Environmental Science
Processes & Impacts

RSC Publishing

PAPER

View Article Online
View Journal | View Issue

Occurrence, profiling and prioritization of halogenated disinfection by-products in drinking water of China†

Cite this: *Environ. Sci.: Processes Impacts*, 2013, **15**, 1424

Huanhuan Ding,[a] Liping Meng,[b] Haifeng Zhang,[a] Jianwei Yu,[a] Wei An,[a] Jianying Hu[b] and Min Yang*[a]

Received 27th February 2013
Accepted 1st May 2013

DOI: 10.1039/c3em00110e

rsc.li/process-impacts

The occurrence of 28 disinfection by-products (DBPs), which were divided into 5 groups, in 70 drinking water treatment plants in 31 cities across China was investigated, and the toxic potency of each DBP group was calculated using mammalian cell toxicity data from previous studies for profiling. Of the 28 DBPs, 21 were detected with an average frequency of detection of 50%. Trihalomethanes (THM4) and haloacetic acids (HAAs) were the most predominant species, whose median concentration levels were at 10.53 and 10.95 μg L^{-1}, respectively. Two of four iodinated trihalomethanes (I-THMs) were detected, and the concentration of the I-THMs ranged from under the detection limit to 5.58 μg L^{-1}. The total concentration of haloacetonitriles (HANs) in different water samples ranged from under the limit of detection to 39.20 μg L^{-1}, with a median concentration of 1.11 μg L^{-1}. Two of four halonitromethanes (HNMs) were detected, and the maximum concentrations of chloronitromethane (CNM) and trichloronitromethane (TCNM) were 0.96 and 0.28 μg L^{-1}, respectively. HANs were found to be the most potent DBP group in terms of cytotoxicity, and HANs and HAAs had the same level of genotoxic potency. These results indicate that although at a low concentration level, the toxic potency of the unregulated HANs in drinking water may not be neglected.

Environmental impact

Identification and control of disinfection by-products (DBPs) have long been major issues for securing drinking water safety. The occurrence patterns of 28 DBPs, including the regulated trihalomethanes (THMs), haloacetic acids (HAAs), and the emerging iodinated trihalomethanes (I-THMs), haloacetonitriles (HANs) and halonitromethanes (HNMs), in the finished water of 70 water treatment plants across 31 cities in China were revealed for the first time. Prioritization of the DBP groups was performed using mammalian cell toxicity data from previous studies. HANs were found to be the most potent DBP group in terms of cytotoxicity and genotoxicity.

1 Introduction

Identification and control of disinfection by-products (DBPs) have long been major issues for securing drinking water safety.[1,2] With the rapid development of analytical technologies, more and more emerging halogenated DBPs with potential toxicity, including iodinated-THMs (I-THMs), haloacetaldehydes (HCAs), haloacetonitriles (HANs), haloacetamides (HAcAms), and halonitromethanes (HNMs), have been detected in drinking water.[3–7] Up to now, more than one thousand disinfection by-products (DBPs) have been reported in the literature, most of which are chlorinated DBPs.[8,9] Of these reported DBPs, only a small percentage have been quantified in drinking waters, and even less have been regulated.[10,11] In comparison with the regulated DBPs like trihalomethanes (THMs) and haloacetic acids (HAAs), the emerging DBPs including I-THMs, HNMs and HANs are in general, present in drinking water at a much lower level.[12–16] For example, in a nationwide DBPs survey conducted in the United States,[17] I-THMs, HNMs and HANs were detected with a median concentration of 0.40, 1.00, and 3.00 μg L^{-1}, in comparison with the most abundant halogenated DBPs including 4 THMs and 9 HAAs (median concentrations, 31.00 and 34.00 μg L^{-1}, respectively). In a regional investigation of DBPs from ten water treatment plants in China,[18] the median THMs, HAAs and HANs levels were 17.70, 8.60 and 1.80 μg L^{-1}, respectively, which were much lower than those of the United States and the United Kingdom.[17,19] Due to the lack of a nationwide survey, however, information regarding the occurrence of DBPs in China's drinking water is still very limited.

