

Occurrence of Halogenated Transformation Products of Selected Pharmaceuticals and Personal Care Products in Secondary and Tertiary Treated Wastewaters from Southern California

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Principal Component Analysis

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Synthesis, Purification, and Structure Determination of Analytical Standards

Chemicals and suppliers. A 13% active Cl₂ solution of NaOCl was obtained from Acros (Geel, Belgium). Gemfibrozil was obtained from Spectrum Chemical Manufacturing Company (New Brunswick, NJ). Sodium formate, potassium bromide, formic acid, acetic acid, hydrochloric acid, methanol, technical nonylphenol, naproxen, bisphenol A, *tert*-octylphenol, p-dioxane, bisphenol A-*d*₁₆ and sodium thiosulfate were obtained from Sigma Aldrich (St. Louis, MO). LC-MS grade acetonitrile and salicylic acid were obtained from Fisher Scientific (Pittsburgh, PA). HPLC-grade water was obtained from Burdick and Jackson (Morristown, NJ). Diclofenac was obtained from Cayman Chemical Company (Ann Arbor, MI). Tetrachlorobisphenol A was obtained from TCI America (Portland, OR). Salicylic acid-*d*₄, diclofenac-*d*₄, gemfibrozil-*d*₆, naproxen-*d*₃, bisphenol A-*d*₆ and 4-n-octylphenol-*d*₁₇ were obtained from C/D/N Isotopes (Quebec, Canada).

Synthesis and isolation of halogenated standards. Halogenated transformation product (TP) standards of the PPCPs in this study were generated by the addition of NaOCl solution to a stirred mixture of the parent PPCP dissolved in methanol:water 1:1 (p-dioxane:water 1:1 for the alkylphenols to prevent the formation of methoxylated TPs¹) as previously described for gemfibrozil.² Evolution of halogenation reactions was monitored by LC-QTOF/MS, and once the parent compound had fully attenuated into its TPs the reactions were quenched with sodium thiosulfate. The solutions were acidified to pH ~3, concentrated by C18 SPE and evaporated to near-dryness in a 40 °C water bath under a gentle stream of compressed air.

The concentrated reaction mixtures were purified by analytical scale RP-HPLC-UV using an Agilent 1100 HPLC with UV detection at 254 nm. Separations were performed on a 4.6x150 mm Inertsil ODS-2 column from MetaChem (Torrance, CA) with mobile phase A: water + 0.1% formic acid and B: acetonitrile. Fractions containing the desired product were collected

manually, pooled and evaporated to dryness with a Savant SC110 SpeedVac from Thermo Scientific (Asheville, NC).

TP standard accurate mass MS and NMR characterization. Accurate mass experiments were conducted to confirm the identity of the synthesized standards. A Waters Micromass QTOF mass analyzer equipped with an electrospray ionization (ESI) source operated in negative ion mode was used. The lock-spray mode of the instrument was used with 10 ng/ μ L tetrachlorobisphenol A ($[M-H]^- = 362.9519$ Da) in 50:50 1 mM ammonium acetate:acetonitrile as the lock mass solution. A 10 ng/ μ L naproxen ($[M-H]^- = 229.0870$ Da) solution in the same mobile phase was used as a lock mass for accurate mass determination of tetrachlorobisphenol A. The lock mass solution was directly infused into the reference source by syringe pump at 25 μ L/min and sampled at a frequency of 0.2 Hz. Accurate mass spectra were acquired with 1-5 ng/ μ L solutions of each analyte in methanol, analyzed by direct infusion fed by a syringe pump at 10-20 μ L/min to generate ion counts of 300-600 cps. Spectra were collected for 2 min in the m/z scan range 130-600 Da and 20-30 scans were averaged, then processed for accurate mass measurement using the built-in accurate mass TOF correction in the MassLynx software. The mass spectrometer was calibrated after every 5 accurate mass measurements using a sodium formate solution per the manufacturer's recommendation. Calibration for the time-of-flight sector of the spectrometer was under 3 ppm RMS error for the m/z region 100-1000 Da. Accurate mass results where the mass difference in ppm for the m/z of the measured value for the monoisotopic peak for each analyte was compared to the theoretical m/z as calculated using ACD Labs ChemSketch version 12.0. The accurate mass values determined for each compound had mass errors <5 ppm of the theoretical value.

Confirmation of the regiochemistry of halogenation for protonated TPs was carried out by one-dimensional ^1H and two-dimensional [^1H , ^{13}C] heteronuclear multiple bond correlation (HMBC) NMR spectroscopy using a 600 MHz Bruker Avance spectrometer (Billerica, MA) as previously reported.³

Solid Phase Extraction (SPE) Details

Using a positive pressure automated workstation (Autotrace; Caliper Life Sciences, Hopkinton, MA), 6 cc-200 mg Oasis HLB cartridges were conditioned with 5 mL dichloromethane, 5 mL methanol, and 10 mL of reagent water. The 200 mL samples in clean glass bottles were spiked with internal standard and shaken vigorously for approximately 30 s. Samples were loaded onto the cartridges at 10 mL/min. Cartridges were rinsed with 4 mL of 5% methanol in water prior to drying for 40 min with clean air (10-12 psi). Samples were eluted twice with 3 mL aliquots of methanol at a rate of 3 mL/min with a 2 min pause between elutions, and were then eluted twice with 2.5 mL aliquots of 70/30 methanol/dichloromethane at a rate of 3 mL/min with a 1 min pause between elutions. All the eluent was collected in a 12 mL flint glass test tube (Fischer Scientific, Waltham, MA) and the volume reduced to approximately 200 μL using N_2 or clean air in a water bath with a temperature below 30°C . It is important to avoid reducing the extracts to dryness, which can result in the replacement of deuterium with hydrogen on labeled internal standards. Concentrated extracts were brought to a final volume of 1 mL with methanol.

Best Match Internal Standards

We were unable to obtain exact match isotope labeled internal standards for the chlorinated and brominated alkylphenol compounds. The main reason was the cost of purchasing enough C^{13}

labeled nonylphenol and octylphenol. As an alternative, chloro and bromo 4-n-octylphenol- d_{17} were synthesized. We chose 4-n-octylphenol- d_{17} as a starting material because of its cost and similar chemical structure and chromatographic retention proximity. Results were mixed, with an estimated uncertainty for the reported chloro/bromo-alkylphenols of approximately $\pm 25\%$ based upon matrix spike recoveries. Additionally, bromochlorosalicylic acid was paired with the internal standard dibromosalicylic acid- d_2 because of difficulties isolating the bromochloro analog in the synthetic process.

Principal Component Analysis (PCA)

Differences in plant treatments were examined using k-means clustering and principal component analysis (PCA). The analysis was performed in R, with functions `kmeans()` and `prcomp()`. Non-detected analytes were set to zero. Three cluster centers were specified for k-means analysis. The combined k-means and PCA results are shown in Figure S6, where each symbol represents one sample, and the symbol shapes/colors were set according to the cluster assignments made by the k-means analysis. Cumulatively, the first two principal components represented 97% of the variance in the data. The plot shows three distinct groups of contaminant profiles: plants a-h, plant i, and plant j.

