

Supplementary Information:

A Novel Method to Characterise Levels of Pharmaceutical Pollution in Large-Scale Aquatic Monitoring Campaigns

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Supplementary Tables:

Supplementary Table 1. Mass spectrometer conditions and target ions with precursor, transition 1 (T1) for quantitation and transition 2 (T2) for confirmation mass-to-charge ratios, collision energy and retention times.

Compound	Retention Time (min)	Precursor (m/z)	Product T1, T2 (m/z)	Collision Energy T1, T2 (V)
Amitriptyline	12.5	278.2	191.1, 64.30	25.6, 17.4
Artemisinin	14.3	283.2	247.1, 209.1	10.3, 10.3
Atenolol	4.25	267.2	190.0, 145.0	19.2, 26.1
Caffeine	6.32	195.1	137.9, 110.0	20.0, 25.0
Carbamazepine	11.6	237.1	194.1, 192.1	25.0, 31.0
Cephalexin	17.1	348.3	174.1, 158.1	14.5, 10.3
Cetirizine	13.5	389.2	200.9, 166.1	18.5, 39.7
Cimetidine	4.31	253.2	159.0, 95.20	14.4, 24.2
Ciprofloxacin	6.74	332.2	314.1, 288.1	19.9, 17.8
Citalopram	9.99	325.2	262.0, 109.1	19.6, 26.5
Clarithromycin	13.7	748.6	590.4, 158.1	18.1, 26.1
Clotrimazole	15.2	345.1	277.0, 165.0	10.3, 32.1
Cloxacillin	12.5	436.0	220.0, 178.0	17.8, 24.7
Codeine	4.8	300.1	225.1, 215.1	26.5, 28.1
Cotinine	3.98	177.1	146.1, 98.10	15.0, 20.0
Desvenlafaxine	7.48	264.1	107.1, 58.30	30.3, 17.9
Diazepam	14.0	285.0	193.0, 154.0	31.7, 26.5
Diltiazem	11.1	415.1	177.9, 150.0	24.1, 42.1
Diphenhydramine	10.2	256.0	167.1, 152.1	10.3, 35.6
Enrofloxacin	6.95	360.2	316.2, 245.0	19.2, 26.6
Erythromycin	12.5	734.4	576.3, 158.0	15.2, 24.6
Fexofenadine	12.2	502.4	484.2, 466.2	20.3, 24.6
Fluconazole	7.88	307.1	238.1, 220.1	15.0, 15.0
Fluoxetine	12.8	310.2	148.1, 44.52	10.3, 10.3
Gabapentin	5.47	172.3	154.0, 137.1	11.8, 14.8
Hydrocodone	5.35	300.2	199.0, 171.0	29.5, 38.8
Itraconazole	16.2	705.3	432.3, 392.2	31.3, 35.4
Ketoconazole	13.6	531.1	489.1, 82.10	20.0, 45.0

Ketotifen	8.63	310.2	213.0, 96.22	28.9, 23.0
Lidocaine	6.66	235.2	86.20, 58.30	17.3, 32.8
Lincomycin	6.03	407.3	359.2, 126.2	18.8, 28.2
Loratadine	15.8	383.1	337.1, 267.1	23.2, 42.5
Metformin	1.39	130.2	71.30, 60.30	20.2, 11.7
Metronidazole	4.53	172.3	128.0, 82.30	10.3, 26.2
Miconazole	16.2	417.1	161.0, 159.0	30.1, 29.9
Naproxen	13.6	231.0	184.9, 170.0	13.4, 26.1
Nevirapine	9.07	267.1	226.2, 184.2	25.0, 35.0
Nicotine	1.92	163.2	130.1, 117.1	20.6, 26.9
Noreisterone	13.9	299.2	109.1, 83.20	26.5, 29.5
Norfluoxetine	12.9	296.2	134.1, 105.2	10.3, 15.5
Oseltamivir	10.7	313.2	225.1, 166.1	10.3, 18.4
Oxazepam	12.8	286.9	268.9, 240.9	10.3, 18.4
Oxytetracycline	7.08	461.2	426.1, 337.0	18.9, 29.3
Paracetamol	4.15	152.0	110.1, 93.10	14.2, 20.3
Pregabalin	5.47	160.1	124.2, 97.15	14.9, 14.1
Propranolol	9.88	260.2	183.0, 116.1	17.8, 18.2
Raloxifene	10.3	474.2	112.1, 84.30	30.9, 46.6
Ranitidine	4.33	315.2	176.0, 130.0	16.8, 24.6
Salbutamol	4.4	240.0	222.1, 148.1	10.4, 18.5
Sertraline	13.3	306.1	274.9, 159.0	19.0, 20.0
Sitagliptin	7.88	408.1	235.0, 174.0	18.3, 26.2
Sulfadiazine	4.3	248.9	185.0, 92.18	18.8, 37.9
Sulfamethoxazole	6.08	254.1	156.0, 108.1	17.7, 25.2
Temazepam	13.1	301.1	283.0, 255.0	13.1, 21.6
Tetracycline	6.93	445.2	410.1, 337.0	18.3, 28.7
Thiabendazole	8.15	202.1	175.1, 131.1	28.0, 35.0
Tramadol	7.51	264.1	58.40, 43.40	15.1, 50.3
Triamterene	7.07	254.0	237.0, 104.0	38.0, 60.0
Trimethoprim	6.16	291.2	261.1, 230.1	25.0, 24.0
Tylosin	12.4	916.6	772.5, 174.1	29.2, 38.0
Venlafaxine	9.41	278.2	260.1, 58.10	11.6, 20.0
Verapamil	11.2	455.3	165.0, 150.0	28.5, 38.4
Internal Standards				
Amitriptyline D3	12.5	281.2	91.20	23.9
Atenolol D7	4.19	274.3	145.1	24.9
Atrazine D5	12.4	221.2	179.1	18.3
Cabamazepine D10	11.5	247.2	204.0	20.2
Ciprofloxacin D8	7.04	340.2	322.2	20.5
Citalopram D6	10.0	331.2	109.1	26.1
Codeine D6	4.71	306.3	218.0	23.3
Cotinine D3	3.98	180.1	80.10	25.0
Desvenlafaxine D6	7.22	270.2	64.30	17.4
Diazepam D5	13.9	290.1	198.0	33.8
Diltizem D3	11.1	418.2	178.0	23.5

