REVIEW

The formation and control of emerging disinfection by-products of health concern

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When drinking water treatment plants disinfect water, a wide range of disinfection by-products (DBPs) of health and regulatory concern are formed. Recent studies have identified emerging DBPs (e.g. iodinated trihalomethanes (THMs) and acids, haloacetonitriles, halonitromethanes (HNMs), haloacetaldehydes, nitrosamines) that may be more toxic than some of the regulated ones (e.g. chlorine- and bromine-containing THMs and haloacetic acids). Some of these emerging DBPs are associated with impaired drinking water supplies (e.g. impacted by treated wastewater, algae, iodide). In some cases, alternative primary or secondary disinfectants to chlorine (e.g. chloramines, chlorine dioxide, ozone, ultraviolet) that minimize the formation of some of the regulated DBPs may increase the formation of some of the emerging by-products. However, optimization of the various treatment processes and disinfection scenarios can allow plants to control to varying degrees the formation of regulated and emerging DBPs. For example, pre-disinfection with chlorine, chlorine dioxide or ozone can destroy precursors for N-nitrosodimethylamine, which is a chloramine by-product, whereas pre-oxidation with chlorine or ozone can oxidize iodide to iodate and minimize iodinated DBP formation during post-chloramination. Although pre-ozonation may increase the formation of trihaloacetaldehydes or selected HNMs during post-chlorination or chloramination, biofiltration may reduce the formation potential of these by-products.

Keywords: drinking water; disinfection by-products; iodinated by-products; haloacetaldehydes; halonitromethanes; nitrosamines

1. Introduction

Disinfection of public drinking water supplies with chlorine or other disinfectants has been integral to the prevention of infectious waterborne diseases. The highly reactive nature of chlorine or other oxidants used as disinfectants, which aids

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in microbial inactivation, also causes them to form a number of disinfection by-products (DBPs) with naturally occurring organic and inorganic substances in the source water (Christman et al. 1983). Since the discovery of DBP formation in the mid-1970s (Rook 1974), there has been increasing apprehension about the possible health effects posed by DBPs (National Research Council 1977). Toxicological studies have shown that certain DBPs cause cancer in the liver, kidney and/or large intestine of laboratory animals and that particular DBPs cause adverse reproductive or developmental effects (Boorman et al. 1999). Epidemiological studies have indicated a slightly increased risk for bladder, colon and rectal cancers in individuals who were exposed to chlorinated surface waters for many years (Villanueva et al. 2004). In addition, some epidemiology studies have shown an association between the consumption of chlorinated drinking water and adverse reproductive or developmental health effects, such as spontaneous abortion or foetal anomalies (Nieuwenhuijzen et al. 2000).

As a result, many countries regulate (or provide guidance for) selected DBPs (e.g. trihalomethanes (THMs) and haloacetic acids (HAAs)) in drinking water (US Environmental Protection Agency 2006; Karanfil et al. 2008). However, many of the DBPs that have been evaluated in toxicity studies do not account for the health risks observed in many cancer epidemiology studies: (i) the DBPs do not cause bladder cancer in animal bioassays and/or (ii) the carcinogenic potencies of the DBPs and their concentrations are not high enough to account for the cancer cases ascribed to high-DBP exposure in the epidemiology studies (Bull et al. 2006). An expert toxicology review of the hundreds of DBPs reported in the literature (Richardson 1998) was conducted with an in-depth mechanism-based structure–activity relationship analysis—supplemented by an extensive literature search for genotoxicity and other data—to rank the carcinogenic potential of these DBPs (Woo et al. 2002). Approximately 50 ‘high-priority’ DBPs were identified that received the highest ranking for potential toxicity. Using in vitro mammalian cell assays, the cytotoxicity and genotoxicity of many of these DBPs have been determined (Muellner et al. 2007; Plewa & Wagner 2009). Certain emerging DBPs (halonitromethanes (HNMs), haloacetonitriles (HANs), haloacetaldehydes) were found to be significantly more toxic in these assays than the regulated ones. Moreover, iodine-containing DBPs were found (in general) to be the most toxic and chlorinated species the least, with bromine-containing DBPs of intermediate toxicity. In addition to halogenated DBPs, there are non-halogenated DBPs of health concern, such as nitrosamines (Mitch et al. 2003).

The regulation of THMs (and HAAs in the USA) was based on their use as ‘surrogates’ for the toxicity associated with chlorinated water. Also, it was known that the control of THMs and HAAs also resulted (in general) in a reduction in the concentration of many other DBPs (Reckhow & Singer 1984), as well as unknown chlorination DBPs (based on total organic halogen (TOX) measurements) (Zhang et al. 2000), which may be associated with the adverse health effects. However, recent studies suggest that certain emerging DBPs of potential health concern can be formed when alternative disinfectants to chlorine are used to minimize the formation of the regulated chlorination DBPs (Krasner et al. 2006). Thus, a growing challenge of concern has been finding ways to cost-effectively control the formation of regulated and emerging DBPs while meeting disinfection and other operational requirements.
2. Factors that affect the formation of disinfection by-products

