Advanced Mass Spectrometric Techniques for DOD analytes of interest

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Non-standard MS techniques

- HPLC/MS/MS
- IC/MS/MS
- GC/MS/MS
- Electrospray ionisation
- Atmospheric Pressure Chemical Ionization
- Chemical Ionization
- High Resolution Mass Spectrometry
Electron Impact GC/MS

➢ Advantages
  ▪ Powerful separation
  ▪ Structural information from fragmentation
  ▪ Affordable instrumentation
  ▪ Universal detector (if the analyte gets to the MS)

➢ Disadvantages
  ▪ Most organic compounds will not go through a gas chromatograph
  ▪ Some compounds fragment too much
  ▪ No selectivity
Desirable method characteristics

- **Linearity**: predictable instrument response
- **Sensitivity**: low concentration reliably detected
- **Precision**: reproducibility of results
- **Accuracy**: proximity of results to true value
- **Selectivity**: ability to differentiate compound of interest from interferences
- **Ruggedness**: ability of method to work properly in a variety of types of samples
Standard method is 8330 HPLC/UV

- Insufficient
  - Sensitivity
  - Selectivity
  - Ruggedness

Solution

- LC/MS
- Extraction – similar to 8330 – 2g sonicated in acetonitrile for soil, SPE of 1L water eluted with acetonitrile to 5 mL final volume.
Analysis

- LC- 250 mm C18 column, mobile phase 0.01M ammonium acetate in water and methanol mixture

- MS- APCI negative ion polarity – single stage MS detection of characteristic mass

- 3 isotopic labeled internal standards and one surrogate used for QC compounds

- Calibration – 10 to 300 ug/L instrument concentration
<table>
<thead>
<tr>
<th>Analyte</th>
<th>LC/UV MDL</th>
<th>LC/MS MDL</th>
<th>Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,3,5-Trinitrobenzene</td>
<td>0.037</td>
<td>0.015</td>
<td>2</td>
</tr>
<tr>
<td>1,3-Dinitrobenzene</td>
<td>0.065</td>
<td>0.008</td>
<td>8</td>
</tr>
<tr>
<td>2,4,6-Trinitrotoluene</td>
<td>0.047</td>
<td>0.015</td>
<td>3</td>
</tr>
<tr>
<td>2,4-Dinitrotoluene</td>
<td>0.068</td>
<td>0.013</td>
<td>5</td>
</tr>
<tr>
<td>2,6-Dinitrotoluene</td>
<td>0.075</td>
<td>0.013</td>
<td>6</td>
</tr>
<tr>
<td>2-Amino-4,6-dinitrotoluene</td>
<td>0.058</td>
<td>0.012</td>
<td>5</td>
</tr>
<tr>
<td>2-Nitrotoluene</td>
<td>0.065</td>
<td>0.022</td>
<td>3</td>
</tr>
<tr>
<td>3-Nitrotoluene</td>
<td>0.034</td>
<td>0.016</td>
<td>2</td>
</tr>
<tr>
<td>4-Amino-2,6-dinitrotoluene</td>
<td>0.028</td>
<td>0.015</td>
<td>2</td>
</tr>
<tr>
<td>4-Nitrotoluene</td>
<td>0.042</td>
<td>0.014</td>
<td>3</td>
</tr>
<tr>
<td>HMX</td>
<td>0.068</td>
<td>0.015</td>
<td>4</td>
</tr>
<tr>
<td>Nitrobenzene</td>
<td>0.096</td>
<td>0.020</td>
<td>5</td>
</tr>
<tr>
<td>Nitroglycerin</td>
<td>0.374</td>
<td>0.039</td>
<td>10</td>
</tr>
<tr>
<td>PETN</td>
<td>0.529</td>
<td>0.016</td>
<td>33</td>
</tr>
<tr>
<td>RDX</td>
<td>0.098</td>
<td>0.006</td>
<td>18</td>
</tr>
<tr>
<td>Tetryl</td>
<td>0.084</td>
<td>0.010</td>
<td>9</td>
</tr>
</tbody>
</table>
Groundwater containing 10 mg/L JP4

HPLC/UV

Expected RT RDX

LC/MS
0.05 ug/L RDX
Perfluorooctanoic acid, PFOA

- Used in the manufacture of fluoropolymers – non-stick cookware, water and stain resistant finishes, fire resistant finishes
- Persistent in the environment
- Related compounds, Perfluorooctyl sulfonate (PFOS) and perfluorooctanesulfonic acid (PFOSA) can be analyzed using the same method
Extraction
- Aqueous – SPE extraction using C18 cartridge
- Solids - 10g sonicated with methanol

