Supporting Information for

Selective Uptake and Bioaccumulation of Antidepressants in Fish from Effluent-Impacted Niagara River

Prapha Arnnok[†ϕ], Randolph R. Singh[‡ϕ], Rodjana Burakham[¢], Alicia Pérez-Fuentetaja[§], Diana S. Aga[‡*]

[†]Department of Chemistry, Faculty of Science, Ramkhamhaeng University, Bangkok 10240 Thailand

[¢]Materials Chemistry Research Center, Department of Chemistry and Center for Innovation in Chemistry, Faculty of Science, Khon Kaen University, Khon Kaen 40002 Thailand

[‡]Department of Chemistry, University at Buffalo, The State University of New York (SUNY), Buffalo, New York 14260 United States

[§] Department of Biology and Great Lakes Center, Buffalo State, The State University of New York (SUNY), Buffalo, NY 14222 United States

*Corresponding author. Phone: +1-716-645-4220; fax: +1-716-645-6963,

E-mail: dianaaga@buffalo.edu

[ϕ] P. Arnnok and R.R. Singh contributed equally to this work

Contents

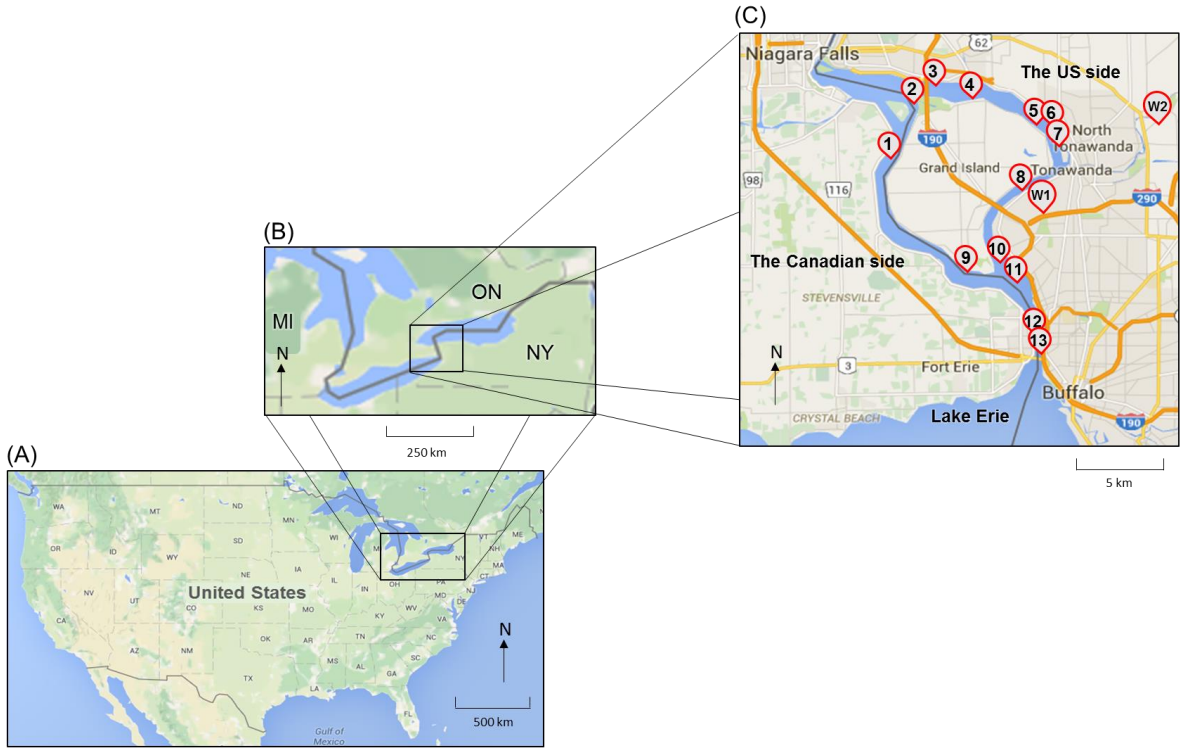
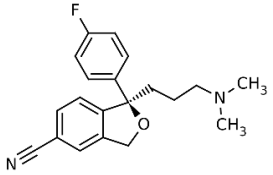
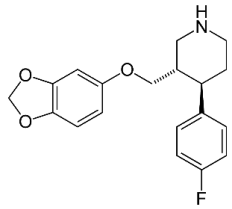
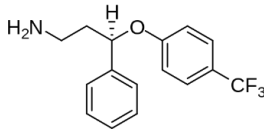
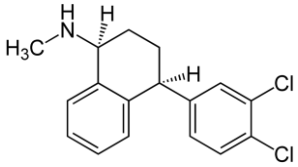
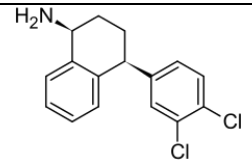
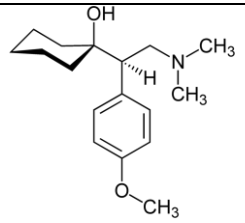
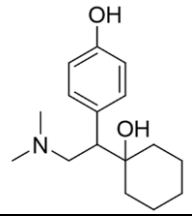
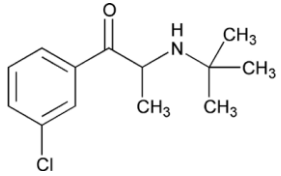
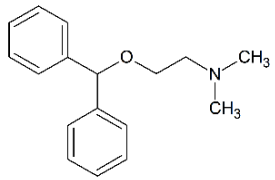
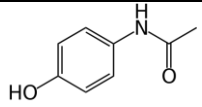
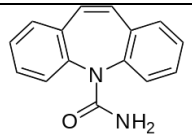
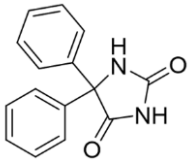
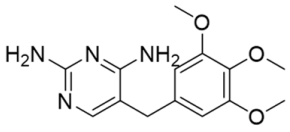
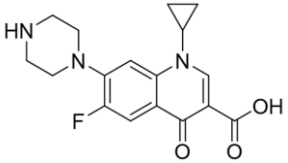
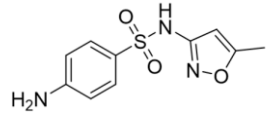
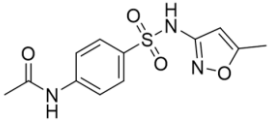
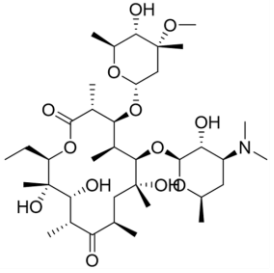


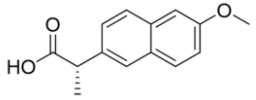
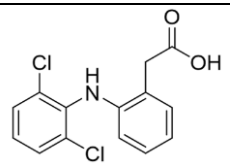
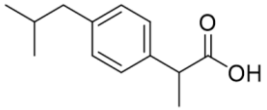
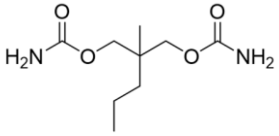
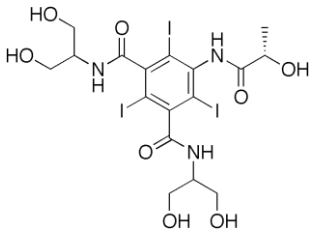
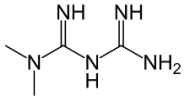
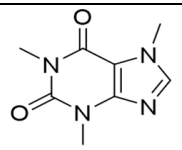
Figure S1. Maps showing the North American Great Lakes (A) and the location of the Niagara River relative to New York State (USA) and the province of Ontario (Canada) (B). The US side and Canadian side are divided by the black line in the river in the inset (C). The inset (C) indicates the locations of the municipal wastewater treatment plants (W1 and W2) where samples were collected, and the locations of sites for fish and surface water sample collection: Site #1, Big Six Mile Creek; Site #2, Burnt Ship Creek (Control site); Site #3, La Salle; Site #4, Sandy Beach; Site #5, Gun Creek; Site #6, Vacant Marina; Site #7, Tonawanda Island; Site #8, Isle View; Site #9, Beaver Island; Site #10, Motor Island; Site #11, Strawberry Island; Site #12, Broderick Park; Site #13, Peace Bridge. The Niagara River, with a distance of about 56 km, originates at the north-east end of Lake Erie and flows north to its mouth at Lake Ontario at a flow rate of 5,796 cubic meters (m^3)/second.

Table S1. List of target selective serotonin reuptake inhibitors, pharmaceuticals and personal care products, and the isotopically-labeled surrogate standards (in parenthesis) used for isotope dilution quantification, their molecular structures, and important physico-chemical properties.

Compound	**Acronym**	**Drug class**	**Molecular structure**	**pK_a**[a]	**log K_{ow}**[b]	**Water solubility (mg L^{-1})**[b,c]
Citalopram (Citalopram-d_6)	CIT	SSRI Antidepressant		9.57	3.74	31.09
Paroxetine (Paroxetine-d_6)	PRX	SSRI Antidepressant		9.68	2.57	537.1
Norfluoxetine (Norfluoxetine-d_6)	NFLX	Metabolite of SSRI antidepressant fluoxetine		-	4.18	35.7
Sertraline (Sertraline-d_3)	SER	SSRI Antidepressant		9.47	5.29	3.517

Norsertraline (Norsertraline-$^{13}C_6$)	NSER	Metabolite of SSRI antidepressant sertraline		-	4.82	10.61
Venlafaxine (Venlafaxine-d_6)	VEN	SNRI Antidepressant		14.84, 9.26	3.28	266.7
Desvenlafaxine (Desvenlafaxine-d_6)	DES	Metabolite of SNRI antidepressant venlafaxine		-	2.72	3670
Bupropion (Bupropion-d_9)	BUP	NDRI Antidepressant		7.16	3.85	140.2
Diphenhydramine (Diphenhydramine-d_3)	DPH	Antihistamine		8.76	3.11	362.7
Acetaminophen (Acetaminophen-d_4)	ACT	Analgesic		9.38	0.27	30350

Carbamazepine (Carbamazepine-d$_{10}$)	CBZ	Anti-seizure		13.94, 0.49	2.25	17.66
Dilantin (Dilantin-*d*$_{10}$)	DIL	Anti-seizure		8.33	-	-
Trimethoprim (Trimethoprim-*d*$_9$)	TMP	Antibiotic		7.12	0.73	2334
Ciprofloxacin (Ciprofloxacin-*d*$_8$)	CIP	Antibiotic		6.09	0.28	11400
Sulfamethoxazole (Sulfamethoxazole-*d*$_4$)	SMX	Antibiotic		1.6, 5.7	0.00	11480
Acetyl-SMX (Acetyl-SMX-*d*$_4$)	ASMX	Antibiotic		6.03	1.21	1216
Erythromycin (Erythromycin-^{13}C)	ERY	Antibiotic		8.88	-	-

Naproxen (Naproxen-*d*$_3$)	NPX	NSAIDs		4.15	3.10	144.9
Diclofenac (Diclofenac-*d*$_4$)	DIC	NSAIDs		4.15	4.02	4.518
Ibuprofen (Ibuprofen-*d*$_3$)	IBU	NSAIDs		4.91	3.79	41.05
Meprobamate (Meprobamate-*d*$_7$)	MEP	Anxiolytic		9.2	0.98	8877
Iopamidol (Trimetoprim-*d*$_9$)	IOPA	Radiocontrast agent		10.7	-	-
Metformin (Trimetoprim-*d*$_9$)	MET	Anti-diabetic		12.4	-1.40	1e+006
Caffeine (Caffeine-*d*$_3$)	CAF	Stimulant		10.4	0.16	2632

[a]Predicted properties Most Acidic Temp: 25 °C/ Most Basic Temp: 25 °C: http://scifinder.cas.org.