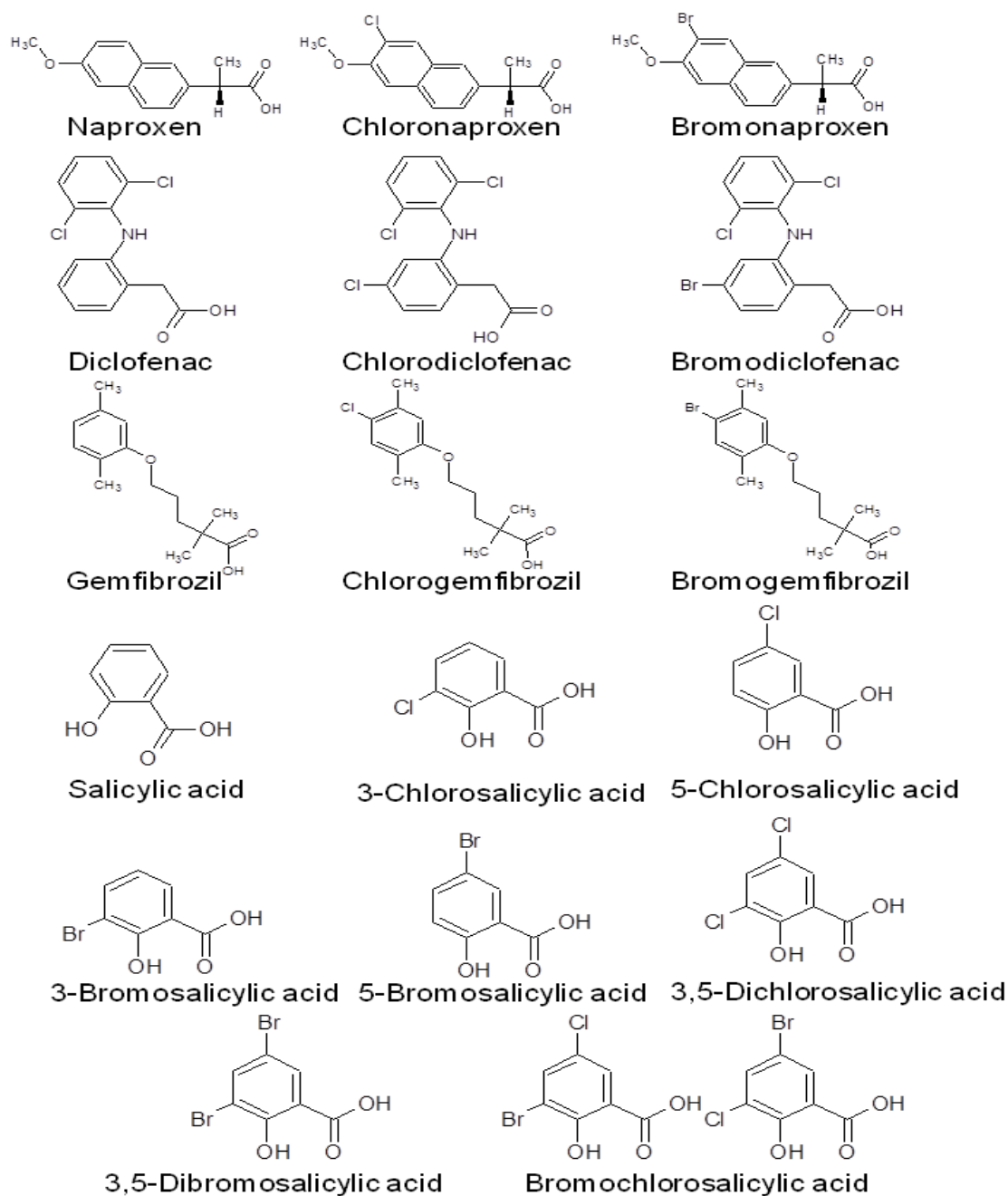


Figure S1. Selected PPCPs and their TP's which were synthesized, isolated and characterized for use as authentic standards. Structures were created using Advanced Chemistry Development Labs (Toronto, CA) 12.0. Continued on page 8.

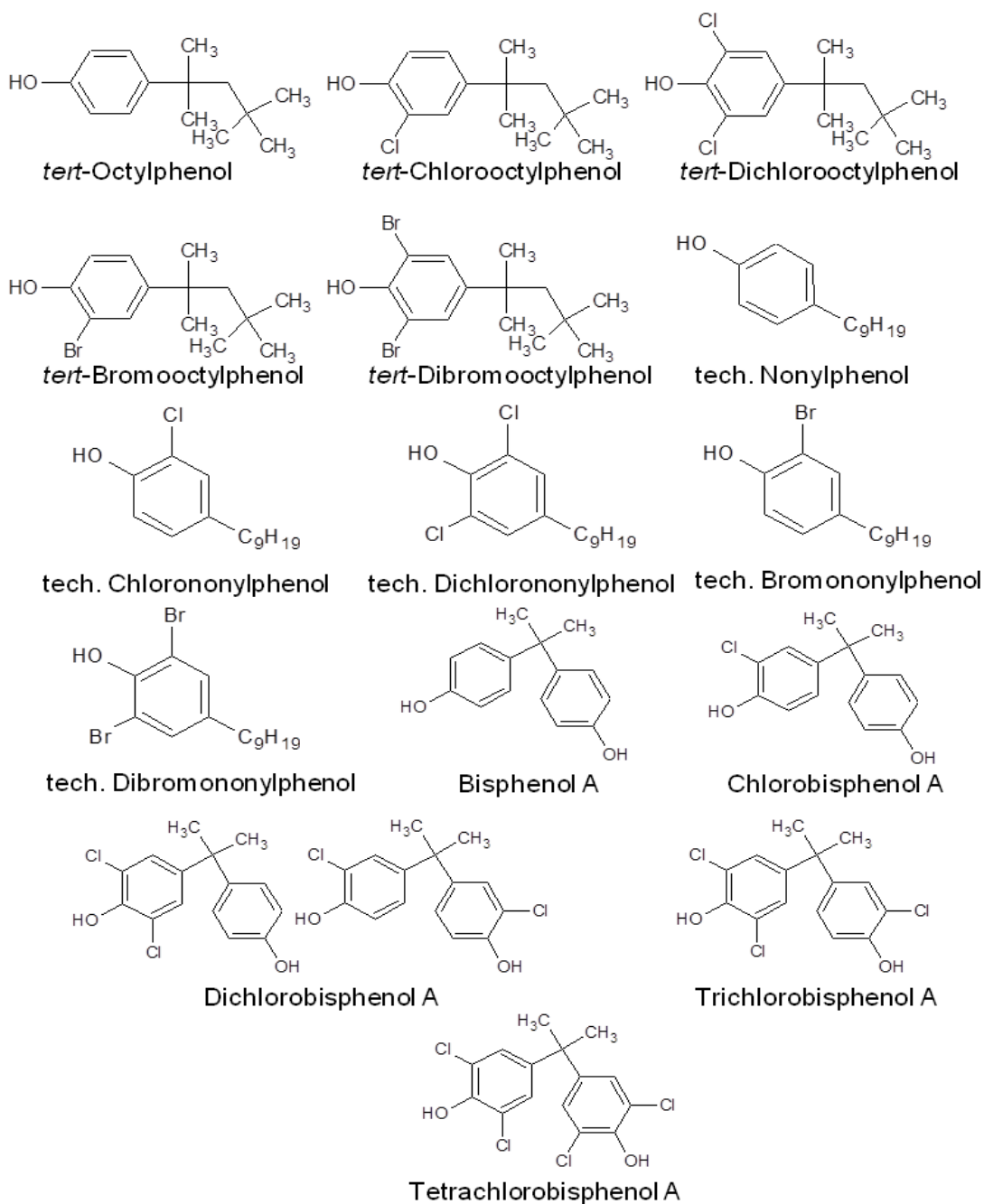


Figure S1 cont. Selected PPCPs and their TPs which were synthesized, isolated and characterized for use as authentic standards. Structures were created using Advanced Chemistry Development Labs (Toronto, CA) 12.0.