DBPs are formed through the reaction of a chemical disinfectant (chlorine, chlorine dioxide, chloramines, ozone) with an organic precursor, represented by various components of natural organic matter (NOM), and an inorganic precursor, most often certain halide ions (figure 1). Any one of these disinfectants can transform (oxidize) a complex NOM molecule into simpler moieties, which are then reactive with additional chlorine or chloramines acting as a halogen substitution agent (Reckhow & Singer 1985). Some of the disinfectants can also oxidize certain halide ions, bromide and iodide, to bromine and iodine, which are less effective oxidants but more effective substitution agents than chlorine (Amy et al. 1991). In a mixture of chlorine and bromide and/or iodide, mixed chlorine-, bromine- and/or iodine-containing DBP species are formed. Besides the presence of halides, other influential factors affecting the formation of halogenated DBPs include NOM concentration as dissolved organic carbon (DOC), pH, temperature, disinfectant concentration and reaction time (Stevens et al. 1989; Singer 1994).

Both the amount and composition of NOM are influential. Principal types/categories of NOM include allochthonous (terrestrially derived, dominated by humic substances) and autochthonous (microbially derived, in which non-humic organic matter becomes more dominant) (Krasner et al. 1996). A principal NOM characteristic, specific ultraviolet absorbance (SUVA), is helpful in differentiating humic (higher SUVA) from non-humic (lower SUVA) NOM components/precursors (Edzwald & Van Benschoten 1990). Emerging sources of DBPs include natural organic matter (NOM), algal organic matter (AOM) and wastewater effluent organic matter (EfOM).
of NOM include algal organic matter (AOM) and wastewater effluent organic matter (EfOM) (Mitch *et al.* 2009). There is extracellular and intracellular AOM, which includes macromolecules and cell fragments. Furthermore, there can be indirect potable reuse, where the watershed for a drinking water treatment plant can contain point source discharges of treated wastewater. In addition to influent refractory substrates (e.g. NOM from the drinking water source) not assimilated by bacteria, EfOM from biological wastewater treatment plants is composed of degradation products and soluble microbial products (SMPs) (Namkung & Rittmann 1986; Barker & Stuckey 1999). SMPs consist of macromolecules and cellular debris with a protein (nitrogen-enriched) and polysaccharide signature. Both AOM and EfOM are microbial in origin and are sources of organic nitrogen.

Amino acids are an important part of the organic-nitrogen content in water (Dotson *et al.* 2008). Chlorination (oxidation) of amino acids can result in the formation of aldehydes and nitriles, with subsequent or concomitant chlorine substitution to form chloral hydrate (the hydrolysed form of trichloroacetaldehyde) and dichloroacetonitrile, respectively (Trehy *et al.* 1986). In other research, acetaldehyde formed during pre-ozonation was found to react during post-chlorination to form chloroacetaldehyde, which in the presence of a sufficient amount of free chlorine rapidly reacted to form chloral hydrate (McKnight & Reckhow 1992). In addition, pre-ozonation was found to increase chloropicrin (trichloronitromethane) formation upon post-chlorination (Hoigné & Bader 1988).

Although the formation of brominated DBPs has been studied for many decades, research on iodinated DBP formation has been an emerging area of concern. Iodide can react with ozone, chlorine, chloramines or chlorine dioxide to first form hypoiodous acid (HOI) (Bichsel & von Gunten 2000; Hua & Reckhow 2006). Ozone or chlorine can then further react with HOI to form iodate, which acts as a sink for the iodide. Alternatively, HOI can react with NOM to form iodinated DBPs. The yield of iodinated DBPs generally follows the order: chloramines (NH₂Cl) > chlorine dioxide (ClO₂) > chlorine (Cl₂) >> ozone (O₃).

Nitrosamines are a group of non-halogenated DBPs. Among them, N-nitrosodimethylamine (NDMA) has been shown to be a by-product of the disinfection of some natural waters and wastewaters with combined chlorine (Mitch *et al.* 2003). Pre-oxidation with chlorine, chlorine dioxide or ozone has been shown to destroy or transform NDMA precursors (Charrois & Hrudey 2007; Lee *et al.* 2007). Certain treatment resins (Mitch *et al.* 2003) or polymers (e.g. polyamine) used during the coagulation process (Kohut & Andrews 2003) may contribute to NDMA precursor material.

### 3. The formation and occurrence of emerging disinfection by-products

Surveys in the USA and Canada in the 1990s and 2000s provided data for assessing the formation, occurrence and control of emerging DBPs that are not currently regulated in the USA. These involved iodinated THMs, which have been detected in various parts of the world, including Australia (Hansson *et al.* 1987), France (Bruchet *et al.* 1989) and Spain (Cancho *et al.* 2000), where they have been associated with medicinal odour problems. Some of the early research on
Iodinated THMs can occur under both chlorination and chloramination conditions. However, studies concur that their formation is highest when chloramines are used with ammonia added before chlorine (Hansson et al. 1987; Bichsel & von Gunten 2000). The impact of disinfection scenario on iodinated THM formation (sum of all six species) in a US DBP occurrence study (Weinberg et al. 2002) is summarized in figure 2. Iodinated THM formation is a function of both precursor (e.g. iodide) concentration and disinfection scenario. Iodide concentrations in source waters were not determined in this study. Nonetheless, these data show that iodinated THM yield was highest for chloramination systems, in particular for those plants that did not use ozone or chlorine as a pre-oxidant. The group with a short free-chlorine contact time followed by chloramine addition had relatively low iodinated THM formation, which may

\[ \text{iodinated THMs (\( \mu \text{g l}^{-1} \))} \]

\[ n = 9 \quad 8 \quad 7 \quad 9 \quad 4 \quad 4 \quad 6 \quad 5 \]

