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Article

Simultaneous Determination of Chlorinated and Brominated Acetic Acids in Various Environmental Water Matrixes by High-Performance Liquid Chromatography–Inductively Coupled Plasma Tandem Mass Spectrometry without Sample Preparation

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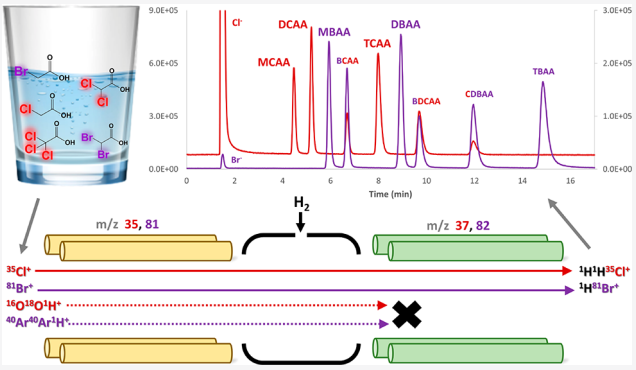
ABSTRACT: The halogenated acetic acids (HAAs) are generally considered as environmental contaminants and are suspected to pose a major public health concern. The inductively coupled plasma mass spectrometry (ICPMS) has been improved by coupling with the tandem mass spectrometry technology (ICPMS/MS), enabling ultratrace determination of heteroatoms. There have been few reports about the determination of chlorine-containing analytes by high-performance liquid chromatography (HPLC)–ICPMS/MS but none about utilizing this technique for the speciation analysis of organic halogenated compounds in environmental matrixes. We report a rapid method for the simultaneous determination of up to nine chlorinated and brominated acetic acids by HPLC–ICPMS/MS in Austrian surface, ground, and tap water. The chromatographic separation of the main five regulated haloacetic acids (so-called HAA5: chloroacetic acid, dichloroacetic acid, trichloroacetic acid, bromoacetic acid, and dibromoacetic acid) could be achieved in <6 min with limits of detection of 1.4–1.6 μg Cl L^{-1} and 0.8–1.5 μg Br L^{-1} for the chlorinated and brominated acetic acids, respectively. The method was validated through recovery experiments at four concentration levels (10–500 μg L^{-1}) as well as by analyzing the U.S. Environmental Protection Agency (EPA) 552.2 CRM (certified reference material) in pure water and in three different water matrixes (tap, river, and groundwater), and thereby validated for repeatability (RSD% 1–10%), accuracy (±1.0–15%), and linearity (r^2 = 0.9996–0.9999). The method fulfills the regulatory concentration limits by the EPA for HAA5 [maximum contaminant level (MCL) 60 μg L^{-1}] and the limits currently being reviewed by the European Union for HAA9 (80 μg L^{-1}) and demonstrates the advantages of HPLC–ICPMS/MS for the analysis of environmental water samples for halogen-tagged contaminants.



Along with trihalomethanes (THMS), the halogenated acetic acids (HAAs) are among the most common groups of known water disinfection byproducts (DBPs).[1] Following the first identification of HAAs in drinking water in 1979, which was attributed to chlorination of natural organic matter,[2] *in vitro* and animal model studies were frequently undertaken in order to investigate the biological mechanisms underlying the cytotoxicity, genotoxicity,[3−10] and teratogenicity[11,12] of these common water contaminants. The general outcome of these studies supports their possible contribution to the elevation of cancer risk in humans which has been assessed by animal[13−15] and epidemiological studies.[16−20] Therefore, the levels of five haloacetic acids in drinking water (the so-called HAA5) including monochloro-, dichloro-, trichloro-, monobromo-, and dibromoacetic acetic acid have been regulated by the U.S. Environmental Protection Agency (EPA) and restricted to a combined maximum contaminant level of 60 μg L^{-1} in drinking water.[21] In the European Union, a proposal for a maximum concentration of 80 μg L^{-1} for the sum of nine haloacetic acids (HAA9) is currently under consideration.[22]

Although the major source of the haloacetic acids involves water disinfection processes, these were also found in precipitation.[23,24] In particular, chloro- and bromoacetates were detected in glacier ice and firn samples of preindustrial origins, which supports the presence of natural sources for their production.[25,26] Another indication of their natural production involves the reported formation of chlorinated

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acetic acids by enzymatic chlorination of humic substances in soil carried out by certain microorganisms.[27−32]

Currently, the most commonly applied method for the determination of the haloacetic acids involves high-performance liquid chromatography (HPLC) coupled with electrospray ionization tandem mass spectrometry (HPLC−ESI-MS/MS).[33−37] Despite its high sensitivity and selectivity, the technique can in general be prone to matrix effects due to ion signal suppression/enhancement in the electrospray source.[38] Ideally, accurate determination by ESI-MS/MS detection would require the utilization of isotopically labeled internal standards for each and every analyte individually. To help eliminate the need for this approach, sample preparation by solid-phase extraction is sometimes employed in HPLC−ESI-MS/MS methods for the combined haloacetic acids determination,[34,36,39,40] in order to mitigate the matrix effects problem. The haloacetic acids have also been determined by methods based on techniques such as gas chromatography coupled with a mass spectrometric (GC−MS)[41−45] or electron capture detector (GC-ECD), with the latter being the basis for the U.S. EPA reference method 552.[46−48] These techniques are not completely devoid of matrix effects and, additionally, require a sample preparation step to convert the HAAs into their ester derivatives, which introduces additional time and labor demands, as well as possible sources of variability and error.

