Analysis of Drugs of Abuse by Laser Diode Thermal Desorption Coupled with Differential Ion Mobility Spectrometry

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ABSTRACT

For Research Use Only. Not for use in diagnostic procedures. The Laser Diode Thermal Desorption™ (LDTD) ionization source has been coupled to a mass spectrometer equipped with the SelexION™ differential ion mobility cell, enabling a high throughput capacity for the analysis of drugs of abuse in biological matrix, with sample-to-sample analysis time of 10 seconds. Sample preparation consisted of a liquid-liquid extraction of urine under both acidic and basic conditions.

INTRODUCTION

LDTD™ Ionization Source:

The LDTD uses a Laser Diode to produce and control heat on the sample support **(Figure 1)** which is a 96 well plate**.** The energy is then transferred through the sample holder to the dry sample which vaporizes prior to being carried by a gas in an APCI region. High efficiency protonation with strong resistance to ionic suppression characterize the ionization, due to the absence of solvent and mobile phase. This allows very high throughput capabilities of 7 seconds sample-to-sample analysis time, without carry over.

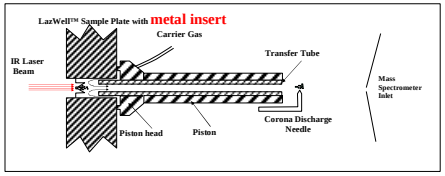


Figure 1. Schematic of the LDTD Ionization Source.

SelexION™ Technology:

The SelexION™ technology is a Differential Mobility Spectrometer (DMS) placed in front of the inlet of the mass spectrometer **(Figure 2).** The ionized molecules travel into the orthogonal geometry shaped DMS.

- Short residence times
- Rapid voltage changes for MRM operation
  - MRM cycle times of 25 msec, (20 msec pause time)
  - Transparent Mode
  - Allows all ions to be transmitted by turning off voltages
- Minimal diffusion losses
- Uniform conditions for the addition of chemical modifiers

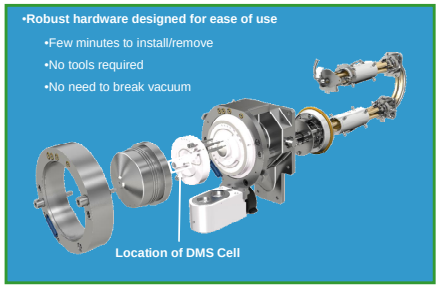
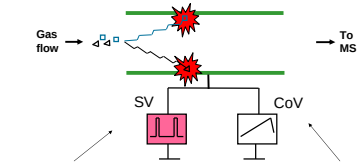


Figure 2. QTRAP® 5500 System Ion Path with SelexION™ Technology

•Differential Mobility Spectrometry (DMS) is the term used for planar geometry



Separation waveform (SV):

Radially displaces ions towards one or the other electrode, depending upon high and low field mobility characteristics

Compensation voltage (CoV):

Restores the trajectory for a given ion to allow them to transmit through the DMS device and enter the mass spectrometer

Figure 3. How the SelexION™ Technology Separates Ions

MATERIALS AND METHODS

Sample Preparation:

Acidic liquid-liquid extraction
- 50 µL of urine
- 50 µL of HCl 0.2 N containing 500 ng/mL of IS mixture
- 200 µL 1-Chlorobutane
- 2 µL of organic phase run in LDTD- QTRAP® 5500

Basic liquid-liquid extraction
- 50 µL of urine
- 50 µL of NaOH 0.2 N containing 500 ng/mL of IS mixture
- 200 µL Ethyl Acetate
- 2 µL of organic phase run in LDTD- QTRAP® 5500

LDTD Instrumentation:

LDTD model S-960, Phytronix Technologies
- •Laser power pattern:
  - Increase laser power to 45 % in 3.0 s
  - Decrease laser power to 0 %
- Carrier gas flow: 3 L/min (Air)
- Spotted sample volume: 2 µL

MS/MS Conditions:

Data was obtained using an AB SCIEX 5500 QTRAP® LC/MS/MS system. The ion source region of the mass spectrometer was modified for incorporation of the AB SCIEX SelexION™ ion mobility separation device. The standard ceramic orifice plate was replaced with a modified ceramic plate that included provisions for sealing the SelexION™ cell.