Figure 2. Impact of disinfection scenario on iodinated THM formation (sum of all six species) in plant effluents in a US occurrence study (iodinated THMs for one plant with chlorine dioxide and chloramines was 6.8\( \mu \text{g l}^{-1} \)). The top and bottom of the box are 75th and 25th percentiles, respectively; the top and bottom of the whiskers are 90th and 10th percentiles, respectively; the line across the inside of the box is the median; and the points \( n \) beyond the whiskers are outliers.

the formation of HNMs was conducted in Switzerland (Hoigné & Bader 1988) and in France (Thibaud et al. 1988). The occurrence of various emerging DBPs (e.g. chloral hydrate) has been studied in Greece (Golfinopoulos & Nikolaou 2005). Recently, a study on the formation and control of nitrosamines was conducted in Europe (Sacher et al. 2008).

\( (a) \) Iodinated disinfection by-products

Iodinated THMs can occur under both chlorination and chloramination conditions. However, studies concur that their formation is highest when chloramines are used with ammonia added before chlorine (Hansson et al. 1987; Bichsel & von Gunten 2000). The impact of disinfection scenario on iodinated THM formation (sum of all six species) in a US DBP occurrence study (Weinberg et al. 2002) is summarized in figure 2. Iodinated THM formation is a function of both precursor (e.g. iodide) concentration and disinfection scenario. Iodide concentrations in source waters were not determined in this study. Nonetheless, these data show that iodinated THM yield was highest for chloramination systems, in particular for those plants that did not use ozone or chlorine as a pre-oxidant. The group with a short free-chlorine contact time followed by chloramine addition had relatively low iodinated THM formation, which may

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have been due (in part) to low levels of iodide in the source waters of this group. The highest formation of iodinated THMs occurred at a plant that added chlorine and ammonia simultaneously to (pre)form chloramines in a water with a moderate amount of bromide (0.15mg l\(^{-1}\)), which presumably had a moderate amount of iodide. At the latter plant, iodinated acids were also detected (Krasner et al. 2006). Subsequently, a follow-up study (Richardson et al. 2008) measured the occurrence of five iodinated acids and two iodinated THMs in chloraminated and chlorinated drinking waters in the USA and Canada. (In the latter study, the researchers only chose to look for the two most commonly formed iodinated THMs.) In the study conducted by Richardson and colleagues, mixed bromo/iodo acids were detected at low \(\mu g l^{-1}\) or ng l\(^{-1}\) levels, with their occurrence being highest at chloramine plants with short free-chlorine contact times (less than 1 min).

TOX consists of total organic chlorine (TOCl), bromine (TOBr) and iodine (TOI). The relative yields of TOI versus TOCl for a surface water spiked with iodide (200\(\mu g l^{-1}\)) was studied under different disinfection scenarios (Hua & Reckhow 2006). The yield order for TOI was \(NH_2Cl > ClO_2 > Cl_2 > O_3\), which was in contrast to that for TOCl, where free chlorine was the most influential. However, the formation of TOI during chloramination was significantly reduced when pre-ozonation was employed. The yield order (on a weight basis) for iodinated THM formation (the sum of the six species) was the same as that of TOI. In this research, the percentage of TOI accounted for by iodinated THMs was not determined. Nonetheless, in one experiment, chloramines produced approximately 27\(\mu g l^{-1}\) of iodinated THMs and approximately 40\(\mu g l^{-1}\) of TOI as \(Cl^-\) (approx. 130\(\mu g l^{-1}\) of TOI as I\(^-\)). In addition to iodinated THMs and acids, other specific iodinated DBPs have been detected in finished waters (e.g. an iodinated aldehyde; Krasner et al. 2006).

