

Ion chromatography

Determination of cationic polar pesticides in oat cereals by ion chromatography and electrospray ionization mass spectroscopy

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Keywords

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RFIC, Reagent-Free IC, ESI-MS,
single quadrupole, diquat, paraquat,
mepiquat, chlormequat

Goal

Demonstrate determinations of cationic polar pesticides by ion chromatography coupled with electrospray ionization mass spectrometry

Introduction

Pesticide contamination in food as a potential health risk is a growing public concern, resulting in increased interest and attention by health researchers and regulatory agencies.¹ Collectively grouped into the category of “Ionic and Highly Polar Pesticides” are herbicides, fungicides, defoliants, and desiccants. For traditional solvent-based pesticides, the regulatory test methods are typically gas and liquid chromatography combined with mass spectrometry. However, polar pesticides, which are ionic and non-volatile, are much more suitable for methods using ion chromatography (IC) separations combined with mass spectrometry (MS) detection. Consequently, determinations of anionic polar pesticide residues, such as glyphosate, glufosinate, and their degradation products, such as AMPA (aminomethylphosphonic acid), have been successfully demonstrated in beer, fruit, cereals, vegetables, and drinking water by the Food Environmental Research Association (Fera Science Ltd.).^{2,3} and others⁴⁻¹⁵ using IC with MS (MS/MS, high-resolution accurate mass (HRAM) MS, or single quadrupole MS).

Determinations of cationic polar pesticides are more challenging than anionic polar pesticides due to their similar chemical structures, resulting in co-elution of paraquat and diquat ions on the previously available columns, and requiring IC-HRAM MS for quantification.^{11,16,17} These challenges have been solved with the recent development of the Thermo Scientific™ Dionex™ IonPac™ CS21-Fast-4µm column, optimized to fully resolve paraquat from diquat and other quaternary amine pesticides. Previous applications demonstrated the determination of cationic pesticide residues in extractions from homogenized fruits and vegetables using IC combined with MS/MS.¹⁸⁻²⁰ Analysis of extracts from cereal samples is well known to be challenging. Analysis of oat cereal samples was previously demonstrated by IC-MS/MS using the Thermo Scientific™ Dionex™ ICS-6000 HPIC™ system and the Thermo Scientific™ TSQ Altis™ Plus triple quadrupole mass spectrometer with sensitivities to 0.5 µg/kg (as indicated by the LODs).²¹

In this application, a targeted screening method is demonstrated for cationic polar pesticides using the Dionex ICS-6000 HPIC system combined with the Thermo Scientific™ ISQ EC™ single quadrupole mass spectrometer. Four cationic pesticides with similar quaternary amine chemical structures—mepiquat (1,1-dimethylpiperidinium chloride), chlormequat (2-chloroethyl(trimethyl)azanium), paraquat (1-methyl-4-(1-methylpyridin-1-ium-4-yl) pyridin-1-ium), and diquat (1,1'-Ethylene-2,2'-dipyridylium)—were separated by cation-exchange chromatography using an electrolytically generated methanesulfonic acid gradient at 0.3 mL/min and 40 °C on the Dionex IonPac CS21-Fast-4µm cation-exchange column. As the quaternary amines eluted from the column, they were detected by suppressed conductivity, heated to ionized gas by heated electrospray ionization (HESI-II), and detected by MS in SIM mode by the ISQ EC single quadrupole mass spectrometer. The method was applied to acid-methanol extractions of ground oat cereal samples (using the EU Reference Laboratories for Food and Vegetables (EURL-FV) Quick Polar Pesticides Extraction (QuPPE) method modified for quaternary amine pesticides²²) and found to be accurate but less sensitive than using MS/MS (TSQ Altis Plus triple quadrupole mass spectrometer). These analyses show that the EU MRL requirements for oat cereals are met.

Experimental

Equipment

- Dionex ICS-6000 HPIC system*
- Dual Pump DP module, isocratic configuration (P/N 22181-6009)* with pump_1 to deliver DI water for eluent generation and pump_2 to deliver DI water as suppressor regenerant.
- Eluent Generator EG module (P/N 22181-60019)
- Detector Chromatography DC module with two 6-port injection valves (P/N 22181-600499)**
- CD Conductivity Detector (P/N 079829)
- Thermo Scientific™ Dionex™ AS-AP Autosampler with temperature control option (P/N 074926)
- 100 µL syringe (P/N 074305)
- 1 to 3 8-position sample trays for 10 mL vials (P/N 069877) typically used for standards
- 1 to 3 19-position sample trays for 10 mL vials (P/N 074938)
- ISQ EC single quadrupole mass spectrometer with HESI-II probe (P/N ISQEC-IC)

*Alternative pump configuration: Thermo Scientific ICS-6000 system with single pump SP module (P/N 22181-6003) to deliver eluent with Thermo Scientific™ Dionex™ Auxiliary Pump AXP-MS (P/N 063973) to deliver DI water for the suppressor regenerant.

**Alternative valve configuration: Thermo Scientific ICS-6000 DC with single injection valve (P/N 22181-60047) and Automation Manager with one (IC PEEK) 6-port valve (P/N 075952) used as the diverter valve.

Software

Thermo Scientific™ Chromeleon™ Chromatography Data System (CDS) v. 7.3 or above.

Table 1. Consumables list for the Dionex ICS-6000 HPIC system coupled to the ISQ EC single quadrupole mass spectrometer

Product name	Description	P/N
Thermo Scientific™ Dionex™ IC PEEK Viper™ fitting tubing assembly kit	Dionex IC Viper fitting assembly kit for the Dionex ICS-6000 HPIC system with CD Detector	302965
Thermo Scientific™ Dionex™ EGC 500 MSA Eluent Generator cartridge	Cation eluent generator cartridge for HPIC high pressure systems	075779
Thermo Scientific™ Dionex™ CR-CTC™ III Continuously regenerated trap column	Continuously regenerated cation trap column required for determining quaternary amine analytes, as in this application note. The cable is standard for the Dionex Integriion HPIC and ICS-6000 HPIC instruments.*	104-30001
Thermo Scientific™ Dionex™ ICS-6000 EG Eluent Generator kit	Degasser installed after Dionex CR-CTC III trap column and before the injection valve, used with eluent generation	075522
Thermo Scientific™ Dionex™ CDRS™ 600 suppressor, 2 mm	Suppressor for 2 mm cation columns	088670
Thermo Scientific™ Dionex™ IonPac™ CG21-Fast-4µm Guard Column	Cation guard column, 2 × 30 mm	303349
Thermo Scientific™ Dionex™ IonPac™ CS21-Fast-4µm Analytical Column	Cation analytical column, 2 × 150 mm	303348
Thermo Scientific™ Dionex™ AS-AP Autosampler vial kit options	10 mL polystyrene, package of 100 caps and septa	055058
Thermo Scientific™ Dionex™ IC PEEK Viper™ Sample Loop	10 µL PEEK Viper sample loop	302895
Thermo Scientific™ ISQ EC Mass Calibrant	Replacement calibrant solution, 250 mL	1R120590-6204
IC-MS Installation Kit	IC-MS installation kit includes tubing, mixing tee	22153-62049
HESI-II needle	Replacement HESI-II needle	1R120590-6211
ISQ EC Inlet union (PEEK)	Replacement union	1R4035-0600
Centrifuge tubes	50 mL centrifuge tubes for sample preparation	14-432-22
Syringe filters	0.45 µm polypropylene syringe filters	44513-PP

* P/N for cable adapter to Dionex ICS-5000+ HPIC system: 22181-98150

IC-MS conditions (part 1)

