The Measurement of Haloacetic Acids in Drinking Water Using IC-MS/MS–Method Performance

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ABSTRACT

Haloacetic acids (HAAs) are among disinfection by-products produced during chlorination of water containing natural organic matter and bromide. EPA Methods 552.1, 552.2 and 552.3 used to determine HAAs require derivatization and multiple extraction steps followed by gas chromatography (GC) with electron capture detection (ECD) and mass spectrometry (MS). Ion chromatography-mass spectrometry (IC-MS and IC-MS/MS) offers a sensitive and selective alternative that does not require sample pretreatment. Water samples are directly injected into an ion chromatograph coupled to a triple quadrupole mass spectrometer. The separation of all 9 HAAs (HAA9) and bromate addressed in EPA methods is achieved on the new Thermo Scientific™ Dionex™ IonPac™ AS24 anion-exchange column using a hydroxide gradient. The unique selectivity of this column allows separation of these analytes from common inorganic matrix ions so that the chloride, sulfate, nitrate, and bicarbonate can be diverted to waste during the analytical run, thus avoiding contamination of the ESI-MS/MS instrument.

Excellent peak resolution and linearity are achieved between 0.4 µg/L and at least 20 µg/L in a matrix containing up to 250 mg/L each of chloride and sulfate, 150 mg/L bicarbonate, and 30 mg/L of nitrate. This matrix also contains 100 mg/L ammonium chloride preservative for a total chloride concentration of 316 mg/L. Four stable-labeled internal standards have been studied and the current regulatory levels (MRLs) of 1 and 2 µg/L for HAA5 are easily achieved. Similar sensitivity is observed for HAA9 targets and bromate. Recoveries of all nine HAAs are greater than 90% in a simulated matrix of the above concentrations. This poster discusses several important method features and compares results from this method to those generated by Method 552.2 for natural southwestern waters.

UNIQUE NEEDS OF IC FOR MS DETECTION

- Sensitive low mass detection, e.g., <100 amu
- Negative polarity ESI
- Usually 100% aqueous eluents
- Quantification, even on a gradient
- Coupling to ion exchange polymers (separator, suppressors, etc.)
- IC-MS and IC-MS/MS methods that are rugged enough to be official EPA methods
- Internal standards are needed for all methods with diverse matrix requirements

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HALOACETIC ACID IC-MS/MS METHOD OBJECTIVES

Goals

- No sample pretreatment
- No preconcentration
- Minimize matrix effects

- Good peak efficiency and resolution
- Separate HAAs and common matrix ions
  - Achieve MDL of < 0.5 µg/L

Solution IC-MS or IC-MS/MS

- Anion-exchange separation of all analytes and common matrix ions
- Dionex IonPac AS24 column

- Significantly higher capacity than other IC columns
  - Good separations
  - Good peak shape and retention time stability in high matrix concentration
  - Mass spectrometric detection
- Structural information for peak identification
- Sensitive detection
  - No preconcentration necessary