[b]Estimated values, from database of Chemspider (EPISuite): http://www.chemspider.com.

[c]Water solubility at 25 ◎°C estimate from log *Kow*

Table S2. List and locations of sites for surface water sample collection

List of water samples and their collection location		
Site #	**Location Name**	**Geographic Coordinates**
2	Burnt Ship Creek*	N 43°03.648' W 79°00.103'
3	La Salle	N 43°04.407' W 78°59.637'
4	Sandy Beach	N 43°03.786' W 78°58.596'
6	Vacant Marina	N 43°02.822' W 78°53.549'
7	Tonawanda Island	N 43°02.078' W 78°53.304'
8	Isle View	N 43°00.900' W 78°53.795'
*Control site		

Table S3. General information on fish samples and their collection sites

Sample ID	Fish species	Sampling site	Sex	Total Length (mm)	Weight (g)
SMB1	Smallmouth bass	Isle View	Female	400	780.8
SMB2	Smallmouth bass	Vacant Marina	Female	390	867.6
SMB3	Smallmouth bass	Tonawanda Island	Male	390	854.0
SMB4	Smallmouth bass	La Salle	Female	332	553.5
SMB5	Smallmouth bass	La Salle	Female	380	968.2
LMB1	Largemouth bass	Tonawanda Island	Male	360	639.2
LMB2	Largemouth bass	Sandy Beach	Female	330	529.7
LMB3	Largemouth bass	Sandy Beach	Male	370	823.6
LMB4	Largemouth bass	Strawberry Island	Male	790	655.7
LMB5	Largemouth bass	Strawberry Island	Male	370	677.6
RUD1	Common rudd	Sandy Beach	Female	351	744.0
RUD2	Common rudd	Sandy Beach	Female	415	1202.0
RUD3	Common rudd	Sandy Beach	Female	382	899.6
RUD4	Common rudd	Burnt Ship Creek	Male	365	872.9
RUD5	Common rudd	La Salle	Female	404	1220.4
RB1	Rock bass	Strawberry Island	Female	190	112
RB2	Rock bass	Isle View	Male	190	136.2
RB3	Rock bass	Vacant Marina	Male	220	198.7
RB4	Rock bass	Strawberry Island	Unknown	190	119.9
RB5	Rock bass	Broderick Park	Female	189	121.2
WB1	White bass	Tonawanda Island	Female	340	465.1
WB2	White bass	Strawberry Island	Male	325	382.3
WB3	White bass	Isle View	Male	315	341.7
WB4	White bass	Isle View	Female	360	567.9
WB5	White bass	Vacant Marina	Female	305	360.8
WP1	White perch	Burnt Ship Creek	Male	209	108.9
WAL1	Walleye	Broderick Park	Male	603	2034.9

WAL2	Walleye	Broderick Park	Female	720	3008.7
WAL3	Walleye	Broderick Park	Male	619	2368.3
WAL4	Walleye	Broderick Park	Unknown	469	887.7
WAL5	Walleye	Big Six Mile Creek	Male	221	98.2
BF1	Bowfin	Big Six Mile Creek	Male	201	123.5
SH1	Steelhead Trout	Peace Bridge	Female	561	1974.6
SH2	Steelhead Trout	Peace Bridge	Male	613	2410.5
SH3	Steelhead Trout	Peace Bridge	Male	612	2472.1
YP1	Yellow perch	Strawberry Island	Male	170	55.8
YP2	Yellow perch	Strawberry Island	Unknown	140	30.2
YP3	Yellow perch	Beaver Island	Male	253	173.1
YP4	Yellow perch	Motor Island	Male	161	36.9
YP5	Yellow perch	Beaver Island	Female	235	133.2
YP6	Yellow perch	Strawberry Island	Unknown	151	34
YP7	Yellow perch	Gun Creek	Unknown	158	34.3
YP8	Yellow perch	Sandy Beach	Male	197	86.1
YP9	Yellow perch	La Salle	Female	176	48.6
YP10	Yellow perch	Sandy Beach	Female	190	59
YP11	Yellow perch	Burnt Ship Creek	Male	176	54.7
YP12	Yellow perch	Burnt Ship Creek	Unknown	164	40.5
YP13	Yellow perch	Burnt Ship Creek	Unknown	195	72.4

Table S4. Mass spectrometer parameters and ions (m/z) used for multiple reaction monitoring (MRM) of target analytes and their respective isotope-labeled surrogate standards

Analyte	retention time (min)	fragmentor voltage (v)	precursor ion	quantifying ion	collision energy (v)	qualitative ion	collision energy (v)
Iopamidol	2.3	170	777.9	686.5	18	558.9	20
Metformin	1.5	50	130	60	10	71	20
Trimethoprim	1.9, 2.5	140	291.2	123	22	230.1	22
Desvenlafaxine	3.3	100	264.4	246.2	5	107	19
Acetaminophen	3.3	100	152.1	110.1	14	65.1	29
Caffeine	4.5	126	195.1	42.2	33	138	18
Bupropion	8.8	100	240	184	5	131	20
Venlafaxine	10.3	50	278	260	5	121	25
Diphenhydramine	11.4	90	256	167	15	152	35
Sulfamethoxazole	11.5	120	254.1	108	22	92.1	25
Ciprofloxacin	11.8	150	322	314	15	288	15
Citalopram	11.9	150	325	109	25	262	15
Meprobamate	12.4	100	219	158.2	5	-	-
Acetyl-SMX	12.4	100	296	134	10	198	10

Paroxetine	12.7	100	330	192	20	123	25
Anhydro-erythromycin	13.1	164	716.5	158.1	29	558.5	9
Norfluoxetine	13.2	50	296	30	5	134	2
Sertraline	13.5	80	306	159	25	275	5
Norsertraline	13.5	100	275	159	15	129	10
Dilantin	14.1	130	253.1	182.1	15	104	39
Carbamazepine	14.2	140	237.1	194.1	18	179.2	37
Naproxen	15.6	100	231.1	185.1	10	115	60
Diclofenac	16.9	100	296	214	34	250	10
Ibuprofen	17.0	60	207.1	161.1	6	117.2	37
Trimethoprim-d_9	1.9, 2.5	180	300.2	123.1	25	234.2	25
Desvenlafaxine-d_6	3.3	100	270.4	252.2	5	207.5	15
Acetaminophen-d_4	3.3	80	80	156	114	25	
Caffeine-d_3	4.5	80	198	53.1	73	138.2	17
Bupropion-d_9	8.8	100	249	185	5	131	20
Venlafaxine-d_6	10.3	100	284	226	5	121	25
Diphenhydramine-d_3	11.4	50	259	167	5	152	40
Sulfamethoxazole-d_4	11.5	122	258.1	112.1	25	96.1	29
Ciprofloxacin-d_8	11.8	130	340	322	20	235	40
Citalopram-d_6	11.9	100	331	109	30	262	15
AcetylSMX-d_4	12.4	80	300	138	15	202	15
Meprobamate-d_7	12.4	60	226	165	5	-	-
D6-Paroxetine	12.7	150	336	198	20	153	20
^{13}C-Erythromycin-H_2O	13.1	164	717.5	159.1	29	559.5	9
Norfluoxetine-d_6	13.2	50	302	30	5	140	2
Sertraline-d_3	13.5	100	309	159	30	275	5
$^{13}C_6$-Norsertraline	13.5	100	281	159	15	135	10
Dilantin-d_{10}	14.1	135	263	235.3	5	-	-
Carbamazepine-d_{10}	14.2	118	247.2	204.1	21	202.1	37
Naproxen-d_3	15.6	60	234	188	10	109	15
Diclofenac-d_4	16.9	90	254	218	-	-	-
Ibuprofen-d_3	17.0	32	210	146.1	10	164.3	9

Table S5. Analytical figures of merit for various fish tissues. The linear range for each analyte was observed from its method detection limit to 40 ng/g in most matrices, with the exception of brain tissue (up to 500 ng/g). All concentrations are based on dry weight.

Pharmaceutical	Matrix	MDL (ng/g)	MQL (ng/g)	Calibration parameter	
				Equation	r^2
CIT	Brain	0.229	0.728	y = 114,575x + 308	0.9998
	Gonad	0.062	0.197	y = 250,686x - 23,998	0.9995
	Liver	0.078	0.249	y = 138,174x - 83,801	0.9998
	Muscle	0.026	0.084	y = 159,548x - 197,527	0.9994
PRX	Brain	0.980	3.12	y = 24,179x - 139,393	0.9991
	Gonad	0.036	0.114	y = 19,542x - 5,430	1.0000
	Liver	3.57	11.4	y = 19,718x - 27,762	0.9995
	Muscle	0.097	0.309	y = 26,107x - 42,068	0.9995
NFLX	Brain	0.326	1.04	y = 63,044x - 148,505	0.9991
	Gonad	0.011	0.034	y = 40,016x - 17,769	0.9998
	Liver	0.038	0.122	y = 37,679x - 78,673	0.9993
	Muscle	0.013	0.040	y = 53,085x - 68,934	0.9994
SER	Brain	0.193	0.613	y = 99,670x - 611,203	0.9992
	Gonad	0.013	0.041	y = 65,563x - 9,987	0.9998
	Liver	0.057	0.182	y = 57,884x - 233,528	0.9984
	Muscle	0.029	0.092	y = 55,979x - 110,700	0.9994
NSER	Brain	0.308	0.980	y = 84,047x - 446,475	0.9982
	Gonad	0.074	0.235	y = 46,287x - 23,900	0.9982
	Liver	0.181	0.567	y = 41,338x - 203,361	0.9987
	Muscle	0.306	0.974	y = 45,609x - 68,448	0.9991
VEN	Brain	0.306	0.973	y = 125,844x - 71,035	0.9997
	Gonad	0.098	0.311	y = 65,139x - 23,031	0.9997
	Liver	0.346	1.10	y = 76,900x - 50,648	0.9992
	Muscle	0.082	0.260	y = 69,306x - 75,451	0.9996
DES	Brain	0.152	0.485	y = 135,876x - 51,123	0.9994
	Gonad	0.072	0.230	y = 91,670x – 19,136	0.9996
	Liver	0.472	1.50	y = 67,927x - 92,786	0.9994
	Muscle	0.078	0.249	y = 60,164x - 89,944	0.9996
BUP	Brain	0.109	0.348	y = 256,124x - 337,723	0.9997
	Gonad	0.004	0.014	y = 117,911x - 25,334	0.9998
	Liver	0.072	0.230	y = 134,062x - 198,834	0.9996
	Muscle	0.172	0.546	y = 98,612 x - 117,490	0.9997
DPH	Brain	0.249	0.791	y = 175,679x + 2,398	0.9999
	Gonad	0.048	0.154	y = 163,220x - 1,127	0.9994
	Liver	0.041	0.130	y = 273,960x - 308,776	0.9994
	Muscle	0.015	0.048	y = 282,975x - 388,244	0.9996
ACT	Brain	0.429	1.36	y = 69,501x - 23,002	0.9997
	Gonad	0.125	0.398	y = 41,241x - 3,289	1.0000

