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Relationships between regulated DBPs and emerging DBPs of health concern in U.S. drinking water

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ABSTRACT

A survey was conducted at eight U.S. drinking water plants, that spanned a wide range of water qualities and treatment/disinfection practices. Plants that treated heavily-wastewater-impacted source waters had lower trihalomethane to dihaloacetonitrile ratios due to the presence of more organic nitrogen and HAN precursors. As the bromide to total organic carbon ratio increased, there was more bromine incorporation into DBPs. This has been shown in other studies for THMs and selected emerging DBPs (HANs), whereas this study examined bromine incorporation for a wider group of emerging DBPs (haloacetaldehydes, halonitromethanes). Moreover, bromine incorporation into the emerging DBPs was, in general, similar to that of the THMs. Epidemiology studies that show an association between adverse health effects and brominated THMs may be due to the formation of brominated emerging DBPs of heath concern. Plants with higher free chlorine contact times before ammonia addition to form chloramines had less iodinated DBP formation in chloraminated distribution systems, where there was more oxidation of the iodide to iodate (a sink for the iodide) by the chlorine. This has been shown in many bench-scale studies (primarily for iodinated THMs), but seldom in full-scale studies (where this study also showed the impact on total organic iodine. Collectively, the THMs, haloacetic acids, and emerging DBPs accounted for a significant portion of the TOCl, TOBr, and TOI; however, ~50% of the TOCl and TOBr is still unknown. The correlation of the sum of detected DBPs with the TOCl and TOBr suggests that they can be used as reliable surrogates.

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Introduction

Trihalomethanes (THMs) and haloacetic acids (HAAs) are the major classes of disinfection by-products (DBPs) unintentionally formed during the chlorination/disinfection process (Krasner et al., 2006). THMs and HAAs are associated with various adverse outcomes in epidemiology studies (e.g., cancer and adverse pregnancy outcomes) (Villanueva et al., 2004; Villanueva et al., 2021; Wright et al., 2017) . However, these studies do not confirm a cause and effect relationship with THMs specifically. Nonetheless, most countries have regulations for THMs (Karanfil et al., 2008; Richardson, 2021), whereas in the U.S., both THMs and HAAs are regulated (U. S. Environmental Protection Agency, 2006) . However, the occurrence of THMs and HAAs do not account for the number of bladder cancer cases reported (Bull et al., 2011). Recent toxicological studies indicate that certain emerging DBPs are orders of magnitude more cyto- and genotoxic than the THMs and HAAs (Richardson and Plewa, 2020; Wagner and Plewa, 2017). These include certain nitrogenous (N)-DBPs (Plewa et al., 2008b) (i.e., haloacetonitriles (HANs) (Muellner et al., 2007; Wei et al., 2020), haloacetamides (HAMs) (Plewa et al., 2008a), halonitromethanes (HNMs)) (Plewa et al., 2004a) and certain carbonaceous (C)-DBPs (i.e., haloacetaldehydes (HALs) (Jeong et al., 2015)). The regulation of THMs (and HAAs) are considered by many as chemical surrogates for emerging (known and unknown) DBPs of health concern, however, this notion was recently discounted (Furst et al., 2021). The belief is that the control of regulated DBPs can result in the control of emerging (and unknown) DBPs as well. Also of concern is the speciation of each class of DBPs. The regulated DBPs include chlorinated (Cl) and brominated (Br) species, where iodinated (I)-DBPs (which are not regulated) are more toxic than the Br species, which are more toxic than the Cl analogues (Richardson et al., 2007; Wagner and Plewa, 2017; Yang et al., 2014). One of these I-DBPs, iodoacetic acid, is the most genotoxic DBP studied to-date (Plewa et al., 2004b; Richardson et al., 2008; Wagner and Plewa, 2017), it is tumorigenic in mice (Wei et al., 2013) as well as a rodent teratogen (Gonsioroski et al., 2022; Gonsioroski et al., 2020a; Gonsioroski et al., 2021; Gonsioroski et al., 2020b; Jeong et al., 2016).

Historically, organic precursors to DBPs focused on natural organic matter (NOM) (Reckhow et al., 1990 Subsequently, certain watersheds were found to also be impacted by more N-rich organic matter, i.e., algal organic matter (AOM) (Liu et al., 2018, 2019, 2020, 2022; Oliver, 1983) and treated wastewater effluent organic matter (EfOM) (Dong et al., 2019; Dong et al., 2016; Dong et al., 2017, 2018; Dong et al., 2021; Krasner et al., 2009a; Page et al., 2020). Historically, inorganic precursors to DBPs focused on bromide (Symons et al., 1993) and subsequently on iodide (Bichsel and von Gunten, 2000; Plewa et al., 2004b; Richardson et al., 2008). More recently, another source of iodide was found to be iodine-containing X-ray contrast agents (Duirk et al., 2011), which can be found in treated wastewater.

The nature of these precursors and their amounts in the source waters impact the quality and quantity of DBPs formed. Total or dissolved organic carbon (TOC, DOC) provides a quantitative measure of the NOM, AOM or EfOM present. More TOC results in the formation of more DBPs in general. Ultraviolet absorbance at 254 nm (UVA_{254}) provides a qualitative measure of the NOM. Specific UVA (SUVA) provides an indication of the humic substance content and SUVA <2.0 L/mg-m corresponds to low in humic substances, whereas >4.0 L/mg-m corresponds to high in humic content) (Krasner et al., 1996). High humic substances content indicates high THM and HAA precursor levels (Reckhow et al., 1990). Thus, both the quantity (TOC) and quality (SUVA) impact how much humic-derived DBPs form.

AOM and EfOM have more nitrogenous organic matter than NOM (Krasner et al., 2012; Krasner et al., 2009b). Thus, there are more N-DBP precursors in AOM or EfOM than in NOM. For example, in drinking water, the median ratio of THMs to the dihalogenated HANs (DHANs) was ~10:1 (Oliver, 1983 However, this ratio was often <10:1 in AOM- and/or EfOM-impacted waters (Krasner et al., 2012). An indicator of wastewater impact is the artificial sweetener sucralose (Prescott et al., 2017; Wu et al., 2014). In a study conducted in the U.S., the median occurrence of sucralose in treated wastewater effluent was 27 μg/L (Oppenheimer et al., 2011). Waters that have more wastewater-derived precursors form more N-DBPs, some of which are of higher health concern than some of the humic-derived C-DBPs.

