DIONEX

Application Note 269

Identification and Quantification at ppb Levels of Common Cations and Amines by IC-MS

INTRODUCTION

Ion chromatography (IC) has been extensively used as the preferred separation technique for ionic species such as inorganic anions/cations, small amines, organic acids, peptides and proteins, nucleic acids, and carbohydrates. In recent years, the increasing demands for higher sensitivity, selectivity, structural, and confirmatory information has led to the emergence of mass spectrometry (MS) as a powerful complementary detector to conductivity, UV, and electrochemical detections.

Given the mass range of the target analytes, common cations and small amines are usually below 100 mass-to-charge ratio (*m/z*); therefore, an ideal MS detector for these analyses will have the features of mass accuracy and high mass transmission efficiency in the low mass range (15–100 *m/z*) while maintaining the necessary mass resolution. Compared with other commercially available MS detectors, the MSQ Plus™ single quadrupole MS detector requires low maintenance, is reasonably affordable, and provides substantially enhanced performance for low molecular weight analyses, covering most analytes for small-molecule IC applications.

The work shown here demonstrates the use of IC with MS detection for the determination of six commonly found cations and selected amines. Confirmatory information was obtained using full-scan MS spectra showing positively charged cation species and characteristic adduct patterns. Quantification was achieved using selected ion monitoring (SIM) acquisitions for each target analyte. This IC-MS method was applied to the analysis of real-world water samples and the results are presented. Method performance with respect to calibration range, reproducibility, and method detection limits is also presented.

EQUIPMENT

Dionex ICS-2000 or ICS-2100 Reagent-Free™ Ion Chromatography (RFIC™) system

MSQ Plus single quadrupole mass spectrometer

Chromeleon® Chromatography Data System (CDS) software, Version 6.8, SR9 (for instrument control, data acquisition, data processing, and report generation)

CHROMATOGRAPHIC CONDITIONS

Column:	IonPac® CS12A 5 µm (3 × 150 mm) with guard column (3 × 50 mm)
Temperature:	30 ºC
Eluent:	Isocratic 33 mM methanesulfonic acid (MSA)
Eluent Source:	EGC II MSA with CR-CTC
Flow Rate:	0.5 mL/min
Injection Volume:	100 µL
Detection:	Suppressed conductivity (external water at 2 mL/min delivered by an AXP-MS pump), MSQ Plus mass spectrometric detector
Ionization Interface:	Electrospray ionization (ESI) with positive polarity
Desolvation Solvent:	0.2 mL/min isopropanol delivered by an AXP-MS auxiliary pump
Needle Voltage:	2 kV
Probe Temperature:	500 ºC
Nebulizer Gas:	Nitrogen at 85 psi
MS Detection Mode:	Selected Ion Monitoring (SIM) Details of SIM scans (Table 1)

Table 1. SIM Scans for Studied Analytes

Analyte	t_R (min)	*m/z*	Adduct*	Cone Voltage (V)
Potassium	3.5	39.0	K^+	45
Trimethylamine	3.9	60.0	$[M+H]^+$	50
Ethanolamine	3.0	62.0	$[M+H]^+$	40
Ammonium	2.9	78.1	$[NH_4+IPA]^+$	20
Diethanolamine	3.1	106.1	$[M+H]^+$	40
Lithium	2.3	127.1	$[Li+2IPA]^+$	30
Sodium	2.6	143.1	$[Na+2IPA]^+$	20
Triethanolamine	3.5	150.1	$[M+H]^+$	60
Magnesium	4.0	192.2	$[Mg+6IPA]^{2+}$	30
Calcium	4.8	265.2	$[3Ca+5OH^-+IPA]^+$	50

* Proposed adduct structures were based on observed *m/z*.

Reagents and Standards

Prepared stock solutions at 1000 ppm were purchased from Ultra Scientific:

Ammonium (NH_4) (Ultra Scientific P/N CC-101)
Lithium (Li) (Ultra Scientific P/N ICC-104)
Sodium (Na) (Ultra Scientific P/N ICC-107)
Potassium (K) (Ultra Scientific P/N ICC-106)
Magnesium (Mg) (Ultra Scientific P/N ICC-105)
Calcium (Ca) (Ultra Scientific P/N ICC-103)

Dilute the cation stock solutions in deionized water to 10 ppm as the mixed working standard.