Parameter	Setting																		
Columns	Dionex IonPac CG21-Fast-4µm guard (2 × 30 mm) Dionex IonPac CS21-Fast-4µm analytical (2 × 150 mm)																		
MSA gradient	3 mM MSA (-4 to 0 min), 3–6 mM (0.1 to 3.6 min), 6–22 mM (3.6 to 6 min), 22–25 mM (6 to 15 min), 1 mM (15-30 min wash), 3 mM (30 min)																		
Eluent source	Dionex EGC 500 MSA eluent cartridge, Dionex CR-CTC III trap column and HP EG degas kit																		
Flow rate	0.30 mL/min																		
Injection volume	10 µL																		
Column temperature	40 °C																		
Detection/suppressor compartment	20 °C																		
Detection 1:	Suppressed conductivity, Dionex CDRS 600 suppressor, 2 mm, 22 mA, constant current and external water modes																		
Suppressor regenerant	DI water by DP Pump 2 at 0.3 mL/min.																		
Conductivity	Background: < 1 µS/cm, Noise: < 1 nS/cm																		
IC-MS system backpressure	~3,000 psi																		
IC-MS run time	34 min																		
DC Valve 2 functioning as a diverter valve	<table><tr><th>Timing (min)</th><th>Valve position</th><th>IC flow path</th></tr><tr><td>Prerun</td><td>DC.InjectValve_2.InjectPosition</td><td>Divert IC flow away from MS. DI water for suppressor Regen flows through diverter valve to MS</td></tr><tr><td>-4.0 Equilibration</td><td>--</td><td>Same</td></tr><tr><td>0.0 Run</td><td>--</td><td>Same</td></tr><tr><td>4.0</td><td>DC.InjectValve_2.LoadPosition</td><td>IC flow to MS Start MS acquisition</td></tr><tr><td>15 min</td><td>DC.InjectValve_2.InjectPosition</td><td>Divert away from MS</td></tr></table>	Timing (min)	Valve position	IC flow path	Prerun	DC.InjectValve_2.InjectPosition	Divert IC flow away from MS. DI water for suppressor Regen flows through diverter valve to MS	-4.0 Equilibration	--	Same	0.0 Run	--	Same	4.0	DC.InjectValve_2.LoadPosition	IC flow to MS Start MS acquisition	15 min	DC.InjectValve_2.InjectPosition	Divert away from MS
Timing (min)	Valve position	IC flow path																	
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-4.0 Equilibration	--	Same																	
0.0 Run	--	Same																	
4.0	DC.InjectValve_2.LoadPosition	IC flow to MS Start MS acquisition																	
15 min	DC.InjectValve_2.InjectPosition	Divert away from MS																	

IC-MS conditions (part 2)*

Parameter	Setting			
Detection 2	ISQ EC single quadrupole mass spectrometer, HESI-II, +ESI, +2,800 V, Full Scan 60–300 <i>m/z</i> , SIM mode			
Flow (N ₂)	Sheath: 45 (psi), Aux: 2.5 (psi), Sweep: 1 (psi)			
MS temperatures	Vaporizer: 300 °C, Ion transfer tube: 350 °C			
SIM conditions				
Method type:	Scan mode, Advanced			
Polarity:	Positive			
Scan time (s):	0.2			
Use calibrated RF lens:	(check box)			
Scans:	Scan window (min)	Ion	<i>m/z</i>	CID (V)
	4–9	Chlormequat	122.1	15
		Chlormequat-d ₄	126.1	15
		Mepiquat	114.1	15
		Mepiquat-d ₁₆	130	15
	12–15	Paraquat	186	10
		Paraquat-d ₈	97	10
		Diquat	184	10
		Diquat-d ₈	96	10

*This method demonstrates using a single quadrupole mass spectrometer. This method does not meet the SANTE identification requirements of using three ions for quantitation (ref 36, Table 3).

Reagents

- Degassed deionized (DI) water, ASTM Type I grade²⁹
- Solvents for sample extraction
 - Formic acid, 88%, ACS grade ([P/N A118P-100](#))
 - Hydrochloric acid, 37%, ACS grade ([P/N AC423795000](#))
 - Methanol, Optima™ HPLC grade ([P/N A454-1](#))
- Chlormequat (2-chloroethyl(trimethyl)azanium;chloride), 98%, Alfa Aesar™ (MW= 158.066 g/mol, CAS 999-81-5, [P/N AAA1563006](#))
- Chlormequat-1,1,2,2-d₄ chloride, 100 µg/mL, Absolute Standards, Inc. ([P/N 96081](#))
- Diquat dibromide, monohydrate (1,1'-ethylene-2,2'-dipyridylium dibromide), SPEX CertiPrep™ (MW = 362.07 g/mol; CAS 6385-62-2, [P/N S1752](#))
- Diquat-d₈ dibromide (dipyridine-D₈) C/D/N Isotopes Inc., 50 mg (MW = 352.08 g/mol; [P/N D-7990](#))
- Mepiquat chloride (1,1-dimethylpiperidinium chloride), 98%, Honeywell Fluka™ PESTANAL™ (MW=149.662 g/mol, CAS 24307-26-4, [P/N 11-101-3665](#))
- Mequat-d₁₆ chloride, 100 µg/mL, Absolute Standards, Inc. ([P/N 96082](#))
- Paraquat dichloride, tetrahydrate (1-methyl-4-(1-methylpyridin-1-ium-4-yl) pyridin-1-ium;dichloride), SPEX CertiPrep (MW = 257.158 g/mol; CAS 1910-42-5, [P/N S2915](#))
- Paraquat dichloride-d₈ (ring-d₈), 100 µg/mL, Absolute Standards, Inc. (CAS 347841-45-6, [P/N 95305](#))

Standard and sample preparation

Standard preparation

Stock and intermediate standards: To prepare 100 mL of 1,000 mg/L individual stock standards, add the solid reagent (Table 2) into a 125 mL HDPE bottle. Add 100 g of ASTM Type I DI water. Swirl to dissolve. Refrigerate at 20 °C. The 1,000 mg/L standards are stable for 2 to 3 months.

Table 2. Preparation of 100 mL of 1,000 mg/L individual standards

	MW of hydrated salt (g/mol)	Formula weight of cation (g/mol)	Ratio (hydrated salt)/(cation)	Reagent (hydrated salt), weight (mg)	DI water (g)
Chlormequat chloride	158.066	122.62	1.29	129	100
Mepiquat chloride	149.662	114.21	1.31	131	100
Paraquat dichloride	257.158	186.26	1.38	138	100
Diquat dibromide monohydrate	362.07	202.27	1.96	196	100

Mixed intermediate and working standards: To prepare the mixed 5 mg/L intermediate standard, pipet 500 µL of the individual 1,000 mg/L stock standards into a 125 mL HDPE bottle. Dilute with DI water to 100 g total weight. Swirl to mix. Refrigerate at 20 °C or lower.

Working standards (1, 2, 5, 10, 20, 50, 100 and 200 µg/L) were prepared from the 5 mg/L intermediate standard and DI water. Twenty-five µg/L ISTD was added to each 5 mL working standard from the 10 mg/L mixed isotopic spiking standard (prepared below).

ISTD isotopic standards: To prepare 500 mg/L (µg/mL) stock standard of the diquat isotopic standard, 9.2 mg of diquat-d₈ dibromide (dipyridine-d₈) (1.83 salt/cation ratio) were dissolved in 10 mL of DI water and further diluted (2,000 µL in 10 mL) to 100 mg/L working standard.

