Desalination and Water Treatment
www.deswater.com

doi: 10.5004/dwt.2018.23200

129 (2018) 325–331
October

Research progress on the precursors and formation mechanisms of typical N-DBPs in drinking water

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Received 7 August 2017; Accepted 27 May 2018

ABSTRACT

Recently, the highly pathogenic and carcinogenic nitrogen disinfection byproducts (N-DBPs) have been found to be prevalent in disinfected drinking water, causing widespread concern. This review summarizes the major findings related to N-DBPs in drinking water over the previous decade. In particular, the review focuses on the known precursors and formation mechanisms of N-DBPs. New information regarding precursors and mechanisms is also discussed. N-DBPs include the halonitromethanes (HNMs), haloacetonitriles (HANs), nitrosamines (NAs), and haloacetamides (HAcAms), among other chemicals. HNMs are mainly generated through disinfectant oxidation and halogen atom substitution, while HANs are formed through a decarboxylation pathway and an aldehyde pathway. The formation of *N*-nitrosodimethylamine (NDMA) occurs in two steps: in the first, nitrite reacts with dimethylamine (DMA) to generate NDMA, while in the second, the unsymmetrical oxidation of dimethylhydrazine (UDMH) generates NDMA indirectly. The control of *N*-DBPs remains challenging, and the area requires additional research. This review can act as a reference for the research and control of *N*-DBPs.

Keywords: *N*-DBPs; Precursors; Mechanism; Review; Drinking water

1. Introduction

Drinking water disinfection plays an important role in reducing pathogenic bacteria and stabilizing water quality. However, organic pollutants can react with disinfectants during this process and generate a variety of disinfection byproducts (DBPs) with high toxicity and carcinogenicity [1]. Moreover, drinking water sources have been severely polluted from municipal wastewater discharges and agricultural non-point source pollution discharges in many countries and regions worldwide, which increases the concentrations of dissolved organic nitrogen in the water [2] and results in the production of higher concentrations and more varieties of *N*-DBPs during disinfection. Wang et al. [3] surveyed the water from a water supply plant in a city in northern China and found that the concentrations of haloacetic acids (HAAs), NDMA, and trihalomethanes (THMs) in the water after conventional treatment were 18.5 μg/L, 2.9 ng/L, and 32.7 μg/L, respectively. Although the concentrations were within water quality standards, they were still considered high [3]. Tan et al. [4] found the highest concentration of dichloroacetonitrile (DCAN), 9.05 μg/L, in a water sample from Taihu Lake. Bei et al. [5] examined samples from treated water and tap water from 44 cities in 23 provinces in China; the average concentration of NDMA was 11–13 ng/L, and the maximum concentration was 27–28.5 ng/L. Moreover,

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Presented at 2017 Qingdao International Water Congress, June 27–30, 2017, Qingdao, China.

the concentrations of NDMA in the sampled water reached up to 204 ng/L. Kosaka et al. [6] found that at least one of six HAcAms was found in all of the drinking water samples examined, and the total concentration of HAcAms ranged from 0.3 to 3.8 mg/L across Japan. These studies showed that a complex variety of *N*-DBPs were present in relatively high concentrations in water from water supply plants, and in some cases, the contamination was severe. This review presents an analysis of the variety of *N*-DBPs and the precursors and formation mechanisms of these pollutants; in addition, suggestions for future studies on *N*-DBPs are made.

2. N-DBP speciation

The organic/inorganic precursors of DBPs in water can react with disinfectants during the disinfection process, generating the DBPs. At present, more than 700 DBPs have been identified [7]. These are divided into nitrogenous and carbonaceous DBPs (*N*-DBPs and C-DBPs, respectively) according to whether or not they contain nitrogen. *N*-DBPs are unregulated and include HANs, HNMs, NAs, and HAcAms. *N*-DBPs have attracted widespread interest because of their strong cytotoxicity and genotoxicity [8–11]. For example, researchers have found that nitromethane, especially dibromonitromethane and tribromonitromethane, is potentially highly toxic to humans [12]. Compared with THMs and HAAs, the emerging iodo-trihalomethanes (I-THMs), HANs and HNMs are more toxic [13]. As *N*-DBPs have not been included in the Standards for Drinking Water Quality (GB5749-2006, China), the water supply plants in China seldom make routine measurements of *N*-DBP concentrations. Methods for detecting and controlling *N*-DBPs are still being studied, and no standards for *N*-DBPs have been implemented in China or elsewhere. The varieties and molecular structures of *N*-DBPs in drinking water are shown in Table 1.