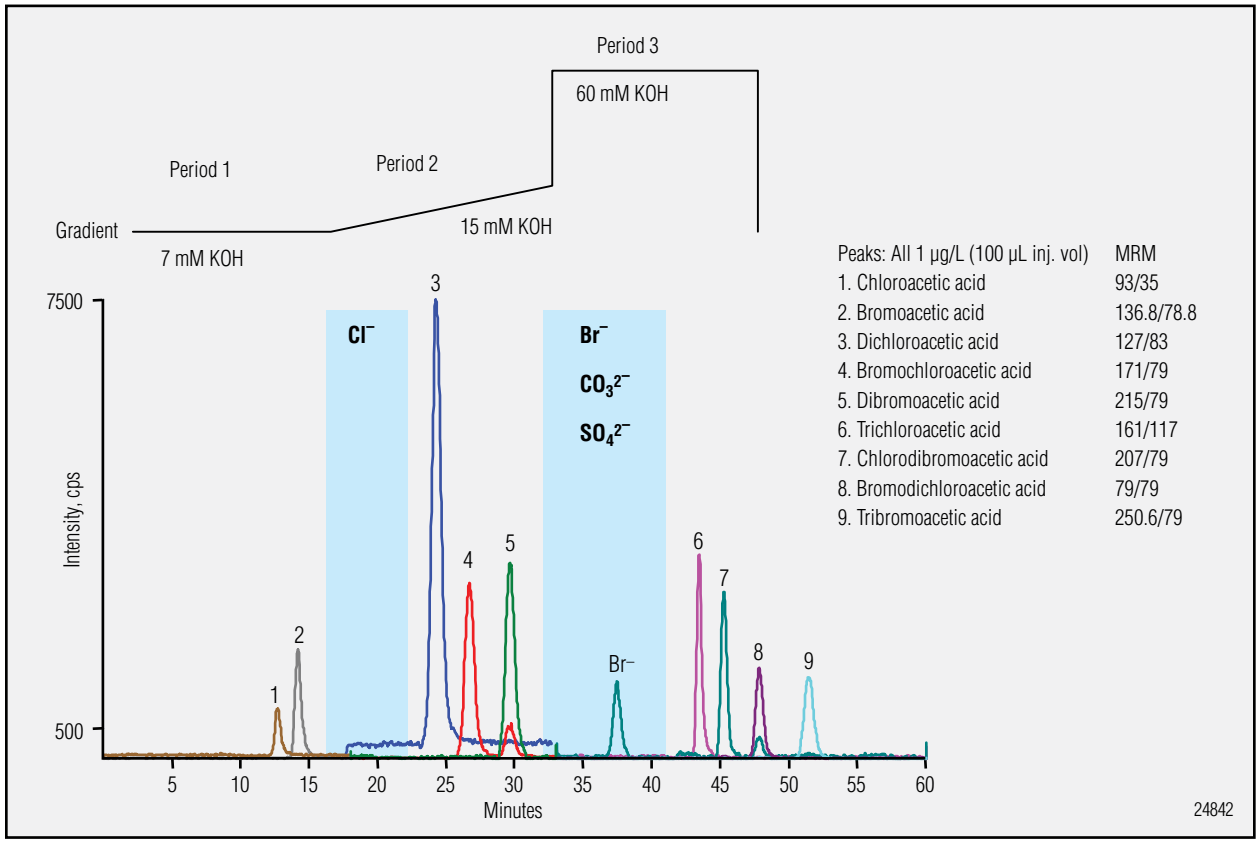

Figure 1. IC-MS/MS MRM channel overlay of nine haloacetic acids using a Thermo Scientific™ Dionex™ ICS-3000 ion chromatography system and an ABI-Sciex API 2000™ mass spectrometer. The colored boxes show the matrix diversion windows where the analytical flow is diverted to waste during elution of the matrix ions. Peaks 1, 2, 3, and 6 have stable-labeled internal standards. The IC hydroxide gradient is illustrated above the chromatogram overlay. Analytical and solvent flow rates are 0.3 mL/min using the system shown in Figure 2. The column compartment temperature is 15 °C and the autosampler sample tray is held at 8 °C for analyte stability, as discussed later.

