SUPPORTING INFORMATION

for

The Forest or the Trees: A Critical Review on the Analysis of Total Organic Halogen (TOX) in Drinking Waters and Its Utility as Water Quality Parameter

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Table S1 Reported recoveries of TOX analysis (adsorption-combustion-detection) of model halogenated compounds

Analyte	% Recovery	Log K_{ow}	Adsorbent	Reference
Trihalomethanes				
Chloroform	90.5	1.97[a]	Sugar activated carbon (Merck)	1
	94		Activated carbon	2
	89		Filtrasorb 400 and APC carbon (Calgon)	3
	93[b]; 84[c]		Activated carbon	4
	95 ± 11		Activated carbon (CPI International)	5
Bromodichloromethane	98	1.61[f]	Activated carbon	2
	102 ± 1[d]; 101± 4[e]		Activated carbon (CPI International)	6
	TOCl: 118 ± 0.6; TOBr: 120 ± 2		Activated carbon (CPI International)	5
Chlorodibromomethane	86	2.16[a]	Activated carbon	2
	103 ± 3[d]; 104 ± 2[e]		Activated carbon (CPI International)	6
	TOCl:120 ± 17; TOBr: 92 ± 2		Activated carbon (CPI International)	5
Bromoform	95.3[b]; 97.7[c]	2.40[f]	Activated carbon	4
	90.6		Sugar activated carbon (Merck)	1
	98 ± 5a		Activated carbon (CPI International)	6
	98 ± 4b		Activated carbon (CPI International)	6
	101		Filtrasorb 400 and APC carbon (Calgon)	3
	101		Activated carbon	2
	119 ± 2		Activated carbon (CPI International)	5
Iodoform	100 ± 2	3.03[g]	Activated carbon (CPI International)	5
Haloacetic acids				
Chloroacetic acid	56.0	0.2[h]	Sugar activated carbon (Merck)	1
	91 ± 3[d]; 92 ± 4[e]		Activated carbon (CPI International)	6
	0		Filtrasorb 400 and APC carbon (Calgon)	3
	35		Activated carbon (Mitsubishi)	7

	96 ± 2 78 ± 6		Activated carbon (CPI International) Activated carbon (CPI International)	5 8
Bromoacetic acid	96 ± 2[d]; 95 ± 1[e] 69 95 ± 4	0.41[a]	Activated carbon (CPI International) Activated carbon (Mitsubishi) Activated carbon (CPI International)	6 7 8
Bromochloroacetic acid	97 ± 5[d]; 100 ± 5[e] TOCl: 109 ± 2; TOBr: 110 ± 0.6 TOCl: 94 ± 4; TOBr: 111 ± 4	0.61[f]	Activated carbon (CPI International) Activated carbon (CPI International)	6 5 8
Dichloroacetic acid	98 ± 4[d]; 101 ± 5[e] 110 ± 12	0.942[h]	Activated carbon (CPI International) Activated carbon (CPI International)	6 8
Dibromoacetic acid	102 ± 3[d]; 101 ± 4[e] 95 ± 6	0.70[f]	Activated carbon (CPI International) Activated carbon (CPI International)	6 8
Chlorodibromoacetic acid	TOCl: 80 ± 10; TOBr: 97 ± 2	1.62[a]	Activated carbon (CPI International)	8
Bromodichloroacetic acid	TOCl: 87 ± 6; TOBr: 92 ± 8	1.53[a]	Activated carbon (CPI International)	8
Trichloroacetic acid	109 83 100 ± 2[d]; 97 ± 4[e] 85 ±4	1.645[h]	Sugar activated carbon (Merck) Activated carbon (Mitsubishi) Activated carbon (CPI International) Activated carbon (CPI International)	1 7 6 8
Tribromoacetic acid	98 ± 3[d]; 98 ± 5[e] 108 ± 0.9	1.71[f]	Activated carbon (CPI International) Activated carbon (CPI International)	6 5
Iodoacetic acid	103 99 ± 3[d]; 94 ± 5[e]	0.85[f]	Activated carbon (Mitsubishi) Activated carbon (CPI International)	7 6
Haloacetonitriles				
Chloroacetonitrile	85 ± 10 80 ± 8	0.11[g]	Activated carbon (CPI International) Activated carbon (CPI International)	5 8
Bromoacetonitrile	127 ± 2 108 ± 2	0.20[g]	Activated carbon (CPI International) Activated carbon (CPI International)	5 8

