Chloramination of iopamidol- and bromide-spiked waters containing natural organic matter

Nana Osei B. Ackerson, Hannah K. Liberatore, Susan D. Richardson, Michael J. Plewa, Thomas A. Ternes and Stephen E. Duirk

ABSTRACT

Iopamidol (an iodinated X-ray contrast medium) and bromide are precursors in the formation of halogenated disinfection byproducts (DBPs). The interactions of these precursors are vital to elucidate the formation of halogenated DBPs during chloramination. This work investigated the formation of total organic halogen and select individual DBPs in two laboratory-chloraminated source waters containing iopamidol and bromide. Experiments were carried out in batch reactors containing Barberton source water (BSW) and Cleveland BSW (CSW), spiked with iopamidol (5 μM), bromide (15 μM), and 100 μM monochloramine. Total organic iodine concentrations were approximately equal regardless of source water since they are mostly unreacted iopamidol and iopamidol DBPs. Almost equal amounts of total organic chlorine (3–4 nM) were produced in the source waters, but higher quantities of total organic bromine were formed in BSW than CSW. Substantial quantities of regulated trihalomethanes (THMs) and haloacetic acids (HAAs) were formed in the source waters, along with appreciable concentrations of iodinated trihalomethanes (CHBrClI, $CHCl_2I$, and $CHBr_2I$). Low concentrations of iodo-HAAs were detected, especially at low pH. Overall, bromide concentrations appeared to suppress iodo-DBP formation during chloramination of iopamidol in the presence of natural organic matter. A good correlation ($R^2 = 0.801$) between the yields of regulated DBPs and iodo-DBPs was observed.

Key words | bromide, disinfection byproducts, iopamidol, monochloramine, source water, total organic halogen

Nana Osei B. Ackerson (corresponding author)
Stephen E. Duirk
Department of Civil Engineering,
University of Akron,
Akron, OH 44325,
USA
E-mail: *nba5@zips.uakron.edu*

Hannah K. Liberatore
Susan D. Richardson
Department of Chemistry and Biochemistry,
University of South Carolina,
631 Sumter St., Columbia, SC 29208,
USA

Michael J. Plewa
Department of Crop Sciences and Safe Global Water Institute,
University of Illinois at Urbana-Champaign,
1101 West Peabody Drive, Urbana, IL 61801,
USA

Thomas A. Ternes
Federal Institute of Hydrology (BfG),
Am Mainzer Tor 1, D-56068, Koblenz,
Germany

HIGHLIGHTS

- Bromide suppressed the formation of iodo-THMs without bromine atoms.
- Approximately equal quantities of total organic chlorine were formed regardless of NOM characteristics.
- Iodoacetic acids showed substantial formation at low pH irrespective of NOM.

INTRODUCTION

To alleviate the risk of water-borne diseases, chlorine has been employed to disinfect potable water since before the 1900s. Achieving adequate disinfection is paramount to public health; however, addition of chlorine results in the formation of appreciable concentrations of disinfection byproducts (DBPs), especially regulated trihalomethanes (THMs) and haloacetic acids (HAAs). Difficulty in complying with regulations has led some water utilities in the USA to switch from free chlorine to monochloramine (NH_2Cl) as a secondary disinfectant (Luh & Marinas

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2012). Generally, NH_2Cl is used for maintaining residual disinfectant in distribution systems since it is less reactive with natural organic matter (NOM) and results in lower concentrations of regulated DBPs (Vikesland *et al.* 1998). However, studies have revealed that other DBPs are formed in chloraminated waters that elicit greater toxicity than regulated DBPs (Plewa *et al.* 2004; Krasner *et al.* 2006; Richardson *et al.* 2008a; Duirk *et al.* 2011).

Monochloramine reacts with different precursor materials to form relatively higher concentrations of different classes of DBPs, including total iodinated DBPs (iodo-DBPs), haloacetonitriles (HANs), cyanogen halides, *N*-nitrosodimethylamine (NDMA), haloacetamides, halonitromethanes, and haloacetaldehydes (Plewa *et al.* 2004; Krasner *et al.* 2006; Richardson *et al.* 2008a; Luh & Marinas 2012; Shah & Mitch 2012; Chuang *et al.* 2015). Haloacetamides, halonitromethanes, haloacetaldehydes and HANs have been found to be up to two orders of magnitude more genotoxic and cytotoxic than THMs and HAAs in mammalian cells (Krasner *et al.* 2006). These nitrogenous DBPs are formed during chloramination (Krasner *et al.* 2006) or chlorination of precursor material containing organic nitrogenous compounds and phenols, among others (Chuang *et al.* 2015). Also, iodo-DBPs elicit high genotoxicity and cytotoxicity, with iodoacetic acid (IAA) being the most genotoxic DBP identified to date (Plewa *et al.* 2004; Richardson *et al.* 2008a). Iodo-DBPs are produced in chlorinated or chloraminated source waters containing inorganic iodide or organic iodinated compounds (Plewa *et al.* 2004; Krasner *et al.* 2006; Richardson *et al.* 2008b; Duirk *et al.* 2011; Wang *et al.* 2014; Tian *et al.* 2017; Ackerson *et al.* 2018; Postigo *et al.* 2018).

Iodinated X-ray contrast media (ICM) are a class of pharmaceuticals with three iodines bonded to a benzene ring at the 2, 4, and 6 positions with other side-chain moieties. ICM have been detected in surface waters, creeks, rivers, and effluents of wastewater (especially from medical facilities) around the world (Ternes & Hirsch 2000; Drewes *et al.* 2001). They are recalcitrant to conventional wastewater and drinking treatment (Ternes & Hirsch 2000; Drewes *et al.* 2001), but can be transformed somewhat during chemical treatment processes. Chlorination of iopamidol yields both mono- and dimeric iopamidol DBPs (Wendel *et al.* 2014) as well as iodinated THMs (iodo-THMs) and iodinated HAAs (iodo-HAAs) (Duirk *et al.* 2011). Additional studies have shown rapid transformation of iomeprol during TiO_2 photolysis and degradation through photochemical processes, including UV/$S_2O_8^{2-}$ for diatrizoate (Duan *et al.* 2016) and Fe(III)-oxalate/H_2O_2 using ultraviolet (UV) and visible light irradiations for iopamidol (Zhao *et al.* 2014).