Diphenhydramine D3	10.2	259.0	167.0	11.2
Gabapentin D10	5.17	182.2	163.9	10.3
Hydrocodone D3	5.33	303.2	199.1	30.4
Itraconazole D4	16.2	709.4	454.3	31.1
Lidocaine D6	6.66	241.3	86.20	18.4
Metformin D6	1.39	136.2	77.30	21.0
Metronidazole D3	4.42	175.2	131.1	14.8
Naproxen D3	13.8	234.2	188.1	12.9
Norfluoxetine D6	13.1	302.2	140.2	10.3
Oxazepam D5	12.7	292.2	274.0	10.3
Paracetamol D4	4.12	156.2	114.1	17.1
Propranolol D7	9.84	267.2	116.2	17.8
Raloxifene D4	10.2	478.2	116.2	29.4
Salbutamol D9	4.06	249.2	231.3	10.3
Sertraline D3	13.2	308.9	274.9	10.3
Sitagliptin D4	7.88	412.2	239.1	17.7
Sulfamethoxazole D4	6.73	258.2	160.0	16.7
Temazepam D5	13.1	305.8	260.1	22.4
Triamterene D5	7.03	259.2	242.1	27.9
Trimethoprim D9	5.95	300.2	234.0	24.2
Venlafaxine D6	9.45	284.2	121.1	28.1
Verapamil D7	11.2	462.4	165.1	29.0

Supplementary Table 2. Concentrations of the 15 calibration levels used in this method with the volumes and concentrations of mixed stock solutions used to create final calibrants with an equal amount of organic solvent in each.

Level	Original solution (mix. of all chemicals)	Vol.* of Original Solution (mix. of all chemicals) <i>mL</i>	Amt. of MeOH to Dilute Orig. Solution aliquot with <i>mL</i>	Final Vol. of Concentrated Calibration Solution <i>mL</i>	Conc.** of Concentrated Calibration Solution $\mu\text{g/L}$	Final Calibration Conc. After final dilution ^a <i>ng/L</i>
15	Mix at 20ppm	0.5	24.5	25	400	8000
14	L15	5	5	10	200	4000
13	L15	6.25	18.75	25	100	2000
12	L15	1.75	8.25	10	70	1400
11	L15	1	9	10	40	800
10	L15	0.5	9.5	10	20	400
9	L15	0.625	24.375	25	10	200
8	L15	0.175	9.825	10	7	140
7	L15	0.1	9.9	10	4	80
6	L15	0.05	9.95	10	2	40
5	L15	0.025	9.975	10	1	20
4	L15	0.0125	9.9875	10	0.5	10
3	L15	0.0125	24.9875	25	0.2	4
2	L15	0.0063	24.9937	25	0.1	2
1	L15	0.0063	49.9937	50	0.05	1

^a **Final Dilution:** Final Calibration solution is formed by spiking 975 μL LCMS-grade water with 20 μL of each respective level's Concentrated Calibration Solution plus 5 μL of the internal standards mixture (at 80 $\mu\text{g/}$).

*Volume **Concentration

Supplementary Table 3. Stability of monitored chemicals over 2 and 7 days at three temperatures.

Chemical	Mean Stability after 2 Days (%)			Mean Stability after 7 Days (%)		
	4°C	20°C	35°C	4°C	20°C	35°C
	(n=6)	(n=6)	(n=6)	(n=6)	(n=6)	(n=6)
Amitriptyline	88.7	90	91	92.8	92.4	97.7
Artemisinin	72.8	71.2	68.9	69.2	50.4	48.5
Atenolol	103	99.9	104	91.8	88.2	96.9
Caffeine	89.2	87	79.5	70.1	72.2	69
Carbamazepine	101	96.3	105	93.2	92.7	96.6
Cetirizine	99.5	98	99.9	91.8	95	104
Cimetidine	101	95.6	103	85.7	83.6	84.3
Ciprofloxacin	86.3	86.6	83.9	72.7	67.7	70.4
Citalopram	83.8	82.5	88.4	93.3	92.1	104
Clarithromycin	87.2	85.3	81.3	76.6	77.9	77.3
Clotrimazole	76.3	75.8	74.2	67.3	53.3	50.8
Cloxacillin	85.7	77.8	69.3	71.2	64.2	50.3
Codeine	98.9	97.4	109	87.4	80.2	93.2
Cotinine	95.3	94.5	95.8	90.1	84.3	80.8
Desvenlafaxine	94.4	90.8	99.2	89.4	88.6	89.1
Diazepam	97.5	95.6	107	95.7	93.8	97.5
Diltiazem	91.3	87.2	93.5	84.2	59.8	50.1
Diphenhydramine	89.1	90.8	88.4	76.3	70.2	71.4
Enrofloxacin	78.2	75.8	71.1	63.2	59.4	55
Erythromycin	99.6	92.6	60.3	105	86.4	26.8
Fexofenadine	96.1	97.1	97.4	92.2	92.5	97.2
Fluoxetine	70.3	69.9	62.5	58.8	55.4	49.7
Fluconazole	86.5	86	85.5	71.8	69.6	62.8
Gabapentin	92.6	93.1	95.7	93.7	92.6	86.8
Hydrocodone	95.8	89	90.8	85.8	78.1	89.4
Itraconazole	91.4	91	89	75.3	76.3	72.8
Ketoconazole	77.8	79.1	75.4	69.1	65.6	60.3
Ketotifen	91.4	88.5	92.6	87.9	80.7	88.3
Lidocaine	103	95.3	103	90.1	88	95
Lincomycin	94.2	91.9	91	88.9	84.3	82
Loratadine	90.2	89.1	89.9	82.7	82	79.1
Metformin	89.6	83.5	82.4	83.3	74.5	82.7
Metronidazole	97	98.7	107	92.5	92.5	90.8
Miconazole	84.3	82.8	80.2	69.2	70	65.7
Naproxen	94.4	92.8	99.4	89	86.9	90.7
Nevirapine	91.3	91.1	89.3	83.3	80.7	79.9
Nicotine	95.7	95.1	93.3	88.3	83.7	79.1
Noreistherone	97	95.9	105	97.7	96.2	96.7

Norfluoxetine	70.7	68.2	65.8	58.4	55.4	50.8
Oseltamivir	97.2	93.1	86.9	70.9	73.7	62.9
Oxazepam	98.7	99.1	97.2	91.3	90.1	88.8
Oxytetracycline	78.9	75.8	70.7	67.7	65.9	60.7
Paracetamol	104	98	110	91.5	90.9	90.6
Pregabalin	93.3	90.6	91.1	88.9	85.3	82.2
Propranolol	96.9	92.6	93.4	91.9	90.9	88.9
Raloxifene	99.2	78.8	93.2	66.5	55.9	30.7
Ranitidine	86.6	84.3	81.9	83.3	60.7	53.7
Salbutamol	96.4	94.1	101	91.4	88.2	83.4
Sertraline	89.3	90.9	87.7	81.3	78.8	73.6
Sitagliptin	106	94.7	104	86.8	88.5	43.6
Sulfadiazine	93.4	90.1	90	88.3	82.2	80.7
Sulfamethoxazole	97.5	93.6	108	92.3	95.7	96.6
Temazepam	92.4	93.2	105	97.8	93.7	91.5
Tetracycline	79.1	76.3	75.8	65.2	66.6	56.9
Thiabendazole	82.6	83.3	80.5	70.4	68.6	62.8
Tramadol	91.1	86.9	95.2	96.9	94.5	102
Triamterene	101	98.1	110	93.3	91.3	88.9
Trimethoprim	101	95.8	105	90.8	90.5	96.1
Tylosin	75.3	76.2	73.3	64.7	60.8	58
Venlafaxine	98	95.2	90.8	94.5	90.3	85.2
Verapamil	98.2	96.8	90.8	88.6	90.8	96.5
Mean Stability (%)	91.5	89.0	90.3	83.3	79.5	76.8
Median Stability (%)	93.3	90.9	91.0	87.9	83.6	82.0
Mean Degradation (%)	8.5	11.0	9.7	16.7	20.5	23.2
Median Degradation (%)	6.7	9.1	9.0	12.1	16.4	18.0