Four amines were purchased from Sigma-Aldrich:

Ethanolamine (EA) (Sigma Aldrich P/N 411000)
Diethanolamine (DEA) (Fluka P/N 31589)
Triethanolamine (TEA) (Fluka P/N 90279)
Trimethylamine (TMA) (Fluka P/N 92262)

Prepare stock solution for each of the four amines in deionized water and then dilute to 10 ppm as working standards.

Deionized water with 18.2 MΩ-cm resistivity (Millipore Corporation)
Isopropanol (IPA) (General Chemical Corporation 119-9758-011-09, Class 10 certified grade)
Acetonitrile (CH_3CN) (Burdick & Jackson Cat. No. 015-4, HPLC/GC grade, Honeywell)
Methanol (CH_3OH) (Burdick & Jackson Cat. No. 230-4 HPLC/GC grade, Honeywell)

Prepare calibration standards in deionized water at 1 part-per-billion (ppb or µL), 2 ppb, 5 ppb, 10 ppb, 20 ppb, 50 ppb, 100 ppb, and 200 ppb.

RESULTS AND DISCUSSION

Chromatography

Typical IC-MS chromatograms for six cations and four amines using suppressed conductivity and SIM detection are shown in Figure 1. The six commonly seen cations—lithium, sodium, ammonium, potassium, magnesium, and calcium—were separated using an IonPac CS12A 5 µm cation-exchange column within 6 min. The four selected common amines—ethanolamine, diethanolamine, triethanolamine, and trimethylamine—were not baseline resolved from the six common cations (i.e., coelution of some analytes was observed). However, using SIM detection, coeluted analytes are differentiated by mass-to-charge ratio (*m/z*), can be accurately quantified, and are a single peak in each monitored SIM channel in Figure 1.

Mass Spectrometry

Mass spectrometers are not inherently compatible with ion-exchange chromatography due to two factors: first, the highly ionic mobile phase can cause fouling or premature wear of the mass spectrometer entrance apertures, consequently leading to more frequent interruptions of normal operation for instrument maintenance; and second, the mobile phase used in IC is essentially 100% aqueous, and the ESI interface will require higher temperatures and/or higher nebulizer gas flow for optimization of the thermally assisted pneumatic nebulization process.

To enable MS detection for IC, a self-regenerating suppressor and the addition of a desolvation solvent are used to ameliorate the afore-mentioned considerations for IC-MS applications. The suppressor currently used on IC instruments electrolytically replaces potassium/sodium with hydronium ions (anion-exchange applications) or methanesulfonate anion (MSA) with hydroxide ions (cation-exchange applications) in the mobile phase, thus converting the mobile phase to virtually deionized water which is more compatible with mass spectrometers.

A desolvation solvent, such as acetonitrile, methanol, or IPA, can be added and mixed into the IC stream before entering the mass spectrometer to improve the evaporation of the mobile phase, thus improving the release of the ions from the liquid to gas phase.

Chromatographic Conditions

Column:	IonPac CS12A 5 µm (3 × 150 mm) with guard column (3 × 50 mm)	Ionization Interface:	Electrospray ionization (ESI) with positive polarity
Temperature:	30 °C	Desolvation Solvent:	0.2 mL/min isopropanol delivered by an AXP-MS auxiliary pump
Eluent:	Isocratic 33 mM MSA	Needle Voltage:	2 kV
Eluent Source:	EGC II MSA with CR-CTC	Probe Temp.:	500 °C
Flow Rate:	0.5 mL/min	Nebulizer Gas:	Nitrogen at 85 psi
Inj. Volume:	100 µL	MS Detection Mode:	Selected Ion Monitoring (SIM) Details of SIM scans (Table 1)
Detection:	Suppressed conductivity (external water at 2 mL/min delivered by an AXP-MS pump), MSQ Plus mass spectrometric detector		