Dichloroacetonitrile	105 ± 4	0.29[h]	Activated carbon (CPI International)	8
Dibromoacetonitrile	107 ± 6	0.47[h]	Activated carbon (CPI International)	8
Bromochloroacetonitrile	TOCl: 135 ± 15; TOBr: 118 ± 10	0.38[h]	Activated carbon (CPI International)	8
Trichloroacetonitrile	124 ± 2 115 ± 10	1.21[g]	Activated carbon (CPI International) Activated carbon (CPI International)	5 8
Halophenols				
2-Chlorophenol	101 ± 6	2.16[h]	Activated carbon (CPI International)	8
4-Chlorophenol	90.7 99 89 ± 4	2.39[h]	Sugar activated carbon (Merck) Activated carbon (Mitsubishi) Activated carbon (CPI International)	1 7 8
2,4-Dichlorophenol	98	3.17[a]	Activated carbon (Calgon F400)	9
2,6-Dichlorophenol	93 ± 8	2.8[h]	Activated carbon (CPI International)	8
2,4,6-Trichlorophenol	96.8[b]; 96.8[c] 101 104 ± 4 91 ± 5	3.69[a]	Activated carbon Filtrasorb 400 and APC carbon (Calgon) Activated carbon (CPI International) Activated carbon (CPI International)	4 3 5 8
Pentachlorophenol	93 82 ± 12	5.86[g]	Activated carbon Activated carbon (CPI International)	2 8
4-Bromophenol	97 99.2 96 99 ± 2	2.33[a]	Activated carbon (Calgon F400) Sugar activated carbon (Merck) Activated carbon (Mitsubishi) Activated carbon (CPI International)	9 1 7 8
2,4-Dibromophenol	108 ± 0.9 83 ± 6	3.29[h]	Activated carbon (CPI International) Activated carbon (CPI International)	5 8
2,4,6-Tribromophenol	90.6 102 102 ± 4	4.08[a]	Activated carbon Filtrasorb 400 and APC carbon (Calgon) Activated carbon (CPI International)	4 3 5

	91 ± 2		Activated carbon (CPI International)	8
2-Iodophenol	85 ± 1	2.68[h]	Activated carbon (CPI International)	8
4-Iodophenol	98 96 ± 4	2.90[a]	Activated carbon (Mitsubishi) Activated carbon (CPI International)	7 5
Halobenzenes				
4-Amino-chlorobenzene	80	1.83[a]	Activated carbon (Mitsubishi)	7
4-Amino-bromobenzene	88	2.26[h]	Activated carbon (Mitsubishi)	7
4-Amino-iodobenzene	80	2.80[a]	Activated carbon (Mitsubishi)	7
Chlorobenzene	67.9	2.89[h]	Sugar activated carbon (Merck)	1
1,2-Dichlorobenzene	40.6 94 ± 4	3.38[a]	Sugar activated carbon (Merck) Activated carbon (CPI International)	1 8
1,3-Dichlorobenzene	107	3.53[f]	Filtrasorb 400 and APC carbon (Calgon)	3
1,4-Dichlorobenzene	55	3.45[a]	Activated carbon (Mitsubishi)	7
1,3,5-Trichlorobenzene	83.9	4.15[a]	Sugar activated carbon (Merck)	1
Bromobenzene	79.8 95 113 ± 6 109 ± 6	2.99[h]	Sugar activated carbon (Merck) Filtrasorb 400 and APC carbon (Calgon) Activated carbon (CPI International) Activated carbon (CPI International)	1 3 5 8
1,2-Dibromobenzene	94 ± 4	3.28[a]	Activated carbon (CPI International)	8
1,4-Dibromobenzene	46.1 49 93 ± 3 98 ± 2	3.79[h]	Sugar activated carbon (Merck) Activated carbon (Mitsubishi) Activated carbon (CPI International) Activated carbon (CPI International)	1 7 5 8
2-Bromoethylbenzene	56.4	3.783[h]	Sugar activated carbon (Merck)	1
1,4-Diiodobenzene	78	4.11[a]	Activated carbon (Mitsubishi)	7
4-Bromobenzylbromide	28.4	3.77[f]	Sugar activated carbon (Merck)	1
1-Bromonaphthalene	57.1	4.35[h]	Sugar activated carbon (Merck)	1