	Liver	0.190	0.605	y = 26,221x - 51,139	0.9993
	Muscle	0.032	0.101	y = 35,377x - 53,771	0.9996
CBZ	Brain	0.128	0.409	y = 324,456x - 290,752	0.9995
	Gonad	0.014	0.045	y = 219,936x - 126,095	0.9986
	Liver	0.020	0.065	y = 120,112x - 194,033	0.9995
	Muscle	0.011	0.035	y = 190,436x - 229,114	0.9991
DIL	Brain	1.78	5.67	y = 8,336x - 3,445	0.9999
	Gonad	0.114	0.364	y = 2,451x - 795	1.0000
	Liver	0.937	2.98	y = 1,785x - 665	0.9993
	Muscle	0.374	1.19	y = 3,735x - 2,570	0.9993
TMP	Brain	0.261	0.832	y = 107,013x - 19,327	0.9998
	Gonad	0.023	0.073	y = 74,706x – 25,660	0.9995
	Liver	0.136	0.434	y = 33,105x - 3,627	0.9998
	Muscle	0.051	0.162	y = 30,092x - 15,757	0.9998
CIP	Brain	5000	-	-	-
	Gonad	400	-	-	-
	Liver	400	-	-	-
	Muscle	400	-	-	-
SMX	Brain	0.205	0.653	y = 33,183x - 74,851	0.9991
	Gonad	0.093	0.294	y = 18,155x – 6,735	0.9987
	Liver	1.42	4.51	y = 10,922x - 44,874	0.9994
	Muscle	0.208	0.662	y = 20,075x - 35,603	0.9995
ASMX	Brain	1.95	6.20	y = 584x - 885	0.9996
	Gonad	0.368	1.17	y = 638x + 712	0.9995
	Liver	6.72	21.4	y = 521x + 6,199	0.9996
	Muscle	1.40	4.46	y = 752x + 318	0.9999
ERY	Brain	0.263	0.837	y = 66,266x - 231,312	0.9992
	Gonad	0.012	0.037	y = 87,834x + 9,468	0.9995
	Liver	0.015	0.047	y = 72,426x - 47,843	0.9997
	Muscle	0.031	0.098	y = 76,930x - 132,648	0.9994
NPX	Brain	6.34	20.2	y = 7,291x + 7,534	0.9997
	Gonad	4.56	14.5	y = 1,150x + 7,258	0.9996
	Liver	4.45	14.2	y = 2,049x + 36,082	0.9992
	Muscle	2.360	7.53	y = 6,686x + 32,692	0.9995
DIC	Brain	1.16	3.70	y = 5,271x + 624	0.9996
	Gonad	0.168	0.533	y = 3,192x – 2,036	0.9992
	Liver	0.353	1.12	y = 1,645x - 4,312	0.9995
	Muscle	0.109	0.345	y = 9,303 - 14,385	0.9992
IBU	Brain	250	795	y = 169x + 718	0.9997
	Gonad	7.82	24.9	y = 679x + 1,725	0.9992
	Liver	3.10	9.87	y = 1,559x + 3,968	0.9994
	Muscle	19.2	60.9	y = 423x + 2,247	0.9997

MEP	Brain	1.18	3.75	y = 13,588x - 17,088	0.9993
	Gonad	0.065	0.208	y = 9,941x – 3,231	0.9991
	Liver	2.09	6.65	y = 8,026x - 6,743	0.9996
	Muscle	0.047	0.151	y = 15,196x - 22,893	0.9996
IOPA	Brain	122	388	y = 232x + 3,065	0.9997
	Gonad	1.82	5.78	y = 434x + 2,773	0.9987
	Liver	4.00	12.7	y = 254x - 176	0.9989
	Muscle	10.0	31.8	y = 207x - 4,288	0.9995
MET	Brain	0.482	1.53	y = 28,912x - 31,593	0.9996
	Gonad	0.070	0.224	y = 17,173x – 7,494	0.9989
	Liver	0.401	1.28	y = 7,313x - 12,755	0.9998
	Muscle	0.182	0.578	y = 11,157x - 17,872	0.9993
CAF	Brain	1.67	5.32	y = 17,587x - 60,899	0.9993
	Gonad	0.273	0.869	y = 10,855x - 772	1.0000
	Liver	0.191	0.606	y = 10,067x - 4,076	0.9998
	Muscle	0.178	0.565	y = 9,794x - 29,959	0.9992

- Not evaluated

Table S6. Accuracy and precision of the method in terms of absolute percent recovery (%R) and relative standard deviation (%RSD), performed at two levels of concentrations: spiked level 1 is at 10 ng/g dry weight, and spiked level 2 is at 100 ng/g dry weight for all analytes, with the exception of iopamidol in brain tissue where 500 ng/g dry weight was used.

Analyte	Mean recoveries and relative standard deviation for triplicate extraction															
	Brain				Gonad				Liver				Muscle			
	Spiked level 1		Spiked level 2		Spiked level 1		Spiked level 2		Spiked level 1		Spiked level 2		Spiked level 1		Spiked level 2	
	%R	RSD	%R	RSD	%R	RSD	%R	RSD	%R	RSD	%R	RSD	%R	RSD	%R	RSD
CIT	84	3	100	7	79	1	103	3	88	8	98	5	93	2	98	3
PRX	66	4	104	10	58	7	77	3	49	3	64	7	61	2	64	1
NFLX	78	3	106	4	58	2	78	6	42	6	77	6	56	3	79	5
SER	82	8	103	2	48	5	62	9	63	1	83	3	60	6	97	3
NSER	80	2	99	2	66	3	88	10	62	10	76	6	63	3	108	6
VEN	68	6	101	10	73	6	106	4	72	9	102	6	91	7	94	8
DES	71	3	110	10	56	3	77	4	54	6	90	8	89	5	84	3
BUP	64	6	80	9	84	2	92	6	104	9	98	4	78	2	114	3
DPH	78	2	107	7	92	2	99	4	99	8	100	7	110	8	102	2
ACT	54	4	75	6	65	5	99	8	54	3	59	3	62	8	69	9
CBZ	70	3	112	11	73	8	75	3	76	4	104	6	106	8	98	6
DIL	60	2	81	2	57	3	63	5	57	5	100	7	70	2	83	3
TMP	68	5	93	7	50	4	80	5	60	6	85	12	72	4	67	8
CIP	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
SMX	56	2	67	5	69	6	93	3	55	9	74	6	79	2	97	2
ASMX	50	2	80	4	74	3	98	2	63	6	67	9	88	4	91	5
ERY	75	4	103	11	61	3	83	2	80	1	98	2	72	4	102	3
NPX	-	-	118	8	-	-	144	6	-	-	66	3	66	3	109	2
DIC	62	1	122	6	58	2	61	2	39	5	66	3	92	4	101	9
IBU	-	-	-	-	-	-	124	5	-	-	61	3	-	-	107	3
MEP	48	6	98	3	55	4	103	10	58	7	90	7	63	3	81	10
IOPA	-	-	63	4	-	-	59	2	-	-	44	3	-	-	41	10
MET	57	4	88	1	41	2	57	3	31	6	50	4	40	2	52	6
CAF	69	5	94	6	24	2	40	2	37	3	55	2	33	2	45	7

Table S7. Average concentrations (n=3) of selective serotonin reuptake inhibitors (SSRIs), and other pharmaceuticals and personal care products (PPCPs), in the wastewater treatment plant (WWTP) influents (pre-treatment) and effluents (post-treatment).

	WWTP 1 (Average concentration in ng/L)		**WWTP 2** (Average concentration in ng/L)	
SSRI and PPCPs	**Pre-treatment**	**Post-treatment**	**Pre-treatment**	**Post-treatment**
CIT	3861	3374	2505	2219
PRX	293	278	351	352
NFLX	247	238	283	338
SER	588	680	997	930
NSER	293	296	481	423
VEN	902	936	291	264
DES	1521	1646	422	383
BUP	2558	2649	359	475
DPH	12249	11877	4004	5098
ACT	<LOD	<LOD	14	<LOD
CBZ	134	155	30	27
DIL	44	70	26	17
TMP	574	720	226	262
SMX	1793	2134	136	302
ASMX	161	162	4769	2407
ERY	70	79	11	11
DIC	1	<LOD	1	1
IBU	<LOD	<LOD	7688	2852
MEP	1362	1355	783	827
MET	3440	5823	289	249
IOPA	1384	1568	311	461
CAF	10	55	8784	1274

Information on Wastewater Treatment Plants (WWTPs) and Concentrations of SSRIs and PPCPs Detected

Grab wastewater samples were obtained from two different local WWTPs and were collected before and after secondary treatment (chlorination). Samples were prepared using a published method from our group.[1]

WWTP 1: The treatment train is as follows: influent, screens, grit chamber, primary settling, dual-stage oxygen activated sludge process (stage 1 removes carbonaceous oxygen demand, and stage 2 is for nitrification), cloth filter, chlorine disinfection, and then effluent.

WWTP 2: The treatment train is as follows: influent, aerated grit chambers, oxygen contact reactors, bioclarifiers, solids contact bioclarifiers, sand filters, chlorination, and then effluent.

Average concentrations (n=3) for each target analytes in the WWTP influents and effluents are listed in Table S7. Wastewater analysis revealed that WWTP effluents are significant sources of PPCP residues into the Niagara River, and consequently into the lower Great Lakes system. While it is not the intention of this current work to quantify the removal efficiencies of the two WWTPs sampled, previous study using the same WWTPs have shown incomplete removal of antibiotics during the treatment process.[2] It has been previously reported that the WWTPs around the Lake Erie watershed are sources of antibiotics for surface waters, but information on the occurrence of antidepressants in the Niagara River is lacking.[3] Therefore, this present study took a snapshot of the concentration of SSRIs and other PPCPs in the effluent of two WWTPs that discharge into the Niagara River, to determine "typical" levels of PPCPs and SSRIs that are being discharged into the river.

The anti-allergy medicine diphenhydramine was found to have the highest concentration (up to 11.9 μg/L), followed by caffeine and ibuprofen in the WWTP effluents. All antidepressants included in the list of target analytes were detected in the effluents, with bupropion, citalopram, and desvenlafaxine showing concentrations greater than 1 μg/L. Also, sulfamethoxazole and its metabolite acetyl-sulfamethoxazole, ibuprofen, meprobamate, iopamidol, and the anti-diabetic drug metformin were all found at levels greater than 1 μg/L in the effluents, further indicating these two WWTPs as important sources of PPCP contamination in the Niagara River.