To prepare 10 mL of 1 mg/L mixed isotopic spiking standard, pipet:

- 128 µL (1.28 salt/cation ratio) of 100 mg/L chlormequat-d₄ chloride
- 128 µL (1.28 salt/cation ratio) of 100 mg/L mequat-d₁₆ chloride
- 100 µL of 100 mg/L diquat-d₈
- 192 µL (1.92 salt/cation ratio) of 100 mg/L paraquat-d₈ dichloride

into a 20 mL HDPE bottle. Dilute with DI water to 10 g total weight. Swirl to mix. Refrigerate at 20 °C or lower.

Sample preparation

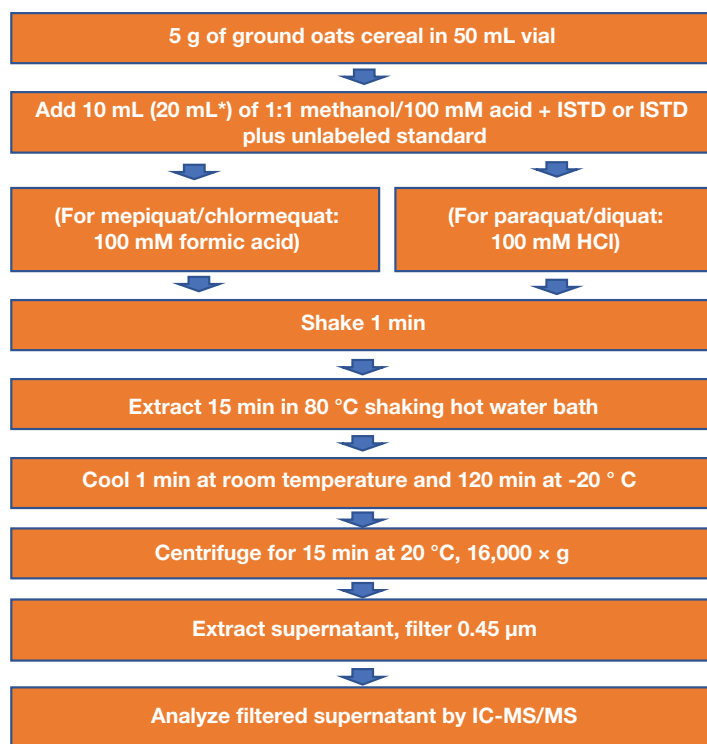
100 mM formic acid extraction acid: In an exhaust hood, pipet 4.2 mL (5.22 g) of 88% formic acid into a 1 L volumetric flask containing 300 mL of DI water. Swirl to mix. Dilute to the 1 L mark. Mix by inverting the flask several times.

100 mM HCl extraction acid: In an exhaust hood, pipet 8.35 mL (9.85 g) of 37% (concentrated) hydrochloric acid (HCl) into a 1 L volumetric flask containing 300 mL of DI water. Swirl to mix. Dilute to the 1 L mark. Mix by inverting the flask several times.

Samples

Commercial oatmeal (referred to as "oatmeal") and toasted whole grain oats (referred to as "toasted oats cereal") cereal samples were evaluated.

The sample extraction follows the EURL-FV Quick Polar Pesticide Extraction method (QuPPE)²² optimized for quaternary amines (Figure 1). The oatmeal and toasted oats cereal samples were ground in a food-grade processor. Twelve replicate 5 g ground samples were weighed into 50 mL vials and were extracted with 10 mL (20 mL for toasted oats samples) each of a 1:1 solution of 100 mM acid and methanol (Table 3). The acid-methanol solutions were spiked with 25 µg/L mixed ISTD. To determine recoveries, a mixed unlabeled standard, 25 µg/L, was added to three replicates of the formic acid-methanol extractions. Similarly, the 25 µg/L mixed standard was added to three replicates of the hydrochloric acid-methanol extraction.



*Added 20 mL of methanol/acid to extract toasted oats cereal samples

Figure 1. EURL-FV QuPPE extraction method recommended for quantitation of quaternary amine pesticides in cereals

Table 3. Extraction solutions recommended by the EURL-FV QuPPE method

Compound	100 mM formic acid	100 mM hydrochloric acid	Methanol
Chlormequat	5 mL	--	5 mL
Mepiquat	5 mL	--	5 mL
Paraquat	--	5 mL	5 mL
Diquat	--	5 mL	5 mL

During the extractions, the ground toasted oats cereal sample immediately absorbed the 10 mL of acid/methanol solution, therefore an additional 10 mL were used to extract the toasted oats cereal (20 mL total). Twice the amount of ISTD (to 50 µg/L) and spiked standard (50 µg/L) were added to correct for the additional volume.

Instrument setup and installation

Physical and electronic configuration

The Dionex ICS-6000 is a modular, high-pressure, Reagent-Free IC™ (RFIC™) dual IC system. This application runs on one side of the dual system: System 1 (Pump_1, EGC_1, CR-CTC_1, DC_Valve_1, CD_1) with a second pump and valve. In this case, the second pump of the DP module is used to deliver DI water as the regenerant solution to the suppressor. The second DC Injection Valve 2 is used as the IC PEEK diverter valve to facilitate the flow to the suppressor regenerant (Inject mode) and to the MS (Load mode) (Figure 2).

In IC-MS applications, a PEEK valve should be used as the diverter valve. The valve timing is intended to divert most of the sample matrix away from the mass spectrometer (-4 to 4 min; >15 min). In IC-MS, a heated electrospray source transfers chromatographically separated ions in solution to ions in a gas stream. Make-up solvent is not needed.

For the best results, position the Dionex ICS-6000 system near the MS source. Install the power and USB cables, and power up the IC, autosampler, and computer. Add DI water to the eluent bottles and prime the pumps. Use Dionex IC PEEK Viper fittings

(from the IC-MS Installation kit) to complete the connections from the IC effluent to the diverter valve (Inj.Valve_2) to the MS source.

Installing the ISQ EC mass spectrometer

To install the ISQ EC mass spectrometer, first remove the shipping material located under the power supply inside the MS and then follow the installation instructions in the ISQ EC mass spectrometer instrument manual.²³ These include installing a nitrogen source, preferably a nitrogen generator, a mechanical vacuum pump, the correct power needed by the MS, exhaust lines, and power, USB, ethernet communication lines as described in AN73339¹⁴.

Power up the nitrogen generator so that the N₂ pressure output is ~100 psi. The foreline vacuum pump is plugged into the mass spectrometer and will automatically start with the mass spectrometer. After the mass spectrometer achieves vacuum (by mechanical (foreline) and turbo pumps), set the source conditions to standby mode (ISQEC ePanel, select *More Options, Standby*).

Electronic configuration

This application is operated solely through the Chromeleon Chromatography Data System (CDS). To electronically configure the IC system, start the Chromeleon Instrument Services program, then start the Instrument Controller program by selecting the *Configure instruments link*. Add the Dionex ICS-6000 system modules: DP, EG, and DC, the AS-AP Autosampler, and the ISQ EC single quadrupole mass spectrometer, as described in Table 4. Check and then correct any errors in the configuration. Save and close the configuration.