1-Bromonitrobenzene	58.4	2.5[h]	Sugar activated carbon (Merck)	1
4-Bromotoluene	93.4	3.42[f]	Sugar activated carbon (Merck)	1
Haloamides				
2-Chloroacetamide	14	-0.53[a]	Activated carbon (Mitsubishi)	7
2,2,2-Trichloroacetamide	121 ± 2	0.83[g]	Activated carbon (CPI International)	5
3-Chloropropionamide	79.3 107 ± 2	-0.42[f]	Sugar activated carbon (Merck) Activated carbon (CPI International)	1 5
2-Iodoacetamide	37	-0.19[a]	Activated carbon (Mitsubishi)	7
X-ray contrast media (iodinated organic compounds)				
Iopromide[h]	98 98 ± 2	-2.05[a]	Activated carbon (Mitsubishi) Activated carbon (CPI International)	7 5
Iopamidol	99 + 0.1		Activated carbon (CPI International)	5
Iothalamic acid	112 ± 4	-0.056[g]	Activated carbon (CPI International)	5
Iodipamide	97 ± 5	5.10[g]	Activated carbon (CPI International)	5
Iohexol	100 ± 0.2		Activated carbon (CPI International)	5
Diatrizoic acid	94 104 ± 4	0.49[g]	Activated carbon (Mitsubishi) Activated carbon (CPI International)	7 5
Haloketones				
Chloroacetone	90	0.02[f]	Filtrasorb 400 and APC carbon (Calgon)	3
Halobenzoic acids				
3-Chlorobenzoic acid	100 ± 2	2.52[g]	Activated carbon (CPI International)	5
4-Chlorobenzoic acid	83.7	2.65[h]	Sugar activated carbon (Merck)	1
3-Bromobenzoic acid	104	2.75[a]	Filtrasorb 400 and APC carbon (Calgon)	3
4-Bromobenzoic acid	96.2	2.86[h]	Sugar activated carbon (Merck)	1
3,5-Dichloroisonicotinic acid	100 ± 2[d]; 101 ± 3[e]	1.62[i]	Activated carbon (CPI International)	6