(b) Haloacetaldehydes

In addition to chloral hydrate, there are mono- and dihalogenated acetaldehydes, as well as bromine-containing analogues of chloral hydrate. In a US nationwide DBP occurrence study, chlorine/chloramine disinfection at one plant produced 13\(\mu g l^{-1}\) of chloral hydrate and 3\(\mu g l^{-1}\) of dichloroacetaldehyde, whereas ozone (without biofiltration) and chloramines at a second plant—which treated groundwater from the same aquifer as the first plant—produced 0.3\(\mu g l^{-1}\) of chloral hydrate and 12\(\mu g l^{-1}\) of dichloroacetaldehyde (Krasner et al. 2006). Either ozone or chlorine can produce acetaldehyde, which can react with additional chlorine to form chloral hydrate (McKnight & Reckhow 1992; Trehy et al. 1986). At the second plant, in the presence of a chloramine residual, the reaction terminated with dichloroacetaldehyde. At another ozone/chloramine plant in this US study using biofiltration, the formation of dichloroacetaldehyde was controlled (Weinberg et al. 2002), possibly because acetaldehyde formed by ozonation could be removed on the biofilters (Weinberg et al. 1993). In a subsequent US survey of drinking water treatment plants (Mitch et al. 2009), the highest formation of dihalogenated acetaldehydes (i.e. 5.1–11\(\mu g l^{-1}\)) occurred at three plants that used ozone and chloramines, where two did not use biological filtration. Alternatively, another plant with ozone, biological filtration and chloramines in the latter study did not produce dihalogenated acetaldehydes.
At the two ozone/chloramine plants without biofiltration that produced high levels of dihalogenated acetaldehydes, the highest levels of acetaldehyde in this study were detected (i.e. 8–12 μg l⁻¹), whereas at the ozone/chloramine plant with biofiltration and no dihalogenated acetaldehydes, acetaldehyde was not detected in one sample event and was detected at a low level (1.9 μg l⁻¹) during a second sampling. At the former two ozone/chloramine plants without biofiltration, one had no trihalogenated acetaldehydes (and a relatively low level of THMs) and the other had 16 μg l⁻¹ of trihalogenated acetaldehydes (and a substantial amount of THMs). Based on the THM data and other information, it is likely that the first plant had little or no free-chlorine contact time and, thus, did not form the trihalogenated acetaldehydes, whereas the second plant had considerable free-chlorine contact and was able to form the trihalogenated DBPs. In general, the formation of trihalogenated acetaldehydes is higher at plants that use chlorine than at those that use chloramines, when similar types of water quality are being treated. If ozonation is used without biofiltration, there should be increased formation of trihalogenated acetaldehydes during post-chlorination. In terms of dihalogenated acetaldehydes, the database for plants that use chlorine, with or without ozonation, is too small to make any generalizations. The formation of the dihalogenated acetaldehydes was in general low, except for the ozone/chloramines plants without biofiltration discussed above.

In a study of US wastewater treatment plants, EfOM was found to be a significant source of precursors for trihaloacetaldehydes (Krasner et al. 2008). In that study, DBP formation at the wastewater treatment plants was also evaluated. For well-nitrified EfOM, where the addition of chlorine achieved a free-chlorine residual, the formation of haloacetaldehydes (sum of three di- and four trihalogenated species) was significantly higher (range = 5.9–61 μg l⁻¹, median = 24 μg l⁻¹ (n = 7)) than what was detected at drinking water treatment plants (range = not detected to 27 μg l⁻¹, median = 5.3 μg l⁻¹ (n = 25)). For the well-nitrified EfOM with haloacetaldehyde data, the ratio of chlorine to total organic carbon (Cl₂/TOC) ranged from 0.2 to 2.2 mg mg⁻¹ (median = 1.9 mg mg⁻¹), whereas the range of Cl₂/TOC ratios at the US drinking water treatment plants studied was not as high. Thus, the use of a high Cl₂/TOC ratio may have contributed (in part) to higher haloacetaldehyde formation in some EfOM samples. In one study of US drinking water treatment plants (Mitch et al. 2009), the (chlorine/chloramine) plant with the highest level of trihalogenated (chlorine- and bromine-containing) acetaldehydes (i.e. 19 μg l⁻¹) had the highest algal count in the plant influent prior to the addition of chlorine (i.e. 22 700 ml⁻¹). Amino acids in EfOM or AOM can be a source of precursors for this class of DBPs (Trehy et al. 1986). Trehy and colleagues found similar amounts of chloral hydrate and dichloroacetonitrile in chlorinated lake waters as in a chlorinated wastewater they evaluated, but much higher levels of chloroform (a THM) in the chlorinated lake waters. The independence of chloroform formation with respect to that of dichloroacetonitrile and chloral hydrate suggested different precursors for these chlorination by-products (i.e. humic substances versus amino acids or other nitrogenous substances). The different precursors were not characterized; rather Trehy and colleagues assumed that the lake waters were substantially higher in humic substances, whereas treated wastewater would have relatively more nitrogenous substances.
(c) Halonitromethanes