Studies have shown that transformation of commonly detected ICMs result in the release of iodine and subsequent formation of iodo-DBPs. Chlorination and chloramination of water spiked with iopamidol, in the presence of NOM and algae organic matter extracts formed dichloroiodomethane ($CHCl_2I$), chlorodiiodomethane ($CHClI_2$), triiodomethane (CHI_3) and IAA (Duirk *et al.* 2011; Wang *et al.* 2014; Ackerson *et al.* 2018). Similarly, UV irradiation of iopamidol followed by either chlorination or chloramination produced similar iodo-DBPs (Tian *et al.* 2014). Source waters containing naturally occurring bromide (Br^-) dosed with either iopamidol or iodide (I^-) and monochloramine produced different speciation of iodo-DBPs (Wang *et al.* 2014). Thus, the presence of organic or inorganic iodine, bromide, and type of chemical oxidant DBP affects the speciation of DBPs in natural waters.

The main objective of this study was to investigate the formation of total organic halogen (TOX) and the distribution of individual DBPs in chloraminated source waters containing iopamidol and Br^-. The study specifically investigated how different NOM sources and pH affected halogen-specific TOX and DBP formation. Since both constituents are precursors in the formation and speciation of DBPs and bromide oxidation/incorporation is faster than iopamidol transformation, we wanted to investigate whether the presence of Br^- might suppress the formation of choro-iodo/iodo-DBPs in chloraminated iopamidol-containing waters.

MATERIALS AND METHODS

Reagents

All reagents used were of the highest available purity and are described in detail elsewhere (Ackerson *et al.* 2018). Purified water (18.2 MΩ-cm) used for preparing buffer solutions was produced from Barnstead ROPure Infinity/NANOPure system (Barnstead-Thermolyne Corp. Dubuque, IA, USA). An Orion 5-star pH meter equipped with a Ross ultra-combination electrode (Thermo Fisher Scientific, Waltham, MA) was used

to measure pH. Phosphate buffer was used to maintain pH at 6.5 and 7.5, and borate buffer for pH 8.5 and 9.0. pH adjustments were carried out with 1 N H_2SO_4 and 1 N NaOH. All glassware and polytetrafluoroethylene (PTFE) containers were soaked in a chlorine bath for 24 hours, rinsed with large amounts of purified water and dried before use.

Water samples and oxidants

Source waters were collected from drinking water treatment plants from Northeast Ohio, USA – Barberton source water (BSW) from the Barberton water treatment plant (Barberton, OH) and Cleveland source water (CSW) from the Garret Morgan water treatment plant (Cleveland, OH). Naturally occurring iodide levels in the source waters were below detection limits (0.5 μM) (Table S1, Supplementary Information). The source waters were filtered with 0.45 μm Whatman nylon membrane filters (West Chester, PA) and stored at 4 °C until use. Detailed chemical and fluorescence spectral characteristics of the source waters can be found in Ackerson *et al.* (2018).

Preformed monochloramine was used in this study to examine the oxidant's impact on TOX and DBP formation. Sodium hypochlorite (5.65–6%, Thermo Fisher Scientific, Waltham, MA) was used to prepare aqueous chlorine solutions. Aqueous chlorine was prepared monthly and the concentration was verified prior to use using ferrous ammonium sulfate (FAS)/*N*,*N*′-diphenyl-p-phenylenediamine (DPD) titration (APHA *et al.* 2005). Preformed monochloramine was prepared from aqueous chlorine and ammonium chloride at pH 8.5, using borate buffer, to achieve a Cl/N molar ratio of 0.7. A UV-visible spectrophotometer and FAS/DPD titration were used to determine the concentration of the preformed monochloramine (APHA *et al.* 2005). The full procedure for monochloramine preparation is shown elsewhere (Ackerson *et al.* 2018).

Experimental methods

To investigate the impact of bromide and iopamidol on DBP and TOX formation and speciation, 1,000- and 250-mL Erlenmeyer flasks were filled with BSW or CSW dosed with buffer solutions (1 mM for TOX and 4 mM for DBPs), 5 μM iopamidol, and 15 μM Br^- concentrations at pH 6.5–9.0. Phosphate buffer was used to maintain pH 6.5 and 7.5, while borate buffer was used at pH 8.5 and 9.0. Monochloramine was added to achieve a final concentration of 100 μM under rapid mixing conditions on a magnetic stir plate with a PTFE stir bar. After uniform mixing, aliquots of the samples were transferred into 128-mL amber bottles and 40-mL amber vials with PTFE septa screw caps and stored headspace-free in the dark at 25 °C for 0–48 hours prior to DBP and TOX analyses, respectively.

At the end of each reaction time, the residual monochloramine in the samples was quenched with aqueous sulfite solution (120% of the initial total oxidant concentration). Samples were analyzed using the method used by Hua & Reckhow (2006) with slight modification. Samples were then extracted for subsequent DBP and TOX analyses. About 30 mL of quenched-water samples for TOX analysis were acidified with 70% nitric acid to <pH 2 and concentrated on prepacked granular activated carbons. Inorganic halides were rinsed with 15 mL KNO_3 solution, combusted in a TOX-100 analyzer (Cosa Instruments/Mitsubishi, Horseblock Road, NY), and the off-gas (hydrogen halides) was absorbed into a 20 mL phosphate solution (100 μmol/L). Detailed extraction procedures can be found elsewhere (Ackerson *et al.* 2018).

Analytical methods

Extracted and combusted TOX samples were analyzed on a Dionex ICS-3000 column (Dionex Corporation, Sunnyvale, CA) with conductivity detector and an ASRS®300 4 mm anion self-regenerating suppressor. Detection of TOX was accomplished with an AS20 analytical column (4 × 250 mm) and a guard column (Dionex Corporation, Sunnyvale, CA) with 10 mM KOH as the mobile phase (flow rate of 1 mL/min). The specific TOX species analyzed were total organic bromine (TOBr), total organic chlorine (TOCl), and total organic iodine (TOI). TOBr, TOCl, and TOI were detected respectively on the ICS-3000 as Br^-, Cl^- and I^-. The recoveries of all TOX species were 98–100% with a limit of quantitation of 0.50 μM and a detection limit of 0.25 μM.