[a]*State Key Laboratory of Environmental Aquatic Chemistry, Research Center for Eco-Environmental Sciences, Chinese Academy of Sciences, P. O. Box 2871, Beijing 100085, China. E-mail: yangmin@rcees.ac.cn; Fax: +86-10-62923541; Tel: +86-10-62923475*

[b]*College of Urban and Environmental Sciences, Peking University, Beijing 100871, China*

† Electronic supplementary information (ESI) available. See DOI: 10.1039/c3em00110e

On the other hand, the occurrence and concentration levels of different types of DBPs in drinking water could be impacted by multiple factors including the size and fractionation of dissolved organic matter,[20] amino acids,[21] bromide ions,[22] iodine ions,[23] and the type of disinfectants[24] *etc.* The most promising approaches for the control of DBPs include reducing DBP precursors and adopting alternative disinfectants (chloramine, chlorine dioxide, ultraviolet, *etc.*) instead of chlorine.[24–26] While alternative disinfection has been demonstrated to be very effective in reducing the formation of the regulated DBPs including the 4 THMs and 5 HAAs, it may lead to an enhancement in the formation of emerging DBPs,[2,17,24] which have exhibited a higher cytotoxic and/or genotoxic potential in mammalian cell tests.[27–29] So it is clear that prioritizing the most potent DBP groups is vital for establishing a reasonable strategy to control the adverse health effects of DBPs.

In this study, a total of 70 finished water samples from 31 cities across major watersheds of China were collected for a DBPs survey, and the concentration levels of four I-THMs (dichloroiodomethane, bromochloroiodomethane, dibromoiodomethane and iodoform), seven HANs (chloroacetonitrile, dichloroacetonitrile, trichloroacetonitrile, bromoacetonitrile, dibromoacetonitrile, bromochloroacetonitrile, and iodoacetonitrile), and four HNMs (chloronitromethane, trichloronitromethane, bromochloronitromethane, and tribromonitromethane) were compared with the conventional THM4 (chloroform, bromodichloromethane, dibromochloromethane and bromoform) and nine HAAs (chloroacetic acid, dichloroacetic acid, trichloroacetic acid, bromoacetic acid, dibromoacetic acid, tribromoacetic acid, bromochloroacetic acid, bromodichloroacetic acid, and chlorodibromoacetic acid). In addition, the mammalian cell toxicity index values based on cytotoxicity and genotoxicity tests of each DBP group were calculated to prioritize the DBP groups with high potency in these regions.[27,30–32] The occurrence patterns and toxicity index of each DBP obtained from this study will provide useful information for better understanding the potential adverse health effects of DBPs and for making national level regulations.

2 Materials and methods

2.1 Chemicals and reagents

The structures and acronyms of target analytes are shown in Fig. S1 and Table S1 in the ESI.† Chloronitromethane (90% pure), bromochloronitromethane (90% pure) and tribromonitromethane (95% pure) were purchased from AccuStandard, Inc (New Haven, CT, USA). The 9 HAAs (99% pure) were all purchased from Dima Technology TNC (USA). Haloacetonitriles except for iodoacetonitrile, regulated THM4 and trichloronitromethane were purchased from Sigma Aldrich Chemical Co. (St. Louis, Mo, USA). Iodinated THMs (I-THMs) including dichloroiodomethane, bromochloroiodomethane, dibromoiodomethane, iodoform, and iodoacetonitrile were purchased from CanSyn Chem. Corp. (Toronto, ON, Canada), Their purity was all >95%. Bromofluorobenzene (98% pure), decafluorobiphenyl (99% pure) and 1,2-dibromopropane (97% pure) were purchased from Sigma Aldrich Chemical Co. (St. Louis, Mo, USA), and used as internal standards in the process of detection.

Methanol, methyl *tert*-butyl ether (MtBE), acetonitrile and acetone obtained from Fisher Chemicals (New Jersey, USA) were all of HPLC grade. HPLC grade acetic acid was purchased from Dima Technology TNC (USA). L-Ascorbic acid, sodium sulfate, and copper sulfate from Alfa Aesar (USA) were of analytical reagent grade. Distilled water was prepared by a Milli-Q Synthesis water purification system (Millipore, Bedford, MA, USA). A syringe driven filter was purchased from Anpel (China).

2.2 Sample collection

Effluent samples were collected from 70 full-scale drinking water treatment plants (DWTPs) of 31 cities in China between 2010 and 2011, as shown in Fig. 1. To the samples for HAAs analysis, 20 mg L^{-1} L-ascorbic acid was immediately added to remove residual oxidants according to Meng *et al.*[4] To the remaining DBPs, 31 mg L^{-1} L-ascorbic acid and sufficient sulfuric acid (to lower the pH to 3.5) were added according to Weinberg *et al.*[16] The samples were collected in amber glass bottles and delivered under cooling conditions (4 °C in cooling boxes) within 48 h to the lab. Once they arrived in the lab, the samples were stored in the dark at 4 °C until they were used. Information regarding the source water characteristics and disinfectants is shown in Table S3 in the ESI.†