In addition to chloropicrin, there are mono- and dihalogenated HNMs, as well as bromine-containing analogues of chloropicrin (Thibaud et al. 1988). Pre-ozonation sometimes was found to increase the levels of some of the HNMs at plants in US DBP occurrence studies (Weinberg et al. 2002; Krasner et al. 2006; Mitch et al. 2009). For example, two plants that treated water from the same high-bromide source but used different primary disinfectants (i.e. chlorine and ozone) formed 2.4 and 5.7 μg l⁻¹ of HNMs (sum of bromonitromethane, three di- and four trihalogenated species), respectively (Krasner et al. 2006). Another pair of plants treated water from another source (lower in bromide), used chlorine dioxide or ozone as the primary disinfectant and produced 0.3 and 2.9 μg l⁻¹ of HNMs (sum of eight species), respectively (Krasner et al. 2006). In addition, chloropicrin formation during subsequent chlorination was increased by medium-pressure ultraviolet (UV) disinfection, but not by low-pressure UV, where both were evaluated (on waters with approx. 1 mg l⁻¹ of TOC) at the same fluence rates (Kashinkunti et al. 2006). For example, in one set of tests, chloropicrin formation during post-chlorination was approximately 0.2, 0.5, 0.8 and 1.1 μg l⁻¹ when the UV doses for the medium-pressure system were 0, 40, 105 and 140 mJ cm⁻², respectively (Kashinkunti et al. 2006). This phenomenon may have been due to photonitration, where ortho- and para-nitrophenols, if present in the water, can be fairly productive precursors (Reckhow 2005). In addition, medium-pressure UV can generate nitrite from nitrate, where nitrite has been shown to be a potential source of nitrogen in the nitro group of chloropicrin through labelling studies carried out with ¹⁵N-labelled nitrite (Choi & Richardson 2004). In a survey of US wastewater treatment plants, chloropicrin and dihalogenated HNM concentrations were both low (each were less than 1.0 μg l⁻¹) (Krasner et al. 2008). However, in an effluent-dominated river that received poorly nitrified EfOM, nitrification occurred in the river, and there was an increase in the chloropicrin formation potential (FP) in the stretch of the river in which the level of nitrite had increased (Krasner et al. 2008).

(d) Nitrosamines

In a survey of drinking water treatment plants in the USA and Canada (Valentine et al. 2005), which primarily treated surface water supplies (a few used groundwater), where cationic polymers were used at some plants, and ozone/chloramines were used at one plant, the median and 90th percentile NDMA concentrations in the chlorinated finished waters (for plants that did not use anion-exchange resins) were less than 1 ng l⁻¹ and less than 1 and 3.2 ng l⁻¹, respectively, for the chloraminated systems (figure 3). The concentrations increased somewhat in the chloraminated distribution systems (median and 90th percentile were 1.8 and 4.5 ng l⁻¹, respectively). At one plant using chloramines, the annual average concentration of NDMA increased in the distribution system from 5.4 to 16 ng l⁻¹. Higher NDMA levels (up to 30 ng l⁻¹) were found in a groundwater treated with anion-exchange resin and free chlorine (no other chemicals (e.g. polymers) were used), where the resin was most likely a source of NDMA precursors (Mitch et al. 2003, 2009).
In a subsequent US study of drinking water treatment plants, all but one of the surveyed source waters and plant influents (sampled before any chemical addition (e.g. polymers)) had measurable amounts of NDMA precursors based on FP testing (NDMAFP) (Krasner et al. 2004). [In the FP tests, samples were dosed in laboratory-controlled studies with relatively high concentrations of chloramines (ratios of chlorine to total organic carbon and to ammonia nitrogen $\text{Cl}_2/\text{TOC} = 3:1$ and $\text{Cl}_2/\text{NH}_3-N = 3:1$ on a weight basis, where ammonia was added before the chlorine) and held at $25 ^\circ \text{C}$ at $\text{pH} \sim 8$ for 3 days, in order to produce NDMA, which could be measured by gas chromatography/mass spectrometry (GC/MS) analysis. FP tests for DBPs (DBPFPs) are used routinely in drinking water studies to determine the levels of DBP precursors in water; however, they are not meant to represent actual levels in finished drinking water.] The 25th percentile, median, 75th percentile, 90th percentile and maximum values were 12, 22, 52, 83 and 261 ng l$^{-1}$, respectively (Mitch et al. 2009). The presence of NDMA precursors was significantly higher in the EfOM-impacted waters. In the low-impacted group, NDMAFP ranged from 10 to 76 ng l$^{-1}$ (median = 20 ng l$^{-1}$), whereas in the group with higher impact, NDMAFP was 22–261 ng l$^{-1}$ (median = 53 ng l$^{-1}$). In the full-scale plant effluent samples that were chlorinated (by plant operations), NDMA was not detected. In the full-scale plant effluent samples that were chloraminated (by plant operations), the median value of NDMA was not detected (with a minimum reporting level of 2 ng l$^{-1}$). The 75th and 90th percentile NDMA occurrences in the full-scale chloraminated waters were 3.3 and 10 ng l$^{-1}$, respectively. As all of the full-scale chloramine plants in this study used a strong pre-oxidant (in their plant operations), this may explain (in part) the low occurrence of NDMA in the full-scale finished waters (relative to their laboratory-scale FPs), as previous research has shown that pre-oxidation with
chlorine, chlorine dioxide or ozone may destroy or transform NDMA precursors (Charrois & Hrudey 2007; Lee et al. 2007). Regardless of source-water impact, effluent NDMA concentrations at full-scale chloramine plants generally increased with increasing usage of the polymer poly(diallyldimethylammonium) chloride (polyDADMAC) (Mitch et al. 2009).

