Application Note

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# Determination of Haloacetic Acids in Drinking Water by LC/MS/MS


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## Abstract

A fast, simple, and sensitive direct injection LC/MS/MS method has been developed for the determination of nine haloacetic acids (HAAs), bromate, and chlorate in drinking water. The workflow uses an Agilent 1290 Infinity II LC coupled to an Agilent 6470A triple quadrupole LC/MS. Water samples were directly injected without filtration and nine HAAs, bromate, and chlorate were separated in less than 8.0 minutes using an Agilent InfinityLab Poroshell 120 HPH-C18 column. The developed method is approximately five times faster than the current US EPA Method 557, achieving limits of detection (LODs) from 0.003 to 0.04 µg/L. These limits are lower than required in the EU, US, and many other parts of the world. Linear calibration curves with determination coefficients ($R^2$) greater than 0.997 for all analytes in a range of 0.02 to 100 µg/L were achieved. The mean recoveries of target compounds in spiked drinking water samples were from 85.2 to 107.7%, and no apparent signal suppression was observed in drinking water. Satisfactory method performance was also demonstrated in a synthetic matrix containing high ionic concentration. Finally, the method was applied to determine HAAs, bromate, and chlorate in tap (drinking) water samples collected from different regions of São Paulo city, Brazil.

## Introduction

In the 19th century, one of the most important advances in public health was the introduction of drinking water disinfection. This process helped to reduce and prevent the incidences of waterborne diseases such as typhoid, cholera, dysentery, and diarrhea.[1,2] There are several methods of disinfecting drinking water, but chlorination is still the most used due to its effectiveness and cost. However, chlorine reacts with organic and inorganic matter present in the water, and forms a series of compounds called disinfection by-products (DBPs).[3,4,5] DBPs include regulated compounds (trihalomethanes, haloacetic acids (HAAs), bromate, and chlorite) as well as unregulated compounds, all of them posing health concerns or linked to possible harmful human health effects.[6]

In the United States, the US Environment Protection Agency (EPA) regulates HAAs, establishing the maximum contaminant level (MCL) as close to health goals as possible. Cost, benefits, and the ability of public water systems to detect and remove contaminants using suitable treatment technologies are taken into consideration.[7] The MCL established for five of the HAAs, known as the HAA5—namely monochloroacetic acid (MCAA), monobromoacetic acid (MBAA), dichloroacetic acid (DCAA), dibromoacetic acid (DBAA), and trichloroacetic acid (TCAA)—is 60 µg/L.[8] These five HAAs, along with tribromoacetic acid (TBAA), bromochloroacetic acid (BCAA), bromodichloroacetic acid (BDCAA), and chlorodibromoacetic acid (CDBAA), make up the HAA9, which are recommended compounds for monitoring.[9] In Europe, the Drinking Water Directive 98/83/EC does not currently propose any guideline values for HAAs in drinking water.[10]

However, in March 2019, the European Parliament proposed a revision of the Drinking Water Directive defining the sum of the HAA9 as 80 µg/L.[11]

The determination of HAAs in drinking water is a challenge because, in addition to the low concentration levels, they are strongly hydrophilic and acidic compounds. Gas chromatography (GC) with electron capture (GC-ECD) and mass spectrometry (GC/MS) detection are the most commonly used methods to analyze HAAs after sample extraction and derivatization.[12,13] However, these methods are tedious and laborious, and are also more subject to unexpected errors and reduced reproducibility. Capillary electrophoresis (CE) with ultraviolet (CE-UV), contactless conductivity (CE-C4D), and mass spectrometry (CE/MS) detection has also been used in HAAs analysis. Although it does not require derivatization of the sample, as in GC, preconcentration steps are required to increase the sensitivity.[14,15,16] To improve ruggedness, ionic chromatography (IC) coupled to mass spectrometry with direct injection of the sample have been used in HAAs analysis. This is the method proposed by the US EPA,[17] but the long analysis time can significantly reduce the sample throughput. Liquid chromatography with tandem mass spectrometry (LC/MS/MS) detection is an alternative method due to its sensitivity and specificity. Reversed-phase liquid chromatography is the most used technique, but it is difficult to find a suitable stationary phase capable of retaining small and charged polar molecules such as HAAs.[18,19] Reversed-phase ion-pairing liquid chromatography and hydrophilic interaction liquid chromatography (HILIC) were used to increase the retention and separation of the HAAs. However, neither of the techniques was able to simultaneously improve separation and signal intensity of HAAs.[20,21]

This Application Note describes a sensitive and specific LC/MS/MS method for simultaneously analyzing nine HAAs as well as bromate and chlorate in drinking water using an Agilent InfinityLab Poroshell 120 HPH-C18 column without the use of ion pairing reagents and sample concentration steps. Figure 1 shows the molecular structure of the haloacetic acids analyzed in this work. The developed method was validated according to US EPA Method 557 protocols, and it was applied to the analysis of drinking water samples collected in São Paulo city, Brazil.