Table S8. Individual concentrations (ng/g dry weight) of selective serotonin reuptake inhibitors and other pharmaceuticals and personal care products in brains of fish samples collected from the Niagara River. The sample extracts were analyzed in 3 replicates.

Sample ID	Pharmaceutical (mean ± SD, 3 replicates)														
	CIT	NFLX	SER	NSER	VEN	BUP	DPH	ACT	CBZ	DIL	TMP	ERY	MET	IOPA	CAF
SMB1	ND	12.6 ± 1.5	ND	121.9 ± 6.2	ND	1.5 ± 0.1	1.0 ± 0.02	ND	0.6 ± 0.1	ND	ND	13.4 ± 0.4	ND	ND	23.5 ± 3.2
SMB2	ND	5.5 ± 1.7	ND	101.0 ± 12.0	ND	0.8 ± 0.04	<LOQ	ND	<LOQ	ND	ND	11.4 ± 0.6	ND	ND	13.4 ± 1.3
SMB3	ND	ND	ND	ND	ND	1.6 ± 0.2	1.0 ± 0.1	ND	ND	ND	ND	12.9 ± 0.7	ND	ND	19.2 ± 2.5
SMB4	ND	9.5 ± 2.8	6.7 ± 1.1	197.7 ± 2.6	ND	0.6 ± 0.2	1.3 ± 0.1	ND	0.9 ± 0.2	ND	ND	21.2 ± 0.1	ND	ND	23.2 ± 3.7
SMB5	ND	4.0 ± 0.9	6.0 ± 1.1	119.2 ± 5.6	ND	ND	1.6 ± 0.1	ND	0.6 ± 0.1	ND	ND	11.6 ± 1.3	ND	ND	24.5 ± 2.0
LMB1	ND	14.6 ± 2.0	ND	174.5 ± 8.8	ND	1.4 ± 0.3	1.1 ± 0.1	ND	ND	ND	ND	18.6 ± 1.3	ND	ND	23.6 ± 1.4
LMB2	ND	ND	ND	182.4 ± 5.8	ND	ND	<LOQ	ND	0.7 ± 0.1	ND	ND	18.7 ± 0.9	ND	ND	17.5 ± 0.4
LMB3	ND	3.9 ± 2.2	ND	128.3 ± 4.0	ND	ND	<LOQ	ND	0.5 ± 0.04	11.3 ± 1.2	ND	13.0 ± 0.4	ND	ND	12.6 ± 0.7
LMB4	1.5 ± 0.2	25.0 ± 4.0	16.9 ± 8.0	230.0 ± 9.8	ND	ND	3.7 ± 0.3	ND	0.7 ± 0.1	ND	ND	20.1 ± 1.0	ND	ND	14.7 ± 1.5
LMB5	ND	ND	ND	254.4 ± 4.8	ND	ND	<LOQ	ND	1.0 ± 0.03	ND	ND	27.9 ± 1.8	ND	ND	43.5 ± 1.8
RUD1	ND	5.3 ± 3.1	ND	100.9 ± 1.4	ND	ND	4.7 ± 0.3	ND	ND	ND	ND	10.4 ± 0.3	ND	ND	23.4 ± 3.0
RUD2	ND	ND	ND	98.8 ± 11.2	ND	ND	<LOQ	ND	<LOQ	ND	ND	10.1 ± 0.5	ND	ND	7.3 ± 1.1
RUD3	<LOQ	5.9 ± 0.3	ND	129.7 ± 2.1	ND	ND	1.0 ± 0.1	ND	0.6 ± 0.03	ND	ND	15.6 ± 0.7	ND	ND	11.6 ± 2.3
RUD4	ND	ND	ND	146.5 ± 11.5	ND	ND	1.1 ± 0.2	ND	ND	ND	ND	16.5 ± 1.4	ND	ND	25.5 ± 1.6
RUD5	0.8 ± 0.05	6.3 ± 1.8	4.5 ± 1.1	91.4 ± 2.9	ND	ND	1.6 ± 0.04	ND	ND	ND	ND	10.2 ± 0.6	ND	<LOQ	14.7 ± 2.7
RB1	3.3 ± 0.3	33.9 ± 12.1	ND	400.1 ± 41.0	ND	ND	7.3 ± 0.4	ND	ND	ND	ND	31.7 ± 2.1	ND	ND	90.9 ± 8.3
RB2	ND	3.9 ± 0.3	7.1 ± 2.0	254.7 ± 24.0	ND	ND	2.6 ± 0.2	ND	1.3 ± 0.1	ND	ND	24.5 ± 0.9	ND	<LOQ	24.7 ± 1.9
RB3	<LOQ	ND	ND	126.3 ± 5.6	ND	ND	1.3 ± 0.1	ND	0.7 ± 0.01	ND	ND	13.5 ± 1.1	ND	<LOQ	7.8 ± 3.2
RB4	ND	<LOQ	ND	171.1 ± 11.2	ND	ND	<LOQ	ND	1.0 ± 0.1	ND	ND	19.6 ± 1.6	ND	<LOQ	22.8 ± 0.8
RB5	<LOQ	1.5 ± 0.3	ND	109.1 ± 2.6	ND	ND	<LOQ	ND	0.6 ± 0.1	ND	ND	11.8 ± 0.7	ND	<LOQ	16.0 ± 0.6
WB1	<LOQ	ND	ND	109.6 ± 7.2	ND	ND	<LOQ	ND	<LOQ	ND	ND	10.0 ± 0.5	ND	ND	8.4 ± 1.8
WB2	ND	4.8 ± 1.2	ND	133.6 ± 14.4	ND	ND	<LOQ	ND	<LOQ	ND	ND	12.7 ± 1.4	ND	ND	12.3 ± 1.5
WB3	1.1 ± 0.1	17.2 ± 2.7	5.7 ± 1.2	183.8 ± 16.6	ND	ND	2.2 ± 0.1	ND	0.5 ± 0.1	ND	ND	16.0 ± 0.8	ND	ND	15.7 ± 1.5
WB4	ND	ND	ND	117.8 ± 7.0	ND	ND	<LOQ	ND	ND	ND	ND	13.6 ± 1.2	ND	ND	10.0 ± 0.6
WB5	1.2 ± 0.3	ND	ND	198.5 ± 8.8	ND	ND	2.1 ± 0.2	ND	1.0 ± 0.1	ND	ND	19.3 ± 2.2	ND	1058.5 ± 287.3	278.6 ± 14.3
WP1	ND	ND	ND	182.4 ± 4.6	ND	ND	1.1 ± 0.1	ND	0.8 ± 0.2	ND	ND	19.5 ± 0.1	ND	ND	14.8 ± 1.8
WAL1	ND	ND	3.8 ± 1.4	99.6 ± 12.5	ND	ND	<LOQ	ND	0.6 ± 0.02	ND	ND	10.9 ± 0.6	ND	<LOQ	19.6 ± 1.9
WAL2	ND	ND	ND	78.4 ± 6.4	ND	ND	<LOQ	ND	<LOQ	ND	ND	7.6 ± 0.3	ND	<LOQ	8.6 ± 0.3
WAL3	ND	ND	4.4 ± 0.7	75.5 ± 6.9	ND	ND	1.3 ± 0.05	ND	<LOQ	ND	ND	8.8 ± 0.7	ND	<LOQ	25.8 ± 3.0
WAL4	ND	ND	4.9 ± 1.1	118.2 ± 8.8	ND	ND	2.7 ± 0.2	ND	0.7 ± 0.2	ND	ND	12.8 ± 1.6	ND	396.6 ± 51.2	255.7 ± 5.8
WAL5	ND	ND	ND	145.6 ± 16.6	ND	ND	<LOQ	ND	1.0 ± 0.1	ND	ND	16.4 ± 2.3	ND	<LOQ	20.3 ± 1.5
BF1	ND	ND	ND	317.4 ± 16.0	ND	ND	<LOQ	ND	1.6 ± 0.2	17.2 ± 2.2	ND	36.4 ± 1.1	ND	404.0 ± 108.2	37.3 ± 4.1
SH1	ND	ND	ND	54.2 ± 4.6	ND	ND	<LOQ	ND	<LOQ	ND	ND	5.7 ± 0.4	ND	<LOQ	5.8 ± 1.1
SH2	ND	ND	ND	34.3 ± 1.2	ND	ND	<LOQ	ND	<LOQ	ND	ND	3.7 ± 0.1	ND	<LOQ	6.8 ± 0.2
SH3	ND	ND	ND	129.4 ± 14.7	ND	ND	<LOQ	ND	0.7 ± 0.1	ND	ND	14.8 ± 0.3	ND	<LOQ	8.9 ± 2.0
YPG1	ND	ND	<LOQ	<LOQ	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
YPG2	ND	ND	ND	53.6 ± 4.2	ND	ND	<LOQ	ND	<LOQ	ND	ND	6.0 ± 0.1	ND	<LOQ	15.3 ± 0.3
YPG3	0.8 ± 0.3	ND	ND	<LOQ	ND	ND	ND	ND	ND	ND	ND	54.1 ± 7.8	ND	ND	ND

Table S9. Individual concentrations (ng/g dry weight) of selective serotonin reuptake inhibitors and other pharmaceuticals and personal care products in gonads of fish samples collected from the Niagara River. The samples were analyzed in 3 replicates.