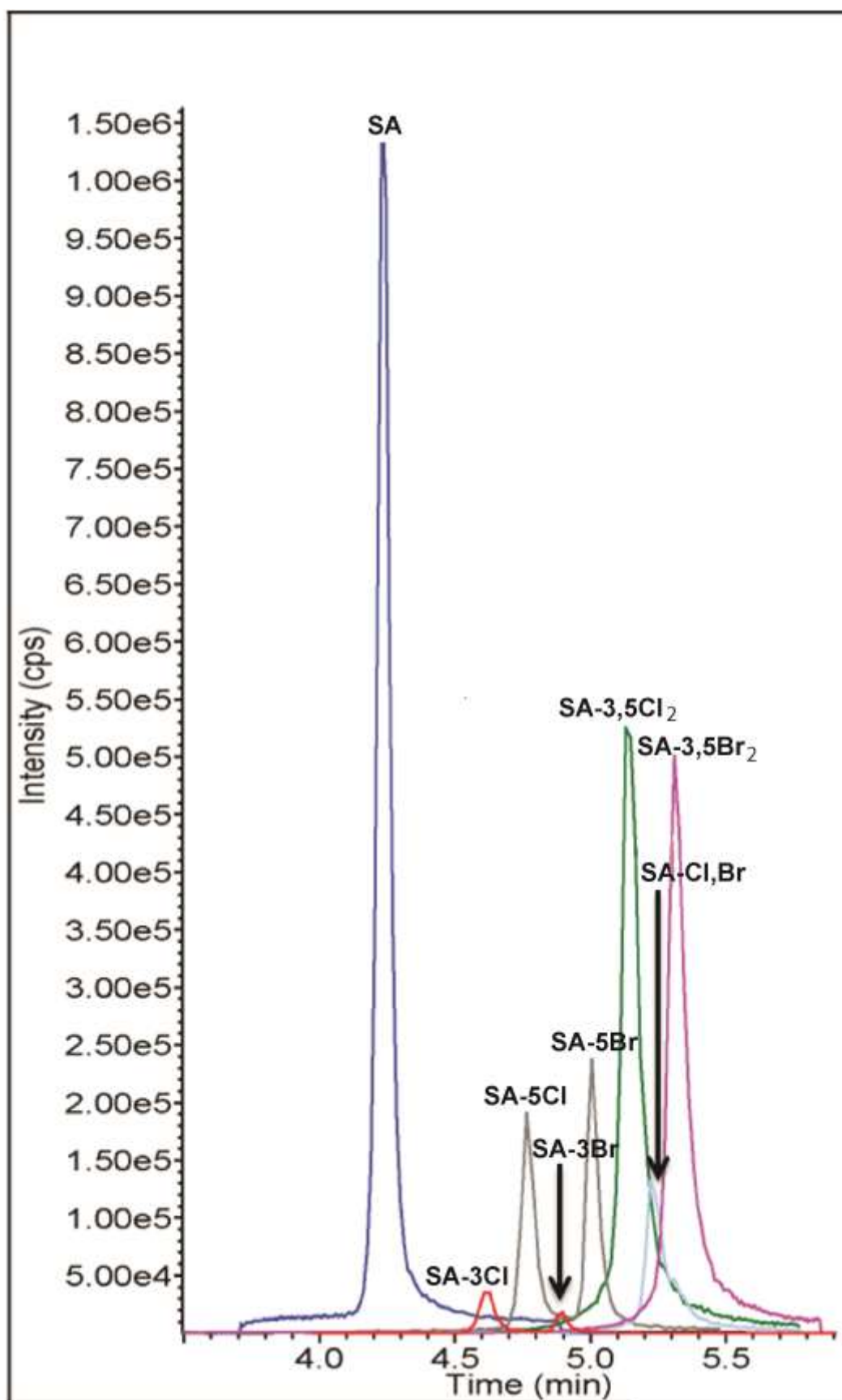


Figure S2. Extracted ion chromatograms for salicylic acid (SA) and its transformation products.

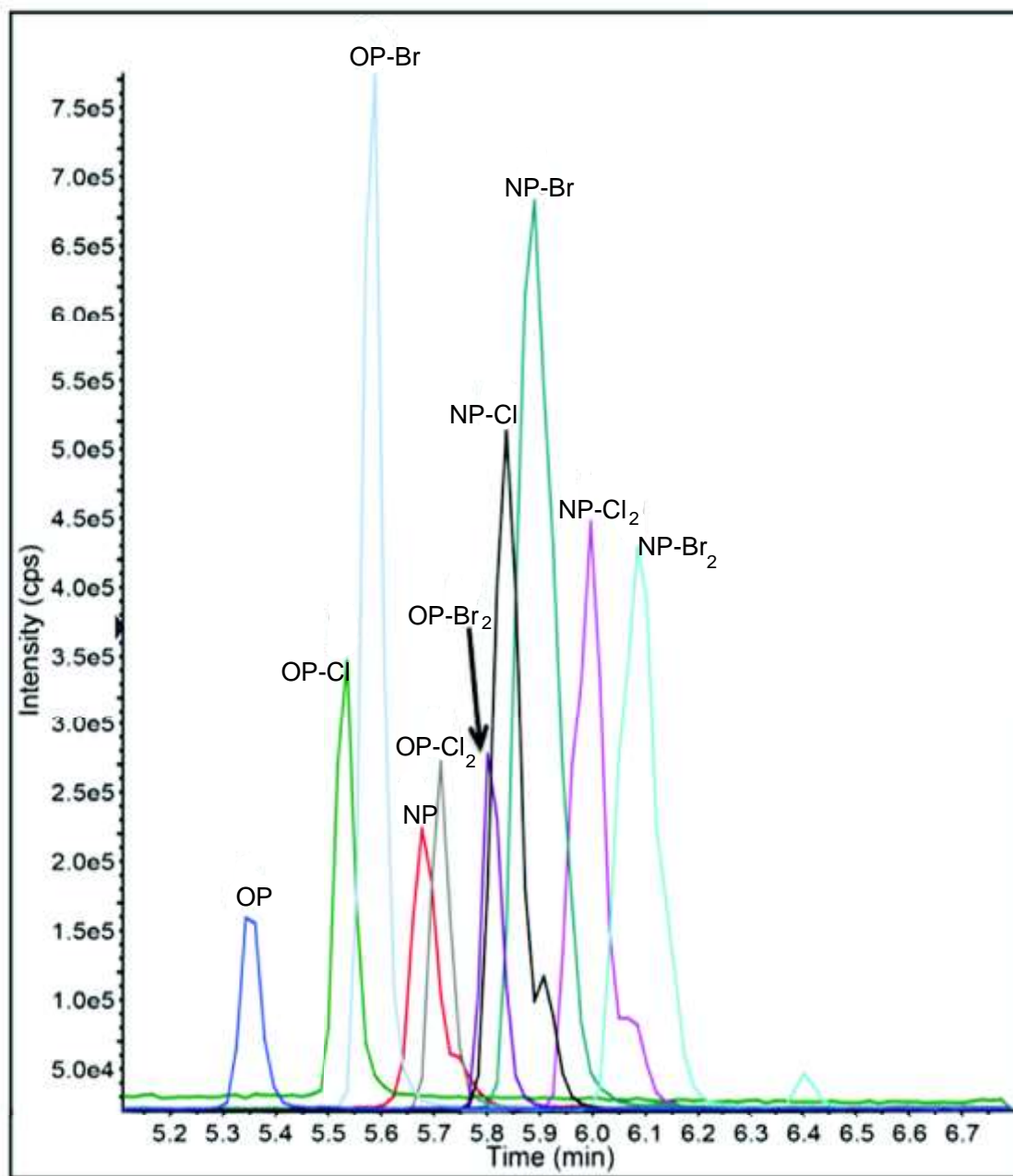


Figure S3. Extracted ion chromatograms for the alkylphenols *tert*-octophenol (OP) and technical nonylphenol (NP), and their halogenated disinfection byproducts.