2.3 Sample preparation

HAAs were analyzed using an ultra performance liquid chromatography-electrospray tandem mass spectrometry (UPLC-ESI-MS/MS) method described by Meng *et al.*[4] Prior to analysis by UPLC-MS/MS, water samples were filtered through 0.22 μm syringe driven filters. The other halogenated DBPs, including THM4, I-THMs, HANs, and HNMs were analyzed using a liquid–liquid extraction (LLE)-gas chromatography/electron capture detection (GC/ECD) method described by Weinberg *et al.*[16] Briefly, the samples and standards were extracted according to USEPA Method 551.1 with some modifications. 30 mL water

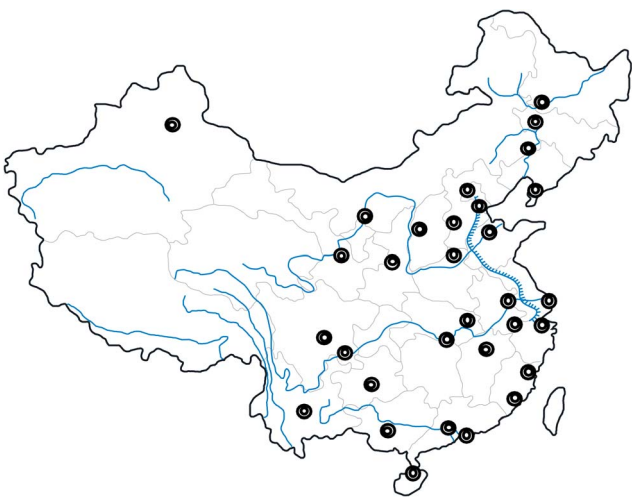

Fig. 1 Map of sampling locations of drinking water in China.

samples were transferred into 40 mL glass vials. Then 3 mL of MtBE was added followed by ten grams of anhydrous sodium sulfate (for salting out effect) and one gram of copper sulfate (for visual phase separation). The samples were capped and shaken briefly by hand before being shaken in a vortex mixer for 20 min. Then the vials were allowed to stand until there was a sharp demarcation line between the two layers, and approximately two milliliter of extract was transferred evenly into two autosampler vials using a disposable Pasteur pipette. One vial was stored in a freezer as a backup extract, and the other vial was used for analysis.

2.4 Instrumental analysis

Separation of HAAs was performed using an ACQUITY UPLC™ system (Waters, Milford, MA, USA), as described by Meng *et al.*[4] A Waters ACQUITY UPLC BEH C8 column (1.7 μm; 2.1 × 100 mm) was used to separate the nine HAAs. The column was maintained at 40 °C and a flow rate of 0.3 mL min^{-1}, and the injection volume was 15 μL. Acetonitrile (A) and ultrapure water containing 0.1 (v/v) acetic acid (B) were used as mobile phases. Mass spectrometry was performed using a Waters Micromass Quattro Premier XE (triple-quadrupole) detector equipped with an electrospray ionization source (Micromass, Manchester, UK) in negative ion mode. The operating conditions for the selected reaction monitoring (SRM) mode consisted of a source temperature of 110 °C, desolvation temperature of 350 °C, 3.00 kV capillary voltage, 650 V multiplier, 800 L h^{-1} desolvation gas flow, and 50 L h^{-1} cone gas flow.

Separation of the other target analytes was performed using an Agilent6890 gas chromatography (Agilent, Palo Alto, CA) with a DB-1 column (Agilent 30 m × 0.25 mm × 1 μm), and interfaced with an electron capture detector (ECD). The GC temperature program was as follows: hold at 35 °C for 23 min, then increase to 139 °C at a rate of 4 °C min^{-1}; and then increase to 301 °C at a rate of 27 °C min^{-1} and hold at 301 °C for 5 min. A 2 μL injection volume was used in splitless mode. The carrier gas was ultra-high purity (UHP) nitrogen. The injector temperature was set at 90 °C, while the detector was set at 300 °C.

2.5 Quality assurance and quality control

Identification of DBPs in drinking water was accomplished by comparing the retention time (within 2%) with the corresponding standards, and each sample was analyzed three times ($n = 3$). Seven point calibration curves were constructed for the standard solutions in a concentration range between 0.01 and 120 μg L^{-1} for quantification, depending on the individual compound. Bromofluorobenzene, 1,2-dibromopropane, and decafluorobiphenyl were used as the internal standards for GC-ECD analysis.

Equipment rinsing was performed with methanol to avoid sample contamination, and laboratory blanks were analyzed to confirm that no sample contamination occurred. For each DBP, recovery was evaluated by spiking standard solutions to a drinking water sample at three concentration levels in replicates of three. The limits of detection (LODs) and limits of quantization (LOQs) were defined as signal-to-noise (S/N) ratios at 3 and 10, respectively.