Supplementary Table 4. Concentrations of 30 medicinal chemicals quantified in Muddy Creek (Iowa, USA) by the USGS (Central Midwest Water Science Center, Iowa City, Iowa) and University of York (York, UK).

Compound	USGS Quantifications (ng/L)				University of York Quantifications (ng/L)			
	Site 1*	Site 2*	Site 3*	Site 4*	Site 1*	Site 2*	Site 3*	Site 4*
Amitriptyline	<37	<37	<37	<37	<8.66	<8.66	<8.66	<8.66
Atenolol	<13	206	111	84	<11.5	197	85.9	71.7
Carbamazepine	<11	286	148	84	<6.02	219	114	69.6
Cimetidine	<80	97	83	<84.8	ND	70.2	66.6	51.4
Citalopram	<6.6	166	43	<6.6	ND	139	58.2	3.6
Codeine	<88	26	22	15	ND	ND	ND	ND
Desvenlafaxine	<84	1210	613	357	ND	1620	895	319
Diazepam	<4	<4	<4	<4	ND	ND	ND	ND
Diltiazem	<20	42	22	10	ND	36.7	16.7	5.6
Erythromycin	<80	<80	<80	<80	ND	ND	ND	ND

Fexofenadine	<96	1870	1070	650	ND	1640	926	575
Fluconazole	<71	108	52	40	<10.9	102	59.3	42.6
Gabapentin	<400	1300	790	620	12.6	946	525	642
Hydrocodone	<20	<20	<20	<20	ND	12.2	6.3	4.1
Lidocaine	<38	345	182	104	<2.66	258	115	67.4
Loratadine	<7	3	2	1	<20.6	<20.6	<20.6	<20.7
Metformin	15	1050	672	543	<18.4	923	539	419
Noreistherone	<20	<20	<20	<20	ND	ND	ND	ND
Propranolol	<26	93	54	21	<14.86	85.7	43.1	20.1
Raloxifene	<80	<80	<80	<80	ND	ND	ND	ND
Ranitidine	<192	441	261	271	ND	315	205	219
Salbutamol	<6.7	8	5	4	<10.3	<10.3	<10.3	<10.3
Sitagliptin	<97	81	42	22	ND	113	53.4	28.5
Sulfamethoxazole	<26	510	289	192	ND	410	201	188
Temazepam	<20	25	<20	<20	<35.3	<35.3	<35.3	<35.3
Tramadol	<15	402	216	118	<13.4	419	220	111
Triamterene	<5.2	55	27	12	<4.78	71.1	27.3	12.3
Trimethoprim	<19	39	25	14	ND	39.7	19.6	12.7
Venlafaxine	<5.2	920	480	247	<2.37	681	306	197
Verapamil	<140	<140	<140	<140	ND	ND	ND	ND

* Site 1 (USGS ID 05454050) is roughly 100 m upstream of wastewater treatment plant (WWTP) outfall, Site 2 (USGS ID 05454051) is the wastewater effluent at the WWTP outfall to Muddy Creek, Site 3 (USGS ID 05454052) is roughly 200 m downstream of the WWTP outfall, and Site 4 (USGS ID 05454090) is roughly 5 km downstream of WWTP outfall.
ND= Not Detected

Supplementary Table 5. Linearity (n=3) and relative standard deviation (%) of both Intra-day repeatability (n=6) and intermediate precision (n=6) for the 61 APIs in the presented method validation with cells shaded in red indicating RSD > 20%.

API	Linearity r ² (n=3)	Intra-Day Repeatability (RSD, %)			Inter-Day Intermediate Precision (RSD, %)		
		10 ng/L	100 ng/L	1000 ng/L	10 ng/L	100 ng/L	1000 ng/L
		n=10	n=10	n=10	n=10	n=10	n=10
Amitriptyline	0.9967	6.4	5.6	5	15.2	5	3.7
Artemisinin	0.9264	36.9	32.1	25.5	41.2	30.1	11.8
Atenolol	0.9946	14.2	8.3	5.9	23.1	23.4	7
Caffeine	0.9532	29.6	18.4	15.8	31.2	19.8	16.4
Carbamazepine	0.9955	5.4	2.7	3.5	5.2	2.4	2
Cetirizine	0.9857	21.6	5.9	11.3	33.1	15.9	18
Cimetidine	0.9958	15.3	2.5	2.9	30.5	6.8	5.2
Ciprofloxacin	0.9444	32.6	12.5	7	30.1	18.1	8.1
Citalopram	0.9972	8.0	3.1	3	10.2	4.1	2.9
Clarithromycin	0.9943	44.8	16.4	13.8	56.6	22.6	19.9
Clotrimazole	0.9611	31.2	26.5	15.7	40.4	29.1	18.9
Cloxacillin	0.9509	35.4	6.7	16.3	24.1	18.3	16.8
Codeine	0.9921	19.4	5.8	10	17.2	14.3	10.6
Cotinine	0.9980	38	9.3	5.9	39	12.6	6.2

