

Comparison of High-Field Asymmetric Waveform Ion Mobility Spectrometry with GC Methods in Analysis of Haloacetic Acids in Drinking Water

Wojciech Gabryelski,* Fengwu Wu, and Kenneth L. Froese

Department of Public Health Sciences, University of Alberta, Edmonton, Alberta, Canada T6G 2G3

Haloacetic acids (HAAs) are major byproducts of chlorination of drinking water. Electrospray ionization high-field asymmetric waveform ion mobility spectrometry mass spectrometry (ESI-FAIMS–MS) provides a tool for direct monitoring of these compounds. However, treated drinking water samples can be challenging to analyze due to the large number of chemicals present and due to matrix effects that can hinder quantitation of analytes. We developed a standard addition ESI-FAIMS–MS method that permits submicrogram per liter detection of haloacetic acids and overcomes matrix effects. An advantage of FAIMS is increased selectivity through a significant reduction in the chemical background from ESI. Moreover, detection limits with this method are much lower than with previously existing GC and GC/MS methods, and quantitation results compare favorably with other existing methods. This new method does not require sample preparation or chromatographic separation and provides a fast, simple, sensitive, and selective method for monitoring HAAs.

Haloacetic acids (HAAs) are one of the two major groups of compounds that have been identified as products of drinking water chlorination.¹ In 1998, HAAs were added to the list of compounds to be monitored by water treatment utilities in the United States as part of the Stage 1 Disinfectants/Disinfection Byproducts Rule² with a maximum contamination level of 60 µg/L established for the sum of five HAAs: monochloro-, dichloro-, trichloro-, monobromo-, and dibromoacetic acid. HAAs have also been detected in vegetation, fog, rain, snow, and ocean waters.^{3–8} This wide

distribution in nature signifies possible environmental and public health implications of this class of compounds.^{3,9,10} Consequently, efforts have been made to develop fast and accurate analytical methods of monitoring concentration, behavior, and distribution of HAAs in water.

Most of the methods used to determine HAAs involve gas chromatography (GC) with electron capture detection (ECD). U.S. EPA method 552.2¹¹ for the analysis of nine HAAs involves liquid–liquid extraction followed by derivatization prior to GC analysis. Procedural steps in this method are labor-intensive and time-consuming and involve reagents that are toxic or carcinogenic. Although modifications to EPA method 552.2 were investigated¹² to eliminate existing problems, new methods for direct determination of the haloacetic acids are desirable. The application of ion chromatography^{13,14} and capillary electrophoresis^{15–18} with UV or conductivity detectors to HAA analysis requires preconcentration of the sample, but both of these methods still may not meet detection limits necessary for routine water monitoring. Electrospray ionization mass spectrometry (ESI-MS) has also been used to investigate HAAs. The direct analysis of HAAs in drinking water was not feasible because of high detection limits and matrix effects

* Corresponding author. Tel: 780-4925096. Fax: 780-4927800. E-mail: wg@ualberta.ca.

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caused by the presence of other organic species in the water.¹⁹ Various approaches intended to reduce matrix effect and improve detectability of HAAs in ESI-MS include the following: HPLC separation,²⁰ formation of stable association complexes in ESI,²¹ tandem mass spectrometry,²² and ion mobility separation.²³ The first two methods avoid the derivitization step but still rely on preconcentration of HAAs in the sample. The last two methods depend on reduction of chemical noise and could be applied in direct analysis of drinking water. Tandem mass spectrometry utilizes selected reaction monitoring in combination with HPLC or more often with a fast on-line sample cleanup. Time spent on sample purification is critical, particularly in trace analysis, to improve the selectivity and reliability of this method.

High-field asymmetric waveform ion mobility spectrometry (FAIMS) was applied to HAA analysis²³ and was shown to be capable of reducing chemical noise and separating HAAs in the gas phase, but detection limits of HAAs were insufficient to allow for direct monitoring of water samples. Further advances in the design and application of the FAIMS analyzer led to evaluation of this technique for direct analysis of HAAs.²⁴ High sensitivity combined with selectivity of ions transmitted by FAIMS improved the detection limits by 3–4 orders of magnitude (5–36 ng/L) over conventional ESI-MS when HAA standards dissolved in deionized water were analyzed. This level of detectability could provide a tool for direct monitoring of HAAs in treated drinking water with no extraction, preconcentration, derivitization, or chromatographic separation. In contrast to standard methods for HAAs requiring significant resources to provide a sufficient degree of selectivity, the FAIMS method avoids time-consuming steps to speed up the time of analysis.

Treated drinking water, however, presents an additional challenge in separation, detection, identification, and quantification of HAAs. In standard analysis methods, treated drinking water samples require additives to dechlorinate the water, preserve sample components, or both. The presence of these additives along with thousands of other DBPs and other chemicals in water²⁵ introduces matrix-induced ionization suppression hindering quantitative analysis by ESI-MS. The complexity of the drinking water matrix creates problems in trace analyses because sample constituents are a potential source of interferences. The quantitative aspect and selectivity of ESI-FAIMS-MS in relation to such samples must be evaluated. To further demonstrate the applicability of this technique, water samples from different sources and different methods of treatment were analyzed to account for variations in matrix effects. The focus of this paper is on the analytical merits of ESI-FAIMS-MS in such applications. The evaluation of this new method in comparison to conventional GC methods is based on quantitative results of HAAs.

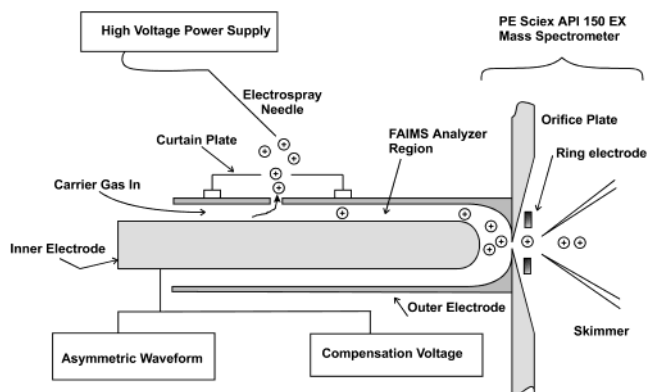


Figure 1. Schematic diagram of the ESI-FAIMS-MS instrument.