An ideal analytical method would involve direct, selective, sensitive, and simultaneous determination of multiple analytes in their native chemical form in untreated samples using simple external standardization. The potential of the inductively coupled plasma mass spectrometry (ICPMS) has been gaining increased recognition as a chromatographic detector, as it fulfills many aspects in the above-mentioned criteria. The applicability of ICPMS to the determination of halogenated acetic acids has already been realized[49,50] but has been recently significantly improved with the introduction of the tandem mass spectrometry technology (ICPMS/MS),[51−54] allowing a decrease in the detection limits by orders of magnitude and selective speciation analysis of several nonmetal elements, including inorganic chlorine-containing analytes (e.g., perchlorate and chlorate) in blood[55] and environmental samples[56] as well as chlorine-containing active pharmaceutical ingredients (e.g., diclofenac) in blood.[57]

The aim of the present work was to develop and validate a simple and rapid HPLC−ICPMS/MS method for the direct and concurrent determination of chlorinated and brominated acetic acids in drinking, ground, and river water matrixes, as well as to generally highlight the advantages of HPLC−ICPMS/MS as an element-selective tool for the trace speciation analysis of halogen-tagged environmental contaminants.

■ EXPERIMENTAL SECTION

Sample collection was generally performed as described in our previous work.[56] Briefly, about 200 mL of tap water (pH = 7.9, water hardness 268 mg L^{-1} $CaCO_3$, conductivity 554 μS cm^{-1}) was collected in 300 mL Corning polypropylene bottles (Corning Inc., New York, U.S.A.) on August 20, 2019 within the place of residence of the authors in the city of Graz. Ground water [total organic carbon (TOC), 1.2 mg L^{-1}, pH = 7.1, water hardness 109 mg L^{-1} $CaCO_3$, conductivity 432 μS cm^{-1}] was collected by the Austrian agency for health and food safety (AGES) on July 31, 2018 from a well in Leutschach, Styria, Austria using sterile 500 mL polypropylene bottles. River water samples (pH = 7.8, water hardness 203 mg L^{-1} $CaCO_3$, conductivity 341 μS cm^{-1}) were collected on August 20, 2019 from the bank along the Austrian river Mur in the center of the city of Graz (Innere Stadt region, 47°04′26.6″ N 15°26′05.1″ E) using 300 mL Corning polypropylene bottles. The studied matrixes were further characterized by total element concentrations in the various matrixes (Table S1), determined by ICPMS/MS in the no gas (Na and K), oxygen mode (S, P, Ca, Mg, and Si 0.3 mL min^{-1}), and hydrogen mode (Cl, 3.0 mL min^{-1}). The tap and river water samples were freshly collected and stored at 4 °C before analysis within ca. 72 h. The groundwater was stored at −80 °C, thawed, and stored at 4 °C before analysis within ca. 72 h. A quenching reagent was not employed since Austrian drinking water is not chlorinated.

The matrix of the collected water samples as well as the HAA standards (purchased from Sigma-Aldrich, Steinheim, Germany, and prepared in pure water, 18.2 MΩ·cm) was matched with the acidity of the mobile phase with the addition of 0.3% trifluoroacetic acid (TFA), 0.5% nitric acid, or 50 mM oxalic acid (trace metal basis grade, Sigma-Aldrich, Steinheim, Germany) in order to enable the injection of larger volumes (see below) and lower limits of detection (LODs). The water samples were withdrawn by polypropylene syringes (2.0 mL capacity, NORM-JECT, Henke Sass Wolf, Tuttlingen, Germany) and filtered with 0.22 μm nylon filters (Chromafil Xtra PA-20/13, Macherey-Nagel GmbH, Dueren, Germany) into polypropylene HPLC vials (Bruckner, Linz, Austria) prior to injection onto the chromatographic column by the HPLC autosampler.

The accuracy and repeatability (n = 3) of the developed method were evaluated based on three different approaches: (1) by spiking the three different matrixes with the halogenated acetic acids (including the regulated HAA5 at four different levels, namely, 10, 25, 100, and 500 μg L^{-1}), (2) by analyzing the EPA 552.2 certified reference material (CRM) (see below), and (3) by spiking the three matrixes with the EPA 552.2 certified reference material.

The certified reference material EPA 552.2 [Haloacetic Acid Mix, Sigma-Aldrich, Steinheim, Germany, labeled to contain 2.000 g L^{-1} of each of nine haloacetic acids, namely, chloroacetic acid (CAA), dichloroacetic acid (DCAA), bromoacetic acid (BAA), chlorobromoacetic acid (CBAA), trichloroacetic acid (TCAA), dibromoacetic acid (DBAA), dichlorobromoacetic acid (DCBAA), chlorodibromoacetic (CDBAA) acid, and tribromoacetic acid (TBAA)], was prepared by a 1 + 999 dilution in pure water and in the three above-mentioned water matrixes including a final concentration of 50 mM oxalic acid.