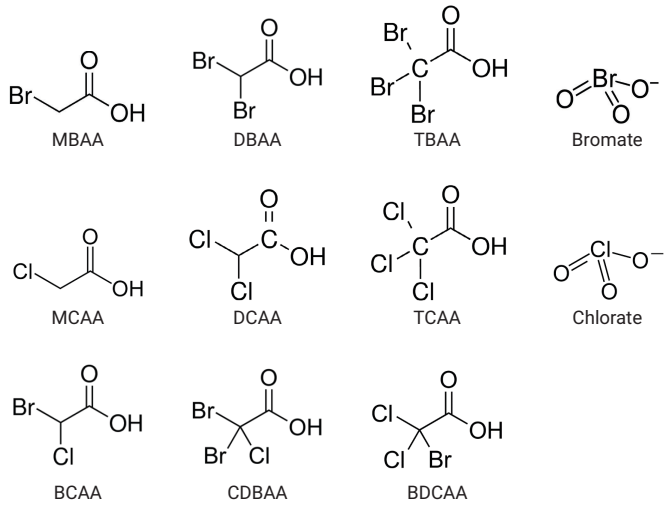


**Figure 1.** Molecular structure of analyzed haloacetic acids, bromate, and chlorate.

# Experimental

## Standards and reagents

LC/MS grade methanol (J.T. Baker) was used to prepare mobile phase with ultrapure water obtained from a Milli-Q unit (Millipore, Bedford, MA, USA) and formic acid (p/n G2453-85060). A certified reference material (CRM) of an EPA 552.2 haloacetic acids mix composed by MBAA, MCAA, DBAA, DCAA, TBAA, TCAA, BCAA, BDCAA, and CDBAA (2,000 µg/mL each) in methyl *tert*-butyl ether was obtained from Merck (Supelco). Chloroacetic acid-2-$^{13}$C (99 atom % $^{13}$C) was obtained from Sigma-Aldrich, and it was used as internal standard. Potassium bromate (≥ 99.8%, Sigma-Aldrich), potassium chlorate (≥ 99.0%, JT Baker), potassium chloride (≥ 99.5%, Fluka), potassium sulfate (≥ 99.0%, Honeywell Riedel-de-Haën), ammonium bicarbonate (≥ 99.5%, Sigma-Aldrich), and potassium nitrate (≥ 99.0%, Merck) were available in the laboratory. All HAAs, bromate, and chlorate standards were initially combined to make an intermediate stock solution at 200 µg/L. This solution was used for the preparation of calibration standards in ultrapure water. Calibration standard solutions from 0.02 to 100 µg/L were prepared daily in amber glass vials.

## Sample preparation

Residual chlorine present in the drinking water samples was quenched with 100 mg/L of ammonium chloride, in accordance with US EPA Method 557. The samples were stored at 4 °C, and protected from light until analysis. For the analysis of drinking water, there was no need to filter the samples or any further sample preconcentration/preparation step. Prior to LC/MS/MS analysis, monochloroacetic acid-2-$^{13}$C was added as internal standard to the samples and standard solutions for final a concentration of 5.0 µg/L.

## Instrumental

An Agilent 1290 Infinity II LC, configured with an Agilent 1290 Infinity II high speed pump (G7120A), 1290 Infinity II multisampler (G7167B), and 1290 Infinity II multicolumn thermostat (G7116B), coupled to an Agilent 6470A triple quadrupole LC/MS (G6470AA), was used to determine HAAs, bromate, and chlorate, using AJS (Agilent Jet Stream) ion source in negative mode. Table 1 shows the LC/MS/MS optimized conditions.

The MS was operated in dynamic multiple reaction monitoring (dMRM) mode using one specific transition for each target compound, which was obtained using the Agilent MassHunter Optimizer software tool and infusing individual 500 ng/mL standards prepared in water into the MS. Table 2 lists the retention time (Rt), and the optimized multiple reaction monitoring (MRM) parameters for the 6470A triple quadrupole LC/MS system.

**Table 1.** Liquid chromatography and triple quadrupole MS-optimized run parameters.

| Liquid Chromatography | | | |
|---|---|---|---|
| Column | Agilent InfinityLab Poroshell 120 HPH-C18, 3.0 × 150 mm, 2.7 µm (p/n 693975-502) | | |
| Column Temperature | 40 °C | | |
| Injection Volume | 20 µL | | |
| Mobile Phase | (A) Water with 0.05% formic acid | | |
| | (B) Methanol | | |
| Gradient | Time (min) | A (%) | B (%) |
| | 0.0 | 95 | 5 |
| | 9.0 | 5 | 95 |
| | 9.1 | 95 | 5 |
| Stop Time | 12 minutes | | |
| Flow Rate | 0.250 mL/min | | |
| **Triple Quadrupole MS** | | | |
| Sheath Gas Heater | 150 °C | | |
| Sheath Gas Flow | 10 L/min | | |
| Drying Gas Flow ($N_2$) | 6 L/min | | |
| Drying Gas Temperature | 120 °C | | |
| Nebulizer Pressure | 40 psi | | |
| Capillary Voltage | 2,500 V | | |
| V Charging | 0 V | | |