Sample ID	Pharmaceutical (mean ± SD, 3 replicates)													
	CIT	NFLX	SER	NSER	VEN	BUP	DPH	ACT	CBZ	DIL	TMP	ERY	MET	IOPA	CAF
SMB1	<LOQ	10.0 ± 1.2	6.7 ± 0.9	31.5 ± 5.1	0.5 ± 0.1	2.0 ± 0.1	1.3 ± 0.04	ND	ND	ND	ND	2.7 ± 0.1	ND	ND	8.3 ± 5.4
SMB2	ND	1.8 ± 0.8	ND	ND	ND	0.5 ± 0.1	0.4 ± 0.01	ND	<LOQ	ND	ND	1.4 ± 0.03	ND	139.2 ± 20.2	1.9 ± 0.5
SMB3	ND	ND	ND	ND	ND	0.5 ± 0.1	0.3 ± 0.01	ND	<LOQ	ND	ND	1.5 ± 0.1	ND	85.3 ± 10.7	3.5 ± 0.5
SMB4	ND	1.3 ± 0.7	ND	ND	ND	0.6 ± 0.01	0.4 ± 0.02	ND	<LOQ	ND	ND	1.4 ± 0.1	ND	264.4 ± 31.0	3.4 ± 0.4
SMB5	ND	ND	ND	ND	ND	0.6 ± 0.04	0.6 ± 0.01	ND	<LOQ	ND	ND	1.6 ± 0.1	ND	103.1 ± 12.2	3.7 ± 0.5
LMB1	ND	3.4 ± 1.6	ND	ND	ND	0.3 ± 0.01	0.4 ± 0.01	ND	<LOQ	ND	ND	1.7 ± 0.1	ND	426.9 ± 22.5	1.9 ± 0.05
LMB2	0.9 ± 0.002	ND	ND	34.8 ± 2.1	ND	ND	<LOQ	ND	<LOQ	<LOQ	ND	2.7 ± 0.1	ND	ND	7.8 ± 0.7
LMB3	ND	2.1 ± 0.8	ND	ND	1.6 ± 0.1	0.7 ± 0.1	0.4 ± 0.03	ND	ND	ND	ND	3.3 ± 0.3	ND	ND	10.0 ± 5.3
LMB4	ND	ND	ND	27.1 ± 8.3	ND	ND	0.3 ± 0.02	ND	0.9 ± 0.1	ND	ND	16.8 ± 1.4	ND	ND	12.9 ± 7.0
LMB5	0.8 ± 0.1	ND	ND	ND	1.1 ± 2.7	ND	0.6 ± 0.02	ND	0.6 ± 0.04	ND	ND	1.9 ± 0.8	ND	ND	3.3 ± 0.5
RUD1	0.5 ± 0.04	2.4 ± 1.4	ND	ND	ND	ND	<LOQ	ND	<LOQ	ND	ND	1.4 ± 0.1	ND	184.3 ± 41.7	1.3 ± 0.1
RUD2	0.7 ± 0.03	ND	ND	32.2 ± 3.2	ND	ND	0.2 ± 0.01	ND	<LOQ	0.4 ± 0.1	ND	2.8 ± 0.03	ND	ND	7.7 ± 0.3
RUD3	0.5 ± 0.03	1.2 ± 0.5	ND	ND	ND	ND	<LOQ	ND	<LOQ	ND	ND	1.5 ± 0.1	ND	118.0 ± 11.1	2.2 ± 0.2
RUD4	ND	ND	ND	ND	ND	ND	0.2 ± 0.02	ND	<LOQ	ND	ND	2.3 ± 0.1	ND	ND	4.4 ± 0.7
RUD5	ND	ND	ND	ND	ND	ND	0.4 ± 0.01	ND	0.4 ± 0.01	ND	ND	1.1 ± 0.8	ND	ND	1.6 ± 0.1
RB1	0.6 ± 0.5	ND	3.6 ± 0.1	44.0 ± 8.4	ND	ND	0.5 ± 0.04	ND	6.6 ± 0.9	ND	ND	22.7 ± 6.8	ND	749.8 ± 123.0	140.1 ± 4.3
RB2	0.5 ± 0.02	ND	3.8 ± 0.1	ND	ND	ND	2.4 ± 0.1	ND	<LOQ	ND	ND	2.7 ± 0.1	ND	ND	11.5 ± 1.6
RB3	ND	ND	ND	ND	ND	ND	0.9 ± 0.2	ND	1.8 ± 0.1	ND	ND	28.7 ± 0.5	ND	ND	111.1 ± 11.1
RB4	0.3 ± 0.1	12.7 ± 2.3	ND	ND	ND	ND	0.2 ± 0.01	ND	<LOQ	ND	ND	2.2 ± 0.1	ND	ND	6.1 ± 0.8
RB5	0.3 ± 0.1	ND	ND	28.6 ± 4.5	ND	ND	0.3 ± 0.05	ND	0.8 ± 0.1	ND	ND	13.5 ± 0.4	ND	480.1 ± 89.0	33.2 ± 3.1
WB1	ND	ND	ND	ND	ND	ND	0.4 ± 0.01	1.2 ± 0.1	0.4 ± 0.1	ND	ND	2.7 ± 0.9	ND	ND	2.5 ± 0.2
WB2	ND	ND	ND	ND	ND	ND	0.5 ± 0.01	ND	0.6 ± 0.1	ND	ND	1.3 ± 0.5	ND	111.1 ± 3.9	1.9 ± 0.2
WB3	ND	ND	ND	ND	ND	ND	0.4 ± 0.01	ND	0.5 ± 0.05	ND	ND	1.3 ± 0.1	ND	70.8 ± 10.1	2.8 ± 0.1
WB4	1.7 ± 0.1	ND	0.5 ± 0.03	ND	2.3 ± 0.6	5.5 ± 2.3	0.5 ± 0.01	ND	0.4 ± 0.03	ND	ND	2.4 ± 1.0	ND	ND	3.7 ± 0.3
WB5	ND	ND	ND	ND	ND	0.2 ± 0.04	0.3 ± 0.02	ND	0.6 ± 0.1	ND	ND	8.5 ± 0.9	ND	ND ± ND	99.5 ± 3.1
WP1	1.6 ± 0.1	0.3 ± 0.03	0.1 ± 0.01	ND	ND	13.5 ± 2.2	2.0 ± 0.2	ND	1.6 ± 0.3	ND	ND	<LOQ	ND	211.6 ± 30.9	1.9 ± 0.3
WAL1	0.9 ± 0.1	ND	0.5 ± 0.02	ND	4.3 ± 1.1	ND	0.5 ± 0.01	ND	0.5 ± 0.1	ND	ND	1.4 ± 0.2	ND	69.4 ± 4.3	5.3 ± 0.1
WAL2	ND	ND	0.4 ± 0.04	ND	2.7 ± 1.5	ND	0.5 ± 0.01	ND	0.4 ± 0.02	ND	ND	1.6 ± 0.6	ND	ND	3.3 ± 0.1
WAL3	ND	ND	ND	ND	ND	ND	0.4 ± 0.00	ND	<LOQ	ND	ND	ND	ND	ND	18.6 ± 0.5
WAL4	ND	ND	ND	42.2 ± 8.0	ND	ND	<LOQ	1.7 ± 0.2	<LOQ	ND	ND	2.3 ± 0.2	ND	ND	7.7 ± 1.2
WAL5	ND	ND	ND	ND	5.5 ± 1.4	10.1 ± 0.6	0.3 ± 0.01	ND	0.4 ± 0.04	ND	ND	1.2 ± 0.6	ND	ND	3.8 ± 0.4
BF1	ND	ND	ND	ND	ND	ND	<LOQ	4.7 ± 0.3	<LOQ	ND	ND	2.2 ± 0.1	ND	ND	4.5 ± 0.6
SH1	ND	ND	ND	ND	ND	ND	<LOQ	ND	<LOQ	ND	ND	2.3 ± 0.2	ND	ND	3.5 ± 0.6
SH2	ND	ND	ND	ND	ND	ND	<LOQ	2.8 ± 0.2	2.2 ± 0.2	ND	ND	9.4 ± 0.8	ND	ND	5.3 ± 0.5
SH3	<LOQ	ND	ND	ND	ND	ND	<LOQ	3.0 ± 0.3	2.3 ± 0.1	ND	ND	9.7 ± 0.5	ND	ND	2.9 ± 0.3
YPG1	ND	ND	ND	ND	ND	ND	0.5 ± 0.02	ND	<LOQ	ND	ND	1.6 ± 0.3	ND	ND	4.0 ± 0.1
YPG2	0.2 ± 0.02	ND	ND	ND	3.6 ± 0.2	ND	0.3 ± 0.003	ND	2.3 ± 0.1	ND	ND	9.8 ± 0.2	ND	ND	6.1 ± 0.6
YPG3	0.7 ± 0.1	ND	ND	ND	ND	6.6 ± 1.6	0.4 ± 0.01	ND	<LOQ	ND	ND	2.0 ± 0.5	ND	ND	3.3 ± 0.3

Table S10. Individual concentrations (ng/g dry weight) of selective serotonin reuptake inhibitors and other pharmaceuticals and personal care products in liver of fish samples collected from the Niagara River. The samples were analyzed in 3 replicates.