The haloacetic acids were chromatographically separated on an HPLC system (Agilent 1100, Agilent Technologies, Waldbronn, Germany) consisting of a quaternary pump (G1311A, max pressure 400 bar), an autosampler ALS G1367C, a degasser G1379A, a column compartment COLCOM (G1316A), and a sample chiller ALSTherm G1330B.

The separation of nine haloacetic acids was performed using the following chromatographic conditions: stationary phase, YMC Triart-C18 (3.0 mm i.d. × 150 mm long, 3 μm particle size, operating pH range according to the manufacturer, 1−12); mobile phase, 22 mM oxalic acid (pH = 1.8); column temperature, 40 °C; mobile phase flow rate, 0.5 mL min^{-1}; injection volume, 50 μL. An expedited chromatographic

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Table 1. Recovery and Repeatability (RSD%) of the Determination of Six HAAs in Various Water Matrixes[a]

	tap water				ground water				river (Mur) water			
	L1	L2	L3	L4	L1	L2	L3	L4	L1	L2	L3	L4
CAA	9.8	25	98	500	10	25	97	486	9.7	25	98	491
	98%	100%	98%	100%	100%	100%	97%	97%	97%	100%	98%	98%
	(2%)	(4%)	(1%)	(2%)	(7%)	(4%)	(2%)	(2%)	(7%)	(4%)	(3%)	(3%)
DCAA	11	26	101	504	11	26	100	493	11	27	102	497
	110%	104%	101%	101%	110%	103%	100%	99%	110%	112%	102%	99%
	(7%)	(4%)	(1%)	(2%)	(8%)	(4%)	(1%)	(1%)	(7%)	(4%)	(4%)	(3%)
TCAA	10	26	100	498	11	26	99	485	10	26	100	498
	100%	103%	100%	99%	110%	104%	99%	97%	100%	104%	100%	100%
	(10%)	(4%)	(2%)	(4%)	(10%)	(4%)	(3%)	(2%)	(3%)	(4%)	(1%)	(4%)
BAA	10	26	103	517	10	26	101	510	10	26	104	517
	100%	104%	103%	103%	100%	104%	101%	102%	100%	104%	104%	104%
	(5%)	(4%)	(4%)	(4%)	(2%)	(4%)	(4%)	(3%)	(4%)	(4%)	(4%)	(5%)
DBAA	9.8	26	103	516	10	26	103	509	10	26	104	518
	98%	104%	103%	103%	100%	102%	103%	102%	100%	104%	104%	104%
	(6%)	(4%)	(3%)	(4%)	(1%)	(4%)	(2%)	(3%)	(6%)	(8%)	(3%)	(4%)
TBAA	10	26	103	512	10	25	101	506	10	27	104	516
	100%	102%	103%	102%	100%	100%	101%	101%	100%	111%	104%	103%
	(5%)	(8%)	(2%)	(5%)	(1%)	(8%)	(5%)	(4%)	(5%)	(8%)	(4%)	(5%)

[a]The values show the mean recovered concentration (in μg Cl/Br L^{-1}), mean recovery (%), and the relative standard deviation (%) in brackets (n = 3). The spiked levels were as follows: L1, 10 μg Cl/Br L^{-1}; L2, 25 μg Cl/Br L^{-1}; L3, 100 μg Cl/Br L^{-1}; L4, 500 μg Cl/Br L^{-1}. CAA, chloroacetic acid; DCAA, dichloroacetic acid; TCAA, trichloroacetic acid; BAA, bromoacetic acid; DBAA, dibromoacetic acid; TBAA, tribromoacetic acid.

method using the same conditions above with the exception of using 0.15% of trifluoroacetic acid, pH = ca. 1.8 (≥99%, purified by redistillation by the manufacturer, Sigma-Aldrich, Steinheim, Germany) in pure water and a flow rate of 0.8 mL min^{-1} was used for the separation of six haloacetic acids including the regulated HAA5 in addition to tribromoacetic acid.

The outlet of the chromatographic column was connected directly with the nebulizer of an ICPMS/MS system (Agilent 8800 ICPQQQ, Agilent Technologies, Waldbronn, Germany) using PEEK capillary tubing (0.127 mm in internal diameter and ca. 30 cm in length). The ICPMS/MS system consisted of an AriMist PEEK nebulizer (maximum operating nebulizer gas flow rate 0.8 L min^{-1}), a glass double-pass spray chamber cooled at 2 °C, nickel/copper sampler and skimmer cones, and a quartz plasma torch with an inner diameter of 2.5 mm.