3. Precursors of N-DBPs

Studying the control of *N*-DBP precursors is of great significance, as identifying the precursors' classifications and structural characteristics could help define the formation mechanisms of *N*-DBPs and thus enable the reduction of *N*-DBP production through source control.

The precursors of *N*-DBPs mainly consist of dissolved organic nitrogen (DON) compounds in the water [8]. The organic precursors include natural organic matter (humic acid, fulvic acid, proteins, polysaccharides, etc.), chemical and human emissions (amido polymers and flocculants introduced by the domestic sewage drainage and supply process, drugs, cosmetics and personal care products, etc.), and microorganisms and their metabolites (bacteria, algae, and their respective metabolites). The inorganic precursors consist of halide ions, such as Br and I, in the water. At least in some waters, a significant proportion of NDMA formation can be explained by the presence of known precursors [16]. Identified *N*-DBP precursors tend to be of low molecular weight and low electrostatic charge relative to bulk natural organic matter. This makes them recalcitrant to removal by water treatment processes, notably coagulation, as confirmed by a number of bench-scale studies.

3.1. Precursors of HANs

Wang et al. [47] chlorinated 20 typical amino acids and found that DCAN was the main product of HAN chlorination. The potential of asparagine to form HANs was the highest of all the amino acids (0.027 mol/mol), although that of aspartic acid, glutamic acid, glutamine, lysine, arginine, proline, histidine, tryptophan, phenylalanine, and tyrosine were also high. Studies in which nine amino acids (tyrosine, uracil, tryptophan, threonine, asparagine, adenine, cytosine, thymine, and glycine) were chlorinated revealed that only tyrosine, tryptophan, and asparagine chlorination produced DCAN [48]. Other studies found that a variety of organic nitrogen compounds could produce a certain amount of HANs in the chlorination process; among these compounds, the HAN formation potential of kynurenine was the highest [49]. Heterocyclic nitrogen and albuminoid substances in free amino acids and nucleic acids can produce HAN during the chlorination process [8]. Zhang et al. [50] chlorinated soluble microbial products (SMPs) in activated sludge and found that the SMPs could produce DCAN and trichloroacetonitrile (TCAN) during the chlorination process, thereby showing that SMPs may also be precursors of HANs. In comparison with free AAs, combined AAs generate more chloroform (125%–671%) but less DCAN (4.66%–87.5%) at all chlorine doses [51].

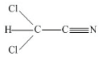
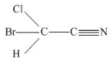
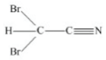
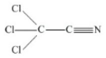
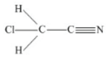
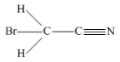
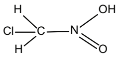
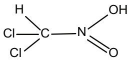
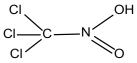
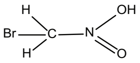
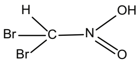
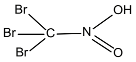
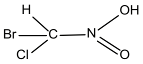
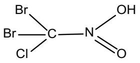
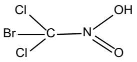
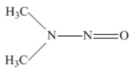
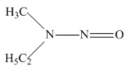
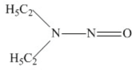
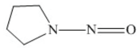
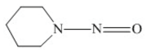
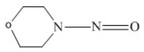
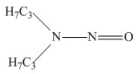
3.2. Precursors of HNMs

Trichloronitromethane (TCNM), which was the first HNM to be discovered, usually accounts for most of the measured HNMs and is generally considered a representative HNM. The main precursors of TCNM are not proteins or aromatic carbons but DON components with amino sugar structures [8]. Hu et al. [29] further found that DON components with short-chain amino acid structures were precursors of TCNM, but amino acids with highly stable functional groups (such as phenylalanine) were less likely to be precursors. The HNM formation potential was relatively high in water with low $SUVA_{254}$, while the formation potential was lower in water with high concentrations of aromatic carbons and high hydrophobicity. In addition, some specific synthetic organic compounds (such as benzene and methylbenzene) might also become precursors of HNMs under certain disinfection conditions [52]. Consequently, water containing DON with amino sugars and amino acid structures and water with high concentrations of dissolved organic carbon are more likely to promote the formation of HNMs.

