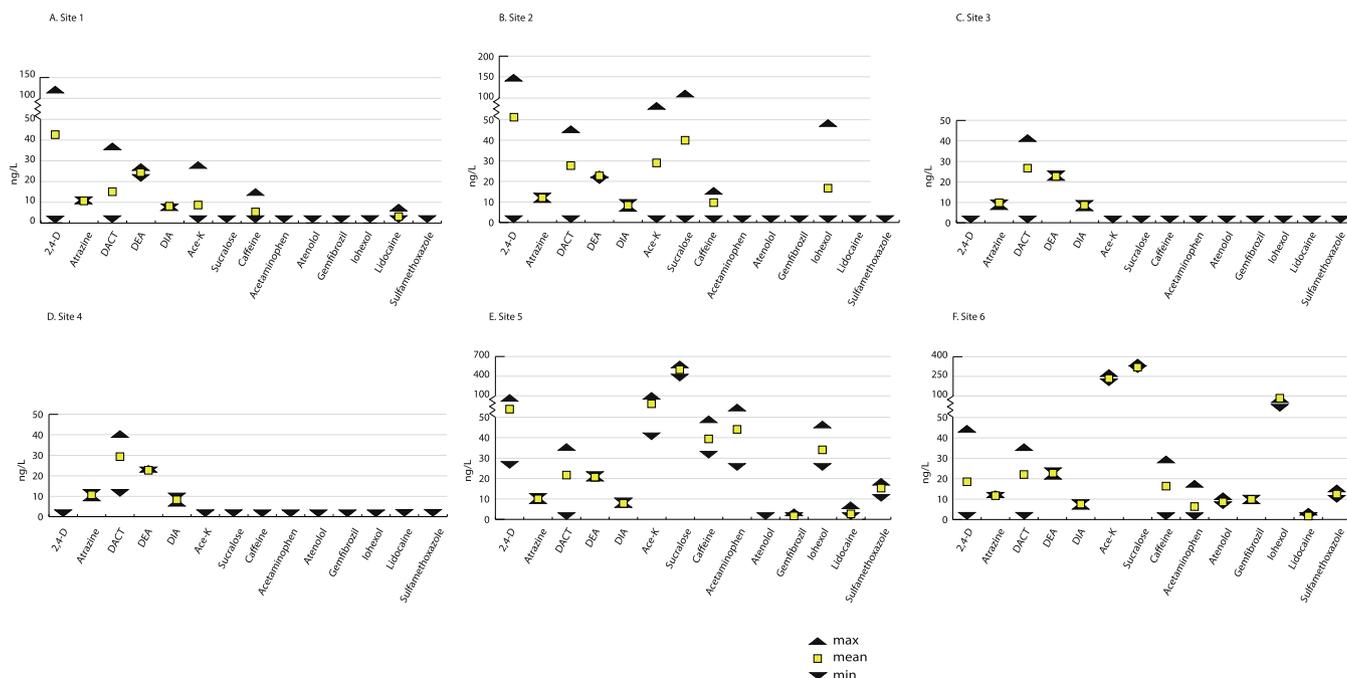


Fig. 3. PPCPs consistently detected across sampling events (F18 - F19). A) Site 1. B) Site 2. C) Site 3. D) Site 4. E) Site 5. F) Site 6.

have potentially greater toxicity in aquatic ecosystems than the parent compounds, but remain understudied (Belton et al., 2020).

Antimicrobials

Of the pharmaceuticals detected, the sulfonamide antibiotic, sulfamethoxazole, was found consistently across sampling events

at Sites 5 and 6 (mean: 15.3 ng/L and 12.5 ng/L, respectively; range: 8.9 – 20 ng/L and 8.6 – 17 ng/L, respectively; Fig. 3) with no detections at Sites 1 – 4. However, sulfamethoxazole was detected at relatively lower concentrations at Sites 2 (3 ng/L) and 4 (1 ng/L) during the initial sampling event (S18; Table S1). Similar to the synthetic sweeteners, the highest amount detected was in the WWTP effluent (680 ng/L), indicating sulfamethoxazole as a