The ICPMS/MS was operated in the reaction cell mode with 4.0 mL min^{-1} hydrogen as the reaction gas (H_2 purity 6.0). The operating ICPMS/MS parameters were as follows: RF power, 1550 W; RF matching, 1.86; sampling depth, 3.0 mm; nebulizer gas flow rate, 0.65 L min^{-1}; makeup gas flow rate, 0.35 L min^{-1}; OctP bias, −10 V; Oct RF, 190; energy discrimination, −4.0 V; extract 1, 0.0 V; extract 2, −190 V; omega bias, −115 V; omega lens, 6.4 V; deflect, −0.8 V; cell focus, −3.0; cell entrance, −50 V; cell exit, −60 V; plate bias, −60 V; Q1 entrance, −3.0 V; Q1 exit, −3.0 V; Q1 bias, −2.0 V; Q1 prefilter bias, −48 V; Q1 postfilter bias, −18; SLS factor, 0.5; SLG factor, 1. Chlorine and bromine were measured by monitoring the mass transitions 35 → 37 and 81 → 82, respectively. Concentrations in the present work are generally reported as elemental concentration (μg Cl/Br L^{-1}) unless otherwise indicated.

For regular quality control and instrument tuning, we monitor m/z 59 (Co), 89 (Y), and 205 (Tl) in a standard tuning solution containing 1.0 μg L^{-1} of Li, Co, Y, Tl, Ce, As, and Se in 1% nitric acid. Typical counts in the no gas mode are around 65 000, 400 000, and 190 000 counts/s (cps) for m/z 59, 89, and 205, respectively. The oxide and doubly charged ion formation were monitored by recording the ratios 156/140 (CeO^+/Ce^+) and 70/140 (Ce^{2+}/Ce^+), which were generally <1.5% and <2.0%, respectively.

RESULTS AND DISCUSSION

A chromatographic method was initially developed for the separation of six haloacetic acids [chloroacetic acid (CAA), dichloroacetic acid (DCAA), trichloroacetic acid (TCAA), bromoacetic acid (BAA), dibromoacetic acid (DBAA), and tribromoacetic acid (TBAA)], including the regulated five haloacetic acids (the so-called HAA5), using trifluoroacetic acid as the eluent, which was found to achieve a fast separation of the six haloacetic acids in ca. 7 min. The accuracy and the repeatability of the developed method for the determination of the six haloacetic acids in the tap, river, and groundwater matrixes were validated by recovery experiments at four different concentration levels based on external standardization (Table 1). The linearity of the method was tested over the concentration range of 10−1000 μg Cl/Br L^{-1} (r^2 = 0.9996−0.9999). The calculated instrumental LODs (based on the S/N = 3 definition) were 1.4−1.6 μg Cl L^{-1} for the chlorinated acetic acids and 0.8−1.5 μg Br L^{-1} for the brominated acetic acids (injection volume 50 μL). Figure 1 shows the detection and separation of the six haloacetic acids in the three water matrixes spiked at a concentration of 10 μg Cl/Br L^{-1}. The concentrations of all HAAs in the native (nonspiked) water matrixes were <LOD.

The method was later expanded by substituting the 0.15% TFA mobile phase with a mobile phase of 22 mM oxalic acid (pH 1.8), and the mobile phase flow rate was decreased to 0.5 mL min^{-1}, enabling baseline separation of the nine haloacetic acids found in the EPA 552.2 certified reference material in ca. 15 min (Figure 2). The optimization of oxalic acid mobile phase pH is illustrated in Figure S2A−E. Note that different pH values yield different selectivities and elution orders depending on the positioning of the pH relative to the widely