Although dimethylamine is a precursor to NDMA formation (Mitch & Sedlak 2002), its yield in laboratory-controlled studies is low (Sacher et al. 2008). The pharmaceutical ranitidine, which is often used to prevent gastritis, had the highest conversion efficiency to NDMA among selected tertiary amines during chloramination in laboratory-scale studies (Sacher et al. 2008). Because treated wastewater is a major source of NDMA precursors and many pharmaceuticals have been found in wastewater treatment plant discharges, amine-based pharmaceuticals may be part of the NDMA precursor pool in EfOM. Although ranitidine has not been detected in EfOM, a breakdown product of this pharmaceutical (which is reactive with chloramines to form NDMA) could be present in EfOM. In addition, selected agricultural chemicals have been found to be NDMA precursors. For example, the phenylurea herbicide diuron reacts with chlorine or chloramines, especially dichloramine, to form NDMA (Chen & Young 2008). Recently, the fungicide tolylfluanide was found to undergo microbial degradation to \( N,N \)-dimethylsulphamide, which during ozonation had a high conversion rate to NDMA (Schmidt & Brauch 2008).

4. The control of emerging disinfection by-products

DBPFP tests using chlorine or chloramines can be used to evaluate the impact of various unit processes (e.g. coagulation, lime softening, ozonation, filtration) on DBP precursors. For example, figure 4 shows the effects of these processes on precursors for regulated THMs, trihaloacetaldehydes, chloropicrin and NDMA for a single sampling event at a lime softening plant in the USA (Mitch et al. 2009). This plant ozonated the softened water and then filtered the ozonated water through a biologically active filter. The removal of precursors
for trihaloacetaldehydes and THMs (57–58%) by lime softening was in between that of the removal of DOC (41%) and the reduction in ultraviolet absorbance (UVA) at 254 nm (61%). The removal of precursors for chloropicrin (33%) by lime softening was more similar to that of the removal of dissolved organic nitrogen (DON) (29%). The removal of NDMA precursors by lime softening, however, was low (12%, where the NDMAFPs of the plant influent and the softened water were 59 and 52 ng l\(^{-1}\), respectively). Because polyDADMAC polymer was added before secondary flocculation at this plant, the apparent low removal of NDMA precursors during softening may have been due (in part) to the addition of NDMA precursors from the polymer.

Ozonation at this plant resulted in a 47 per cent reduction in UVA, whereas the bulk organic matter (i.e. DOC and DON) was not significantly impacted (3 and 15% removal, respectively). Likewise, the percentage of THM precursors removed by ozonation was low (8%). The concentration of bromide at this plant was 0.09 mg l\(^{-1}\). There was no substantial change in the distribution of bromine- and chlorine-containing THMs after the ozone process (e.g. the concentration of chloroform decreased somewhat (from 79 to 70 \(\mu\)g l\(^{-1}\)), whereas the amount of bromoform increased to some extent (from 1.1 to 1.6 \(\mu\)g l\(^{-1}\)). Alternatively, there was a significant reduction in NDMA precursors from ozonation (65%, where the NDMAFPs of the softened and ozonated waters were 52 and 18 ng l\(^{-1}\), respectively). This is consistent with other research showing that ozone can destroy or transform NDMA precursors (Lee et al. 2007). However, there was an increase in precursors for trihaloacetaldehydes and chloropicrin. This is consistent with previous research that showed that pre-ozonation increased chloral hydrate or chloropicrin formation during subsequent chlorination (Hoigné & Bader 1988; McKnight & Reckhow 1992).

Biologically active filters resulted in removing some DOC (25%), DON (18%) and—to a lesser extent—UVA (12%). Removal of THM precursors through the filtration process was low (3%), while the removal of precursors (relative to what was found by DBPPF testing of ozonated water) for trihaloacetaldehydes, chloropicrin and NDMA was high (55, 75 and 67%, respectively). For example, the NDMAFPs of the ozonated and filtered waters were 18 and 5.9 ng l\(^{-1}\), respectively (where the concentration of NDMAFP for the filtered water was substantially above the minimum reporting level of 2 ng l\(^{-1}\)). Relative to the plant influent NDMAFP (i.e. 59 ng l\(^{-1}\)), a total of 90 per cent of the NDMA precursors were removed through the entire treatment process at this softening plant. (Note that the Cl\(_2\)/TOC ratio was kept constant in the NDMAFP tests, such that, as TOC was removed through the treatment process, an appropriately lower chlorine (chloramine) dose was used in each successive sample.) Acetaldehyde produced by ozonation was most likely removed in the biologically active filters, which is consistent with the reduction in precursors for trihaloacetaldehydes. Although acetaldehyde was not measured at this plant after ozonation, it was analysed for in the filter effluent and was barely present (1.9 \(\mu\)g l\(^{-1}\)). The FP test for trihaloacetaldehydes was conducted with chlorine, so more acetaldehyde could have formed in the laboratory-scale test; however, ozonation typically forms substantially more aldehydes than chlorination does. Filtration removed some of the precursors for chloropicrin that were formed during the ozonation process. Furthermore, some of the NDMA precursors (perhaps some of the polymer) were removed on the filters.
During this sample event, dihalogenated HNMs were not detected in FP tests at this plant. However, in a previous sampling, where they were detected, lime softening did not remove their precursors, ozonation increased their FP (from 1.7 to $6.9 \mu \text{gl}^{-1}$) and filtration brought them down somewhat (to $4.9 \mu \text{gl}^{-1}$). Thus, the impact of the unit processes at this plant on the precursors for the dihalogenated HNMs was similar to that for chloropicrin.

