Environmental Science & Technology

Article

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Toxic Impact of Bromide and Iodide on Drinking Water Disinfected with Chlorine or Chloramines

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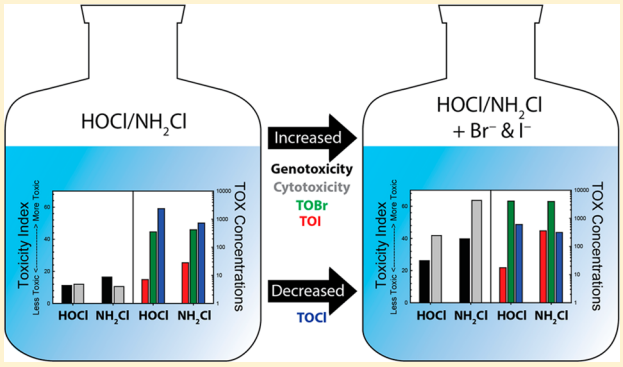
Supporting Information

ABSTRACT: Disinfectants inactivate pathogens in source water; however, they also react with organic matter and bromide/iodide to form disinfection byproducts (DBPs). Although only a few DBP classes have been systematically analyzed for toxicity, iodinated and brominated DBPs tend to be the most toxic. The objectives of this research were (1) to determine if monochloramine (NH_2Cl) disinfection generated drinking water with less toxicity than water disinfected with free chlorine (HOCl) and (2) to determine the impact of added bromide and iodide in conjunction with HOCl or NH_2Cl disinfection on mammalian cell cytotoxicity and genomic DNA damage induction. Water disinfected with chlorine was less cytotoxic but more genotoxic than water disinfected with chloramine. For both disinfectants, the addition of Br^- and I^- increased cytotoxicity and genotoxicity with a greater response observed with NH_2Cl disinfection. Both cytotoxicity and genotoxicity were highly correlated with TOBr and TOI. However, toxicity was weakly and inversely correlated with TOCl. Thus, the forcing agents for cytotoxicity and genotoxicity were the generation of brominated and iodinated DBPs rather than the formation of chlorinated DBPs. Disinfection practices need careful consideration especially when using source waters containing elevated bromide and iodide.



INTRODUCTION

Although the disinfection of drinking water to reduce waterborne disease was a spectacular public health achievement of the 20th century, the unintended formation of disinfection byproducts (DBPs) continues to be a concern.[1] Chemical disinfectants inactivate pathogens in source water, however, their high oxidizing capacity allows them to react with natural organic matter (NOM), anthropogenic contaminants and bromide/iodide to form DBPs.[2] DBP formation is affected by the concentration and type of organic matter, pH, temperature, disinfectant type and concentration, and contact time.[3,4] Common disinfectants include chlorine, chloramines, chlorine dioxide, and ozone; each disinfectant generates DBPs with different chemical class distributions.[5,6] Since the discovery of DBPs more than 40 years ago,[7,8] a total of over 600 DBPs have been identified[9] which represents a fraction of the total organic halogen (TOX) generated in disinfected water. Only a small number of these have undergone systematic, quantitative, comparative toxicological analyses.[10−12] Epidemiological studies demonstrated low but significant associations between disinfected drinking water and adverse health effects[13] including cancer of the bladder,[14−16] colon[17,18] and rectum.[19] Studies report a weak association with adverse pregnancy outcomes and DBPs; however, the evidence is inconclusive.[20−30]

Recently the occurrence and toxicity of emerging DBPs has gained attention, especially nitrogen-containing and iodinated DBPs (I-DBPs).[31−40] In the U.S. Environmental Protection Agency (EPA) Nationwide Disinfection Byproduct Occurrence Study, iodo-acids were identified for the first time as DBPs in drinking water disinfected with chloramines.[31,41,42] In addition these iodo-acids were quantified in a 23-city study in the U.S. and Canada and iodo-THMs were previously reported.[43−45] Disinfection with chloramines produced lower levels of the regulated trihalomethanes and haloacetic acids (HAAs), as well as TOX, compared to free chlorine.[5,6,46] Due to the more

Received: July 25, 2014
Revised: September 14, 2014
Accepted: September 15, 2014
Published: September 15, 2014

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stringent EPA Stage 2 Disinfectants/DBP Rule,[47] many U.S. utilities switched or are switching from free chlorine to chloramines.[48] The formation of I-DBPs is enhanced by monochloramine because monochloramine, unlike free chlorine, does not rapidly oxidize hypoiodous acid (HOI). Thus, HOI has a longer half-life with monochloramine and can react with NOM to form I-DBPs.[39,49] In general I-DBPs were more cytotoxic and genotoxic in mammalian cells than their brominated and chlorinated analogues (Figure 1).[12,42,50,51] When source waters contain high levels of iodide, switching from free chlorine to chloramine disinfection may inadvertently increase the toxicity of the finished water.