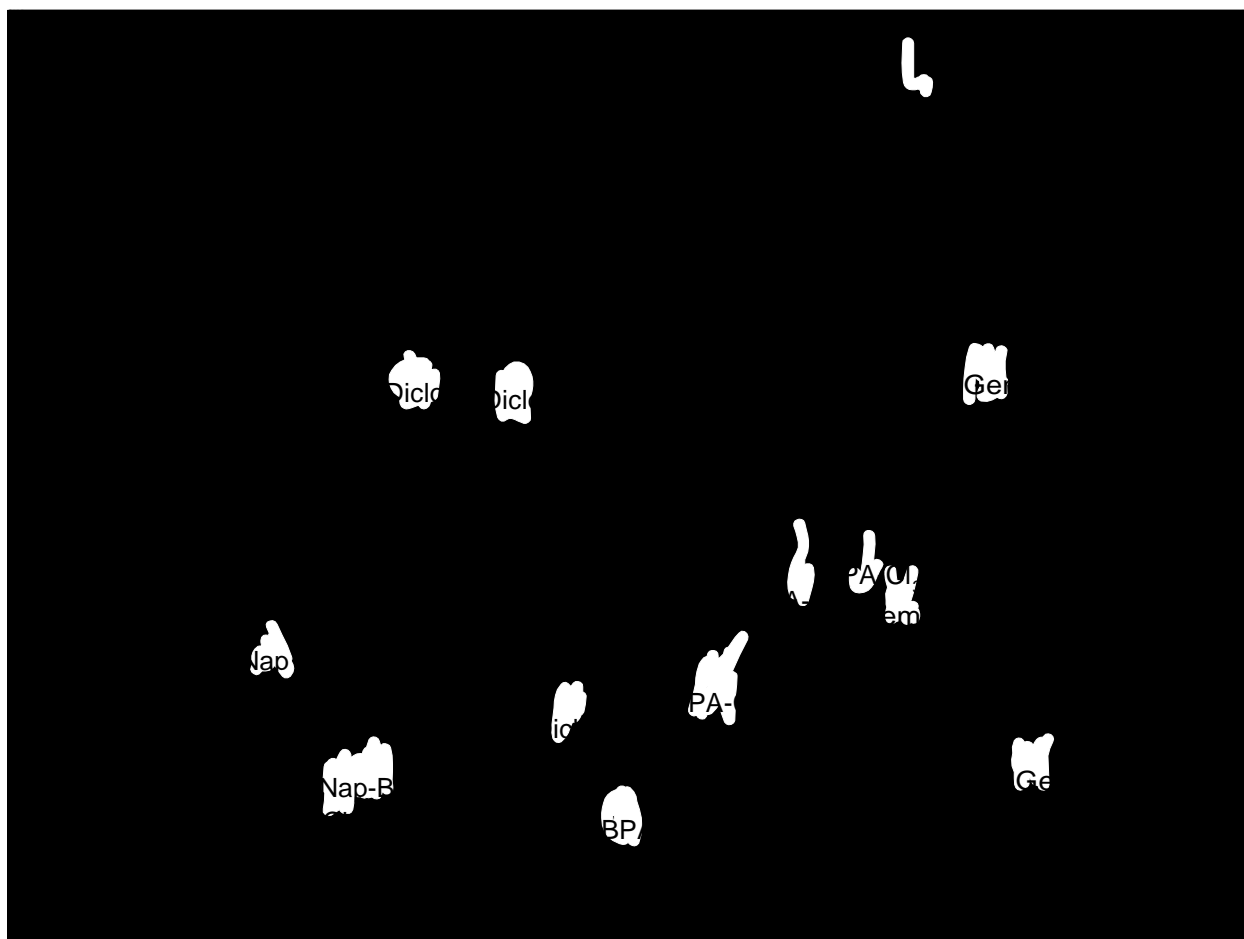


Figure S4. Extracted ion chromatograms for the PPCPs naproxen (Nap), diclofenac (Diclof), bisphenol A (BPA) and gemfibrozil (Gem) and their transformation products.

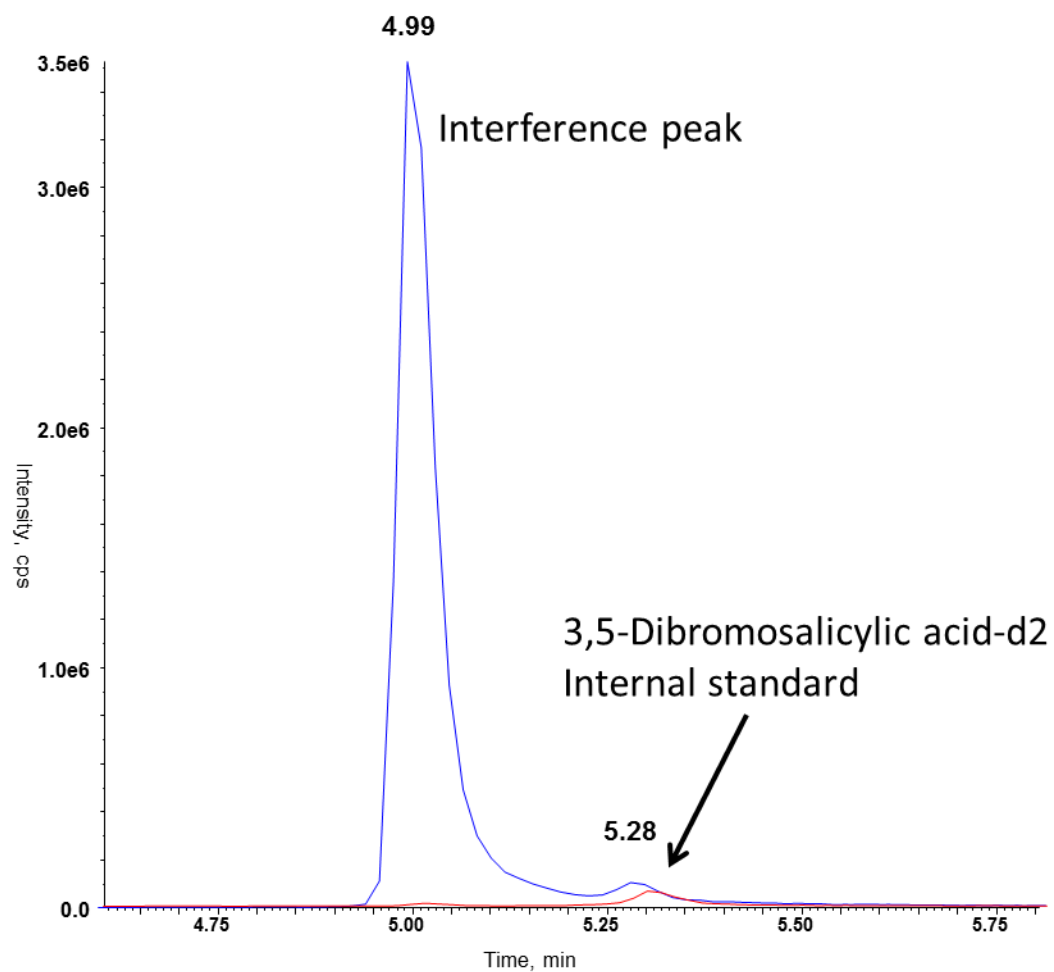
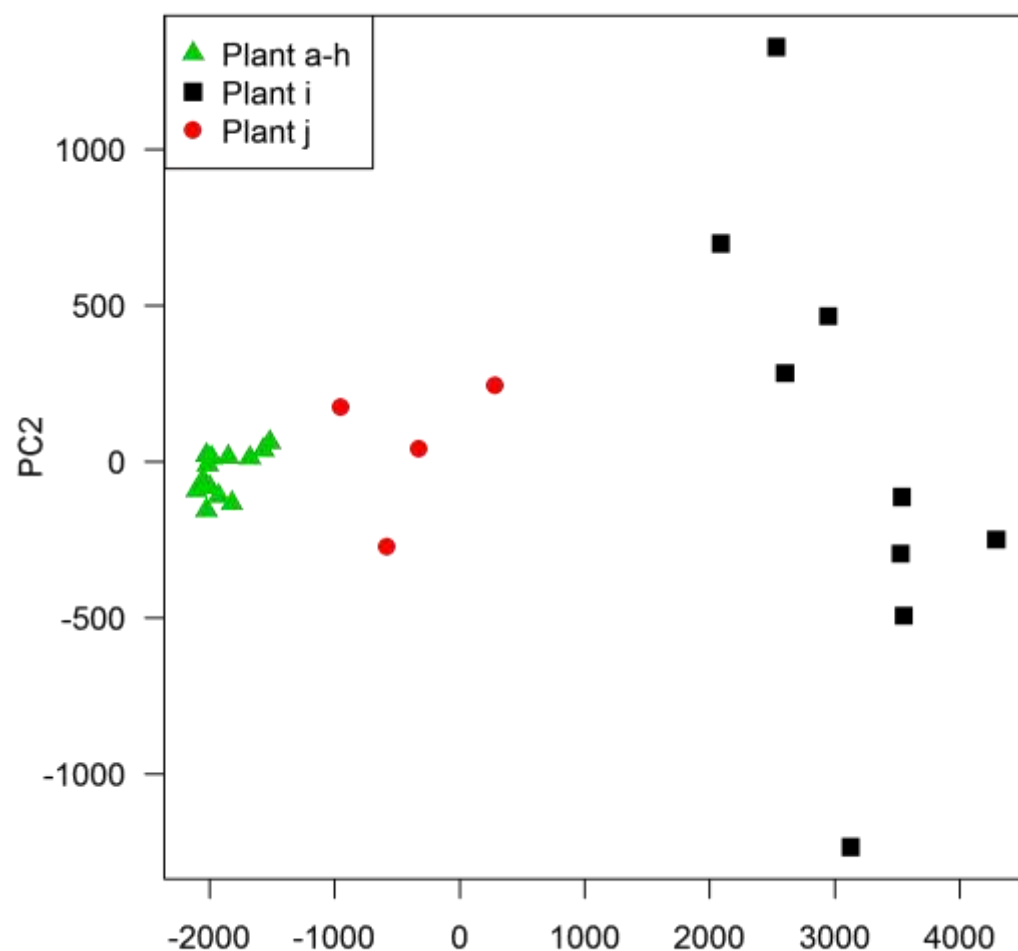