LC – 250 mm C18 column, aqueous formic acid and methanol mobile phase

MS – ESI negative ion MS/MS detection

C13 labeled PFOA used as an internal standard and PFNA (closely related cmpd) used for a surrogate

Calibration - 1 to 50 ug/L instrument concentration
Compound: APFO
Coefficient of Determination: 0.998740
Calibration curve: 0.107086 * x + 0.0231085
(Response type: Internal Std (Ref 1), Area * (IS Conc. / IS Area))
Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None
PFOA low std
Perchlorate

- Extraction – soils tumbled with DI water, waters are analyzed directly
- IC Analysis
  - IC – AG16/AS16 column, using an eluant generator producing a potassium hydroxide mobile phase, a suppressor system and time actuated valves for sample diversion during the analysis
- MS – ESI negative ion MS/MS detection, heavy chlorine isotope monitored for confirmation
- O18 labeled perchlorate internal standard
- Calibration – 10 – 500 ng/L
ESI Ionization Suppression (without IS correction)

Note: 1,000 MCT = 1,000 mg/L each chloride, sulfate, bicarbonate
De-ionized water > 18 Megohm-cm

To which was added:

- Chloride (NaCl) = 5,000 mg/L
- Sulfate (Na₂SO₄) = 5,000 mg/L
- Bicarbonate (KHCO₃) = 5,000 mg/L

Total dissolved solids = 22,600 mg/L
Blank : 3 replicates of high TDS water
0.01 ug/L: 4 replicates in high TDS water
0.25 ug/L: 4 replicates in high TDS water
0.50 ug/L: 4 replicates in high TDS water

Notes:
- 1.0 ug/L O-18 perchlorate added to each
- Entire series prepared & analyzed on 3 days
IC/MS/MS Calibration

<table>
<thead>
<tr>
<th>Level</th>
<th>(ug/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.005</td>
</tr>
<tr>
<td>2</td>
<td>0.01</td>
</tr>
<tr>
<td>3</td>
<td>0.02</td>
</tr>
<tr>
<td>4</td>
<td>0.05</td>
</tr>
<tr>
<td>5</td>
<td>0.10</td>
</tr>
<tr>
<td>6</td>
<td>0.20</td>
</tr>
<tr>
<td>7</td>
<td>0.50</td>
</tr>
<tr>
<td>8</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Each day of analysis:

\[
r = 0.9998_{\text{day 1}}, \ 0.9999_{\text{day 2}}, \ 0.9983_{\text{day 3}}
\]
Compound 1 name: Perchlorate
Coefficient of Determination: 0.996726
Calibration curve: 0.00404910 * x = 0.010066
Response type: Internal Std (Ref 2), Area * (IS Conc. / IS Area)
Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axes trans: None

Response

Conc

Analyser: Stunn Celling
0.01 ug/L Perchlorate Calibration Standard

True RT = 10.5 + 3.4 = 13.9 min.

← 85 ion
1,074 area counts

← 83 ion
2,669 area counts
After running high TDS samples for hours:

True RT = 10.5 + 3.5 = 14.0 min.
Perchlorate contamination in all samples at 0.06 - 0.08 ug/L

Contamination control proved to be more challenging at ppt levels

Previously confirmed perchlorate in some lab detergents at low mg/kg levels

This time traced to vinyl lab gloves
Day 2 & Day 3:

<table>
<thead>
<tr>
<th>Test No.*</th>
<th>True Value (ug/L)</th>
<th>Recovery (%)</th>
<th>RSD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.01</td>
<td>116.8</td>
<td>14.9</td>
</tr>
<tr>
<td>2</td>
<td>0.25</td>
<td>99.2</td>
<td>2.71</td>
</tr>
<tr>
<td>3</td>
<td>0.5</td>
<td>93.6</td>
<td>2.84</td>
</tr>
</tbody>
</table>

- Spikes prepared in water with 22,600 mg/L TDS
- No pretreatment
- 8 replicates tested per concentration, 4 on each of 2 days
- O-18 labeled perchlorate used as internal standard
N-Nitrosodimethylamine, NDMA

- GC/Cl/MS/MS positive ion analysis
  - CI gas – ammonia

- Extraction – CLLE of 1L water with CH$_2$Cl$_2$, concentration to 1.0 ml final volume