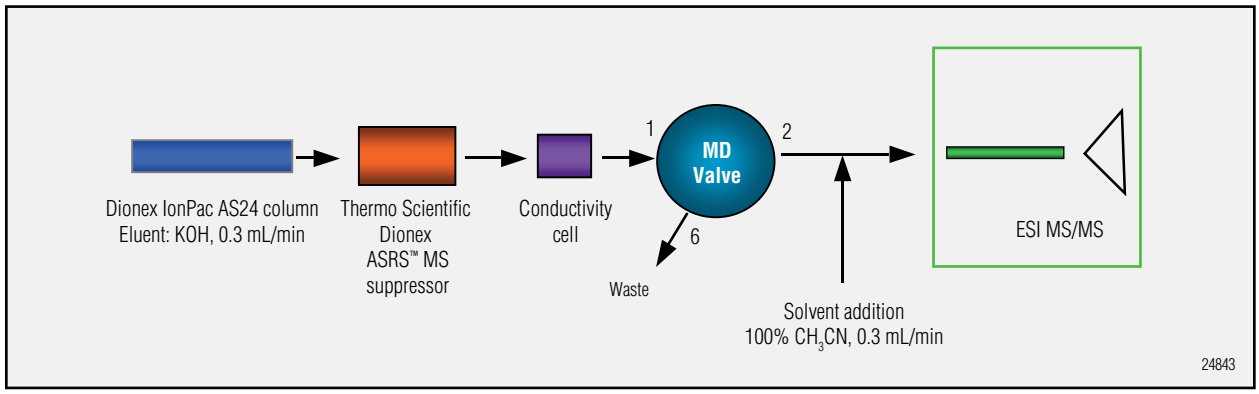

Figure 2. Flow diagram with matrix diversion valve.

In this configuration, acetonitrile is delivered to the mass spectrometer continuously; the matrix diversion (MD) valve is used to divert sample matrix to waste and send the analytes to the MS instrument; the analytical stream is mixed with solvent in a mixing tee before entering the mass spectrometer.

INSTRUMENTATION AND SOFTWARE

Ion Chromatograph:	Dionex ICS-3000
Mass Spectometer:	MS/MS ABI/Sciex API 2000
Software:	Thermo Scientific™ Dionex™ DCMS^{Link}™ 2.0 and MDS Sciex Analyst® 1.4.2

METHOD DETAILS

Separation

With insufficient column capacity, overloading with sample matrix will cause peak broadening and significant shifts in retention times. Reduced peak heights have an adverse effect on detection limits and recoveries, and shifting retention times increase the need for method modifications by the chromatographer. When sample lots include several matrix compositions, this can cause a significant decrease in the ability to operate in an unattended mode. Table 1 shows stable retention times and peak efficiencies, even in a high ionic strength matrix.

Table 1. Matrix Effects: Recovery and Retention Time Stability

Analyte	Concentration	Area × 10^4	Area × 10^4	% Recovery	R.T. (min)	R.T. (min)	Shift (min)
		DI Water	Matrix		DI Water	Matrix	
	µg/L	N = 7	N = 7		N = 7	N = 7	
MCAA	3	11.1	11.6	104	10.56	10.48	–0.08
MBAA	2	16.0	17.2	107	11.86	11.80	–0.06
DCAA	3	126	132	105	19.26	19.28	0.02
BCAA	2	19.3	20.0	103	20.72	20.72	0.00
DBAA	1	11.6	12.0	102	23.08	23.10	0.02
TCAA	1	9.15	9.22	100	37.16	36.70	–0.46
BDCAA	2	8.96	9.13	101	40.18	40.10	–0.08
CDBAA	5	14.8	15.3	103	43.34	43.34	0.00
TBAA	10	14.8	15.5	104	47.00	47.02	0.02

* Simulated Matrix: SO_4^{2-} 250 mg/L; Cl^- 250 mg/L; NO_3^- 20 mg/L; NH_4Cl 100 mg/L

Detection

In this method we optimized the MRM conditions for maximum sensitivity. The MS/MS method conditions are provided in Table 2A and 2B. The voltages are generally low, which indicates a general fragility for these analytes.