Utilities have installed and modified treatment practices to control the formation of regulated DBPs (e.g. THMs). In order to balance the control of regulated DBPs with that of emerging DBPs of health concern, utilities will need to optimize a series of various unit processes to minimize the formation of a wide range of DBPs. However, optimizing the unit processes will be site-specific, as no one scenario will work best for all plants. Nonetheless, the softening plant discussed above, as well as other full-scale plants studied in the USA (Mitch et al. 2009), indicate the following:

(i) coagulation or lime softening can be used to remove a portion of the precursors for THMs, trihaloacetaldehydes and chloropicrin; however, certain polymers used during coagulation or softening may contribute to NDMA precursors;
(ii) ozonation may destroy or transform NDMA precursors, but may concurrently increase the FP for trihaloacetaldehydes and HNMs;
(iii) biologically active filtration can remove acetaldehyde, one of the precursors for trihaloacetaldehydes, and may remove precursors for chloropicrin that were formed during the ozonation process; and
(iv) filtration may be used to keep NDMA precursors (e.g. certain polymers) from the finished water.

Although iodinated DBPs were not detected at the lime softening plant discussed above, studies show that the use of certain strong oxidants (i.e. chlorine, ozone) for primary disinfection can minimize the formation of either iodinated DBPs or NDMA upon subsequent chloramination. However, the use of these pre-oxidants to control the formation of these chloramine DBPs must be balanced with the formation of regulated chlorination and ozonation DBPs (THMs, HAAs, bromate) that can be concurrently produced.

5. Other emerging disinfection by-products of concern

Plewa & Wagner (2009) found that nitrogenous DBPs were significantly more toxic in single-cell mammalian studies (i.e. Chinese hamster ovary cells) than the regulated carbonaceous DBPs. In addition to HANs and HNMs, another emerging nitrogenous DBP class of health concern was haloacetamides (Plewa et al. 2008a). Alkaline hydrolysis of HANs can form haloacetamides (and ultimately HAAs) (Exner et al. 1973). Haloacetamides have been found in drinking water at low $\mu \text{gl}^{-1}$ levels (Krasner et al. 2006). In new studies (Plewa et al. 2008b), toxicogenomic analysis of DBPs is being conducted with non-transformed human embryonic cells.
Halogenated furanones are a class of highly mutagenic compounds (Kronberg et al. 1988). The chlorinated furanone 3-chloro-4-(dichloromethyl)-5-hydroxy-2-(5H)-furanone (MX), its geometric isomer (E)-2-chloro-3-(dichloromethyl)-4-oxobutenoic acid (EMX), their oxidized and reduced forms, and brominated analogues of MX (BMX) have been identified (primarily MX and EMX) in a limited number of studies in various countries (Kronberg et al. 1990; Suzuki & Nakanishi 1995; Smeds et al. 1997; Simpson & Hayes 1998; Wright et al. 2002). A survey was conducted in the USA that examined the formation and control of MX and 12 MX analogues (Krasner et al. 2006; Onstad et al. 2008). In addition to the chlorinated furanones that have been measured previously, brominated furanones—which have seldom been analysed—were detected, especially in high-bromide waters. Although MX and its analogues have typically been detected at low ng l$^{-1}$ levels, they were found in the latter study at high ng l$^{-1}$ levels at certain sites that treated water high in DOC and/or bromide. However, pre-treatment with ozone and biologically active granular activated carbon minimized MX-analogue formation upon subsequent chlorination or chloramination (Onstad et al. 2008).

A recently conducted study (Bull et al. 2006) used a quantitative structure–activity relationship model and other health-effect information to examine the likely carcinogenic potential of a group of other possible DBPs. These researchers came up with a list of plausible candidates for chemicals that could be associated with bladder cancer from the consumption of chlorinated drinking water: (i) haloquinones, (ii) halocyclopentenoic acids and related cogeners of MX, (iii) nitrosamines derived from alkaloids and nitrosamides, (iv) halonitriles aside from the HANs, and (v) organic N-haloamines. Thus, there are newly measured DBPs (e.g. haloacetamides, halogenated furanones) as well as newly proposed chemicals that require further study to better explain the adverse health outcomes associated with exposure to chlorinated and chloraminated drinking water.