Haloalkanes				
Dichloromethane	98.1 50 $\pm$ 9	1.25[h]	Sugar activated carbon (Merck) Activated carbon (CPI International)	1 5
1-Chloro-2-Bromoethane	106	1.92[f]	Filtrasorb 400 and APC carbon (Calgon)	3
1,1,1-Trichloroethane	92.1	2.49[h]	Sugar activated carbon (Merck)	1
1,1-Dibromoethane	64.4	1.94[f]	Sugar activated carbon (Merck)	1
1-Bromo-3-chloropropane	87.0	2.2[h]	Sugar activated carbon (Merck)	1
1-Chlorohexane	82.5	3.58[h]	Sugar activated carbon (Merck)	1
Haloalkenes				
Tetrachloroethylene	47.9	3.40[h]	Sugar activated carbon (Merck)	1
Ƴ-Hexachlorocyclohexane	105.0	4.14[f]	Sugar activated carbon (Merck)	1
4-Bromo-1-butene	69.1	2.34[a]	Sugar activated carbon (Merck)	1
Other halogenated nitrogen-containing compounds				
Chloramine-T (Cl_2)	3.4	1.85[i]	Sugar activated carbon (Merck)	1
Tribromonitromethane	114 $\pm$ 8	1.59[g]	Activated carbon (CPI International)	5
4-Chloroaniline	102.6 110 $\pm$ 3	1.83[a]	Sugar activated carbon (Merck) Activated carbon (CPI International)	1 5
2-Bromoaniline	95.4	2.11[h]	Sugar activated carbon (Merck)	1
Halogenated sulphur containing compounds				
2-Bromothiophene	42.1	2.75[a]	Sugar activated carbon (Merck)	1
3’,3”-Dibromophenol-sulfonphthaleine	98		Activated carbon (Mitsubishi)	7
3’, 3”-Dichlorophenol-sulfonphthaleine	92		Activated carbon (Mitsubishi)	7
Other model compounds				
Bis(2-chloroethyl)ether	92	1.29[a]	Activated carbon	2
2-Chloroethanol	20	0.107[j]	Filtrasorb 400 and APC carbon (Calgon)	3

	6.6 50 ± 2		Sugar activated carbon (Merck) Activated carbon (CPI International)	1 5
(6-Bromo-pyridin-2-yl) methanol	101 ± 2[d]; 99 ± 4[e]	0.994[j]	Activated carbon (CPI International)	6

[a] http://logKow.cisti.nrc.ca/logKow/search.html
[b] analysis done by Mitsubishi TOX Analyser
[c] analysis done by Dohrmann TOX Analyser
[d] detection by microcoulometer
[e] detection by ion chromatograph
[f] http://www.chemspider.com
[g] http://www.epa.gov/oswer/riskassessment/ragse/pdf/appendix_a.pdf
[h] https://pubchem.ncbi.nlm.nih.gov/compound
[i] http://www.chemicalize.org/structure
[j] SciFinder Website: Under 'Explore the substances'

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Table S2: Summary of outcomes from studies reporting toxicity of TOX in disinfected water

Sample/Disinfection conditions	[TOX]	Bioassay method	Cell/organism type	Toxicological endpoint	Toxicity measure	Ref
Water samples from various locations in a water treatment plant (WTP)	31.8 – 325 $\mu g\ L^{-1}$	Microtox	*Vibrio fischeri*	Cytotoxicity	EC_{50} (REF): 2.04 – 17.25 TEQ (mg L^{-1}): 0.71 – 6.61	1
		Mammalian cell cytotoxicty	Human colon cancer cell line (Caco-2)	Cytotoxicity	Assay was insensitive	
		UmuC assay (without metabolic activation)	*Salmonella typhimurium*	Genotoxicity	$EC_{IR1.5}$– S9 (REF): 16 – 198 4NQO-EQ – S9 ($\mu g\ L^{-1}$): 0.05 – 0.72	
		UmuC assay (with metabolic activation)	*Salmonella typhimurium*		$EC_{IR1.5}$ + S9 (REF): 26 – 244 2AA-EQ ($\mu g\ L^{-1}$) + S9: 0.18 – 1.63	
		E.coli biosensor	*E.coli* GSH$\pm$	Reactive toxicity to protein	Ratio EC_{50}(GSH+) : EC_{50}(GSH-): 3.09 – 3.68	
		AREc32 assay	AREc32 cell	Oxidative stress	$EC_{IR1.5}$ (REF): 2 – 35 tBHQ-EQ (mg L^{-1}): 0.01 – 0.11	
Drinking water samples from various WTPs and tap waters; various sample enrichment methods for bioassays	1.3 – 2.8 μM	Microtox	*Aliivibrio fischeri*	Cytotoxicity	EC_{50} (REF): 13.9 – 26.0	2
		AREc32 assay	AREc32 cell	Oxidative stress	$EC_{IR1.5}$ (REF): 1.5 – 2.2	
Disinfection of treated water samples from 3 WTPs	0.3 – 8 μM	Microtox	*Vibrio fischeri*	Bacterial cytotoxicity	EC_{50} (REF): 2.40 – 51.3 TEQ (mg L^{-1}): 0.24 – 5.22	3
Chlorination or chloramination, pH 7, 72hr contact time		*UmuC* assay (without metabolic activation)	*Salmonella typhimurium*	Genotoxicity	$EC_{IR1.5}$ – S9: 14 – >150 4NQO-EQ – S9 ($\mu g\ L^{-1}$): <0.06 – 0.87	
		UmuC assay (with metabolic activation)	*Salmonella typhimurium*	Genotoxicity	$EC_{IR1.5}$ + S9: 27 – >150 2AA-EQ + S9 ($\mu g\ L^{-1}$): <0.71 – 4.05	
		E.coli biosensor	*E.coli* GSH$\pm$	Reactive toxicity to protein	Ratio of EC_{50}(GSH+) : EC_{50}(GSH-): 0.7 – 6.9	
		AREc32 assay	AREc32 cell	Oxidative stress	$EC_{IR1.5}$: 1.8 – 50 tBHQ-EQ (mg L^{-1}): <5 – 123	