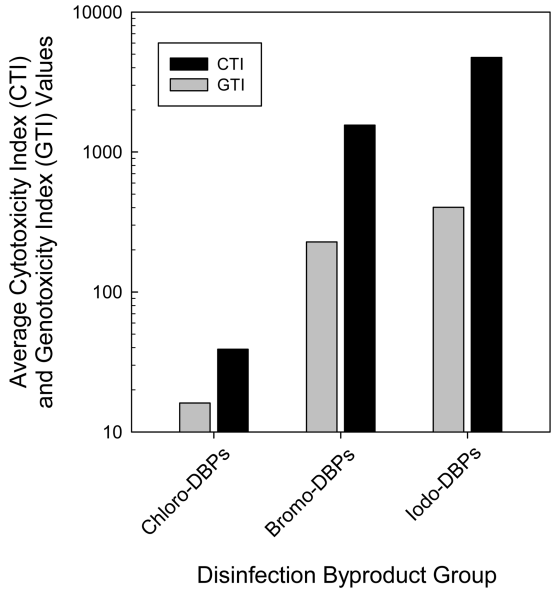

Figure 1. Relative toxic potencies of chloro-, bromo-, and iodo-DBPs in inducing chronic cytotoxicity or acute genotoxicity in mammalian cells. The cytotoxic index value was calculated as the reciprocal of the LC_{50} multiplied by 1000. The genotoxic index value was the reciprocal of the midpoint of the SCGE tail moment or the 50% Tail DNA value multiplied by 1000. These data were derived from two studies.[12,43]

Past studies demonstrated that the levels of Br^- and I^- strongly influenced the generation of brominated and iodinated DBPs.[31,39,43,49,52,53] The impact of global climate change,[54] extended periods of droughts, rising sea levels and the increasing human population, cause pristine source water demand to exceed available resources. Using recycled wastewaters,[55,56] bromide-rich desalinated seawater[57] and compromised source waters with increased levels of Br^- and I^-, as well as impacts from the disposal of fossil fuel wastewaters,[58] may generate conditions that enhance the formation of brominated and iodinated DBPs.[2,43] Brominated and iodinated DBPs are of concern for their cytotoxicity and genotoxicity in model mammalian and human cell systems;[11,12,42,59,60] brominated DBPs are gaining attention in epidemiological studies.[25,61]

The objectives of this research were (1) to determine, under controlled conditions, if monochloramine (NH_2Cl) disinfection generated drinking water with less toxicity than water disinfected with free chlorine (HOCl) and (2) to determine the impact of added bromide and iodide in conjunction with HOCl or NH_2Cl disinfection on mammalian cell cytotoxicity and genomic DNA damage induction.

MATERIALS AND METHODS

Reagents and Solutions. Sodium hypochlorite (5−6% laboratory grade), ammonium chloride (≥99.5%), sodium bicarbonate (≥99.7%), ethylenediaminetetraacetic acid (EDTA) (>95%), nitric acid (optima grade), ammonium hydroxide (optima grade), sodium bromide (>99%), ethyl acetate (≥99.9%), dimethyl sulfoxide (DMSO, ≥99.7%), media, and fetal bovine serum (FBS) were purchased from Fisher Scientific (Pittsburgh, PA). Potassium iodide (>99%), *N*,*N*-diethyl-1,4-phenylenediamine oxalate (DPD, >98%), sulfuric acid (95−98%), sodium phosphate dibasic (>99%), potassium phosphate monobasic (>99%), ethyl acetate (CHROMASOLV Plus), and resins (Supelite DAX-8; Amberlite XAD-2) were purchased from Sigma-Aldrich (St. Louis, MO): these resins are referred to as XAD-8 and XAD-2. Chloride, iodide, and bromide standards (1000 mg/L) for inductively coupled plasma-mass spectrometry (ICP-MS) were purchased from Inorganic Ventures (Christiansburg, VA). Germanium and rhodium standards (1000 mg/L) were purchased from High-Purity Standards (Charleston, SC). Sodium hypochlorite stock was standardized spectrophotometrically (λ_{max} = 292 nm, 350 $M^{-1}cm^{-1}$) with a UV−vis spectrophotometer model 2550 (Shimadzu Scientific Instruments, Columbia, MD). Monochloramine solutions were prepared as described elsewhere[35] with 5 mM carbonate buffer. Monochloramine solutions were standardized using 4500-Cl DPD colorimetric method.[62] General biological reagents were purchased from Sigma-Aldrich (St. Louis, MO) and Fisher Scientific (Pittsburgh, PA).