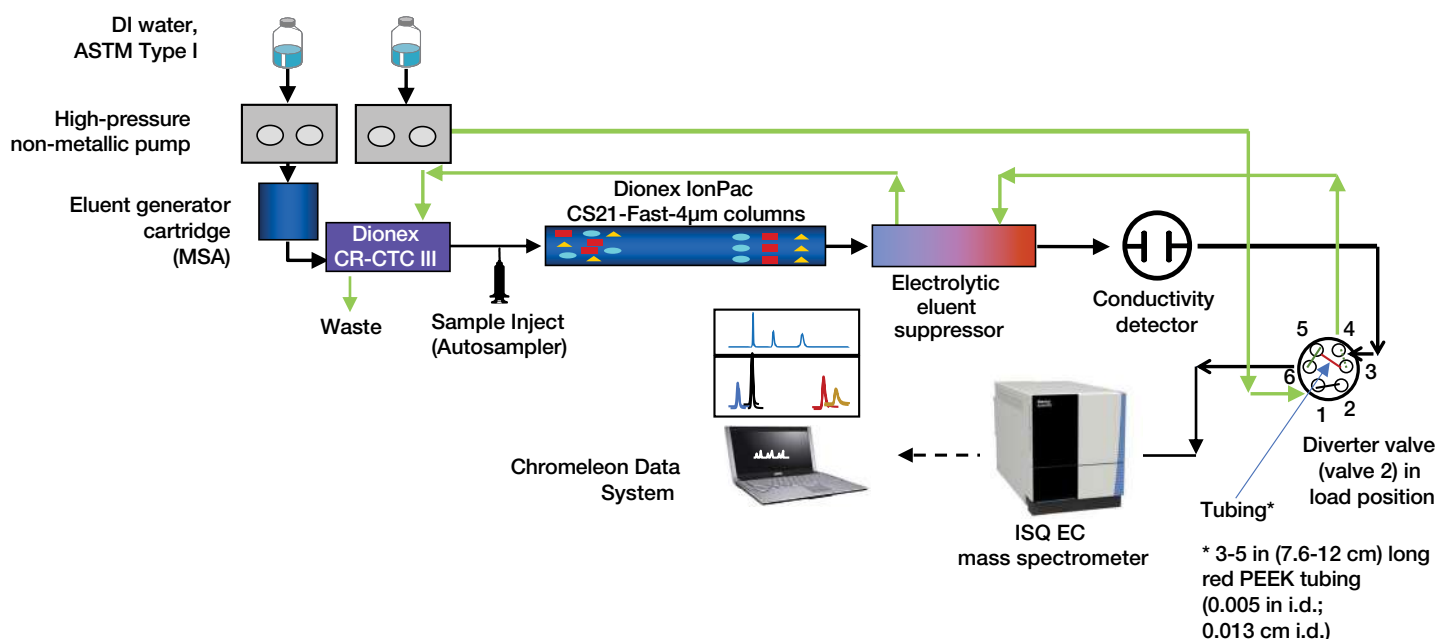


Figure 2. IC-MS flow diagram

Table 4. Electronic configuration parameters

Module	Tab	Action
ICS-6000 DP	General	Select <i>Browse</i> . Select the serial number to link the module to the instrument
	Device	Link Pump_1 and Pump_2 to the instrument
	Top Pump	Set the minimum pressure to 500 psi
	Bottom Pump	Set the minimum pressure to 500 psi
	Error Levels	Set "System pressure below limit" to <i>abort</i>
ICS-6000 EG	General	Select the serial number to link the module to the instrument
	Cartridges	Link to the instrument. Check <i>EGC_1</i> and link to <i>Pump_1</i>
ICS-6000 DC	General	Select serial number to the link module to instrument, Select instrument
	Detectors	Double click on CD, Link to <i>Pump_1</i>
	Thermo Controls	Check <i>Compartment_TC</i> and <i>Column_TC</i>
	Suppressors	Double click <i>Suppressor_1</i> , Link to Pump_1
	High Pressure Valves	Double click <i>InjectValve_1</i> , Link to <i>Pump_1</i> , select control by autosampler. Double click <i>InjectValve_2</i> , Link to <i>Pump_1</i> , select control by DC.
AS-AP Autosampler	General	Select serial number to link module to Instrument
	Sharing	If this option is present, select instrument
	Segments / Pump Link	Select <i>10 mL PolyVials</i> for "Red", "Blue", and Green. Leave the pump and TTL links empty.
	Options	Select <i>1200 buffer loop</i> , <i>250 µL syringe</i> , <i>temperature control</i> , and <i>push mode</i> . Enter "10" µL in sample loop.
ISQ Mass Spectrometer	Add module	Mass spectrometry, ISQ ICMS family
	General	Device model: <i>ISQ EC</i>
		Deselect the hardware inject synchronization. This is not needed for Chromeleon CDS.
		Remote Start: Select <i>ActiveLow</i> (ASAP autosampler)
		Deselect <i>split flow</i> , <i>fraction collection</i> , <i>Warn on source change</i> and <i>Simulation mode</i> boxes.
		Vacuum pressure units: <i>Torr</i>
		Source gas pressure units: <i>psig</i>
	Maintenance	Enable all boxes. Select "OK".
	Associate Pump Flow	Optional: Select <i>Associate</i> — a pump box will automatically enter flow rate when setting source conditions. If using this option, select pump_1 used for eluent flow.

Plumbing the Dionex ICS-6000 HPIC system

Plumb the Dionex ICS-6000 IC system as a standard Reagent-Free™ IC (RFIC™) system, as shown in Figure 2. Use the IC PEEK Viper fittings as indicated on their labels. Install a 2,000 psi backpressure tubing loop on Injection Valve 2 position 6 for DP.Pump_2 to maintain similar pressure as the IC system and to maintain backpressure well above the 500 psi lower limit. Temporarily direct the liquid flow away from the ISQ EC mass spectrometer until the IC system, and IC consumables are fully conditioned. The schematics are also illustrated on the inside doors of the Dionex ICS-6000 IC system. Further information can be found in the operator's and installation manuals.^{24,25} Direct the waste lines to waste containers.

Conditioning consumable devices

Important: If consumable tracking is installed, do not remove consumable tracking tags on the columns and consumable devices. These tags are required for consumables monitoring functionality.

Temporarily direct the liquid flow away from the mass spectrometer until the IC system and IC consumables are fully conditioned. Hydrate and condition the Dionex EGC 500 MSA eluent generator cartridge and Dionex CR-CTC III continuously regenerated trap column according to product manuals or the instructions in the drop-down menu (Chromeleon Console, under Consumables drop-down menu).^{26,27} The Dionex CR-CTC III trap column is required for this application. Note: Long-term use of a Dionex CR-CTC II or Dionex CR-CTC 500 trap column for this application will damage the Dionex IonPac CS21-Fast-4µm column.

Condition the columns as described in the Dionex IonPac CS21-Fast-4µm product manual²⁸ or Consumables Conditioning instructions (Chromeleon Console, under Consumables drop-down menu), using 4 mM MSA, 40 °C at 0.30 mL/min for 30 min or more while directing the effluent to waste. Install the conditioned columns according to Figure 2.

To hydrate the Dionex CDRS 600 suppressor, follow the instructions in the Suppressor Installation Checklist included with the suppressor.²⁹

Install the suppressor according to Figure 2 and ensure that the suppressor is within backpressure specifications. For cation suppressors, the optimum results are achieved by minimizing the hydrating and waiting times to those stated in the suppressor installation checklist and immediately installing the suppressor, starting the pump, eluent generation and CR-CTC III trap column, and powering the suppressor.

Plumbing the IC system to the MS system

Use Dionex IC PEEK Viper fittings (from the IC-MS Installation kit) to complete the connections from the IC system effluent to the diverter valve (Inj.Valve_2) to the MS source. Monitor and minimize backpressure to the suppressor (< 100 psi) to prevent damage to the suppressor. Check the backpressure to the suppressor as part of the start-up and daily checklist. Additional information can be found in the ISQ EC and ISQ EM Tips and Tricks issues #2, 4–6 and Technical Notes 73050 and 73878, regarding recommended replacement intervals for consumables, using restrictive tubing for calibration³¹, installing the oil mist filter³², effects of the chromatography filter³³, tuning and troubleshooting³⁴, and direct infusion³⁵.

Additional maintenance of the Dionex AS-AP autosampler may be required after six months due to cross-contamination and resulting carryover of diquat and paraquat. The following parts should be replaced every six months: AS-AP injection port, transfer line tubing, and buffer loop.