Using liquid-liquid extraction, samples for DBP analysis were extracted in methyl *tert* butyl ether (MtBE) with 1,2-dibromopropane as the internal standard. The extracted organic phase was divided into 1.5 mL (for THM and HAN analyses) and 0.5 mL aliquots for derivatization of HAAs. Derivatization was conducted with diazomethane to form

methyl esters. Table S2 shows the lists of THMs, HANs, and HAAs analyzed in this study. DBPs were analyzed on 7890A gas chromatograph (GC) equipped with a ^{63}Ni micro-electron capture detector (μECD) from Agilent Technologies (Santa Clara, CA). A Restek Rxi-5Sil MS GC column (30 m × 0.5 μmand 0.25 mm i.d.; Restek Corporation, Bellefonte, PA) was used to separate the DBP species. Splitless injection was employed. The make-up and carrier gases were ultrahigh pure nitrogen and ultrahigh pure helium, respectively. The μECD temperature was 250 °C. The temperature programs for the separation of THMs/HANs and non-iodinated HAAs are shown in Tables S3 and S4 respectively. Gas chromatography–tandem mass spectrometry (GC-MS/MS) with a ThermoScientific Quantum GC-triple quadrupole mass spectrometer coupled to a TRACE GC Ultra gas chromatograph (ThermoScientific, Waltham, MA) was used to analyze iodo-HAAs (Table S2). The temperature program for the iodo-HAAs analysis is shown in Table S5 while the MS-MS transitions are shown in Table S6.

RESULTS AND DISCUSSION

TOX speciation

TOI did not change substantially when the source waters were spiked with 5 μM iopamidol, 15 μM Br^-, and 100 μM NH_2Cl. In both Barberton and Cleveland source waters, TOI exhibited marginal losses at the end of 48 hours (Figure 1 and Figure S2, Supplementary Information). This is due to unreacted iopamidol, iopamidol transformation products (IDOL-DBPs), or iodide released from the IDOL-DBPs that has been oxidized and incorporated into DBP precursors in the NOM structure. Monochloramine undergoes hydrolysis, especially at pH < 8.5 (Vikesland *et al.* 2001). The hydrolysis product, HOCl, is in equilibrium with OCl^-, which can act as a nucleophile, reacting with one of the amide side chains of iopamidol and forming IDOL-DBPs (Wendel *et al.* 2014). The DBPs continue to react with the chlorinated oxidants present and release the iodine from the IDOL-DBP ring structure (Figure S1). It has been observed that chloramine cannot degrade iopamidol effectively (Tian *et al.* 2017). The iodide is then oxidized to HOI and subsequently incorporated into NOM structures, possibly forming different TOI structures.

Like TOI, TOBr did not show substantial differences as a function of pH. However, different quantities of TOBr were produced with respect to the different source waters (Figure 1 and Figure S2). An appreciable level of bromine incorporation (67–90%) was found in BSW. By contrast, only 25–32% bromide was incorporated into chloraminated CSW. The amounts of TOBr generated during chloramination were 12–35% and two- to threefold less in BSW and CSW, respectively, than when these source waters were chlorinated in a previous study (Ackerson *et al.* 2020). Chlorination and chloramination of organic matter isolates in finished water from Bloomington water treatment plant (IL), containing Br^- and iodide also showed marginal a difference between TOBr levels (Yang *et al.* 2014). Other studies have likewise reported both marginal and substantial differences between TOBr concentrations in chlorinated

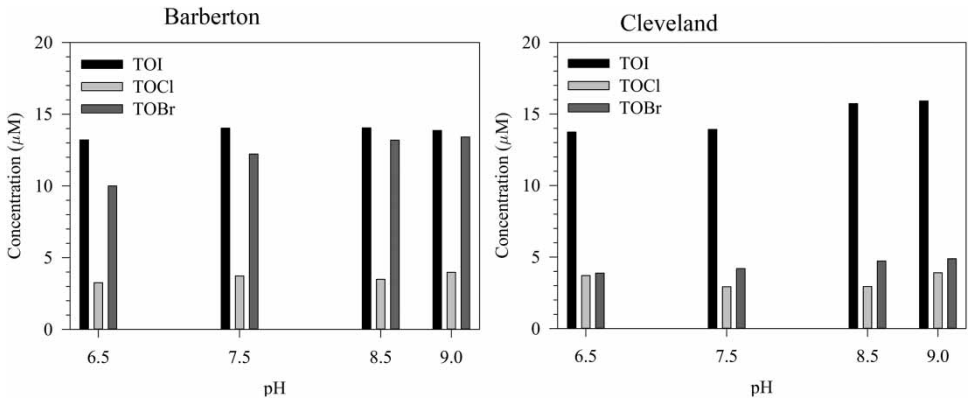

Figure 1 | Total organic halogen formation in chloraminated Barberton and Cleveland source waters at 48 hours as a function of pH. [Iopamidol] = 5 μM, [Br^-] = 15 μM, [NH_2Cl] = 100 μM, $[buffer]_T$ = 1 mM, temp = 25 °C, $DOC_{Barberton}$ = 4.47 mg/L-C, $DOC_{Cleveland}$ = 2.51 mg/L-C.

and chloraminated NOM-containing waters (Kristiana *et al.* 2009). The results indicate that the type of NOM influences the quantities of TOBr produced. The NOM in BSW and CSW are rich in fulvics and aromatic protein-like structures respectively (Ackerson *et al.* 2018).

Bromide is a direct precursor to the formation of brominated DBPs during chloramination. Monochloramine reacts with Br^- to form bromochloramine (Trofe *et al.* 1980). The reaction is proposed to occur through a general acid-assisted Cl^+ transfer that forms bromine chloride (BrCl) as an intermediate (Gazda & Margerum 1994). Bromochloramine, a very reactive species (Valentine *et al.* 2005), reacting with NOM forms TOBr. Also, HOCl, the hydrolysis product of NH_2Cl, oxidizes Br^- to HOBr, which incorporates into NOM to yield TOBr (Hua & Reckhow 2007). Thus, TOBr formation occurred through two known pathways.

Degradation of iopamidol in the presence of Br^-, NOM, and NH_2Cl produced a relatively small quantity of TOCl, and the observed formation of TOCl was approximately equal in both source waters (Figure 1 and Figure S2). Formation of TOCl possibly occurred via two pathways. The first would be the direct reaction of NH_2Cl with NOM (Vikesland *et al.* 1998). The second is the hydrolysis of NH_2Cl to form HOCl, which can react with IDOL-DBPs and reactive sites in NOM (Duirk *et al.* 2010). Iopamidol and IDOL-DBPs are known for excessive TOCl formation in comparison to NOM (Wendel *et al.* 2014; Ackerson *et al.* 2018). In addition, TOCl yield was lower in the chloraminated source waters than chlorinated source waters (Ackerson *et al.* 2018). This can be ascribed to aqueous chlorine being more reactive than NH_2Cl (Vikesland *et al.* 1998).