Disinfection of NOM solution using MP UV-Cl_2/NH_2Cl, pH 7, 24hr contact time	95 – 859 μM as Cl	*In vitro* chronic cytotoxicity assay	Normal human colon cells	Cytotoxicity	IC_{50}: 80 – 564 μM as Cl (inhibitory concentration at which 50% reduction in cell density occurred)	4
Chlorination and chloramination of treated water sample from a WTP (with and without addition of bromide/iodide), pH 8, 48hr contact time. Organic materials extracted by XAD resin	TOCl: 500 – 3000 μg L^{-1} TOBr: 500 – 6000 μg L^{-1} TOI: 8 – 500 μg L^{-1}	Cytotoxicity assay Single cell gel electrophoresis (SCGE) assay	CHO cell CHO cell	Cytotoxicity Genotoxicity	Cytotoxicity index (CTI): 12 – 40 Genotoxicity index (GTI): 10 – 65	5
Chlorination of treated water samples, 4 hr contact time	52 – 881 μg L^{-1}	Cytotoxicity assessment (cell counting kit-8) Single cell gel electrophoresis (SCGE) assessment Oxidative stress assessment	Human hepatocyte cell line (HepG2) HepG2 cells HepG2 cells	Cytotoxicity Genotoxicity Oxidative stress	Cytotoxicity index: 1.3 – 2.7 Olive Tail Moment: 1.7 – 40 Total superoxide dismutase (T-SOD): 0.7 – 2.3 nmol/mg protein Glutathione (GSH): 220 – 360 nmol/mg protein Malondialdehyde (MDA): 0.3 – 3.5 nmol/mg protein	6
Chlorinated simulated tap water samples, pH 8.5, 15hr contact time	0.2 – 0.7 mg L^{-1} as Cl	Chronic cytotoxicity assay	CHO cells	Cytotoxicity	Cytotoxicity index: 3.1 – 13.5	7
Chlorination and bromination of humic acid solution, pH 7, 24 hr contact time	14.4 – 185.7 μg Cl L^{-1}	Chromosomal aberration test	Chinese hamster lung (CHL) cells	Mutagenicity	No. of abnormal chromosomes per TOX: 9.9 – 56.7 count/100 cells mmol	8
NOM solution treated with UV/Cl_2	10 – 17 μM	Cytotoxicity assay	Chinese hamster ovary (CHO) cells	Cytotoxicity	20 – 35 mg-phenol L^{-1}	9

Disinfection of simulated raw water (Cl_2, NH_2Cl, ClO_2, O3+Cl_2) 48 hr contact time	5 – 550 μg L^{-1} as Cl	Developmental toxicity bioassay	*Platynereis dumerilii* embryos	Developmental toxicity	2 – 95% normal development (presented in graphs)	10

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