Table 2A. Compound-Dependent Parameters for API 2000 Using Automatic Optimization Routine in Analyst

Analyte	Retention Time	Transition	Declustering Potential (V) *At Ion Path Entrance*	Collision Energy (eV) *Q2 Offset from Q0*	Collision Cell Exit Potential (V) *Q2 to Q3 Entrance Lens*
MCAA	11.7	92.9/34.9	–20	–12	–6
MBAA	13.0	137/78.8	–11	–12	–14
Dalapon	20.9	141/97	–13	–11	–6
DCAA	22.1	127/82.9	–11	–12	–6
BCAA	24.2	170.8/78.8	–16	–28	–8
DBAA	27.3	214.7/170.7	–11	–12	–10
TCAA	42.7	161/116.9	–6	–7	–13.7
BDCAA	44.2	207/81 or 79/79	–12	–6	–14
CDBAA	46.5	207/78.8	–11	–20	–6
TBAA	49.6	250.75/78.8	–15	–28	–12

Table 2B. Source-Dependent Parameters for API 2000 Mass Spectrometer

	Period 1	Period 2	Period 3
Curtain gas (psig)	20	25	25
Gas 1 (psig)	90	90	90
Gas 2 (psig)	90	90	90
Collision gas (psig)	2	4	4
Ionspray (V)	–4500	–4500	–4500
Temperature (°C)	475	475	475
Probe position (x, y)	8, 4	8, 4	8, 4

INTERNAL STANDARDS

In this method we used four stable-labeled internal standards for all analytes due to cost and availability issues. We chose internal standards that elute in each of the three sections of the gradient method since the composition of the background changes over the course of the run.

In Figure 1, period 1 of the gradient uses 7 mM KOH eluent and the analytes are MCAA and MBAA. Chloride elutes at the end of this region so a matrix diversion window separates this first section of the gradient from the second section. The brominated acetic acids, especially MBAA, are known to be susceptible to decomposition at elevated temperature and pH, so the use of the stable-labeled MBAA-1-13C is used for accurate tracking of the MBAA analyte. MCAA-1-13C is also used as an internal standard in the first section of the chromatogram for the quantification of MCAA. The stable-labeled internal standard for Period 2 is DCAA-2-13C. This section ramps the concentration of KOH to 18 mM and the analytes are the dihaloacetic acids including, DCAA, BCAA, DBAA, and dalapon (dichloropropionic acid). The second section ends with the diversion of sulfate, nitrate, and bicarbonate to waste. The concentration of KOH eluent is ramped to 60 mM in Period 3 and the trihaloacetic acids, TCAA, BDCAA, DBCAA, and TBAA elute. The internal standard for this section is TCAA-2-13C, which is not commercially available.