wastewater contaminant. These surface water detections are similar to the range previously found within surface waters in the Great Lakes (Ferguson 2013), and also consistent with studies showing that sulfamethoxazole is among the most frequently detected compounds in urban watersheds (Bai et al., 2018; Ferguson et al., 2013; Kolpin et al., 2002). The persistence of sulfamethoxazole in aquatic environments, even at low levels, can drive antibiotic resistance with implications for human, animal, and ecosystem health (Gullberg et al., 2011; Martin-Laurent et al., 2019). Trimethoprim, which is commonly combined with sulfamethoxazole for medication purposes but detected at a relatively lower frequency in the environment, was also found in the WWTP effluent at 230 ng/L and in surface water samples at low levels compared to other studies (3 ng/L at Sites 5 and 6 during S18; ESM Table S1) (Bai et al., 2018; Ferguson et al., 2013; Kolpin et al., 2002).

Two additional sulfonamide antibiotics, sulfamerazine and sulfadiazine, were found in the WWTP effluent at 14 and 42 ng/L, respectively, but not at Sites 1 – 6. Similarly, amoxicillin (beta-lactam antibiotic), quinolones, and triclosan (antimicrobial agent) were detected only in the WWTP effluent at 1100, 41, and 120 ng/L, respectively. However, triclocarban, an antimicrobial agent similar to triclosan, was found at S18 (1.3 ng/L at Site 5; ESM Table S1). Triclosan and triclocarban have been largely restricted from use in personal care products since 2016, but not necessarily in other household products, due to wide-ranging human health and ecotoxicological concerns related to endocrine disruption, cancer, and antimicrobial resistance mediated by both the parent compounds and their degradation products (Halden et al., 2017). This restricted use may explain the low surface water detection frequency and concentrations in this study compared to older studies (Ferguson et al., 2013; Kolpin et al., 2002). Additionally, these compounds preferentially partition into sludge during the wastewater treatment process (Halden et al., 2017). Because measurable levels in WWTP effluent and nearby surface water were found in the current study, follow-up investigation of potential human and environmental exposure via agricultural biosolids and runoff is warranted.

#### Other pharmaceuticals

In addition to sulfamethoxazole, the other pharmaceuticals that were consistently detected across sampling events were acetaminophen, lidocaine, atenolol, gemfibrozil, and iohexol (Table 1 and Figs. 1 and 3). Acetaminophen, an analgesic and antipyretic that was frequently detected in a nationwide stream survey in the US (Kolpin et al., 2002), was consistently detected at Site 5 (mean: 44 ng/L; range: 24 – 77 ng/L; Fig. 3), including during S18 (247 ng/L; ESM Table S1). Acetaminophen was also detected at Site 6 during F18 (19 ng/L), as well as at Sites 2 and 6 during S18 (6 and 65 ng/L, respectively). These detections are higher than concentrations detected in Lake Michigan adjacent to urban watersheds (Ferguson et al., 2013). Environmentally-relevant acetaminophen concentrations are associated with potential oxidative damage, as well as reproductive and neurobehavioral toxicity in freshwater organisms with transgenerational effects demonstrated in aquatic invertebrates (Nunes, 2020; Overturf et al., 2015). The environmental risk linked to acetaminophen is considered greater than that for non-steroidal anti-inflammatories (NSAIDs), specifically compared to diclofenac, ibuprofen, and naproxen (Nunes, 2020). These and other analgesics were detected in the WWTP effluent: diclofenac (97 ng/L), ibuprofen (26 ng/L), naproxen (130 ng/L), and ketoprofen (32 ng/L; NSAID), and butalbital (12 ng/L; barbiturate). However, only two of these compounds were detected in surface waters: naproxen (14 ng/L at Site 5 during S19; 35 and 12 ng/L at Sites 5 and 6, respectively during S18; ESM Table S1) and

diclofenac (1 ng/L at Site 6 during S18; Table S1), both of which are below or within the range of previous detections (Bai et al., 2018; Ferguson et al., 2013; Hua et al., 2006a; Jasim et al., 2006; Metcalfe et al., 2003).

