LDTD-MS/MS in 1.8 seconds with RSD of 2.4 % : Paracetamol in Human Plasma Crash

Pierre Picard and Patrice Tremblay

Keywords: High-throughput, LDTD, Tandem mass spectrometry, Paracetamol, Acetaminophen, Human Plasma

Overview

- High-throughput determination of paracetamol in human plasma crash is performed by LDTD-MS/MS;
- Calibration range from 0.6 to 5000 ng/mL with $r^2 = 0.9944$;
- 1008 samples in 1.26 hours;
- Sample-to-sample run time of 4.5 seconds;
- Desorption peak width of 1.8 seconds;
- RSD of 2.4 % for 1008 replicates.

Instrumentation

- Phytronix Technologies LDTD ion source (model T-960);
- Thermo Fisher Scientific TSQ® Quantum™ Ultra AM mass spectrometer.

LDTD ionization process

The LDTD ion source uses an infrared laser diode to desorb sample that have been dried onto a well of a LazWell™ (96-well plate). The desorbed gas phase molecules are carried into a corona discharge region to undergo APCI, then they are transferred directly into the mass spectrometer for detection.

Samples Preparation

Stripped human plasma was spiked with paracetamol and paracetamol-d4 (ISTD). Plasma proteins were precipitated with the addition of acetonitrile (1:4 v/v). A volume of 2.0 µL of the supernatant was manually transferred into a well of a LazWell™ and was allowed to dry at room temperature.

Results and Discussion

LDTD-MS/MS allows high-throughput analysis of paracetamol in human plasma as shown in **Figure 1** where 96 replicates are analyzed in 7.2 minutes.

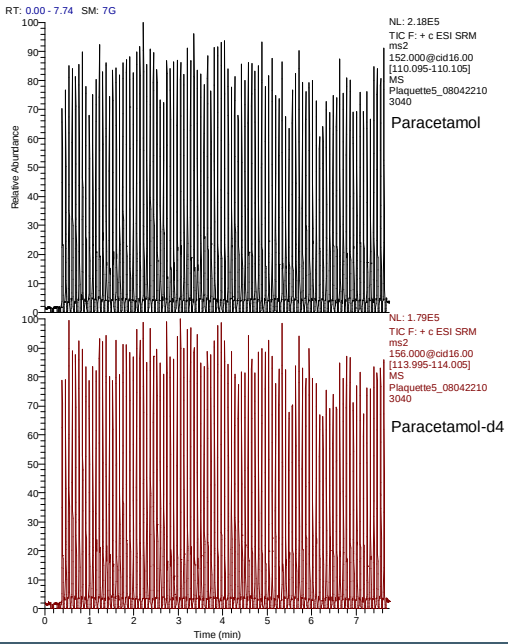

Figure 1 Area count of 96 replicates of paracetamol (40 ng/mL) in human plasma crash determined in LDTD-MS/MS.

Analysis Repeatability

Using only the raw area count of 1008 replicates, the RSD for paracetamol (40 ng/mL) and paracetamol-d4 (40 ng/mL) signal are 9.9 %. With the ISTD correction, the **RSD is lowered to 2.4 %** showing the stability of the LDTD-APCI process (**Figure 2**).

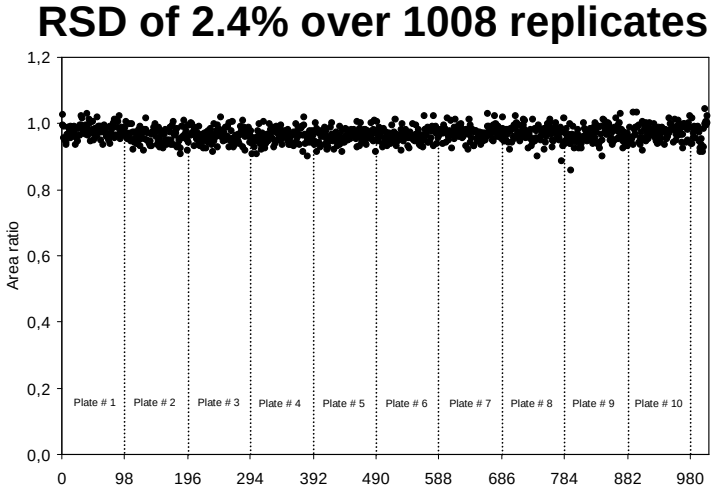

Figure 2 LDTD-MS/MS repeatability on paracetamol/ISTD ratio over 1008 human plasma crash replicates.