**Table 2.** RT and optimized MRM acquisition parameters used for the identification and quantification of HAAS, bromate, and chlorate in drinking water.

| Compound | RT (min) | Q1 (*m/z*) | Q3 (*m/z*) | Fragmentor (V) | CE (V) |
|---|---|---|---|---|---|
| $BrO_3^-$ | 2.71 | 126.9 | 110.9 | 90 | 24 |
| $ClO_3^-$ | 2.93 | 82.9 | 67.1 | 25 | 24 |
| DCAA | 4.31 | 127 | 83 | 85 | 6 |
| MCAA | 4.44 | 93 | 35 | 80 | 7 |
| M$^{13}$CAA | 4.44 | 94 | 35 | 80 | 7 |
| BCAA | 4.80 | 173 | 81 | 49 | 5 |
| MBAA | 5.09 | 137 | 79 | 80 | 8 |
| DBAA | 5.38 | 217 | 173 | 85 | 3 |
| TCAA | 6.06 | 161 | 117 | 65 | 2 |
| BDCAA | 6.36 | 163 | 81 | 60 | 6 |
| CDBAA | 6.66 | 207 | 79 | 80 | 3 |
| TBAA | 6.93 | 251 | 79 | 50 | 24 |

## Results and discussion

The mobile phase composition, gradient, and injected volume were optimized to achieve the best sensitivity and resolution. The proposed method for HAAs, bromate, and chlorate analysis takes only 12 minutes. Good separation was achieved using the InfinityLab Poroshell 120 HPH-C18 column, compared to the 60-minute method in EPA 557 on IC-MS/MS. Figure 2 shows a typical dynamic MRM chromatogram of all compounds analyzed at 2 µg/L in ultrapure water. The separation performance was also evaluated in a synthetic water matrix containing, in addition to target compounds at the same concentration, 320 mg/L chloride, 250 mg/L sulfate, 150 mg/L of bicarbonate, and 20 mg/L nitrate.

Figure 3 shows the dMRM chromatogram of the same compounds, under the same analysis conditions, in a synthetic water matrix. It is possible to see that the synthetic matrix interferes directly not only with the sensitivity, but also with the peak shape of some compounds. This behavior was also observed in the official method 557, and must be related not only to the matrix effects, but also to column capacity issues in relation to high-ionic-strength samples. This behavior affects all analytes to some degree. The synthetic matrix solution is prepared at an ionic concentration higher than that typically observed in drinking water. Such effects were minimal or not observed in the evaluated drinking water matrices evaluated.

Calibration curves, from 9 to 13 different levels, were built with standard solutions in a concentration ranging from 0.02 to 100 µg/L, depending on the individual compound and using the MCAA isotopically labeled as internal standard. Each concentration level was analyzed in triplicate. A linear fitting with no weighting was used for all analytical curves prepared in ultrapure water, and the values of the coefficient of determination ($R^2$) were higher than 0.997 for all compounds, with relative standard deviations (RSDs) ranging from 0.1 to 5.1% for run-to-run precision. Figure 4 shows an example of the response for BDCAA in drinking water using Agilent MassHunter Quantitative software (Version 10.0).