Sources of bromide and iodide include saltwater intrusion (Krasner et al., 1994; Luther et al., 1988), connate water (Braitsch, 1971; Richardson et al., 2008), oil-field brines (Hildenbrand et al., 2016), and certain anthropogenic wastes, including hydraulic fracturing wastewaters (Good and VanBriesen, 2016; Harkness et al., 2015; Liberatore et al., 2017; Liberatore et al., 2020) . In two major surveys in the U.S. Amy et al., 1994; Krasner et al., 1989), the median occurrence of bromide was 56 and 110 μg/L and the 90th percentile was 266 and 548 μg/L. In a recent study (Westerhoff et al., 2021), the median, 75th, and 95th percentile for iodide was < 1, 5, and 26 μg/L, respectively. In some surveys in the U.S., the ratio of bromide to iodide was ~5:1 to ~10:1 (Richardson et al., 2008). Note, the level of bromide in water can vary significantly between wet years and during droughts (Krasner et al., 1994). Measurement of bromide and iodide in the source waters provides an indicator of how much bromine- and iodine-containing DBPs–which are of higher health concern than the chlorine-containing DBPs–can form.

DBP control includes the removal of TOC via enhanced coagulation (Krasner and Amy, 1995) or softening, granular activated carbon (GAC) adsorption (Chiu et al., 2012; Cuthbertson et al., 2019), and biologically active carbon (BAC) or biologically active filtration (BAF) (Cuthbertson et al., 2020; Farré et al., 2011) and/or the use of alternative disinfectants (i.e., ozone (O_3) (Bichsel and von Gunten, 2000; Jacangelo et al., 1989), chlorine dioxide (ClO_2) (Aieta and Berg, 1986), chloramines (NH_2Cl) (Diehl et al., 2000), or UV irradiation (Plewa et al., 2012; Reckhow et al., 2010). However, there can be tradeoffs with the use of these control measures. GAC removes TOC, but neither bromide nor iodide. Thus, the GAC effluent will have a higher bromide to TOC ratio and can result in the formation of more Br-DBPs (Allen et al., 2022; Cuthbertson et al., 2019; Krasner et al., 2016). Based on the potency of the HANs and HNMs, in particular that of the bromi-

nated species, these nitrogen-containing DBPs were the driving agents of the predicted genotoxicity in one GAC study (Krasner et al., 2016). For example, the bromine-containing DHANs are substantially more geno- and cytotoxic, have sufficient concentration and bromine incorporation, and their formation was not controlled by GAC treatment, which resulted in their accounting for much of the predicted geno- and cytotoxicity of the sum of the measured halogenated DBPs (Krasner et al., 2016).

Ozone can form bromate (a regulated DBP in the U.S. and elsewhere), but recent studies using the chlorine or ammonia process and/or pH suppression have minimized bromate formation (Buffle et al., 2004). Chlorine dioxide forms chlorite (a regulated DBP in the U.S.), which can be controlled by limiting the chlorine dioxide dose (Aieta and Berg, 1986). Chloramines can form N-nitrosodimethylamine (NDMA) (which is being considered for regulation in the U.S.) and I-DBPs (which are highly toxic but are currently not regulated). However, pre-oxidation with chlorine or ozone can destroy NDMA precursors (McCurry et al., 2015) and can oxidize iodide to iodate, a sink for the iodide (Bichsel and von Gunten, 1999). Thus, controlling the formation of regulated and emerging DBPs requires careful balancing.

In addition to controlling regulated and emerging DBPs, there is concern over unknown DBPs. Total organic halogen (TOX) is a measure of the known and unknown halogenated DBPs. THMs and HAAs account for the highest percentage of the TOX in chlorinated or chlorinated/chloraminated waters (Zhang et al., 2000; Krasner et al., 2006). The emerging DBPs account for a small portion of the TOX (Zhang et al., 2000; Krasner et al., 2006). Typically, the regulated and emerging DBPs that are detected account for ~50% of the TOX. Although ozone or chloramines form less TOX than chlorine, more of the TOX from ozone or chloramines is unknown (Zhang et al., 2000). TOX measurements can be broken down to total organic chlorine (TOCl), total organic bromine (TOBr), and total organic iodine (TOI) (Cuthbertson et al., 2019; Hua and Reckhow, 2006). This allows for a better assessment of the more toxic Br- and I-DBPs. Another way in which Br-DBPs are examined is via the bromine incorporation factor (BIF), which represents the molar amount of bromine in a class of DBPs divided by the molar amount of that class of DBPs (Symons et al., 1993). For THMs, BIF ranges from 0 (all chloroform) to 3 (all bromoform) (where 1 corresponds to bromodichloromethane on average). For DHANs, BIF ranges from 0 (all dichloroacetonitrile) to 2 (all dibromoacetonitrile) (where 1 corresponds to bromochloroacetonitrile on average). Alternatively, BIF divided by the number of halogens (X) (BIF/X or the normalized bromine incorporation factor) ranges from 0 to 1 for all classes of DBPs, which allows easier comparisons between different DBP classes. In some studies, there was more bromine incorporation into DHANs than into THMs (Obolensky and Singer, 2005). As the BIF for THMs increases, there is more formation of known and unknown Br-DBPs, which are of higher health concern.

As the sum of the four regulated THMs (THM4) is typically used in regulations and epidemiology studies, it is important to determine if this and/or other parameters can best guide regulators, epidemiologists, researchers, and utilities. The objectives of this paper include determining what percentage of the TOCl, TOBr, and TOI are accounted for by the measured (regulated and emerging) DBPs and to what extent each class of DBPs accounts for this percentage. Is bromine incorporation into emerging DBPs similar to that of the THMs? Does the presence of wastewater impact the THM/DHAN ratio? How does pre-oxidation impact I-DBP formation? These questions were examined using data from a group of U.S. utilities that represent a range of water quality issues, as well as different treatment options to control DBP formation.