Paracetamol Calibration Curve

Quantitative determination of paracetamol in human plasma crash can be achieved over a nominal concentration range of 0.6 to 5000 ng/mL (**Figure 3**). An excellent linearity is obtained over the concentration range (R^2 = 0.9944).

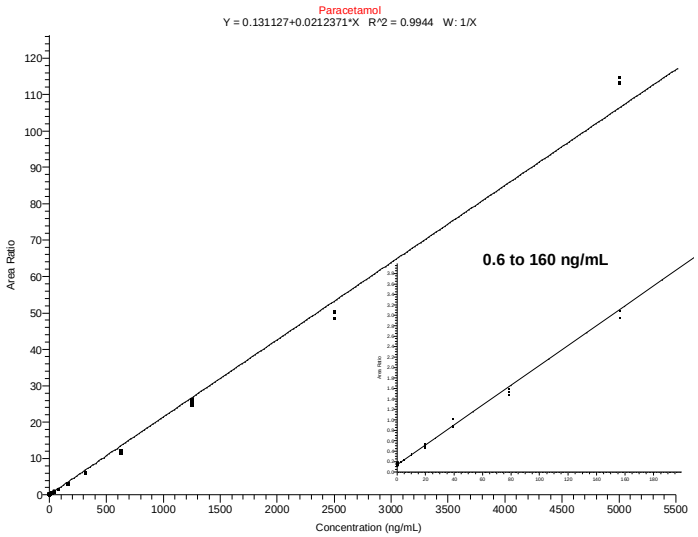

Figure 3 Paracetamol calibration curve in human plasma crash (3 replicates at each concentration).

Paracetamol and Paracetamol-d4 LDTD Desorption Profile

The Laser Diode Thermal Desorption process performed in **1.5 seconds** allows an excellent paracetamol signal width of 1.8 seconds. No carryover, no overlapping peak and no matrix effect are observed (**Figure 4**).

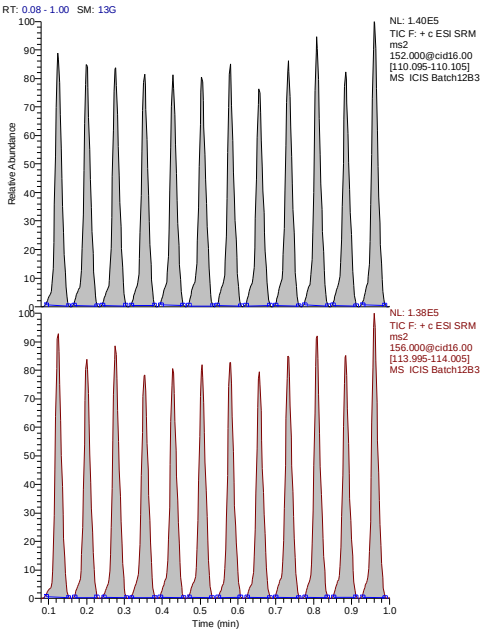

Figure 4 Area count of 12 samples of paracetamol in human plasma crash (40 ng/mL) analyzed in LDTD-MS/MS.

MS Parameters

APCI (+)	
Collision gas pressure	1.5 mTorr (Argon)
Collision energy	16 V
Tube lens	51 V
Scan time	0.050 s
Scan width	0.010 amu
Needle voltage	4500 V
Q1 width	0.30 amu
Q3 width	0.70 amu
Paracetamol SRM transition	152.0 → 110.1 amu
Paracetamol-d4 SRM transition	156.0 → 114.1 amu

LDTD Parameters

Laser power pattern	0 to 25 % in 1.0 s Hold at 25 % for 0.5 s
Carrier gas flow	3.0 L/min (Air)

Conclusions

LDTD-MS/MS allows ultra-fast paracetamol thermal desorption in **1.8 seconds** with a sample-to-sample run time of 4.5 seconds. The LDTD-MS/MS signal is stable over 1008 replicates as show by a RDS of 2.4 % with no matrix effect and no observed carryover. Paracetamol quantification can be performed over a 4-fold concentration range with an excellent linearity.

High-throughput analysis with excellent repeatability and linearity can be achieved using LDTD as ion source in mass spectrometry.

For more information about your specific application, visit www.phytronix.com

Phytronix Technologies
337 rue Saint-Joseph E.
Québec, Qc Canada G1K 3B3
Phone : +1 (418) 692-1414
Fax : +1 (418) 692-4940