Source Water Sampling. The Bloomington, Illinois water treatment plant uses Lake Bloomington or Lake Evergreen as their water source. The day of the sampling, water from Lake Bloomington was being treated. A cationic polymer was added at the lake intake followed by the addition of powdered activated carbon and ferric sulfate before inline static mixers. An anionic polymer was added immediately before a lime softening process, followed by pH adjustment to 9 and the addition of orthophosphates. Water was then passed through granular activated carbon/sand/gravel filters. At this stage we obtained our source water sample. The dissolved organic carbon (DOC) content was measured using a Shimadzu TOC-VCPH oxidation/combustion TOC analyzer (Shimadzu Scientific Instruments, Columbia, MD) after passing the water sample through a 0.45 μm filter. The absorbance at 254 nm ($UVA_{254\ nm}$) was determined by a Shimadzu UV-2550 UV−vis spectrophotometer (Shimadzu Scientific Instruments, Columbia, MD).

Disinfection Experiments. Using four reactors, 20 L each of source water were treated with free chlorine (2 mg/L Cl_2) or chloramines (preformed chloramine, molar ratio of N/Cl = 1.05, 2 mg/L as total Cl_2) with or without the addition of bromide (500 μg/L as Br^-) and iodide (100 μg/L as I^-) ions. Chlorine and chloramine doses were determined so that only a slight chlorine residual remained after 48 h to avoid the addition of a quencher. The reaction was carried out at room temperature for 48 h at pH ∼ 8.

Isolation of Organic Compounds from Disinfected Waters. We employed a method developed at the U.S. EPA with resins to isolate organic materials from the finished waters.[63] Resins were Soxhlet cleaned sequentially with HPLC grade methanol, ethyl acetate, and methanol (detailed procedure in Supporting Information (SI)). A chromatography

column (3.5 cm id ×70 cm with a 1 L reservoir) was packed with 30 mL of XAD-2 followed by 30 mL of XAD-8 resin. Samples were acidified with concentrated sulfuric acid to pH < 2 and slowly pumped through the packed resin beds using a peristaltic pump equipped with Masterflex/easy-load pump head (Millipore Corporation, Bedford, MA). The adsorbed organics were eluted with 200 mL of spectroscopy grade ethyl acetate. The ethyl acetate extracts were reduced to 3−4 mL using a rotary evaporator at 240 mbar, 60 °C and 90 rpm, and further reduced to 1 mL under a gentle stream of N_2 gas. One fifth of the final ethyl acetate extract was aliquoted for chemical analysis, while the remainder was solvent exchanged into DMSO such that the organics from 1 L of finished water were concentrated into 10 μL DMSO resulting in a 10^5 × concentration. Controls to test carryover of inorganic Br^- and I^- from water to ethyl acetate extracts were negative.

TOX Analyses. The ethyl acetate extracts were analyzed to determine total organic chlorine (TOCl), bromine (TOBr), and iodine (TOI) by quantifying Cl^-, Br^- and I^- ions directly with a NexION 300X ICP-MS (PerkinElmer, Waltham, MA) equipped with a Meinhard nebulizer, cyclonic spray chamber, and platinum sampler and skimmer cones. Cl^- standards and samples were prepared in 2% HNO_3. Br^- and I^- standards and samples were prepared in 0.1% NH_4OH. Ethyl acetate extracts (20 μL) were diluted separately in 2% HNO_3 or 0.1% NH_4OH. The internal standards were 10 μg/L germanium (for chloride and bromide) and 5 μg/L rhodium (for iodide). Duplicate samples were analyzed. Calibration curves, instrument conditions, and method details are described in SI.