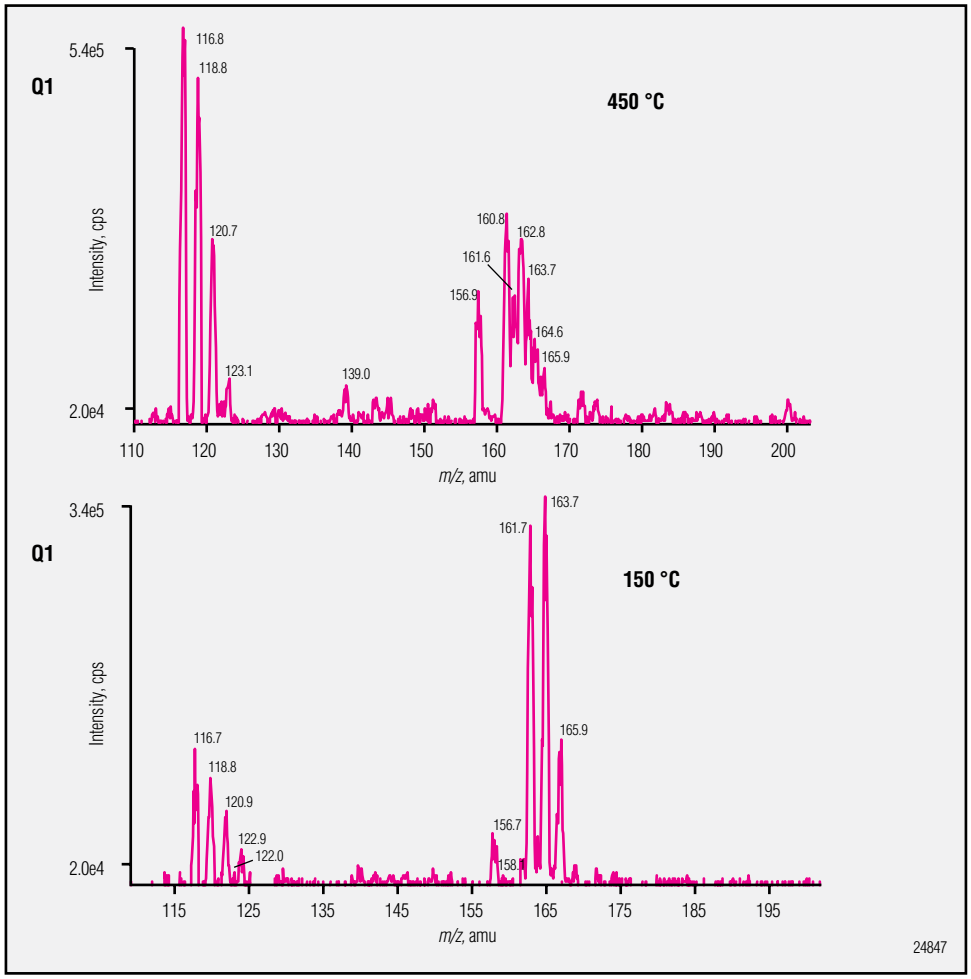

Figure 3. Q1 ions of TCAA-1-13C as a function of source gas temperature.

Figure 3 shows Q1 ions of TCAA-1-13C as a function of source gas temperature. TCAA-1-13C interconverts to TCAA-1-12C, probably through a decarboxylation process in the electrospray source as the temperature of the nitrogen gas is increased. The TCAA-2-13C does not show the exchange from *m/z* 162 to 161 over the temperature range of 150–450 °C. We found that the ratio percentage of 12C/13C for TCAA-2-13C is about 1.8 and stable. Based on this information, we used TCAA-2-13C as the Period 3 internal standard.

SIGNAL INTENSITY AS A FUNCTION OF COLUMN COMPARTMENT TEMPERATURE

Table 3. Peak Areas as a Function of Column Temperature

Analyte	Temperature (°C)	Peak Area µS*min	% (Relative to 10 °C)	Peak height (µS)	% (Relative to 10 °C)
MCAA	10	2.12		8.22	
	15	2.13	100.6	7.92	96.3
	20	2.14	100.7	7.73	94.0
MBAA	10	0.157		0.455	
	15	0.125	79.6	0.353	63.1
	20	0.990	63.0	0.263	57.8
DCAA	10	1.319		2.710	
	15	1.286	97.5	2.598	95.9
	20	1.312	99.5	2.475	91.3
BCAA	10	0.859		1.563	
	15	0.856	100.3	1.500	96.0
	20	0.834	97.1	1.417	90.7
DBAA	10	0.658		1.037	
	15	0.635	96.5	0.936	90.2
	20	0.361	54.8	0.672	64.8
TCAA	10				
	15	0.590	106.6	2.535	113.2
	20	0.557	100.7	2.517	112.4
BDCAA	10	0.361		0.688	
	15	0.367	101.6	0.692	100.5
	20	0.381	105.5	0.691	100.4
CDBAA	10	0.361		0.688	
	15	0.241	66.7	0.365	53.0
	20*				
TBAA	10	0.647		0.697	
	15	0.719	90.0	0.612	87.8
	20	0.580	90.7	0.540	77.5

*interference

In order to determine the best column temperature for this method, the stabilities of all nine HAAs in the gradient method using a chromatographic temperature of 20 °C, 15 °C and 10 °C were compared using conductivity detection. Formic acid was used as a reference. The results are shown in Table 3. Relative to the area counts and peak heights calculated at 10 °C, we found better than 90% recovery for seven of the haloacetic acids. MBAA and CDBAA show losses at both 15 °C and 20 °C relative to 10 °C, and DBAA only showed significant loss at 20 °C. This means that the only HAA with significant loss at 15 °C and one that does not have its own stable-labeled internal standard is CDBAA For method simplicity, 15 °C was chosen as the method column temperature.