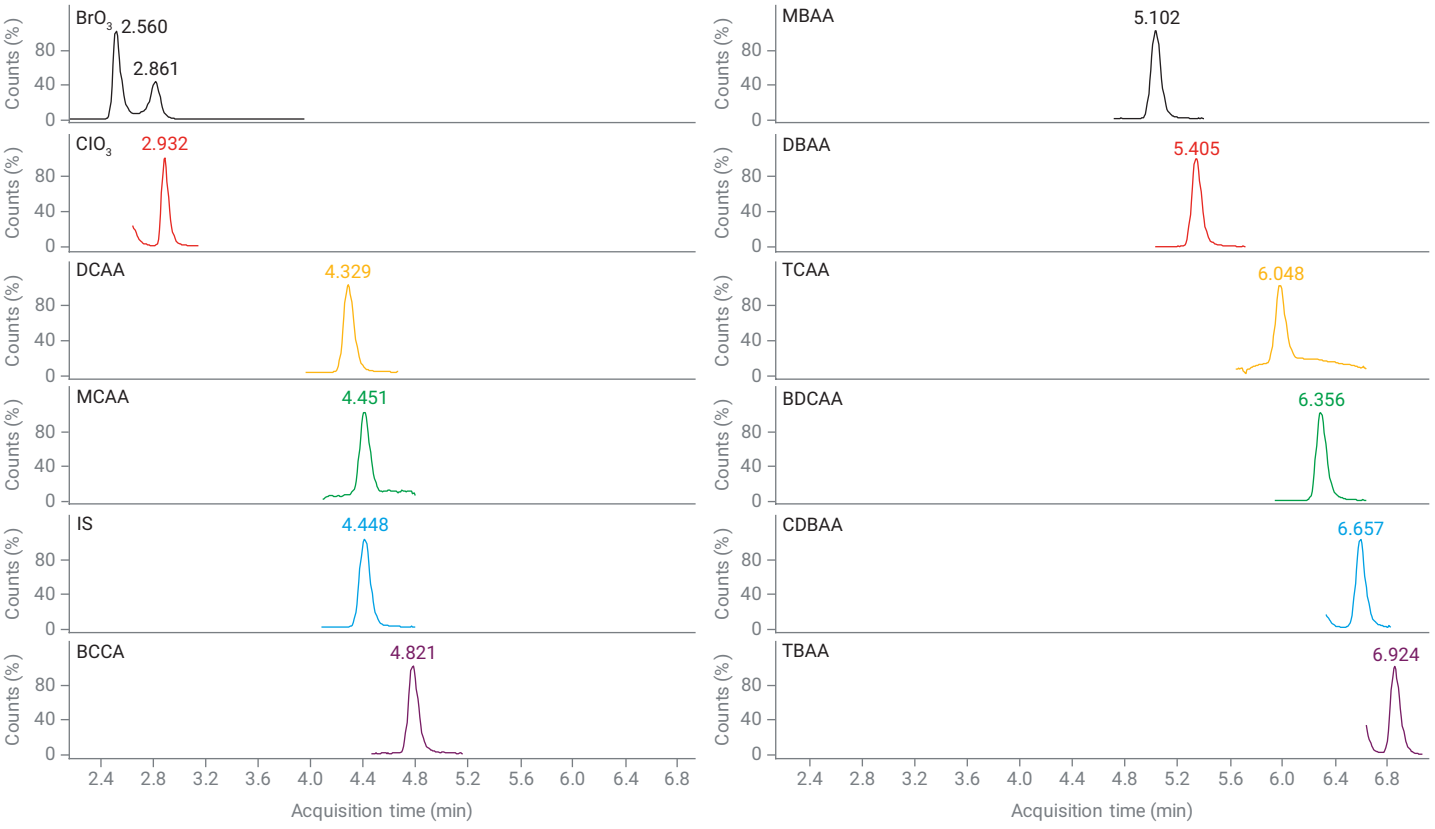


**Figure 2.** Dynamic MRM chromatogram of HAAs, bromate, chlorate, and isotopically labeled standard at 2 µg/L in ultrapure water.