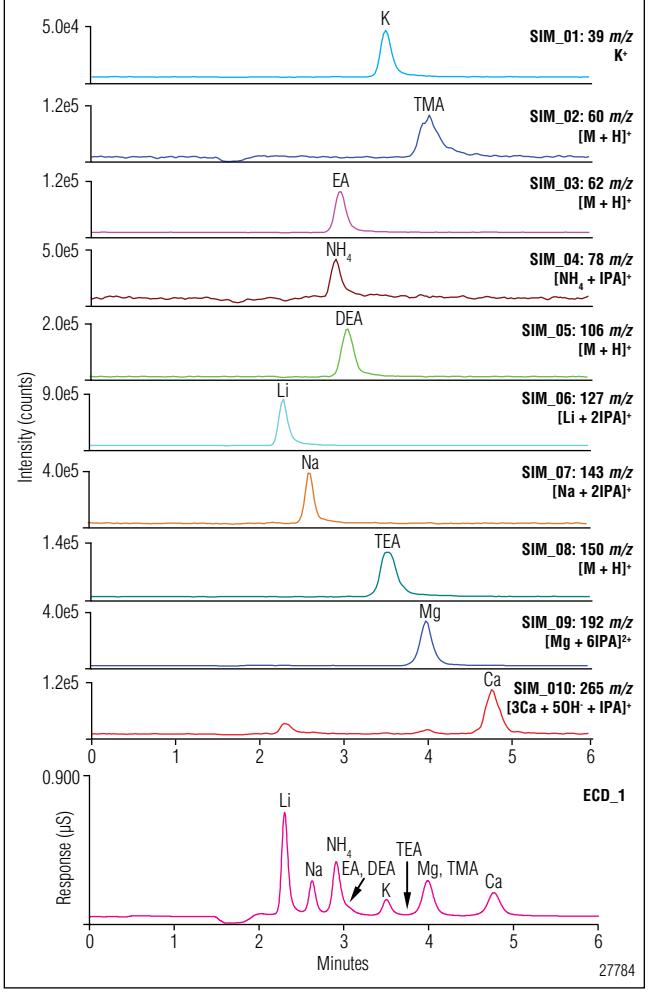

Figure 1. SIM and conductivity chromatograms of six cations and four amines.

The addition of a moderate volume of an organic solvent not only improves the desolvation/ionization efficiency, but adding organic solvent to the IC eluent also promotes formation of analyte-solvent adducts with improved response intensity, and these adducts may be used as quantitative ions to achieve lower detection limits.

Isopropanol was selected as the desolvation solvent because it showed relatively cleaner full-scan MS spectra, and higher observed analyte and/or adduct intensity. An example is shown in Figure 2 for the comparison of lithium mass spectra with three organic solvents. When using IPA as the desolvation solvent, the cleanest MS spectrum with the lowest background was observed, compared to the spectra obtained using CH_3CN and CH_3OH solvents. Higher intensity was also observed for the major IPA adduct ion: $[Li+2\ IPA]^+$ at 4.75×10^5, compared to the major CH_3CN adduct $[Li+3CH_3CN]^+$ at 1.05×10^5. The specificity of each adduct to the original analyte was evaluated by extracting the individual adduct ion from the full-scan spectrum and confirmed by comparing the retention times of the adduct ion in extracted MS and the conductivity channels. The details of SIM scans for quantitative ions and adduct assignments are shown in Table 1.

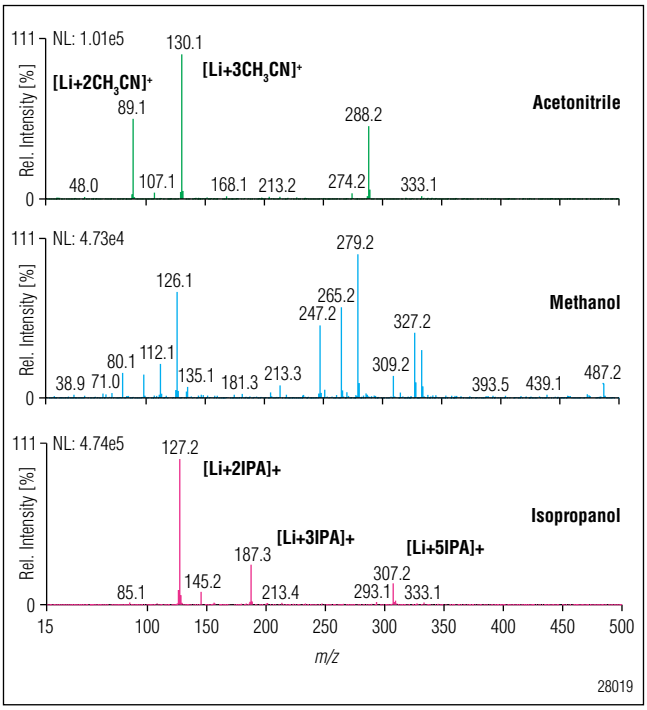

Figure 2. MS spectra of Li with different desolvation solvents. The cone voltage was 50 V.