Chinese Hamster Ovary Cells. Chinese hamster ovary (CHO) cell line AS52, clone 11−4−8 was used for the mammalian cell toxicity studies.[12,64] The CHO cells were maintained in Ham's F12 medium containing 5% FBS, 1% antibiotics (100 U/mL sodium penicillin G, 100 μg/mL streptomycin sulfate, 0.25 μg/mL amphotericin B in 0.85% saline), and 1% L-glutamine at 37 °C in a humidified atmosphere of 5% CO_2.

CHO Cell Chronic Cytotoxicity Assay. This 96-well microplate assay measures the reduction in cell density as a function of the water concentrate sample (WCS) concentration factor over a period of 72 h (>3 cell cycles).[12,65] The detailed procedure is presented in the SI. In general, for each WCS concentration factor, 4−8 replicates were analyzed and the experiments were repeated. A concentration−response curve was generated for each WCS and a regression analysis was conducted for each curve. The LC_{50} values were calculated from the regression analysis, where the LC_{50} represents the WCS concentration factor that induced a 50% reduction in cell density as compared to the concurrent negative controls.

CHO Cell Single Cell Gel Electrophoresis Assay. Single cell gel electrophoresis (SCGE, or Comet) assay quantitatively measures genomic DNA damage in individual nuclei.[66,67] The detailed procedure of the microplate methodology used in this study is presented in the SI.[68] The SCGE metric for genomic DNA damage was the %Tail DNA value which is the amount of DNA that migrated from the nucleus into the microgel (range from 0 to 100%).[69] For each WCS concentration factor range where the cell viability was >70%, a concentration−response curve was generated. A regression analysis was used to fit the curve, and the concentration factor that induced a 50%Tail DNA value was calculated.

Statistical Analyses. For the cytotoxicity assay, a one-way analysis of variance (ANOVA) test was conducted to determine if each WCS induced a statistically significant level of cell death. If a significant F value ($P \leq 0.05$) was obtained, a Holm-Sidak multiple comparison versus the control group analysis was performed to identify the lowest cytotoxic concentration factor. The power of the test statistic ($1-\beta$) was maintained as ≥0.8 at $\alpha = 0.05$. For the SCGE assay, the %Tail DNA values are not normally distributed which limits the use of parametric statistics.[70] The mean %Tail DNA value for each microgel was calculated and these values were averaged among the microgels for each WCS concentration. A one-way ANOVA test was conducted on these averaged %Tail DNA values. If a significant F value of $P \leq 0.05$ was obtained, a Holm-Sidak multiple comparison versus the control group analysis was conducted with the power ($1-\beta$) ≥ 0.8 at $\alpha = 0.05$. To determine significant differences among the WCS groups, a bootstrap statistical approach was used to generate a series of multiple LC_{50} values and multiple 50%Tail DNA values for each WCS.[71,72] For each LC_{50} value, a cytotoxicity index (CTI) value was calculated as $(LC_{50})^{-1}(10^3)$. For each 50%Tail DNA value, a genotoxicity index (GTI) value was calculated as $(50\%\ \text{Tail DNA})^{-1}(10^3)$. These dimensionless values were then analyzed using an ANOVA test. These statistics provided a quantitative assessment of the impact of the disinfection method and the addition of Br^- and I^- on the toxicity of the water concentrate samples. For correlation analyses a Pearson Product Moment Correlation test was used.