2.6 Toxicity calculation and data analyses

The unit cytotoxicity and genotoxicity index values were defined as the reciprocal of the median CHO cell cytotoxicity $\%C_{1/2}$ value for each DBP group or the reciprocal value of the median CHO SCGE genotoxic potency values for each DBP chemical group.[27] With data derived from previous studies,[27,30–32] we calculated the unit cytotoxicity and genotoxicity index values for each DBP group (details shown in ESI Tables S5–S8†).

3 Results and discussion

3.1 Occurrences of different groups of DBPs

The concentrations of each group of DBPs in drinking water are shown in Fig. 2 and Table S4.† As has been observed previously,[17,33] THMs and HAAs are the two major groups of the halogenated DBPs with a relatively high frequency of detection. Of the eight THMs, $CHCl_3$ (frequency of detection, freq. 100%), $CHBrCl_2$ (freq. 100%), $CHBr_2Cl$ (freq. 94%), and $CHBr_3$ (freq. 54%) were found in most samples, while $CHCl_2I$ (freq. 31%) and CHClBrI (freq. 4%) were less frequently detected, and $CHBr_2I$ and CHI_3 were not found in any samples. The concentrations of four I-THMs ranged from below the detection limit to 5.58 μg L^{-1}, significantly lower than those of THM4 (0.79–107.03 μg L^{-1}) (Table S4†). The ratio of the I-THMs (0.50 μg L^{-1}) to THM4 (23.86 μg L^{-1}) was 2.1% on the 75th percentile value basis, with the maximum value being 5.2%. The median level of THM4 (10.53 μg L^{-1}) in this study was significantly lower than those acquired during the US (31.00 μg L^{-1}) and the UK surveys (14.90–44.70 μg L^{-1} in three regions).[17,19] The median and maximum concentrations of the four I-THMs in this study were below the detection limit and 5.58 μg L^{-1}, respectively, whereas in the US survey the sum of six species was 0.40 and 19.00 μg L^{-1}, respectively. Dichloroiodomethane was the most abundant I-THMs detected in this study, which is in agreement with the US survey results.

Among the 9 HAAs analyzed, DCAA (freq. 91%) and TCAA (freq. 83%) were found in most of the samples, BCAA (freq. 34%), DBAA (freq. 23%), DCBAA (freq. 9%), and DBCAA (freq.

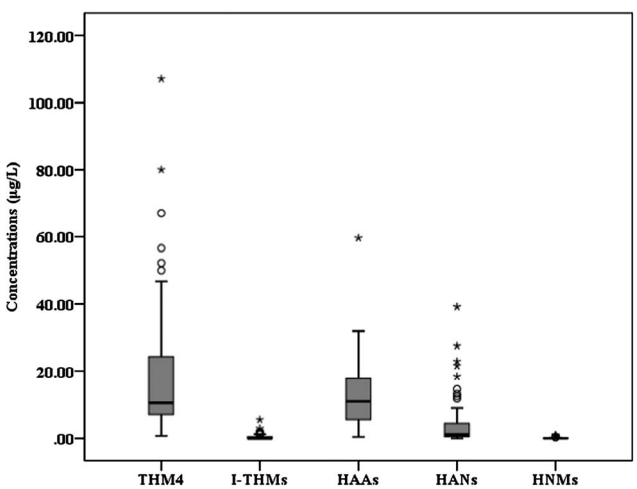

Fig. 2 Concentrations of DBPs in drinking water in China.

3%) were less frequently detected, while CAA, BAA, and TBAA were not detected. The total concentrations of the 6 detected HAAs in different water samples ranged from 0.45 to 59.64 μg L^{-1} with a median value of 10.95 μg L^{-1} (Table S4†), which was lower compared with the previous study in the US.[17] Similar to other environmental survey results,[19] DCAA and TCAA were found to be the two most abundant species with a median concentration of 3.93 and 3.97 μg L^{-1}, respectively. In spite of the low median concentration, however, the maximum concentration of DCAA (52.85 μg L^{-1}) was higher than the guideline value (50 μg L^{-1}) of the WHO.[10]

Among the seven HANs, CAN (freq. 57%), DCAN (freq. 86%), TCAN (freq. 77%), and BAN (freq. 56%) were frequently detected, while BCAN (freq. 40%), DBAN (freq. 8%), and IAN (freq. 7%) were detected at a relatively low frequencies. As shown in Fig. 2 and Table S4,† the total concentrations of the 7 HANs in different water samples ranged from below the detection limit to 39.20 μg L^{-1}, with the median value of total concentration being 1.11 μg L^{-1}, which was lower than those reported for the United States (3.00 μg L^{-1}), Korea (2.34 μg L^{-1}), and a previous survey in China (1.80 μg L^{-1}).[12,17,18]