DBP formation and speciation

Addition of monochloramine to source waters containing iopamidol and bromide generated both regulated THMs and iodo-THMs. Generally, most of the regulated THMs exhibited a slow initial formation, especially at high pH, probably due to monochloramine being the dominant oxidant and being extremely stable at high pH (Jafvert & Valentine 1992). All four regulated THMs – $CHCl_3$, $CHBrCl_2$, $CHBr_2Cl$, and $CHBr_3$ – were detected in both source waters. Appreciable quantities of $CHCl_3$ were formed in BSW compared to CSW (Figure 2). Nonetheless, formation rates were faster in CSW than BSW. Almost 74–91% and 50–64% of $CHCl_3$ formed at 48 hours was detected at 6 hours in CSW and BSW, respectively, except for CSW at pH 6. Since the direct reaction of monochloramine with iopamidol is minimal (Duirk *et al.* 2011; Wendel *et al.* 2014; Ackerson *et al.* 2018), chlorinated THM formation is likely due to the direct reaction of NH_2Cl with NOM and monochloramine hydrolysis, resulting in HOCl formation and reaction with NOM (Vikesland *et al.* 1998; Duirk *et al.* 2010). While $CHCl_3$ increased with time, it decreased with increasing pH because of the decreasing rate of monochloramine auto-decomposition. The concentration of $CHBr_3$ detected in source waters after exposure to NH_2Cl was relatively low (Figure 2). Both source waters showed up to 12% formation (of the total amount after 48 hours) of $CHBr_3$ at 6 hours. In CSW, $CHBr_3$ yields were detected at 24 hours at pH 8.5 and 9.0. Formation of brominated oxidants (i.e., NH_2Br, NHBrCl and HOBr) and reaction/incorporation into NOM and IDOL-DBPs may have enhanced $CHBr_3$ formation. NHBrCl and other bromamines have been assumed to exhibit slow reaction with NOM (Duirk & Valentine 2007). This may account for the slow rate of formation seen for $CHBr_3$ especially as pH increased, reducing brominated oxidant formation.

The formation of two bromo-chloro-THMs was observed in both source waters. However, pH and source water impacted the concentrations of the mixed brominated/chlorinated THMs formed. Mixed halo-THM (i.e., $CHBr_2Cl$ and $CHBrCl_2$) formation was substantially greater in BSW than CSW (Figure S3). This was likely the result of BSW being more reactive with brominated/chlorinated oxidants than CSW and IDOL-DBPs. Ackerson *et al.* (2018) have previously shown that BSW has more DBP precursors than CSW and IDOL-DBPs, generally resulting in unknown TOX and unknown DBPs. Therefore, the formation of these species may be a simultaneous incorporation of chlorine and bromine found in NH_2Cl, HOCl, NHBrCl, and HOBr. Since the reactivity of each oxidant or haloamine species is pH dependent, their relative abundance at each pH will vary. This pH-dependent oxidant formation would likely have impacted the formation of these THMs.

The use of monochloramine as a disinfectant in water treatment has been an increasing topic of research because of the enhanced formation of more toxic iodo-DBPs. This happens because HOI, the oxidation product of iodide, is

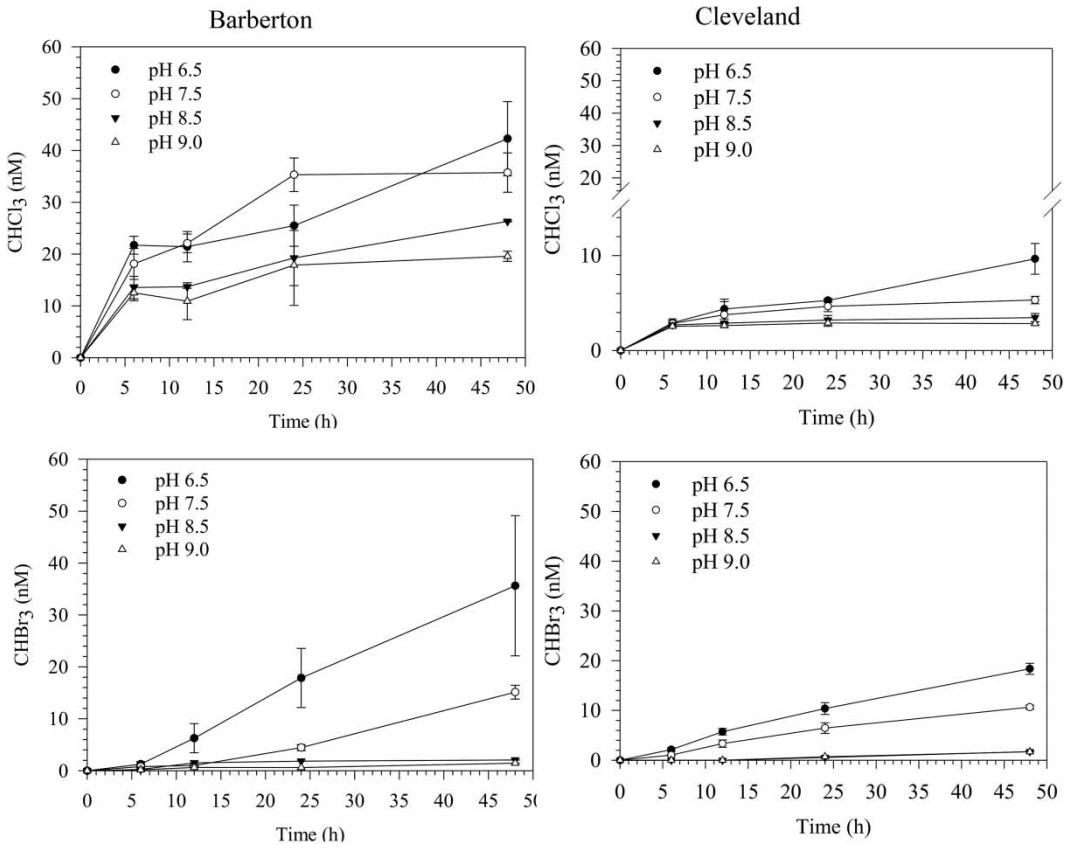

Figure 2 | $CHCl_3$ and $CHBr_3$ formation in chloraminated Barberton and Cleveland source waters as a function of pH. [Iopamidol] = 5 μM, $[Br^-]$ = 15 μM, $[NH_2Cl]$ = 100 μM, $[buffer]_T$ = 4 mM, temp = 25 °C, $DOC_{Barberton}$ = 4.47 mg/L-C, $DOC_{Cleveland}$ = 2.51 mg/L-C. Error bars represent 95% confidence interval for two replicates.