■ RESULTS AND DISCUSSION

The increased employment of chloramine as a disinfectant to comply with the U.S. EPA Stage 2 Disinfectants and Disinfection Byproducts Rule[47,48] may enhance the generation of I-DBPs when treating source waters containing inorganic and organic iodine species.[31,39,43] Increased Br^- levels in source waters also leads to higher levels of brominated DBPs many of which are highly toxic.[12] Although several studies demonstrated the relationship between bromide, or bromide and iodide concentrations and the enhanced generation of brominated and iodinated DBPs, no direct assessment on the toxicity of these disinfected waters was measured. Although a study showed a reduction in genotoxicity in *Salmonella* of wastewaters with added bromide, no analytical chemistry was available.[73] The present study was conducted to discover the impact of disinfectant (HOCl versus NH_2Cl) and the impact of Br^- and I^- on the mammalian cell toxicity of finished water. To the best of our knowledge this is the first study that directly connects DBP formation chemistry mediated by Br^- and I^- with mammalian cell toxicity. We chose Br^- and I^- concentrations that reflected high yet environmentally relevant levels (500 μg/L Br^-, 100 μg/L I^-). From our previous work bromide concentration ranged from 24 to 1120 μg/L while iodide levels were between 0.4 and 104 μg/L in source waters from 23 cities.[43] Based on this and on the significant findings of Karanfil and his colleagues,[52,53] we used a single source water with low levels of Br^- and I^- that we amended with bromide and iodide at a Br^-/I^- ratio of 5:1 prior to disinfection with chlorine or chloramine. The organics from these disinfected waters were isolated and analyzed for TOX as well as for induced chronic cytotoxicity and acute genomic DNA damage in mammalian cells. The dissolved organic carbon concentration in the sampled water was 3.35 mg/L and this is in the range of 25th percentile to 50th percentile in the 23 source waters studied by Richardson et al. (2008).[43] The UV absorbance at 254 nm was 0.041 cm^{-1} and specific UV absorbance (SUVA)

level was calculated as 1.22 L/mg-m, which is lower than the 23 source waters previously studied.[43]

Extraction of Organic Material from Finished Water. We extracted the organic materials from the disinfected water by passing over XAD-8 and XAD-2 resins in a column using a previously developed method.[63] XAD-8 resins isolate hydrophobic acid fractions, aliphatic carboxylic acids, aromatic carboxylic acids, phenols and humic substances while XAD-2 isolates polyfunctional organic acids, aliphatic acids with 5 or fewer carbons and low molecular weight solutes.[74,75] We have previously employed XAD resins to isolate organics from water samples for toxicological and chemical analyses.[25,43,63,76] XAD resins are able to recover various classes of DBPs and have been successfully employed to study DBP occurrence and toxicity from water samples.[25,76−79]

TOX Analyses. Samples with a dilution factor of 2000 and 20 000 were within the calibration curve range. Sample concentrations with relative standard deviations (RSD) <10% were used for quantification of the analytes. Internal standard recovery was between 96 and 111% for the chloride method and 97−118% for the bromide and iodide method. Method accuracy was determined to be in the range of 89−117% for bromide and iodide, and 94% for chloride concentration in the ethyl acetate extracts (SI Table S2, S3).

TOCl, TOBr, and TOI concentrations in XAD-8/XAD-2 ethyl acetate extracts are shown in Figure 2. The highest TOCl concentration (mean ± SD) was produced by chlorination alone (2350 ± 502 mg/L as Cl), followed by chloramination alone (725 ± 87 mg/L as Cl). However, in the reactors with added bromide and iodide, TOCl for chlorination or chloramination was reduced (602 ± 31 mg/L and 314 ± 30 mg/L as Cl, respectively). There was a simultaneous increase of TOBr with chlorination (352 ± 19 mg/L to 4110 ± 612 mg/L as Br) and with chloramination (421 ± 147 mg/L to 3950 ± 735 mg/L as Br). Increases in TOI, while more pronounced for chloramination, were observed in the chlorination (7.08 ± 0.05 mg/L to 17.6 ± 1.6 mg/L as I) and chloramination (28.2 ± 2.0 mg/L to 359 ± 10.8 mg/L as I) reactors with added Br^- and I^-. It is likely that the high levels of TOBr were the result of hypobromous acid (HOBr) produced by bromide oxidation by free chlorine,[80] and bromochloramine produced by bromide reaction with monochloramine,[81] reacting with organic matter to produce brominated DBPs. While TOBr formation has been reported to be higher for chlorination compared to chloramination, our results show that both disinfection treatments produce similar levels of TOBr.[5,82,83] A possible explanation is that the pH was slightly higher (pH 8) for both disinfection treatments. At pH 8, monochloramine and bromochloramine are more stable compounds than at pH 7.4 and will further react with organics in the water until it has been consumed.[81] Another possibility is that in this study the disinfected water was not quenched before extraction to avoid artifacts produced from quenching. Furthermore, chloraminated reactors produced higher levels of TOI than the chlorinated reactors; similar results were reported by others.[32,39,49] Such results are consistent with the formation and slow decay of HOI in the presence of monochloramine that can further react with organic matter to form I-DBPs, whereas free chlorine can quickly oxidize HOI to form IO_3^-.[39,49]