EXPERIMENTAL SECTION

Instrumentation. A schematic diagram of the ESI-FAIMS-MS instrument is shown in Figure 1. The FAIMS device consists of two concentric cylinders. The end of the inner cylinder (16-mm o.d.) facing the mass spectrometer was machined to a spherical shape. The inner part of the outer cylinder (20-mm i.d.) facing the mass spectrometer was machined to a concave spherical shape. The spacing between the inner and the outer electrodes in the cylindrical part of the FAIMS analyzer region was 2 mm. The distance between spherical surfaces of the inner and the outer electrodes was adjusted to 2.32 mm. The surface of the outer cylinder at the mass spectrometer side is flat with a 1-mm aperture in the center and makes electrical contact with the orifice plate of the PE Sciex API 150 EX quadrupole mass spectrometer (MDS Sciex, Concord, ON, Canada). An asymmetric waveform,²⁶ at a dispersion voltage of -3500 V and frequency of 750 kHz, was applied to the inner cylinder of the FAIMS device along with a dc compensation voltage. The relative amplitude of the sinusoidal wave and its harmonic²⁷ was $\sim 3:1$.

The electrospray source consisted of a length of fused-silica capillary (FSC) ($30\text{ cm} \times 50\text{ }\mu\text{m i.d.} \times 180\text{ }\mu\text{m o.d.}$) that protruded through a stainless steel capillary ($10\text{ cm} \times 200\text{ }\mu\text{m i.d.} \times 430\text{ }\mu\text{m o.d.}$). The stainless steel capillary, in turn, protruded beyond the end of a larger stainless steel capillary that was used for support and contact for application of the high voltage required for ESI. The polyimide coating was removed from the tip of the FSC. The extension of the FSC end from the tip of the metal capillary was adjusted to provide stable ESI operation. The electrospray needle was kept at a potential of -3300 V. The tip of the needle was located ~ 1 cm from the 2-mm opening in the curtain plate and was positioned at 45° with respect to the curtain plate. An in-house-built floating digital ammeter with nanoampere sensitivity was placed in-line with the power supply and the tip of the metal capillary. Both the magnitude and stability of the electrospray current were used to optimize signal intensity and electrospray stability. The electrospray source was slightly modified to permit a more stable electrospray for pure aqueous solutions. The capillary tip was placed ~ 2 mm from the stainless steel supporting tubing. The electrospray voltage (-4000 to -6000 V) was applied to the fused-silica tip through the solution in the

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capillary. A second voltage (-1000 V) was applied to the stainless steel tubing. The electrospray tip was enshrouded by a bath gas (sulfur hexafluoride) delivered through tubing surrounding the stainless steel support at a flow rate of ~ 0.8 L/min.

The curtain plate of the FAIMS device was electrically insulated from the outer cylinder of the FAIMS device and kept at a potential of -1000 V. The carrier gas (97.5%/2.5% N_2/CO_2) was purified by charcoal/molecular sieve filters and introduced into the FAIMS analyzer region at a total flow of 2 L/min. The gas was split into two flows with a larger portion of the gas flowing out of the opening in the curtain plate as a countercurrent flow against the arriving electrospray-generated ions and a smaller portion of the total gas flow carried these ions through the FAIMS analyzer region to the entrance of the mass spectrometer. Before mass detection, ions were transported from the atmospheric pressure region of the FAIMS device through the $250\text{-}\mu\text{m}$ -diameter opening in the orifice plate (-9 V), into the low-pressure region of the mass spectrometer source equipped with the ring electrode (-50 V) assembly and the skimmer.

Quantitation was performed using the standard addition method, where an original water sample is spiked with known quantities of the analytes, and results are corrected by subtraction of a blank. The analyzed water sample (0.1 mL) was placed in a 2-mL precleaned amber vial with a Teflon cap and diluted with methanol (0.9 mL). After mixing, 0.25 mL of this solution was analyzed by ESI-FAIMS-MS, and the remaining solution was spiked with an EPA 552.2 Acid Calibration Mix solution. The solutions of this calibration mixture at different HAA concentrations were prepared before analysis by dilution of the stock solution with methanol. Care was taken to minimize the contact of samples and solvents with plastic by using glassware and glass syringes. Samples were delivered to the electrospray source by a Harvard Apparatus model 22 syringe pump at a flow rate of $1\text{ }\mu\text{L}/\text{min}$. To eliminate pulsation of the pump and improve stability of the flow, a small air gap was introduced inside the gastight syringe between the piston and sample solution. Each sample was analyzed in five replicates.

Sensitive trace level methods rely on the preconcentration of sample components. The ESI-FAIMS-MS method uses a 10-fold dilution of the sample with methanol. The reason for this step is related to difficulties with electrospraying purely aqueous solution in the negative ion mode. However, this dilution step may compromise the sensitivity of this method by a factor of 10. A modified ESI source (described in the Experimental Section) was also evaluated to overcome this limitation. Stable electrospray was achieved for pure water samples; however, the detection sensitivity for HAAs was much lower than for methanol solutions and severe signal suppression was observed for the least sensitive HAAs. The addition of methanol to the sample was found to be necessary for improving the ionization efficiency and reducing matrix suppression effects.

Ion Separation in FAIMS. The principles of ion separation in FAIMS have been described in detail^{28,29} and are only briefly summarized here. To separate two ions by FAIMS, the relative ion mobility (at high electric field vs low electric field) must be different for these two ions. High and low electric field conditions

are generated between the cylindrical plates of the FAIMS device (Figure 1) by application of the asymmetric waveform to the inner cylinder electrode. During one cycle of the waveform, an ion experiences a short duration of high electric field and moves at high-field mobility toward one of the cylinder electrodes. During the same cycle of the waveform, the ion also experiences a longer duration of oppositely directed low electric field and moves with low field ion mobility toward the opposite cylinder electrode. The waveform is designed in such a way that if the mobility of the ion is the same under high- and low-field conditions, the ion does not experience any displacement from the center in the space between two cylinders. The difference in relative ion mobility at high and low field, however, will result in a constant drift of the ion toward one of the cylindrical electrodes. To transport the ion through the FAIMS analyzer, a dc voltage (compensation voltage (CV)) is applied to the inner electrode to compensate for the ion drift. The ion can be transmitted through FAIMS and sampled by the mass spectrometer only when the appropriate value of the compensation voltage is used.