stable in the presence of NH_2Cl (Bichsel & von Gunten 1999), not oxidizing further to from iodate, but reacting with NOM to form iodo-DBPs. The predominant iodo-THM identified in BSW and CSW was CHBrClI (Figure 3). Concentrations as high as 812 nM and 48 nM were determined in BSW and CSW, respectively, at pH 6.5. The high concentrations of iopamidol and bromide could have affected the observed CHBrClI concentrations. This result is consistent with data from Wang *et al.* (2014), who observed that the dominant iodo-THM in two chloraminated source waters from China dosed with Br^- and iopamidol was CHBrClI. When iodide was present as the primary iodo-DBP precursor, they found that iodide favored CHI_3 formation in fulvic and humic acids, as well as the same source waters from China. It is possible that HOI formed from IDOL-DBPs, bromamines, and the other oxidants listed above may have concurrently incorporated into NOM to produce CHBrClI. $CHCl_2I$ was detected in both BSW and CSW (Figure 3). Also, up to 6.5 nM of $CHClI_2$ was found only in BSW at pH 6.5 and 7.5. $CHBr_2I$ was produced in both source waters (Figure 3), whereas $CHBrI_2$ was identified only in BSW in small quantities at pH 6.5. All the iodo-THMs exhibited a decreasing formation trend with increasing pH. The same iodo-THM species were formed in two source waters from China spiked with iopamidol, Br^-, and NH_2Cl at pH 7 (Wang *et al.* 2014). As explained above, the long half-life of HOI in chloraminated aqueous systems enhanced the formation of the iodo-THMs. However, the higher concentrations of THMs in BSW than CSW are attributed to the higher specific ultraviolet absorbance ($SUVA_{254}$) and dissolved organic carbon (DOC) concentration in BSW than CSW.

The only HAN detected in BSW, but below detection in CSW, was dibromoacetonitrile (DBAN). DBAN in BSW was detected at pH 6.5 and 7.5 at concentrations up to 9.4 nM and 1.4 nM, respectively. Hua & Reckhow (2007)

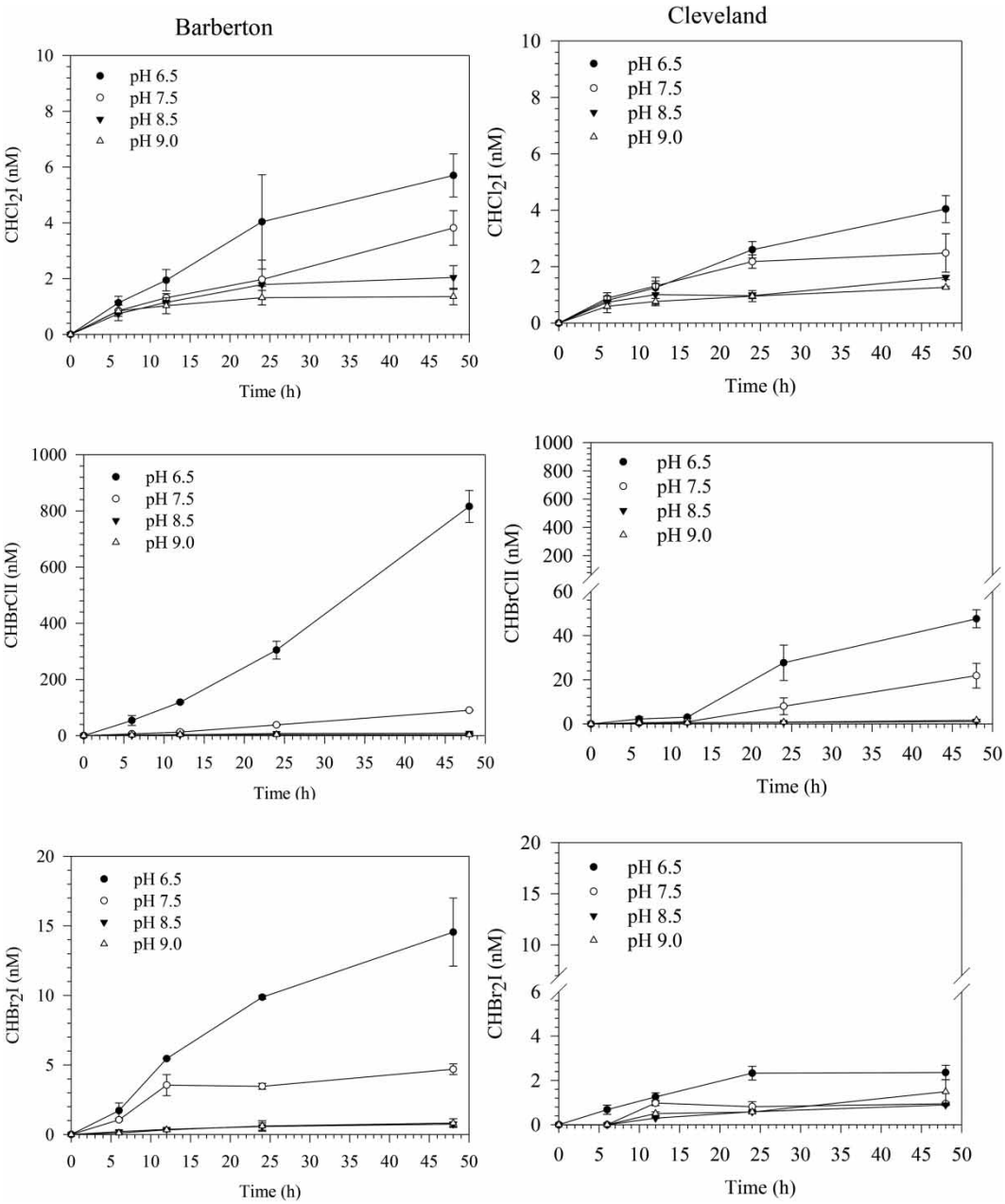

Figure 3 | Iodo-THM formation in chloraminated Barberton and Cleveland source waters as a function of pH. [Iopamidol] = 5 μM, $[Br^-]$ = 15 μM, $[NH_2Cl]$ = 100 μM, $[buffer]_T$ = 4 mM, temp = 25 °C, $DOC_{Barberton}$ = 4.47 mg/L-C, $DOC_{Cleveland}$ = 2.51 mg/L-C. Error bars represent 95% confidence interval for two replicates.

observed that dihaloacetonitriles (DHANs), which include DBAN, were the primary HAN species in chloraminated source waters in North America. Compared to chlorinated source waters under the same experimental conditions, lower quantities of DBAN were formed in the chloraminated source waters because of the high oxidation capacity of chlorine.