1. Materials and methods

1.1. *Survey*

Eight representative utilities in the U.S. were studied (two from the Pacific west, two from the Rocky Mountain region, one from the south-central region, two from the Midwest, and one from the Southeast). Appendix A Table S1 summarizes the treatment processes and water quality of each plant. Note, plant 6 had 2 parallel trains (plants 6A and 6B), which had very different source waters and treatment processes. The DBPs formed in the distribution system were derived from the 2 trains. The 8 plants show how different treatment and disinfection processes can be used for source waters with different water qualities. There are no group classifications *per se*. Plants 1 and 2 used GAC, with chlorine as the secondary disinfectant. All other plants used chloramines as the secondary disinfectant. Plant 3, which used ozone for pre-oxidation, treated water from the same source as plant 2 (which had a moderate amount of bromide). Plant 4 (which also treated water with a moderate amount of bromide) used chlorine for pre-oxidation with a very short free chlorine contact time. Plants 5 and 6A treated water from the same watershed, which was significantly impacted by wastewater. Plant 6A used riverbank filtration (RBF) and soil aquifer treatment (SAT), which are often used to treat wastewater (Karakurt et al., 2019). Plant 6B was from a reservoir that was much less wastewater impacted. Plant 7 went to a chlorine "burn" once per year (used chlorine as the secondary disinfectant instead of chloramines) to control nitrifying bacteria that may develop in a chloraminated distribution system (Alfredo, 2021; Seidel al., 2005). The chlorine burn is a common practice by many public water systems throughout the U.S. to reduce the number of the bacteria so that a satisfactory disinfectant residual can be maintained throughout the distribution system. Chlorine conversions can be used as a preventative strategy to stop nitrification. Plant 8 used several different source waters, which included seawater that was desalinated, groundwater, and a high-TOC surface water. This plant also underwent a chlorine burn once a year.

Each plant was sampled two to three times in each of three years. Samples were collected on a seasonal basis (e.g., a cold/wet season, a warm/dry season). Plants 7 and 8 were sampled with chloramines and with a chlorine burn. The plant influents were sampled for TOC, UV_{254}, bromide, iodide, and sucralose (Appendix A Table S1). The plant effluents were sampled for TOC and UV_{254} to determine how much organic matter was removed (Appendix A Table S1). The treated water in the distribution system was sampled at an average detention time (which was usually of the order of several days or more).

The treated water was sampled for THM4, the nine HAAs (HAA9) (two monohalogenated, three dihalogenated (DXAAs), and four trihalogenated (TXAAs)), the nine bromochloro HANs plus iodoacetonitrile (IAN), the nine bromochloro HAMs plus iodo HAM (IAM), chloroiodo HAM (CIAM), bromoiodo HAM (BIAM), and diiodo HAM (DIAM), the three dihalo HNMs and the four trihalo HNMs (THNMs), the nine HALs and iodo HAL (IAL), nine haloketones (HKs), the six I-THMs, four iodo acetic acids (IAAs), TOCl, TOBr, and TOI.

1.2. *Analytical methods*

TOC and UV_{254} were analyzed with standard methods (American Public Health Association, 2005). Bromide and iodide were measured using ion chromatography (IC) with a conductivity detector Allen et al., 2022). Sucralose was determined using direct injection liquid chromatography (LC)-mass spectrometry (MS)/MS (Prescott et al., 2017). THMs (Munch and Hautman, 1995) and HAAs (Munch et al., 1995) were analyzed with liquid-liquid extraction (LLE), derivatization with acidic methanol for the HAAs, and gas chromatography (GC)-electron capture detection (ECD). HANs, HAMs, HNMs, HALs, HKs, and I-THMs were measured using LLE and GC-MS (and o-(2,3,4,5,6-pentafluorobenzyl)hydroxylamine (PFBHA) derivatization for mono- and di-HALs) (Allen et al., 2022; Cuthbertson et al., 2020). IAAs were determined by LLE, diazomethane derivatization, and GC-MS/MS (Allen et al., 2022; Cuthbertson et al., 2020). TOCl, TOBr, and TOI were analyzed with GAC sorption, combustion, measurement of Cl^-, Br^-, and I^- with IC and a conductivity detector or an inductively coupled plasma (ICP)-MS (Allen et al., 2022).

1.3. *Box-and-whisker plots*

The box represents the 25th and 75th percentile values, and the two whiskers represent the minimum and maximum (excluding outlier values). The line running horizontally through the box is the median value. Potential outliers are marked as "o" (values >1.5 times but <3 times the length of the box) and extreme values are marked as "*" (values >3 times the length of the box (e.g., Fig. 5). Box-and-whisker plots were generated with IBM SPSS Statistics software.

1.4. *Pearson product moment correlation*

Pearson product moment correlation (*r*) analyzes was conducted on the data to determine the strength of association between pairs of variables. A strong, medium and low correlation are associated with *r*-values of ±0.50 and ±1.0, ±0.30 and 0.49, and below ±0.29, respectively. The *P* value for the correlation analyzes is the probability from *t*-tests run on the null hypothesis that the two variables are not linearly related (Box et al., 1978).

2. Results and discussion

2.1. *Overview*

The interquartile range (25th to 75th percentile) THM4 for the 8 plants was 20 to 42 µg/L (Appendix A Fig. S1). The 10th to 90th percentile range was 14 to 74 µg/L. The minimum, median, and maximum values were 11, 32, and 248 µg/L, respectively. These concentrations provide some perspective to that found in other studies and surveys (e.g., most of the THM4 results in this study were less than the U.S. regulatory level of 80 µg/L).

GAC plants 1 and 2 removed 69%–77% of the TOC, except for one sample event at plant 1. In that instance, they removed 48% of the TOC (lowered the TOC from 1.96 to 1.01 mg/L). Note, the treatment goal at plant 1 was to lower the TOC down to 1.0 mg/L, which was achieved. Plant 1 had THM4 of 12–20 µg/L, whereas plant 2 had THM4 of 39–64 µg/L (both plants used chlorine). Plant 2 had higher THMs, in part, because the bromide levels were much higher in plant 2's source water. Note, hypobromous acid/hypobromite ion (formed during the chlorination of bromide-containing water) forms halogenated DBPs more strongly than chlorine (Krasner et al., 1994). Moreover, bromine-containing DBPs weigh more than chlorine-containing DBPs.