Table 4. Comparisons of Analyte Ratios and Internal Standard Peak Areas as a Function of Column Temperature and Concentration Ratio

Analyte / Internal Standard 1 µg/L / 5µg/L; 2.5 µg/L / 5 µg/L	Temperature (°C)	Ratio Peak Area (Analyte / Internal Standard) 1µg/L / 5 µg/L; 2.5 µg/L / 5 µg/L	% Ratio Peak Area at 15 °C / Ratio Peak Area at 20 °C
MCAA/MCAA-1-13C	15 20	0.219 0.221; 0.575	 99; 96
MBAA-12C /MBAA-1-13C	15 20	0.157 0.148; 0.554	 106; 102
MBAA-12C /MCAA-1-13C	15 20	0.275 0.221	 124
DCAA/DCAA-2-13C	15 20	0.235 0.218; 0.726	 108; 105
BCAA/DCAA-2-13C	15 20	0.0459 0.0406 ;0.153	 113; 119
DBAA-12C /DCAA-2-13C	15 20	0.077 0.067; 0.224	 115; 117
DBAA/MBAA-1-13C	15 20	0.533 0.711; 2.49	 75; 72
TCAA/TCAA-2-13C	15 20	0.143 0.137; 0.469	 104; 99
CDBAA-12C / TCAA-2-13C	15 20	0.013 0.013; 0.054	 100; 102
CDBAA-12C / MBAA-1-13C	15 20	0.040 0.070; 0.297	 57; 56
TBAA/TCAA-2-13C	15 20	0.023 0.017; 0.068	 135; 116
TBAA/MBAA-1-13C	15 20	0.068 0.093; 0.379	 73; 63
BDCAA/TCAA-2-13C	15 20	0.011 0.006; 0.189	183; 81

Table 5. Linearity, Detection Limits, and Accuracy for the Nine HAAs					
Analyte	**ISTD 3 or 5 µg/L**	**R^2 (Calibration range 0.250–20 µg/L) DIW/Matrix***	**R^2 (Calibration range 0.250–5 µg/L) Matrix with NH_4Cl***	**MDL µg/L/%RSD (n=7, 1 µg/L) In Matrix**	**Accuracy (%) (at 500 ng/L) DIW/HI Matrix with NH_4Cl**
MCAA	MCAA-1-13C	0.9997/0.9989	0.9962	0.440/14.7	87.5/81.6
MBAA	MBAA-1-13C	0.9999/0.9990	0.9981	0.126/4.2	102/74.
DCAA	DCAA-2-13C	0.9999/0.9991	0.9924	0.095/3.3	96.7/73.3
BCAA	DCAA-2-13C	0.9999/0.9992	0.9964	0.100/0.8	93.5/88.8
DBAA	DCAA-2-13C	0.9999/0.9993	0.9957	0.325/10.8	107.0/79.9
TCAA	TCAA-2-13C	0.9999/0.9993	0.9970	0.091/0.3	113.0/87.3
BDCAA 207/81	TCAA-2-13C	0.9991/0.9991	0.9963	0.637/18.9	105/89.0
CDBAA	TCAA-2-13C	0.9992/0.9994	0.9972	0.521/16.4	128/108.0
TBAA	TCAA-2-13C	0.9994/0.9998	0.9954	0.360/9.9	102/95.6