Creating IC-MS methods with emergency shutdown subprograms

Create an IC-MS instrument method using the Chromeleon Instrument Method Wizard and the settings listed in the Conditions section, including the DC.InjectValve_2 valve timing and the SIM table. For IC-only methods, uncheck the mass spectrometer box on the mass spectrometer page. In the instrument configuration, the low-pressure error setting was previously set to “abort”. This error setting is as a result of the DP.Pump_2 pressure falling below the lower pressure (500 psi) will cause the IC system to abort (sequence, methods, flow). Save the instrument method.

Unexpected failures in the suppressor or in the regenerant pump directing water to the suppressor can damage the mass spectrometer. For IC-MS applications, during emergency failures

the diverter valve should be rotated to direct the CD effluent away from the mass spectrometer. In this configuration, the Dionex ICS-6000 Automation Manager the DC.InjectValve_2 valve is in the “Inject” position directing DI water to the mass spectrometer and the suppressor is in the recycle mode.

High conductivity emergency trigger

The high conductivity trigger, using the Chromeleon Conditional Trigger function, implements emergency actions when the total conductivity signal exceeds a high level (50 µS/cm) for a set time (180 s). The action commands for DC.InjectValve_2 to direct water to the mass spectrometer and put the suppressor in recycle mode. The high conductivity could be due to an unexpected suppressor failure. (Note: when the trigger conditions are met, the pump will turn off, which turns off the RFIC consumables and suppressor.) These conditions were selected for the application and can be adjusted to lower or higher conductivity or a different elapsed time, depending on the sample.

To create an emergency trigger:

1. Open the IC-MS program.
2. Open the Script Editor.
3. Insert a Conditional Trigger on the 0.00 Time, Run line.

Name	“HighConductivity”
Condition	CDet.CD_1_total.signal>=50
TrueTime	180
Delay	5
AllowImmediate	Yes

4. Place the cursor on the End Trigger row and Command column. Select *Insert Command*.
5. Enter the command to divert IC flow away from the MS while diverting DI water to the MS and to turn-off the Pump_1 motor.

```
DC.InjValve_2.InjectPosition  
  
Pump_1.Motor    off
```

6. Save the trigger.
7. Save the instrument method.

For more details on creating emergency triggers, see AN73339.¹⁴

Results and discussion

Column selection

The Dionex IonPac CS21-Fast-4 μ m column, a high-capacity weak cation-exchanger, was selected for this application because it is optimized for separation of monovalent and divalent quaternary amine pesticides. The column is functionalized with carboxylic acid groups and composed of DVB macroporous resin beads with 80% cross-linking. As a result, the column has both cation-exchange and reversed-phase properties that allow fast elution of the quaternary amines. The column chemistry creates elution windows for the quaternary amines, resolving the quaternary amines from other cations and from each other. Figure 3 shows a chromatogram of a mixed quaternary amine standard (3.5 mg/L chlormequat and mepiquat, 5.0 mg/L paraquat and diquat) with

Column: Dionex IonPac CG21-Fast-4 μ m, 2 $\times$ 30 mm
Dionex IonPac CS21-Fast-4 μ m, 2 $\times$ 150 mm
Eluent source: Dionex EGC 500 MSA,
Dionex CR-CTC III trap column, HP EG degas kit
MSA gradient: 3 mM (-3 to 0.1 min), 3–6 mM (0.1 to 3.6 min),
6–22 mM (3.6 to 6 min), 22–25 mM (6 to 15 min)
Flow rate: 0.30 mL/min
Inj. volume: 10 μ L
Column temp.: 40 $^{\circ}$ C
Detection 1: Suppressed conductivity, 20 $^{\circ}$ C,
Dionex CDRS 600, 2 mm, 22 mA, external water mode
Detection 2: ISQ EC single quadrupole mass spectrometer
Peaks: 1. Lithium -- mg/L
2. Sodium --
3. Ammonium --
4. Potassium --
5. Chlormequat 3.5
6. Mepiquat 3.5
7. Magnesium --
8. Calcium --
9. Paraquat 5.0
10. Diquat 5.0

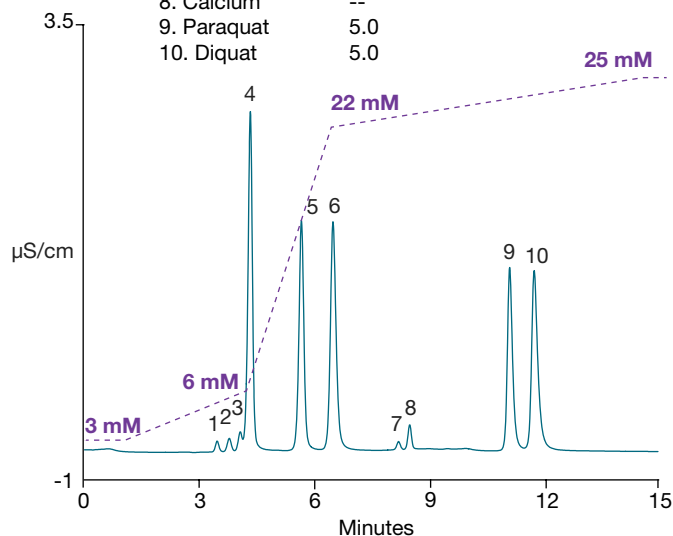


Figure 3. Mixed quaternary amine standard with trace cations using gradient conditions

trace amounts of inorganic cations. The monovalent cations elute first (lithium, sodium, ammonium, potassium) and then chlormequat and mepiquat, followed by the divalent cations (magnesium and calcium), paraquat and diquat. The quaternary amines of interest elute within 15 min.

Method qualification

To qualify the method, experiments using mixed cation and quaternary amine standards were evaluated for MS peak area and retention time reproducibilities. Mixed quaternary amine standards from 10 to 200 μ g/L with 25 μ g/L ISTDs were used to determine the calibration ranges and estimated limits of detection by MS detection (Figure 4).

Column: Dionex IonPac CG21-Fast-4 μ m, 2 $\times$ 30 mm
Dionex IonPac CS21-Fast-4 μ m, 2 $\times$ 150 mm
Eluent source: Dionex EGC 500 MSA,
Dionex CR-CTC III trap column, HP EG degas kit
MSA gradient: 3 mM (-3 to 0.1 min), 3–6 mM (0.1 to 3.6 min),
6–22 mM (3.6 to 6 min), 22–25 mM (6 to 15 min),
3 mM (15 min)
Flow rate: 0.30 mL/min
Inj. volume: 10 μ L
Column temp.: 40 $^{\circ}$ C
Detection 1: Suppressed conductivity, 20 $^{\circ}$ C
Dionex CDRS 600, 2 mm, 22 mA, external water mode
Detection 2: ISQ EC single quadrupole mass spectrometer
Standard: 50 μ g/L standard, 25 μ g/L ISTD
Peaks: 1. Chlormequat
2. Chlormequat-d₉
3. Mepiquat-d₁₆
4. Mepiquat
5. Paraquat
6. Paraquat-d₈
7. Diquat
8. Diquat-d₈

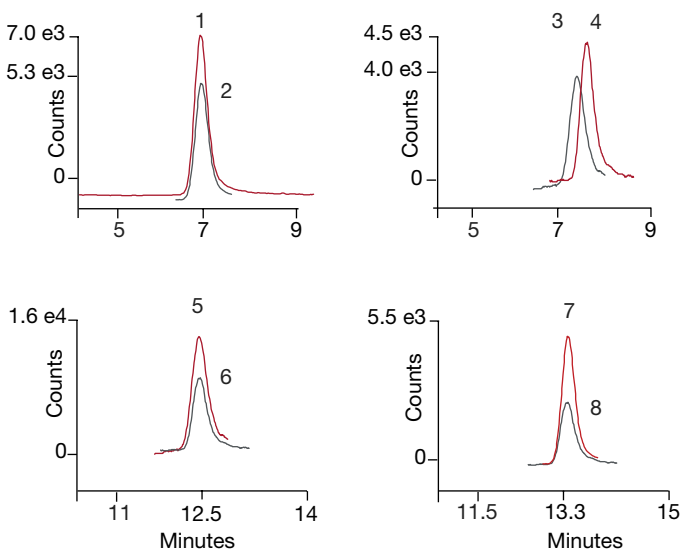


Figure 4. 50 μ g/L standard, 25 μ g/L ISTD

To correct for matrix effects, the ratios of the 25 µg/L target analytes and their isotopically labeled versions were determined (Table 5). These ratios were applied to all measured isotopically labeled internal standards.