Scanning the CV generates CV spectra representing the distribution of ions transmitted through the FAIMS analyzer at different separation conditions. CV scanning can be fast, requiring only ~ 100 ms to change FAIMS separation conditions and transmit ions at a new CV, but because of the slower scanning ability of the quadrupole mass spectrometer, the CV rate is adjusted accordingly. Selected ion monitoring or full-scan mass spectra can be acquired at each CV. The fast CV scanning rate can be adjusted to the slow rate of quadrupole detection. For the analysis of HAAs, multiple ion monitoring was used for simultaneous detection of eight selected ions.

HAA anions move faster at a high electric field than at a low electric field. Ions with the opposite relative ion mobility characteristic that move slower at a high electric field, and that could interfere during conventional ESI-MS detection, are easily eliminated by FAIMS. Compounds separated from HAAs in the process include constituents of natural organic matter (fulvic and humic acids), products of their decomposition, plasticizers, and chloride complexes. After rejection of these compounds, there is still a large group of ions with relative ion mobilities similar to those of HAAs. The separation of all these ions was not possible with the limited resolution of FAIMS. It is reasonable, however, to establish separation conditions that provide good selectivity for HAAs by minimizing the contribution of interferences originating from the sample matrix.

GC Methods. Different GC methods were used to analyze water samples. EPA method 552.2¹¹ was used in water utility laboratories in cities A and C and also in the Environmental Health Sciences (EHS) laboratory at University of Alberta, where ESI-FAIMS-MS analyses were performed. The water utility laboratory in city B used standard methods 6251 B. These methods are the same, except they differ in the derivatization agent used: method 552.2 employs acidified methanol, standard methods 6251 B uses diazomethane. A liquid-liquid extraction solid-phase microextraction gas chromatography method was implemented in the EHS laboratory for HAA analysis. This nonstandard method was intended to provide detection of HAAs at a submicrogram per liter concentration level.

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EPA Method 552.2. A water sample (40 mL) was acidified to pH 0.5 and extracted with 4 mL of methyl *tert*-butyl ether (MTBE). Acidified methanol (1 mL, 10% H₂SO₄ in MeOH) is added to the MTBE extract, followed by heating at 50 °C for 120 min to allow derivitization. After neutralization, the MTBE fraction was analyzed by GC-ECD on a DB-5.625 column (30m × 0.25 mm i.d., 0.25- μ m film; J&W, Folsom, CA). Each sample was analyzed in triplicate. GC analyses were performed on an HP 6890 gas chromatograph with ECD (Agilent Technologies, Wilmington, DE). EPA method 552.2 Acid Calibration MIX ICR and 2,3-dichloropropanoic acid (the internal standard) from Supelco (Oakville, ON) were used in analyses.

Liquid–Liquid Extraction Solid-Phase Microextraction Gas Chromatography Method (LLE-SPME-GC). A water sample (220 mL) was placed in a Boston bottle with 59 g of sodium sulfate, 7 g of copper carbonate, and 20 mL of sulfuric acid. Three milliliters of MTBE was added to extract HAAs. MTBE was removed and evaporated, and 0.1 g of sodium sulfate, 40 μ L of methanol, and 30 μ L of sulfuric acid were added to derivatize HAAs at 50 °C for 10 min. SPME was used to concentrate the HAA methyl esters. A poly(dimethylsiloxane) fiber (100 μ m) was used to absorb sample components from the headspace. A 10-min absorption at room temperature was followed by 2-min desorption (230 °C) into the injector for GC analysis. A DB-1 column (20 m × 0.18 mm, 0.4 μ m; J&W Scientific, Folsom, CA) was used for separation. The temperature program used was a modified version of that used in EPA method 552.2 to provide a faster chromatographic run. GC analyses were performed on a Varian (Varian Canada Inc., Mississauga, ON, Canada) 3800 GC with ECD and a Saturn 2000 ion trap mass spectrometry detector.

Water Samples and Reagents. Water samples were acquired at multiple locations in three Canadian cities (A–C). Sample sites in these cities are designated by numbers (e.g., A-1–2, B-1–6, C-1–3). City A uses a conventional treatment (coagulation, flocculation, sedimentation, and filtration) of raw river water, followed by disinfection with chloroamines. City C draws raw surface water from a river/reservoir system and uses a similar procedure, except that chlorine is added to raw water and treated water after filtration. City B obtains its water from a lake via a 160-km aqueduct. The lake source water is disinfected by chlorination at three points along the water supply, which leads to higher DBP formation. Sampling, preservation, and transport of samples were carried out according to requirements of EPA method 552.2. Sequential 1-L samples were collected at each sampling site, with one sample shipped to the EHS Laboratory at the University of Alberta, which was analyzed upon arrival. The sample duplicates were sent to the respective water utility laboratories and analyzed as a part of their water quality monitoring programs.

HPLC-grade methanol and HPLC-grade water, ammonium chloride, sodium sulfate, copper carbonate, and sulfuric acid were purchased from Fisher Scientific Co. (Nepean, ON, Canada). EPA 552.2 Acid Calibration Mix of trichloroacetic acid (TCA), dichloroacetic acid (DCA), and monochloroacetic acid (MCA), bromochloroacetic acid (BCA), bromodichloroacetic acid (BDCA), dibromoacetic acid (DBA), monobromoacetic acid (MBA), chlorodibromoacetic acid (CDBA), and tribromoacetic acid (TBA) was supplied by Supelco (Oakville, ON, Canada).

RESULTS AND DISCUSSION

Figure 2 shows CV spectra for selected ions (m/z 161 for TCA, m/z 127 for DCA, m/z 93 for MCA, m/z 173 for BCA, m/z 207 for BDCA, m/z 217 for DBA, m/z 137 for MBA, and m/z 251 for CDBA and TBA) acquired for the A-1 water sample. The m/z of the selected ions used for detection of HAAs corresponds to the mass of deprotonated haloacetic acids with the exception of TBA for which the decarboxylation product of the deprotonated acid at m/z 251 was used for identification. CV separations resemble GC or HPLC chromatograms. A unique aspect of CV spectra is that they illustrate separation of ESI-generated ions that takes place in the gas phase and is much quicker than GC or HPLC. The acquisition time for a complete CV spectrum presented in Figure 2 is \sim 1 min.