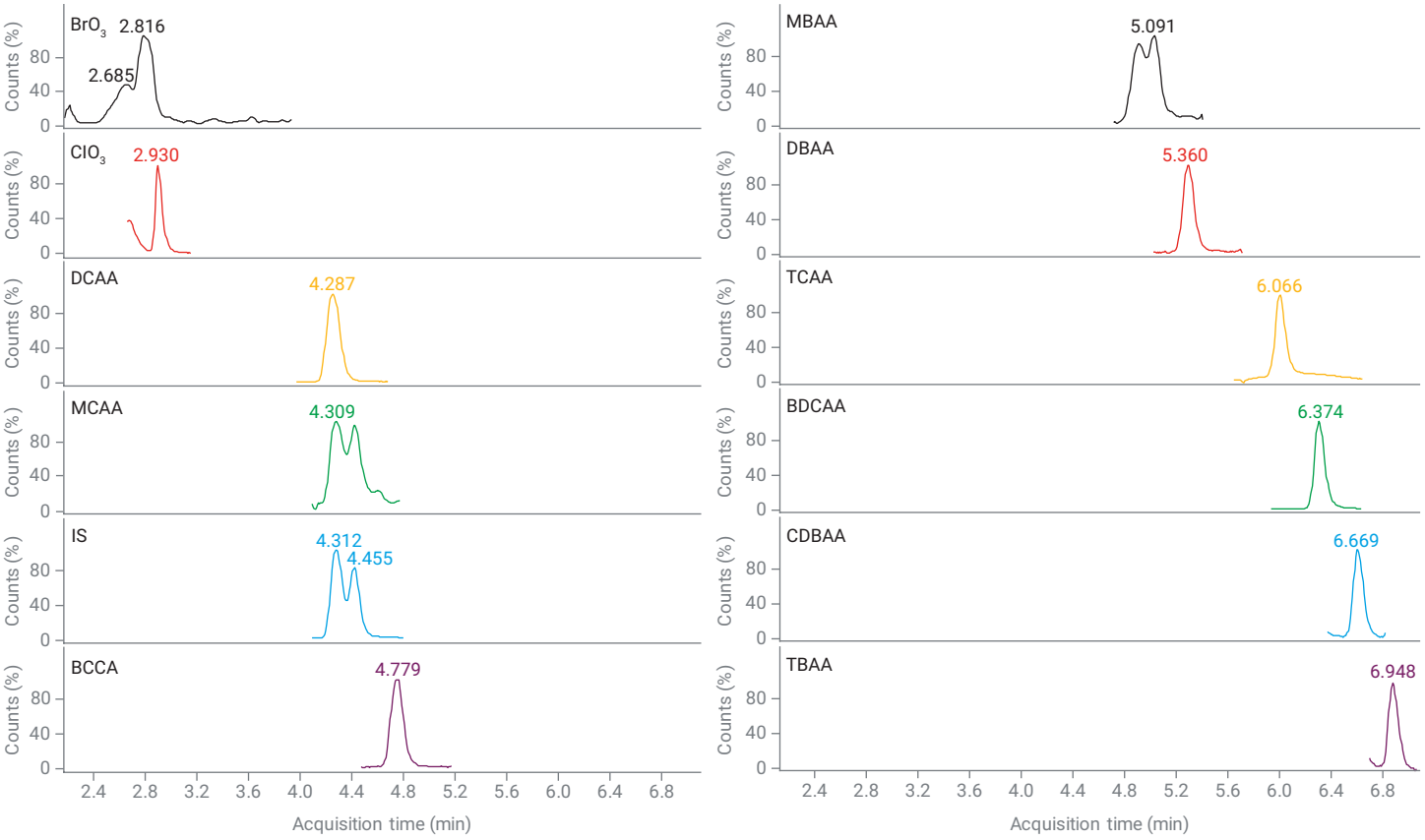


**Figure 3.** Dynamic MRM chromatogram of HAAs, bromate, chlorate, and isotopically labeled standard at 2 µg/L in synthetic matrix containing 320 mg/L chloride, 250 mg/L sulfate, 150 mg/L of bicarbonate, and 20 mg/L nitrate.

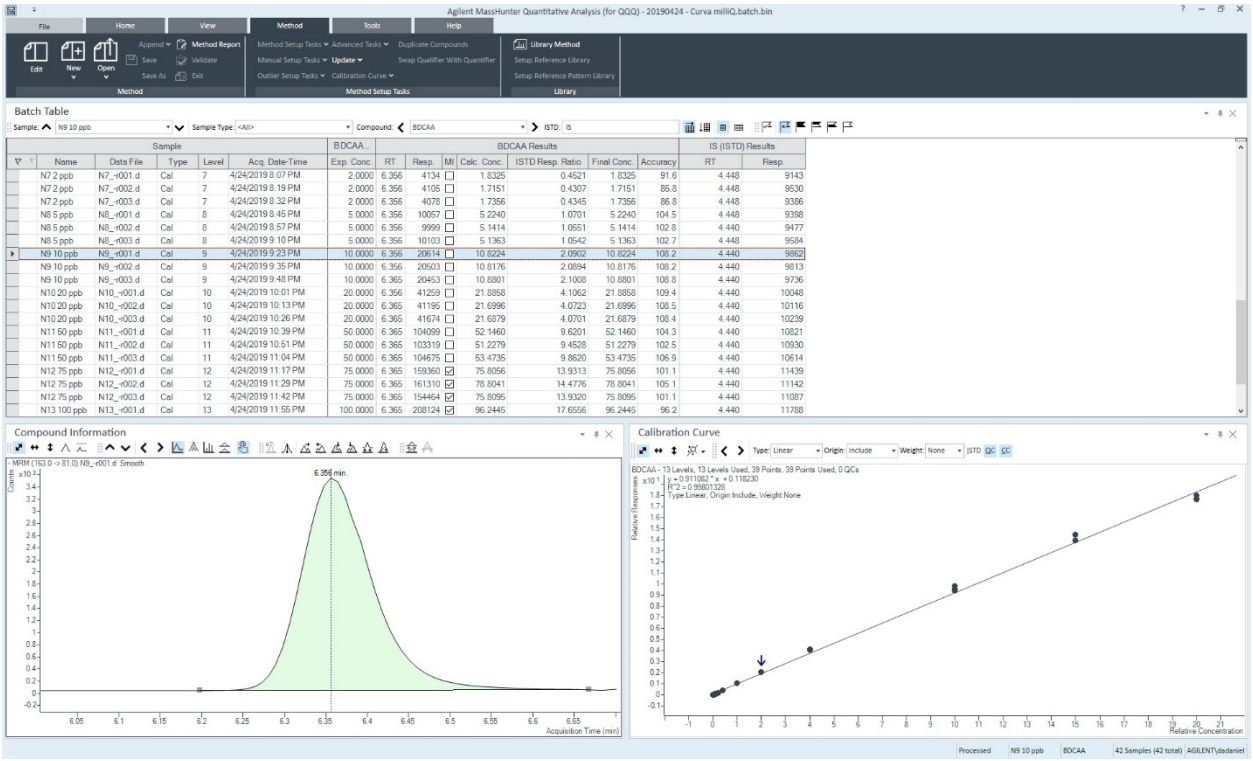


**Figure 4.** Calibration curve of BDCAA in ultrapure water using Agilent MassHunter Quantitative software (Version 10.0).

