

Simultaneous Measurement of an Anion and Cation

Quantitative analysis of ions is an important aspect of pharmaceutical development and manufacturing QC. This includes pharmaceutical salt selection, confirmation of stoichiometry, and detection of impurities and process contaminants. Since many of these analytes are highly polar and are weak chromophores, a common approach for their measurement is ion-exchange chromatography with conductivity detection. The ability to measure anions and cations simultaneously can greatly simplify these analyses, reduce sample usage and improve throughput.

This application note describes the use of a standard HPLC system with the Corona[®] charged aerosol detector (CAD[®]), for the simultaneous measurement of sodium and chloride ions. These ions were first separated using a zwitterionic stationary phase operated in hydrophilic interaction chromatography (HILIC) mode (see Risley and Pack, (2006) LCGC, 24, 776-785) prior to detection by the Corona CAD.

This is an extremely versatile, sensitive and reliable approach for the determination of counter ions.

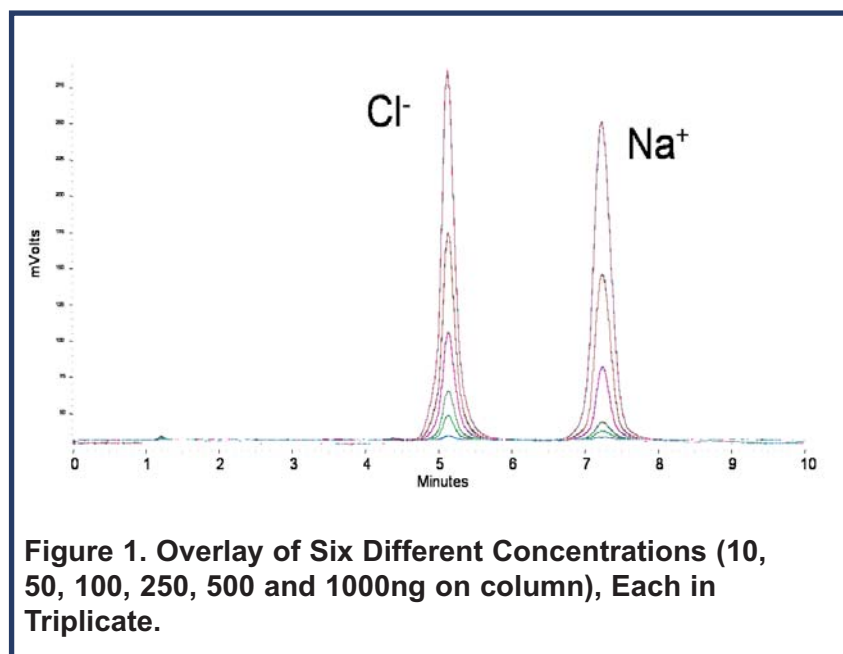


Figure 1. Overlay of Six Different Concentrations (10, 50, 100, 250, 500 and 1000ng on column), Each in Triplicate.

Method Parameters

| | |
|-------------------|--|
| Column: | Sequant ZIC [®] -pHILIC; 4.6 x 150mm, 5 μ m |
| Column Temp: | 30 $^{\circ}$ C |
| Mobile Phase: | 75:25 acetonitrile/100mM ammonium acetate (pH 7.00) |
| Flow Rate: | 1.0mL/min |
| Injection Volume: | 10 μ L |
| Run Time: | 10mins |
| Corona: | 100pA range, no filter |
| Sample Vial: | Polypropylene or certified borosilicate |

Sample Preparation

Chloride (ammonium chloride) and sodium (sodium acetate) ions were prepared in mobile phase. All dilutions were in mobile phase.

The Corona[®] Charged Aerosol Detector

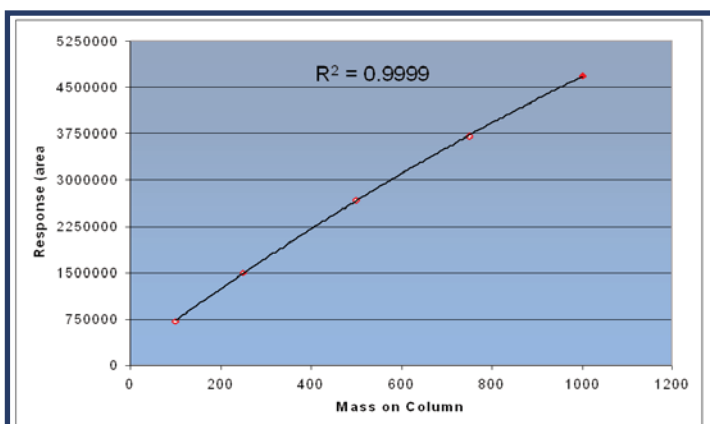


Figure 2A. Chloride Standardization Curve (ng).

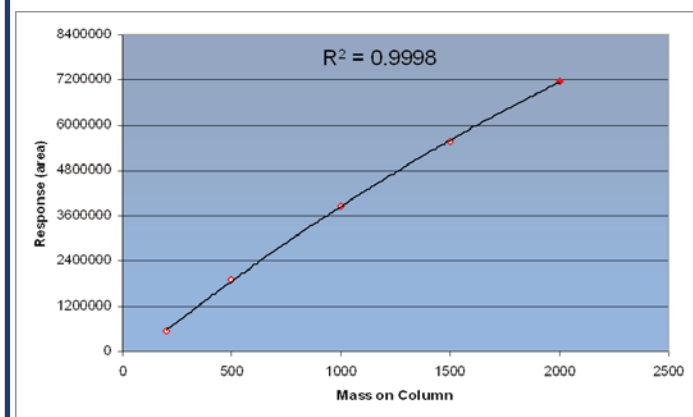


Figure 2B. Sodium Standardization Curve (ng).

Results and Discussion

Sodium and chloride ions were separated in under eight minutes (Figure 1) and showed good linearity (Figure 2A and 2B). The precision (%RSDs) for sodium and chloride were 0.64 and 0.32 (1000ng on column), respectively, and 2.66 and 1.77 (100ng on column), respectively.

Method precision (defined as the reproducibility of 5 measurements at 5 different concentration levels, each standard set run twice a day for three days): Intra-day: %RSD was <3.0% for both analytes. Inter-day: %RSD was <5.0% for both analytes. The limit of detection was <20ng (on column) for both ions.

HILIC-CAD is an extremely versatile approach to the simultaneous measurement of anions and cations in pharmaceutical preparations. This technique uses standard, readily-available HPLC equipment. In addition, the HILIC-CAD combination reproducibly detects anions and cations at nanogram limits of detection.

Product Information

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|---|-----------|
| Corona Charged Aerosol Detector | 70-6350 |
| Thermal Organizer Module | 70-5499TA |
| Corona <i>ultra</i> [™] Detector | 70-8773 |
| Nitrogen Generator | 70-6003 |



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