The CV spectra in Figure 2 were acquired by ramping the CV from 8 to 38 V at 0.1-V intervals, and the intensity of the selected ions was recorded for each compensation voltage step. CV spectra of the blank, sample, and spiked sample are included in each segment illustrating detection of a particular HAA. The blank was represented by a solution of ammonium chloride dissolved in methanol at the concentration present in samples during the ESI-FAIMS–MS analysis. Spiked samples were obtained by elevation of HAA concentrations to 1–30 μ g/L. The concentration of HAAs in sample A-1 was found to be the lowest among all analyzed water samples, and the selectivity of this technique at optimized separation conditions is demonstrated for this sample in Figure 2. Note, that isobaric interferences are observed even at this relatively high concentration of chloroacetates. In the case of TCA (Figure 2 A) transmitted through the FAIMS at CV 10.4 V, there is another m/z 161 ion transmitted at CV 20.5 V. Isobaric interfering ions of DCA include ionic species at CV 9.5 V and CV 16 V. The separation of the m/z 127 ion of DCA at CV 17.5 V from the CV 16-V interfering ion depends strongly on the composition of the buffer gas. The partial separation of these ions was achieved by setting the concentration of carbon dioxide in nitrogen carrier gas at 2.5%. Note that the CV 16.0-V peak is present also in the methanol/ammonium chloride blank, and for determination of DCA at lower concentration, the resolution of these adjacent CV peaks should be improved to avoid overestimation of the DCA concentration. MCA detection indicates the presence of abundant interfering species detected at CV 10 and 15.5 V. The ion detected at CV 15.5 V originates from the methanol/ammonium chloride mixture whereas the ion detected at CV 10 V originates from the water sample. Interfering ions are separated from TCA, DCA, and MCA but high blank signals are observed at CVs corresponding to transmission of these compounds due to the presence of small amounts of TCA, DCA, and MCA in ammonium chloride. Panels D–H of Figure 2 show that the same mixture contains small concentrations of BCA, BDCA, DBA, and MBA. The blank signals of these compounds at corresponding CVs are small. This low level of background is critical in the analysis of these HAAs. The detection of these species, present in the water sample at submicrogram per liter concentrations, results in CV peaks at intensities of tens or hundreds of ion counts. The level of chemical background depends greatly on the concentration of carbon dioxide in the buffer gas, which determines the CV distribution of interfering ions originating from ESI.²⁵ Detection or quantification, or both,

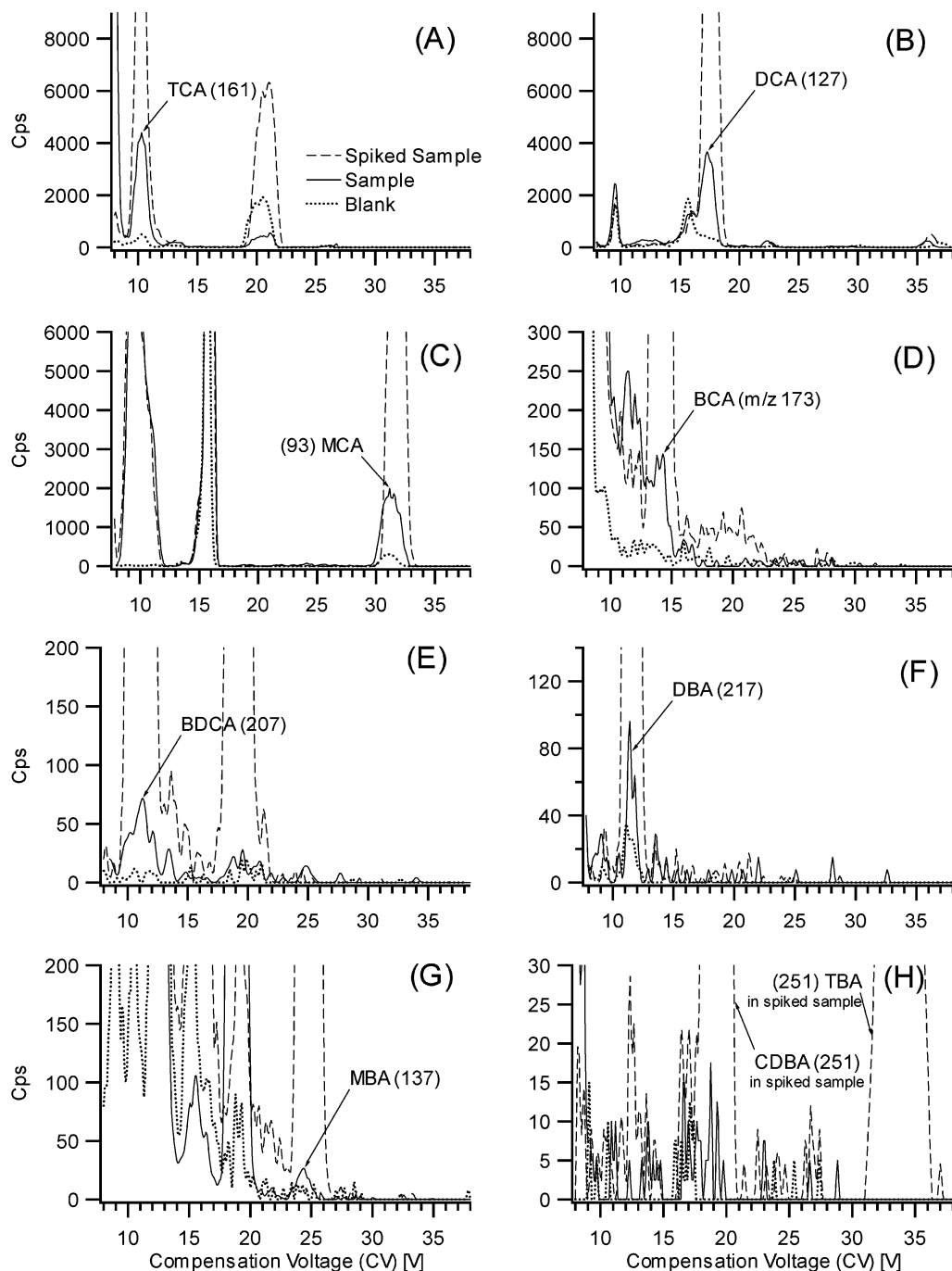


Figure 2. Compensation voltage spectra obtained for the A-1 drinking water sample. (A) TCA at m/z 161, (B) DCA at m/z 127, (C) MCA at m/z 93, (D) BCA at m/z 173, (E) BDCA at m/z 207, (F) DBA at m/z 217, (G) MBA at m/z 137, (H) CDBA at m/z 251, and TBA at m/z 251. Diagnostic ions of HAAs were monitored by the API 150 EX quadrupole in the multiple ion monitoring mode (eight mass windows). CV spectra of the blank, the water sample, and the spiked water sample are presented for each HAA.

of HAAs at submicrogram per liter concentrations (Figure 2D–H) is possible due to good selectivity of FAIMS. The CV peaks of HAAs are separated from other abundant isobaric ions. Note that CDBA (CV = 19 V) and TBA (CV = 34 V) (Figure 2H) do not show any signals in the blank. CDBA and TBA were not detected in the water sample. The signal variation around a CV of 19 V (Figure 2H) is too large to confirm detection of CDBA. Considering the variation of the blank, the detection of DBA (Figure 2F) in the water sample illustrates analysis at the quantification limit ($10\text{ sd}_{\text{blank}}$) whereas the detection of MBA (Figure 2G) in the water

sample represents analysis approximately at the detection limit ($3\text{ sd}_{\text{blank}}$).

