Comparison of Electrospray and Impactor Ionization for Pharmaceutical Compounds

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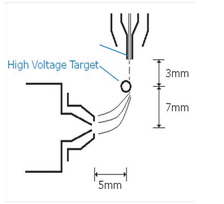
INTRODUCTION

Impactor ionization, is the formation of ions by directing a heated nebulized spray of liquid onto a curved surface with applied voltage. The spray is aimed off center and on impact, the ions flow downstream in a path that follows the curvature of the surface (in this case a pin), called the Coandă effect. Commonly used electrospray ionization involves a heated high velocity spray from a charged capillary. These two techniques have similar effects of ionization, producing predominantly $M+H^+$ (or $M-H^-$) ions, yet their mechanisms appear to be different. This work shows the comparison of ionization of a selection of pharmaceutical compounds by electrospray and UniSpray™.



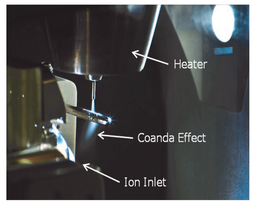


Figure 1. Graphic representation and photo of UniSpray source

METHODS

Compound libraries with molecular weights ranging from 151 to 824 were purchased from Enzo Life Sciences. The standards were diluted to 100 nM and 1nM, or 0.1nM with 30:70:0.1 ACN/water/formic acid for high-throughput compound optimization of M+H or M-H by QuanOptimize followed by injection on column. Plasma robustness studies were performed by protein precipitation with ACN at a 3:1 ratio, vortex mixed and then centrifuged at 16.1 x g for 10 minutes. The supernatant was taken and standards were spiked to 1nM before injection. ACQUITY® I-Class UPLC® with a BEH C18 2.1x50mm column and mobile phases of water and ACN with 0.1% formic acid was coupled to a Xevo® TQ-S tandem quadrupole mass spectrometer equipped with electrospray and Impactor (UniSpray™) ionization sources. Data was collected in both positive and negative ionization modes and processed using MassLynx v.4.1. All results are calculated on chromatographic peak area.

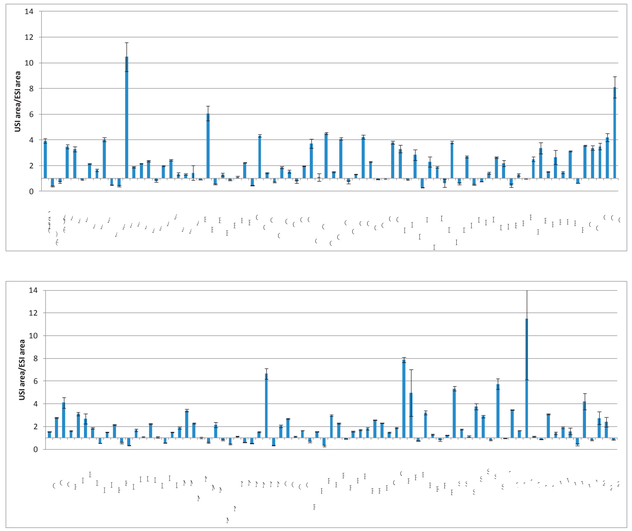


Figure 2. Chromatographic peak area ratios USI/ESI showing UniSpray ionization response compared to electrospray

RESULTS AND SUMMARY

Compound libraries consisting of 157 compounds were screened using a short chromatographic gradient from 1 - 95% B over 2 minutes (4 minute total run time) and collected in positive and negative ionization modes of electrospray (ESI) and UniSpray (USI). Over 70% of the compounds had greater or comparable peak area response in USI compared to ESI (defined as the ratio of USI to ESI response above 1.0) and are summarized in figure 2. To test ionization efficiency at lower concentration levels, samples were further diluted to 0.1 nM. Figure 3 shows two examples, amantadine and amlodipine, where increased ionization was observed in USI relative to ESI. Plots of USI/ESI response with respect to such chemical properties as pKa and LogP showed no discernible trend (figure 4). This, with the correlation results in figure 4C, suggest USI is not discriminatory and behaves similarly to ESI for the compounds tested.
Robustness in human serum was performed on a subset of the compound library. Peak areas for injections 5-1800 are plotted and then summarized in figures 5 and 6 representing nearly 6 days of continuous operation. The RSD for the 37 compounds tested ranged from 1.9 - 16. Higher RSD was observed for compounds that were at the lower end of detection.

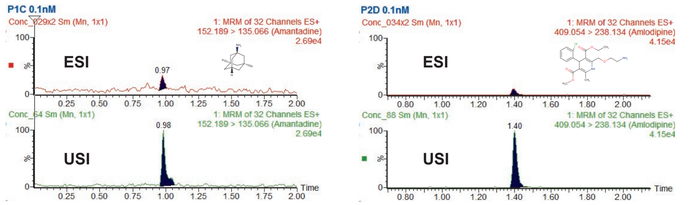


Figure 3. Ionization of amantadine and amlodipine at 0.1nM comparing ESI (top trace) and USI (bottom trace) in solvent

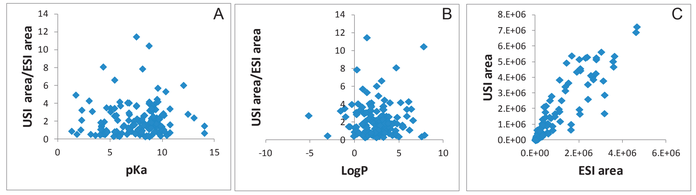


Figure 4. Plots of USI and ESI chromatographic peak area ratio with respect to pKa (A) and LogP.(B) as well as USI area vs. ESI area (C)

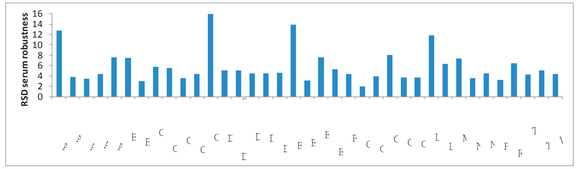


Figure 5. Summary of compounds tested for robustness in human serum up to 1800 injections

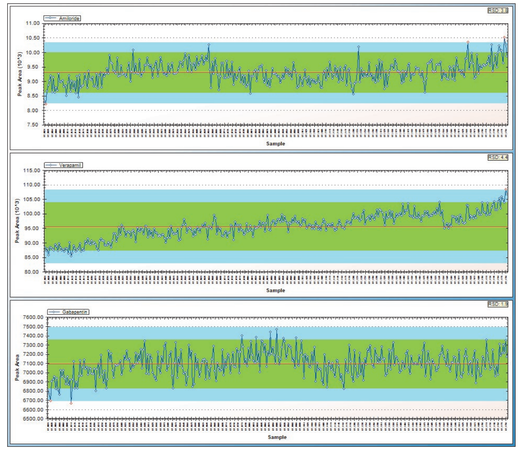


Figure 6. Representative human serum robustness results for amiloride (top), verapamil (middle), and gabapentin (bottom); Every 5th injection is plotted

CONCLUSION

- UniSpray is an ionization technique that produces results similar to electrospray
- Chromatographic peak area ranged from 0.3 to 11.4 and was an average of 2.1 times greater for UniSpray for the compounds tested
- Peak area serum robustness ranged from 1.9 - 16% RSD for 1800 injections

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