Plant 3, which treated water from the same watershed as plant 2, used ozone and chloramines and had THM4 of 11–14 µg/L. Removal of TOC or the use of alternative disinfectants can control THM formation. In this case, the use of ozone/chloramines reduced THM formation more than GAC (with chlorine).

Plant 7 had THM4 of 15–26 µg/L with chloramines and THM4 of 248 µg/L during the chlorine burn. The effluent TOC was 4.8 mg/L, which is moderately high. Plant 8 had THM4 of 36 µg/L with chloramines and THM4 of 75–79 µg/L during the chlorine burn. The treatment plant effluent and groundwater TOC was 1.2–3.9 mg/L.

Plant 4 had THM4 of 29–43 µg/L. Although the plant had moderate levels of TOC and bromide, the free chlorine contact time before choramine addition was very short (0.5–4.8 min).

Plants 5 and 6A treated water high in wastewater impact. Plant 5 used ultrafiltration (UF) with chlorine and chloramines. They had 39%–49% TOC removal and THM4 was 34–35 µg/L. Plants 6A and 6B had miscellaneous treatment processes (e.g., BAC), where TOC removal at plant 6B was 41%–44%. They used chlorine and chloramines and THM4 was 20–24 µg/L.

The eight plants in this study treated waters with a range of water qualities (many moderately high in TOC and/or bromide) with a range of precursor removal processes and/or alternative disinfectants. They all complied with the U.S. THM regulatory limit, except for during the chlorine burn at plant 7; however, the U.S. standard is based on a running annual average (it is not based on a maximum allowable concentration). (Moreover, the current standard is based on sampling during a representative time period in each quarter, where the chlorine burn is not sampled.) Bladder cancer has a long latency period (long-term exposure) and is not due to short-term exposure, thus, individual excursions are not regulated in the U.S.

As N-, Br-, and I-DBPs are more toxic, the rest of the results section will focus on these types of DBPs. Moreover, unknown DBPs are of concern, as they likely include unknown DBPs of health concern (the emerging DBPs account for some of the toxicity, but likely not all).

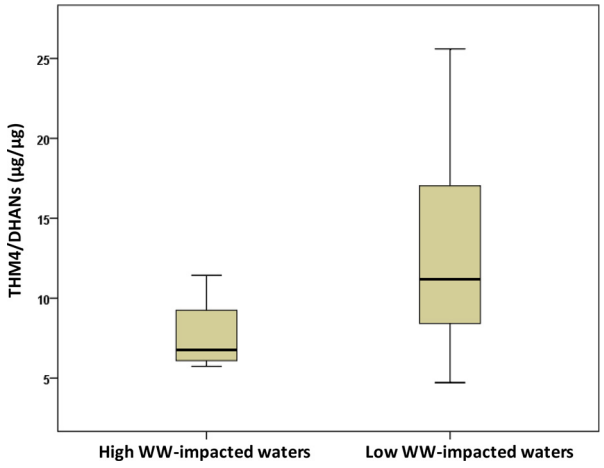

Fig. 1 – Impact of the presence of wastewater on the relative formation of an N-DBP (i.e., DHANs) to a C-DBP (i.e., THMs).

2.2. *Impact of wastewater on DHAN formation*

Fig. 1 shows the impact of the presence of wastewater (sucralose as an indicator) on the relative formation of a group of N-DBPs (i.e., DHANs) to a C-DBP group (i.e., THMs). Plants with low sucralose (0.1–1.4 (median = 0.5) µg/L) had THM4/DHAN ratios of 4.7 to 72 (median = 13). Excluding 2 outliers from plant 4, the THM/DHAN ratio ranged from 4.7 to 26. As noted, typically the THM/DHAN ratio in drinking water samples in the U.S. is ~10:1 on average (Oliver, 1983). Note, most of the THM/DHAN ratios for the low-sucralose group was <20:1. Plants 5 and 6 with high sucralose (4.6–10 (median = 6.9) µg/L) (results for plant 6 based on the flow-weighted amounts in plants 6A and 6B) had THM4/DHAN ratios of 5.7 to 11 (median = 6.8). High wastewater impact means more organic nitrogen, which means more DHAN precursors (and lower THM4/DHAN ratio (e.g., <10]) (Krasner et al., 2012). Note, based on a median occurrence of sucralose in wastewater effluent (i.e., 27 µg/L) (Oppenheimer et al., 2011), plant 6A was 44% to 78% wastewater impacted. This watershed is known to be effluent dominated in certain times of the year (e.g., low river flow). One of the samples from plant 5 had an intermediate value of sucralose (2.8 µg/L) and was not included in the high sucralose group. Its THM4/DHAN ratio (22:1) was higher than the other plant 5 sample (THM4/DHAN = 11:1) because it had less sucralose in this event (2.8 versus 8.0 µg/L). There was a small overlap between the interquartile ranges for the high and low wastewater-impacted groups (THM4/DHAN ratios of 6–9 versus 8–17, respectively), but the general trend was that low wastewater-impacted waters had a higher THM4/DHAN ratio.