In other research, it was found that a significant portion of the TOX produced during chlorination or chloramination was of a high molecular weight (Khiari et al. 1997; Hua & Reckhow 2007). An analytical constraint in further identification of TOX components has been that GC/MS, a principal measurement tool, can only typically be used to identify DBPs with molecular weights of up to approximately 650 Da. Zhang and colleagues (Zhang & Minear 2002; Zhang et al. 2004) have evaluated different analytical approaches to characterize the high-molecular-weight DBPs, including ultrafiltration, size exclusion chromatography and electrospray ionization tandem mass spectrometry (MS/MS). For example, chlorine-containing DBPs were found to form chloride ion fragments by MS/MS, which can be used as a fingerprint for chlorinated DBPs (Zhang et al. 2004). In another study, NOM was chlorine substituted with radioactive $^{36}$Cl. The fractionation techniques of ultrafiltration and size exclusion chromatography were combined with the detection of $^{36}$Cl, UVA and DOC in order to identify the molecular weight distribution of high-molecular-weight chlorinated DBPs (Zhang & Minear 2002). For example, Zhang & Minear found that the molecular weight distribution of chlorinated Suwannee River fulvic acid produced high-molecular-weight chlorinated DBPs that were highly dispersed, with an average molecular weight of 2000 Da, and that the Cl/C atomic ratios of the high-molecular-weight DBPs were approximately constant (i.e. 0.025), which is much

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lower than those of the commonly known low-molecular-weight chlorinated DBPs. These types of studies are at the forefront of helping to elucidate the formation and occurrence of high-molecular-weight DBPs; however, substantially more research is needed in this area.

Another emerging area of research in terms of DBPs is the identification of transformation products of micropollutants in water by the treatment plant disinfectants/oxidants. Although DBPs have traditionally been associated with NOM as the source of precursors, new research has shown that pharmaceuticals, personal care products and agricultural chemicals may be transformed to by-products during the disinfection/oxidation process. As discussed above, this has been studied for NDMA. In other research, the widely used antimicrobial agent triclosan was shown to react with chlorine to form chloroform and other chlorinated organic compounds (Rule et al. 2005). Bisphenol A—which is a building block of several important polymers and polymer additives—is an endocrine disruptor. The chlorination by-products of bisphenol A have also been studied for their oestrogenic activity (Hu et al. 2002).

6. Conclusions

Contributions from treated wastewater discharges and algal activity in drinking water supplies can lead to elevated levels of DON, which can increase the likelihood for the formation of emerging nitrogenous DBPs of health concern (e.g. HANs, nitrosamines). In addition, there are emerging carbonaceous DBPs of concern (e.g. haloacetaldehydes, halogenated furanones), as well as iodine-containing species (e.g. THMs, haloacids). Although many of these emerging DBPs are of higher health concern than the regulated DBPs (based in part on toxicology studies conducted with Chinese hamster ovary cells), drinking water utilities are currently only required to control the formation of regulated DBPs such as bromine- and chlorine-containing THMs and some of the HAAs in certain countries (e.g. the USA).

Because the commonly used alternative disinfectants to chlorine (i.e. ozone, chloramines, chlorine dioxide) produce lower levels of the regulated THMs and most of the bromine- and chlorine-containing HAAs, as well as TOX, many water utilities have switched (or are in the process of switching) from chlorine to these alternative disinfectants to meet regulatory limits. However, some of the emerging DBPs were higher in concentration with the use of alternative disinfectants. For example, iodinated THM and haloacid levels were highest in waters disinfected with chloramines only; dichloroacetaldehyde was highest in concentration in some waters disinfected with chloramines and ozone (with no biological filtration); some of the HNMs were formed at higher levels during post-disinfection when pre-ozonation was used; and NDMA formation was primarily associated with waters that were chloraminated.

However, disinfection/oxidation and treatment practices may be optimized to minimize (within limits) the formation of both the regulated and emerging DBPs. Pre-oxidation with chlorine, chlorine dioxide or ozone may destroy or transform the precursors for NDMA, and pre-oxidation with chlorine or ozone can oxidize iodide to iodate, which can minimize the formation of iodinated DBPs during post-chloramination. However, pre-ozonation can increase...
the FP for trihaloacetaldehydes and HNMs (and form bromate), whereas subsequent biological filtration may reduce the FP of these two classes of organic DBPs.

Although many newly identified DBPs have been incorporated into new studies, these compounds are not the end of the story. Emerging DBPs of potential health concern are being identified in disinfected drinking water. Because all chemical disinfection processes produce DBPs, it is important to include a wide range of potential DBPs in treatment studies to determine how best to minimize the formation of as many DBPs as possible, recognizing that not all will be minimized (and some may be increased). Unlike some micropollutants that are regional in their impact, exposure to DBPs is highly prevalent because of the use of some disinfectant or oxidant at drinking water treatment plants in most parts of the world. The challenge to scientists, engineers, utility staff, regulators, toxicologists and epidemiologists is to be aware of both emerging DBPs and emerging sources of DBP precursors and how their formation and control may be similar to and/or different from that of the regulated DBPs. Continued research needs to offer cost-effective means of controlling a wide range of DBPs, all of which have varying degrees of toxicity with consequences for human health.

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References


Bull, R. J., Reckhow, D. A., Rotello, V., Bull, O. M. & Kim, J. 2006 Use of toxicological and chemical models to prioritize DBP research. Denver, CO: AWWA & AWWA.


Review. Emerging by-products of concern


Agency Workshop on Optimizing the Design and Interpretation of Epidemiologic Studies to Consider Alternative Disinfectants of Drinking Water, Raleigh, NC.