Of the four HNMs, only CNM (80%) and TCNM (7%) were detected. The median and maximum values of the total HNMs were 0.05 μg L^{-1} and 0.96 μg L^{-1}, respectively. The concentrations of HNMs detected in this study were lower than those in the US (nd–10 μg L^{-1}), but in accordance with those in Australia (nd–0.97 μg L^{-1}).[6,17] Although the LODs of HANs and HNMs were comparable with EPA 551.1 and the previous study,[17] it is desirable to improve the sensitivity of the analytical method in order to detect the concentration levels of HANs and HNMs.

In order to explore the possible effects of disinfection strategies on the production of DBPs, the DBP concentrations from 15 DWTPs with their source water taken from the Yangtze River, the longest river in China with a total length of 6398 km and annual runoff of 960 billion cubic meters, were compared, as shown in Fig. 3. In comparison with the median concentrations of THM4 and HAAs (18.10 and 9.92 μg L^{-1}) in samples using chlorine as the disinfectant, those in the samples using chloramines (disinfected with chlorine but with an NH_3-N concentration level of 0.5 mg L^{-1} or higher) were significantly lower (6.47 and 2.15 μg L^{-1}). It is well known that switching the disinfectant from chlorine to chloramines could minimize the formation of THM4 and HAAs.[34,35] However, as shown in Table S3,† the THM4 concentrations in some DWTPs with chloramine disinfection (such as #7) were quite high in comparison with other DWTPs with chlorine disinfection (such as #17). Except for the disinfectants, the concentration and characteristics of natural organic matter could also impact THM4 formation. As for HANs, the median concentrations in samples using chlorine and chloramine were 0.54 and 0.20 μg L^{-1}, respectively. The findings are in agreement with a previous study which found that the median concentration of HANs changed from 1.70 μg L^{-1} for chlorinated water to 1.30 μg L^{-1} when using chloramines.[15] The impacts of chloramine disinfection on the formation of HANs, however, needs further study. I-THMs were detected in 3 of the 15 samples. Previous research has shown that the concentrations of iodoform increased rapidly as the initial iodide concentration increased from 30 μM to 100 μM.[23] In this study, iodide was not detected in source water (the method detection limit was 5 μg L^{-1}). So the low detection frequency of I-THMs should be related to the low levels of iodide in the source water. The median HNMs concentrations for chloramine and chlorine were 0.04 and 0.05 μg L^{-1}, respectively, showing that using chloramine and chlorine may not affect the production of HNMs, which was in accordance with previous investigation.[15,36]

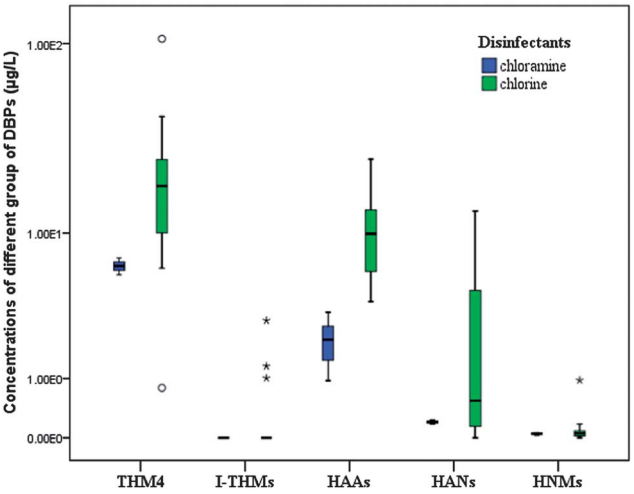

Fig. 3 Concentrations of DBPs in drinking water using the Yangtze river as the source water.

3.2 Prioritization of DBPs based on mammalian cell cytotoxicity and genotoxicity

Although THM4 and HAAs were found to be the most abundant DBPs in almost all of the drinking water samples, the health effects of the emerging DBPs may not be neglected because of their higher toxicities. Since it is difficult to acquire the animal test based toxicity data, this study tried to evaluate the potential health effects of each DBP groups using the mammalian cell cytotoxicity and genotoxicity data. The unit toxicity index values of each DBP group were calculated according to the results of previous studies,[27,30–32] and are shown in Fig. 4. HANs were approximately 923×, 116×, 92× and 34× more cytotoxic than THM4, HAAs, I-THMs and HNMs, respectively. As for the genotoxicity, HNMs were 21× and 3× more genotoxic than HAAs and HANs, respectively. However, according to the CHO cell SCGE assay result,[32] halomethanes including THM4 and I-THMs do not exhibit genotoxicity, and were thus excluded from the comparison.