Desvenlafaxine	0.9984	10.2	5	5.3	27.9	8.8	5.2
Diazepam	0.9973	19.5	2.9	3.9	15.3	4.3	3.3
Diltiazem	0.9960	9	3.3	1.8	7.5	3.8	2
Diphenhydramine	0.9816	22.0	10.4	7.1	28.7	16.2	10.1
Enrofloxacin	0.9294	34.5	4.5	5.2	38.1	29.2	7.8
Erythromycin	0.9879	15.8	14.5	10.2	26.3	34.2	13
Fexofenadine	0.9979	17.6	9.1	4.2	32.5	7.3	4.4
Fluoxetine	0.9605	37.1	25.7	18.4	41.2	34.6	24.1
Fluconazole	0.9997	16.5	7.1	6.1	63.4	25.6	20.7
Gabapentin	0.9912	21.3	11.8	9.7	61.8	15.7	10.7
Hydrocodone	0.9965	15.5	3.6	3.7	17.1	6.5	3.9
Itraconazole	0.9332	44.7	21.2	12.7	69.3	27.7	11.2
Ketoconazole	0.9917	29.0	12.1	3.9	22.0	19.6	6.1
Ketotifen	0.9960	6.7	4.5	2.3	5.9	3.2	3.5
Lidocaine	0.9972	5	4.4	1.6	7.6	4.5	2.2
Lincomycin	0.9956	25.9	5.6	5.5	7.3	6.3	3.3
Loratadine	0.9785	35.4	3	6.3	44.1	15.2	9.8
Metformin	0.9917	18.1	10.8	3.7	26.3	10.5	3.5
Metronidazole	0.9939	28.4	22.6	9.8	49.2	22.3	8.6
Miconazole	0.9646	17.5	10.4	5.1	3.8	7.1	11
Naproxen	0.9882	23.7	8.5	8.4	91.2	23.7	7
Nevirapine	0.9841	15.3	9.7	8.2	19.2	17.1	9.1
Nicotine	0.9937	19.1	11.2	4.9	12.2	10.5	9.5
Noreistherone	0.9943	52.4	13.2	2.8	84.7	11.1	4
Norfluoxetine	0.9595	78.2	50.3	19.1	112.4	61.2	20.1
Oseltamivir	0.9810	83.2	18.7	8.2	40.2	9.6	10.2
Oxazepam	0.9722	44.5	21.2	20.1	32.9	24.3	19.7
Oxytetracycline	0.9870	68.4	4.5	15.4	89.7	14.8	14.7
Paracetamol	0.9943	32.9	8.2	3.8	36.1	8.5	5.1
Pregabalin	0.9816	28.9	12.6	12.6	90.2	27.3	13.5
Propranolol	0.9968	19.3	5.2	5.3	47.9	7.4	4.9
Raloxifene	0.9974	9.8	7.2	2.4	13.2	7	3.8
Ranitidine	0.9962	32.8	10.5	3	42.9	11.2	5
Salbutamol	0.9944	37.2	6.5	2.4	38.5	10	3.9
Sertraline	0.9720	24.1	12.7	10.9	30.2	17.5	16.9
Sitagliptin	0.9949	21.4	5.6	5.1	28.7	9.5	4.5
Sulfadiazine	0.9394	64.9	36.2	21.3	123.1	52.1	16.2
Sulfamethoxazole	0.9928	19.4	5	2.2	17.2	7.5	3.1
Temazepam	0.9856	51.0	12.5	11.7	162.7	18.2	13.1
Tetracycline	0.9905	59.0	26.8	14.5	125.9	40.2	20.4
Thiabendazole	0.9925	9.2	6.1	4.8	11.8	10.2	6.1
Tramadol	0.9956	10.5	6.9	4.3	13.4	5.8	4.4
Triamterene	0.9972	17.7	6.4	2	18.2	7.2	3.9
Trimethoprim	0.9967	7.6	2.4	1.3	7.6	4.3	1.7
Tylosin	0.9779	79.3	10.6	8.4	235.5	31.4	17.4
Venlafaxine	0.9949	16.9	2.4	3.8	19.2	5.5	4.5

Verapamil	0.9976	6.3	3.6	1.5	10.3	4.2	1.7
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Supplementary Table 6. Recovery (%) of 61 APIs from LCMS-grade water (n=10) with cells shaded in green indicating a recovery between 60-130%.

API	<u>Analyte Response in LCMS-grade water (Recovery, %)</u>		
	10 ng/L n=10	100 ng/L n=10	1000 ng/L n=10
Amitriptyline	93.1	113	97.9
Artemisinin	39.4	52.1	65.4
Atenolol	92.3	117	99.3
Caffeine	73.3	109	105
Carbamazepine	101	124	106
Ceterizine	81.4	115	92.8
Cimetidine	104	113	99.4
Ciprofloxacin	140	89.2	116
Citalopram	102	114	101
Clarithromycin	96.2	88.3	81.6
Clotrimazole	46.1	59.4	87.9
Cloxacillin	59.7	83.8	60.5
Codeine	113	122	101
Cotinine	86.2	115	69.5
Desvenlafaxine	92.1	116	101
Diazepam	94.7	122	102
Diltiazem	96.5	117	101
Diphenhydramine	135	92.7	88.4
Enrofloxacin	88.9	94.9	109
Erythromycin	115	89.4	72.9
Fexofenadine	119	107	89.8
Fluoxetine	38.1	55.9	75.8
Fluconazole	109	112	75.4
Gabapentin	92.9	109	99.4
Hydrocodone	104	124	101
Itraconazole	113	96.9	103
Ketoconazole	126	98.4	81
Ketotifen	96.6	121	97.7
Lidocaine	94.4	120	100
Lincomycin	53.5	78	87.9
Loratadine	69.7	117	114
Metformin	112	106	90
Metronidazole	68.7	109	111
Miconazole	39.0	78.1	87.8
Naproxen	141	109	106
Nevirapine	94.1	102	98.3
Nicotine	141	118	80.4

Noreistherone	81.8	115	109
Norfluoxetine	207	187	133
Oseltamivir	108	98.7	86.7
Oxazepam	27.4	58.1	69.9
Oxytetracycline	39.1	72.0	92.5
Paracetamol	118	122	103
Pregabalin	92.5	83.1	71.0
Propranolol	121	118	104
Raloxifene	175	119	99.2
Ranitidine	106	109	101
Salbutamol	117	119	102
Sertraline	58.7	77.6	84.9
Sitagliptin	93.8	114	98.2
Sulfadiazine	48.1	55.8	59.4
Sulfamethoxazole	99.2	120	103
Temazepam	106	103	121
Tetracycline	84.5	91.7	94.1
Thiabendazole	92.1	96.8	99.0
Tramadol	97.2	109	98.7
Triamterene	101	120	105
Trimethoprim	99.6	118	104
Tylosin	72.7	78.0	74.4
Venlafaxine	102	117	102
Verapamil	104	110	95.1

Supplementary Table 7. Recovery (%) of 61 APIs from drinking (tap) water obtained from the University of York (n=10) with cells shaded in green indicating a recovery between 60-130%.