The limits of detection (LODs) and quantification (LOQs) were determined with reference to the corresponding concentration to 3 to 10 times, respectively, the baseline noise. Table 3 shows the regression equations and other characteristic parameters for the developed method.

The lowest concentration minimum reporting level (LCMRL) is defined as the lowest true concentration for which future recovery is predicted to fall, with high confidence (99%), between 50 and 150% recovery. The detection limit (DL) is defined as the statistically calculated minimum concentration that can be measured with 99% confidence that the reported value is greater than zero. These values were statistically calculated according to EPA's LCMRL statistical protocol[22] and are shown in Table 4 with the values reported for official Method 557.

**Table 3.** Quality parameters for the LC/MS/MS analysis method of the HAAs, bromate, and chlorate in ultrapure water.

| ID | Linear Range | Equation | $R^2$ | LOD | LOQ |
|---|---|---|---|---|---|
| MCAA | 0.2 – 100 | y = 0.0838x + 0.0662 | 0.998 | 0.04 | 0.13 |
| MBAA | 0.1 – 100 | y = 0.1029x + 0.0632 | 0.999 | 0.02 | 0.06 |
| DCAA | 0.05 – 100 | y = 0.7764x + 0.6448 | 0.997 | 0.01 | 0.03 |
| DBAA | 0.05 – 100 | y = 0.3356x + 0.2898 | 0.997 | 0.01 | 0.03 |
| TCAA | 0.05 – 100 | y = 1.4504x + 1.9362 | 0.997 | 0.01 | 0.03 |
| TBAA | 0.05 – 100 | y = 0.0497x + 0.0627 | 0.997 | 0.01 | 0.04 |
| BCAA | 0.1 – 100 | y = 0.0601x + 0.0447 | 0.999 | 0.01 | 0.05 |
| BDCAA | 0.02 – 100 | y = 0.1818x + 0.1407 | 0.997 | 0.004 | 0.012 |
| CDBAA | 0.05 – 100 | y = 0.0726x + 0.0749 | 0.997 | 0.005 | 0.016 |
| $BrO_3^-$ | 0.02 – 100 | y = 0.5771x - 0.1079 | 0.998 | 0.004 | 0.012 |
| $ClO_3^-$ | 0.02 – 100 | y = 0.3586x + 0.0182 | 0.998 | 0.003 | 0.01 |

**Table 4.** Values of LCMRL and DL for the LC/MS/MS analysis method of HAAs, bromate, and chlorate.

| ID | Fortification Level (µg/L) | Proposed Method (µg/L) | | Method 557 EPA (µg/L) | |
|---|---|---|---|---|---|
| | | LCMRL | DL | LCMRL | DL |
| MCAA | 0.2 | 0.45 | 0.09 | 0.58 | 0.20 |
| MBAA | 0.1 | 0.1 | 0.03 | 0.19 | 0.064 |
| DCAA | 0.05 | 0.05 | 0.01 | 0.13 | 0.055 |
| DBAA | 0.05 | 0.09 | 0.02 | 0.062 | 0.015 |
| TCAA | 0.05 | 0.08 | 0.02 | 0.25 | 0.090 |
| TBAA | 0.05 | 0.07 | 0.02 | 0.27 | 0.067 |
| BCAA | 0.1 | 0.1 | 0.04 | 0.16 | 0.11 |
| BDCAA | 0.02 | 0.04 | 0.01 | 0.19 | 0.050 |
| CDBAA | 0.05 | 0.08 | 0.02 | 0.08 | 0.041 |
| $BrO_3^-$ | 0.02 | 0.02 | 0.01 | 0.042 | 0.020 |
| $ClO_3^-$ | 0.02 | 0.03 | 0.01 | NA | NA |

Recovery experiments were carried out, in duplicate, at three concentration levels by spiking standard solutions to a blank water sample. The analyte percent recoveries were between 84.1 to 107.7%, with RSD (relative standard deviation) <15%. Table 5 presents these results.

This method was applied to determine the HAAs, bromate, and chlorate in tap drinking water samples collected from different areas in Sao Paulo city, Brazil. Table 6 shows the results.

Out of the nine HAAs, TCAA was the most abundant species. Apart from samples 4 and 6, TCAA corresponds to more than 80% of the total concentration of HAAs in the samples. Sample 6 had a total concentration above the limit set by USEPA of 60 µg/L.