In this study, the toxicity index values, which are defined as the product of the unit toxicity index value and the concentration of each DBP group, were created to evaluate the potential health effects of the different DBP groups. Fig. 5 and 6 show the cytotoxicity and genotoxicity index values of the target DBPs in 70 drinking water samples, respectively. The median cytotoxicity index values for HANs in drinking water samples were the highest among all of the DBP groups analyzed, and were approximately one and two orders of magnitude higher than

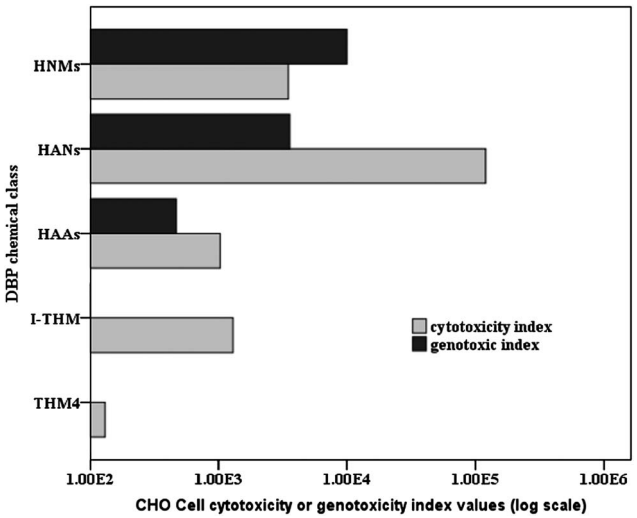

Fig. 4 Unit CHO cell cytotoxicity and genotoxicity for each DBP group.

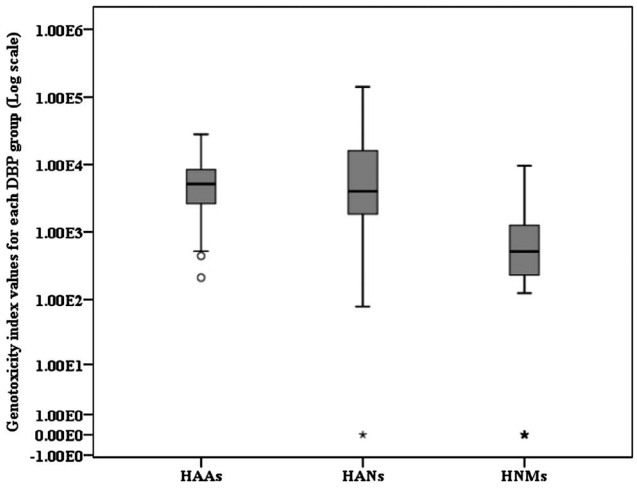

Fig. 6 Genotoxicity index values for each DBP group (log scale).

those of the HAAs and the THM4, respectively. In spite of their relatively high unit cytotoxicities, I-THMs and HNMs were found to have the lowest toxicity index values because of the low detection frequencies (30% for I-THMs) and median concentration levels (under detection limit and 0.05 μg L^{-1} for I-THMs and HNMs, respectively). On the other hand, the median genotoxicity index values for HAAs and HANs were at the same order of magnitude, and were higher than that of HNMs.

As demonstrated above, the potential health effects of HANs may not be neglected since they exhibited the highest cytotoxicity index values among all of the 5 groups of DBPs and the highest genotoxicity values among the 3 groups of DBPs evaluated in this study, although their concentration levels in drinking water samples were very low in comparison with the regulated DBPs including THM4 and HAAs. Previous studies found that HANs were formed at plants that used chlorine, chloramines, chlorine dioxide, or ozone disinfection.[33,37,38] At the same time, nitrogenous precursors from algae or aquatic humic substances have been related to HANs.[39] As the most predominant species of HANs, DCAN could increase relative liver weights,[40] and clear carcinogenic activity evidence was found for DBAN in male and female mice.[41] Drinking water guideline values of 20 μg L^{-1} and 70 μg L^{-1} were determined for DCAN and DBAN, respectively, by the WHO.[10] However, studies regarding the formation and potential health effects of HANs in drinking water are still quite insufficient, and none of these HANs have been regulated in China or other countries. Further studies are required in order to provide sufficient proof for making regulations.