3.3. *BIFs of the different classes of DBPs*

Table 1 summarizes the linear regressions and the correlation analyzes of the different classes of DBPs. Appendix A Fig. S2 shows selected correlation analyzes of the BIFs of the THMs with that of DXAAs ($r = 0.96$; $P \leq 0.001$), TXAAs ($r = 0.93$; $P \leq 0.001$) and DHANs ($r = 0.87$; $P \leq 0.001$). Most of the linear regressions between the THMs and the other classes of DBPs had slopes ≤1.2 or ≥0.8. Thus, the degree of bromine incorporation into the other classes of DBPs was similar to that of the THMs (slope >1.0 means more bromine incorporation into the other class of DBPs, whereas slope <1.0 means more bromine incorporation into the THMs). For example, the slope for the linear regression between the DHANs and THMs was 0.99 and a strong significant correlation of $r = 0.87$ (Appendix A Fig. S2), which means bromine incorporation into each of these classes of DBPs was essentially the same (which is in contrast to some other studies) (Obolensky and Singer, 2005). What is important is that as bromine incorporation in the THMs (or HAAs) increases, it also increases for the emerging DBPs. *Thus, epidemiology studies that suggest an association between the occurrence of brominated THMs and an adverse health effect also suggest an association with brominated emerging DBPs*. This is important, as many toxicology studies indicate that brominated emerging DBPs are of higher health concern than the THMs or HAAs (Richardson and Plewa, 2020; Richardson et al., 2007; Wagner and Plewa, 2017).

Fig. 2 shows a strong correlation ($r = 0.63$; $P \leq 0.002$) of the normalized bromine incorporation factor (BIF/X) and that of

Table 1 – Linear regressions and Pearson's product moment correlation analyzes of bromine incorporation factors (BIFs).

Y-axis	X-axis	Slope	R^2 [c]	r [d]	P [e]
DXAAs	THMs	1.24	0.92	0.96	$P \leq 0.001$
TXAAs	THMs	1.11	0.87	0.93	$P \leq 0.001$
DHANs	THMs	0.99	0.76	0.87	$P \leq 0.001$
THANs[a]	THMs	1.10	0.60	0.78	$P \leq 0.05$
THAs	THMs	0.86	0.71	0.84	$P \leq 0.001$
DHAMs	THMs	0.86	0.44	0.66	$P \leq 0.002$
THAMs	THMs	0.80 (1.42[b])	0.38 (0.91[b])	0.62	$P \leq 0.05$
THNMs	THMs	0.86	0.57	0.76	$P \leq 0.001$
TXAAs	DXAAs	1.01	0.90	0.95	$P \leq 0.001$
DHANs	DXAAs	0.81	0.78	0.88	$P \leq 0.001$
THANs[a]	DHANs	0.83	0.68	0.82	$P \leq 0.03$
THAMs	DHAMs	0.37 (0.56[b])	0.09 (0.20[b])	0.30	$P = 0.36$

[a] Limited data. [b]Removed a significant outlier. [c]R^2, the coefficient of determination, expressing the proportion of the variance in the response variable that can be explained by the predictor variables in the regression model. [d]r The coefficient of correlation. [e]P is the probability from t-tests run on the null hypothesis that the two variables are not linearly related.

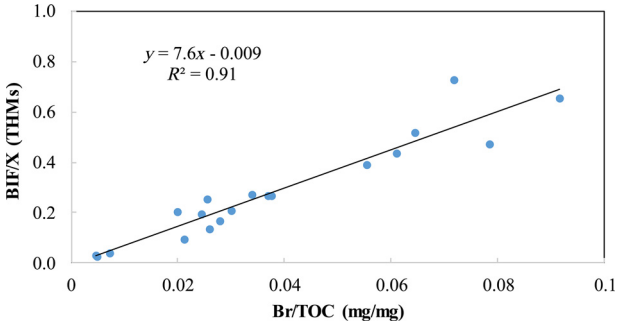

Fig. 2 – Correlation of BIF/X with that of the Br/TOC ratio for THMs.

the bromide to TOC (Br/TOC) ratio for the THMs. As the Br/TOC ratio increased, there was more bromine incorporation. Note, in this study, TOC was measured at the plant influent and plant effluent. An important question is which TOC to use in the Br/TOC ratio. If a plant used pre-chlorination and post-chloramination (e.g., plant 5), most of the DBPs were formed during pre-chlorination, so the raw water TOC was used in the Br/TOC ratio. If chlorine (and chloramines) was added to the treated water (e.g., plants 1, 3, 6), the treated water TOC was used, as the raw water was not chlorinated. Plant 2 was removed from this analysis, as it had very high bromide (e.g., 334 µg/L) and very low TOC after GAC usage (e.g., 1.0 mg/L), resulting in a much higher Br/TOC ratio (e.g., 0.33 mg/mg) than any other plants in the study (i.e., Br/TOC <0.10 mg/mg). Appendix A Table S2 summarizes the linear regressions and the correlations for the other DBPs classes. Except for the DXAAs (slope = 9.2), the slopes were quite similar (i.e., 7.0–7.7). For example, for a Br/TOC ratio of 0.06 mg/mg, the normalized bromine incorporation factors for the THMs and TXAAs were 0.45 and 0.40 (based on the linear regression slope and intercept, respectively (e.g., for the THMs, $y = 7.6\,x - 0.009$ (Fig. 2)). The latter normalized bromine incorporation factors indicate that the average species was a mixed bromochloro DBP (e.g., normalized bromine incorporation factor is 0.33 and 0.67 for the average DBP being a bromodichloro and dibromochloro species, respectively). Thus, these relationships show how the Br/TOC ratio impacted bromine incorporation in the same way for each of the different DBP classes (where there was more bromine incorporation in the DXAAs in this data set). Note, the linear regressions were ($R^2 = 0.72$–0.91), except for the THNMs and DHAMs, ($R^2 = 0.48$–0.56). Note, the coefficient of determination (R^2) measures the percent of variation in the y variable that can be attributed to variation in the x variable. An R^2 value of 0.9, for example, means that 90% of the variation in the y data is due to variation in the x data. The correlation coefficients for the BIF/X with Br/TOC had significant r values, ranging from 0.80 to 0.63 for most of the DBPs, indicating strong correlations. The r values for the THNMs and DHAMs expressed a medium strength of correlation, with both having $r = 0.48$; $P \leq 0.05$.

In addition, brominated DBPs that are not measured can be predicted. This was first done to predict the concentrations of the brominated analogues of trichloroacetic acid (TCAA) based on the concentration of TCAA and that of each of the four THM species (e.g., bromodichloroacetic acid = TCAA * bromodichloromethane/chloroform (based on molar concentrations)) (Singer, 2002). To this day, the vast majority of HAA data from U.S. utilities does not include the brominated analogues of TCAA, as these brominated HAAs are not regulated and not widely measured.