API	<u>Matrix Recovery (Drinking Water, %)</u>		
	10 ng/L n=10	100 ng/L n=10	1000 ng/L n=10
Amitriptyline	76.8	107.1	107.3
Artemisinin	NA	45.0	127.6
Atenolol	92.7	112.5	116.8
Caffeine	90.1	133.2	116.0
Carbamazepine	88.4	112.6	108.5
Ceterizine	93.4	90.9	83.4
Cimetidine	93.0	93.3	91.1
Ciprofloxacin	70.6	79.0	93.3
Citalopram	182.3	106.3	103.3
Clarithromycin	NA	34.9	149.2
Clotrimazole	49.1	60.7	78.9
Cloxacillin	472.3	113.7	72.2
Codeine	96.9	118.7	119.6

Cotinine	94.9	101.7	118.1
Desvenlafaxine	90.5	107.4	109.2
Diazepam	98.6	109.8	107.4
Diltiazem	87.3	106.6	109.1
Diphenhydramine	167.2	131.1	110.2
Enrofloxacin	93.4	118.7	92.7
Erythromycin	148.0	109.0	76.1
Fexofenadine	92.1	99.5	90.3
Fluoxetine	49.9	45.0	89.8
Fluconazole	62.9	94.8	61.6
Gabapentin	70.8	124.7	89.7
Hydrocodone	91.8	112.0	104.9
Itraconazole	121.2	84.0	82.9
Ketoconazole	NA	46.5	130.8
Ketotifen	81.9	102.0	104.6
Lidocaine	84.6	109.4	114.8
Lincomycin	NA	64.8	103.7
Loratadine	59.8	89.1	90.4
Metformin	251.2	71.2	76.6
Metronidazole	44.0	115.4	105.3
Miconazole	163.3	45.6	95.4
Naproxen	151.7	119.6	97.0
Nevirapine	89.9	96.2	100.3
Nicotine	366.8	105.8	65.8
Noreisterone	73.7	104.4	98.7
Norfluoxetine	NA	242.5	195.2
Oseltamivir	38.3	81.5	105.2
Oxazepam	54.3	60.1	78.7
Oxytetracycline	432.0	97.4	117.5
Paracetamol	80.5	108.7	110.0
Pregabalin	272.6	105.4	144.8
Propranolol	77.5	111.2	108.6
Raloxifene	67.1	106.3	122.7
Ranitidine	64.5	76.2	112.9
Salbutamol	80.3	141.7	138.6
Sertraline	41.1	68.9	89.4
Sitagliptin	76.3	105.2	108.8
Sulfadiazine	15.9	144.4	234.1
Sulfamethoxazole	104.3	129.5	120.7
Temazepam	35.5	115.8	99.8
Tetracycline	37.5	87.3	78.6
Thiabendazole	88.8	93.2	97.4
Tramadol	100.7	137.1	128.6
Triamterene	98.6	120.1	119.9
Trimethoprim	86.7	110.5	105.4
Tylosin	67.2	58.8	66.2

Venlafaxine	116.3	109.3	104.1
Verapamil	90.0	104.8	116.0

Supplementary Table 8. Recovery (%) of 61 APIs from surface water obtained from the River Ouse in York City Centre, UK (n=10) with cells shaded in green indicating a recovery between 60-130%.

API	<u>Matrix Recovery (Surface Water, %)</u>		
	10 ng/L n=10	100 ng/L n=10	1000 ng/L n=10
Amitriptyline	66.5	107.1	101.4
Artemisinin	NA	75.5	94.0
Atenolol	98.2	123.5	115.6
Caffeine	73.1	63.9	78.7
Carbamazepine	90.1	115.1	107.8
Ceterizine	186.6	104.5	98.5
Cimetidine	90.8	113.8	115.5
Ciprofloxacin	68.4	70.1	87.3
Citalopram	178.9	110.0	102.2
Clarithromycin	NA	66.9	137.2
Clotrimazole	39.2	76.9	98.1
Cloxacillin	651.2	144.7	114.4
Codeine	125.5	129.4	115.6
Cotinine	142.0	122.3	130.6
Desvenlafaxine	93.8	115.8	103.2
Diazepam	84.4	116.9	105.9
Diltiazem	95.7	116.7	107.4
Diphenhydramine	203.6	176.1	90.4
Enrofloxacin	42.3	144.4	173.5
Erythromycin	57.9	104.5	113.8
Fexofenadine	67.3	95.8	92.3
Fluoxetine	62.1	130.1	99.1
Fluconazole	38.2	82.3	86.2
Gabapentin	108.8	97.0	94.7
Hydrocodone	94.7	113.3	103.1
Itraconazole	71.0	167.5	90.8
Ketoconazole	NA	117.6	111.4
Ketotifen	93.7	108.9	103.8
Lidocaine	72.6	111.9	112.6
Lincomycin	NA	71.4	124.8
Loratadine	67.1	92.7	91.3
Metformin	95.6	116.3	107.1
Metronidazole	124.8	107.0	96.8
Miconazole	NA	119.9	135.4
Naproxen	144.2	99.0	91.1

Nevirapine	76.1	86.3	92.7
Nicotine	NA	113.7	125.9
Noreistherone	5.5	106.6	99.5
Norfluoxetine	NA	38.1	73.2
Oseltamivir	99.8	130.7	126.1
Oxazepam	59.2	67.1	65.4
Oxytetracycline	87.9	93.6	120.2
Paracetamol	92.4	110.4	109.8
Pregabalin	191.1	119.6	120.3
Propranolol	39.8	100.7	103.0
Raloxifene	74.2	111.3	97.6
Ranitidine	93.9	111.6	115.0
Salbutamol	55.3	125.8	123.9
Sertraline	48.7	55.1	72.6
Sitagliptin	53.2	116.4	110.9
Sulfadiazine	64.7	71.5	127.7
Sulfamethoxazole	99.2	123.9	117.2
Temazepam	28.3	99.1	98.5
Tetracycline	NA	50.8	84.4
Thiabendazole	76.4	81.1	87.0
Tramadol	174.0	131.1	118.1
Triamterene	106.2	130.2	119.2
Trimethoprim	81.2	115.5	104.0
Tylosin	116.3	146.3	136.1
Venlafaxine	91.5	109.5	99.3
Verapamil	87.3	120.2	110.9

Supplementary Table 9. Recovery (%) of 61 APIs from wastewater treatment plant (WWTP) effluent obtained from a WWTP in Barnsley, UK (n=10) with cells shaded in green indicating a recovery between 60-130%.