3.3. Precursors of NDMA

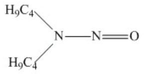
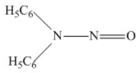
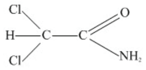
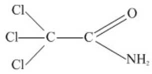
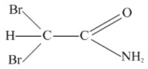
According to recent studies on the formation mechanisms of NDMA, DMA is the most significant precursor of NDMA. Li et al. [53] found that, in *Microcystis aeruginosa* in the growth stage, the NDMA formation potential of intracellular organic matter was 96 ng/mg DOC, and that of extracellular organic matter reached 189 ng/mg DOC. Chu et al. [41] found that the precursors of NDMA in drinking water sewage treatment plants mainly consist of DMA, tertiary amines with DMA functional groups, and

Table 1
Varieties and structures of *N*-DBPs in drinking water reported in the literature

Reported varieties of *N*-DBPs		Chemical structural formula
Haloacetonitriles, HANs	Dichloroacetonitrile, DCAN [14–22]	
	Bromochloroacetonitrile, BCAN [14,15,22–24]	
	Bromoacetonitrile, DBAN [14,15,17,22]	
	Trichloroacetonitrile, TCAN [15,20,22]	
	Chloroacetonitrile, CAN [25]	
	Bromoacetonitrile, BAN [26]	
Halonitromethanes, HNMs	Chloronitromethane, CNM [27–29]	
	Dichlorodinitromethane, DCNM [28–30]	
	Trichloronitromethane, TCNM [15,27–30]	
	Bromonitromethane, BNM [28,29]	
	Dibromonitromethane, DBNM [28,29]	
	Tribromonitromethane, TBNM [28–30]	
	Bromochloronitromethane, BCNM [28–30]	
	Dibromochloronitromethane, DBCNM [28–30]	
	Bromodichloronitromethane, BDCNM [28–30]	
Nitrosamines, NAs	*N*-Nitrosodimethylamine, NDMA [15–17,31–38]	
	N-nitrosomethylethylamine, NMEA [39,40]	
	N-nitrosodiethylamine, NDEA [31–36]	
	N-nitrosopyrrolidine, NPYR [35,36]	
	N-nitrosopiperidine, NPIP [35,36]	
	N-nitrosomorpholine, NMOR [36]	
	N-nitrosodipropylamine, NDPA [35,36]	

(Continued)

Table 1 *(Continued)*

Reported varieties of *N*-DBPs		Chemical structural formula
	N-nitrosodibutylamine, NDBA [32,36]	
	N-nitrosodiphenylamine, NDPhA [35,36]	
Haloacetamides, HAcAms	Dichloroacetamide, DCAcAm [6,15,19,20,22,41–45]	
	Trichloroacetamide, TCAcAm [6,15,20,22,41,44,45]	
	Dibromoacetamide, DBAcAm [6,15,22,43,46]	

dimethylformamide. Amino polymer flocculants (such as poly-DADMACs and cationic polyacrylamide) can release DMA during the ozone oxidation process and then form NDMA [54]. The precursors of NDMA are specific and are mainly composed of functional compounds such as DMA and UDMH, which are only present at very low background levels in natural waters. Therefore, the production rate of NDMA in water after disinfection is not high, and concentrations are approximately at the nanogram per litre level. However, the carcinogenicity of NDMA has necessitated thorough study.

3.4. Precursors of HAcAms

HAcAms are emerging DBPs whose toxicity is much higher than that of the traditional DBPs [55]. However, there are fewer reports on the HAcAms, and their precursors and formation mechanisms are still not fully understood. Chu et al. [56] found that aspartic acid was an important precursor of DCAcAm and TCAcAm; chloramphenicol is also an important precursor of DCAcAm [27].