2.4. *Impact of pre-oxidation on TOI formation*

Fig. 3 shows a strong, significant correlation ($r = 0.97$; $P \leq 0.001$) of the impact of free chlorine contact time (before ammonia addition to form chloramines for the chloramine plants) on TOI formation. For plants with very short contact times (0.5–4.8 min), 14%–16% of the iodide was transformed into I-DBPs (as TOI) in the chloraminated distribution systems. Higher contact times (143–187 min) resulted in 6%–11% of the iodide

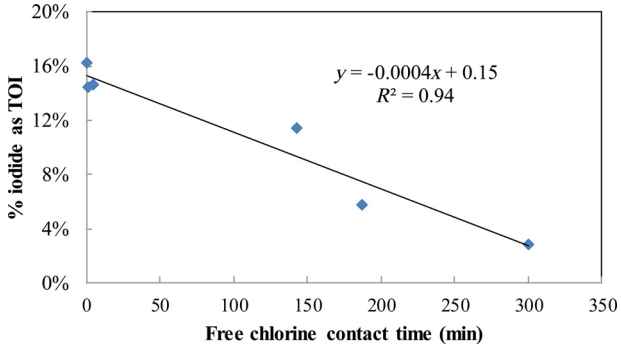

Fig. 3 – Impact of free chlorine contact time on TOI formation.

as TOI. The remaining plant (plant 2) used chlorine for primary and secondary disinfection. So, the impact of chlorine in this plant was compared to TOI formation in the plant effluent. Only 3% of the iodide was transformed to TOI. Thus, some I-DBPs can form from chlorine (not all the iodide was converted to iodate). In a previous study, in which only IAAs were examined, 0.2% of the iodine was transformed to IAAs when there was a long free chlorine contact time (20 min to 1.3 hr) and 0.7%–1.6% of the iodine as IAAs were detected with a short contact time (1–5 min) (Krasner, 2012). Jones et al. (2011) studied the impact of free chlorine contact time on I-THM formation. For two samples with 80 µg/L of iodide, the iodide utilization factors were 9.6%–18% and 1.5%–5.0% for free chlorine contact times of 5 and 20 min, respectively. The iodide utilization for the I-THMs was of the same order of magnitude as that of the TOI, whereas that of the IAAs was much lower, as the I-THMs make up a larger percentage of the TOI than the IAAs (Fig. 6).

Because there were limited iodide results at or above the reporting level (10 µg/L) in the current study, the impact of free chlorine contact time could only be evaluated for a limited number of samples. As the 75th percentile occurrence of iodide in a previous survey was 5 µg/L (Westerhoff et al., 2021) this shows that a reporting level of 10 µg/L would preclude the detection of iodide in a number of samples. Appendix A Fig. S3 shows the relationship of iodide to bromide in the current study. The surface waters had a bromide to iodide ratio of 5:1 to 10:1, which is consistent with that reported previously (Richardson et al., 2008). Groundwaters from one region in the U.S. had a bromide to iodide ratio less than 5:1. For the samples with iodide <10 µg/L, it was assumed that the bromide to iodide ratio was 10:1. This suggested that the missing iodide results ranged from 2.0 to 33 µg/L with a median of 6.6 µg/L. This confirms that iodide was not detected in several samples, as their likely occurrence was <10 µg/L. Note, in this study, 6 of 22 samples had 22–32 µg/L of iodide (≥73rd percentile), whereas the 95th percentile occurrence in U.S. waters in a nationwide study was 26 µg/L (Westerhoff et al., 2021).

2.5. *Percentage of TOCl, TOBr, and TOI accounted for*

In a previous study, halogenated DBPs accounted for 12%–33% (median = 24%) of the TOCl and 6%–58% (median = 39%)

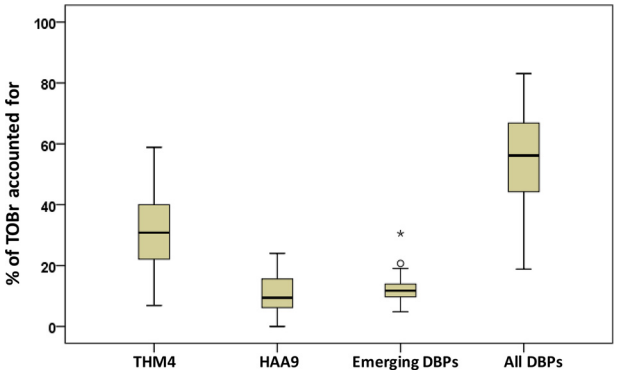

Fig. 4 – Percentage of TOBr accounted for by THMs, HAAs, and emerging DBPs.

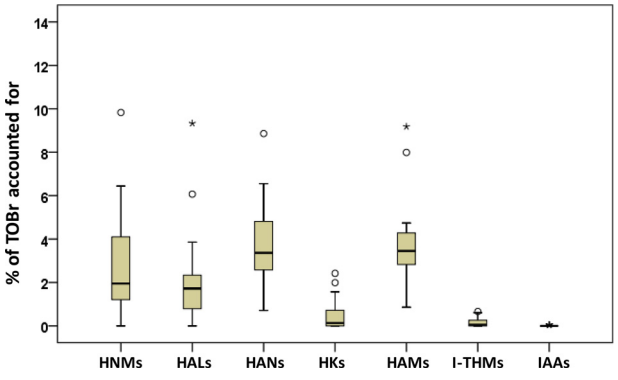

Fig. 5 – Percentage of TOBr accounted for by emerging DBPs.

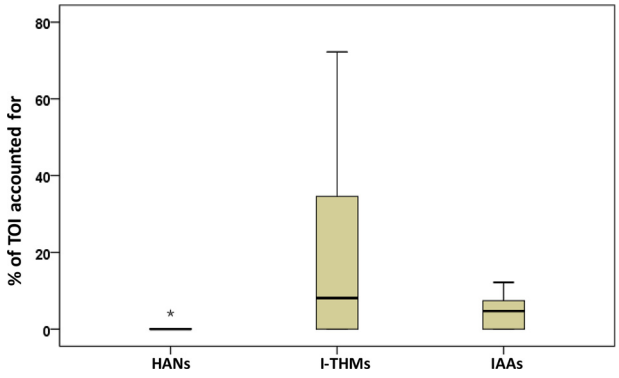

Fig. 6 – Percentage of TOI accounted for by emerging DBPs.