API	<u>Matrix Recovery (WWTP Effluent, %)</u>		
	10 ng/L n=10	100 ng/L n=10	1000 ng/L n=10
Amitriptyline	109.8	125.6	108.0
Artemisinin	NA	105.5	99.3
Atenolol	116.5	127.5	114.4
Caffeine	276.1	172.1	124.4
Carbamazepine	245.4	146.0	113.7
Ceterizine	620.3	173.3	96.4
Cimetidine	125.1	128.9	126.6
Ciprofloxacin	129.4	73.1	80.4
Citalopram	198.9	120.7	105.8
Clarithromycin	NA	76.1	108.3
Clotrimazole	56.8	98.1	93.4

Cloxacillin	NA	85.0	82.6
Codeine	67.5	129.3	125.0
Cotinine	85.7	96.5	87.1
Desvenlafaxine	972.6	136.7	120.2
Diazepam	103.0	127.7	109.9
Diltiazem	76.7	142.5	128.2
Diphenhydramine	267.9	144.4	112.1
Enrofloxacin	23.5	60.1	130.0
Erythromycin	NA	89.4	114.6
Fexofenadine	273.6	125.3	88.1
Fluoxetine	NA	67.3	74.8
Fluconazole	118.1	110.3	100.6
Gabapentin	1047.2	154.3	93.1
Hydrocodone	102.2	118.7	105.0
Itraconazole	82.0	147.4	127.7
Ketoconazole	312.9	77.4	101.7
Ketotifen	100.2	125.2	110.0
Lidocaine	132.5	132.3	119.8
Lincomycin	NA	50.6	91.0
Loratadine	87.1	97.2	99.0
Metformin	NA	55.8	103.8
Metronidazole	105.4	127.3	95.4
Miconazole	NA	59.3	92.1
Naproxen	57.8	88.6	77.9
Nevirapine	145.2	131.6	130.2
Nicotine	240.7	156.1	120.0
Noreisterone	101.4	117.7	104.6
Norfluoxetine	NA	36.8	49.8
Oseltamivir	134.8	187.3	160.5
Oxazepam	46.8	58.2	76.9
Oxytetracycline	NA	100.8	114.2
Paracetamol	96.4	127.5	110.1
Pregabalin	220.2	195.9	114.3
Propranolol	123.0	126.2	107.7
Raloxifene	99.2	129.9	108.2
Ranitidine	128.2	167.3	129.9
Salbutamol	181.7	171.3	138.8
Sertraline	57.7	62.1	86.7
Sitagliptin	721.5	184.5	119.4
Sulfadiazine	298.9	120.6	132.3
Sulfamethoxazole	300.5	177.2	124.2
Temazepam	154.9	142.8	107.4
Tetracycline	NA	67.0	102.9
Thiabendazole	59.3	79.9	98.7
Tramadol	74.2	85.1	115.8
Triamterene	106.3	136.7	121.7

Trimethoprim	105.8	128.2	108.8
Tylosin	108.7	109.8	118.3
Venlafaxine	267.8	138.8	104.0
Verapamil	101.3	127.8	121.0

Supplementary Table 10. Recovery (%) of 61 APIs from wastewater treatment plant (WWTP) influent obtained from a WWTP in Barnsley, UK (n=10) with cells shaded in green indicating a recovery between 60-130%.

API	<u>Matrix Recovery (WWTP Influent, %)</u>		
	10 ng/L n=10	100 ng/L n=10	1000 ng/L n=10
Amitriptyline	108.7	105.8	124.3
Artemisinin	77.5	122.6	125.8
Atenolol	261.6	156.7	129.2
Caffeine	948.4	142.9	128.6
Carbamazepine	1470.5	475.8	182.3
Ceterizine	63.8	68.8	129.9
Cimetidine	41.6	262.6	220.2
Ciprofloxacin	324.7	191.0	128.7
Citalopram	329.0	148.3	129.3
Clarithromycin	22.9	129.7	116.4
Clotrimazole	79.2	102.4	107.5
Cloxacillin	809.2	125.7	158.9
Codeine	115.0	147.6	126.6
Cotinine	232.0	172.6	149.6
Desvenlafaxine	5401.2	177.4	166.3
Diazepam	114.8	129.6	122.1
Diltiazem	189.7	180.9	167.4
Diphenhydramine	302.1	134.9	118.3
Enrofloxacin	176.1	174.8	145.6
Erythromycin	143.6	104.9	183.6
Fexofenadine	475.5	141.9	152.7
Fluoxetine	410.3	154.1	129.6
Fluconazole	539.5	267.9	203.1
Gabapentin	5565.7	206.8	84.3
Hydrocodone	382.5	357.5	185.9
Itraconazole	194.0	333.8	257.9
Ketoconazole	531.9	91.9	103.7
Ketotifen	65.6	184.9	161.4
Lidocaine	243.1	148.8	129.7
Lincomycin	651.1	129.9	140.5
Loratadine	91.1	94.3	99.1
Metformin	153.7	95.5	94.4
Metronidazole	183.3	134.8	142.5

Miconazole	198.9	138.2	127.3
Naproxen	82.0	234.7	183.6
Nevirapine	139.1	122.7	115.3
Nicotine	478.2	157.3	139.2
Noreistherone	239.8	148.8	151.2
Norfluoxetine	46.6	63.7	70.7
Oseltamivir	770.0	275.8	184.4
Oxazepam	66.5	78.1	83.2
Oxytetracycline	189.7	127.6	128.1
Paracetamol	260.1	156.8	138.5
Pregabalin	956.0	217.1	129.1
Propranolol	208.5	329.6	172.2
Raloxifene	188.9	105.2	103.1
Ranitidine	97.9	129.2	126.6
Salbutamol	140.8	381.2	352.2
Sertraline	75.2	88.1	93.5
Sitagliptin	53.1	95.8	94.7
Sulfadiazine	361.9	132.5	120.7
Sulfamethoxazole	145.5	116.6	117.7
Temazepam	173.3	156.6	136.6
Tetracycline	46.6	84.7	81.2
Thiabendazole	72.5	82.8	95.2
Tramadol	175.5	192.7	194.8
Triamterene	201.3	179.3	177.1
Trimethoprim	30.8	163.1	189.4
Tylosin	272.8	186.7	189.3
Venlafaxine	1922.0	254.2	124.8
Verapamil	96.7	228.6	266.6

Supplementary Table 11. Limits of Detection (LOD) and Quantification (LOQ) determined in respective matrices.

API	LCMS-grade water		Drinking Water		Surface Water		WWTP Effluent		WWTP Influent	
	LOD	LOQ	LOD	LOQ	LOD	LOQ	LOD	LOQ	LOD	LOQ
	ng/L	ng/L	ng/L	ng/L	ng/L	ng/L	ng/L	ng/L	ng/L	ng/L
	n=10	n=10	n=10	n=10	n=10	n=10	n=10	n=10	n=10	n=10
Amitriptyline	1.67	3.34	2.96	5.92	4.83	8.66	8.34	16.68	23.11	46.22
Artemisinin	3.85	7.70	3.37	6.74	5.75	11.51	8.04	16.08	18.61	37.22
Atenolol	2.57	5.14	2.78	5.55	3.01	6.02	14.72	29.43	36.91	73.82
Caffeine	14.98	29.96	15.07	30.13	21.23	42.46	25.78	51.56	51.78	103.56
Carbamazepine	0.74	1.49	0.74	1.48	0.70	1.40	7.06	14.11	19.32	38.64
Cetirizine	2.48	4.96	3.13	6.27	4.92	9.84	13.92	27.85	17.51	35.02
Cimetidine	1.08	2.16	1.77	3.55	1.75	3.51	15.52	31.03	30.02	60.04
Ciprofloxacin	12.36	24.72	11.91	23.82	12.83	25.65	18.40	36.80	41.87	83.74
Citalopram	1.48	2.96	1.32	2.64	0.78	1.56	18.50	36.00	50.66	101.32
Clarithromycin	10.37	20.75	14.38	28.77	13.46	26.92	39.51	79.01	61.45	122.9