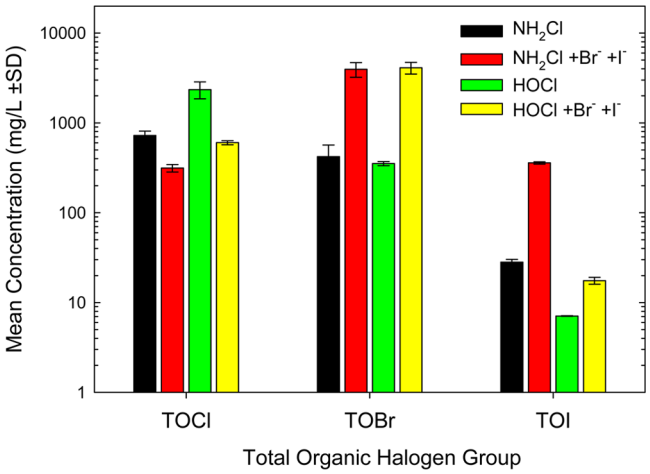

Figure 2. Comparison of the components of the total organic halogen as TOCl, TOBr, and TOI in the ethyl acetate extract generated by the four reactors (NH_2Cl, NH_2Cl +Br^- +I^-, HOCl, HOCl +Br^- +I^-).

Cytotoxicity and Genotoxicity of Reactor Samples. One objective of this research was to determine if the addition of 500 μg/L Br^- and 100 μg/L I^- to the source water affected the cytotoxicity and genotoxicity of the extracted DBPs after disinfection with chlorine or chloramines. The concentration metric for the quantitative biology was expressed as the concentration factor (CF) of the original water sample.

After 72 h exposure, the CHO cell cytotoxicity of each water concentrate sample derived from each reactor is presented as a concentration−response curve (Figure 3). The LC_{50} value for each WCS was determined by regression analysis of each concentration response curve and the lowest cytotoxic concentration was determined after an ANOVA test of the data (Table 1A). The LC_{50} values indicated that the lowest levels of cytotoxicity were associated with NH_2Cl or HOCl disinfection alone (LC_{50} = 62.1 and 89.4 concentration factors, respectively). The addition of Br^- and I^- significantly increased the cytotoxicity of the WCS with chloramine disinfection (LC_{50} = 24.7 CF) or chlorine disinfection (LC_{50} = 37.8 CF).

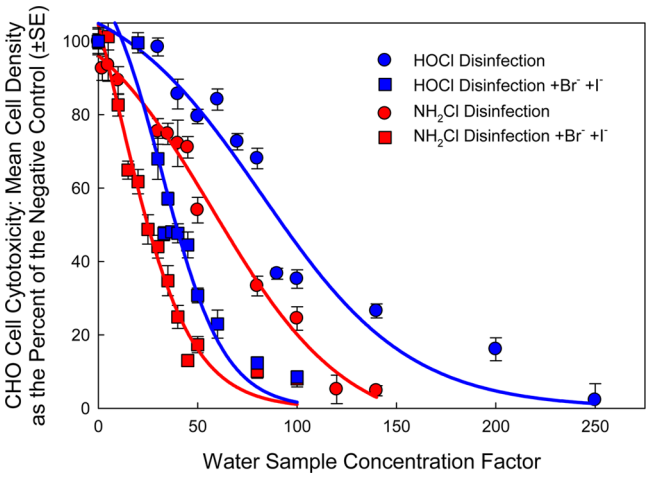

Figure 3. CHO cell chronic cytotoxicity concentration−response curves generated by the XAD-8/XAD-2 extracted organics from the disinfected water derived from the four reactors (NH_2Cl, NH_2Cl +Br^- +I^-, HOCl, HOCl +Br^- +I^-).

The induction of acute (4 h exposure) genomic DNA damage by the four WCS is presented as their individual concentration−response curves (Figure 4). The data for each

Table 1A. CHO cell chronic cytotoxicity metrics derived from the concentration-response curves of the water concentrate samples.