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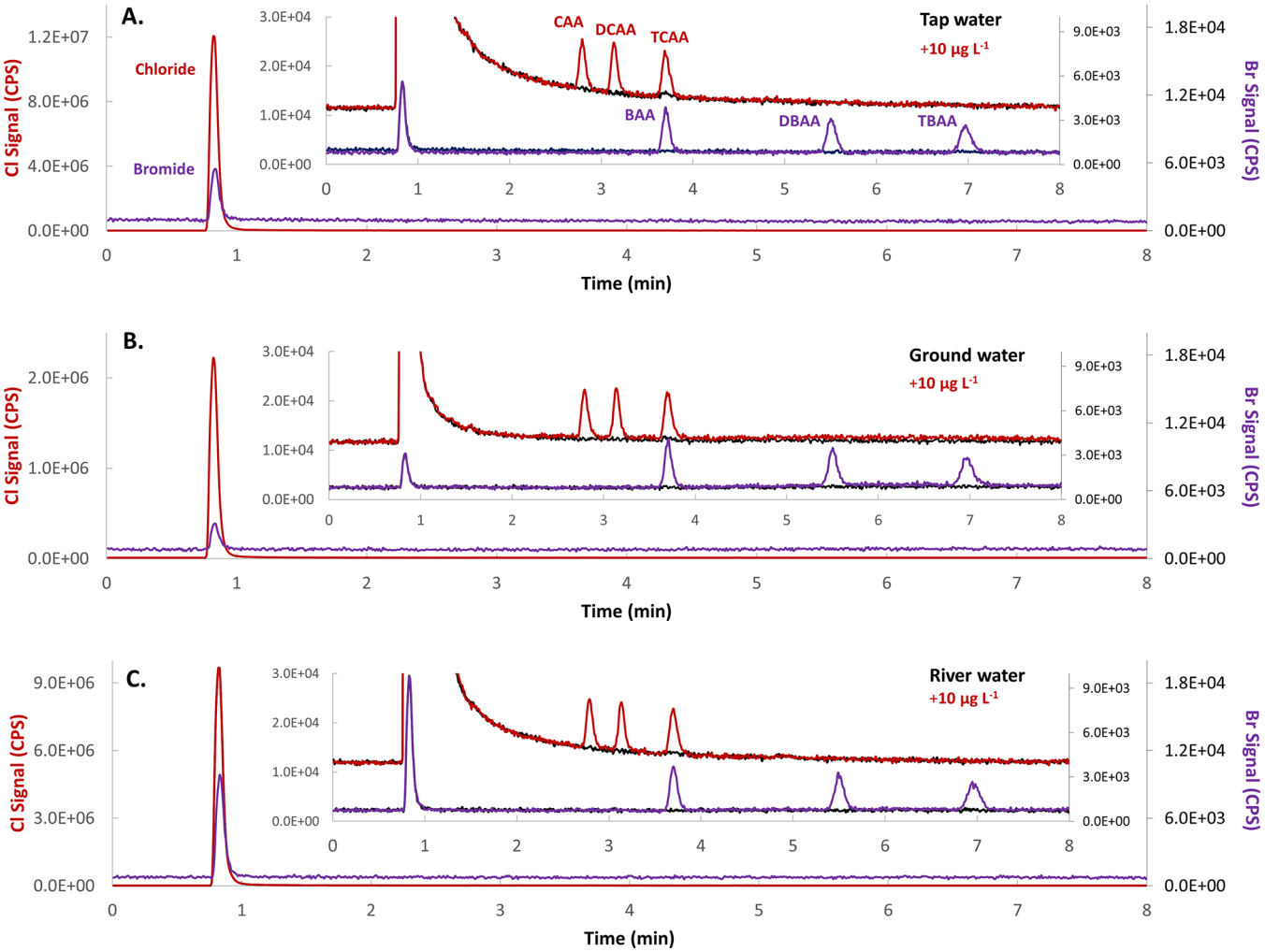

Figure 1. Detection and separation of haloacetic acids in spiked water samples. The chromatograms show native (black) and spiked tap (A), ground (B), and river water (C) (red and violet). The spiking concentration was 10 μg L^{-1} (elemental concentration). All samples were acidified prior to injection with TFA to a final concentration of 0.3%. Mobile phase, 0.15% TFA in pure water (18.2 MΩ·cm); stationary phase, YMC Triart-C18 (3.0 mm i.d. × 150 mm long, 3 μm particle size, pH range 1−12); column temperature, 40 °C; mobile phase flow rate, 0.8 mL min^{-1}; injection volume, 50 μL.

different pK_a values for the different haloacetic acids (pK_a 0.7−2.9). The accuracy and repeatability of the method were reassessed by quantifying the nine haloacetic acids in a 1 + 999 dilution of the EPA 552.2 CRM in pure water as well as in the three studied water matrixes using external calibration (Table 2). The determined concentrations were in agreement with the certified concentrations (within ±10% on average) in all four matrixes (Table 2).

In order to maximize the injection volume and therefore achieve the lowest possible LOD, we recommend acidifying the water samples in order to decrease the gap in pH between the mobile phase and the alkaline hard water matrixes. Figure S1 shows the effects of injecting different volumes of tap water spiked with the six haloacetic acids, without acidification (Figure S1A−C) and with acidification with different concentrations of TFA (Figure S1D−F). A 5-fold increase in the injection volume was enabled and a corresponding improvement in the LOD was achieved by acidification with 0.1−0.5% TFA. Precaution must be taken by using high-purity TFA as this could otherwise possibly contain traces of other HAAs as impurities which must be assessed by blank inspection. Alternatively, other acids can also be used (e.g., 50 mM oxalic acid or 0.5% nitric acid which were tested and found to yield similar results). The retention times (min) ± SD (standard deviation) for chloro-, dichloro-, trichloro-, bromo-, dibromo-, and tribromoacetic acid (Figure 1) were 2.79 ± 0.01, 3.13 ± 0.01, 3.70 ± 0.01, 3.70 ± 0.01, 5.50 ± 0.02, and 6.96 ± 0.03 in pure water and 2.78 ± 0.01, 3.14 ± 0.06, 3.69 ± 0.04, 3.69 ± 0.01, 3.69 ± 0.01, 5.48 ± 0.02, and 6.93 ± 0.01 in all three sample matrixes, all analyzed cyclically over a period of ca. 9 h. This indicates that acidification provides robust chromatographic behavior under high-volume injection in all sample matrixes tested.