The selectivity of FAIMS for MBA that is present in water sample A-1 at the detection limit ($\sim 0.1\text{ }\mu\text{g/L}$) is illustrated in Figure 3. The CV spectrum (Figure 3A) indicates that in addition to the m/z 137 ion of MBA there are a number of m/z 137 ions present in the sample. MBA is transmitted through the FAIMS analyzer at CV 25.4 V, and the CV peak of this compound is shown in the inset of Figure 3A. To monitor ions transmitted through the FAIMS device at the maximum of the CV peak for MBA, the

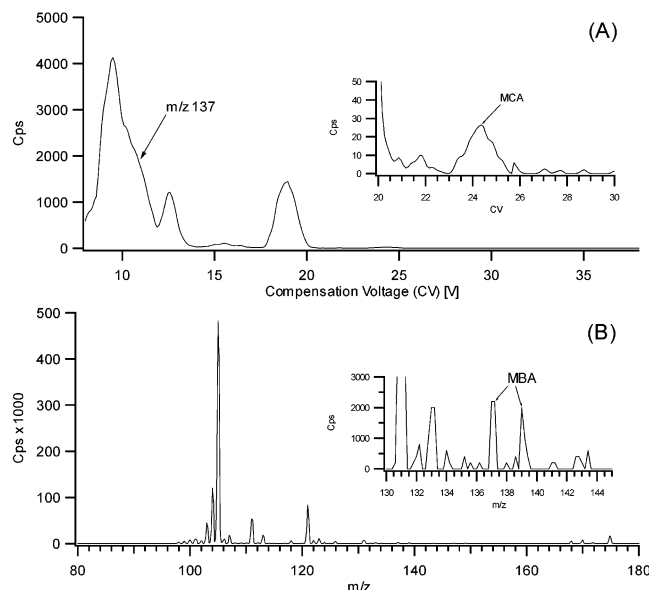


Figure 3. Detection of MBA in the A-1 drinking water sample by FAIMS. (A) CV spectrum of the selected ion at m/z 137. (B) Mass spectrum at CV 24.4 V (100 scans).

CV was set at 25.4 V and the mass spectrum (Figure 3B) was acquired by collecting a sum of 100 spectra in the 80–180 m/z range. MBA isotopic peaks at m/z 137 and 139 constitute only a small fraction of ions transported at this CV. The inset in Figure 3B shows the extended mass range in the vicinity of the MBA isotopic peaks. The peaks at m/z 137 and 139 represent closely the isotopic pattern of MBA. A slight distortion of the isotopic pattern is due to the FAIMS separation of MBA species containing a heavier or lighter isotope of bromine. The acquisition time for the mass spectrum in Figure 3B was just over 1 h.

In contrast to liquid separation methods, the ion availability in FAIMS is not restricted by time (peak width in chromatographic separation methods) or low intensities of target ions. FAIMS is a continuous ion filter that transforms the entire population of ions entering the FAIMS device to a small fraction of these ions that are able pass through the device at particular conditions. Species separated at a particular CV are available for MS analysis as long as the ionization method provides a continuous stream of ions. Signal from low-intensity ions can be collected and summed over an extended period of time to enhance spectral information.

CV spectra can be used to quantify HAAs in water. The ion intensity measured at the maximum transmission CV of particular ions is proportional to the quantity of these ions introduced into the FAIMS device. This analytical signal could be measured sequentially at selected maximum transmission CVs or determined from the entire CV spectrum. In this application, analytical signals were extracted from CV spectra. To design a quantitative ESI-FAIMS–MS method, the correlation between concentrations of HAAs in a water sample and their instrument responses must be known. Table 1 shows the standard addition calibration data for water samples from different locations A-1, B-1, and C-1. Each water sample was fortified with HAAs at six different concentration levels. The final concentrations of the standards added to the spiked samples were in the range between 0.5 and 20 times the original component concentration. The original water sample and fortified solutions were diluted with methanol and analyzed by

Table 1. Detection Sensitivities of HAAs in ESI-FAIMS–MS Determined by the Standard Addition Method for Different Drinking Water Samples from Different Locations

HAA	sample A-1		sample B-1		sample C-1	
	slope ^a	X^c ($\mu\text{g/L}$)	slope	X ($\mu\text{g/L}$)	slope	X ($\mu\text{g/L}$)
TCA	750 (0.997) ^b	4.9	680 (0.998)	80	150 (1.000)	13
DCA	530 (0.997)	6.2	450 (0.999)	35	3.8 (0.988)	19
MCA	290 (0.997)	5.0	220 (0.999)	13	1.1 (0.997)	
BCA	360 (0.997)	0.30	250 (0.999)	1.3	5.3 (0.992)	
BDCA	140 (1.00)	0.36	91 (0.999)	4.7	21 (0.998)	0.53
DBA	240 (0.999)	0.23	160 (0.997)	0.5	3.6 (0.989)	
MBA	74 (0.993)	0.12	66 (0.999)			
CDBA	160 (0.998)		100 (0.999)		9 (0.989)	
TBA	13 (0.998)		11 (0.995)			

^a The slope of standard addition plots is given for (counts $\text{s}^{-1} \mu\text{g}^{-1} \text{L}^{-1}$ HAA in water). ^b Linear correlation coefficient for standard addition plots (sic points, $n = 5$ for each point). ^c Concentrations of HAAs determined by the standard addition method ($n = 5$).

ESI-FAIMS. Parameters of standard addition plots obtained from these experiments are given in Table 1. The slope of the standard addition plot determines the detection sensitivity of HAAs in ESI-FAIMS for a particular water sample. The linear correlation coefficient shows the linearity of the signal response. The intercept gives the signal of HAA in the sample. This signal could be background-corrected and was used to obtain the concentration of HAA in the sample.