Figure S5. Overlaid extracted ion chromatograms showing interference that complicates integration of internal standard 3,5-dibromosalicylic acid-d₂. The blue chromatogram is from Plant *h*, the red trace is from Plant *b*.



	PC1						
	PC1	PC2	PC3	PC4	PC5	PC6	PC7
Standard deviation	2359.55086	426.13111	289.65773	215.56443	142.11787	66.92435	62.25481
Proportion of Variance	0.94167	0.03071	0.01419	0.00786	0.00342	0.00076	0.00066
Cumulative Proportion	0.94167	0.97238	0.98657	0.99443	0.99785	0.99860	0.99926
	PC8	PC9	PC10	PC11	PC12	PC13	PC14
Standard deviation	49.93665	31.64722	18.88321	17.52122	10.98065	6.469081	5.193095
Proportion of Variance	0.00042	0.00017	0.00006	0.00005	0.00002	0.000010	0.000000
Cumulative Proportion	0.99968	0.99985	0.99991	0.99996	0.99998	0.999990	0.999990
	PC15	PC16	PC17	PC18	PC19	PC20	PC21
Standard deviation	3.367801	2.645891	2.196601	1.517266	1.393341	1.056242	1.048025
Proportion of Variance	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000
Cumulative Proportion	1.000000	1.000000	1.000000	1.000000	1.000000	1.000000	1.000000
	PC22	PC23	PC24				
Standard deviation	0.9239062	0.4311117	0.2422011				
Proportion of Variance	0.0000000	0.0000000	0.0000000				
Cumulative Proportion	1.0000000	1.0000000	1.0000000				

Figure S6. Principal component analysis and associated statistics for all plant samples using 3 groupings from k means results.

Table S1. Characteristics of individual surveyed WWTPs (mean values)

Parameter	a	b	c	d	e	f	g	h	i	j
TOC (mg/L as C)	1.25	1.35	6.74	4.85	1.31	2.74	3.46	2.71	N.D.	1.2
TSS (mg/L)	0.89	0.94	1.00	1.20	0.84	1.22	0.90	0.4	6.9	13.0
BOD (mg/L)	2.48	1.95	2.30	2.04	2.61	1.81	3.30	3.0	5.7	5.1
Cl ₂ residual (mg/L)	3.6	2.9	3.7	2.7	2.3	4.1	3.4	0.8	0.5	0.5
Ammonia (mg/L as N)	1.30	0.92	1.20	0.8	1.3	1.2	0.9	0.2	27.3	15.2
Bromide (mg/L)	<0.2	< 0.2	< 0.2	< 0.2	< 0.2	< 0.2	< 0.2	< 0.2	0.5	1.2
pH	7.1	7.2	7.0	7.3	7.3	7.2	7.4	7.9	7.9	7.2

N.D.= not determined, Ammonia measurements are taken in secondary treatment effluent prior to the addition of disinfectant

Table S2. Sampling locations, times and dates (MS= matrix spike, MSD=matrix spike duplicate)

Sample Date	Sample Location	Sample Type	Time	Associated QA/QC
3/4/2013	e	24h Comp		
3/12/2013	d	24h Comp		
3/13/2013	b	24h Comp		
3/26/2013	i	Grab	0730	
3/26/2013	i	Grab	Pm	
3/26/2013	i	24h Comp		MS/MSD (no MSD for PPCPs)
4/1/2013	i	Grab	Am	
4/1/2013	i	Grab	Pm	
4/1/2013	i	24h Comp		
4/2/2013	i	Grab	Am	
4/2/2013	i	Grab	Pm	
4/2/2013	i	24h Comp		
4/4/2013	a	24h Comp		
4/4/2013	b	24h Comp		MS/MSD
4/4/2013	f	24h Comp		
4/4/2013	g	24h Comp		
4/9/2013	d	24h Comp		
4/9/2013	e	24h Comp		
4/10/2013	a	Grab	1415	
4/10/2013	h	24h Comp		
4/11/2013	c	24h Comp		
5/7/2013	j	24h Comp		
5/7/2013	j	Grab	0830	
5/7/2013	j	Grab	1500	MS/MSD
5/8/2013	j	24h Comp		MS/MSD
5/7/2013	d	24h Comp		
5/7/2013	a	24h Comp		MS/MSD
4/10/2013	a --unchlor sec	Grab	1300	

Table S3. Calculated vs. measured accurate mass m/z and normalized isotopic intensity QTOF-MS data for labeled and unlabeled PPCPs and TPs