**Table 5.** Recoveries of the HAAs, bromate, and chlorate from spiked water.

| ID | Linear Range | Recovery (%) (mean ± RSD, n =6) | | |
|---|---|---|---|---|
| | | Lowest Level | 1 µg/L | 100 µg/L |
| MCAA | 0.2 – 100 | 96.2 ± 11.7 | 98.0 ± 7.0 | 106.7 ± 7.4 |
| MBAA | 0.1 – 100 | 88.9 ± 6.4 | 100.9 ± 9.2 | 95.6 ± 4.9 |
| DCAA | 0.05 – 100 | 107.1 ± 6.5 | 100.5 ± 0.8 | 94.0 ± 3.3 |
| DBAA | 0.05 – 100 | 102.0 ± 9.2 | 98.0 ± 2.4 | 96.2 ± 2.1 |
| TCAA | 0.05 – 100 | 100.2 ± 8.6 | 97.4 ± 4.2 | 98.7 ± 4.7 |
| TBAA | 0.05 – 100 | 102.0 ± 7.4 | 101.5 ± 13.7 | 104.2 ± 4.7 |
| BCAA | 0.1 – 100 | 94.0 ± 9.5 | 99.3 ± 4.4 | 98.2 ± 3.2 |
| BDCAA | 0.02 – 100 | 98.9 ± 13.7 | 100.7 ± 1.7 | 96.4 ± 4.0 |
| CDBAA | 0.05 – 100 | 100.5 ± 8.1 | 98.4 ± 9.0 | 88.5 ± 12.6 |
| $BrO_3^-$ | 0.02 – 100 | 99.9 ± 9.8 | 84.1 ± 3.5 | 102.9 ± 8.4 |
| $ClO_3^-$ | 0.02 – 100 | 107.7 ± 9.9 | 88.9 ± 4.9 | 100 ± 9.4 |

**Table 6.** Concentrations of HAAs, bromate, and chlorate found in the tap drinking water of São Paulo city, Brazil.

| Compound | LOQ | Sample 1 | Sample 2 | Sample 3 | Sample 4 | Sample 5 | Sample 6 |
|---|---|---|---|---|---|---|---|
| MCAA | 0.13 | 0.45 ± 0.01 | nd | 0.41 ± 0.01 | nd | 1.29 ± 0.06 | 5.75 ± 0.16 |
| MBAA | 0.06 | nd | nd | nd | nd | 0.07 ± 0.01 | 0.37 +0.01 |
| DCAA | 0.03 | 0.74 ± 0.04 | nd | 0.27 ± 0.03 | 1.67 ± 0.02 | 5.59 ± 0.03 | 44.81 ± 0.93 |
| DBAA | 0.03 | nd | nd | <LOQ | <LOQ | 0.06 ± 0.01 | 0.48 ± 0.01 |
| TCAA | 0.03 | 34.90 ± 0.12 | 25.47 ± 0.73 | 31.91 ± 0.11 | 1.02 ± 0.03 | 31.83 ± 0.35 | 32.56 ± 0.35 |
| TBAA | 0.04 | 0.25 ± 0.01 | 0.16 ± 0.02 | 0.28 ±0.03 | nd | 0.28 ± 0.04 | 0.13 ± 0.02 |
| BCAA | 0.05 | <LOQ | nd | <LOQ | 0.15 ± 0.01 | 0.85 ± 0.03 | 6.69 ± 0.20 |
| BDCAA | 0.012 | 4.19 ± 0.05 | 3.59 ± 0.05 | 3.76 ± 0.04 | 0.13 ± 0.01 | 4.63 ± 0.05 | 4.48 ± 0.03 |
| CDBAA | 0.016 | 0.57 ± 0.03 | 0.46 ± 0.02 | 0.70 ± 0.04 | 0.02 ± 0.004 | 0.54 ± 0.03 | 0.47 ± 0.04 |
| $BrO_3^-$ | 0.012 | <LOQ | <LOQ | nd | nd | <LOQ | nd |
| $ClO_3^-$ | 0.01 | 1.56 ± 0.01 | 2.06 ± 0.04 | 0.43 ± 0.02 | 0.62 ± 0.06 | 1.33 ± 0.05 | 1.09 ± 0.07 |
| Σ of HAAs | | 41.1 µg/L | 29.7 µg/L | 37.3 µg/L | 3.0 µg/L | 45.1 µg/L | 95.7 µg/L |

nd = not detected. ΣΣ: sum of HAAs concentrations in µg/L.

## Conclusion

This Application Note demonstrates an easy, fast, and robust LC/MS/MS method for the analysis of HAAs, bromate, and chlorate in drinking water samples. The proposed method allows the direct injection of the sample without any preparation or preconcentration step, thus greatly improving laboratory productivity and eliminating extraction variables. The developed method is approximately five times faster than the current US EPA Method 557, achieving LODs from 0.003 to 0.04 µg/L, and recoveries between 84.2 to 107.7% with RSD lower than 15%. The results clearly demonstrate the applicability and effectiveness of the developed method for analyzing HAAs, bromate, and chlorate residues in drinking water samples.

