A Comparative Study of ESI, Nano ESI, and HPLC-Chip/MS Ion Sources for Optimum Sensitivity and Sample Throughput

Craig Love1, Uwe Effelsberg2 and Alex Mordehai1, Agilent Technologies, Inc. 1Santa Clara, CA and 2Waldbronn, Germany

Introduction
Non-flow techniques generally offer excellent chromatographic resolution with high sensitivity, but problems with clogging have limited their use for high throughput analysis. With the introduction of microfluidic LC chips, many of the robustness issues with conventional nanoelectrospray (nanoES) sources have been overcome. In this study we compare the ionization efficiencies of an HPLC-Chip/MS interface vs. conventional nanoES and pneumatically assisted electrospray (ES) sources using a variety of samples.

Experimental

ES Source: The Agilent G1982A nanospray ion source uses a grounded, orthogonal pneumatic nebulizer with an 0.12 mm (120 µM) I.D. needle. Variable nebulizer pressure from 0 to 68 psi allows effective nebulization at LC flow rates from 0.1 to 1.0 µL/min (Figure 2).

NanoES Source: The Agilent G1982A nanospray ion source uses a grounded, orthogonal emitter which can be fitted with PicoTips (New Objective, Inc) with I.D. ranging from 5 to 30 µM. For this investigation, a distal coated PicoTip with an I.D. of 15 µm was used (Figure 3).

HPLC-Chip/MS Source: The Agilent HPLC-Chip/MS interface uses a polystyrene microchip with an integral 15 µm I.D. emitter. The HPLC-Chip includes a metal cartridge that simplifies handling includes an RF tag for identification (Figure 4). For this investigation, a G4240-61002 infusion chip was used.

Results and Discussion

The performance of the ES source was used as the reference for the nanoES source and HPLC-Chip/MS interface. In order to compare the results of this study graphically, the extracted ion response of the nanoES source and the HPLC-Chip/MS interface were both normalized to the ES source response at 100 µL/min.

NanoES Source: The nanoES source showed significantly lower response vs the ES source for all masses at flow rates above 200 nL/min. Below 200 nL/min, the response for higher molecular weight ions increased dramatically, reaching 90% of the normalized API-ES source response at 100 µL/min, while the response of the lower molecular weight ions remained relatively constant throughout the investigated flow range.

HPLC-Chip/MS Interface: In contrast to the nanoES source, the response of the HPLC-Chip/MS did not show significant ion selectivity throughout the investigated flow range. The relative ion response track quite closely with the reference ES source for singly charged ions. The overall ion response was also better than the nanoES source and was comparable to the reference ES source from 117 to 500 nL/min.

Conclusions

• The HPLC-Chip/MS interface provided good sensitivity for small molecule ions without the ion suppression effects of conventional nanoES.

• The HPLC-Chip/MS interface exhibited superior response across a much broader flow range than conventional nanoES. With chromatographic applications that allows shorter run times and greater sample throughput.

• The HPLC-Chip/MS interface also provided greater ease-of-use, yielding consistent response without the extensive optimization required for nanoES.

These results are consistent with previously reported observations that this type of microfluidic chip is less susceptible to Taylor cone variations and has a greater dynamic range that conventional nanoES sources.

References
It has been observed by Mann et al. (Int. J. Mass Spectrom. Ion Processes 136 (1994), pp 167-180) that ions with the highest surface concentration in the electrospray droplets are favored. The surface concentration is a function of the ion solubility and charge density of the analyte.