Compound	Accurate mass m/z (Da)			Calculated/measured isotopic intensities (normalized counts)		
	Calc. [M-H] ⁺	Meas. [M-H] ⁺	Error (ppm)	M	M+2*	M+4**
Salicylic acid	137.0244	137.0242	-1.46	100/100	7.8/9.2	-
3-Chlorosalicylic acid	170.9854	170.9849	-2.92	100/100	33.2/34.8	-
5-Chlorosalicylic acid	170.9854	170.9859	2.92	100/100	33.2/34.7	-
3,5-Dichlorosalicylic acid	204.9435	204.9433	-0.98	100/100	65.6/67.2	11/12.3
3-Bromosalicylic acid	214.9349	214.9351	0.93	100/100	98.4/98.3	-
5-Bromosalicylic acid	214.9349	214.9346	-1.40	100/100	98.4/98.4	-
3,5-Dibromosalicylic acid	292.8454	292.8452	-0.68	51.1/52.8	100/100	49.4/50.8
Bromochlorosalicylic acid	248.8960	248.8960	0	76.5/78.4	100/100	25/27.4
Salicylic acid- <i>d</i> ₄	141.0495	141.0498	2.13	100/100	7.7/9.0	-
3-Chlorosalicylic acid- <i>d</i> ₃	174.0043	174.0050	4.02	100/100	33.2/34.6	-
5-Chlorosalicylic acid- <i>d</i> ₃	174.0043	174.0037	-3.45	100/100	33.2/34.5	-
3,5-Dichlorosalicylic acid- <i>d</i> ₂	206.959	206.9586	-1.93	100/100	65.6/66.9	11/11.6
3-Bromosalicylic acid- <i>d</i> ₃	217.9538	217.9540	0.92	100/100	98.4/98.1	-
5-Bromosalicylic acid- <i>d</i> ₃	217.9538	217.9529	-4.13	100/100	98.4/97.1	-
3,5-Dibromosalicylic acid- <i>d</i> ₂	294.8580	294.8590	3.39	51.1/50.9	100/100	49.4/49.6
Naproxen	229.0870	229.0866	-1.75	100/100	15.3/17.1	-
Chloronaproxen	263.0480	253.0475	-1.90	100/100	34.1/35.1	-
Bromonaproxen	306.9975	306.9966	-2.93	100/100	99.2/99.2	-
Naproxen- <i>d</i> ₃	232.1058	232.1051	-3.02	100/100	15.3/16.6	-
Chloronaproxen- <i>d</i> ₃	266.0669	266.0677	3.01	100/100	33.5/35.3	-
Bromonaproxen- <i>d</i> ₃	310.0164	310.0159	-1.61	100/100	98.6/96.6	-
Diclofenac	294.0094	294.0089	-1.70	100/100	66.3/66.5	11.4/12.4
Chlorodiclofenac	327.9704	327.9691	-3.96	100/100	98.7/99.2	33/34.2
Bromodiclofenac	371.9199	371.9188	-2.96	61/61.6	100/100	46.5/46.6
Diclofenac- <i>d</i> ₄	298.0345	298.0341	-1.34	100/100	66.3/67.3	11.4/12
Chlorodiclofenac- <i>d</i> ₃	330.9893	330.9878	-4.53	100/100	98.7/100	33/33.4
Bromodiclofenac- <i>d</i> ₃	374.9387	374.9380	-1.87	61/62.1	100/100	46.5/48
Gemfibrozil	249.1496	249.1497	0.40	100/100	16.7/18.6	-
Chlorogemfibrozil	283.1106	283.1105	-0.35	100/100	34.3/35.7	-
Bromogemfibrozil	327.0601	327.0604	0.92	100/100	99.4/99.2	-
Gemfibrozil- <i>d</i> ₆	255.1873	255.1875	0.78	100/100	16.6/18.2	-
Chlorogemfibrozil- <i>d</i> ₆	289.1483	289.1491	2.77	100/100	34.2/34.8	-
Bromogemfibrozil- <i>d</i> ₆	333.0978	333.0983	1.50	100/100	99.3/99.9	-
Bisphenol A	227.1078	227.1077	-0.44	100/100	16.5/15.7	-
Chlorobisphenol A	261.0688	261.0701	4.98	100/100	34/35.6	-
Dichlorobisphenol A	295.0298	295.0291	-2.37	100/100	66.4/68.2	11.6/13.1
Trichlorobisphenol A	328.9908	328.9903	-1.52	100/100	98.8/98.6	33.1/34.3
Tetrachlorobisphenol A	362.9519	362.9524	1.38	76.2/77.6	100/100	49.6/51.5
Bisphenol A- <i>d</i> ₆	233.1454	233.1443	-4.72	100/100	16.5/18.1	-
Chlorobisphenol A- <i>d</i> ₁₃	274.1504	274.1501	-1.09	100/100	34/35.6	-
Dichlorobisphenol A- <i>d</i> ₁₂	307.1051	307.1049	-0.65	100/100	66.4/68	11.6/12.3
Trichlorobisphenol A- <i>d</i> ₁₁	340.0599	340.0614	4.41	100/100	98.8/99.5	33.1/33.5
Tetrachlorobisphenol A- <i>d</i> ₁₀	373.0146	373.0151	1.34	76.2/77.6	100/100	49.6/50.9

*M+1 for non-halogenated compounds

**Only reported if M+4 > 2% base ion normalized intensity

Table S3 cont. Calculated vs. measured accurate mass m/z and normalized isotopic intensity QTOF-MS data for labeled and unlabeled PPCPs and TPs

Compound	Accurate mass m/z (Da)			Calculated/measured isotopic intensities (normalized counts)		
	Calc. [M-H] ⁻	Meas. [M-H] ⁻	Error (ppm)	M	M+2*	M+4**
<i>n</i> -Octylphenol- <i>d</i> ₁₇	222.2665	222.2668	1.35	100/100	15.2/15.4	-
<i>n</i> -Chlorooctylphenol- <i>d</i> ₁₇	256.2275	256.2277	0.78	100/100	33.7/34	-
<i>n</i> -Dichlorooctylphenol- <i>d</i> ₁₇	290.1885	290.1888	1.03	100/100	66.4/66.8	11.3/11.8
<i>n</i> -Bromooctylphenol- <i>d</i> ₁₇	300.1770	300.1768	-0.67	100/100	98.8/99.8	
<i>n</i> -Dibromooctylphenol- <i>d</i> ₁₇	378.0875	378.0868	-1.85	50.9/51.7	100/100	49.7/50.8
<i>t</i> -Octylphenol	205.1598	205.1597	-0.49	100/100	15.5/16.8	-
<i>t</i> -Chlorooctylphenol	239.1208	239.1202	-2.51	100/100	33.7/34.5	-
<i>t</i> -Dichlorooctylphenol	273.0818	273.0831	4.76	100/100	66.1/67.7	11.3/12.2
<i>t</i> -Bromooctylphenol	283.0703	283.0711	2.83	100/100	98.8/97.7	-
<i>t</i> -Dibromooctylphenol	360.9808	360.9823	4.16	50.9/49.5	100/100	49.7/51
tech. Nonylphenol	219.1754	219.1753	-0.46	100/100	16.6/18.2	-
tech. Chlorononylphenol	253.1365	253.1354	-4.35	100/100	33.9/34	-
tech. Dichlorononylphenol	287.0975	287.0963	-4.18	100/100	66.3/66.1	11.4/12.8
tech. Bromononylphenol	297.0859	297.0870	3.70	100/100	99/99.5	-
tech. Dibromononylphenol	374.9964	374.9963	-0.27	50.9/52.2	100/100	49.9/50.6

*M+1 for non-halogenated compounds

**Only reported if M+4 > 2% base ion normalized intensity

Table S4. MRM transitions and MS-MS parameters for studied analytes

Compound	Q1→ Q3 m/z (Da)	Second Q1→ Q3 m/z (Da)	Collision Energy (V)	Collision Cell Exit Pot. (V)	Declust. Pot. (V)
Salicylic acid	137→93		-35	-10	-60
3-Chlorosalicylic acid	170.8→91	170.8→34.9	-30	-15	-55
5-Chlorosalicylic acid	170.8→91	170.8→34.9	-30	-15	-55
3,5-Dichlorosalicylic acid	204.8→125	204.8→89.2	-31	-15	-55
3-Bromosalicylic acid	214.7→78.9	214.7→171	-50	-9	-70
5-Bromosalicylic acid	214.7→78.9	214.7→171	-50	-9	-70
3,5-Dibromosalicylic acid	294.8→80.8	292.8→78.8	-55	-9	-40
Bromochlorosalicylic acid	249→78.9	250.9→80.9	-46	-9	-40
Salicylic acid- <i>d</i> ₄	141→97		-35	-10	-60
3-Chlorosalicylic acid- <i>d</i> ₃	173.9→129.9	173.9→34.9	-20	-15	-40
5-Chlorosalicylic acid- <i>d</i> ₃	173.9→93.9	173.9→34.9	-35	-11	-50
3,5-Dichlorosalicylic acid- <i>d</i> ₂	210.8→129	210.8→36.9	-31	-15	-35
3-Bromosalicylic acid- <i>d</i> ₃	219.8→80.9		-50	-9	-45
5-Bromosalicylic acid- <i>d</i> ₃	219.8→80.9		-50	-9	-45
3,5-Dibromosalicylic acid- <i>d</i> ₂	298.8→80.9	296.8→78.8	-55	-9	-40
Naproxen	229→170		-20	-10	-40
Chloronaproxen	263→204	265→206	-20	-10	-55
Bromonaproxen	306.9→79	306.9→262.9	-30	-8	-35
Naproxen- <i>d</i> ₃	232→171		-42	-10	-40
Chloronaproxen- <i>d</i> ₃	266→207		-20	-13	-55
Bromonaproxen- <i>d</i> ₃	310→251		-24	-8	-60
Diclofenac	294→249.8	294→35	-20	-15	-50
Chlorodiclofenac	328→284	330→286	-17	-25	-60
Bromodiclofenac	371.9→79	373.8→81	-65	-8	-40
Diclofenac- <i>d</i> ₄	298→217		-30	-15	-50
Chlorodiclofenac- <i>d</i> ₃	332.8→288.9		-24	-15	-90
Bromodiclofenac- <i>d</i> ₃	376.8→80.9		-60	-9	-40
Gemfibrozil	249.2→120.8		-50	-17	-145
Chlorogemfibrozil	283.2→154.9	285.2→156.9	-22	-20	-150
Bromogemfibrozil	329→81	327→79	-50	-8	-150
Gemfibrozil- <i>d</i> ₆	255→120.9		-58	-17	-135
Chlorogemfibrozil- <i>d</i> ₆	288.9→154.9		-45	-15	-150
Bromogemfibrozil- <i>d</i> ₆	332.9→198.9		-28	-10	-150
Bisphenol A	227→132.8		-35	-15	-145
Chlorobisphenol A	260.9→210.1	260.9→181.9	-33	-13	-130
Dichlorobisphenol A	294.9→244	294.9→34.9	-33	-12	-140
Trichlorobisphenol A	328.7→249.8	328.7→34.9	-43	-15	-170
Tetrachlorobisphenol A	362.8→312	362.8→34.9	-35	-25	-120
Bisphenol A- <i>d</i> ₆	233→215		-27	-20	-50
Chlorobisphenol A- <i>d</i> ₁₃	274→220.4		-33	-13	-100
Dichlorobisphenol A- <i>d</i> ₁₂	306.9→34.9		-68	-12	-140
Trichlorobisphenol A- <i>d</i> ₁₁	339.7→34.9		-85	-12	-160
Tetrachlorobisphenol A- <i>d</i> ₁₀	374.8→34.9		-100	-12	-165
<i>n</i> -Chloro octylphenol- <i>d</i> ₁₇	255→34.9		-70	-11	-140
<i>n</i> -Dichloro octylphenol- <i>d</i> ₁₇	290.1→34.9		-80	-12	-180
<i>n</i> -Bromo octylphenol- <i>d</i> ₁₇	300→78.9		-26	-8	-130
<i>n</i> -Dibromo octylphenol- <i>d</i> ₁₇	379.8→80.8		-45	-8	-170