We collected peak area data at 1 µg/L and 2.5 µg/L for all analytes and 5 µg/L internal standards at three column compartment temperatures. We calculated ratios of peak areas for analytes versus internal standards at two concentration ratios as shown in Table 4. We also compared area ratios at 15 °C to those at 20 °C, as percentages, in an effort to assess any response differences between the analytes-internal standard pairs over this 5 °C temperature range. We think that the most desireable choice for an internal standard for a given analyte is one that is fairly immune to the temperature change as shown by the % ratio peak area at 15 °C/ ratio peak area at 20 °C being close to 100%. For example, we compared these ratios for CDBAA using both TCAA-2-13C and MBAA-1-13C with the idea that perhaps a brominated internal standard would track the CDBAA better than TCAA-2-13C, even though TCAA-2-13C elutes closer to CDBAA. From the data it appears that TCAA-2-13C will track CDBAA better if there are changes in the column temperature than MBAA-1-13C. The pink/blue lines show the comparison data for four HAAs using two different internal standards.

Table 5 provides linearity in deionized water and high ionic strength matrix for this method. Standards in matrix were used to calculate worst-case minimum detection limits against the DI water calibration. Accuracy for the 500 ppt standard was automatically calculated by the Analyst software for both the DI water data and the matrix data. The high ionic strength matrix comprised 315 mg/L chloride, 250 mg/L sulfate, 150 mg/L bicarbonate, and 30 mg/L nitrate. This chloride content includes 250 mg/L sodium chloride salt and 100 mg/L ammonium chloride that is added as a preservative to each sample. The transition for bromodichloroacetic acid is 207/81. The intensities for this transition are low, leading to the high %RSD and MDL. Better quantification is produced by monitoring the 79/79 signal for this analyte.

Table 6. Recovery at Two Analyte Concentrations and Two Matrix Concentrations (Synthetic Matrix)			
Analyte	**ISTD**	**% Recovery* 100 matrix** 0.5; 2.5 ppb**	**% Recovery* 250 matrix** 0.5; 2.5 ppb**
MCAA	MCAA	101; 103	103; 101
MBAA	MBAA	102; 110	81; 104
DCAA	DCAA	100; 107	87; 103
BCAA	DCAA	119; 113	103; 111
DBAA	DCAA	114; 124	108; 115
TCAA	TCAA	89; 99	73; 94
BDCAA	TCAA	96; 94	101; 94
CDBAA	TCAA	105; 87	109; 92
TBAA	TCAA	107; 95	109; 91

* vs. calibration in DI water
**100 matrix = 100 ppm chloride, and sulfate, 60ppm bicarbonate, 20 ppm nitrate plus 100 ppm ammonium chloride;
250 matrix = 250 ppm chloride and sulfate, 150 ppm bicarbonate, 30 ppm nitrate plus 100 ppm ammonium chloride

APPLYING THE METHOD TO PUBLIC WATER UTILITY SAMPLES

We obtained three samples from a southwest public water utility whose source is primarily surface water. One sample is from a treated water reservoir and two samples were from the distribution system within the pressure zone. These samples were routinely analyzed using U.S. EPA Method 552.2 before being sent to us for comparative analysis. We determined chloride and sulfate levels using ion chromatography and did not dilute the samples prior to IC-MS/MS. These samples had already been preserved using the ammonium chloride specified in Method 552.2.

The features of EPA Method 552.2 are provided below along with the achievable detection limits published in the method. Since Method 552.2 is a GC-ECD method, no structural information is produced. This method uses liquid-liquid extraction and methylation of the carboxylic acids before determination by GC-ECD.