The developed method achieves instrumental limits of quantification (LOQs) within the range of 4.6−12 μg L^{-1} (calculated based on molecular concentration), which can be considered comparable to some of the LOQs recently reported by (U)HPLC−ESI-MS/MS methods not employing sample preconcentration (e.g., 0.5−5,[33] 0.5−5.8,[58] 0.5−3.3,[37] and 0.1−2.0[59] μg L^{-1}). Furthermore, recoveries determined in the present method based on external calibration (see Table 1) for the three different hard water matrixes tested demonstrate the advantage of HPLC−ICPMS/MS in terms of a much higher resistance to matrix effects and indicate that the reported

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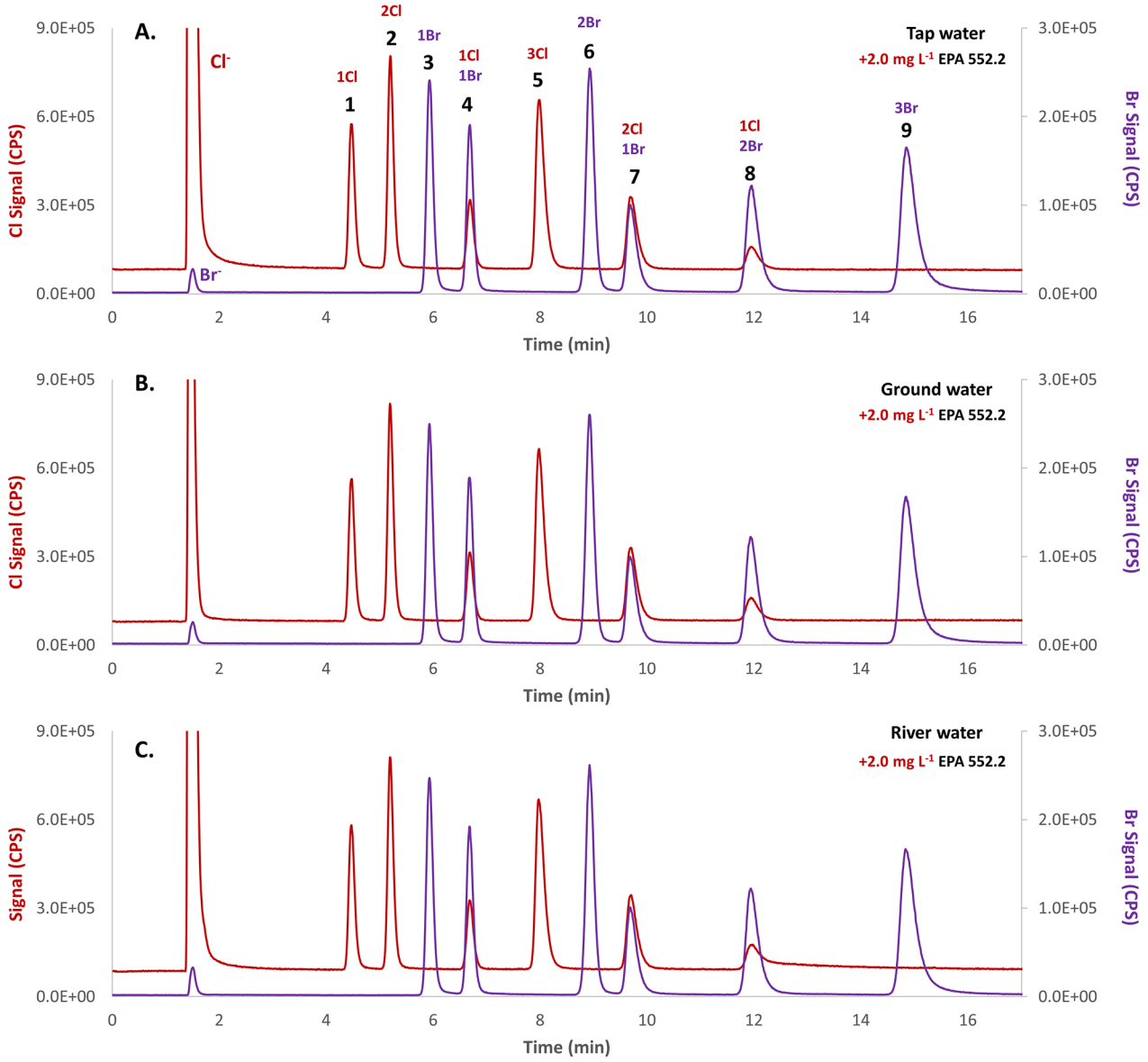

Figure 2. Detection and separation of haloacetic acids in water samples spiked with the EPA 552.2 certified reference material. The EPA 552.2 CRM is stated to contain 2.000 g L^{-1} of each haloacetic acid (1, chloroacetic acid; 2, dichloroacetic acid; 3, bromoacetic acid; 4, chlorobromoacetic acid; 5, trichloroacetic acid; 6, dibromoacetic acid; 7, dichlorobromoacetic acid; 8, chlorodibromoacetic acid; 9, tribromoacetic acid). The chromatograms show tap (A), ground (B), and river water (C) spiked with the EPA 552.2 CRM at a final concentration of 0.1% v/v (2.0 mg L^{-1} of each HAA). All samples were acidified prior to injection with oxalic acid to a final concentration of 50 mM. Mobile phase, 22 mM oxalic acid in pure water (18.2 MΩ·cm), pH = 1.8; stationary phase, YMC Triart-C18 (3.0 mm i.d. × 150 mm long, 3 μm particle size, pH range 1−12); column temperature, 40 °C; mobile phase flow rate, 0.5 mL min^{-1}; injection volume, 50 μL.

