Effect of Sample Introduction on ICP-MS Detection of Nonmetal Analytes in a Simulated HPLC Matrix

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Overview

- With the increase in heteronatom moieties (P, S, Cl, F, for example) in pharmaceutical compounds and impurities, the detection and quantification of nonmetals has become increasingly important to the pharmaceutical industry.
- Demand for heteronatom detection in the pharmaceutical industry is a function of the high sensitivity and genotoxic impurity requirements for the manufacturing of pharmaceutical compounds.
- An argon inductively coupled plasma (ICP) is a versatile, robust, and nearly structurally independent source that can be applied to the detection of heteronatom moieties in pharmaceutical compounds.
- Solutions containing the active pharmaceutical ingredient phosphomycin in one of these buffers common LC buffers; ammonium acetate, ammonium hydroxide, and formic acid, are used to monitor phosphorus.

1. Experimental Setup

The experimental setup for all experiments is diagrammed below:

ICP-MS operating parameters are listed below in Table 1:

<table>
<thead>
<tr>
<th>CPM-MS Parameters</th>
<th>Setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nebulizer Power (W)</td>
<td>475</td>
</tr>
<tr>
<td>Auxiliary Gas Flow Rate (L/min)</td>
<td>0.8</td>
</tr>
<tr>
<td>Carrier Gas Flow Rate (L/min)</td>
<td>1.0</td>
</tr>
<tr>
<td>Deoxidizer Counter Gas Flow Rate (L/min)</td>
<td>2.4</td>
</tr>
</tbody>
</table>

2. Methods and Materials

Materials:
- Phosphorus containing solutions were continuously nebulized and phosphorus was monitored at m/z=31
- All solutions were 80:20 (v/v%) methanol:water and contained one of three buffers.
  1. 0.1% (v/v%) Ammonium Hydroxide
  2. 10% Ammonium Acetate
  3. 0.1% (v/v%) Formic Acid
- Qg (nebulizer gas flow rate) varied by Ar(g) calibrated mass flow controller
- All solutions were 80:20 (v/v%) methanol:water and contained one of three buffers.
  1. 0.1% (v/v%) Ammonium Hydroxide
  2. 10% Ammonium Acetate
  3. 0.1% (v/v%) Formic Acid

Methods:
- Qg (L/min) Qg (L/min) Qg (L/min)
- Ql (mL/min) Ql (mL/min) Ql (mL/min)
- Signal To Background Ratio
- Signal To Noise Ratio
- Detection Limit (ppb)

3. Results for U500AT

- See section 12 for a graphical representation of the data

4. U500AT Discussion

- Best detection occurs at higher values of Qg and Ql
- Can easily nebulize entire range of Qg values tested
- Droplets formed such that residence time affects overall detection limit at most by one order of magnitude
- Large range of Qg and Ql (1.0 subscript and test) work well for optimal detection with this nebulizer
- RSD% of all signals higher than other nebulizers:
  - May be poor for maintaining peak shape post UV detection
  - See table comparing signal RSD% of all nebulizers in section 11
- Performance profile (surface plot) seen in section 12 is similar in shape to other high efficiency nebulizers such as HEN90A and HEN90A:
  - High signal to background ratio and size distribution
  - Efficiently nebulizes with only a small range of Qg and Ql values tested
  - May pose a problem

5. Results for TR30-C1

- See section 13 for a graphical representation of the data

6. TR30-C1 Discussion

- Best detection occurs at moderate and lower values of Qg and Ql
- Efficiency improves and cover a small range of Qg values tested
- All lower Qg there is an increase in the ratio of gas kinetic energy to liquid mass ratio
- Droplets formed such that residence time affects overall detection limit at most by a factor of 3
- RSD% of all signals higher than HEN90A but lower than USN
- Likely less problematic than USN for maintaining peak shape post UV detection
- See table comparing signal RSD% of all nebulizers in section 11
- Performance profile (surface plot) seen in section 13 is similar in shape to other high efficiency nebulizers such as HEN90A and USN:
  - Likely a result of similar droplet size and size distribution
  - Performance makes nebulizer attractive for coupling to HPLC

7. Results for HEN170A

- See section 14 for a graphical representation of the data

8. HEN170A Discussion

- Best detection occurs at higher values of Qg and Ql
- Can easily nebulize entire range of Qg values tested
- Droplets formed such that residence time affects overall detection limit at most by a factor of 3
- Large range of Qg and Ql work well for optimal detection with this nebulizer
- RSD% of all signals lower than USN or C30
- May be poor for maintaining peak shape post UV detection
- See table comparing signal RSD% of all nebulizers in section 11
- Performance profile (surface plot) seen in section 12 is similar in shape to other high efficiency nebulizers such as HEN90A and USN:
  - May be good for maintaining peak shape post UV detection
  - Performance makes nebulizer attractive for coupling to HPLC
  - Performance equivalent or better than C30 with ~10X less sample

9. Results for HEN90A

- See section 15 for a graphical representation of the data

10. HEN90A Discussion

- Best detection occurs at higher values of Qg and Ql
- Can easily nebulize entire range of Qg values tested
- Droplets formed such that residence time affects overall detection limit at most by a factor of 3
- Large range of Qg and Ql work well for optimal detection with this nebulizer
- RSD% of all signals lower than USN or C30
- May be good for maintaining peak shape post UV detection
- See table comparing signal RSD% of all nebulizers in section 11
- Performance profile (surface plot) seen in section 12 is similar in shape to other high efficiency nebulizers such as HEN90A and USN:
  - Likely a result of similar droplet size and size distribution
  - Performance makes nebulizer attractive for coupling to HPLC
  - Performance equivalent or better than C30 with ~10X less sample

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We gratefully acknowledge the NIU Department of Chemistry and Biochemistry and NIU Graduate School. Special thanks to members of NIU technical staff. [Meinhard We gratefully acknowledge the NIU Department of Chemistry and Biochemistry and NIU Graduate School. Special thanks to members of NIU technical staff. (Meinhard]