Lidocaine, a sodium channel blocker used as a local anesthetic and antiarrhythmic in a wide variety of species across both human and veterinary medicine (Carpenter and Marion, 2018; Grubb and Lobprise, 2020; Plumb, 2018), was found consistently across sampling events at Sites 5 or 6 (mean: 8.5 ng/L and 5.8 ng/L, respectively; range: 8.3 – 8.6 ng/L and 5.7 – 5.9 ng/L, respectively; Fig. 3), below surface water concentrations detected in other urban areas (Bai et al., 2018), but at a >30-fold concentration in the WWTP effluent (280 ng/L). Though lidocaine can cause toxicity affecting the musculoskeletal, cardiovascular, and neurological systems at doses exceeding clinical uses (Grubb and Lobprise, 2020), studies are lacking that investigate ecotoxicological outcomes related to chronic, environmentally-relevant exposures.

The cardiovascular medications, atenolol (beta-blocker) and gemfibrozil (lipid regulator), were consistently found at Site 6 with respective mean concentrations of 8.6 ng/L (range: 5.5 – 13 ng/L) and 9.9 ng/L (range: 8.6–11 ng/L; Fig. 3) that are at the low end of detections associated with urban land use (Bai et al., 2018; Ferguson et al., 2013; Kolpin et al., 2002). Gemfibrozil was also detected at Site 5 (5.5 ng/L during S19; Fig. 3). Relatively higher concentrations in the WWTP effluent at 460 ng/L atenolol and 580 ng/L gemfibrozil, representing a >35-fold and >50-fold increase compared to surface water samples, is not surprising for atenolol given low metabolism and excretion of predominantly unchanged drug (Kuster et al., 2010). On the other hand, gemfibrozil is largely glucuronidated to a more potent metabolite, suggesting that our results likely underrepresent this pharmaceutical in both WWTP effluent and surface water samples, thus highlighting the importance of including transformation products in environmental investigations and risk assessments (Celiz et al., 2009). The parent compounds are considered a low acute ecotoxicity risk, however available studies lack non-standard endpoints and indicate the potential for transgenerational effects on non-target organisms, a particular concern for continuous environmental exposures (Kuster et al., 2010; Overturf et al., 2015; Zurita et al., 2007).

Iohexol, a non-ionic, water-soluble, iodine-based contrast agent for medical imaging, was consistently detected across sampling events at Sites 5 (mean: 34 ng/L; range: 24 – 48 ng/L) and 6 (mean: 83.7 ng/L; range: 53 – 100 ng/L), but only once at Site 2 (50 ng/L during S19; Fig. 3). The iohexol concentration in the WWTP effluent (6600 ng/L) was >65-fold higher than detected concentrations in the surface water samples. The closely related contrast agents, iopamidol and iopromide, were only detected at Site 5 (1000 ng/L during F19) and in the WWTP effluent (250 ng/L), respectively. Interestingly, iopamidol, which was only analyzed during F19 at Site 5, was found at the highest surface water concentration, possibly due to its relatively low transformation efficiency in the WWTP process compared to other contrast agents (Nowak et al., 2020). These compounds are metabolically stable in humans, and are thus excreted unchanged after diagnostic medical imaging (Nowak et al., 2020). Little is known about the ecotoxicity of these compounds despite consistent release into aquatic ecosystems up to concentrations of 100 ug/L, much less about the numerous transformation products generated by processes in wastewater treatment and the natural environment (Nowak et al., 2020). As an example of the existing knowledge gaps for these compounds, iopromide does not appear to be associated with toxicity following short-term exposure in aquatic species (Steger-Hartmann et al., 2002), but is nonetheless the only contrast agent to be classified as an environmental hazard that is “very toxic to aquatic life with

long-lasting effects” by the Globally Harmonized System of Classification and Labeling of Chemicals (PubChem, 2020).

