Chemically Etched Open Tubular and Silica Monolithic Electrospray Emitters

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Overview

A new procedure for fabricating silica emitters for electrospray ionization-mass spectrometry (ESI-MS) has been developed

Emitter features include:

- Excellent signal stability at nanospray flow rates
- No internal taper (clogging is reduced or eliminated)
- A high degree of inter-tip reproducibility

The etching procedure can also be used to create emitters with protruding silica monolithic material, enabling:

- Direct integration with monolithic liquid chromatography (LC) columns
- Greater ion currents due to the formation of multiple Taylor cones at the emitter surface

Introduction

Nanoelectrospray

- Smaller charged droplets are generated by ESI at low flow rates (e.g., <100 nL/min) compared with conventional flow rates (e.g., >1 μL/min)[1]
- Improved ionization efficiency leads to enhanced MS sensitivity
- Ion supression and matrix effects are minimized, improving quantitation[2]
- Very small emitter orifice or liquid flow is required

Conventional Nanospray Emitters

- Silica capillaries are heated and pulled until they break
- The inner and outer diameters (i.d. and o.d., respectively) taper to a small aperture
- The mechanical process is difficult to control, leading to poor reproducibility between emitters[3]
- The internal taper promotes clogging[4]

Porous Monolithic Emitters

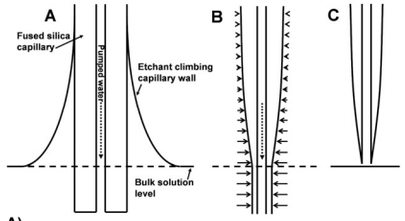
- Large number of fluid paths minimize blockage
- Multiple Taylor cones from rough surface or different fluid paths increase ion current
- Direct integration with monolithic liquid chromatography (LC), eliminating post-column dead volume

Our Approach

- Chemical etching in a concentration gradient
- Improves the fabrication of both open tubular and monolithic electrospray tips

Methods

Chemical Etching Procedure



A)

- The end of a fused silica capillary (polyimide removed) is immersed into 49% HF
- Water is pumped through the capillary (~100 nL/min) to prevent etching of the interior
- A meniscus forms on the capillary exterior above the bulk solution

B)

- A gradient in HF concentration forms in the meniscus
- The etch rate decreases further up, causing a taper to form

C)

- Etching process stops automatically when all silica in contact with the HF reservoir is removed
- Tip is rinsed with water and ready for use
- Same procedure for open and monolithic emitters

Mass Spectrometry

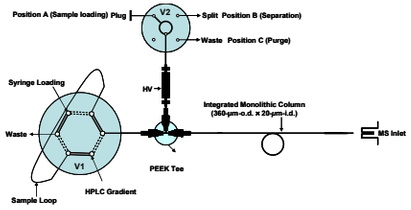
Open Tubular Emitter Characterization

Agilent MSD1100 single quadrupole with its standard ESI interface replaced by an ion funnel interface[5]

Proteomics Analysis using Monolithic LC-ESI-MS

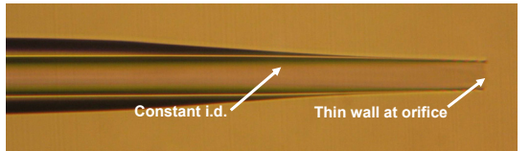
LTQ XP (Thermo) linear ion trap, unmodified

Monolithic LC with Integrated ESI Tips



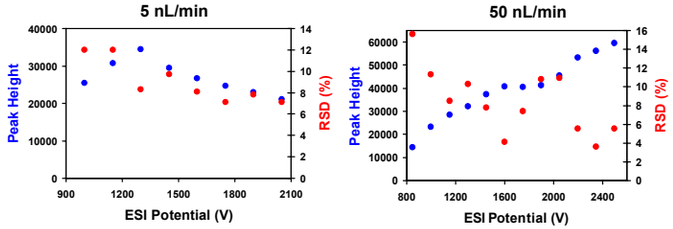
Results

Etched Open Tubular Emitters



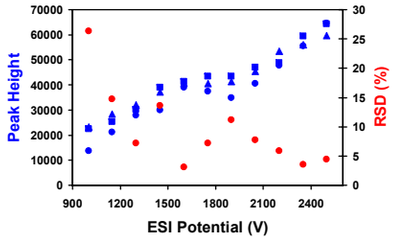
Emitter shown: 20 μm i.d., 200 μm o.d. Tips ranging from 5–50 μm i.d. and 150–360 μm o.d. were tested and showed similar quality.

Nanospray Stability



- Sample: 5 μM reserpine in 99% water, 1% acetic acid
- Emitter: 5 μm i.d., 150 μm o.d.
- Peak heights and relative standard deviation (% RSD) were calculated from 20 consecutive scans
- % RSD reached as low as 7% at 5 nL/min and 4 % at 50 nL/min
- Very similar performance when solvent was 90% water or 50% water (1% acetic acid, balance methanol; not shown)

Inter-tip Reproducibility

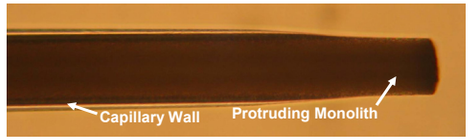


- Blue shapes indicate average peak heights (20 scans per point) for 3 runs using different emitters
- Sample: 5 μM reserpine in 99% water, 1% acetic acid
- Emitters: 5 μm i.d., 150 μm o.d.
- % RSD was calculated from the average peak heights of the replicates (red circles)

Evaluation of Tip Longevity

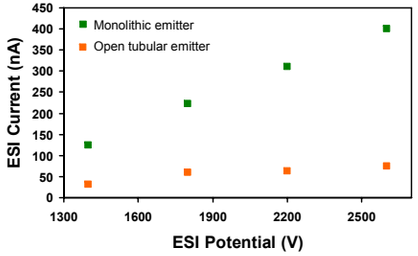
- Pulled silica tips were replaced with 20-μm-i.d. chemically etched emitters on the LC systems at PNNL's High Performance Mass Spectrometry Facility
- Each emitter used 200–300 h/month
- Flow rates: 0.3–1.8 mL/min
- Pulled tip lifetimes were highly variable, from less than 1 day to ~1 month
- Etched emitters typically lasted 1–2 months

Etched Silica Monolithic Emitters



Emitter shown: 50 μm i.d., 200 μm o.d. Monolith prepared according to Ref. 6

Increased Ion Currents



- Electrospray currents produced from monolithic and open tubular silica emitters
- For both emitters, the i.d. was 50 μm, and the flow rate was 200 nL/min.
- Solvent: 49.5% water, 49.5% methanol, 1% acetic acid

LC-MS with Integrated Monolithic ESI Tips

- As an example, 5,748 unique peptides, covering 1,429 distinct *Shewanella oneidensis* proteins, were identified from a 100 ng tryptic digest in a single 3-h LC-MS/MS analysis
- Post-column dead volume was completely eliminated
- Integration of the monolithic emitters is simple and reliable

Conclusions

- Chemical etching in a concentration gradient enables the creation of high aspect ratio silica ESI emitters with no internal taper
- Emitters can be used for hundreds of hours, and clogging is essentially eliminated
- Stable ESI-MS signals were obtained for model analytes from 5-μm-diameter emitters at 5 nL/min
- A high degree of reproducibility has been demonstrated for different tips
- Monolithic emitters produced ion currents ~8-fold higher than open tubular emitters, indicating the formation of multiple Taylor cones

Acknowledgements

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