Clotrimazole	22.14	44.28	19.76	39.52	27.11	54.22	46.28	92.56	61.98	123.96
Cloxacillin	16.11	32.21	19.56	39.12	28.72	57.44	31.84	63.67	66.86	133.72
Codeine	0.14	0.28	0.73	1.46	1.32	2.64	2.93	5.86	22.81	45.62
Cotinine	3.83	7.66	7.43	14.86	6.97	13.95	8.15	16.29	19.67	39.34
Desvenlafaxine	2.24	4.49	3.40	6.81	4.33	8.66	14.44	28.88	31.18	62.36
Diazepam	1.05	2.11	1.47	2.94	0.78	1.56	10.56	21.11	27.65	55.3
Diltiazem	0.85	1.70	0.88	1.76	0.50	1.00	4.11	8.22	23.31	46.62
Diphenhydramine	5.61	11.22	5.35	10.71	8.46	16.92	10.93	21.86	45.98	91.96
Enrofloxacin	1.70	3.41	2.66	5.32	4.23	8.45	8.40	16.79	48.61	97.22
Erythromycin	1.77	3.54	1.06	2.13	1.57	3.13	9.63	19.26	52.58	105.16
Fexofenadine	2.13	4.25	3.07	6.14	4.64	9.29	6.43	12.86	36.71	73.42
Fluoxetine	5.42	10.84	6.63	13.25	7.00	13.99	11.72	23.44	51.16	102.32
Fluconazole	1.21	2.42	1.57	3.13	5.49	10.98	7.85	15.70	38.61	77.22
Gabapentin	5.57	11.15	7.63	15.26	7.70	15.40	21.41	42.82	70.12	140.24
Hydrocodone	1.13	2.25	1.31	2.63	1.65	3.30	8.78	17.56	25.61	51.22
Itraconazole	14.05	28.09	21.84	43.68	29.22	58.44	41.76	83.53	98.21	196.42
Ketoconazole	2.92	5.84	3.03	6.06	2.19	4.38	16.27	32.55	44.47	88.94
Ketotifen	0.74	1.48	0.68	1.37	0.56	1.12	2.25	4.50	18.51	37.02
Lidocaine	1.48	2.96	1.20	2.41	1.33	2.66	6.96	13.91	28.37	56.74
Lincomycin	0.73	1.46	0.97	1.94	1.27	2.55	5.01	10.03	31.83	63.66
Loratadine	7.73	15.45	7.25	14.50	10.31	20.62	12.89	25.78	42.95	85.9
Metformin	3.55	7.11	6.34	12.68	9.21	18.42	12.19	24.38	48.51	97.02
Metronidazole	5.97	11.93	5.93	11.85	5.79	11.59	11.20	22.40	51.82	103.64
Miconazole	1.92	3.84	3.90	7.80	4.13	8.26	3.94	7.88	16.25	32.5
Naproxen	9.42	18.83	16.12	32.24	17.92	35.85	27.83	55.67	67.15	134.3
Nevirapine	4.29	8.58	5.05	10.10	5.95	11.90	6.99	13.99	17.27	34.54
Nicotine	2.53	5.07	2.54	5.08	2.37	4.74	2.86	5.71	11.78	23.56
Noreistherone	10.60	21.20	9.08	18.15	6.57	13.14	14.58	29.16	40.67	81.34
Norfluoxetine	148.68	297.36	133.94	267.87	139.42	278.84	184.95	369.90	427.81	855.62
Oseltamivir	1.99	3.98	3.33	6.66	4.80	9.61	6.15	12.30	22.01	44.02
Oxazepam	15.95	31.90	15.68	31.36	20.38	40.77	28.93	57.86	68.45	136.9
Oxytetracycline	2.67	5.33	2.40	4.80	8.10	16.20	17.01	34.02	41.11	82.22
Paracetamol	9.91	19.81	11.54	23.08	21.68	43.36	30.61	61.22	67.29	134.58
Pregabalin	8.21	16.41	10.02	20.05	10.50	21.00	24.26	48.52	59.03	118.06
Propranolol	6.58	13.17	7.79	15.59	7.43	14.86	10.02	20.04	36.71	73.42
Raloxifene	2.33	4.67	1.82	3.65	4.55	9.10	11.12	22.25	38.88	77.76
Ranitidine	0.36	0.71	0.43	0.85	2.34	4.68	12.91	25.82	42.09	84.18
Salbutamol	5.73	11.46	5.03	10.07	5.17	10.34	13.60	27.21	45.89	91.78
Sertraline	10.31	20.62	10.85	21.70	12.94	25.88	15.97	31.95	44.18	88.36
Sitagliptin	3.27	6.54	3.63	7.26	4.17	8.33	11.58	23.16	30.05	60.1
Sulfadiazine	110.46	220.93	114.80	229.60	127.97	255.94	159.13	318.26	389.28	778.56
Sulfamethoxazole	2.56	5.12	4.82	9.65	1.76	3.52	14.32	28.63	36.21	72.42
Temazepam	14.06	28.12	10.87	21.74	17.64	35.27	24.44	48.89	57.24	114.48
Tetracycline	10.08	20.15	13.34	26.67	12.83	25.65	17.05	34.11	48.76	97.52
Thiabendazole	1.71	3.42	1.84	3.68	2.22	4.44	5.21	10.43	18.72	37.44
Tramadol	3.58	7.17	3.61	7.22	6.69	13.38	19.25	38.51	58.67	117.34

Triamterene	2.39	4.78	2.31	4.63	2.39	4.78	12.63	25.26	39.74	79.48
Trimethoprim	1.35	2.70	1.53	3.06	0.88	1.75	6.12	12.25	18.88	37.76
Tylosin	1.87	3.73	3.85	7.70	22.89	45.78	61.30	122.59	202.85	405.7
Venlafaxine	5.01	10.03	4.81	9.61	4.92	9.85	6.69	13.38	26.69	53.38
Verapamil	1.14	2.28	0.84	1.68	1.19	2.37	2.34	4.68	8.84	17.68

Supplementary Table 12. Concentrations, in ng/L, of all 61 APIs determined by the method presented in this paper found in the Muddy Creek (North Liberty, Iowa, USA).