Though not consistently detected across sampling events, the pharmaceuticals, metformin (anti-hyperglycemic/diabetic) and carbamazepine (anticonvulsant), were detected at multiple sites and/or during multiple sampling events (Fig. 1 and Table 1). Metformin was detected during S19 at Sites 3, 4, and 6 at a mean concentration of 5.7 ng/L (range: 5–6.2 ng/L), which was the same concentration found in the DWTP influent, whereas the concentration in the WWTP effluent was 42 ng/L. As a potentially non-traditional EDC, metformin is linked to adverse behavior and reproductive outcomes for non-target, aquatic organisms at multiple trophic levels, but at exposures exceeding those found in this study and other streams (Bai et al., 2018; Godoy et al., 2018; Kolpin et al., 2004; Niemuth, and Klaper, 2015). Nonetheless, as prescription use of this pharmaceutical is expected to continue increasing with a concomitant increase in WWTP effluents and aquatic environments, understanding the effects of chronic, low level metformin exposure, particularly in environmentally-relevant mixtures, is critical (Godoy et al., 2018; Briones et al., 2016). Carbamazepine, which has evidence of inducing impaired reproduction in fish (Overturf et al., 2015), was detected during three sampling events (S18, S19, and F19) at Sites 5 and/or 6 with a mean concentration of 4.6 ng/L (range: 3–5.1 ng/L), as well as in the WWTP effluent (140 ng/L). These concentrations are similar to other surface water and WWTP effluent detections (Ferguson et al., 2013; Metcalfe et al., 2003; Hua et al., 2006a; Bai et al., 2018), however as is the case for many CECs, ecotoxicological studies at doses and exposure durations relevant to aquatic environments are lacking (Hai et al., 2018).

### Pesticides

In contrast to Sites 5 and 6, Sites 3 and 4 had the lowest number of compounds detected across sampling events with 7 and 5 compounds, respectively (Table 1). These sites are predominantly upstream of the WWTPs and CSOs in the study area and also had the highest mean water velocity compared to all other sampling locations at  $0.39 \pm 0.14$  m/s and  $0.50 \pm 0.23$  m/s, respectively (ESM Table S3), suggesting potentially lower contaminant burdens due to a dilution effect (Hua et al., 2006a; Metcalfe et al., 2003). The compounds consistently detected at these sites were the triazine herbicide, atrazine, and its degradation products: diaminochlorotriazine (DACT), deethyl-atrazine (DEA), and deisopropylatrazine (DIA). Some of the degradation products can also arise from simazine and cyanazine (US EPA 2016b), but no other triazine herbicides were detected during the current study. In contrast, atrazine, along with DEA and DIA, were detected at every sampling location for each sampling event with a mean concentration of 10.8 ng/L (range: 9.2 – 13 ng/L), 22.6 ng/L (range: 19 – 28 ng/L), and 8.1 ng/L (range: 7.1 – 9.1 ng/L), respectively (Fig. 3). DACT was only found at Site 4 during F19 at 10 ng/L, but was found at every site for all other sampling events with a mean concentration of 34.8 ng/L (range: 7.4 – 47 ng/L; Fig. 3). The one-time sampling event at the DWTP intake showed similar results to Sites 1 – 6 with 12 ng/L atrazine, 38 ng/L DACT, 23 ng/L DEA, and 9.8 ng/L DIA; while the one-time sampling event at the WWTP effluent did not detect DACT or DIA, but relatively high atrazine (23 ng/L) and relatively low DEA (8.9 ng/L) compared to Sites 1 – 6. In aquatic environments, atrazine toxicity is of greater concern than that for the degradates, for which levels necessary for aquatic toxicity tend to be higher than the maximum water solubility (US EPA, 2016b). For atrazine, the current study found a comparatively lower mean concentration than the monitoring results and steady-state predictions of previous surface water investigations within the Great Lakes basin, including for adjacent urban land cover specifically (Bai et al., 2018; Baldwin et al., 2016; Hua et al.,

2006a; Jasim et al., 2006; Metcalfe et al., 2019; Tierney et al., 1999). However, our findings were similar to the relatively consistent detection of atrazine in the Detroit River at concentrations <30 ng/L outside of the summer months, potentially representing a steady-state level related to transport from Lake Huron (Hua et al., 2006a; Jasim et al., 2006). Atrazine-contaminated source waters for DWTPs, such as the Detroit River, are of increasing concern for human health since the EPA found developmental risks for children stemming from combined exposure to drinking water, food, and residential landscaping (US EPA, 2018b). Chronic atrazine exposure studies have also shown impaired survival, growth, and reproduction in aquatic species, ranging from plants to vertebrates, notably freshwater fish, but at shorter durations and higher concentrations than the persistent, low levels found here (Baldwin et al., 2016; US EPA 2016b). However, as an endocrine-disrupting compound (EDC), atrazine has been shown to exhibit a non-monotonic response with measurable toxic endpoints at concentrations below water quality benchmarks, particularly when exposure occurs during development/early life (Vandenberg et al., 2012).

