

## B46924 pharm-analyt excursion into anorganic chemistry analytics

At a user meeting in Vienna earlier this year, I saw the Trinity P1 column and fell in love with it. It promised to open up the field of analysis of very small organic and inorganic compounds with polar or ionic properties. And indeed, the column has delivered on (most of) that promise.

In order to use charged aerosol detection (CAD) and compare it to both ELSD and Orbitrap XL detection (2008 system), only a volatile mobile phase (ammonium acetate) was used. Both acetonitrile and methanol were used as organic modifiers, but the baseline for the latter was quite poor with CAD, so methanol was omitted further on. Gradient elution was used by increasing the buffer concentration only, not the organic modifier concentration as usual. For CAD and ELSD detection, only aqueous solutions were considered and LLOQs determined from these, as selectivity from a complex matrix such as plasma would not be sufficient for these two detectors. For Orbitrap detection, plasma samples were also examined to get a feel for both selectivity and recovery. In general, CAD detection was more sensitive than ELSD detection by a factor of 3-5 for most of the compounds analysed.

### **Anions determined successfully:**

Halogens such as chloride, bromide and iodide: LLOQ in the low  $\mu\text{M}$  range with CAD; for chloride, only the ion trap MS mode can be used on the Orbitrap XL (molecular weight of analyte < 50 amu), hence no improvement in LLOQ; for bromide and iodide, selective detection even in the upper nM range could be achieved (also from plasma).

Nitric acid and perchloric acid: determination in the high nM range possible with CAD, sensitivity improved about 5-fold with Orbitrap (and selective determination with XIC with high mass accuracy from plasma).

Nitrous acid: difficult to determine with CAD, LLOQ with Orbitrap also only in the low  $\mu\text{M}$  range, as ion trap MS mode can only be used on the Orbitrap XL (molecular weight of analyte < 50 amu).

Sulphuric acid: determination in the low  $\mu\text{M}$  range possible with CAD, sensitivity greatly improved with Orbitrap to achieve LLOQ in the high nM range (and selective determination with XIC with high mass accuracy from plasma). However, the HPLC part of the system was not "clean" enough. Selective determination from plasma is possible with Orbitrap.

Phosphoric acid: Determination in the low  $\mu\text{M}$  range possible with CAD, selective determination in the very low  $\mu\text{M}$  range possible with Orbitrap from plasma (XIC with high mass accuracy). High concentrations in some animal plasma matrices.

As small organic acid: Citric acid: determination in the low  $\mu\text{M}$  range with CAD, determination in the mid nM range with Orbitrap (and selective with XIC from plasma with high mass accuracy).

Trichloroacetic acid and methanesulfonic acid: determination in the low  $\mu\text{M}$  range with CAD, selective determination in the high nM range with Orbitrap from plasma (XIC with high mass accuracy).

### **Cations determined successfully:**

Alkaline metal ions such as lithium, sodium, potassium and cesium: LLOQ in the high nM range with CAD; for Lithium no MS data could be generated (7 amu), for sodium and potassium the ion trap MS mode can only be used on the Orbitrap XL (molecular weight of analytes < 50 amu), hence no improvement in LLOQ, but selective determination from plasma seems possible, however MS transmission for sodium is still quite poor (23 amu) compared to potassium (39 amu); for caesium, selective detection even in the upper nM range could be achieved (also from plasma).

Alkaline earth metals such as magnesium, calcium and barium: chromatography is more difficult than for the previously mentioned compounds/ions; magnesium works best, calcium somehow shows relatively wide peaks and high blanks even from the HPLC/detection systems; and barium elutes as a wide peak (for both pH values tested at pH 4.0 and 5.8). Determination in the low  $\mu\text{M}$  range is possible with CAD for Mg, medium  $\mu\text{M}$  range for both, Ca and Ba; for Mg the ion trap MS mode can only be used on the Orbitrap XL (molecular weight of analytes < 50 amu) with rather poor transmission (24 amu), hence no improvement in LLOQ, but selective determination from plasma seems possible. Selective determination in the high nM range is possible with Orbitrap for Ba, but extraction efficiency from plasma (XIC with high mass accuracy) was poor.

Manganese, silver, cobalt, zinc, iron(II), cerium: determination in the low  $\mu\text{M}$  range possible with CAD, selective determination in the high nM range theoretically possible with Orbitrap from plasma (XIC with high mass accuracy). However, for most of them the recovery from plasma was somehow poor, although the selectivity would be very good; it may be that recovery at native plasma levels is sufficient, which was not investigated in detail. The recovery of iron (II) from plasma seemed to be quite good; iron (III) was detectable with CAD detection at a very late retention time, but could not be detected with the Orbitrap.