A New Platform for High-Throughput Mass Spectrometry: Acoustic Droplet Ejection with an Open Port Probe Sampling Interface

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Introduction

We demonstrate a system combining acoustic droplet ejection (ADE) with the open port probe sampling interface for high-throughput mass spectrometry (MS). We use a customized Labcyte Echo® acoustic liquid handler to eject 2.5 nL droplets directly from a 384-well assay plate into an Open Port Probe (OPP) sampling interface. Captured droplets are diluted into a continuous flow of solvent and the OPP fluid stream is aspirated into the MS detector where sample is ionized by standard electrospray prior to entering a Sciex Q5000 Qtrap mass spectrometer. This new ADE-OPP platform leverages the high speed and excellent accuracy of ADE liquid handling technology into sample delivery for mass spectrometry.

Acoustic Droplet Ejection

The Labcyte Echo® ADE instrument is a robust platform that can eject 2.5 nL droplets from a fluid meniscus at high speed with excellent accuracy (< 10%) and precision (< 8% CV). The instrument can address a broad range of fluid classes utilizing Dynamic Fluid Analysis (DFA), a real-time auditing, sensing and calibration technology.

Acoustic Droplet Ejection into Open Port Probe (ADE-OPP)

The Labcyte Echo® ADE instrument is customized to move the dispensing module external to commercial chassis for interface to Sciex Q5000 Qtrap MS.

Matrix Effects

We address the question: does decoupling of sample fluid delivery and ionization with ADE-OPP have an impact on ion suppression? It is known that ionization by sample fluid injection directly into gas phase may be impacted by ion suppression. Matrix effects were studied with 100 nM reserpine spiked into diluted digested plasma. For single droplet injection, no matrix effects were observed up to pure digested plasma with reserpine. With larger volumes, we observe onset of ion suppression at around 200 nL when using 10X dilution of plasma digest as matrix.

Initial Results

A precision solvent delivery pump allows us to explore the solvent flow rate effects on peak width and intensity. We tested a range of pump flow rates relative to the fixed aspiration rate, going from balanced flow rates with a small solvent vortex to unbalanced flows with a hanging droplet of solvent. The larger droplet volume of the hanging droplet leads to higher dilution and broader, lower intensity peaks. We observe that operation in Vortex mode with a single 2.5 nL droplet injection is desirable and Reserpine at 0.01 microM (25 nanoM) gives a 2 second peak at baseline. The flow rate stability of our pump provides good reproducibility and peak shape and allows us to generate calibration curves with excellent linearity. The continuous flow of solvent also mitigates carryover.

Conclusions

• A new ADE-OPP platform leverages the speed and precision of ADE nanoliter droplets for high-throughput MS.
• Range of conditions explored to evaluate precision of the ADE-OPP combination with regard to sample concentration, sample volume and sample matrix.
• Flow control (key) and important for system stability and data precision.
• Operation in Vortex Mode is desirable.
• Good linearity with regards to volumes and concentrations.
• Matrix effects explored to point where observed.