instrumental LOQs are also applicable to real samples. However, it is noteworthy that the presence of high concentrations of inorganic ions, particularly chloride, can result in a broad peak tailing for the chloride peak (Figure 1). This can be minimized by careful optimization of the chromatographic separation. The LOD values in the studied matrixes were calculated using the signal-to-noise ratio (S/N) value for the lowest spiking level (10 μg L^{-1}) and found to be in the range of 1.8−2.0 μg Cl L^{-1} and 1.0−1.5 μg Br L^{-1}, which is comparable with the instrumental LOD values above. In water matrixes with exceptionally high chloride content (e.g., wastewater or seawater), sample preparation to remove chloride (e.g., by precipitation with silver nitrate) can be considered.

Furthermore, the recoveries shown in Table 1 also indicate that the HPLC−ICPMS/MS is relatively less prone to matrix effect than HPLC−ESI-MS/MS and, provided that instrument drift is properly controlled (usually by inserting drift standards inserted at regular intervals over long sequences), the use of internal standards for speciation analysis by HPLC−ICPMS/MS is generally deemed unnecessary. This is in contrast with ESI-MS/MS where the use of isotopically labeled internal standards for each analyte is desirable. Furthermost, the response factor in ICPMS is generally independent of the molecular structure and dependent on the elemental content, which can further simplify the calibration process. For example, the relative response factor between the different chlorine- and bromine-containing compounds (normalized to the elemental

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Table 2. Recovery and Repeatability of the Determination of Nine HAAs in the EPA 552.2 Certified Reference Material and Various Water Matrixes Spiked with EPA 552.2 CRM[a]

	CAA	DCAA	BAA	CBAA	TCAA	DBAA	DCBAA	DBCAA	TBAA
EPA 552.2 HAA mix	2.02 (0.04)	1.97 (0.02)	1.83 (0.03)	2.00 (0.03)	1.86 (0.04)	1.78 (0.03)	1.95 (0.03)	1.71 (0.02)	2.01 (0.02)
tap water	1.98 (0.03)	1.94 (0.02)	1.80 (0.02)	1.95 (0.02)	1.84 (0.02)	1.74 (0.01)	1.90 (0.01)	1.67 (0.04)	1.95 (0.04)
ground water	2.02 (0.03)	1.97 (0.02)	1.82 (0.03)	1.97 (0.03)	1.85 (0.04)	1.74 (0.01)	1.95 (0.06)	1.67 (0.02)	1.97 (0.02)
river water	2.01 (0.04)	1.97 (0.05)	1.82 (0.03)	1.99 (0.03)	1.84 (0.04)	1.74 (0.03)	1.96 (0.09)	1.66 (0.02)	1.96 (0.04)

[a]The values show the mean recovered concentration (in milligrams per liter, based on the mass concentration) and the standard deviation in brackets ($n = 3$). The nine HAAs were determined in the certified reference material EPA 552.2 Haloacetic Acids Mix prepared by a 1:999 dilution in pure water or in various water matrixes. The certified concentration was stated as 2000 μg mL^{-1} (based on the molecular concentration). The concentrations are reported as milligrams per liter (based on the molecular concentration). CAA, chloroacetic acid; DCAA, dichloroacetic acid; TCAA, trichloroacetic acid; BAA, bromoacetic acid; DBAA, dibromoacetic acid; TBAA, tribromoacetic acid; CBAA, chlorobromoacetic acid; DCBAA, dichlorobromoacetic acid; DBCAA, dibromochloroacetic acid.

composition) was within the range of 0.95−1.06 (see also Figures 1 and 2).

Although more robust than ESI-MS/MS, it is noteworthy that the ICPMS/MS is not completely immune to matrix effects. In particular, the signal of high ionization potential elements, particularly chlorine, can be influenced by high carbon load in the plasma.[56] However, this problem is far less significant when ICPMS/MS is employed as a chromatographic detector due to the relatively small injection volumes relative to the mobile phase flow rate (in contrast with total element determination by ICPMS) and the use of a chromatographic column for separation. As a proof of concept, we previously showed that artificially high concentrations of carbonate, which is abundant in hard water matrixes, lead to disturbance in an artificially elevated chlorine baseline.[56] The bicarbonate ion, however, elutes close to the void time on reversed-phase columns and is therefore unlikely to interfere with the chromatographically well-retained HAAs, which is supported by the obtained recovery levels in the various matrixes (Tables 1 and 2).

