Direct Mass Spectrometry Analysis of Wet Biofluid Samples Using Slug-Flow Microextraction

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The translation of the mass spectrometry analysis from the analytical laboratories to the clinical settings will be highly dependent on the development of sampling and analysis methods using extremely simple procedures while retaining the high sensitivity and quantitation precisions set by traditional methods in laboratory involving HPLC-MS. A series of ambient ionization methods have been developed for direct quantitative analysis of biofluid samples, such as the paper spray (*Angewandte Chemie International Edition*, 2010, 49, 877) and extraction spray (*Analytical Methods*, 2013, 5, 6686). These two methods have been incorporated into a miniaturized MS analysis system (*Analytical Chemistry*, 2014, 86, 2909) for point-of-care applications.

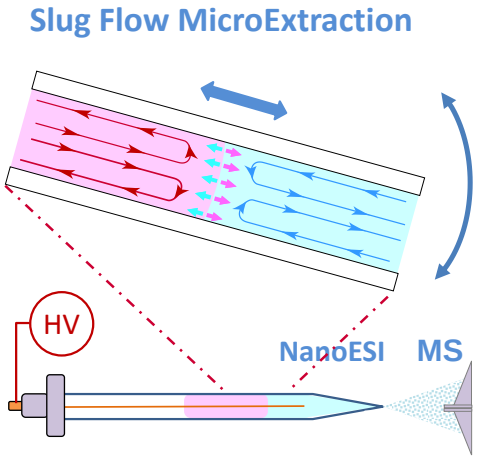

Figure 1. Direct analysis of biofluid samples by SFME-nanoESI.

The current study reports the development of the slug-flow microextraction (SFME) with nano-electrospray (nanoESI), a single-step sampling ionization method incorporating real-time reaction, internal standard addition and MS quantitation for the direct analysis of wet blood and urine samples. (Figure 1, *Angewandte Chemie International Edition*, doi: 10.1002/anie.201409949) Limits of detection (LODs) better than 1 ng/mL were achieved were achieved for the direct analysis of therapeutic drugs and drugs of abuse in 5 μL blood or urine samples. In a quantitation study, linearity of R^2=0.999 and quantitative precision of RSD <15% were obtained in the analysis of imatinib, nicotine and methamphetamine from wet blood or urine samples. Real-time chemical derivatization has also been incorporated for analyzing anabolic steroids. The achieved LODs for (5α-androstan-3β, 17β-diol-16-one), epitestosterone, 4,6-cholestadien-3-one, and

stigmastadienone in urine were 0.2, 0.7, 0.6, 0.8 ng/mL respectively. Furthermore, the direct monitoring of enzymatic functions by SFME-nanoESI has been developed with cholinesterase in wet whole blood as a demonstration. The enzyme activity in blood samples with different levels of cholinesterase inhibition were assessed by SFME, and the significant differences on cholinesterase deficiency level were identified. The reported study encourages the future development of disposable cartridges, which function with simple operation to replace the traditional complex laboratory procedures for MS analysis of biological samples.