Improving Mass Spectrometric Sensitivity and Ionization Efficiency Using a nanoESI Emitter Array at Subambient Pressures

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Overview

- Arrays of chemically etched emitters with individual sheath gas have been developed.
- Emitter arrays were incorporated in a subambient pressure with nanoelectrospray (SPIN) source.
- Stable electrospray array was obtained and improved MS sensitivity was demonstrated.
- Ion transmission efficiency and ESI efficiency were evaluated using both a SPIN-MS and a conventional heated capillary ESI-MS.

Introduction

The achievable sensitivity of electrospray ionization mass spectrometry (ESI-MS) is largely determined by the ionization efficiency and the ion transmission efficiency through the ESI-MS interface. The ESI efficiency can be greatly enhanced by using an array of electrosprays and the ion losses at the ESI-MS interface can be effectively eliminated by operating the electrospray at subambient pressures adjacent to an electrodynamic ion funnel.

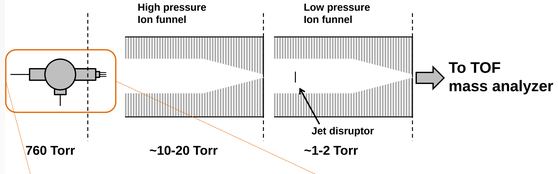
In this study, we present the development of a new emitter array with individualized sheath gas and their incorporation in a subambient pressure ionization with nanoelectrospray (SPIN) source. The utility of operating an emitter array at subambient pressures was evaluated by coupling the emitter array/SPIN source with a time of flight mass spectrometer. The instrument sensitivity of the emitter array was compared to a single emitter in the SPIN source and a conventional ESI source using a peptide mixture. The overall ion utilization efficiency was also systematically evaluated under different ESI-MS and SPIN-MS interface configurations.

Methods

Experimental

- Emitter arrays were fabricated by chemically etching fused silica capillaries (150 µm o.d./ 10 µm i.d.) arranged in radial patterns for electrical field uniformity.
- The instrument sensitivity using emitter array was compared to a single emitter in the SPIN source and a conventional ESI source using a peptide mixture. A 1 µM sample was infused at a total liquid flow rate of 200 nL/min for all configurations.
- The overall ion utilization efficiency was evaluated under different ESI source and MS interface configurations by measuring the electrical current transmitted through the high pressure ion funnel as a function of the RF voltage and using the second funnel as a charge collector. This current was correlated to the gas phase ion current detected at the mass spectrometer.

Ion Source Configuration



Emitter Assembly

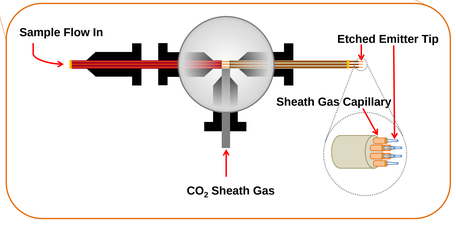


Figure 1. Configuration of the SPIN source interface coupled with an emitter array positioned at the entrance of the high pressure ion funnel. In the completed emitter assembly, each emitter is housed within a larger fused silica capillary (360 µm o.d./ 200 µm i.d.) providing CO_2 sheath gas for added stability.

Results

"Brighter" Ion sources

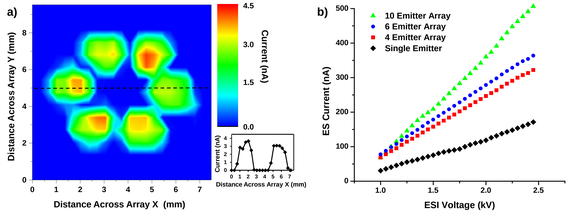


Figure 2. Two-dimensional ESI spray profile generated from a six-emitter array infusing 0.1% formic acid in 10% acetonitrile at a flow rate of 100 nL/min. The distance between the emitter and the counter electrode was fixed at 2 mm **(a)**. The inset shows the one-dimensional current profile taken along the dotted line. Current versus voltage curves for various emitter arrays under the same experimental conditions **(b)**.