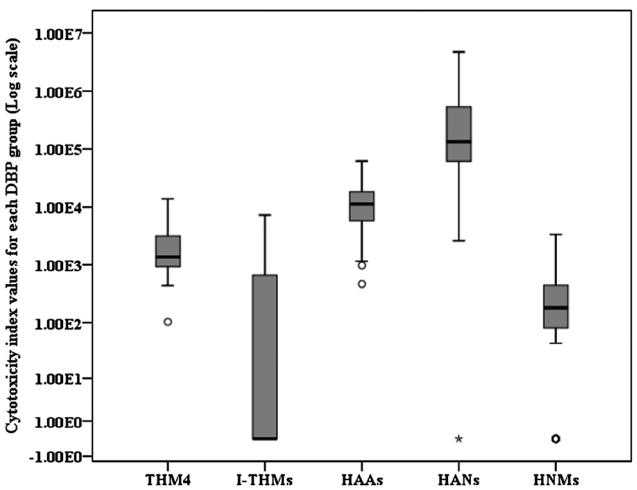

Fig. 5 Cytotoxicity index values for each DBP group (log scale).

4 Conclusions

This study investigated the occurrence of 28 halogenated DBPs in 70 water treatment plants from 31 cities across China, and calculated the toxic index values of each DBP class in drinking water plants. The main findings of this work include:

1. THM4 and HAAs were the two major groups of the halogenated DBPs in drinking water samples of China with median concentrations of 10.53 and 10.95 μg L^{-1}, respectively, which were lower than those reported for the US and UK. The median concentrations of I-THMs, HANs and HNMs in drinking water were under the detection limit, 1.11 and 0.05 μg L^{-1}, respectively.

2. The cytotoxicity index values for HANs in drinking water samples were highest among the 5 DBP groups analyzed, followed by HAAs and THM4 with much lower values. The genotoxicity index values for HAAs and HANs were at the same level among the 3 groups, and were higher than that of HNMs. This study suggested that in spite of the much lower concentration levels in drinking water, the adverse health effects of HANs should not be neglected, and further studies are required to evaluate the necessity of making regulations.

Acknowledgements

Financial supports from NSFC (210077118) and Major Science and Technology Program for Water Pollution Control and Treatment (2009ZX07419-001) are gratefully acknowledged.