Thus far, studies have mainly focused on the precursors of *N*-DBPs, but the structural characteristics of *N*-DBPs are not yet entirely clear. Therefore, further studies should be conducted as follows: (1) quantitative and qualitative analysis should be performed to identify the structural characteristics of the *N*-DBP representative groups based on their different kinds of precursors. The characteristic substances and structures involved in the formation of *N*-DBPs should be identified. This would create a foundation for including *N*-DBPs in national water quality standards. (2) Targeted treatment technology that operates under conditions optimized for maximum efficiency of *N*-DBP removal from the source should be developed based on the characteristics and structures of the different *N*-DBP precursors.

4. Formation mechanisms of N-DBPs

Studies clarifying the formation mechanisms of *N*-DBPs can provide a theoretical basis for improving treatment technology and optimizing operation parameters. Therefore, the current findings regarding *N*-DBP formation are reviewed here.

4.1. Formation mechanism of HANs

HANs are formed by the reaction of free amino acids, nucleic acids, proteins, humic acid, and small molecular amines with chlorine or chloramine. At present, there are two known HAN formation pathways [57]: the first is the aldehyde pathway, in which a halogen is substituted for an atom of H on an amino acid and the nearest carboxyl forms a C=N imine after decarboxylation and dehalogenation. The imine and water continue to react to form NH_3 and aldehyde, and the aldehyde and chlorine/chloramines ultimately react to form nitriles. The second pathway is the decarboxylation pathway, in which halogens are substituted for two H atoms on an amino acid, and decarboxylation, after the removal of HCl, forms nitriles. Ding et al. [58] studied the formation mechanism of DCAN from aspartic acid during the chlorination process. It has been shown that the amino functional group of aspartic acid is first chlorinated to form chloraspartic acid [8,29,42], and the chloraspartic acid is decarboxylated via the removal of carboxylate and two molecules of carbon dioxide [8,42,59]. The decarboxylated chloraspartic acid is then oxidized by HClO, and acetonitrile is formed after one molecule of HCl is removed from the amino functional group to form a carbon-nitrogen triple bond. Finally, the methyl group of the acetonitrile continues to be oxidized by HClO to form DCAN [42,59,60]. When the ratio between free chlorine/chloramine and amino acids is greater than 1, the decarboxylation pathway is more likely to occur. Yang et al. [61] also studied the pathway of nitrile formation from the reaction of chlorine/chloramine and amino acids. Ammonia reacts with chlorine to form organic chloramines. Based on different chlorine–nitrogen ratios, there are two potential products: when the chlorine–nitrogen ratio is less than or equal to 1, R–CH(COOH)–NHCl is formed, while $R–CH(COOH)–NCl_2$ is formed when the chlorine–nitrogen ratio is greater than 1. R–CH (COOH)–NHCl and $R–CH (COOH)–NCl_2$ form R–C≡N after elimination and hydrolysis reactions; when the R group is CH_3, it can react with chloride ions to form DCAN/TCAN.

Organic nitrogen in natural waters is involved in the majority of cases of HAN production, and free chlorine and chloramine in organic nitrogen can also be involved in the reaction. Therefore, it is necessary to improve the removal of organic nitrogen precursors of HANs and to intensify source control.

4.2. Formation mechanism of HNMs

Studies have found that the concentration of HNMs increases markedly when chlorine and chloramine are applied after ozonation [28,62]. Thus, it is clear that ozone can promote the formation of HNMs. Recent studies on HNMs have mainly focused on TCNM. And and Mitch [63] studied the formation mechanism of TCNM from methylamine precursors and found that during disinfection by chlorination, methylamine rapidly reacts with HOCl to form dichloramine, which is then oxidized into nitroalkane. Cl from the disinfectant is then substituted for H on the nitroalkane to form TCNM. Hu et al. [29] explored the formation mechanism of TCNM from aspartic acid precursors. The reaction process is very complicated and has been divided into 13 steps; alternating oxidation and elimination reactions promote the decomposition of alkyl groups and the formation of TCNM. Taken together, the findings of current studies on the formation mechanism of HNMs through chlorination suggest that the process can be described by two steps: disinfectant oxidation and halogen atom substitution. Ammonia derived from the precursors is first oxidized by the disinfectant into nitro compounds, which are then formed into nitroalkanes. The increased acidity of the C–H bond on the α-C makes it easier for halogen atoms to substitute for H atoms on the C–H bond, deprotonating the compound [64] and ultimately forming TCNM.

