

# Ultra-high-throughput and chromatography-free bioanalysis of polar analytes with Acoustic Ejection Mass Spectrometry

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## Gold statement

- High throughput analysis of polar analytes directly from the complex biological matrix
- Chromatography free
- No sample clean-up

## Introduction

Bioanalysis of polar analytes using LC-MS remains a significant challenge, due to their poor chromatographic retention on the commonly used reversed-phase LC columns, and the resulting severe ionization suppression from co-eluting matrix components. Here we present a novel approach to perform ultra high-throughput and chromatography-free bioanalysis of polar compounds, using a prototype acoustic ejection mass spectrometer (AEMS). Ionization suppression was minimized due to the >1000-fold dilution of the original sample by the carrier solvent. Using several model polar analytes, we have demonstrated the ultra-high-throughput bioanalysis of in-vitro transporter inhibition assay samples at a speed of 2.3 seconds/sample.

## Body

Taking full advantage of the chromatography-free and suppression-resistant features of the prototype AEMS instrument, we demonstrated ultra high-throughput bioanalysis of several polar substrates commonly used in high-throughput in vitro transporter inhibition assays in the early ADME profiling space in drug discovery. Important AEMS parameters including ejection volume, pause time between wells, and selected reaction monitoring (SRM) transitions were optimized to achieve a final analysis speed of 2.3 seconds/sample using only 10 nL of sample. Similar metformin concentration results were obtained by AEMS from actual assay samples, when compared to those obtained by the fastest LC-MS method previously reported. The calculated IC<sub>50</sub> values were within 2-fold for all testing compounds. In addition, the AEMS approach offered a ~20-fold speed advantage and ~1000-fold less sample consumption. The general applicability of this novel approach to bioanalysis of several classes of polar analytes including metformin, ethambutol, isoniazid and ephedrine in biological matrices (cell extracts) was further demonstrated using spiked samples.

## Conclusion

Ultra high-throughput (~2 seconds/sample) and chromatography-free bioanalysis of polar analytes with a novel prototype acoustic ejection mass spectrometer.