Poster

[P25-6] P25-6: Immunosuppressive drugs (1): LC-MS/MS assay

Chair: Tsutomu Nakamura, Japan

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[P25-6-3] An 8 second analytical method for Tacrolimus in whole blood by LDTD-MS/MS

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Background

Therapeutic drug management of immunosuppressive drugs is imperative for organ transplant recipients. LC-MS/MS is considered gold standard; however, immunoassays provide rapid turnaround time to result. New technology was developed to reduce the analytical run-time of LC-MS/MS methods. The Laser Diode Thermal Desorption (LDTD) source eliminated liquid chromatographic separation to increase analytical throughput.

Methods

A rapid, 8 second, LDTD-MS/MS analytical method was developed for the quantification tacrolimus in whole blood. Whole blood samples were lysed, followed by protein precipitation and solid phase extraction. The extracted samples were spotted into wells in the LaZwell plate and desorption solution was added. The LaZwell plate was dried under a gentle stream of nitrogen gas then the plate was loaded on the LDTD source and analyzed by a SCIEX 5500 mass spectrometer. The four transitions monitored, using multiple reaction monitoring in positive mode, were 821.5 -> 768.5 (quantitative ion), 821.5 -> 718.5 (qualitative ion) for tacrolimus and 824.5 -> 771.6 (quantitative ion), 824.5 ->721.5 (qualitative ion) for the tacrolimus internal standard. The LDTD laser profile ramps from 0 to 65% of full power over 6 seconds and is held at 65% for 2 seconds before returning to initial conditions.

Results

Method validation data presented for tacrolimus by LDTD-MS/MS includes method comparison to LC-MS/MS, imprecision and sensitivity. Method comparison between LDTD-MS/MS and a validated in-house LC-MS/MS assay with 95% confidence intervals (±) yielded: (LDTD-MS/MS) = 1.185 ±0.035(HPLC-MS/MS) + 0.19 ±0.39 ng/mL, Sy/x=0.86, r=0.9945 (n=52). The limit of quantitation by LDTD-MS/MS for tacrolimus was 1.7 ng/mL and total imprecision was <10%.

Conclusions

Laser Diode Thermal Desorption Tandem Mass Spectrometry technology can provide rapid turnaround time to result for tacrolimus. The sample to sample analytical time for LDTD-MS/MS was 8 seconds compared to 180 seconds by LC-MS/MS, which was about a 95% decrease in analytical time.