In addition, HAA formation trends were observed in the source waters containing iopamidol and bromide. As known, iodo-HAAs were formed in limited quantities compared to other HAAs. Iodo-HAAs detected in both source waters were IAA, chloroiodoacetic acid (CIAA), bromoiodoacetic acid (BIAA), and diiodoacetic acid (DIAA). Formation of these iodo-HAAs was observed at

pH 6.5 and 7.5 and a reaction time of 48 hours. The highest detected iodo-HAA in BSW and CSW was BIAA, with amounts of 7.4 nM and 4.8 nM, respectively, at pH 6.5. Similarly, the greatest amounts of CIAA (5.0 nM) and IAA (3.0 nM) detected in BSW were formed at pH 6.5 at 48 hours. The highest concentrations of these species formed in CSW were approximately equal at pH 6.5 and 7.5 at 48 hours.

Regulated HAA yields were lower in chloraminated than chlorinated source waters (Ackerson *et al.* 2020). Previous studies have reported comparable reductions in HAA concentrations in chloraminated waters compared to chlorinated waters (Kristiana *et al.* 2009; Bougeard *et al.* 2010). Reductions have also been reported for the sum of all HAA9 (nine regulated HAAs; usually 90–95%) when the oxidant was changed from aqueous chlorine to preformed monochloramine (Cowman & Singer 1996). Aqueous chlorine is a stronger oxidant than monochloramine, and that accounts for the higher yields. The major HAAs formed in chloraminated waters are dihaloacetic acids (DHAAs), comprising dibromoacetic acid (DBAA), dichloroacetic acid (DCAA), and bromochloroacetic acid (BCAA) (Cowman & Singer 1996; Duirk & Valentine 2007; Bougeard *et al.* 2010).

Based on each HAA species, BCAA and tribromoacetic acid (TBAA) were the most prevalent HAAs at low and high pH, respectively in BSW at 48 hours. In CSW, TBAA and DCAA were the dominant HAAs produced. BSW has more reactive fulvic and humic fractions than CSW (Ackerson *et al.* 2018). Since bromine is also more reactive than chlorine, BCAA and DCAA may have predominated in BSW and CSW, respectively. Bougeard *et al.* (2010) identified DCAA as the predominant HAA in source waters dosed with NH_2Cl. The differences in identifiable dominant species may be due to the Br^- concentrations in the different experiments as well as the reactivity of the NOM. The concentration of Br^- used in this study was higher.

On the other hand, when the HAAs were grouped into monohaloacetic acids (MHAAs), DHAAs, and trihaloacetic acids (THAAs), DHAAs were the most predominant in BSW and CSW at 48 hours. DHAAs represented 47–61% of the total HAAs in BSW and CSW. DHAAs increased with decreasing pH, as found elsewhere (Cowman & Singer 1996; Duirk & Valentine 2007). Duirk & Valentine (2007) suggested that the active bromine species with a valence of +1 (designated as Br(I)), which is formed by the reactions between Br^- and NH_2Cl, may be very reactive with DHAA precursors. These DHAA precursors have been assumed to contain fast-reacting chromophores, which enhance bromine incorporation (Korshin *et al.* 2007).

The only MHAA detected was bromoacetic acid (BAA) (Figure S4). Of the total produced BAAs at 48 hours, 16–28% and 20–30% were found, respectively, in BSW and CSW at 6 hours. DCAA yields were the highest (33–56%) produced DHAAs in BSW at all pH values (Figure 3). This was consistent with the findings that the depletion of the fast-reacting chromophores in NOM was as a result of the rapid formation of DCAA (Korshin *et al.* 2007). About 3–23% of the total DCAA observed in CSW was produced at 6 hours (Figure 4). The lower yields of DCAA observed in CSW could be attributed to the low DOC concentration of the precursor NOM. BCAA was quantified at all pH levels at the end of 48 hours in the source waters (Figure 3), and although it was detected in BSW from 6 hours at all levels of pH, BCAA showed a slow formation especially at pH 8.5 and 9.0. Appreciable amounts of DBAA were also formed in BSW at low pH, but dropped substantially at higher pH (Figure 3). Formation of DBAA in CSW was observed at pH 6.5–8.5 but was below detection limits at pH 9.0. In modeling DHAA formation, Duirk & Valentine (2007) assumed that bromine and chlorine independently incorporate into DHAA precursors to form each species of DHAA, and is linearly proportional to the quantity of each halogen reacting with NOM. Therefore, the relative concentration of each halogen will impact their incorporation into NOM.

TBAA was the most abundant THAA in the source waters. In BSW, 31–72 nM of TBAA was detected at 48 hours (Figure S5). The concentrations of TBAA in BSW were twofold higher than the yields in CSW (8–34 nM). At higher pH, TBAA was the dominant HAA in BSW, but only 13–35% was formed at 6 hours. In contrast to the yields of TBAA, trichloroacetic acid (TCAA) was formed in smaller quantities in both BSW and CSW (Figure S5). The low yields of TCAA may be attributed in part to the possible direct reactions of NH_2Cl with NOM and HOCl (monochloramine hydrolysis product) with NOM as well as the high concentration of Br^-. Furthermore, small quantities of