Sample ID	Pharmaceutical (mean ± SD)														
	CIT	NFLX	SER	NSER	VEN	BUP	DPH	ACT	CBZ	DIL	TMP	ERY	MET	IOPA	CAF
SMB1	ND	ND	ND	64.9 ± 5.4	ND	0.9 ± 0.2	0.9 ± 0.1	ND	ND	ND	ND	5.7 ± 0.1	<LOQ	ND	5.3 ± 0.6
SMB2	ND	ND	ND	67.6 ± 7.1	5.6 ± 0.1	0.7 ± 0.1	0.4 ± 0.1	ND	ND	ND	ND	5.9 ± 0.4	<LOQ	ND	3.3 ± 0.5
SMB3	ND	ND	ND	52.8 ± 4.4	7.8 ± 0.8	0.8 ± 0.2	1.1 ± 0.1	ND	ND	ND	ND	6.1 ± 0.7	ND	ND	869.7 ± 6.1
SMB4	ND	ND	ND	60.1 ± 2.3	5.5 ± 0.5	ND	0.8 ± 0.1	ND	ND	ND	ND	5.6 ± 0.6	ND	ND	ND
SMB5	ND	ND	ND	68.1 ± 9.3	<LOQ	1.0 ± 0.1	1.0 ± 0.1	ND	ND	ND	ND	5.5 ± 0.03	<LOQ	ND	4.9 ± 0.2
LMB1	ND	ND	ND	69.1 ± 10.9	2.7 ± 0.1	0.3 ± 0.1	0.7 ± 0.01	ND	ND	ND	ND	5.3 ± 0.2	ND	ND	ND
LMB2	ND	ND	ND	85.9 ± 11.0	ND	0.5 ± 0.8	ND	ND	ND	ND	ND	5.5 ± 0.2	ND	ND	3.3 ± 1.0
LMB3	ND	ND	ND	82.0 ± 9.1	1.2 ± 0.2	ND	0.2 ± 0.01	ND	ND	ND	ND	5.4 ± 0.5	<LOQ	ND	3.5 ± 1.9
LMB4	0.9 ± 0.03	ND	ND	102.9 ± 16.3	ND	ND	0.7 ± 0.05	ND	ND	ND	ND	9.3 ± 0.2	ND	ND	82.2 ± 2.6
LMB5	ND	ND	ND	89.3 ± 4.0	<LOQ	ND	<LOQ	ND	ND	ND	ND	8.9 ± 0.2	ND	ND	4.6 ± 0.7
RUD1	ND	ND	ND	132.5 ± 23.7	ND	ND	<LOQ	ND	ND	ND	ND	5.6 ± 0.3	<LOQ	ND	747.4 ± 17.7
RUD2	ND	ND	ND	109.7 ± 5.4	ND	ND	ND	ND	ND	ND	ND	5.5 ± 0.3	<LOQ	ND	ND
RUD3	ND	ND	ND	141.3 ± 7.0	ND	ND	ND	ND	ND	ND	ND	5.2 ± 0.4	<LOQ	ND	ND
RUD4	ND	ND	ND	64.6 ± 2.9	ND	ND	0.9 ± 0.1	ND	ND	ND	ND	5.8 ± 0.2	<LOQ	ND	4.9 ± 0.6
RUD5	3.7 ± 0.2	ND	ND	647.3 ± 111.5	ND	ND	5.2 ± 0.1	ND	ND	ND	ND	27.3 ± 0.4	1.5 ± 0.3	ND	20.1 ± 2.0
RB1	ND	ND	ND	347.4 ± 28.8	ND	ND	0.6 ± 0.02	ND	ND	ND	ND	36.3 ± 0.9	ND	ND	25.6 ± 1.0
RB2	1.7 ± 0.1	ND	ND	167.7 ± 10.9	1.7 ± 0.1	ND	1.7 ± 0.1	ND	ND	ND	ND	13.9 ± 0.5	ND	ND	8.4 ± 1.7
RB3	ND	ND	ND	ND	<LOQ	ND	1.7 ± 0.05	ND	ND	ND	ND	11.3 ± 0.1	ND	ND	7.1 ± 0.8
RB4	<LOQ	ND	ND	149.5 ± 10.8	ND	ND	0.2 ± 0.04	ND	ND	ND	ND	11.8 ± 0.8	ND	ND	7.8 ± 2.4
RB5	<LOQ	ND	ND	174.8 ± 2.6	ND	ND	0.2 ± 0.02	ND	ND	ND	ND	14.2 ± 0.1	ND	ND	25.5 ± 3.0
WB1	0.3 ± 0.01	ND	ND	32.4 ± 0.8	<LOQ	ND	0.1 ± 0.004	ND	ND	ND	ND	11.2 ± 0.5	ND	ND	2.4 ± 0.2
WB2	0.7 ± 0.1	ND	ND	101.7 ± 9.4	ND	ND	0.4 ± 0.03	ND	ND	ND	ND	9.1 ± 0.1	ND	ND	6.8 ± 0.8
WB3	2.1 ± 0.2	ND	ND	ND	ND	ND	2.9 ± 0.1	ND	ND	ND	ND	9.4 ± 0.5	ND	ND	6.0 ± 0.9
WB4	3.6 ± 0.1	ND	ND	111.8 ± 4.4	ND	ND	3.8 ± 0.1	ND	ND	ND	ND	8.7 ± 0.3	ND	ND	6.5 ± 0.5
WB5	ND	ND	ND	ND	ND	ND	0.3 ± 0.03	ND	ND	ND	ND	9.1 ± 0.3	ND	ND	6.9 ± 1.7
WP1	ND	ND	ND	245.8 ± 6.1	4.2 ± 4.1	ND	0.3 ± 0.01	ND	ND	ND	ND	46.9 ± 2.6	1.5 ± 0.7	ND	8.9 ± 0.8
WAL1	ND	ND	ND	ND	ND	ND	0.7 ± 0.03	ND	ND	ND	ND	9.1 ± 0.5	ND	ND	21.7 ± 2.1
WAL2	ND	ND	ND	ND	ND	ND	0.8 ± 0.03	ND	ND	ND	ND	8.9 ± 0.2	ND	ND	14.0 ± 0.7
WAL3	ND	ND	ND	ND	ND	ND	0.9 ± 0.1	ND	ND	ND	ND	8.5 ± 0.2	ND	ND	49.8 ± 0.3
WAL4	0.5 ± 0.01	ND	ND	62.5 ± 3.2	ND	ND	0.5 ± 0.01	ND	ND	ND	ND	5.3 ± 0.1	ND	ND	39.9 ± 1.3
WAL5	ND	ND	ND	ND	<LOQ	ND	0.7 ± 0.05	ND	ND	ND	ND	9.7 ± 0.5	ND	ND	13.1 ± 1.1
BF1	0.3 ± 0.1	ND	ND	55.4 ± 2.5	ND	ND	<LOQ	ND	ND	ND	ND	5.7 ± 0.3	ND	ND	2.6 ± 0.8
SH1	<LOQ	ND	ND	136.0 ± 31.3	ND	ND	0.2 ± 0.05	ND	ND	ND	ND	5.5 ± 0.1	ND	ND	2.7 ± 0.7
SH2	3.2 ± 0.05	ND	ND	66.6 ± 15.7	ND	ND	<LOQ	ND	ND	ND	ND	5.4 ± 0.2	ND	ND	3.1 ± 0.8
SH3	ND	ND	ND	57.9 ± 10.4	ND	ND	<LOQ	ND	ND	ND	ND	5.5 ± 0.2	ND	ND	ND
YPG1	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	5.3 ± 0.1	ND	ND	11.8 ± 0.5
YPG2	ND	ND	ND	ND	56.8 ± 1.0	ND	0.2 ± 0.02	ND	ND	ND	ND	8.9 ± 0.2	ND	ND	7.5 ± 0.3
YPG3	ND	ND	ND	ND	32.6 ± 1.7	ND	<LOQ	ND	ND	ND	ND	5.6 ± 0.3	ND	ND	9.5 ± 1.6

Table S11. Individual concentrations (ng/g dry weight) of selective serotonin reuptake inhibitors and other pharmaceuticals and personal care products in muscle of fish samples collected from the Niagara River. The samples were analyzed in 3 replicates.

Sample ID	Pharmaceutical (mean ± SD, 3 replicates)													
	CIT	NFLX	SER	NSER	VEN	BUP	DPH	ACT	CBZ	DIL	TMP	ERY	MET	IOPA	CAF
SMB1	ND	0.4 ± 0.1	ND	19.1 ± 1.1	<LOQ	<LOQ	0.1 ± 0.01	ND	0.04 ± 0.004	ND	ND	1.6 ± 0.1	ND	ND	3.2 ± 0.8
SMB2	ND	0.2 ± 0.04	ND	18.5 ± 0.2	ND	<LOQ	0.1 ± 0.01	ND	ND	ND	ND	1.8 ± 0.1	ND	ND	2.3 ± 0.4
SMB3	ND	0.4 ± 0.1	ND	18.3 ± 1.3	<LOQ	<LOQ	0.1 ± 0.00	ND	0.0 ± 0.0	ND	ND	1.7 ± 0.2	ND	ND	3.5 ± 0.4
SMB4	ND	ND	ND	31.5 ± 2.0	ND	ND	0.2 ± 0.02	ND	1.0 ± 0.1	ND	ND	2.7 ± 0.1	ND	ND	36.7 ± 3.0
SMB5	ND	0.8 ± 0.1	ND	32.2 ± 1.5	ND	ND	0.2 ± 0.01	ND	1.2 ± 0.04	ND	ND	2.8 ± 0.1	ND	ND	4.6 ± 3.4
LMB1	0.4 ± 0.01	1.8 ± 0.2	ND	37.7 ± 2.0	0.4 ± 0.02	<LOQ	0.2 ± 0.00	ND	0.2 ± 0.01	ND	ND	2.8 ± 0.2	ND	ND	4.2 ± 0.3
LMB2	ND	ND	ND	29.6 ± 1.5	0.4 ± 0.03	ND	<LOQ	ND	0.2 ± 0.02	ND	ND	2.8 ± 0.1	ND	ND	17.0 ± 1.7
LMB3	ND	ND	ND	35.5 ± 3.2	0.6 ± 0.03	<LOQ	0.3 ± 0.003	ND	1.3 ± 0.1	ND	ND	2.9 ± 0.2	ND	ND	8.6 ± 3.8
LMB4	ND	ND	ND	30.4 ± 1.2	0.4 ± 0.04	ND	<LOQ	ND	ND	ND	ND	1.6 ± 0.01	ND	ND	3.7 ± 0.3
LMB5	ND	0.2 ± 0.1	ND	34.9 ± 0.6	0.4 ± 0.1	ND	<LOQ	ND	0.8 ± 0.1	ND	ND	2.8 ± 0.1	ND	ND	4.6 ± 2.1
RUD1	ND	ND	ND	34.5 ± 3.4	0.4 ± 0.1	ND	<LOQ	ND	1.0 ± 0.03	ND	ND	2.6 ± 0.2	ND	ND	22.6 ± 1.5
RUD2	ND	ND	ND	37.6 ± 4.5	ND	ND	<LOQ	ND	0.2 ± 0.02	<LOQ	0.6 ± 0.1	2.8 ± 0.1	ND	ND	38.3 ± 4.2
RUD3	ND	ND	ND	66.5 ± 6.0	0.4 ± 0.07	ND	<LOQ	ND	0.3 ± 0.004	ND	ND	2.8 ± 0.1	ND	ND	24.6 ± 1.9
RUD4	ND	ND	ND	48.9 ± 7.4	0.6 ± 0.1	ND	0.1 ± 0.00	ND	0.1 ± 0.02	ND	ND	2.9 ± 0.2	ND	ND	16.2 ± 0.9
RUD5	0.2 ± 0.0	ND	ND	23.7 ± 3.2	ND	ND	0.2 ± 0.01	ND	ND	ND	ND	1.6 ± 0.1	ND	ND	4.1 ± 0.1
RB1	ND	ND	ND	31.8 ± 2.6	0.4 ± 0.08	ND	0.1 ± 0.01	ND	0.8 ± 0.1	ND	ND	2.8 ± 0.3	ND	ND	6.8 ± 5.8
RB2	<LOQ	ND	ND	ND	ND	ND	0.1 ± 0.01	ND	ND	ND	ND	1.6 ± 0.2	ND	ND	4.8 ± 0.2
RB3	<LOQ	ND	ND	20.4 ± 0.4	ND	ND	0.2 ± 0.02	ND	ND	ND	ND	1.7 ± 0.2	ND	ND	2.7 ± 0.3
RB4	<LOQ	ND	ND	20.6 ± 1.3	ND	ND	0.1 ± 0.01	ND	0.4 ± 0.1	<LOQ	ND	1.8 ± 0.1	ND	ND	3.0 ± 0.4
RB5	ND	ND	ND	ND	ND	ND	<LOQ	ND	ND	ND	ND	1.8 ± 0.1	ND	ND	15.6 ± 1.6
WB1	ND	ND	ND	38.4 ± 9.7	ND	ND	0.1 ± 0.01	ND	0.1 ± 0.01	ND	0.7 ± 0.1	2.8 ± 0.2	ND	ND	18.2 ± 4.1
WB2	<LOQ	ND	ND	29.5 ± 0.8	<LOQ	ND	<LOQ	ND	ND	ND	ND	1.7 ± 0.1	ND	ND	1.6 ± 0.2
WB3	ND	1.2 ± 0.2	ND	40.9 ± 1.0	0.5 ± 0.07	ND	0.5 ± 0.04	ND	3.8 ± 0.1	1.2 ± 0.2	ND	2.7 ± 0.03	ND	ND	5.0 ± 3.3
WB4	0.3 ± 0.03	1.5 ± 0.5	ND	29.4 ± 1.2	<LOQ	ND	0.3 ± 0.03	ND	ND	ND	ND	1.6 ± 0.1	ND	ND	2.4 ± 0.2
WB5	ND	0.7 ± 0.2	ND	37.0 ± 2.6	0.5 ± 0.06	ND	0.2 ± 0.00	ND	0.8 ± 0.1	ND	ND	2.7 ± 0.1	ND	ND	60.7 ± 2.0
WP1	ND	ND	ND	31.9 ± 2.8	0.5 ± 0.2	ND	0.2 ± 0.02	ND	0.9 ± 0.1	ND	ND	2.8 ± 0.1	ND	ND	6.4 ± 4.1
WAL1	ND	ND	ND	72.6 ± 2.9	0.4 ± 0.1	ND	0.2 ± 0.02	ND	1.0 ± 0.04	ND	ND	2.9 ± 0.1	ND	ND	22.3 ± 7.7
WAL2	ND	ND	ND	25.2 ± 6.8	<LOQ	ND	0.0 ± 0.00	ND	ND	ND	ND	1.7 ± 0.1	ND	ND	6.6 ± 0.5
WAL3	ND	0.3 ± 0.1	ND	33.5 ± 0.6	0.4 ± 0.03	ND	0.2 ± 0.03	ND	0.8 ± 0.1	ND	ND	2.7 ± 0.1	ND	ND	29.1 ± 8.6
WAL4	ND	ND	ND	28.4 ± 9.1	ND	ND	0.1 ± 0.01	ND	ND	ND	ND	1.5 ± 0.1	ND	ND	14.0 ± 1.1
WAL5	ND	ND	ND	20.8 ± 1.2	ND	ND	<LOQ	ND	ND	ND	ND	1.7 ± 0.04	ND	ND	5.4 ± 0.7
BF1	ND	ND	ND	33.3 ± 1.4	ND	ND	<LOQ	ND	1.0 ± 0.1	ND	ND	2.8 ± 0.1	ND	ND	4.5 ± 1.5
SH1	ND	ND	ND	33.7 ± 1.4	0.4 ± 0.04	ND	<LOQ	ND	0.7 ± 0.02	ND	ND	2.8 ± 0.1	ND	ND	7.6 ± 1.5
SH2	ND	ND	ND	29.5 ± 6.3	ND	ND	<LOQ	ND	ND	ND	ND	1.7 ± 0.1	ND	ND	17.5 ± 0.3
SH3	ND	ND	ND	ND	ND	ND	<LOQ	ND	0.8 ± 0.1	ND	0.4 ± 0.1	2.7 ± 0.05	ND	ND	6.6 ± 7.2
YPG1	ND	ND	ND	ND	ND	ND	0.05 ± 0.01	ND	ND	ND	ND	1.8 ± 0.1	ND	ND	12.2 ± 0.5
YPG2	ND	ND	ND	ND	ND	ND	ND	ND	ND	<LOQ	ND	1.9 ± 0.1	ND	ND	8.7 ± 1.5
YPG3	ND	ND	ND	ND	ND	ND	<LOQ	ND	0.9 ± 0.3	<LOQ	ND	1.8 ± 0.1	ND	ND	9.2 ± 0.6