Method Performance

The method performance was evaluated by measuring analytical parameters such as calibration range, correlation of determination, precision and accuracy, and detection limits. This method was also used to quantify the target analytes in water and beverage samples.

Calibration curves were generated from calibration standards with concentrations from the lower limit of quantitation (LLOQ) to 100 ppb with correlation of determination (r^2) greater than 0.99 for each analyte using linear, quadratic, or cubic fittings. Figure 3 shows the calibration curves for magnesium and trimethylamine as examples. LLOQ was defined as the lowest concentration in calibration standards that consistently showed signal-to-noise ratios greater than 10 (S/N >10) and within 20% bias of quantitation precision and accuracy.

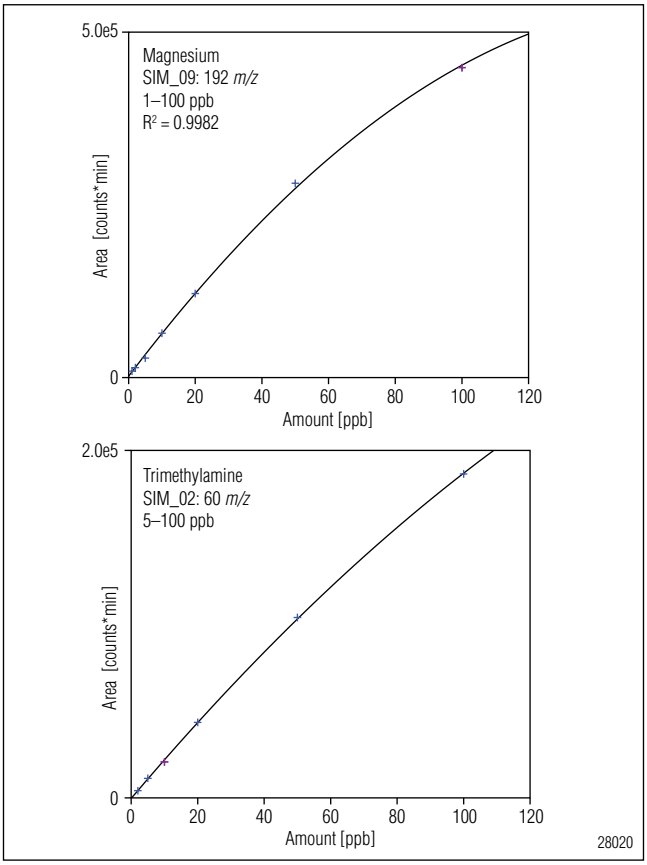

Figure 3. Calibration curves for magnesium and trimethylamine.

Table 2. Calibration, Coefficient of Determination, and Detection Limits							
Analyte	**Calibration Range**	**Fitting**	**r^2**	**RSD***	**MDL (ppb)**	**LLOQ (ppb)**	**S/N at LLOQ**
Potassium	1–100	Quadratic	0.9991	9.94%	0.54	1	53
Trimethylamine	5–100	Quadratic	0.9999	5.60%	1.75	5	26
Ethanolamine	1–100	Cubic	0.9990	3.22%	0.20	1	21
Ammonium	10–100	Quadratic	0.9995	11.0%	3.66	10	24
Diethanolamine	1–100	Cubic	0.9997	7.19%	0.42	1	15
Lithium	1–100	Cubic	0.9991	4.16%	0.26	1	377
Sodium	1–100	Quadratic	0.9984	6.64%	0.37	1	18
Triethanolamine	1–100	Quadratic	0.9995	4.31%	0.27	1	24
Magnesium	1–100	Quadratic	0.9980	5.77%	0.35	1	58
Calcium	10–100	Linear	0.9995	8.50%	1.26	10	150

*RSD was calculated based on 7 replicate injections of a 2 ppb standard, except for trimethylamine, ammonium, and calcium, which were obtained from a 10 ppb standard.

The LLOQ is also related to the background level of target analytes, with various levels of background contamination observed for trace level quantitation. In this study, ~2 ppb of ammonium and calcium were observed (estimated by peak area) in method blanks that may be attributed to the leaching of autosampler vials. Thus, the LLOQ for ammonium and calcium was set as 5× the observed background level, i.e. 10 ppb. Method detection limit (MDL) was statistically calculated by $MDL = S \times t_{99\%,\, n=7}$ where S is the standard deviation and t is the Student's t at 99% confidence interval. Standard deviation was obtained from seven replicate injections of a calibration standard at 2 ppb, and relative standard deviation (RSD) was used to measure the precision of analysis. The evaluation results for method performance are summarized in Table 2.

