

# LDTD-MS/MS Analysis in 9 seconds : Quantification of Mifepristone in Mouse Plasma

Pierre Picard and Patrice Tremblay

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## Overview

- High-throughput determination of mifepristone and two mifepristone analogues in mouse plasma is performed by LDTD-MS/MS;
- Calibration range from 10 to 2000 ng/mL with  $R^2 > 0.995$ ;
- Sample-to-sample run time of 9 seconds;
- Accuracy within 95.1 and 113.4 %;
- Mean precision of  $4.9 \pm 3.2$  %;
- Excellent method selectivity from blank analysis.

## Instrumentation

- Phytronix Technologies LDTD ion source (model T-960);
- Thermo Fisher Scientific TSQ<sup>®</sup> Quantum<sup>™</sup> 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<sup>™</sup> (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.

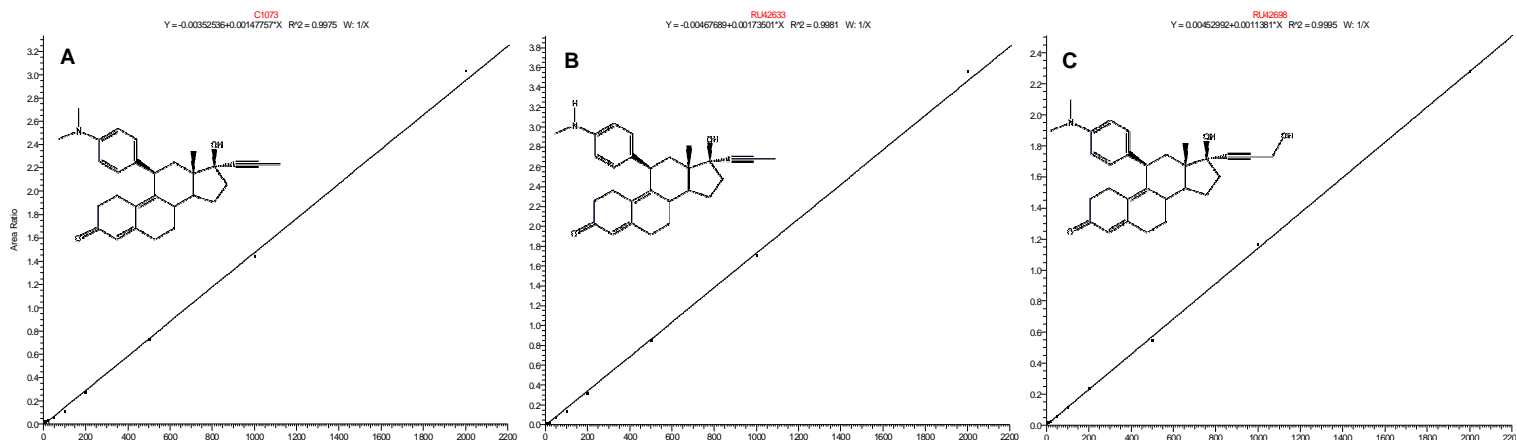
## Samples Preparation

Mouse herapin plasma was spiked with mifepristone and two mifepristone analogues and with ISTD (deuterated drugs). The drugs were extracted with MTBE and Hexane (1:1 v/v) and reconstitute into a water:acetonitrile:formic acid solution (75:25:0.1 v/v/v). A volume of 2.0  $\mu$ L was manually transferred into a well of a LazWell<sup>™</sup> and was allowed to dry at room temperature.

## Results and Discussion

### Calibration Curves

Quantitative determination of mifepristone and two mifepristone analogues in mouse plasma can be achieved over a nominal concentration range of 10 to 2000 ng/mL (**Figure 1**). An excellent linearity is obtained over the concentration range ( $R^2 > 0.995$ ).



**Figure 1** Calibration curve of A) mifepristone and two mifepristone analogues, B) MifA-1 and C) MifA-2 in mouse plasma.

## Accuracy and Precision

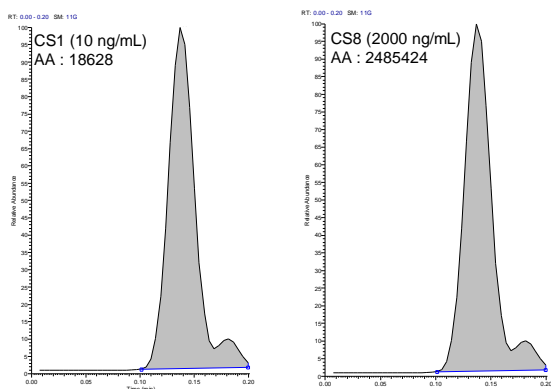
Quality control samples were analyzed to evaluate the LDTD-MS/MS method accuracy and precision. The accuracy was evaluated to be within 95.1 and 113.4 % and the mean precision was  $4.9 \pm 3.2$  % (Table 1)

**Table 1** Within-run accuracy and precision for mifepristone and mifepristone analogues.

	Mifepristone		
	QC1	QC2	QC3
Nominal conc. (ng/mL)	30	300	1600
N	3	3	3
Mean (ng/mL)	30.6	287	1634
RSD (%)	7.0	6.2	1.9
% Nominal conc.	101.8	95.8	102.1
	MifA-1		
	QC1	QC2	QC3
Nominal conc. (ng/mL)	30	300	1600
N	3	3	3
Mean (ng/mL)	29.0	285	1646
RSD (%)	3.8	3.7	5.8
% Nominal conc.	96.7	95.1	102.9
	MifA-2		
	QC1	QC2	QC3
Nominal conc. (ng/mL)	30	300	1600
N	3	3	3
Mean (ng/mL)	30.5	326	1815
RSD (%)	1.9	11.7	2.1
% Nominal conc.	101.6	109.0	113.4

## Mifepristone LDTD Desorption Profile

The LDTD allows fast mifepristone thermal desorption (Figure 2). The blank samples (signal intensity of 557) allows a LOD of 0.9 ng/mL.



**Figure 2** Desorption profile for 2 mifepristone standards.

## Method Selectivity

The selectivity was evaluated from blank samples analysis. The blank signals were interfering from 3.3 to 8.1 % on CS1 samples (10 ng/mL). The interference on the internal standards were lower than 0.05 %. Even without chromatographic separation, LDTD-MS/MS analysis shows an excellent method selectivity.

## MS Parameters

APCI (+)	
Collision gas pressure	1.5 mTorr (Argon)
Collision energy (Mifepristone, MifA-1, MifA-2)	18, 20, 25 V
Tube lens (Mifepristone, MifA-1, MifA-2)	77, 89, 112 V
Scan time	0.030 s
Needle voltage	5000 V
Q1 width	0.70 amu
Q3 width	0.70 amu
Mifepristone SRM transition	430.14 → 372.25 amu
Mifepristone-d4 SRM transition	434.15 → 374.25 amu
MifA-1 SRM transition	416.12 → 358.04 amu
MifA-1-d4 SRM transition	420.12 → 360.04 amu
MifA-2 SRM transition	446.14 → 388.22 amu
MifA-2-d4 SRM transition	450.15 → 390.22 amu

## LDTD Parameters

Laser power pattern	0 to 60 % in 1.0 s Hold at 60 % for 2.0 s
Carrier gas flow	3.0 L/min (Air)

## Conclusions

LDTD-MS/MS allows high-throughput quantification of mifepristone and two mifepristone analogues with a sample-to-sample run time of 9 seconds. LDTD-MS/MS shows no matrix effect and no observed carryover and an excellent method selectivity.

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

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**Phytronix**  
Technologies

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

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