References

1 S. D. Richardson, A. D. Thruston, T. W. Collette, K. S. Patterson, B. W. Lykins and J. C. Ireland, *Environ. Sci. Technol.*, 1996, **30**, 3327–3334.
2 S. D. Richardson, A. D. Thruston, T. V. Caughran, P. H. Chen, T. W. Collette, T. L. Floyd, K. M. Schenck, B. W. Lykins, G.-r. Sun and G. Majetich, *Environ. Sci. Technol.*, 1999, **33**, 3368–3377.
3 L. Silva, M. Bonin, B. McKague and B. Blount, *J. Anal. Toxicol.*, 2006, **30**, 670–678.
4 L. P. Meng, S. M. Wu, F. J. Ma, A. Jia and J. Y. Hu, *J. Chromatogr., A*, 2010, **1217**, 4873–4876.
5 W. Chu, N. Gao, D. Yin, S. W. Krasner and M. R. Templeton, *J. Chromatogr., A*, 2012, **1235**, 178–181.
6 D. Liew, K. L. Linge, C. A. Joll, A. Heitz and J. W. A. Charrois, *J. Chromatogr., A*, 2012, **1241**, 117–122.
7 I. Kristiana, C. Joll and A. Heitz, *J. Chromatogr., A*, 2012, **1225**, 45–54.
8 H. Zhang, Y. Zhang, Q. Shi, J. Hu, M. Chu, J. Yu and M. Yang, *Environ. Sci. Technol.*, 2012, **46**, 4396–4402.
9 H. Zhang, Y. Zhang, Q. Shi, S. Ren, J. Yu, F. Ji, W. Luo and M. Yang, *Water Res.*, 2012, **46**, 5197–5204.
10 WHO, 2006.
11 USEPA, *Fed. Regist.*, 2006, **71**, 387–493.
12 K. J. Lee, B. H. Kim, J. E. Hong, H. S. Pyo, S. J. Park and D. W. Lee, *Water Res.*, 2001, **35**, 2861–2872.
13 S. K. Golfinopoulos, A. D. Nikolaou and T. D. Lekkas, *Proceedings of the 7th International Conference on Environmental Science and Technology*, Syros, Greece, vol. A, 2001.
14 S. K. Golfinopoulos, A. D. Nikolaou and T. D. Lekkas, *Environ. Sci. Pollut. Res.*, 2003, **10**, 368–372.
15 E. H. Goslan, S. W. Krasner, M. Bower, S. A. Rocks, P. Holmes, L. S. Levy and S. A. Parsons, *Water Res.*, 2009, **43**, 4698–4706.
16 H. S. Weinberg, S. W. Krasner, S. D. Richardson and A. D. Thruston, Jr, *The occurrence of disinfection by-products (DBPs) of health concern in drinking water: results of a nationwide DBP occurrence study*, National Exposure Research Laboratory, Office of Research and Development, US Environmental Protection Agency, 2002.
17 S. W. Krasner, H. S. Weinberg, S. D. Richardson, S. J. Pastor, R. Chinn, M. J. Sclimenti, G. D. Onstad and A. D. Thruston, Jr, *Environ. Sci. Technol.*, 2006, **40**, 7175–7185.
18 W. Gan, W. Guo, J. Mo, Y. He, Y. Liu, W. Liu, Y. Liang and X. Yang, *Sci. Total Environ.*, 2013, **447**, 108–115.
19 E. Malliarou, C. Collins, N. Graham and M. J. Nieuwenhuijsen, *Water Res.*, 2005, **39**, 2722–2730.
20 Q. Wei, D. Wang, Q. Wei, C. Qiao, B. Shi and H. Tang, *Environ. Monit. Assess.*, 2008, **141**, 347–357.
21 T. Bond, M. R. Templeton and N. Graham, *J. Hazard. Mater.*, 2012, **235**, 1–16.
22 J. Le Roux, H. Gallard and J. P. Croue, *Environ. Sci. Technol.*, 2012, **46**, 1581–1589.
23 T. Ye, B. Xu, Y.-L. Lin, C.-Y. Hu, S.-J. Xia, L. Lin, S. A. Mwakagenda and N.-Y. Gao, *J. Hazard. Mater.*, 2012, **241–242**, 348–354.
24 C. M. M. Bougeard, E. H. Goslan, B. Jefferson and S. A. Parsons, *Water Res.*, 2010, **44**, 729–740.
25 J. Fang, J. Ma, X. Yang and C. Shang, *Water Res.*, 2010, **44**, 1934–1940.
26 A. Kanan and T. Karanfil, *Water Res.*, 2011, **45**, 926–932.
27 M. G. Muellner, E. D. Wagner, K. McCalla, S. D. Richardson, Y. T. Woo and M. J. Plewa, *Environ. Sci. Technol.*, 2007, **41**, 645–651.
28 S. D. Richardson, M. J. Plewa, E. D. Wagner, R. Schoeny and D. M. DeMarini, *Mutat. Res., Rev. Mutat. Res.*, 2007, **636**, 178–242.
29 S. W. Krasner, *Philos. Trans. R. Soc. London, Ser. A*, 2009, **367**, 4077–4095.
30 M. J. Plewa, J. E. Simmons, S. D. Richardson and E. D. Wagner, *Environ. Mol. Mutagen.*, 2010, **51**, 871–878.
31 M. J. Plewa, E. D. Wagner, P. Jazwierska, S. D. Richardson, P. H. Chen and A. B. McKague, *Environ. Sci. Technol.*, 2004, **38**, 62–68.
32 M. J. Plewa, E. D. Wagner, M. G. Muellner, K.-M. Hsu and S. D. Richardson, in *Disinfection by-Products in Drinking Water: Occurrence, Formation, Health Effects, and Control*, ed. T. Karanfil, S. W. Krasner and Y. Xie, 2008, vol. 995, pp. 36–50.
33 D. T. Williams, G. L. LeBel and F. M. Benoit, *Chemosphere*, 1997, **34**, 299–316.
34 A. C. Diehl, G. E. Speitel, Jr, J. M. Symons, S. W. Krasner, C. J. Hwang and S. E. Barrett, *J. Am. Water Works Assoc.*, 2000, **92**, 76–90.
35 Y. Hong, S. Liu, H. Song and T. Karanfil, *J. Am. Water Works Assoc.*, 2007, 57–69.
36 X. Yang, C. Shang and P. Westerhoff, *Water Res.*, 2007, **41**, 1193–1200.
37 S. W. Krasner, M. J. McGuire, J. G. Jacangelo, N. L. Patania, K. M. Reagan and E. M. Aieta, *J. Am. Water Works Assoc.*, 1989, **81**, 41–53.
38 M. J. McGuire, J. L. McLain and A. Obolensky, *Information collection rule data analysis*, American Water Works Association, 2002.
39 B. G. Oliver, *Environ. Sci. Technol.*, 1983, **17**, 80–83.
40 J. R. Hayes, L. W. Condie, Jr and J. F. Borzelleca, *Environ. Health Perspect.*, 1986, **69**, 183.
41 NTP, *National Toxicology Program*, National Institutes of Health, National Institute of Environmental Health Sciences, Research Triangle Park, NC, 2008.