Three water samples from A-1, B-1, and C-1 vary not only in the concentration of HAAs but also in the sensitivity of detection for HAAs as demonstrated by the slope of the standard addition plots (Table 1). Samples from the same city but different sampling sites show similar detection sensitivity for HAAs. The variation in detection sensitivity for samples from different cities is related to the different nature of the sample matrix. Note that detection sensitivity variations between samples from different cities and among HAAs are much greater than those reported when a liquid–liquid extraction was implemented prior to ESI-MS analysis.²¹ It is evident that at such a high variation of signal responses the external calibration method cannot be used for quantification. A careful examination of data in Table 1 indicates that an internal standard method will also not be effective in quantification of HAAs in real drinking water samples. The internal standard could not compensate for signal suppression for all HAAs because the relative signal suppression of individual HAAs varies with the matrix. This leaves the standard addition method as the most plausible for quantification of HAAs. The standard addition technique can satisfactorily account for changes in signals of HAAs caused by the matrix, as evidenced by high correlation coefficients for standard addition plots. Standard addition plots, however, are linear over a limited range of concentrations (2 orders of magnitude), and this fact should be considered in the preparation of spiked samples.

Table 2. Detection Limits of HAAs in ESI-FAIMS-MS Determined for the A-1 Water Sample

HAA	blank ^a ($\mu\text{g/L}$)	blank SD ^b δ (%)	detection limit ^c ($\mu\text{g/L}$)	quantification limit ^d ($\mu\text{g/L}$)
TCA	0.5	12	0.18	0.60
DCA	0.5	11	0.17	0.55
MCA	0.8	13	0.31	1.0
BCA	0.05	45	0.07	0.23
BDCA	0.06	29	0.05	0.17
DBA	0.09	26	0.07	0.23
MBA	0.08	51	0.12	0.40
CDBA				
TBA				

^a Determined by the standard addition method ($n = 5$). ^b Standard deviation for $n = 5$. ^c Three times the standard deviation of the blank ($n = 5$). ^d Ten times the standard deviation of the blank ($n = 5$).

The standard addition method can compensate for matrix effects. However, in the case of high signal suppression (sample C-1), the sensitivity of detection is low and it prohibits the determination of HAAs present in the sample at low concentrations. The accuracy, precision, and time of analysis are compromised for such samples. It is important to know whether the FAIMS-MS technique could be applied universally to all water samples. To understand matrix-related limitations of the ESI-FAIMS technique, the suppression effects were briefly investigated. For the C-1 water sample, the low detection sensitivity for HAAs resulted from a high conductivity of sample solution. The electrospray current measured during the ionization of samples from location C was a few times higher than that measured for samples from locations B and A. A high ESI current indicates high salt content in samples from location C. The ESI-FAIMS-MS analysis of inorganic anions present in the samples showed that the concentration of chloride in the samples from location C was at least 10 times higher than in other preserved samples. At the same time, other anions such sulfate or bicarbonate that could indicate high mineral content in the water were detected in the sample from location C at levels similar to that in the samples from other locations. It is possible that during preservation of the samples from city C collected for analysis, excess NH_4Cl was added. The detection capabilities of FAIMS-MS demonstrated for the samples from location C are more characteristic of the application of this technique to mineral water rather than tap water. Despite similar conductivities, samples from locations A-1 and B-1 displayed different detection sensitivities for HAAs. This difference between samples A-1 and B-1 is much smaller and comes from natural variations in the sample matrix. A higher concentration of organic matter in sample B-1 combined with more extensive chlorination can result in formation of ionic species that suppress ionization of HAAs.

The standard addition method requires knowledge of chemical background for HAAs originating from sources different from the sample. Sample preparation for ESI-FAIMS relies on dilution of the preserved water sample in methanol. This means that only methanol and ammonium chloride (added to the sample as the dechlorination/preservation component) contribute to blank signals for HAAs. The blank was determined for a solution of ammonium chloride dissolved in methanol at the concentration present in samples during ESI-FAIMS-MS analysis. Table 2

shows results for quantification of the blank and determination of detection and quantification limits of HAAs for sample A-1. Detection limits of HAAs based on three times the standard deviation of the blank were calculated for five replicates. It should be noted that detection limits determined in this way will depend on detection sensitivity and will vary from sample to sample. The lowest (best) detection limits are for sample A-1, slightly higher for sample B-1, and much higher for sample C-1. For CDBA and TBA, detection/quantification limits could not be determined in this way because no signal was observed for these compounds in the blank. Note that the blank signal for HAAs in the running sample will depend on the detection sensitivity of HAAs in this sample. To simplify calculations, the concentration of HAAs determined for the blank was subtracted from the background-uncorrected concentration for each sample.

Table 3 shows ESI-FAIMS-MS results for determination of HAAs in drinking water from different locations and sampling sites. The standard addition method was implemented with analysis of the sample and the spiked sample at a spike level not exceeding 20 times the original component concentration. Five replicates of each sample were analyzed. The blank was subtracted from the sample concentration. The concentration and speciation of HAAs depend on the quality of source water and disinfection conditions. HAAs that contain chlorine only (TCA, DCA, MCA) were detected at microgram per liter concentrations. Compounds containing bromine were detected at submicrogram per liter or just above this concentration. Data from ESI-FAIMS-MS do not include TBA, because this compound was not detected in any of the analyzed samples. Not all results presented in Table 2 could be compared to data reported for these samples from standard GC methods. Only TCA and DCA were detected by method 552.2 or standard methods 6251 B in analyzed water samples. The method quantification limit (MQL) for other HAAs in these methods is generally 1 and 2 $\mu\text{g/L}$ for MCA. The ESI-FAIMS results suggest that the detection and quantification of MCA by GC at concentration levels as high as 10 $\mu\text{g/L}$ (samples B-1 and B-3) should be feasible. Although it is possible that the GC methods did not detect 3 $\mu\text{g/L}$ MCA in sample A-2, the discrepancies of MCA results by the different methods at higher concentrations indicate that some of the MCA results from FAIMS could be overestimated. BDCA was detected by FAIMS in city B samples at levels above the MQL for BDCA with a GC-ECD method but it was not detected by the GC methods. The standard GC methods were originally developed for the five regulated HAAs, which did not include BDCA. Some laboratories have problems with detection and quantification of the nonregulated HAAs.