To determine the estimated limit of detection (LOD) of the standard at 3× S/N, the average peak height response (S/N, n = 7) was measured in a 1 µg/L or 5 µg/L mixed standard with 25 µg/L ISTD. The estimated LODs (Table 5) ranged from 0.43 µg/L to 3.4 µg/L, with diquat the least sensitive at 3.4 µg/L.

Table 5. Response ratios of the naturally occurring and isotopically labeled analytes at 25 µg/L*

Compound	Response (count-min at 25 µg/L)	Ratio
Chlormequat	1569	0.845
Chlormequat-d ₄	1858	
Mepiquat	1817	1.149
Mepiquat-d ₁₆	1582	
Paraquat	894	0.809
Paraquat-d ₈	1105	
Diquat	192	0.975
Diquat-d ₈	197	

* SANTE 11312/2021 ref 36

To determine the estimated LOD of the sample (mg/kg), the LOD results (standard) were corrected for extraction volume (0.01 L), 5× dilution factor, and sample weight (0.005 kg). Table 6 shows that the sample LODs range from 0.0043 to 0.034 mg/kg of oatmeal cereal and 0.0086 to 0.068 mg/kg of toasted oats cereal.

Samples

The method was applied to 5 g samples of ground oatmeal and toasted oats cereal according to version 12 QuPPE sample preparation method using 1:1 HCl-methanol to quantitatively determine paraquat and diquat or 1:1 formic acid-methanol to quantitatively determine chlormequat and mepiquat. Figures 5a and 6a show the IC chromatograms of both samples extracted with formic acid-methanol. The sample matrix is predominant in the chromatograms; however, chlormequat is detected in the expanded scale. That is, the other quaternary amine pesticides are not detectable by suppressed conductivity in the samples due to the overwhelming amount of sample matrix. As reported in Application Note AN000607,¹⁶ the sample matrix interferes with the MS quantification; therefore a 15-min 1 mM MSA wash was applied at the end of the run (15 min). Figures 5b and 6b show the SIM scans of quaternary amine pesticides in the same samples demonstrating the selectivity of using MS. Trace chlormequat was detected in the formic acid-methanol extract of the toasted oats cereal sample.

Table 6. Summary of mass spectrometer calibration results and estimated limit of detection determinations

	Mass spectrometer calibration			Est. standard LOD			Est. oatmeal* LOD**	Est. standard LOQ***
	Range (µg/L)	Type	Coefficient of determination (r ²)	Standard (µg/L)	RSD* (S/N)	Est. LOD (µg/L)	Est. LOD** (mg/kg)*	Est. LOQ*** (µg/L)
Chlormequat	10 to 200	Quadratic, offset	0.9997	1	5.1 (6.9)	0.43	0.0043	0.79
Mepiquat	10 to 200	Quadratic, offset	0.9996	1	3.4 (5.1)	0.59	0.0059	0.60
Paraquat	10 to 200	Quadratic, offset	0.9996	5	3.9 (8.3)	1.8	0.018	3.9
Diquat	10 to 200	Quadratic, offset	0.9994	5	11.6 (4.4)	3.4	0.034	6.3

* Est LOD = 3× S/N

** Est. oatmeal cereal LOD (mg/kg) = corrected for sample weight, extraction volume, and dilution factor. The estimated LODs for toasted oat cereal are 2× those of oatmeal cereal because the extraction volume was 20 mL.

***LOQ = SANTE method: spiked in standard with 20% RSD

Column: Dionex IonPac CS21-Fast-4 μ m, 2 $\times$ 150 mm
 Eluent source: Dionex EGC 500 MSA, Dionex CR-CTC III trap column, HP EG degas kit
 MSA gradient: 3 mM (-3 to 0.1 min), 3–6 mM (0.1 to 3.6 min), 6–22 mM (3.6 to 6 min), 22–25 mM (6 to 15 min), 3 mM (15 min)
 Flow rate: 0.30 mL/min
 Inj. volume: 10 μ L
 Column temp.: 40 $^{\circ}$ C
 Detection 1: Suppressed conductivity, 20 $^{\circ}$ C, Dionex CDRS 600, 2 mm, 4 mA, recycle mode
 Diverter valve: Divert flow to waste
 Detection 2: Not shown
 Peaks: 1. Matrix -- μ g/L
 2. Matrix --
 3. Chlormequat, 25.0
 Chlormequat-d₉

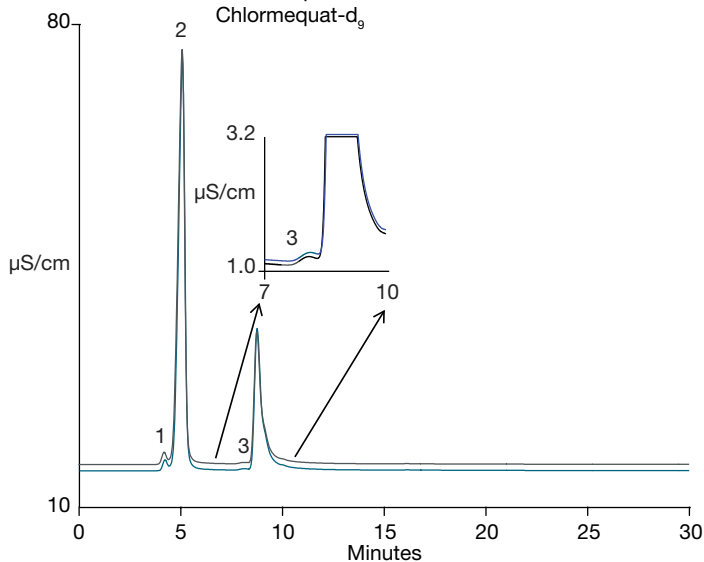


Figure 5a. Formic acid-methanol extract of (A) oatmeal sample and (B) sample A with μ g/L std. Extractant: formic acid-methanol

Column: Dionex IonPac CG21-Fast-4 μ m, 2 $\times$ 30 mm
 Dionex IonPac CS21-Fast-4 μ m, 2 $\times$ 150 mm
 Eluent source: Dionex EGC 500 MSA, Dionex CR-CTC III trap column, HP EG degas kit
 MSA gradient: 3 mM (-3 to 0.1 min), 3–6 mM (0.1 to 3.6 min), 6–22 mM (3.6 to 6 min), 22–25 mM (6 to 15 min), 3 mM (15 min)
 Flow rate: 0.30 mL/min
 Inj. volume: 10 μ L
 Column temp.: 40 $^{\circ}$ C
 Sample prep.: 5 g ground oatmeal cereal, QuPPE method, version 12
 Extract with 20 mL of 1:1 100 mM formic acid-methanol, 80 $^{\circ}$ C, 15 min
 Detection 1: Suppressed conductivity, 20 $^{\circ}$ C, Dionex CDRS 600, 2 mm, 22 mA, external water mode
 Detection 2: ISQ EC single quadrupole mass spectrometer
 A: Sample, B,D: 25 μ g/L ISTD
 C: Sample A + 25 μ g/L

