Comparison of Full Scan High Resolution MS and Triple Quadrupole SRM in Quantitative Bioanalysis

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INTRODUCTION

Triple quadrupole MS has been the workhorse for quantification of drugs for decades. However, this instrument has some limitations: it has a lower mass accuracy and precision, lower selectivity in the presence of matrix interferences, poor sensitivity, and lower endogenous components selectivity without sample re-injection.

Recent advances in LC-HRMS technology have led to the development of high resolution mass spectrometers (HRMS), particularly QTOF HRMS, which provide excellent selectivity, accuracy/precision, mass accuracy and ruggedness. HRMS has gained increasing attention in the field of quantitative drug analysis, particularly in biofluids.

In this study, we compared SRM (triple quadrupole) and HRMS (QTOF) methods to evaluate their performance in the quantitation of drugs in biological matrices.

METHOD

Sample Preparation

- Twenty-eight model compounds were prepared, and analyzed using both methods.
- Human plasma samples were prepared and analyzed, followed by the preparation of a calibration curve using QC samples.

Method Development

- Gradient elution was used to achieve sufficient data points across a chromatographic peak.
- Unit resolutions for Q1 and Q3 were used in method development.
- SRM (triple quadrupole) and HRMS (QTOF) methods were compared.

RESULTS AND DISCUSSION

- Comparison of LLOQ's and linear dynamic ranges: Table 1 shows the results for LLOQ and linear dynamic range of the 28 model compounds. In general, the two methods performed comparably in terms of LLOQ and linear dynamic range, with some exceptions.

- Using HRMS, 58% of the compounds achieved 1 ng/mL; 75% achieved 2 ng/mL; 93% achieved 5 ng/mL; 98% achieved 50ng/mL (Figure 1). Using SRM, 75% of the compounds achieved 1 ng/mL; 93% achieved 5 ng/mL; 98% achieved 50 ng/mL.

- Post-acquisition data-mining: After SRM data acquisition, 85% of the compounds achieved 2 ng/mL; 93% achieved 5 ng/mL; 98% achieved 50 ng/mL. Using HRMS, 89% of the compounds achieved 1 ng/mL; 100% achieved 5 ng/mL; 100% achieved 50 ng/mL.

- Comparison of assay performance: Figure 1 shows the results for assay performance and precision for quantification of buspirone in human plasma standard curve. HRMS achieved a better dynamic range (0.2 – 1000 ng/mL) compared to SRM (0.1 – 50 ng/mL). In both HRMS and SRM methods, %CV was < 15% for all levels except LLOQ.

- Additionally, HRMS-gave excellent mass accuracy over the calibration range for buspirone (Table 4).

CONCLUSIONS

- Overall, the results from this study indicate that HRMS provides better performance in terms of LLOQ, linear dynamic range, assay performance, and precision compared to SRM.

REFERENCES