Available data, summarized in Table 4, can be used to compare results for DCA and TCA by ESI-FAIMS-MS and GC. Figure 4 shows direct comparison of FAIMS with methods used in water utility laboratories (Figure 4A and B) and the 552.2 method used in the EHS laboratory (Figure 4C and D) for TCA and DCA. Linear regression with 95% confidence interval estimation provides a quantitative measure of the comparability of the methods. Ideal agreement between methods would give a slope factor of 1.0 and $R^2 = 1.0$. There is good agreement between FAIMS, EPA 552.2 in EHS, and the water utility laboratories. FAIMS provides a somewhat lower measure of TCA versus water utility laboratories

Table 3. Concentration of HAAs ($\mu\text{g/L}$) in Drinking Water Samples from Different Locations Determined by ESI-FAIMS-MS

sample	TCA $X \pm \delta^a$	DCA $X \pm \delta$	MCA $X \pm \delta$	BCA $X \pm \delta$	BDCA $X \pm \delta$	DBA $X \pm \delta$	MBA $X \pm \delta$	CDBA $X \pm \delta$
A-1	4.9 ± 0.5	6.2 ± 0.9	5.0 ± 0.5	0.30 ± 0.09	0.36 ± 0.03	0.23 ± 0.05		
A-2	6.9 ± 0.5	5.9 ± 0.4	3.2 ± 0.3	0.36 ± 0.08	0.38 ± 0.09			0.09 ± 0.01
B-1	80 ± 4.3	35 ± 2.6	13 ± 1.4	1.3 ± 0.19	4.7 ± 0.3	0.5 ± 0.12		
B-2	68 ± 6.2	12 ± 0.4	5.2 ± 0.2	0.47 ± 0.08	3.2 ± 0.3	0.24 ± 0.02	0.6 ± 0.2	
B-3	66 ± 7.9	23 ± 2.2	11 ± 0.5	0.96 ± 0.08	4.4 ± 0.4	0.4 ± 0.12	0.60 ± 0.05	
B-4	68 ± 3.9	21 ± 0.6	4.0 ± 0.5	0.86 ± 0.07	2.9 ± 0.2	0.32 ± 0.07		
B-5	79 ± 2.9	43 ± 3.0	8.8 ± 0.7	1.4 ± 0.11	3.4 ± 0.2	0.7 ± 0.22	0.52 ± 0.09	0.03 ± 0.01
C-1	13 ± 0.6	19 ± 1.9			0.53 ± 0.05			
C-2	9.8 ± 0.3	7.2 ± 0.5			0.6 ± 0.1			
C-3	13 ± 2.6	14 ± 2.5			0.43 ± 0.06			

^a Average concentration of HAAs \pm standard deviation (in $\mu\text{g/L}$) for $n = 5$.

Table 4. Concentration of TCA and DCA in Drinking Water Samples from Different Locations Determined by ESI-FAIMS-MS and GC

sample	TCA			DCA		
	FAIMS ^a $X \pm \delta$ ($\mu\text{g/L}$)	EPA 552.2 ^b $X \pm \delta$ ($\mu\text{g/L}$)	utility lab ^c $X \pm \delta$ ($\mu\text{g/L}$)	FAIMS ^a $X \pm \delta$ ($\mu\text{g/L}$)	EPA 552.2 ^b $X \pm \delta$ ($\mu\text{g/L}$)	utility lab ^b $X \pm \delta$ ($\mu\text{g/L}$)
A-1	4.9 ± 0.5	5.9 ± 0.1	6.1	6.2 ± 0.9	7.9 ± 2.0	7.4
A-2	6.9 ± 0.5	7.6 ± 0.1	9.6	5.9 ± 0.4	11 ± 0.6	10
B-1	80 ± 4.3	53 ± 2.7	97^d	35 ± 2.6	31 ± 1.6	25^d
B-2	68 ± 6.2	53 ± 1.6	68^d	12 ± 0.4	19 ± 0.8	10^d
B-3	66 ± 7.9	56 ± 0.4	86^d	23 ± 2.2	26 ± 1.1	20^d
B-4	68 ± 3.9	54 ± 2.4	69^d	21 ± 0.6	43 ± 4.8	27^d
B-5	79 ± 2.9	56 ± 3.7	84^d	43 ± 3.0	51 ± 4.8	36^d
C-1	13 ± 0.6	11 ± 0.7	17	19 ± 1.9	17 ± 2.4	16
C-2	9.8 ± 0.3	6.3 ± 0.8	11	7.2 ± 0.5	14 ± 0.7	10
C-3	13 ± 2.6	9.1 ± 0.9	16	14 ± 2.5	15 ± 0.5	13

^a Average concentration of HAAs \pm standard deviation for $n = 5$. ^b Average concentration of HAAs \pm standard deviation for $n = 3$. ^c Results of a single HAAs analysis. ^d Results from standard methods 6251 B (other GC results by method 552.2).

($y = 1.13$) and somewhat higher measure for DCA ($y = 0.87$). According to the slope of the linear regression relationship, there is <15% difference between FAIMS and utility laboratories for TCA and DCA. One can expect this level of deviation between laboratories running the same methods. In fact, 20% difference for QC runs in water utility laboratories is still an acceptable result in HAAs analysis.¹¹ The agreement between FAIMS and either water utility laboratories or method 552.2 in EHS is better than the agreement between the same GC method run at different locations. Correlation between methods appears to be stronger for TCA than for DCA; however, this is largely a function of the spread between two distinct clusters of TCA data.

Among all nonstandard GC methods applied in our laboratory to the water samples, only one method provided detection of HAAs other than TCA and DCA. The liquid-liquid extraction solid-phase microextraction gas chromatography method used preconcentration of sample components (~ 250 factor) during the liquid-liquid extraction and implemented a SPME fiber before GC separation to further preconcentrate HAAs. Table 5 shows results obtained for the C-6 sample by ESI-FAIMS-MS and the LLE-SPME-GC method using ECD and MS detection. Similar results for DCA, BCA, and BDCA were obtained by FAIMS and the GC method with different detectors. The detection of TBA using ECD indicates that this detector may not be specific enough for this method or MS methods are not sensitive enough. At submicrogram per liter concentrations, GC/MS spectra show that coelution of different

Table 5. Concentration of HAAs in the B-6 Drinking Water Sample Determined by ESI-FAIMS-MS and LLE-SPME-GC

HAA	FAIMS ^a $X \pm \delta$ ($\mu\text{g/L}$)	LLE-SPMEGC-ECD ^b $X \pm \delta$ ($\mu\text{g/L}$)	LLE-SPMEGC-MS ^b $X \pm \delta$ ($\mu\text{g/L}$)
TCA	105 ± 4.8	65 ± 8.4	59 ± 6.5
DCA	81 ± 3.5	77 ± 9.2	78 ± 8.6
MCA	9.3 ± 0.7		
BCA	2.3 ± 0.5	1.8 ± 0.3	1.6 ± 0.3
BDCA	3.0 ± 0.6	3.6 ± 0.6	3.2 ± 0.5
DBA	0.5 ± 0.1	0.17 ± 0.05	
TBA		0.6 ± 0.18	

^a Average concentration of HAAs \pm standard deviation for $n = 5$.