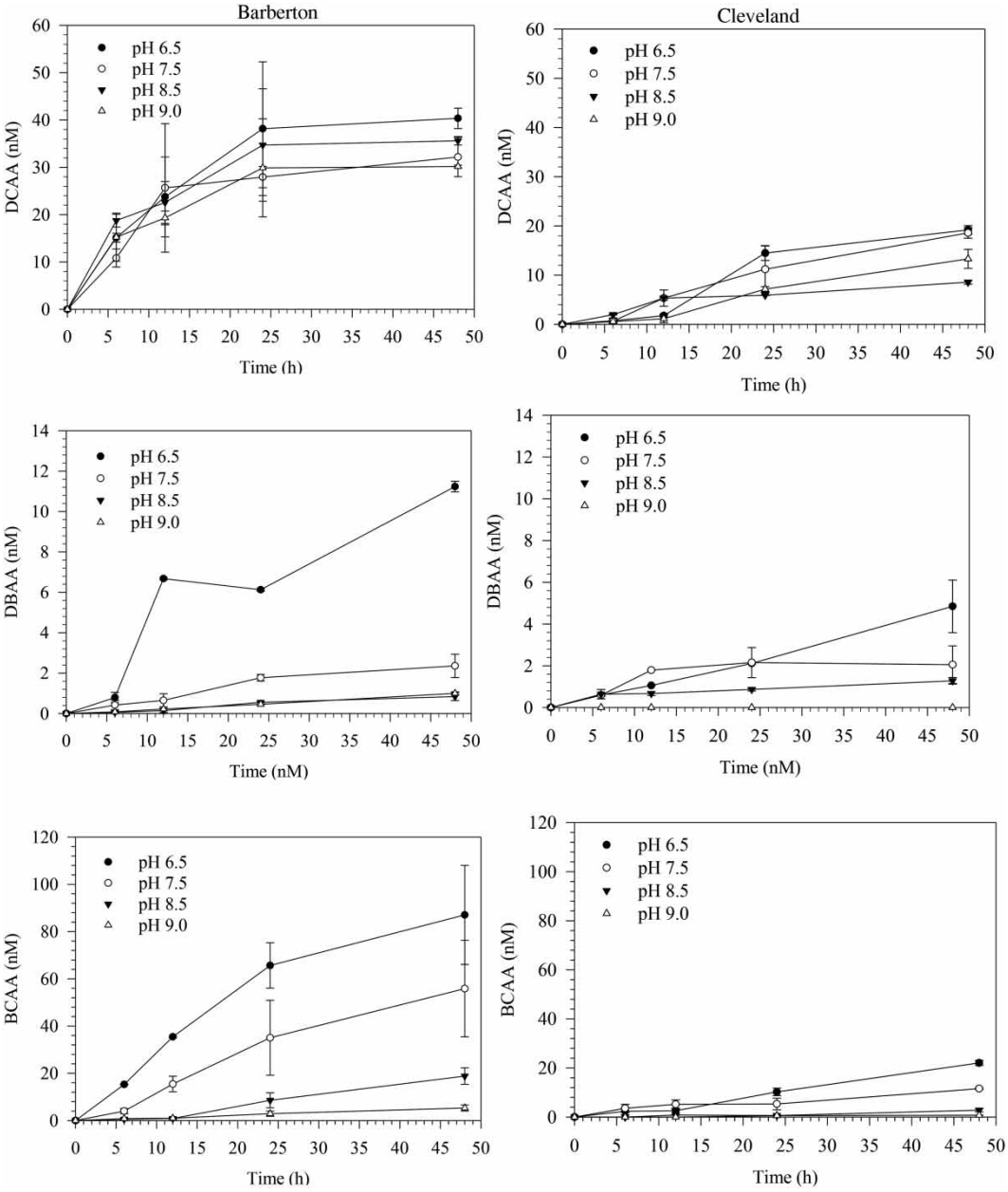

Figure 4 | Formation of DHAA in chloraminated Barberton and Cleveland source waters as a function of pH. [Iopamidol] = 5 μM, $[Br^-]$ = 15 μM, $[NH_2Cl]$ = 100 μM, $[buffer]_T$ = 4 mM, temp = 25 °C, $DOC_{Barberton}$ = 4.47 mg/L-C, $DOC_{Cleveland}$ = 2.51 mg/L-C. Error bars represent 95% confidence interval for two replicates.

bromodichloroacetic acid (BDCAA) was formed at pH 6.5 and 7.5 in BSW and at pH 6.5 in CSW.

TOX distribution

TOX represents the sum of all known halogenated DBPs and unknown TOX (UTOX). TOX comprises TOCl, TOBr, and TOI. Each halogen-specific TOX in this study comprises chloro-THMs ($CHCl_3$), bromo-THMs ($CHBr_3$), bromo-chloro-THMs ($CHBrCl_2$, $CHBr_2Cl$), bromo-iodo-THMs ($CHBr_2I$, $CHBrI_2$), chloro-iodo-THMs ($CHCl_2I$, $CHClI_2$), bromo-chloro-iodo-THMs (CHBrClI), chloro-HAAs (DCAA, TCAA), bromo-HAAs (BAA, DBAA, TBAA), bromo-chloro-HAAs (BCAA, BDCAA), and/or DBAN.

Figure S6 illustrates the distribution of TOI in chloraminated BSW and CSW. The majority of TOI accounted for by individually measured DBPs in both source waters was the bromo-chloro-iodo-THM, B,C,I-THM. In most experiments, B,C,I-THM comprised <1% of TOI. However, at pH 6.5 in BSW, 6.2% of TOI was represented by B,C,I-THM. Generally, all other classes of iodo-DBPs represented <0.5% of TOI. The ratio of quantified iodo-DBPs to TOI was low because of the slow transformation of iopamidol in the presence of NH_2Cl (Ackerson *et al.* 2018). The percentage of unknown TOI (UTOI), which most likely comprises unreacted iopamidol and high-molecular-weight IDOL-DBPs, increased with pH. Earlier studies have shown that more than 90% of iopamidol remain unreacted in the presence of NH_2Cl (Wendel *et al.* 2014).

Of the total produced TOBr, bromo-chloro-THMs (B,C-THMs) and B,C,I-THMs formed >5% each in BSW at pH 6.5 (Figure S7). Bromo-THMs and bromo-HAAs comprised >1% of TOBr at the same pH. As pH increased, a lower proportion of TOBr was accounted for by DBP classes quantified, and the predominant DBP class was bromo-HAAs (except at pH 7.5 in BSW) compared to B,C,I-THMs at pH 6.5. The percentage of bromo-HAA decreased marginally as pH increased but other species saw a larger decrease in BSW. Bromo-HAAs represented the highest percentage of DBPs in CSW at all pH levels (Figure S7). Above pH 6.5, the general observation was that almost all classes of DBPs represented <1% in both source waters. Although a high fraction of Br^- was oxidized to active bromine species (Duirk & Valentine 2007), most of the bromine were not incorporated into precursors to form these specific measured DBPs, thereby increasing the percentage of unknown TOBr (UTOBr) produced. This means a high percentage of active bromine species formed unknown halogenated DBPs in the chloraminated source waters.