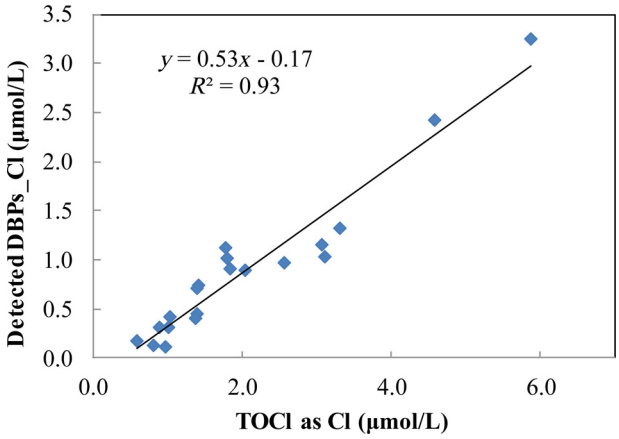

Fig. 7 – Correlation between the sum of the detected DBPs as chlorine and that of TOCl.

of the TOBr (Krasner et al., 2006). (Note, TOI was not measured in the latter study.) In the current study, 9%–82% (median = 39%) of the TOCl (Appendix A Fig. S4) and 19%–83% (median = 56%) of the TOBr (Fig. 4) was accounted for by the halogenated DBPs. In addition, the sum of the halogenated DBPs accounted for 0–72% (median = 17%) of the TOI (Fig. 6). In both studies, THM4 and HAA9 accounted for most of the TOBr and TOCl. Although the emerging DBPs accounted for less of the TOX, it represents a more toxic portion. I-DBPs are more toxic than Br-DBPs, which are more toxic than Cl-DBPs, and N-DBPs are more toxic than C-DBPs (Plewa et al., 2008b; Wagner and Plewa, 2017). In terms of TOBr, HANs and HAMs had the highest medians of the emerging DBPs, followed by HNMs and HALs (Fig. 5). These are the DBPs (HANs, HNMs, HAMs, HALs) that have been found to be more toxic than the THMs and HAAs (Wagner and Plewa, 2017). Appendix A Fig. S5 shows the percentage of TOCl accounted for by the emerging DBPs. In terms of TOI, I-THMs accounted for a larger percentage than the IAAs (Fig. 6), however, IAAs are much more toxic (Plewa et al., 2008a; Richardson et al., 2008; Wagner and Plewa, 2017; Wei et al., 2013). *Therefore, both the toxicity and the mass of each DBP must be considered.*

Fig. 7 shows the strong correlation ($r = 0.96$; $P \leq 0.001$) between the sum of the detected DBPs as chlorine and that of TOCl. Fig. S6 illustrates the correlation between the sum of the detected DBPs as bromine and that of TOBr ($r = 0.85$; $P \leq 0.001$). Note, the point for plant 7 during the chlorine burn was removed from Fig. 7, as its value (16 µM as chlorine) was significantly higher than all the other data (≤3 µM as chlorine). When there is one data point beyond the rest of the data, the outlier greatly impacts the linear regression line. In addition, the point for plant 6 during the third sample event was also removed, as it was a significant outlier from the linear regression line. Significant and very high correlations between the Cl-DBPs and TOCl, and between the Br-DBPs and TOBr were calculated. These strong correlations indicate that TOCl and TOBr are good surrogates for the detected Cl- and Br-DBPs. Although the correlation for the I-DBPs was lower, the association was statistically significant ($r = 0.64$; $P \leq 0.001$) and suggests that TOI was a good surrogate for the detected I-DBPs. Most of the TOI values were quite low (<0.02 µmol/L, whereas most of the TOBr values were >0.4 µmol/L). The linear regression of the detected DBPs as I versus TOI as I expressed a coefficient of determination ($R^2 = 0.40$) that indicated a degree of scatter for the I-DBPs that probably reflects, the low level of occurrence of TOI in this dataset. Nonetheless, the combination of measuring I-THMs, IAAs, and TOI present useful information (Fig. 6) on the occurrence of I-DBPs.

In addition to evaluating the correlation between the sum of the detected DBPs as chlorine and that of TOCl, the correlations between THM4 and TOCl, HAA9 and TOCl, and emerging DBPs and TOCl were examined. The coefficients of determina-

Table 2 – Impact of chlorine burn on THM, HAA, emerging DBP, and TOX formation at plant 7.

	3/14/2018	9/6/2018	6/18/2019
Disimfectant	Chloramines	Chlorine	Chloramines
TOC (mg/L)	6.3	5.8	5.4
Bromide (μg/L)	45	27	27
Iodide (μg/L)	<10	<10	<10
THM4 (μg/L)	15	248	26
HAA9 (μg/L)	36	271	27
TOCl as Cl^- (μg/L)	110	570	117
TOBr as Br^- (μg/L)	16	35	9.8
TOI as I^- (μg/L)	0.9	1.0	1.1
Percentage of TOCl accounted for as			
THM4	11%	37%	18%
HAA9	17%	28%	12%
Emerging DBPs	4%	18%	9%
All DBPs	33%	82%	40%
Percentage of TOBr accounted for as			
THM4	7%	40%	13%
HAA9	7%	24%	12%
Emerging DBPs	5%	19%	31%
All DBPs	19%	83%	56%
Percentage of TOI accounted for as			
Emerging DBPs	6%	18%	20%

tion for linear regression (R^2) were 0.79, 0.93, and 0.86, respectively. The slopes were 0.25, 0.18, and 0.12, respectively. The sum of the slopes (i.e., 0.55) matched that of the linear regression with the sum of the detected DBPs (i.e., 0.55), demonstrating how each of these subclasses of DBPs contributed to the sum.