- **LLE-GC-ECD**
  - – pH-adjust sample
  - – Extract with MTBE
  - – Methylate
  - – Neutralize and back extract
  - – Inject into GC-ECD
- **Advantages:**
  - – Good selectivity
  - – Low MDLs
- **Limitations:**
  - – No mass information
  - – Requires sample pretreatment
  - – Time consuming
  - – Labor intensive
  - – Subject to multiple procedural errors

Analyte	MDL* (µg/L)
MCAA	0.273
MBAA	0.204
DCAA	0.242
BCAA	0.251
DBAA	0.066
TCAA	0.079
BDCAA	0.091
CDBAA	0.468
TBAA	0.820

* Student's t-value 3.143, n=7; data from EPA Method 552.2 Rev.01

Table 7A. Comparison of Analytical Results for High Ionic Strength Samples										
Sample	**Cl^- SO_4^{2-} (mg/L)**	**MCAA ICMSMS (µg/L) % Spike Rec**	**MBAA ICMSMS (µg/L) % Spike Rec**	**DCAA ICMSMS (µg/L) % Spike Rec**	**BCAA ICMSMS (µg/L) % Spike Rec**	**DBAA ICMSMS (µg/L) % Spike Rec**	**TCAA ICMSMS (µg/L) % Spike Rec**	**BDCAA* ICMSMS (µg/L) % Spike Rec**	**CDBAA ICMSMS (µg/L) % Spike Rec**	**TBAA ICMSMS (µg/L) % Spike Rec**
Treated Water Reservoir	163 243	1.11 93%	1.08 103%	15.1 72%	8.56% 76%	3.72 84%	5.85 80%	7.13 104%	4.75 92%	1.07 106%
System A	93 237	2.31 118%	1.16 106%	15.0 56%	9.4 65%	4.40 80%	6.2 70%	7.49 99%	5.12 72%	1.19 125%
System B	170 215	1.21 116%	0.82 105%	6.11 96%	5.83 94%	2.93 98%	1.59 91%	4.27 92%	3.85 100%	0.76 95%

Calculated using 79/79; Reproducibility on duplicates, 98%; Spike recovery is calculated on a 2.5 µg/L spike

Table 7B										
Sample	**Cl^- SO_4^{2-} (mg/L)**	**MCAA (µg/L) 552.2 % Rec**	**MBAA (µg/L) 552.2 % Rec**	**DCAA (µg/L) 552.2 % Rec**	**BCAA (µg/L) 552.2 % Rec**	**DBAA (µg/L) 552.2 % Rec**	**TCAA (µg/L) 552.2 % Rec**	**BDCAA (µg/L) 552.2 % Rec**	**CDBAA (µg/L) 552.2 % Rec**	**TBAA (µg/L) 552.2 % Rec**
Treated Water Reservoir	163 243	1.31 85%	0.95 113%	17.33 87%	10.53 81%	4.74 78%	7.81 75%	7.75 104%	6.39 74%	Na
System A	93 237	2.12 109%	0.89 130%	16.33 92%	9.86 95%	4.44 100%	7.09 87%	7.03 106%	6.03 85%	Na
System B	170 215	1.33 91%	0.64 128%	6.23 98%	6.54 89%	3.43 85%	2.24 71%	4.32 99%	5.95 65%	Na

Reproducibility on duplicates, 98%; Recovery is 100*amount found using IC-MS/MS / amount found using Method 552.2

Table 7A contains the amount found for the nine HAAs using the IC-MS/MS method and recovery calculation for 2.5 µg/L spike into each undiluted sample. The spike recoveries are 56–125% with most in the 70–120% range. Narrower ranges can be achieved if the samples are diluted 1:2, but this study was designed to test without sample preparation of any kind.

The data shown in Table 7B shows the amount found for the HAAs as determined using EPA Method 552.2 at the water treatment site laboratory. The %Rec represents the comparison of the amount found using our IC-MS/MS method to that found using the Method 552.2. The IC-MS/MS data are 70–130% of the Method 552.2 results for all analytes.

SUMMARY

We have described an IC-MS/MS method for the determination of halogenated acetic acids using an anion-exchange separation column with sufficient capacity and selectivity to handle high ionic strength samples without sample preparation. The IC-MS/MS detection provides structural information and sensitive detection without requiring preconcentration. Analytical results show good correlation to data generated using EPA Method 552.2 for high ionic strength, real world samples.

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