Sample	Conc. Factor Range	LC_{50} Conc. Factor [a]	r^2 [b]	Lowest Cytotoxic Conc. Factor [c]	ANOVA Test Statistic [d]
Reactor 1: NH_2Cl	2 − 140	62.1	0.99	30	$F_{12,105} = 58.08$; $P \leq 0.001$
Reactor 2: NH_2Cl +Br^- +I^-	5 − 100	24.7	0.98	10	$F_{12,103} = 120.4$; $P \leq 0.001$
Reactor 3: HOCl	30 − 250	89.4	0.96	40	$F_{11,107} = 107.0$; $P \leq 0.001$
Reactor 4: HOCl +Br^- +I^-	10 − 100	37.8	0.95	30	$F_{12,113} = 97.17$; $P \leq 0.001$

Table 1B. CHO cell genotoxicity metrics derived from the concentration-response curves of the water concentrate samples.

Sample	Conc. Factor Range	50%Tail DNA Conc. Factor [e]	r^2 [f]	Lowest Genotoxic Conc. Factor [g]	ANOVA Test Statistic
Reactor 1: NH_2Cl	100 − 1100	945.4	0.99	700	$F_{13,46} = 94.79$; $P \leq 0.001$
Reactor 2: NH_2Cl +Br^- +I^-	10 − 250	160.5	0.98	100	$F_{7,34} = 44.51$; $P \leq 0.001$
Reactor 3: HOCl	100 − 1000	830.6	0.98	600	$F_{12,47} = 106.9$; $P \leq 0.001$
Reactor 4: HOCl +Br^- +I^-	25 − 400	244.3	0.97	150	$F_{9,38} = 74.17$; $P \leq 0.001$

[a]The LC_{50} is the sample concentration factor that induced a cell density that was 50% of the negative control. [b]The r^2 is the coefficient of determination for the regression analysis from which the LC_{50} value was calculated. [c]Lowest cytotoxic concentration factor was determined from the ANOVA test. [d]ANOVA is the analysis of variance test statistic with the degrees of freedom for the between-groups and residual associated with the calculated F test result and the resulting probability value. [e]The 50%Tail DNA SCGE value is the concentration factor calculated using regression analysis that would induce 50% of the genomic DNA to migrate from the nucleus into the microgel. [f]The r^2 is the coefficient of determination for the regression analysis from which the 50%Tail DNA value was calculated. [g]Lowest genotoxic concentration factor was the lowest concentration factor in the concentration−response curve that induced a significant amount of genomic DNA damage as compared to the concurrent negative control.

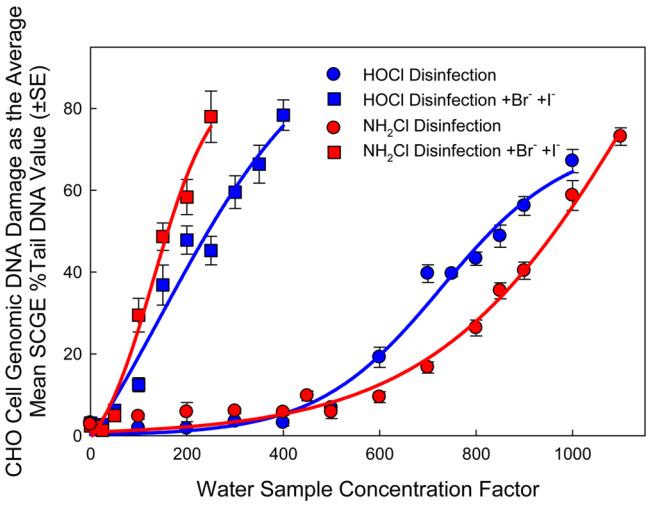

Figure 4. CHO cell genotoxicity concentration−response curves generated by the XAD-8/XAD-2 extracted organics from the disinfected water derived from the four reactors (NH_2Cl, NH_2Cl +Br^- +I^-, HOCl, HOCl +Br^- +I^-).