Improved ion transmission

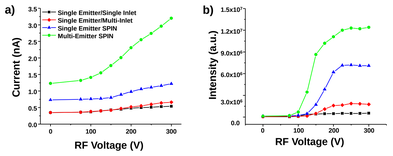
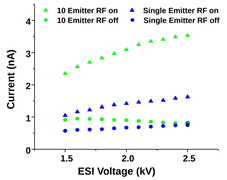


Figure 3. Transmitted electric current through the high pressure ion funnel **(a)**, and extracted ion current for the 3+ neurotensin ion (558.3 *m/z*) at different RF peak to peak voltages for different interface configurations **(b)**.

Enhanced Ionization Efficiency



Ion Source Configuration	Overall ion utilization efficiency
Single Emitter/Single Inlet ESI	4.0 ± 0.3%
Single Emitter/Multi-Inlet ESI	4.2 ± 0.8%
Single Emitter/SPIN	6.4 ± 0.3%
10 Emitter Array/SPIN	13.0 ± 2.3%

Figure 4. Current measurements at different ESI voltages under both high pressure ion funnel rf on and off conditions for both a single emitter and a 10 emitter array.

Increased sensitivity

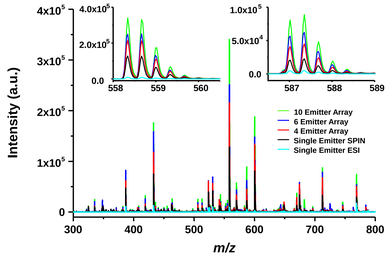


Figure 5. Mass spectra from the analysis of the nine-peptide mixture with various emitter arrays and single emitter configurations operated in optimized conditions. The insets show zoomed images of the mass spectra of the neurotensin +3 charge state (558.3 *m/z*) and angiotensinogen +3 charge state (587.0 *m/z*).

Table 1. Enhancement factors relative to Single Emitter/ESI

m/z	Charge State	Peptide	Single Emitter Spin	4 Emitter Array	6 Emitter array	10 Emitter Array
768.9	2+	Fibrinopeptide A	1.7	2.8	3.1	4.2
712.2	4+	Melittin	12.9	25.5	30.9	34.1
674.4	2+	Substance P	8.1	13.0	14.0	9.5
587.0	3+	Angiotensinogen	4.2	8.7	11.5	17.1
558.3	3+	Neurotensin	13.5	23.1	26.3	35.7
530.8	2+	Bradykinin	3.9	5.3	6.7	6.2
523.8	2+	Angiotensin II	4.9	7.4	7.4	7.4
432.9	3+	Angiotensin I	5.9	9.3	12.6	14.1
386.7	2+	Kemptide	4.3	5.5	7.3	7.3
		Average Enhancement Factor	6.6	11.2	13.3	15.1

Exceptional ESI Stability

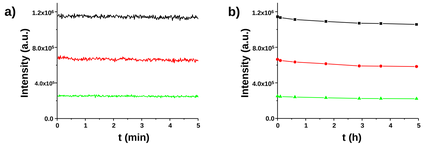


Figure 6. SPIN-MS stability experiments. Extracted ion currents from selected analyte peaks obtained from a six-emitter array during a 5-min data acquisition **(a)** and incrementally over a 5-h duration **(b)**. The neurotensin +3 charge state is shown in *black*, angiotensin +3 charge state in *red*, and angiotensinogen +3 charge state in *green*.

Conclusions

- The emitter arrays produce stable electrospray signal in a pressure range of ~11-30 Torr.
- An increase in ion current and MS signal correlative to the number of emitters in the array was observed with enhancement factors as high has 30-fold.
- The current produced by an emitter array and transmitted through the high pressure ion funnel consisted of a higher fraction of actual gas phase analyte ions leading to an increase in ion utilization efficiency.

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References

1. Cox, J.T. ; Marginean, I.; Kelly, R. T.; Smith, R.D.; Tang, K. *J. Am. Soc. Mass Spectrom.* **2014**, DOI: 10.1007/s13361-014-0856-5
2. Page, J. S.; Tang, K.; Kelly, R. T.; Smith, R. D.; *Anal. Chem.* **2008**, 80, 1800-1805

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