Table S12. Estimated bioaccumulation factor (BAF) for antidepressants and antihistamine DPH in fish muscle, liver, gonad, and brain using the lowest PPCP concentrations in surface water to demonstrate the values for the worst-case scenario.

Species/organ	BAF						
	CIT	NFLX	SER	NSER	VEN	BUP	DPH
Smallmouth bass							
Brain	NA	18 - 57	78 - 84	3400 - 6600	NA	640 – 1600	320 – 520
Gonad	NA	6 - 45	86	1000	498	290 - 2000	100 - 420
Liver	NA	NA	NA	1800 - 2300	2700 – 7800	320 - 860	150 – 360
Muscle	370	1 - 8	NA	610 - 1300	380	NA	370
Largemouth bass							
Brain	1500	18 - 110	390	4300 – 8500	NA	1400	380 – 1200
Gonad	820 - 860	9	NA	900 - 1200	1100 - 1200	580 – 710	85 - 210
Liver	930	NA	NA	2300 – 3400	1200	450 - 1000	54 - 320
Muscle	NA	1 - 3	NA	990 - 1200	360 - 620	NA	63 - 92
Rudd							
Brain	840	24 - 28	61	3000 – 4900	NA	NA	350 – 1600
Gonad	450 - 740	5 - 11	NA	1100	NA	NA	54 - 140
Liver	3900	NA	NA	2200 – 22000	NA	NA	290 - 1700
Muscle	190	NA	NA	790 - 2200	430 - 570	NA	41 - 65
Rock bass							
Brain	3300	7 - 150	92	3700 - 13000	NA	NA	450 - 2400
Gonad	330 - 630	57	47 - 53	950 – 1500	NA	NA	74 – 790
Liver	580 - 1700	NA	NA	5000 -12000	1700	NA	56 - 580
Muscle	NA	NA	NA	680 - 1100	380	NA	32 - 59
White bass							
Brain	1100 - 1200	22 - 73	30	3700 - 6600	NA	NA	710 - 720
Gonad	1700	NA	3	NA	2300	150 - 5500	110 – 180
Liver	250 - 3600	NA	NA	1100 - 3700	NA	NA	45 - 1300
Muscle	320	3 - 7	NA	980 - 1400	470 - 500	NA	25 - 160

White perch							
	Brain	NA	NA	NA	6100	NA	NA	4
	Gonad	1600	2	1	NA	NA	650	8
	Liver	NA	NA	NA	8200	4200	NA	1
	Muscle	NA	NA	NA	1100	460	NA	1
Walleye							
	Brain	NA	NA	20 - 25	2500 – 4900	NA	NA	5 - 11
	Gonad	860	NA	2	1400	2700 – 5500	110 – 160	1 - 2
	Liver	510	NA	NA	2100	NA	170 - 310	2 - 4
	Muscle	NA	2	NA	690 - 2400	350 - 400	NA	1
Bowfin							
	Brain	NA	NA	NA	11000	NA	NA	NA
	Gonad	NA	NA	NA	NA	NA	NA	NA
	Liver	1	NA	NA	1800	NA	NA	NA
	Muscle	NA	NA	NA	1111	NA	NA	NA
Steel head							
	Brain	NA	NA	NA	1100 – 4300	NA	NA	NA
	Gonad	NA	NA	NA	NA	NA	NA	NA
	Liver	3200	NA	NA	1900 - 4500	NA	NA	55
	Muscle	NA	NA	NA	980 - 1100	400	NA	NA
Yellow perch							
	Brain	850	NA	NA	1800	NA	NA	NA
	Gonad	230 - 690	NA	NA	NA	9	6600	98 - 170
	Liver	NA	NA	NA	NA	33000 - 57000	NA	61
	Muscle	NA	NA	NA	NA	NA	NA	15

BAFs were determined in each sample for most of the fish species except yellow perch. BAFs of yellow perch were examined in each group of samples (see *Fish sample and organ collection* section in the SI). NA: unable to calculate BAF because the levels found were below LOD.

Detailed procedure for fish organ preparation, analyte extraction, and clean up

The fish samples were dissected to obtain brain, gonad, liver, and muscle samples. The muscle samples were homogenized while gonad, liver, and brain samples were cut into small pieces. All samples were stored at −40 °C before freeze-drying (T ≤ -40 °C, and pressure ≤133 x 10^{-3} mBar) (Labconco Freeze Dry System). Freeze-dried samples were finely ground and stored at -40 °C prior to extraction.

Muscle, liver, and gonad samples were extracted in the following manner: a 0.5 g aliquot of surrogate-fortified freeze-dried sample was extracted by sonication in 5 mL of the extraction solvent (5% formic acid in acetonitrile/isopropanol (50/50, v/v)) for 5 min. Sample was then centrifuged at 25 °C (3434 x g, 5 min) and the supernatant was decanted to a 15-mL centrifuge tube. Each sample was re-extracted with 5 mL of extraction solvent, and the crude extracts were pooled. The combined crude extract was added into a 50-mL centrifuge tube containing 2 g of lipid removal sorbent (discussed below) and 5 mL of 5-mM ammonium acetate. The sample was immediately vortexed for 1 min and then centrifuged at 25 °C (3434 x g, 5 min). Alumina was chosen to remove lipids from muscle and liver samples; however, it gave poor recoveries for gonad samples that have high lipid content. Thus, the Agilent Bond Elute Enhanced Matrix Removal–Lipid™ (EMR–Lipid) was selected for these samples. After lipid removal, the extract was transferred to a glass bottle and diluted with water to a final volume of 300 mL. Water-diluted samples were adjusted to pH 2.9±0.1 prior to solid phase extraction (SPE).

For brain samples, all freeze-dried brain tissues (25.8 – 256.5 mg) were used. One mL of extraction solvent was added to the fortified brain sample followed by centrifugation (25 °C, 3434 x g, 5 min). The supernatant was decanted and the remaining sample was re-

extracted using 1 mL of extraction solvent. Lipids were removed using 200 mg of alumina and 2 mL of 5 mM ammonium acetate. The brain extract was diluted with Nanopure™ water to 150 mL before SPE.

SPE was performed on Oasis HLB™ cartridges (6 mL, 500 mg). Water-diluted samples were loaded onto the SPE cartridges that have been pre-conditioned with acetonitrile (6 mL) and Nanopure™ water (6 mL), respectively. After all samples were loaded, the cartridges were dried for at least 30 min. The analytes were eluted twice with 4 mL of acetonitrile, then evaporated down to dryness under a gentle N_2 stream. The residues were diluted with 200 μL of 80% (0.1%) formic acid in water, and 20% 50:50 (v/v) acetonitrile:methanol. The samples were kept at -40 °C for at least 20 min and then centrifuged at 11337 x g for 20 min. The clear solution was transferred to 2 mL amber vials for LC-MS analysis.

Method development and optimization for analysis of fish

Even though QuEChERS™ (Quick, Easy, Cheap, Effective, Rugged, and Safe) has been modified for extraction of PPCPs in biological matrices (Agilent Application Notebook, June 2011)[4], it is ineffective for complex and fatty sample matrix like fish tissue. Therefore, we developed a new method for the extraction of PPCPs in fish. Due to sample size limitation, muscle and liver tissues were selected for method optimization; subsequently, the optimized procedure was adapted for gonad and brain tissues.

Selection of extraction solvent. Solid-liquid extraction by vortex was performed to optimize the extraction solvent. To a 1 g of surrogate-spiked freeze-dried tissue, 10 mL extraction solvent was added, then the tissue was extracted for 2 min. The tested extraction

solvents: 0.1 M acetic acid/methanol (50:50), 0.1 M acetic acid/acetonitrile (50:50), and 5% formic acid in acetonitrile were chosen from literature.[5, 6] Among the three, 5% formic acid in acetonitrile showed the highest extraction efficiency for the studied PPCPs; nonetheless some compounds, especially the more hydrophobic compounds, exhibited very low recoveries (less than 27%, spiked level 100 ng/g dry weigh). To improve the extraction of hydrophobic compounds, isopropyl alcohol was added to the extraction solvent to make a final solution of 5% formic acid in 50 acetonitrile/50 isopropyl alcohol (v/v) giving satisfactory extraction efficiency. Percent extractions were higher than 50% (spiked level 100 ng/g dry weigh) for most compounds, especially for the SSRIs.