Therapeutic Class		Compound	Site 1*	Site 2*	Site 3*	Site 4*
			U1	Effluent	D1	D2
Analgesic		Lidocaine	<2.66	257.5	114.6	67.4
		Naproxen	ND	141.9	37.6	ND
		Paracetamol	ND	ND	ND	ND
Anti-epileptic		Carbamazepine	<6.02	219.4	114.4	69.6
		Gabapentin	<15.4	946.2	524.8	641.5
		Pregabalin	ND	<21	ND	ND
Antibiotics	<i>Fluoroquinolones</i>	Ciprofloxacin	54.3	360.5	182.9	127.7
		Enrofloxacin	185.6	160.6	95.4	79.4
	<i>Lincosamide</i>	Lincomycin	ND	ND	ND	ND
	<i>Macrolides</i>	Clarithromycin	ND	ND	ND	ND
		Erythromycin	ND	ND	ND	ND
		Tylosin	ND	ND	ND	ND
	<i>Nitroimidazole</i>	Metronidazole	ND	50.2	21.5	12.2
	<i>Penicillin</i>	Cloxacillin	ND	ND	ND	ND
	<i>Sulfonamides</i>	Sulfadiazine	ND	ND	ND	ND
		Sulfamethoxazole	ND	409.6	201.1	188.4
		Trimethoprim	ND	39.7	19.6	12.7
	<i>Tetracyclines</i>	Oxytetracycline	ND	ND	ND	ND
		Tetracycline	ND	ND	ND	ND
Antidepressant		Amitriptyline	<8.66	<8.66	<8.66	<8.66
		Citalopram	ND	139.0	58.2	3.6
		Desvenlafaxine	ND	1617.0	895.1	318.9
		Fluoxetine	ND	ND	ND	ND
		Sertraline	ND	ND	ND	ND
		Venlafaxine	<2.37	681.3	305.7	197.0
		Norfluoxetine	ND	ND	ND	ND
Antifungal		Clotrimazole	ND	ND	ND	ND
		Fluconazole	<10.98	102.0	59.3	42.6
		Itraconazole	ND	ND	ND	ND
		Ketoconazole	ND	ND	ND	ND
		Miconazole	ND	ND	ND	ND
		Thiabendazole	ND	ND	ND	ND
Antihistamine		Cetirizine	ND	1362.3	742.2	420.6
		Diphenhydramine	ND	ND	ND	ND
		Fexofenadine	ND	1644.0	926.0	575.0

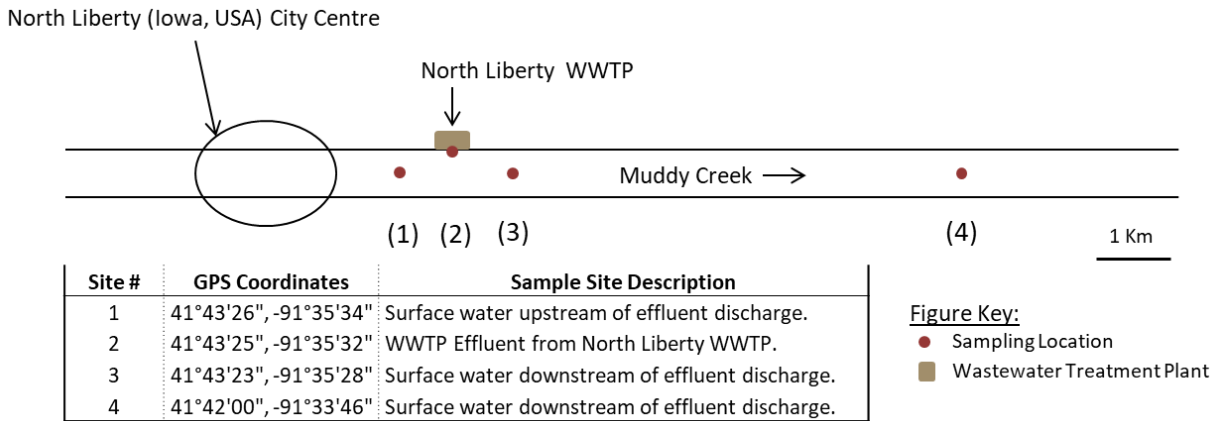
	Ketotifen	ND	ND	ND	ND
	Loratadine	<20.6	<20.6	<20.6	<20.7
Antihyperglycemic	Metformin	<18.42	922.5	539.1	418.5
	Sitagliptin	ND	112.9	53.4	28.5
Antimalarial	Artemisinin	ND	ND	ND	ND
Antiviral/-retroviral	Nevirapine	ND	ND	ND	ND
	Oseltamivir	ND	ND	ND	ND
Benzodiazepine	Diazepam	ND	ND	ND	ND
	Oxazepam	ND	ND	ND	ND
	Temazepam	<35.27	<35.27	<35.27	<35.28
Beta-blocker	Atenolol	<11.51	196.7	85.9	71.7
	Propranolol	<14.86	85.7	43.1	20.1
Calcium channel blocker	Diltiazem	ND	36.7	16.7	5.6
	Verapamil	ND	ND	ND	ND
Diuretic	Triamterene	<4.78	71.1	27.3	12.3
Histamine H ₂ receptor antagonist	Cimetidine	ND	70.2	66.6	51.4
	Ranitidine	ND	314.6	204.8	219.4
Opioid pain medication	Codeine	ND	ND	ND	ND
	Hydrocodone	ND	12.2	6.3	4.1
	Tramadol	<13.38	419.1	220.1	111.4
Oral contraceptive	Noreisterone	ND	ND	ND	ND
Selective estrogen receptor modulator	Raloxifene	ND	ND	ND	ND
Stimulant	Caffeine	ND	<42.46	<42.46	<42.46
	Cotinine	ND	ND	ND	ND
	Nicotine	ND	ND	ND	ND
β ₂ adrenergic receptor agonist (anti-asthma)	Salbutamol	<10.34	<10.34	<10.34	<10.35
Total Concentration:		239.9	10372.9	5561.5	3699.4

ND = Not Detected

Note: Detections between the LOD and LOQ are reported as less than the respective numerical value of the LOQ (<LOQ).

*Site 1 (USGS ID 05454050) is roughly 100 m upstream of wastewater treatment plant (WWTP) outfall, Site 2 (USGS ID 05454051) is the wastewater effluent at the WWTP outfall to Muddy Creek, Site 3 (USGS ID 05454052) is roughly 200 m downstream of the WWTP outfall, and Site 4 (USGS ID 05454090) is roughly 5 km downstream of WWTP outfall.

Supplementary Figures:



Supplementary Figure 1. Map of the sampling locations along Muddy Creek with GPS coordinates and sample site description.

Note: *Site 1 (USGS ID 05454050) is roughly 100 m upstream of wastewater treatment plant (WWTP) outfall, Site 2 (USGS ID 05454051) is the wastewater effluent at the WWTP outfall to Muddy Creek, Site 3 (USGS ID 05454052) is roughly 200 m downstream of the WWTP outfall, and Site 4 (USGS ID 05454090) is roughly 5 km downstream of WWTP outfall.