<i>t</i> -Octylphenol	205.1→132.7		-30	-15	-100
<i>t</i> -Chlorooctylphenol	238.8→34.9	238.8→167.8	-65	-12	-80
<i>t</i> -Dichlorooctylphenol	272.9→34.9	275→35	-70	-12	-130
<i>t</i> -Bromooctylphenol	283→78.9	283.1→239	-50	-9	-100
<i>t</i> -Dibromo octylphenol	362.7→78.9	362.7→291.9	-50	-15	-100
tech. Nonylphenol	219.2→132.8	219.2→146.9	-40	-15	-200
tech. Chlorononylphenol	253→167		-35	-15	-90
tech. Dichlorononylphenol	287.1→200.8	287.1→34.9	-38	-12	-130
tech. Bromononylphenol	296.9→80.9	296.9→78.9	-34	-9	-80
tech. Dibromononylphenol	377→79	379→81	-55	-8	-110
nonylphenol- ¹³ C ₆	225.2→153.2		-35	-15	-105
<i>t</i> -octylphenol- ¹³ C ₆	211.1→138.7		-30	-15	-100

Table S5. Analyte pairs with isotope labeled internal standard matches

Compound	Internal Standard	Alternate Match
Salicylic acid	Salicylic acid-d4	
3-Chlorosalicylic acid	3-Chlorosalicylic acid-d3	
5-Chlorosalicylic acid	5-Chlorosalicylic acid-d3	
3,5-Dichlorosalicylic acid	3,5-Dichlorosalicylic acid-d2	
3-Bromosalicylic acid	3-Bromosalicylic acid-d3	
5-Bromosalicylic acid	5-Bromosalicylic acid-d3	
3,5-Dibromosalicylic acid	3,5-Dibromosalicylic acid-d2	
Bromochlorosalicylic acid	3,5-Dibromosalicylic acid-d2	
Naproxen	Naproxen-d3	
Chloronaproxen	Chloronaproxen-d3	
Bromonaproxen	Bromonaproxen-d3	
Diclofenac	Diclofenac-d4	
Chlorodiclofenac	Chlorodiclofenac-d3	
Bromodiclofenac	Bromodiclofenac-d3	
Gemfibrozil	Gemfibrozil-d6	
Chlorogemfibrozil	Chlorogemfibrozil-d6	
Bromogemfibrozil	Bromogemfibrozil-d6	
Bisphenol A	Bisphenol A-d6	
Chlorobisphenol A	Chlorobisphenol A-d13	
Dichlorobisphenol A	Dichlorobisphenol A-d12	
Trichlorobisphenol A	Trichlorobisphenol A-d11	
Tetrachlorobisphenol A	Tetrachlorobisphenol A-d10	
4- <i>t</i> -Octylphenol	4- <i>t</i> -Octylphenol ¹³ C6	
4- <i>t</i> -Chlorooctylphenol	4- <i>t</i> -Octylphenol ¹³ C6	n-Chloro octylphenol-d17
4- <i>t</i> -Dichlorooctylphenol	n-Chloro octylphenol-d17	
4- <i>t</i> -Bromooctylphenol	4- <i>t</i> -Octylphenol ¹³ C6	n-Bromo octylphenol-d17
4- <i>t</i> -Dibromooctylphenol	n-Bromo octylphenol-d17	
tech. Nonylphenol	tech. Nonylphenol ¹³ C6	
tech. Chlorononylphenol	n-Chloro octylphenol-d17	
tech. Dichlorononylphenol	n-Chloro octylphenol-d17	
tech. Bromononylphenol	n-Bromo octylphenol-d17	
tech. Dibromononylphenol	n-Bromo octylphenol-d17	

The alternate internal standard was used in the case where 4-*t*-Octylphenol ¹³C6 was not spiked into the samples.

Table S6. Quality control/quality assurance parameters. Reporting limit and method blank units are ng/L; laboratory control spike + matrix spike/matrix spike duplicates are %. n=11 for method blanks, n=11 for laboratory control spikes and n=5 for matrix spikes/duplicates; except for *tech.* nonylphenol and *tert*-octylphenol, where n=9 for method blanks, n=9 for laboratory control spikes and n=4 for matrix spike/duplicate. Recoveries are \pm relative standard deviation (=standard deviation/mean).

Compound	Reporting Limit	Mean Method Blank	Mean Laboratory Control Spike	Mean Matrix Spike/Matrix Duplicate
Salicylic acid	10	< 10*	102 \pm 4	103 \pm 3
3-Chlorosalicylic acid	5	< 5	95 \pm 13	106 \pm 9
5-Chlorosalicylic acid	5	< 5	100 \pm 9	106 \pm 6
3,5-Dichlorosalicylic acid	10	< 10	99 \pm 6	103 \pm 5
3-Bromosalicylic acid	2	< 2	104 \pm 7	92 \pm 17
5-Bromosalicylic acid	2	< 2	100 \pm 7	98 \pm 8
3,5-Dibromosalicylic acid	10	< 10	102 \pm 5	105 \pm 8
Bromochlorosalicylic acid	2	< 2	114 \pm 24	100 \pm 4
Naproxen	20	< 20	98 \pm 6	97 \pm 16
Chloronaproxen	4	< 4	96 \pm 6	95 \pm 4
Bromonaproxen	4	< 4	98 \pm 6	100 \pm 7
Diclofenac	10	< 10	109 \pm 7	108 \pm 6
Chlorodiclofenac	4	< 4	100 \pm 10	98 \pm 11
Bromodiclofenac	4	< 4	101 \pm 7	103 \pm 8
Gemfibrozil	20	< 20*	99 \pm 7	95 \pm 15
Chlorogemfibrozil	4	< 4*	97 \pm 8	116 \pm 7
Bromogemfibrozil	4	< 4*	101 \pm 7	103 \pm 5
Bisphenol A	10	< 10	102 \pm 6	105 \pm 17
Chlorobisphenol A	4	< 4	94 \pm 6	102 \pm 2
Dichlorobisphenol A	4	< 4	97 \pm 9	101 \pm 9
Trichlorobisphenol A	4	< 4	97 \pm 8	109 \pm 6
Tetrachlorobisphenol A	4	< 4	97 \pm 8	96 \pm 5
4- <i>t</i> -Octylphenol	10	< 10	96 \pm 3	77 \pm 35
4- <i>t</i> -Chlorooctylphenol	4	< 4	75 \pm 9	73 \pm 17
4- <i>t</i> -Dichlorooctylphenol	4	< 4	166 \pm 14	141 \pm 14
4- <i>t</i> -Bromooctylphenol	4	< 4	93 \pm 13	98 \pm 18
4- <i>t</i> -Dibromooctylphenol	4	< 4	159 \pm 13	124 \pm 17
tech. Nonylphenol	50	< 50*	102 \pm 9	104 \pm 19
tech. Chlorononylphenol	4	< 4	121 \pm 14	122 \pm 12
tech. Dichlorononylphenol	4	< 4	121 \pm 12	116 \pm 12
tech. Bromononylphenol	4	< 4	130 \pm 8	121 \pm 18
tech. Dibromononylphenol	4	< 4	111 \pm 12	105 \pm 11