The herbicide, 2,4-Dichlorophenoxyacetic acid (2,4-D), was also detected across sampling events. Similar to other compounds, 2,4-D was never detected at Sites 3 or 4, but was consistently detected at Site 5 (mean: 63 ng/L; range: 25 – 120 ng/L), at the highest concentration at Site 2 (mean: 87.5 ng/L; range: 15 – 160 ng/L), and variably at Sites 1 (130 ng/L during S19) and 6 (mean: 27.7 ng/L; range: 9.4 – 46 ng/L; Fig. 3). Cumulative 2,4-D burden per sampling event was 68.4, 456, and 25 ng/L for F18, S19, and F19, respectively, suggesting seasonal variability, likely related to runoff due to higher mean rainfall during spring along with impervious surfaces in the surrounding urban environment and agricultural within the Lake St. Clair drainage basin (Metcalfe et al 2019). This is further supported by the relatively low concentration detected in the WWTP effluent compared to surface water samples during S19 (76 ng/L). Though the ester forms are particularly toxic to fish, 2,4-D has a relatively short half-life in aquatic environments and is considered safe for aquatic species at concentrations below 4 ug/L with no known adverse human health or ecotoxicological effects following acute or chronic exposure to the concentrations found in this study (Canadian Water Quality Guidelines, 2014; Gervais et al., 2008). Nonetheless, studies investigating these environmentally-relevant concentrations are scarce, if available at all, and 2,4-D is a known EDC, thus potential exists for these seasonally abundant, low-level exposures to cause physiological consequences (Diamanti-Kandarakis et al., 2009; Gervais et al., 2008).

Other pesticides were detected during S19 only, specifically diuron (6.5 ng/L at Site 1; 9.4 ng/L at Site 2) and sulfometuron-methyl (7.3 ng/L at Site 5), both of which are substituted urea herbicides (Table 1). Unlike 2,4-D, these compounds were detected at a relatively higher concentration in the WWTP effluent (diuron: 43 ng/L; sulfometuron-methyl: 30 ng/L) compared to surface water samples, consistent with use of these compounds for maintenance of roadsides, commercial areas, and/or residential landscaping. The transient, low level concentrations for both of these compounds is not likely to produce significant adverse ecotoxicological effects. The highest detection of N,N-diethyl-meta-toluamide (DEET), the active ingredient in many personal use insect repellants and a frequently detected wastewater contaminant in streams (Kolpin et al., 2002), was also detected in the WWTP effluent (340 ng/L), with a mean concentration of 20 ng/L (range: 10 – 39 ng/L) in surface water samples at Sites 2, 5, and 6, which was similar to the S18 results (mean: 21.5 ng/L; Fig. 1; ESM Table S1). Previous DEET detections in both urban and non-urban Great Lakes tributaries, as well as in other urban watersheds, exceeded the surface water concentrations detected here (Baldwin 2016; Bai et al., 2018). Though DEET is commonly detected in aquatic environments in association with WWTP effluents, the compound is considered

readily biodegradable and not toxic at environmentally-relevant levels (Aronson et al., 2012; Jackson et al., 2008; Pal et al., 2014).

### Stimulants

In addition to synthetic sweeteners, pharmaceuticals, and pesticides, stimulants accounted for 3.5% of the cumulative concentration of compounds detected across sampling events (Fig. 2). No significant difference in cumulative stimulant concentration was observed between sites ( $p > 0.05$ ). Caffeine was consistently found across sampling events at Site 5 (mean: 39.3 ng/L; range: 30 – 54 ng/L), variably at Sites 2 (mean: 14.5 ng/L; range: 12 – 17 ng/L) and 6 (mean: 24.5 ng/L; range: 18 – 31 ng/L), and once at Site 1 (16 ng/L during S19; Fig. 3). The highest concentrations of caffeine were detected during S18 with 200 and 90 ng/L at Sites 5 and 6, respectively (ESM Table S1), while the lowest concentration detected was in the WWTP effluent (12 ng/L). As a frequently detected wastewater contaminant, these concentrations fall within the range previously detected, including on the Canadian side of the Detroit River (Bai et al., 2018; Baldwin et al., 2016; Bruton et al., 2010; Ferguson et al., 2013; Kolpin et al., 2002; Jasim et al., 2006). Previous studies have shown that caffeine exposures at and above  $\mu\text{g/L}$  levels (i.e. above concentrations routinely detected in surface waters) result in developmental toxicity and anxiety-like behavior in a range of species, including aquatic organisms, and these adverse outcomes are exacerbated by co-exposure with synthetic sweeteners (Bruton et al., 2010; Lee and Wang, 2015; Santos et al., 2017), underscoring the potential that lower levels of contaminants in mixtures could induce more severe outcomes than the individual contaminants alone. Thus, the importance of evaluating environmentally-relevant contaminant mixtures.