The percentage of each class of DBPs was >1% of TOCl at pH 6.5 and 7.5 in BSW, except chloro-iodo-THMs (C,I-THMs) and chloro-iodo-HAA (C,I-HAA), which produced <1% of TOCl (Figure S8). As the pH increased, the percentage of each class of DBPs decreased, while unknown TOCl (UTOCl) increased substantially. At pH 6.5, UTOCl represented approximately 47% of TOCl, which increased with pH to 96% UTOCl at pH 9. Only chloro-THMs and chloro-HAAs produced >1% of TOCl at all pH levels in BSW. A lower percentage of TOCl formed in CSW was composed of the specific DBPs quantified, and UTOCl increased with pH (Figure S8). In general, the classes of chlorinated DBPs produced in CSW were <1% except for B,C,I-THMs and chloro-HAAs at low pH. The low formation of the measured chloro-DBPs in the source waters could be ascribed to the weak reactivity of NH_2Cl with NOM, resulting in predominantly unknown chloro-DBPs.

Relationship between the yields of regulated DBPs and iodo-DBPs

The two classes of DBPs identified in this study were regulated DBPs and iodo-DBPs. The amount of regulated DBPs and iodo-DBPs formed in the source waters were normalized to the DOC of the source waters to form DBP yields. Consequently, the relationship between the yields of regulated DBPs (sum of regulated THMs and regulated HAAs) and iodo-DBPs (sum of iodo-THMs and iodo-HAAs) in the source waters was evaluated. The correlation was carried out to determine if the concentration of iodo-DBPs formed in this study can be predicted from the amount formed from regulated DBPs. This is different from other studies that focused on relationship between THMs and HAAs (Bougeard *et al.* 2010).

The study showed a strong positive correlation ($R^2 = 0.801$) between the yields of regulated DBPs and

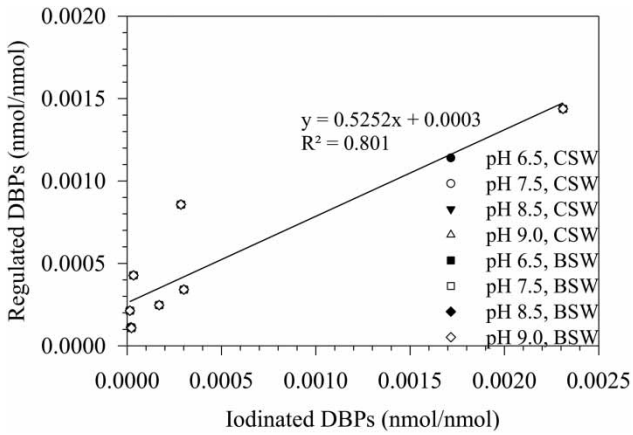

Figure 5 | Relationship between yields of total regulated DBPs and total iodo-DBPs in chloraminated Barberton (BSW) and Cleveland (CSW) source waters. [Iopamidol] = 5 μM, $[Br^-]$ = 15 μM, $[NH_2Cl]_T$ = 100 μM, $[buffer]_T$ = 4 mM, time = 48 hours, temp = 25 °C, $DOC_{Barberton}$ = 4.47 mg/L-C, $DOC_{Cleveland}$ = 2.51 mg/L-C.

iodo-DBPs in the source waters (Figure 5), which was statistically significant ($p = 0.003$). The results show that there is a relationship between the yields of regulated DBPs and iodo-DBPs formed in the source waters. The relationship could be influenced by the types and concentration of precursor in the reactor.

Tian *et al.* (2017) showed that chloramination of pure water containing iopamidol did not produce any regulated THMs or HAAs after a reaction time of 7 days. However, trace to substantial concentrations of iodo-DBPs were formed. It can be inferred that the contribution of iopamidol to non-iodo-DBP formation in this study was minimal, as observed by Duirk *et al.* (2011) using similar experimental conditions. Nonetheless, the addition of Br^- in the presence of NOM increased the total THMs and HAAs formed compared to previous studies (Ackerson *et al.* 2018). Thus, Br^- and NOM contributed substantially to both regulated and iodinated DBP formation with iopamidol. It is possible these precursors in the chloraminated source waters that formed the regulated DBPs may also be responsible for the formation of iodo-DBPs. By contrast, the high concentrations of Br^- and iopamidol in the source waters may have contributed to the observed correlation between regulated DBPs and iodo-DBPs.

CONCLUSIONS

In the presence of bromide and iopamidol, chloramination of source waters produced significant quantities of halogen-specific TOX and DBPs. Of importance to this study were iodo-DBPs, which were formed in significant quantities at low pH in particular. Iodo-DBPs are central to the study because they are highly genotoxic and cytotoxic (Plewa *et al.* 2004; Richardson *et al.* 2008a; Duirk *et al.* 2011). The presence of bromide did not have an impact on TOI, since the bulk of the TOI was unreacted iopamidol or iopamidol DBPs. Approximately equal concentrations of TOCl were formed in the two source waters, whereas higher concentrations of TOBr were formed in BSW, the higher DOC and $SUVA_{254}$ water. The iodo-DBPs formed in appreciable quantities were $CHCl_2I$, CHBrClI, and $CHBr_2I$. Formation of all quantified DBPs, including the iodo-DBPs, was greatest at pH 6.5. Chloramination produced lower concentrations of each of the iodo-DBPs compared to chlorination of the same source waters (Ackerson *et al.* 2020). The addition of Br^- resulted in a decrease in $CHCl_2I$ but an increase in the total quantified iodo-DBP concentration compared to same source waters without Br^- (Ackerson *et al.* 2018). The concentrations of all DBPs formed during chloramination were lower in comparison to chlorination of the same waters. Substantial concentrations of fully chlorinated and brominated DBPs were formed at all pH levels in the waters. Although mixed bromo-chloro-DBPs were observed in the chloraminated waters, there were formation lags at higher pH, especially in the low $DOC/SUVA_{254}$ water. As previously observed in chlorination studies under similar conditions (Ackerson *et al.* 2020), the presence of bromide did suppress the formation iodo-DBPs.

Although substantial concentrations of iodo-DBPs were formed due to high amounts of iopamidol and bromide used in these controlled laboratory reactions, lower concentrations would be expected at environmentally relevant concentrations. However, due to the high toxic potency of iodo-DBPs, their toxicity would still be of concern

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DATA AVAILABILITY STATEMENT

All relevant data are included in the paper or its Supplementary Information.

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