* One or more blanks contained concentrations of analyte that were greater than reporting limits, but the mean was below reporting limits. Concentrations were not blank corrected.

Table S7. Measured concentrations (ng/L) for each sample.

Date	3/4/13	3/12/13	3/13/13	3/26/13	3/26/13	3/26/13	4/1/13	4/1/13	4/1/13
Plant	e	d	b	i am	i pm	i comp	i am	i pm	i comp
SA	76	40	80	181	1680	594	134	138	174
3-Cl SA	12	11	15	21	27	24	24	11	23
5-Cl SA	9	8	6	15	22	22	14	7	25
Cl2 SA	82	60	79	121	166	143	163	101	164
3-Br SA	3	7	4	29	47	40	37	24	34
5-Br SA	< 2	< 2	< 2	6	10	9	61	4	9
Br2 SA	16	19	20	< 10	13	11	12	< 10	10
ClB SA	10	16	9	10	14	12	14	9	11
Napr	34	106	16	2190	2810	3470	2170	1500	3680
Napr Cl	< 4	< 4	< 4	< 4	< 4	< 4	4	< 4	< 4
Napr Br	11	10	5	25	28	33	23	29	23
Diclof	149	116	122	335	438	433	440	301	389
Diclof Cl	13	11	26	< 4	< 4	< 4	< 4	< 4	< 4
Diclof Br	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
Gemfib	179	421	259	3440	3830	3800	2970	3080	3280
Gemfib Cl	5	13	24	< 4	4	4	4	< 4	< 4
Gemfib Br	< 4	4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
BPA	< 10	< 10	< 10	648	617	587	404	483	481
BPA Cl	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
BPA Cl2	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
BPA Cl3	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
BPA Cl4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
OP	No IS	No IS	No IS	1700	1380	1550	1160	1380	1060
OP Cl	< 4	< 4	< 4	12	17	12	18	10	11
OP Cl2	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
OP Br	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
OP Br2	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
<i>tech</i> NP	No IS	No IS	No IS	2720	2740	3610	2920	2380	2140
<i>tech</i> NP Cl	15	10	18	55	91	49	114	53	47
<i>tech</i> NP Cl2	< 4	9	7	8	12	9	16	8	9
<i>tech</i> NP Br	< 4	< 4	< 4	21	34	21	38	18	20
<i>tech</i> NP Br2	< 4	< 4	< 4	60	90	113	60	77	93

Table S7 cont. Measured concentrations (ng/L) for each sample.

Date	4/2/13	4/2/13	4/2/13	4/4/13	4/4/13	4/4/13	4/4/13	4/9/13	4/9/13
Plant	i am	i pm	i comp	a	b	f	g	d	e
SA	136	123	306	67	59	137	127	93	81
3-Cl SA	28	21	25	18	13	20	24	16	11
5-Cl SA	19	10	22	8	9	17	17	9	8
Cl2 SA	186	157	147	64	61	77	66	46	30
3-Br SA	45	25	42	7	2	8	8	5	2
5-Br SA	8	4	10	< 2	3	3	3	2	< 2
Br2 SA	12	< 10	12	< 10	< 10	< 10	< 10	10	< 10
ClB SA	13	10	11	7	13	22	21	8	3
Napr	2980	1310	3310	111	27	49	29	23	138
Napr Cl	< 4	< 4	< 4	< 4	< 4	< 4	8	23	< 4
Napr Br	23	26	27	10	4	7	< 4	6	4
Diclof	430	374	413	184	132	114	10	0	229
Diclof Cl	< 4	6	< 4	21	21	11	5	5	11
Diclof Br	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
Gemfib	3560	3190	3390	829	193	324	142	63	190
Gemfib Cl	< 4	< 4	< 4	56	24	15	35	27	6
Gemfib Br	< 4	< 4	< 4	6	< 4	< 4	12	5	< 4
BPA	545	651	697	10	< 10	< 10	< 10	< 10	< 10
BPA Cl	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
BPA Cl2	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
BPA Cl3	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
BPA Cl4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
OP	1280	1860	1290	64	29	30	15	10	51
OP Cl	14	19	9	7	< 4	< 4	< 4	< 4	< 4
OP Cl2	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
OP Br	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
OP Br2	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
<i>tech</i> NP	3130	2970	2990	169	151	< 50	265	293	< 50
<i>tech</i> NP Cl	106	115	42	18	13	7	4	4	11
<i>tech</i> NP Cl2	18	19	8	7	7	4	< 4	< 4	< 4
<i>tech</i> NP Br	36	39	19	< 4	< 4	< 4	< 4	< 4	< 4
<i>tech</i> NP Br2	352	372	54	< 4	< 4	< 4	< 4	< 4	< 4

Table S7 cont. Measured concentrations (ng/L) for each sample.

Date	4/10/13	4/10/13	4/10/13	4/11/13	5/7/13	5/7/13	5/7/13	5/7/13	5/7/13	5/8/13
Plant	a	a sec	h	c	d	a	j comp	j am	j pm	j comp
SA	43	18	124	168	105	81	248	243	177	289
3-Cl SA	10	< 5	8	23	15	11	10	8	8	8
5-Cl SA	< 5	< 5	6	6	10	8	25	31	18	25
Cl2 SA	24	22	39	71	59	43	183	192	122	150
3-Br SA	2	3	3	7	4	5	3	5	2	3
5-Br SA	< 2	< 2	< 2	< 2	2	< 2	4	6	< 2	4
Br2 SA	9	12	15	28	14	13	208	90	36	183
ClB SA	3	4	7	8	10	5	28	36	24	19
Napr	113	285	146	20	40	45	838	979	353	731
Napr Cl	5	< 4	4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
Napr Br	9	8	10	29	6	8	112	132	104	86
Diclof	207	287	57	303	109	181	302	364	308	286
Diclof Cl	21	< 4	< 4	15	16	29	< 4	< 4	< 4	< 4
Diclof Br	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
Gemfib	886	1110	562	889	184	427	1430	1560	1010	1490
Gemfib Cl	46	< 4	12	42	14	36	6	10	6	10
Gemfib Br	5	< 4	< 4	< 4	5	5	4	6	< 4	8
BPA	< 10	13	< 10	20	< 10	< 10	20	37	< 10	< 10
BPA Cl	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
BPA Cl2	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
BPA Cl3	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
BPA Cl4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
OP	55	104	No IS	No IS	21	32	220	590	257	293
OP Cl	6	< 4	8	7	< 4	< 4	< 4	< 4	< 4	< 4
OP Cl2	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
OP Br	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
OP Br2	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4
tech NP	213	378	No IS	No IS	81	166	530	1660	763	1010
tech NP Cl	27	7	17	17	6	19	30	18	10	40
tech NP Cl2	12	< 4	11	7	5	10	5	< 4	< 4	7
tech NP Br	6	< 4	7	< 4	< 4	< 4	16	5	4	24
tech NP Br2	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4	< 4

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