Peaks: 1. Chlormequat -- 26.4 μ g/L (0.264 mg/kg)
 2. Mepiquat-d₁₆ -- --
 3. Mepiquat -- 24.8 (0.248)
 4. Paraquat -- 26.3 (0.263)
 5. Diquat -- 25.1 (0.251)

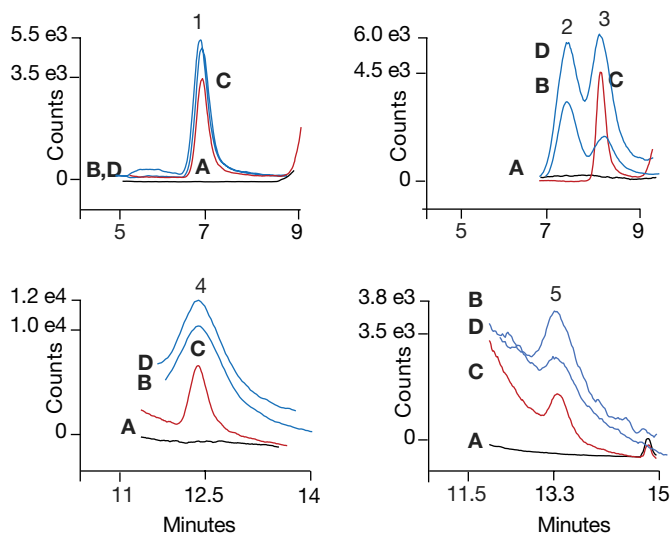


Figure 5b. Extract of (A) oatmeal sample and (C) sample plus 25 μ g/L standard. Extractant: formic acid-methanol

Column: Dionex IonPac CS21-Fast-4 μ m, 2 $\times$ 150 mm
 Eluent source: Dionex EGC 500 MSA,
 Dionex CR-CTC III trap column, HP EG degas kit
 Eluent: 4 mM Methanesulfonic acid (MSA)
 Flow rate: 0.30 mL/min
 Inj. volume: 10 μ L
 Column temp.: 40 $^{\circ}$ C
 Detection 1: Suppressed conductivity,
 20 $^{\circ}$ C, Dionex CDRS 600, 2 mm,
 4 mA, recycle mode
 Diverter valve: Divert flow to waste
 Detection 2: Not shown
 Peaks: 1. Matrix -- μ g/L
 2. Matrix --
 3. Chlormequat, 25.0
 Chlormequat-d₉

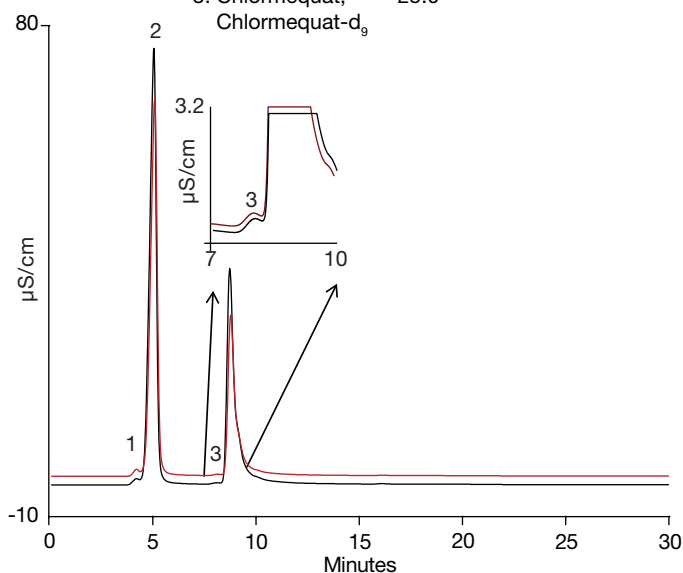


Figure 6a. Formic acid-methanol extract of (A) toasted oats cereal sample and (B) sample A with 25 μ g/L std

Column: Dionex IonPac CG21-Fast-4 μ m, 2 $\times$ 30 mm
 Dionex IonPac CS21-Fast-4 μ m, 2 $\times$ 150 mm
 Eluent source: Dionex EGC 500 MSA,
 Dionex CR-CTC III trap column,
 HP EG degas kit
 MSA gradient: 3 mM (-3 to 0.1 min), 3–6 mM (0.1 to 3.6 min),
 6–22 mM (3.6 to 6 min), 22–25 mM (6 to 15 min),
 3 mM (15 min)
 Flow rate: 0.30 mL/min
 Inj. volume: 10 μ L
 Column temp.: 40 $^{\circ}$ C
 Sample prep.: 5 g ground toasted oat cereal, QuPPE method, version 12.
 Extract with 20 mL of 1:1 100 mM formic acid-methanol,
 80 $^{\circ}$ C, 15 min
 Detection 1: Suppressed conductivity, 20 $^{\circ}$ C, Dionex CDRS 600,
 2 mm, 22 mA, external water mode
 Detection 2: ISQ EC single quadrupole mass spectrometer
 A: Sample, B,D: 25 μ g/L ISTD, C: Sample A + 25 μ g/L

Peaks: 1. Chlormequat 1.0 26.0 μ g/L (0.520 mg/kg)
 2. Mepiquat-d₁₆ -- -- --
 3. Mepiquat -- 26.6 (0.532)
 4. Paraquat -- 20.3 (0.406)
 5. Diquat -- 19.9 (0.398)

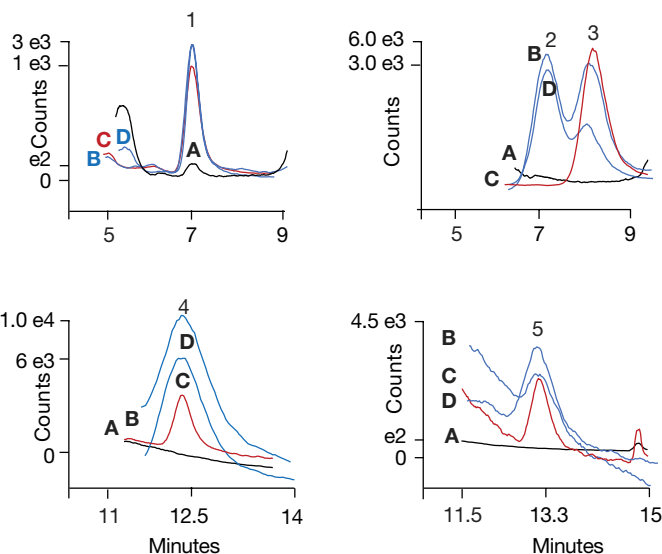


Figure 6b. Extract of (A) toasted oats cereal sample and (C) sample plus 25 μ g/L standard. Extractant: formic acid-methanol

Figures 7 and 8 show similar results in the SIM scans of the samples extracted with HCl-methanol. Trace chlormequat was also detected in the HCl-methanol extract of the toasted oats cereal sample. In contrast, previous analysis using IC-MS/MS (AN000607) reported trace amounts of chlormequat found in oatmeal, <0.001 mg/kg, and trace amounts of paraquat and diquat (0.001–0.002 mg/kg) were found in oatmeal and toasted oats cereal samples.

To determine the accuracy of the method, recoveries were determined from 25 µg/L of added standard (added during

sample preparation). Table 7 summarizes the results, showing good recovery, 80–108%.