^b Average concentration of HAAs \pm standard deviation for three separate GC runs of the same extract.

species is very common. For this reason, MS detection and quantification at low concentrations seems to be more reliable than ECD. DBA was detected at a higher level in FAIMS than with GC-ECD and was not detected with GC/MS. Lower concentrations of TCA determined by SPME-GC should be related to the SPME process because TCA results from the standard GC methods for this sample were in good agreement with the FAIMS results. Either poor detection sensitivity of MCA with the GC methods or false-high MCA estimations from FAIMS could be responsible for the different results observed for this compound.

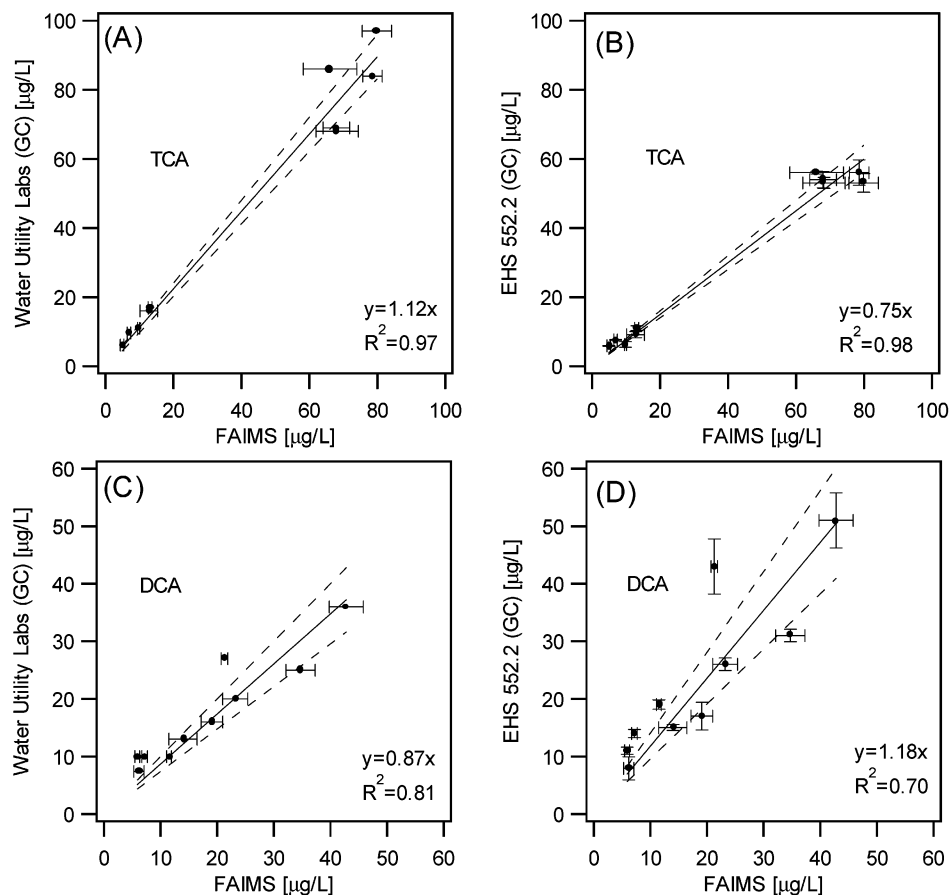


Figure 4. Comparison of results for HAAs by ESI-FAIMS-MS and GC. (A) Water Utility Lab (either method 552.2 or standard methods 6251 B) vs FAIMS for TCA; (B) method 552.2 in EHS vs FAIMS for TCA; (C) Water Utility Lab (either method 552.2 or standard methods 6251 B) vs FAIMS for DCA; (D) method 552.2 in EHS vs FAIMS for DCA. The dashed lines correspond to the 95% confidence interval.

The comparison of these methods with the FAIMS method shows that FAIMS is a viable alternative and offers the advantage of lower detection limits without preconcentration or derivatization.

CONCLUSIONS

The ESI-FAIMS-MS method applied to authentic drinking water samples with the dechlorination agent does not require sample preparation or chromatographic separation and provides a fast, simple and sensitive, and specific method for monitoring HAAs in water. The standard addition method used for quantification can compensate for matrix effects. The ESI-FAIMS results indicate that the concentration of some HAAs is too low to be handled by conventional GC methods. For that reason, a complete evaluation of ESI-FAIMS results could not be accomplished. High-bromide source water sample should be analyzed in the future to extend the ability of comparing FAIMS to the standard GC methods. Some of the MCA and BDCA results from FAIMS were high enough to be detected with the standard GC methods, which indicate either the insufficient selectivity of FAIMS at low concentrations or problems with achieving proper MQL with the standard GC methods. Further comparisons should be done with laboratories that can demonstrate the ability to reliably measure levels of all HAAs at MQL with the standard GC methods. The comparison of results for TCA and DCA obtained by ESI-FAIMS-

MS and GC indicates a good agreement between the methods. The precision of the ESI-FAIMS-MS method is as good as the precision for GC methods. The accuracy of the ESI-FAIMS method concluded from results obtained from GC methods is usually good. The differences in results by FAIMS and GC are observed more for HAAs present in a sample at lower concentrations when the specificity (selectivity) of a method plays the most important role in quantification. A great advantage of the FAIMS method relative to GC methods in HAA analysis is the elimination of time- and labor-intensive steps including extraction and derivitization as well as shortening analysis time from hours to a few minutes. The FAIMS method becomes an attractive alternative to conventional GC methods because the commercial version of the FAIMS system is almost available (summer 2003). The cost of the FAIMS system is estimated to be similar to the cost of a HPLC system.

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