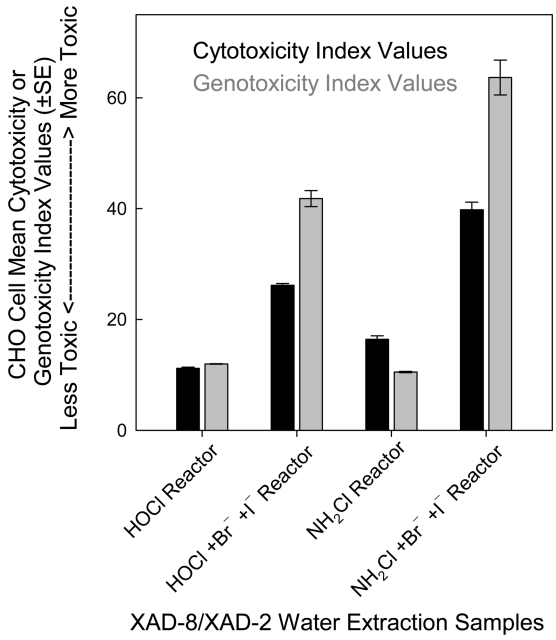

Figure 5. A comparison of the average cytotoxicity and genotoxicity index values of the extracted organics from the disinfected water derived from the four reactors (NH_2Cl, NH_2Cl +Br^- +I^-, HOCl, HOCl +Br^- +I^-).

WCS were regressed and the concentration that induced the SCGE 50%Tail DNA value was calculated (Table 1B). Similar to the cytotoxicity results, the addition of Br^- and I^- increased the genotoxicity for both HOCl and NH_2Cl disinfection.

To compare the toxic responses of the WCS from each reactor we calculated the mean CTI and the mean GTI. These data were generated via a bootstrap statistic which provided an error term with which the groups could be tested for significance using an ANOVA test (Figure 5). Cytotoxicity and genotoxicity were highly and significantly correlated (r = 0.98; P < 0.03), however, there were different responses for the biological assays among the four reactor groups. WCS from NH_2Cl disinfection alone was significantly more cytotoxic than the WCS from HOCl alone. WCS from the reactors with added Br^- and I^- were significantly more cytotoxic with a 2.4× increase as compared to either HOCl or NH_2Cl alone. A more complex response was observed with genotoxicity; there was no significant difference between the NH_2Cl and HOCl samples from reactors without added Br^- and I^-. Thus, under these conditions and with the identical source water, the disinfectant made no difference in the generation of genotoxic DBPs. However, the situation radically changed with the addition of Br^- and I^- in that there was a significant increase in genotoxicity of the WCS for each disinfectant with an increase of 3.5× for the HOCl sample and 6.1× for the NH_2Cl sample. It is interesting to note that with added Br^- and I^-, both cytotoxicity and genotoxicity were 1.5× higher with chloramine disinfection as compared to chlorine disinfection (Figure 5).

This suggests that the formation of highly toxic brominated and/or iodinated-DBPs and the generation of toxic Br/I-NDBPs was favored in the reactors with added Br^- and I^- disinfected with chloramines.

Correlation analyses were conducted for toxicity and the levels of TOCl, TOBr and TOI as a function of the disinfectant with and without Br^- and I^-. Both the cytotoxicity and genotoxicity index values were highly correlated with TOBr (r = 0.85 and r = 0.92, respectively) and TOI (r = 0.88 and r = 0.82, respectively). However, these toxicity metrics were weakly and inversely correlated with TOCl (r = −0.56 and r = −0.39, respectively). Thus, the forcing agents for both cytotoxicity and genotoxicity were the generation of brominated and iodinated DBPs rather than the formation of chlorinated DBPs. In order to reduce the toxicity of finished drinking water, engineering processes to limit the generation of I-DBPs may include increasing the free chlorine contact time prior to ammonia addition or using additional processes to oxidize HOI to IO_3^-.[84,85] These findings indicate that caution is warranted in the use of chloramine disinfection with source waters containing elevated bromide and iodide.

■ ASSOCIATED CONTENT

Supporting Information

Extended materials and methods including extraction resin preparation, description of the ICP-MS optimization and procedure and standards for the TOCl, TOBr and TOI analyses, and an extended presentation of the CHO cell chronic cytotoxicity assay and the SCGE assay for genomic DNA damage and the individual cytotoxicity and genotoxicity concentration−response curves. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ ACKNOWLEDGMENTS

This research was supported by NSF WaterCAMPWS (Award CTS-0120978) and the U.S. EPA STAR grant R834867 and by the China Scholarship Council. Although the research described in the article has been funded in part by the U.S. Environmental Protection Agency's STAR program, it has not been subjected to any EPA review and therefore does not necessarily reflect the views of the Agency, and no official endorsement should be inferred. We acknowledge Sam Youssef from PerkinElmer for his assistance on ICP-MS. Rick Twait and Jill Mayes at the Bloomington Water Department are gratefully acknowledged for their generous assistance for water sampling. The authors thank Bryan Smith for the water analysis.

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