The European Union (EU) has established Maximum Reportable Limits (MRLs) for chlormequat salt (15 mg/kg), mepiquat salt (3 mg/kg), paraquat (0.02 mg/kg), and diquat (2 mg/kg) in oat cereals. Chlormequat was previously found in toasted oats cereals at trace concentrations at 2.6 µg/kg and 6.2 µg/kg, as mepiquat chloride extracted with formic acid-methanol and HCl-methanol, respectively.

Column:	Dionex IonPac CG21-Fast-4µm, 2 × 30 mm
	Dionex IonPac CS21-Fast-4µm, 2 × 150 mm
Eluent source:	Dionex EGC 500 MSA, Dionex CR-CTC III trap column, HP EG degas kit
MSA gradient:	3 mM (-3 to 0.1 min), 3–6 mM (0.1 to 3.6 min), 6–22 mM (3.6 to 6 min), 22–25 mM (6 to 15 min), 3 mM (15 min)
Flow rate:	0.30 mL/min
Inj. volume:	10 µL
Column temp.:	40 °C
Sample prep.:	5 g ground oatmeal cereal, QuPPE method, version 12. Extract with 20 mL of 1:1 100 mM formic acid-methanol, 80 °C, 15 min
Detection 1:	Suppressed conductivity, 20 °C, Dionex CDRS 600, 2 mm, 22 mA, external water mode
Detection 2:	ISQ EC single quadrupole mass spectrometer, SIM
	A: Sample, B,D: 25 µg/L ISTD, C: Sample A + 25 µg/L
Peaks:	
1. Chlormequat	-- 25.3 µg/L (0.253 mg/kg)
2. Mepiquat-d ₁₆	-- --
3. Mepiquat	-- 26.0 (0.260)
4. Paraquat	-- 26.2 (0.262)
5. Diquat	-- 27.1 (0.271)

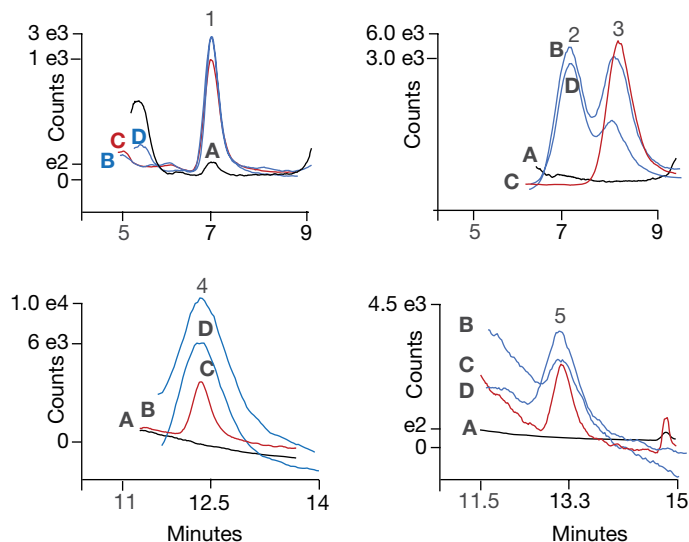


Figure 7. Extract of (A) oatmeal sample and (C) sample plus 25 µg/L standard. Extractant: HCl-methanol

Column:	Dionex IonPac CG21-Fast-4µm, 2 × 30 mm
	Dionex IonPac CS21-Fast-4µm, 2 × 150 mm
Eluent source:	Dionex EGC 500 MSA, Dionex CR-CTC III trap column, HP EG degas kit
MSA gradient:	3 mM (-3 to 0.1 min), 3–6 mM (0.1 to 3.6 min), 6–22 mM (3.6 to 6 min), 22–25 mM (6 to 15 min), 3 mM (15 min)
Flow rate:	0.30 mL/min
Inj. volume:	10 µL
Column temp.:	40 °C
Sample prep.:	5 g ground toasted oat cereal, QuPPE method, version 12. Extract with 20 mL of 1:1 100 mM formic acid-methanol, 80 °C, 15 min
Detection 1:	Suppressed conductivity, 20 °C, Dionex CDRS 600, 2 mm, 22 mA, external water mode
Detection 2:	ISQ EC single quadrupole mass spectrometer
	A: Sample, B,D: 25 µg/L ISTD, C: Sample A + 25 µg/L
Peaks:	
1. Chlormequat	1.2 25.5 µg/L (0.510 mg/kg)
2. Mepiquat-d ₁₆	-- --
3. Mepiquat	-- 26.0 (0.520)
4. Paraquat	-- 26.2 (0.524)
5. Diquat	-- 26.4 (0.528)

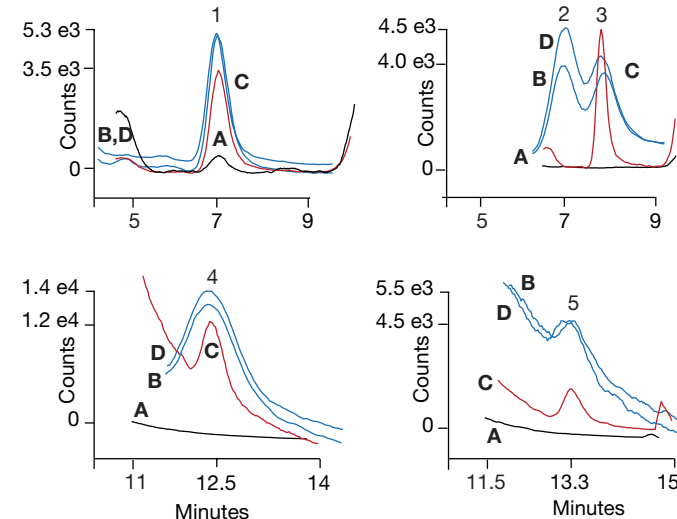


Figure 8. Extract of (A) toasted oats cereal sample and (C) sample plus 25 µg/L standard. Extractant: HCl-methanol

Table 7. Summary of the recovery experiments

	Chlormequat			Mepiquat			Paraquat			Diquat		
	Found (µg/L)	Recovered (µg/L)	(%)	Found (µg/L)	Recovered (µg/L)	(%)	Found (µg/L)	Recovered (µg/L)	(%)	Found (µg/L)	Recovered (µg/L)	(%)
Oatmeal												
Formic acid-methanol	N.D.	26.4 ± 1.4	106	N.D.	24.8 ± 1.3	99	N.D.	26.3 ± 0.43	105	N.D.	25.1 ± 1.0	100
HCl-methanol	N.D.	25.3 ± 0.89	101	N.D.	26.0 ± 0.28	104	N.D.	26.2 ± 0.42	105	N.D.	27.1 ± 0.87	108
Toasted oats cereal												
Formic acid-methanol	1.0	26.0 ± 0.87	100	N.D.	26.6 ± 0.36	95	N.D.	20.3 ± 0.47	80	N.D.	19.9 ± 0.89	81
HCl-methanol	1.2	25.5 ± 1.2	97.3	N.D.	26.0 ± 0.34	104	N.D.	26.2 ± 0.40	105	N.D.	26.4 ± 1.2	106

* N.D.: not detected

Conclusion

This application note demonstrated the determination of quaternary amine pesticides in oat cereal samples by IC with suppressed conductivity and mass spectrometry detections. The method is accurate as indicated by the recoveries (81–106%) and sensitive as indicated by the LODs (0.0043 to 0.068 mg/kg). This method is recommended for screening of cationic polar pesticide contamination of >0.016 mg/kg. To determine lower analyte concentrations and to have greater confidence in analyte identification, use the IC-MS/MS method reported in AN000607.

IC and IC-MS applications, including this application can be found in Thermo Fisher Scientific AppsLab digital library.³⁷

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