The compounds 1,7-dimethylxanthine (caffeine metabolite), cotinine (nicotine metabolite), cocaine, and benzoylecgonine (cocaine metabolite) were each detected once at Site 5 (6.2 ng/L during S19, 12 ng/L during S19, 4.3 ng/L during F19, and 3.7 ng/L during F19 respectively; note that cocaine and benzoylecgonine were only analyzed during F19 at Site 5; Table 1; ESM Table S2). Interestingly, nicotine was detected in surface water samples only during S18 with a mean concentration of 15 ng/L (range: 10 – 20 ng/L; Table S1). Though little is known about how most of these stimulants and metabolites impact ecological health, nicotine targets acetylcholine receptors, and thus has been used as an insecticide in the past with the potential to adversely impact zooplankton in the phylum *Arthropoda* at environmentally-relevant levels (Buerge et al., 2008; Oropesa et al., 2017; Parolini et al., 2017). Despite extensive metabolism, both parent compounds and metabolites were detected in the WWTP effluent (caffeine: 12 ng/L; 1,7-dimethylxanthine: 110 ng/L; nicotine: 0.1 ng/L; cotinine: 140 ng/L; cocaine and benzoylecgonine were not analyzed in the WWTP effluent), hence the use of these compounds as markers of both wastewater and public health in local communities (Centazzo et al., 2019; de Granda-Orive et al., 2018).

### PFAS

Twelve PFAS and 2 branched isomers were detected in the surface water and/or sediment samples (Table 1 and Fig. 4), but unlike the PPCPs and pesticides, none were consistently detected across sampling events. Consistent with previous studies showing that short-chain PFAS replacements for PFOA and PFOS are more frequently detected in surface waters compared to long-chain compounds (Remucal et al., 2019; Hu et al., 2016), perfluorobutanoic acid (PFBA) was the most frequently detected PFAS in water samples (mean<sub>surface</sub>: 7.4 ng/L; mean<sub>1m</sub>: 3.7 ng/L; Fig. 4). Despite being marketed as “safer”, limited available research shows that short-chain

PFAS induce developmental and multisystemic diseases, including cancer, which is not unexpected due to structural similarity with long-chain compounds (Fraleigh et al., 2020; Reade et al., 2019). PFBA was also found in sediment (38 ng/kg; Fig. 4), however sorption of short-chain compounds is poorly understood, and such findings are considered more likely attributable to detections in pore water, which was not excluded during our sample processing (Remucal et al., 2019). The other detected short-chain PFAS, PFBS and perfluoropentanoic acid (PFPeA), were only detected in surface water (mean<sub>1m</sub>: 3.7 and 2.3 ng/L, respectively; Fig. 4). Conversely, long-chain PFAS tend to partition to sediment (Remucal et al., 2019), thus unsurprisingly, the compounds that were exclusively detected in sediment were all long-chain PFAS [PFHxS-linear (PFHxS-LN): 14 ng/kg; PFHxS-branched (PFHxS-BR): 8 ng/kg; perfluorododecanoic acid (PFDoDA): 22 ng/kg; perfluorotridecanoic acid (PFTeDA): 14 ng/kg; perfluorotetradecanoic acid (PFTeDA): 18 ng/kg; Fig. 4]. However, long-chain compounds, PFUnDA (1 ng/L) and perfluorohexanoic acid (1.8 ng/L at the surface; mean<sub>1m</sub>: 2.6 ng/L; PFHxA), were detected only in surface water (Fig. 4).