Table 3. Cation Concentrations in Water Samples (mg/L)				
Sample	**Potassium**	**Sodium**	**Magnesium**	**Calcium**
Municipal Drinking Water	1.70	33.7	8.49	17.3
Bottled Drinking Water	1.51	3.54	2.44	7.31
Bottled Mineral Water	3.77	67.5	48.8	12.4
Bottled Ice Tea Beverage	>100	31.3	2.57	13.0
Bottled Deep Sea Drinking Water	4.37*	99.4	4.79*	2.63*

*Based on 1:100 dilution.

Water Sample Analysis

This method was applied to the quantification of target analytes in several water and beverage samples: local municipal drinking water (A), bottled drinking water (B), bottled mineral water (C), bottled ice tea (D), and bottled deep sea drinking water (E). All water samples were diluted in deionized water at 1:1000 ratio (sample E was diluted 1:100) and directly injected for analysis. (Filtering may be performed as required to remove sample particulates.) The results are shown in Table 3. The MS SIM and suppressed conductivity chromatograms of detected cations in sample E are shown in Figure 4.

CONCLUSION

The methods here demonstrate the use of IC-MS for the determination of six commonly occurring cations and four amines at ppb levels. With MS detection, confirmation of the analyte identity can be achieved from full-scan spectra, and quantitation can be achieved at low ppb levels with greater confidence by using selective SIM scans. Successful applications using this method for analysis of real-world samples have also been demonstrated.

Note: The optimum settings and responses may vary on different instruments; thus, optimization of MSQ Plus local source conditions and acquisition parameters is highly recommended for best results.

Chromatographic Conditions

Column:	IonPac CS12A 5 µm (3 × 150 mm) with guard column (3 × 50 mm)	Ionization Interface:	Electrospray ionization (ESI) with positive polarity
Temperature:	30 °C	Desolvation Solvent:	0.2 mL/min isopropanol delivered by an AXP-MS auxiliary pump
Eluent:	Isocratic 33 mM MSA		
Eluent Source:	EGC II MSA with CR-CTC	Needle Voltage:	2 kV
Flow Rate:	0.5 mL/min	Probe Temp.:	500 °C
Inj. Volume:	100 µL	Nebulizer Gas:	Nitrogen at 85 psi
Detection:	Suppressed conductivity (external water at 2 mL/min delivered by an AXP-MS pump), MSQ Plus mass spectrometric detector	MS Detection Mode:	Selected Ion Monitoring (SIM) Details of SIM scans (Table 1)

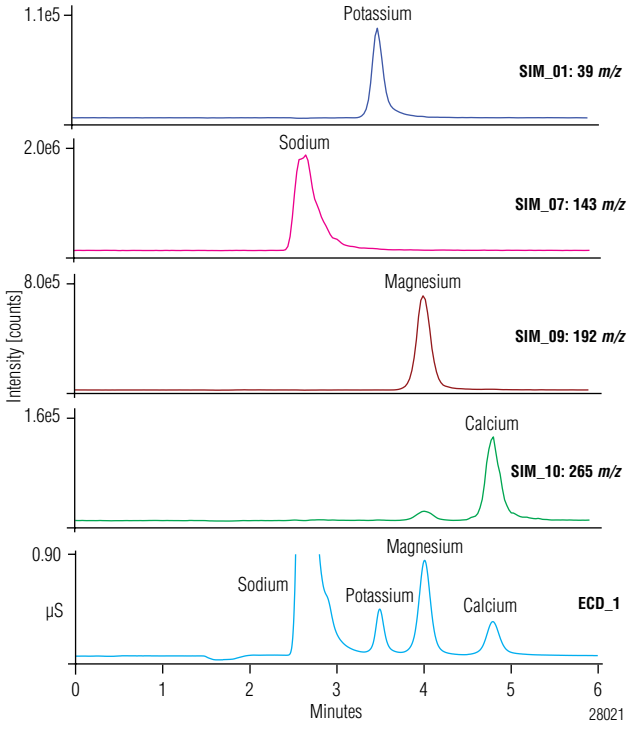

Figure 4. Cations in a bottled deep sea drinking water.

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