In addition to examining the percentage of TOX accounted for by detected DBPs, another issue is identification of the unknown TOX. Although many new DBPs have been identified and measured, the unknown portion still is of the order of 50%. One possibility is the unknown TOX includes high molecular weight NOM that has been halogenated, but not broken down to masses that can be detected with a GC-mass spectrometer (700 Da or less) (Khiari et al., 1996). Another possibility is the switch to alternative disinfectants. It was shown that ozone and chloramines produce less TOX than free chlorine, but a larger percentage of the ozone- and chloramine-generated TOX is unknown (Zhang et al., 2000). Table 2 shows the impact of the chlorine burn on THM, HAA, emerging DBP, and TOX formation at plant 7. Chloramines not only produced much less THMs and HAAs than chlorine, but also produced less TOCl and TOBr. (TOI was low in all cases, as this low-bromide water had no detectable iodide.) When chlorine was used, 82% of the TOCl and 83% of the TOBr was accounted for. When chloramines were used, 33%–40% of the TOCl and 19%–56% of the TOBr was accounted for. Nonetheless, when chloramines were used, 9.8–16 μg/L of TOBr was produced, whereas when chlorine was used, 35 μg/L of TOBr was produced. Therefore, on an absolute basis, chloramines produced less TOBr than chlorine. Allen et al. (2022) also examined the impact of the chlorine burn at plant 8 on TOX (detected and unidentified DBPs), as well as the impact of the chlorine burn on cytotoxicity at both plants.

3. Discussion, summary, and conclusions

The occurrence of a wide range of regulated and emerging DBPs in drinking waters from eight plants in the U.S. were evaluated. These plants treated source waters with a wide range of water qualities (e.g., TOC = 0.8–10 mg/L; <1% to 78% wastewater impacted; bromide = 20–344 μg/L and iodide <10–32 μg/L (not counting the seawater)). The plants used a wide variety of treatment processes (e.g., conventional, GAC, ozonation, biofiltration, membranes) and disinfectants (chlorine, chloramines [including a periodic chlorine burn], ClO_2, ozone, UV).

Plants that treated high-wastewater-impacted waters formed lower THM to DHAN ratios (e.g., median = 6.8) than waters much less impacted (e.g., median = 13) due to the presence of more organic nitrogen and DHAN precursors. Waters with higher bromide to TOC ratios had more bromine incorporation into the different classes of DBPs. The bromine incorporation factors for the regulated and emerging DBPs were similar, suggesting that epidemiology studies that propose an association between brominated THMs and adverse health effects may be due to the presence of brominated emerging DBPs of higher health concern. For plants with very short free chlorine contact times before ammonia addition to form chloramines (e.g., ≤5 min), 15% of the iodide was transformed into I-DBPs (as TOI) in the chloraminated distribution systems. Higher contact times (e.g., 143–187 min) resulted in 6%–11% of the iodide as TOI, where there was more oxidation of iodide to iodate, a sink for the iodide.

On a median basis, 39% of the TOCl, 56% of the TOBr, and 17% of the TOI was accounted for by the measured halogenated DBPs. THMs and HAAs accounted for most of the TOBr and TOCl. Although the emerging DBPs accounted for less of the TOCl and TOBr, it represents a more toxic portion. I-THMs accounted for a larger percentage of the TOI than the IAAs, however, IAAs are much more toxic. Therefore, both the toxicity and the mass of each DBP must be considered. TOCl, TOBr and TOI were found to be good surrogates for the detected Cl-, Br- and I-DBPs. Although many new DBPs have been identified and measured, the unknown portion still is of the order of 50%. One possibility is the unknown TOX includes high molecular weight DBPs. Another possibility is the switch to alternative disinfectants has produced different DBPs.

In addition to the study of emerging DBPs of health concern, the overall study included the determination of chronic mammalian cell (Chinese hamster ovary) cytotoxicity (Allen et al., 2022). Results revealed that unregulated HANs, particularly DHANs, are important toxicity drivers. The toxicity testing found the same forcing factors as that determined by calculated toxicity (Krasner et al., 2016). In bromide/iodide-impacted water treated with chloramines, toxicity was driven by I-DBPs, particularly IAAs. IAAs were particularly higher in plant 4 (which had a very short free chlorine contact time), where samples also had the highest cytotoxicity. Calculated toxicity was not evaluated in this paper, as the companion paper (Allen et al., 2022) involved actual toxicity testing.

This paper showed important relationships and correlations between the formation of the regulated and emerging DBPs and surrogates such as TOCl, TOBr, and TOI. The emerg-

ing DBPs include Br-, I-, and N-DBPs of health concern. Although the emerging DBPs are not regulated at this time, some of them have been under scientific and regulatory consideration. This and other studies indicate that certain changes in operations could be conducted in order to balance the control of regulated and emerging DBPs. For example, plant 4 could increase the free chlorine contact time to minimize I-DBP formation, while still keeping the level of THMs and HAAs within regulatory limits. Plant 4 had THM4 of 29–43 μg/L, which is well below the THM4 regulatory limit of 80 μg/L. Plant 7 had THM4 of 15–26 μg/L with chloramines and THM4 of 248 μg/L during the chlorine burn. Currently, the U.S. THM regulation is based on a running annual average, based on representative quarterly sample events. If the regulatory construct were to change, plants that utilize a chlorine burn might need to utilize other options to control nitrification. Plant 8 had THM4 of 75–79 μg/L during the chlorine burn, so a minor revision in operations might be needed to reliably stay below the regulatory limit during a chlorine burn. Alternatively, plant 7 might need some major revision in operations. For example, another improvement in the practice of nitrification control is the use and maintenance of a slightly higher chloramine residual level throughout the distribution system for effective nitrification detection and preventive monitoring and control (American Water Works Association, 2013). Plant 1 treats a low-bromide water with GAC, whereas plant 2 treats a high-bromide water with GAC. Br-DBPs of health concern likely drove the toxicity at the latter plant. One control option is to increase the carbon usage rate to remove more TOC to compensate for the lack of removal of bromide. The suggestions above provide examples of how treatment processes can be changed or modified to control the formation of both regulated and emerging DBPs.

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Appendix A Supplementary data

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jes.2022.04.016.

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