Extraction procedure and extraction time. Extraction procedure was optimized including manual shaking, vortex, end-over-end inversion, and sonication (data not shown). Spiked tissues (~1 g for each test sample) using 10 mL of extraction solvent were used for optimization. High extraction efficiencies were obtained when using sonication. Then, sonication time was optimized from 1 to 10 min. The optimum sonication time was found to be 5 min; however, extraction yield of some compounds did not show much increase. Thus re-extraction was performed to improve extraction yields. Sample extraction was performed twice for all samples, with 5 mL extraction solvent and sonication for 5 min each time. All extracts were pooled for further analysis.

Sample size. Due to high lipid content, fish tissue extracts appeared hazy. Since increasing sample size proportionally increased the amount of co-extracted lipids, a lipid removal step had to be performed. Sample size was optimized, by testing various amounts (from 0.25, 0.5 and 1 g), to obtain the highest signal-to-noise ratios for all the analytes. Method sensitivity was assessed by spiking a known amount of standard mix at environmentally relevant levels and seeing if the employed method is capable of producing

accurate measurable levels of the spiked standards. The results showed that a 0.5 g sample was the optimum amount that gave enough sensitivity without requiring a laborious process for lipid removal.

Selection of lipid removal sorbent. Residual lipid in the final extract affects method efficiency, chromatographic reproducibility, and mass spectrometer performance over the course of a worklist, thus, introducing a challenge in method development. In this work, lipid removal was first accomplished using alumina as sorbent for unwanted matrix.[7] Effective lipid removal was achieved by using 2 g alumina for 0.5 g of freeze-dried muscle and liver tissues; for brain samples 200 mg alumina was added. However, lipid removal using alumina was not enough for gonad samples, which contains the highest lipid concentration per gram of tissue. The high lipid content in gonad extracts resulted in significantly distorted chromatograms; these extracts could also potentially damage the instrument. To overcome this challenge, Agilent Bond Elut Enhanced Matrix Removal–Lipid[tm] (EMR–Lipid) was considered for lipid removal. Lipids in gonad samples were successfully removed using a 200-mg EMR-lipid sorbent. However, this sorbent is expensive therefore its use was limited to the gonads; alumina was used for the other types of tissues due to its lower cost and sufficient efficiency in lipid removal in muscle, liver, and brain samples.

SPE procedure. The SPE method for extraction of PPCPs in water was applied to cleanup all extracts of fish tissues.[3] Freezing at -40 °C for 20 min, followed by centrifugation (11337 x g, 20 min), was employed as a precautionary step to prevent trace amounts of lipids from negatively affecting the detection system. The clear solution obtained was analyzed by LC-MS/MS.

Method validation and quality assurance protocol

The linearity of the method was evaluated by preparing calibration graphs for all target analytes in all sample matrices. The linear range for muscle, liver, and gonad tissues was between 0 to 40 ng/g, while the linear range for brain tissue was 0 – 500 ng/g. All target compounds, except for ciprofloxacin, had a correlation coefficient (r^2) greater than 0.9982.

Method detection limits (MDLs) and method quantification limits (MQLs) for all fish tissues are presented in Table S5. Both MDLs and MQLs, were determined following the US EPA guidelines.[8] Briefly, seven replicates of the clean tissues were fortified with the standard solution at the lowest concentration in the calibration curve or at the concentration that is well-differentiated from the background. MDLs and MQLs were calculated using equation (1) and (2), respectively.

$$MDL = 3.14\ x\ SD \qquad (1)$$

$$MQL = 10\ x\ SD \qquad (2)$$

Where SD is the standard deviation of 7 replicate measurements and 3.14 is the student's t-value at 99% confidence level.

Accuracy and precision were determined based on percent recoveries (%R) and relative standard deviations (%RSD) of spiked isotope-labeled compounds, respectively. Accuracy and precision were determined using various tissues (brain, gonad, liver and muscle) that were fortified with isotope-labeled compounds; %R was calculated by comparing the measured concentrations with the expected fortified concentrations.

At least one laboratory reagent blank and one fortified laboratory reagent blank were analyzed with each set of 6 - 10 environmental samples to assess potential sample contamination; no analytes were detected in blank samples indicating a clean system and

absence of carry over. Isotope-labeled surrogates of most of the target compounds were added to samples prior the extraction to monitor the method performance. Isotope dilution was used for quantifying analytes, with the exception of iopamidol and metformin that were quantified by internal standard method.

Estimation of bioaccumulation factors

Bioaccumulation is described as a process in which chemicals are taken up by an organism either directly from exposure to a contaminated medium, or by consumption of food containing the chemical contaminant (the US EPA, 2010).[9] According to the US EPA, the bioaccumulation factor (BAF) is calculated as the ratio of the concentration of a chemical in the tissue of an aquatic organism to its concentration in water, in situations where both the organism and its food are exposed and the ratio does not change substantially over time (the US EPA, 2000).[10] The conventional determination of BAFs are based on a steady state of a compound of interest in an organism and the ambient environment. Because fish studied in this work are living in their natural habitat, the Niagara River, and also move significant distances in the river, the BAF values calculated in this study are only estimates since the PPCP concentrations are under dynamic conditions, and their concentrations in both organisms and surrounding media might not be in a steady state. In order to be conservative in our approximation, the highest surface water concentration detected for each PPCP was used to estimate BAFs.

For stable isotopic determination of ◎15N, samples were dried in a pre-heated oven at 60°C for 48 hours and ground using mortar and pestle. About 2 μg of ground dried animal matter were weighed using a Mettler Toledo MX5 micro-analytical balance, placed in

a 4x6 mm aluminum tin capsule and sent to the Colorado Plateau Stable Isotope Laboratory in Northern Arizona for analysis (http://www.isotope.nau.edu). Stable isotopes of C and N in the samples were determined using a Thermo-Finnigan Deltaplus Advantage gas isotope-ratio mass spectrometer interfaced with a Costech Analytical ECS4010 elemental analyzer in continuous-flow. Precision was at least ± 0.10‰ for δ13C and at least ± 0.20‰ for δ15N. Stable isotope abundances were expressed as a ratio of the two most abundant isotopes in the sample to an identical ratio in an international standard using the 'delta' (δ) notation. i.e. δ13C or δ15N = ([Rsample/R standard] - 1) x 1000, where R is 13C:12C or 15N:14N. δ13C data were expressed relative to Vienna Pee Dee Belemnite (VPDB) and δ15N data were expressed relative to air.

Table S13. Pharmaceutical levels in the different sampling sites along Niagara River during summer and fall 2015.

	Sample ID	CIT	PRX	NFLX	SER	NSER	VEN	DES	BUP	DPH	ACT	CBZ	DIL	TMP	SMX	ASMX	ERY	DIC	IBU	MEP	IOPA	MET	CAF
Summer 2015	Burnt Ship	< LOD	37	< LOD	< LOD	33	1	30	< LOD	< LOD	< LOD	1	1	5	3	1	2	< LOD	< LOD	2	< LOD	6	7
	Isle View	1	< LOD	< LOD	< LOD	31	1	32	1	3	< LOD	1	1	7	6	4	3	< LOD	< LOD	3	6	3	10
	La Salle	1	< LOD	< LOD	< LOD	34	2	31	1	5	< LOD	1	1	8	10	5	3	< LOD	< LOD	3	17	5	21
	Sandy Beach	< LOD	< LOD	< LOD	< LOD	34	1	28	< LOD	< LOD	< LOD	1	1	15	4	1	2	< LOD	< LOD	5	< LOD	3	8
	Tonawanda Island	1	< LOD	< LOD	< LOD	30	2	33	1	3	< LOD	1	1	5	6	6	3	< LOD	< LOD	2	< LOD	3	13
	Vacant Marina	1	< LOD	< LOD	< LOD	34	2	32	1	3	< LOD	1	2	6	10	5	3	< LOD	< LOD	3	23	4	21
Fall 2015	Burnt Ship	170	240	230	210	200	390	13	210	200	< LOD	2	2	3	5	3	6	6	< LOD	28	< LOD	5	5
	Clean site	180	230	220	200	180	36	23	210	190	< LOD	2	2	13	10	1	4	4	< LOD	21	< LOD	6	7
	Isle View	180	200	230	210	190	39	30	190	230	< LOD	3	2	26	16	7	3	3	< LOD	28	< LOD	10	7
	La Salle	170	240	230	220	200	40	10	210	190	< LOD	3	1	5	57	< LOD	83	< LOD	< LOD	59	< LOD	5	23
	Sandy Beach	190	230	260	200	170	29	22	190	190	< LOD	2	2	52	6	7	4	2	< LOD	28	< LOD	20	6
	Six mile road	180	210	230	220	210	31	24	180	200	< LOD	2	3	15	3	< LOD	5	6	< LOD	24	< LOD	9	4
	Tonawanda Island	180	270	220	190	200	43	9	220	210	< LOD	3	< LOD	4	260	< LOD	27	0	< LOD	40	1	5	7
	Vacant Marina	190	250	220	220	200	36	29	200	250	< LOD	2	3	24	23	10	5	4	< LOD	38	< LOD	14	40

References

1. Su, L.; Khunjar, W. O.; Aga, D. S., Analysis of trace organic pollutants in wastewater to assess biodegradation using wrong-way-round ionization in liquid chromatography/tandem mass spectrometry. *Rapid Communications in Mass Spectrometry* **2014,** *28*, (11), 1265-1272.
2. Batt, A. L.; Kim, S.; Aga, D. S., Comparison of the occurrence of antibiotics in four full-scale wastewater treatment plants with varying designs and operations. *Chemosphere* **2007,** *68*, (3), 428-435.
3. Batt, A. L.; Bruce, I. B.; Aga, D. S., Evaluating the vulnerability of surface waters to antibiotic contamination from varying wastewater treatment plant discharges. *Environmental Pollution* **2006,** *142*, (2), 295-302.
4. Stevens, J., Analysis of Pharmaceuticals in Whole Blood by Poroshell 120, Using a Modified Mini-QuEChERS Approach for Sample Preparation. *LCGC North America* **2011,** *29*.
5. Du, B.; Perez-Hurtado, P.; Brooks, B. W.; Chambliss, C. K., Evaluation of an isotope dilution liquid chromatography tandem mass spectrometry method for pharmaceuticals in fish. *Journal of Chromatography A* **2012,** *1253*, 177-183.
6. Limian Zhao, D. L., Multiresidue Analysis of Veterinary Drugs in Bovine Liver by LC/MS/MS. *Agilent Application Note-Food Testing and Agriculture, Agilent Technologies, Inc., August 2015* **2015**.
7. Choi, M.; Lee, I.-S.; Jung, R.-H., Rapid determination of organochlorine pesticides in fish using selective pressurized liquid extraction and gas chromatography–mass spectrometry. *Food Chemistry* **2016,** *205*, 1-8.
8. Agency, U. S. E. P., Guidelines establishing test procedures for the analysis of pollutants (App. B, Part 136): Definition and procedures for the determination of the method detection limit. *Fed Reg* **1997,** *40*, 265–267.
9. U.S. Environmental Protection Agency Solid waste and emergency response glossary--Bioaccumulation. (March 23,2016),
10. U.S. Environmental Protection Agency Bioaccumulation testing and interpretation for the purpose of sediment quality assesment. (March 23),