## References


1. Akin, E. W.; Hoff, J. C.; Lippy, E. C. Waterborne Outbreak Control: Which Disinfectant? *Environ. Health Perspect.* **1982**, 46, 7–12.
2. LeChevallier, M. W.; Au. K. -K. Water Treatment and Pathogen Control. Process Efficiency in Achieving Safe. London, United Kingdom: International Water Association; **2004**.
3. Liang, L.; Singer, P. C. Factors Influencing the Formation and Relative Distribution of Haloacetic Acids and Trihalomethanes in Drinking Water. *Environ. Sci. Technol.* **2003**, *37*, 2920–2928.
4. Stevens, A. A.; *et al.* Chlorination of Organics in Drinking Water. *Journal American Water Works Association* **1976**, *68*, 615–620.
5. Richardson, S. D. Disinfection By-Products and Other Emerging Contaminants in Drinking Water. *TrAC Trends in Analytical Chemistry* **2003**, *22*, 666–684.
6. Chaves, R. S.; *et al.* Hazard and Mode of Action of Disinfection By-Products (DBPs) in Water for Human Consumption: Evidences and Research Priorities. *Comparative Biochemistry and Physiology, Part C,* **2019**, *223*, 53–61.
7. U.S. Environmental Protection Agency (US EPA), Disinfectants and Disinfection By-Products: Proposed Rule. Fed. Reg. **1994**, *59*, 38668–38829.
8. U.S. Environmental Protection Agency (US EPA), National Primary Drinking Water Regulations: Stage 2 Disinfectants and Disinfection by-products rule. Fed. Regist. **2006**, *71*, 388–493.
9. U.S. Environmental Protection Agency (US EPA), Revisions to the Unregulated Contaminant Monitoring Rule (UCMR4) for Public Water Systems and Announcement of Public Meeting. Fed. Regist. **2016**, *81*, 92666–92692.
10. European Union, COUNCIL DIRECTIVE 98/83/EC on the quality of water intended for human consumption. *Official Journal of the European Communities* **1998**, *L330*, 1–32.
11. European Parliament. Legislative Resolution of 28 March 2019 on the Proposal for a Directive of the European Parliament and of the Council on the Quality of Water Intended for Human Consumption. available at http://www.europarl.europa.eu/doceo/document/TA-8-2019-0320_EN.html

12. Munch, D. J.; Munch, J. W.; Pawlecki, A. M. Determination of Haloacetic Acids and Dalapon in Drinking Water by Liquid–Liquid Extraction, Derivatization and Gas Chromatography with Electron Capture Detections, EPA Method 552.2, Revision 1, Methods for the Determination of Organic Compounds, Supplement III, EPA Document No. 600-R-95-131, GPO, Washington, DC, **1995**.
13. Li, W.; *et al.* Determination of Ten Haloacetic Acids in Water Using Gas
14. Chromatography-Triple Quadrupole *Mass Spectrometry. Anal. Methods* **2013**, *5*, 2258–2266.
15. Martínez, D.; Borrull, F.; Calull, M. Evaluation of Different Electrolyte Systems and On-Line Preconcentrations for the Analysis of Haloacetic Acids by Capillary Zone Electrophoresis. *Journal of Chromatography A* **1999**, *835*, 187–196.
16. Kubán, P.; *et al.* Determination of Five Priority Haloacetic Acids by Capillary Electrophoresis with Contactless Conductivity Detection and Solid Phase Extraction Preconcentration. *J. Sep. Sci.* **2012**, *35*, 666–673.
17. Zhang, H.; *et al.* Pressure-Assisted Electrokinetic Injection for On-Line Enrichment in Capillary Electrophoresis–Mass Spectrometry: A Sensitive Method for Measurement of Ten Haloacetic Acids in Drinking Water. *Analytica Chimica Acta* **2011**, *706*, 176–183.
18. U.S. Environmental Protection Agency (US EPA). Method 557: Determination of Haloacetic acids, Bromate, and Dalapon in Drinking Water by Ion Chromatography electrospray Ionization Tandem Mass Spectrometry (IC-ESI-MS/MS), 2009. Available at https://nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=P1005OKO.txt.
19. Meng, L.; *et al.* Trace Determination of Nine Haloacetic Acids in Drinking Water by Liquid Chromatography-Electrospray Tandem Mass Spectrometry. *Journal of Chromatography A* **2010**, *1217*, 4873–4876.
20. Luo, Q.; *et al.* Optimized Chromatographic Conditions for Separation of Halogenated Acetic Acids by Ultra-Performance Liquid Chromatography-Electrospray Ionization-Mass Spectrometry. *Journal of Chromatography A* **2013**, *1277*, 26–34.
21. Chen, C. -Y.; Chang, S. -N.; Wang, G. -S. Determination of Ten Haloacetic Acids in Drinking Water Using High-Performance and Ultra-Performance Liquid Chromatography–Tandem Mass Spectrometry. *Journal of Chromatographic Science* **2009**, *47*, 67–74.
22. Loos, R.; Barceló, D. Determination of Haloacetic Acids in Aqueous Environments by Solid-Phase Extraction Followed by Ion-Pair Liquid Chromatography–Electrospray Ionization Mass Spectrometric Detection. *Journal of Chromatography A* **2001**, *938*, 45–55.
23. EPA. Statistical Protocol for the Determination of the Single-Laboratory Lowest Concentration Minimum Reporting Level (LCMRL) and Validation of Laboratory Performance at or below the Minimum Reporting Level (MRL); **2004**, EPA-815-R-05-006.

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