Three pathways forming nitromethane intermediates have been described [65]. –3 amino was oxidized into +3 nitro by the action of disinfectant. When there is NO_2^- in the water, it reacts with chlorine to form $ClNO_2$, which is then oxidized into N_2O_4. During UV disinfection, photolysis can form NO· and OH from NO_2^-; the OH can continue to react with NO_2^- to form N_2O_4, which can be further decomposed into nitrating agents such as NO_2· and ONOOH. These two disinfectant processes can, therefore, accelerate the nitration of HNM precursors.

There have been relatively more studies on the formation mechanism of HNMs during chlorination disinfection than during ozone or UV disinfection. Thus, further study is needed on the formation mechanisms of HNMs during ozone disinfection and UV disinfection to determine the similarities to, and differences from, the formation of HNMs during chlorination. Such studies will lay a foundation for understanding the formation of these byproducts and for improving the removal of HNMs produced through different disinfection methods.

4.3. Formation mechanism of NDMA

NDMA is a typical representative of the NAs. Recent studies have revealed that the formation of NDMA can be divided into two processes. In the first, nitrite reacts with hypochlorous acid to generate a nitrating agent, which then reacts with DMA to generate NDMA. Lü et al. [66] studied the reaction mechanism of NDMA generated by DMA and nitrous acid using the quantum chemical calculation method and found that this reaction is divided into two steps. In the first step, two molecules of nitrous acid react to generate an activated nitrite intermediate, N_2O_3; in the second step, N_2O_3 then reacts with DMA to form NDMA. However, this process is less likely to occur in drinking water, because the concentration of nitrite in treated, filtered water is relatively low, resulting in much lower NDMA production. There have also been studies showing that nitrosation is catalyzed when HClO, CO_2 and CH_2O are present in the water [67,68], although these studies could not directly prove that nitrosation is a primary mechanism of NDMA formation in drinking water. In the second process, UDMH is oxidized into NDMA indirectly. Free chlorine and amine in water react to form monochloramine, which reacts with DMA to generate UDMH. UDMH then reacts with monochloramine to ultimately form NDMA. Studies have also found that formation of an asymmetrically chlorinated dimethylhydrazine intermediate (Cl-UDMH) occurs from a nucleophilic substitution reaction between dimethylamine and $NHCl_2$. However, the production rate of NDMA generated by this reaction pathway is very low (less than 1%), suggesting that it may not be important for NDMA generation [63]. Therefore, some scholars have proposed another pathway: dichloramine + DMA → UDMH + O_2 → NDMA [69]. The precursors of NDMA are specific and mainly contain DMA, UDMH, and other functional groups. Future research should focus on the precise mechanisms that generate NDMA from its precursors.

5. Prospects

N-DBPs in drinking water have become increasingly complicated in their speciation, and their combined concentrations are sufficiently high to confer cytotoxicity and genotoxicity. The presence of *N*-DBPs in drinking water has thus attracted significant concern. To complement current studies on the precursors and formation mechanisms of *N*-DBPs, further studies should be carried out in several areas. First, the structural characteristics of the precursors of *N*-DBPs should be identified by different quantitative and qualitative analysis methods. Moreover, improved and targeted treatment technology should be proposed to remove the precursors from water sources. Second, the formation mechanisms of HNMs and *N*-DBPs during ozone and UV disinfection should be explored to determine the similarities and differences among *N*-DBPs and ultimately to enable the development of targeted combined disinfection technology. Third, a targeted analysis method and evaluation system should be established that combines the characteristic structures of *N*-DBP precursors and the formation processes of various *N*-DBPs. Some new disinfectants and disinfection methods should also be developed, such as extracts of tea polyphenols [70].

Funding

Fund Program: NSFC (51308498), National Spark Plan (2015GA701047).

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