Three long-chain compounds, namely 6:2 fluorotelomer sulfonic acid (6:2 FTSA), PFOA, and PFOS, were detected in both surface water and sediment samples: 6:2 FTSA with 3 ng/L at surface, 8.4 ng/L at 1 m, and 25 ng/kg in sediment; PFOA with 1.6 ng/L for mean<sub>surface</sub>, 2.2 ng/L for mean<sub>1m</sub>, and 7 ng/kg in sediment; PFOS with 2.9 ng/L for mean<sub>1m</sub> and both linear (PFOS-LN) and branched (PFOS-BR) isomers in sediment (29 and 11 ng/kg, respectively; Fig. 4). Though PFOA and PFOS have been phased out of production due to evidence of adverse human and animal health outcomes, bioaccumulation, and trophic magnification, these compounds persist in the environment, likely because of their chemical stability, but also due to the potential for these compounds to form as breakdown products of more complex PFAS (Fraleigh et al., 2020; Furdulj et al., 2007; Giesy and Kannan 2001; Jantzen et al., 2016; Kannan et al., 2005; Rappazzo et al., 2017; Reade et al., 2019; Remucal et al., 2019; Wang et al., 2011). Similar to short-chain compounds, PFHxS-BR and PFOS-BR may represent detections in pore water because branched isomers tend to partition to water, while linear isomers more likely sorb to sediment (Schulz et al., 2020). Measurable sediment concentrations of PFHxS and PFOS at Site 2 may be related to the proximity of a military base that is known to use aqueous fire-fighting foam (Fig. 1) (Fraleigh et al., 2020; Hu et al., 2016). Of the 8 PFAS detected in sediment, all were found at Site 2, except 6:2 FTSA, which was found only at Site 5 (Fig. 4), and the concentrations detected were generally lower than those previously found in the Great Lakes, including in Lake Erie and Lake St. Clair (Codling et al., 2018; Remucal et al., 2019).

In surface water, PFAS detections in this study are within range of previous results within the Great Lakes, including for Lake Erie (Remucal et al., 2019). Though no significant difference in cumulative PFAS concentration in surface water samples was observed between sites ( $p > 0.05$ ), Site 5 had the highest number of PFAS detected in surface water samples (Fig. 4). Site 5 is in proximity to multiple sources of wastewater effluent, a major source of PFAS in the eastern Great Lakes, particularly in association with urban watersheds (Hu et al., 2016; Remucal et al., 2019). In fact, of the 9 PFAS detected in the WWTP effluent [PFBA, PFOA, 6:2 FTSA, PFHxS-LN, PFHxS-BR, PFBS, PFPeA, PFHxA, 4:2 FTSA, perfluorohexanoic acid (PFHpA)], only 2 (4:2 FTSA, PFHpA) were not also detected in water and/or sediment samples. Overall, our findings support that PFAS are present in the environment as mixtures (Table 1) (Rappazzo et al., 2017; Reade et al., 2019). Due to endocrine disrupting properties and structural similarities among the compounds, even low-level exposures to these mixtures are likely to have additive or synergistic effects in humans and other species (Reade et al., 2019).

