Introduction

Nanospray has become an essential tool in high-sensitivity MS, but limited robustness and reproducibility have historically challenged the adoption of nanospray in quantitative applications with triple quadrupole mass spectrometry. MS-based biomarker quantification places strict requirements on the analytical performance of nanospray LC-MS not only in the need for reproducible spraying but also due to the intrinsically complex nature of the samples used in these workflows. Automated emitter positioning with rinsing has been previously demonstrated to improve spray stability and analysis reproducibility on a 12T ion trap MS. Here we investigate the utility of automated tip rinsing to improve emitter spray stability and data quality on a hybrid triple-quadrupole/MS equipped with a heated interface maneuvered by a laminar flow of nitrogen gas.

Methods - QQ/LIT

Instrumentation
- Mass spectrometer: 4000 Q TRAP (AB SCIEX)
- Scan settings: Q1 MS Scan: 400 – 1000 Da; profile mode; unit resolution
- Compound parameters: Declustering potential ~ 70; Entrance potential ~ 30
- Source/Gas parameters: Curtain gas: ~ 10 L/min; spray voltage: ~2200 VDC; Ion source gas: ~ 3 L/min; Interface heater temperature: ~150°C
- Source: Digital PicoView DPV-450 nanospray source (New Objective, Inc.)
- Emitter: uncoated, 360 µm OD x 20 µm ID x 10 µm tip (New Objective, Inc.)
- Autosampler: HTC PAL (Leap Technologies)
- Mobile Phase B: 0.1 formic acid in acetonitrile (J.T. Baker)
- Ion-trap mass spectrometer equipped with Harvard Biosciences syringe pump (LCQ Deca, Thermo Scientific)
- Nanospray source: Digital PicoView 710, New Objective
- 1100 CapLyte pump operated in Normal Mode (Agilent)
- PicoFrit emitter (360 μm OD, 75 μm ID, 15 μm tip ID, New Objective)

Reagents
- TIP Rinses: 10% water/50% methanol, gravity flow (~10 µL/min)
- Mobile Phase A: 0.1% formic acid in water (J.T. Baker)
- Mobile Phase B: 0.1% formic acid in acetonitrile (J.T. Baker)
- Peptides: Angiotensin I, Angiotensin II, [Glu1]-Fibrinopeptide B, Insulin Chain B (Sigma-Aldrich)
- Autosampler: HTV PAL (Leap Technologies)

Flow Injection
- Flow Rate: 1000 nL/min; 50% mobile phase A/50% mobile phase B
- Analyte: 100 nL (4 µg peptide min) in 50% mobile phase A, 30% mobile phase B
- Injection: 1 µL loop

Results

Results With Emitter Rinsing

Results Without Emitter Rinsing

Effects of Positioning on Signal

Ion Trap Methods & Results

Conclusions

- Demonstrated benefits of automated tip rinsing on two different instrument platforms
- Validated regular monitoring of TIC RSD as a good indicator of ion source performance
- Observed finite and variable analyte recovery and emitter performance when regular automated tip rinsing is not enabled
- Enabled robustly stable nanospray and reproducible data using remote controlled automated tip rinsing at regular intervals

Digital PicoView DPV-450 nanospray source installed on an AB SCIEX 4000 Q TRAP instrument.

PicoFrit NanoSpray emitter (360 μm OD, 75 μm ID, 15 μm tip ID, New Objective)