A Separation Voltage of 4000 V was used and the CoV was optimized for each compound (Table 1). The mass spectrometer analysis consisted of an MRM detection.

Compound	Q1	Q3	COV	Compound	Q1	Q3	COV
Codeine 1	282.1	193.0	6	Naloxone 2	328.1	253.1	6
Codeine 2	282.1	175.0	6	Naltrexone 1	342.2	267.1	6
Fentanyl 1	337.2	188.1	10	Naltrexone 2	342.2	212.1	6
Fentanyl 2	337.2	105.1	10	Norfentanyl 1	233.2	84.1	8
Hydrocodone 1	300.1	128.1	8	Norfentanyl 2	233.2	150.1	8
Hydrocodone 2	300.1	199.0	8	Oxycodone 1	316.2	241.0	6
Merperidine 1	248.2	220.0	6	Oxycodone 2	316.2	256.0	6
Merperidine 2	248.2	174.1	6	Oxymorphone 1	302.1	227.0	6
Methadone 1	310.2	265.2	8	Oxymorphone 2	302.1	198.1	6
Methadone 2	310.2	105.0	8	Tramadol 1	264.2	58.1	8
Morphine 1	286.2	152.0	6	Tramadol 2	264.2	42.1	8
Morphine 2	268.1	58.1	6	Hydromorphone 1	286.1	185.0	8
Naloxone 1	328.1	212.0	6	Hydromorphone 2	286.1	243.0	8

Table 1. MRM Transitions and Corresponding Compound Dependent CoV Parameter for Pain Panel Drugs

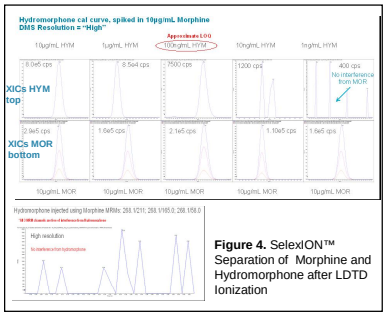


Figure 4. SelexION™ Separation of Morphine and Hydromorphone after LDTD Ionization

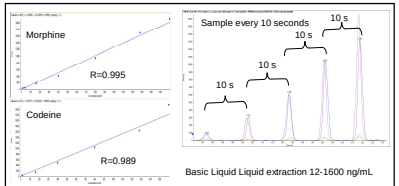


Figure 5. Calibration Curves for Codeine and Morphine from LDTD-SelexION™-QTRAP® 5500 LC/MS/MS System

Representative calibration curves for selected compounds, from the LDTD-QTRAP® 5500 analysis of a mixture of pain panel drugs, are shown in Figure 6. Two MRM transitions for each drug were monitored.

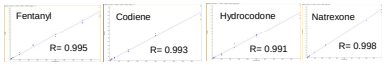


Figure 6. Representative calibration curves for selected compounds, from the LDTD-QTRAP® 5500 analysis

CONCLUSIONS

- •The SelexION™ ion mobility device was interfaced directly to the front of a QTRAP® 5500 mass spectrometer, and was optimized for the detection of the drugs of abuse by optimizing the Compensation Voltage (CoV) for each analyte.
- •The use of the LDTD Source enabled a high throughput capacity for the screening of a panel of drugs of abuse in biological matrix, with sample-to-sample analysis time of ~10 seconds.
- •The combination of SelexION™ with high-selectivity MRM transitions allows intereference-free analysis of morphine and hydromorphone
- •Selectivity is lost when the SelexION™ is removed.

TRADEMARKS/LICENSING