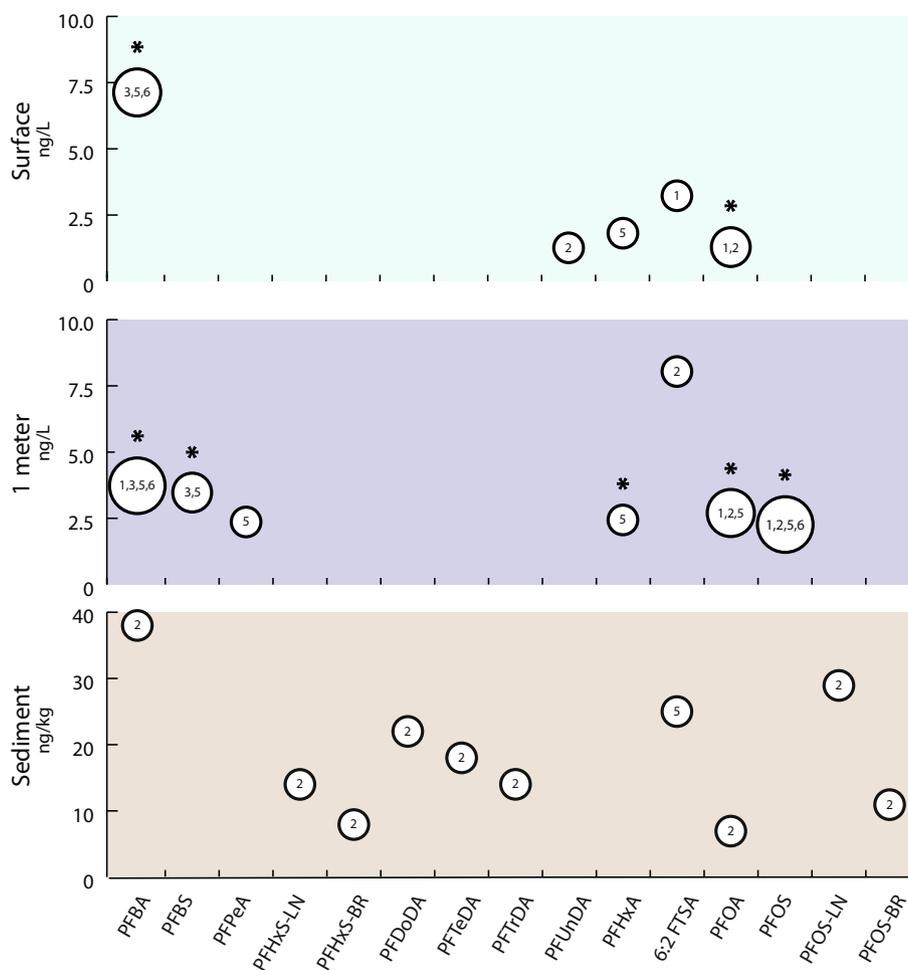


Fig. 4. PFAS detections across sampling events (S18 - F19). Numbers in circles represent sampling site(s) of detections. \* Indicates mean of multiple detections.

**Conclusion**

In summary, 14 compounds comprised of PPCPs and pesticides were consistently detected across sampling events in the Lake Huron to Erie corridor: ACE-K, sucralose, sulfamethoxazole, acetaminophen, lidocaine, atenolol, gemfibrozil, iohexol, atrazine, DACT, DEA, DIA, 2,4-D, and caffeine (Table 1). Factors that predispose these compounds to be persistent in the aquatic environment are multi-faceted, but include frequent use/consumption and physical-chemical properties, such as high water solubility that leads to transport via runoff and/or low recovery rates in WWTPs, and thus consistent release into surface waters. The surface water (ng/L) and sediment (ng/kg) detections in this study are below established water quality criteria for both humans and aquatic organisms (EGLE, 2020; Reade et al., 2019; US EPA AOC 2020). However, current PFAS standards are considered inadequate for protecting public health with suggestions that surface and drinking water limits should be as low as 1 ng/L (Hu et al., 2016; Reade et al., 2019; Remucal et al., 2019). Moreover, such benchmarks are determined for individual compounds using standard toxicological endpoints, and the majority of these frequently detected compounds lack established benchmarks. Thus, most of these compounds are not routinely monitored or regulated despite being environmentally persistent (or pseudo-persistent) and biologically active. Little remains known about contaminant-induced health consequences related to exposures to environmentally-relevant CEC concentrations, durations, temporal variability, and notably

mixtures, that additionally account for population-level or transgenerational impacts. Contaminants are rarely present in the environment alone, and in fact, we had no single compound detections at any site throughout the current study. These compound mixtures became increasingly complex, particularly downstream in the wastewater effluent-dominated Detroit River (Fig. 1). Contaminant mixture investigations are challenging due to potential additive, synergistic, or antagonistic effects depending on the compounds, concentrations, and species evaluated, especially when incorporating compounds that exhibit non-monotonic dose responses (e.g. EDCs). Our sampling methods provide an instantaneous measurement of contaminants at a specific time and location, and analysis for multiple compounds and transformation products was not performed. Thus, our study certainly underrepresents the variability and number of compounds present in this predominantly urban water system. Future studies must incorporate sampling designs to capture a fuller extent of this variability and evaluate the human, animal, and ecological health consequences of environmentally-relevant exposures to frequently detected compounds in the aquatic environment, particularly as complex, real-world contaminant mixtures.

**Declaration of Competing Interest**

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

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jglr.2021.12.001>.

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