ICPMS/MS offers better flexibility in some aspects of mobile phase selection compared with ESI-MS/MS. For example, involatile eluents such as oxalic acid, malonic acid, and citric acid are compatible with ICPMS/MS, and even buffers containing chloride, sodium, phosphate, and sulfate are better tolerated provided that the mobile phase contains <0.2% total dissolved solids (generally equivalent to <50 mM). However, there are some noteworthy disadvantages of HPLC−ICPMS/MS in this respect. First, the background signal and the LOD can be significantly affected by the presence of the element in question in the mobile phase. High-purity reagents for mobile phase preparation are therefore highly desirable. This is especially true for the nonmetals as commercially available buffer salts usually contain 0.5−50 ppm of sulfate, phosphate, and chloride. A further disadvantage is that ICPMS is not directly compatible with high organic solvent contents of the mobile phase. There have been approaches that enable up to 80−100% organic solvent content such as flow splitting, postcolumn eluent dilution, and using oxygen as an optional gas. However, maximum sensitivity is only achievable under mobile phases generally less than 10% organic solvent.

Furthermore, although less significant with newer generation instruments, signal drift (usually <20%) can result with ICPMS over long runs. This can be controlled or corrected for by employing an internal standard and/or repeatedly analyzing a standard solution (so-called drift standard). The drift observed in the present study was within 10% over an 8 h run.

The employment of the tandem mass spectrometry mode in ICPMS/MS greatly improves the selectivity and detection limits for elements suffering from polyatomic interferences. This is particularly relevant for chlorine at both isotope masses where abundant species like $^{16}O^{18}O^{1}H^{+}$ and $^{36}Ar^{1}H^{+}$ result in high background and compromise the LOD. For this reason as well as due to the high first ionization potential of chlorine (12.97 eV), the reported LODs for chlorine-containing species in the very few published methods employing single-quadrupole ICPMS were considerably higher than the general capability of ICPMS (e.g., 500 μg Cl L^{-1},[60] 1.5 mg Cl L^{-1}[61]). The LODs for chlorine speciation by ICPMS/MS in the present study (1.4−1.6 μg Cl L^{-1}) therefore show considerable improvement over single-quadrupole ICPMS. This improvement in the detection of chlorine-containing species was shown in our previous work involving perchlorate determination in water by HPLC−ICPMS/MS, where we also performed a systematic comparison between ICPMS/MS and ICPMS for chlorine speciation, including a detailed discussion about approaches to fully utilize the benefits of ICPMS/MS detection for chlorine.[56]

On the other hand, while the utilization of ICPMS/MS eliminates polyatomic interferences such as $^{40}Ar^{38}Ar^{1}H^{+}$ and $^{40}Ar^{40}Ar^{1}H^{+}$, which can also interfere with the bromine isotopes at m/z 79 and especially 81, the observed LODs in the present study are comparable with those previously reported using single-quadrupole ICPMS (e.g., 0.7−1.0 μg L^{-1} for bromo-, dibromo-, and tribromoacetic acids[50] and 0.8 μg L^{-1} for bromate,[62] based on the ^{79}Br isotope). Although we attempted to find a compromise in the optimum ICPMS/MS instrumental parameters for the simultaneous chlorine and bromine detection, the generally higher drop in sensitivity for bromine (14%) compared with chlorine (45%) in the hydrogen cell gas mode relative to the no gas mode[63] would be expected to offset at least some of the benefit of the decreased background achieved by the elimination of the $^{40}Ar^{38}Ar^{1}H^{+}$ polyatomic interference in ICPMS/MS.

The element-selective detector response of the ICPMS/MS can be exploited for the discovery of new compounds or environmental pollutants naturally tagged with a specific heteroatom. For example, it is reported that the major two

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classes of water disinfection byproducts, the trihalomethanes and the HAAs, contribute by ca. 20% and 13% to total organic halide content in chlorinated drinking water, respectively, and that 62.4% of the chlorine disinfection byproducts are still unknown.[64,65] The HPLC−ICPMS/MS certainly offers attractive options for detecting and identifying these unknown species when used in conjunction with molecular high-resolution mass spectrometry. This general capability of ICPMS/MS as a chromatographic detector for new contaminant/biomarker discovery has been very rarely employed[66] but is nevertheless increasingly gaining recognition since the relatively recent introduction of the technique.[51,67] In a very recent proof-of-concept study, Jamari et al. reported the detection of perfluorinated carboxylic acids in spiked river water and highlighted the advantages of ICPMS/MS in terms of the detection of the esterified nonionizable forms of the studied analytes which are not detectable by ESI-MS/MS.[68]

Finally, the present work was intended to show the applicability of HPLC−ICPMS/MS to the determination of halogenated contaminants in various water matrixes, including the unchlorinated Austrian tap water. We would like to note that specific sample preparation and handling procedures may apply for the case of chlorinated drinking water including the commonly practiced use of a quenching reagent to halt the continued formation of HAAs beyond sample collection, which has been thoroughly assessed in previous work.[69]

■ CONCLUSION

A new method for the determination of trace levels of multiple haloacetic acids applicable to various water matrixes was developed. The method fulfills the current regulatory guidelines in terms of HAA concentration limits in drinking water and offers advantages over the reference and the currently used methods, such as the elimination for the need of internal standards or extensive sample preparation.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.analchem.0c01456.

Effects of sample pH and injection volume, optimization of pH and eluent concentration, and characteristics of the analyzed water samples (PDF)

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Notes

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