- 624 type capillary column with helium carrier gas

- Cryogenic cool on-column injection

- NDMA-d6 used for an isotope dilution standard

- Concentration – 1.0 to 100 ug/L instrument concentration
Sample ID: 1.0 ppb std  
Instrument ID: Varian MS #1  
Measurement Type: Area  
Acquisition Date: 3/2/2004 3:43 PM  
Calculation Date: 3/2/2004 12:55 PM  
Sample Type: Calibration  
Inj. Sample Notes: None  

Operator: nd  
Last Calibration: 3/2/2004 12:56 PM  
Calibration Type: Internal Standard  
Data File: ...\04ind34c0001.xms  
Method: ...\01 initial split.mth  

**Compound Information**

- **Peak Name:** NDMA Adduct  
- **Result Index:** 3  
- **Compound Number:** 3  
- **CAS Number:** None  
- **Identified**

**Identification**

- **Parameter:** Specification  
- **Search Type:** Spectrum  
- **Retention Time:** 15,050 +/- 0.100  
- **Match Result:** N-R >= 700  
- **Status:** Pass  

**Integration and Quantitation**

- **Parameter:** Specification  
- **Quant ms:** 75.0  
- **IS Peak Name:** NDMA-Int  
- **Calibration Equation:** Linear, Include, 1/X  
  - **Area:** >= 100  
  - **Weight:** 8.029m+6  
  - **Amount (RRF):** 3.705  
- **Match Types:** N-R: Normal-Reversed

**MCHTDA:** Quan Instr. 75.0 Merged nd34c0001.xms 1280 CENTROID FILTERED
More than just Dioxins!
How a High Resolution Mass Spectrometer Works

- Target analytes are fragmented in the ion source of a triple-sector instrument

- Ion fragments are selected by energy-dependent trajectory in first electrostatic field (ESA1)

- Exact mass fragments selected by mass-dependent trajectory in magnetic field (Magnet)

- Residual interferences filtered and removed in ESA2

- Exact mass fragments are detected at the photomultiplier with sensitivity at low femtogram levels (on column)
A target analyte’s **exact mass is highly characteristic** of its identity.

Mass resolution measures the ability of the instrument to isolate and detect a particular exact mass.

Triple sector instruments operate at **mass resolution of ~10,000** (high) vs ~100 (low) for quadrupole instruments.

High Res analyses are nominally **100 times better at filtering interferences** than conventional Low Res analysis.

High Res analyses offer **improved sensitivity, selectivity, and ruggedness**.
NDMA
Exact Mass - 74.0480

d$_6$-NDMA
Exact Mass - 80.0857
Brominated Flame Retardant Low Standard (20 pg/L)

**BDE-99**
- Exact Mass - 563.6216

**BDE-99**
- Exact Mass - 565.6196

**$^{13}C_{12}$ - BDE-99**
- Exact Mass - 575.6619

**$^{13}C_{12}$ - BDE-99**
- Exact Mass - 577.6598
Calibration Curve for Low Level Organics by HRMS

- BDE-99
  - Exact Mass: 563.6216
  - Exact Mass: 565.6196
- 13C12 - BDE-99
  - Exact Mass: 575.6619
  - Exact Mass: 577.6598

**Graph:**
- Relative Response vs. Concentration (pg/μL)
- Y-axis: Relative Response
- X-axis: Concentration (pg/μL)
- Lines for NDMA, 1,4-Dioxane, and 1,2,3-Trichloropropane
- NDMA: Black line
- 1,4-Dioxane: Purple line
- 1,2,3-Trichloropropane: Yellow line

Concentration ranges:
- 0 to 1000 pg/μL

Y-axis values:
- 0 to 12

X-axis values:
- 0 to 1000
Conclusions

- Electron impact GC/MS works for many analytes, but not for everything

- LC/MS, LC/MS/MS, IC/MS/MS and CI-GC/MS/MS and High Resolution MS can provide definitive data

- MS/MS is very desirable when soft ionization techniques are used

- Ionization suppression is a concern in LC/MS, and isotopically labeled internal standards are the best solution

- When a lab claims a low detection limit, check the signal to noise!
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- Electron impact GC/MS works for many analytes, but not for everything
- LC/MS, LC/MS/MS, IC/MS/MS, CI-GC/MS/MS and High Resolution MS can provide definitive data
- MS/MS is very desirable when soft ionization techniques are used
- Ionization suppression is a concern in LC/MS, and isotopically labeled internal standards are the best solution
- When a lab claims a low detection limit, check the signal to noise ratio

Acknowledgments

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STL Sacramento

Further Information

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