Nano flow CE-ESI-MS interfacing: Systematic comparison study demonstrates improved robustness and high sensitivity

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Introduction

Nowadays nano spray interfaces for CE-ESI-MS are preferred because of increased sensitivity. Based on the nano flow sheath liquid interface introduced in 1999 (Hsieh et al. 1999) (Wojcik et al. 2010) and commercialized by CMP Scientific, we built our own interface to improve robustness and handling. The interface was investigated in detail to understand its characteristics.
To study the analytical performance, a comparison with the standard sheath liquid interface in negative and positive mode under optimized conditions was performed. Since the setup is able to operate as a porous tip sheathless interface as well, overall a three-way comparison on three molecule classes has been performed.

Methods

A CE instrument was coupled to a QTOF MS. Capillaries with 30 µm i.d. and 365 µm o.d. with 10 % (v/v) acetic acid as electrolyte were used for all experiments. Standard sheath liquid interface experiments were performed using the orthogonal electrospray interface from Agilent. For nano flow sheath liquid interfacing, etched capillaries with reduced o.d. tip were inserted in a 30 µm i.d. orifice opening borosilicate glass emitter filled with sheath liquid. For sheathless interfacing a porous tip capillary, protruding a glass capillary utilizing background electrolyte as conductive liquid, was used.

Results & Discussion

The nano flow sheath liquid interface was modified to improve the handling and robustness. An inline filter to avoid particles and a shut off valve allowing defined flushing were implemented.
Theoretical calculations for the characterization unraveled the functioning of the nano flow interface. Experiments for the determination of the sheath liquid systems resistance, flow rate measurements and examination of different sheath liquids allowed us to understand the performance of the interface.
In comparison with the standard sheath liquid interface, the nano flow interface revealed great improvements in sensitivity mainly due to lower sheath liquid flow. For organic acids in negative mode, an average improvement of 35 times in area and intensity was achieved. In positive mode, for a BSA digest, a higher number of peptides was found due to an improved intensity of up to 30 times. Factors between 60-40 in signal intensities for the light and heavy chain of a reduced antibody were achieved.
By simply exchanging the emitter and using a porous tip capillary, sheathless experiments were performed with the same setup. Although higher gains would be expected for the sheathless interface due to low flow rate (10-20 nL/min), the improvements were slightly lower in comparison to the nano flow sheath liquid interface. This can be explained by the higher ionization efficiency of the sheath liquid, containing organic solvents.

Conclusion

The nano flow setup presented here is a robust, flexible and highly sensitive system for coupling CE with MS. Typical improvement factors of 20-50 in comparison to a standard sheath liquid interface are observed. The setup demonstrated versatility due to the possibility of operating as a porous tip sheathless interface by simple changes.