Application Note : 1211

# Solid-Phase Extraction of MDMA, MDA and MDEA in Urine and analysis by LDTD–MS/MS

*Serge Auger[1] , Alex Birsan[1], Annick Dion-Fortier[1]& David Dubé[2]*
*[1]Phytronix Technologies, Québec, Canada, [2]SiliCycle, Québec, Canada*

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## Introduction

Analysis of certain drugs of abuse in urine can require a sample clean-up step to reduce the interference effect from the matrix. To obtain an optimal sample clean-up, the Silia*Prep*™ CleanDrug SPE cartridges are used in the extraction procedure prior to the Laser Diode Thermal Desorption (LDTD) analysis.

The LDTD ion source uses an infrared laser diode to desorb samples that have been previously dried onto a 96-well LazWell™ plate after sample preparation extraction. The rapid desorption produces neutral species which are carried into a corona discharge region to undergo an efficient protonation and are subsequently transferred directly into the mass spectrometer for detection.

## Solid Phase Cartridge

The Silia*Prep* CleanDrug cartridge is used for the sample extraction procedure.

**Figure 1:** Silia*Prep* CleanDrug SPE cartridge

| Silia*Prep* CleanDRUG Formats | | |
|---|---|---|
| **Formats** | **Qty / Pk** | **Product number** |
| 1 mL / 50 mg | 100 | SPEC-R651230B-01B |
| 1 mL / 100 mg | 100 | SPEC-R651230B-01C |
| 3 mL / 200 mg | 50 | SPEC-R651230B-03G |
| 3 mL / 500 mg | 50 | SPEC-R651230B-03P |
| 6 mL / 500 mg | 50 | SPEC-R651230B-06P |
| 6 mL / 1g | 50 | SPEC-R651230B-06S |
| 2 mL / 50 mg | 1 | 96W-R651230B-B |
| 2 mL / 100 mg | 1 | 96W-R651230B-C |

**Table 1:** Silia*Prep* CleanDRUG product number

## LDTD-MS/MS System


**Figure 2:** LDTD system on AB SCIEX 5500 Qtrap Mass Spectrometer

## Sample Method

### Extraction procedure

| | |
|---|---|
| **Cartridge:** | Silia*Prep* CleanDrug (1 mL / 100 mg) |
| **Activation:** | 1 mL MeOH |
| | 1 mL Water |
| | 1 mL Na Acetate (100 mM, pH 6) in Water |
| **Load:** | 200 µL sample |
| | 40 µL IS (MDMA-d5 at 200 ng/mL in MeOH) |
| | 600 µL Na Acetate (100 mM, pH 6) in Water |
| **Wash 1:** | 1 mL Water |
| **Wash 2:** | 1 mL MeOH |
| **Elution:** | 1 mL EtAc/IPA/$NH_4OH$ (78/20/2) |
| | After elution, add 40 µL Formic Acid. Mix* |
| | Spot: 2 µL in LazWell plate |

*Organic phase can be evaporated and reconstituted to further concentrate the sample

## LDTD-MS/MS Parameters

**LDTD**

| | | |
|---|---|---|
| Gas Flow: | 3 L/min | |
| Laser pattern: | Time (s) | Power (%) |
| | 0 | 0 |
| | 2 | 0 |
| | 5 | 45 |
| | 7 | 45 |
| | 7.1 | 0 |
| | 8 | 0 |

**MS/MS Method**

| | Transition | CE | DP |
|---|---|---|---|
| MDMA | 194->163 | 12 | 30 |
| MDMA-d5 | 199->165 | 12 | 30 |
| MDA | 180->133 | 20 | 30 |
| MDEA | 208->163 | 12 | 30 |
| Mode: | Positive | | |

## Results and Discussion

### Linearity Results

As shown in **Figure 3,** excellent linearity ($r^2 > 0.99$) with no signs of carryover effect is achieved within the quantification range (50 to 5,000 ng/ml).

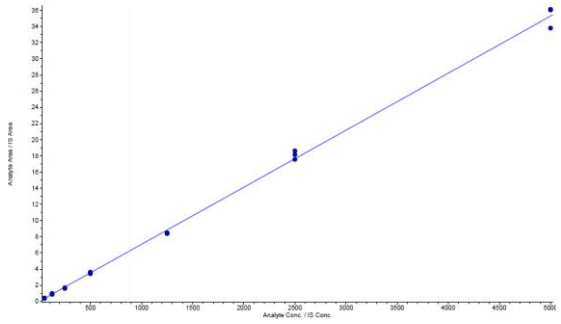

**Figure 3:** Typical standard curve

### Accuracy and Precision

As shown on **Table 2 and 3,** the inter-run and intra-run accuracy and precision are between 96.3 to 111.5% and 1.8 to 11.8% for all three drugs.

| | | Conc. (ng/mL) | N | Mean (ng/mL) | %RSD | %Nom |
|---|---|---|---|---|---|---|
| MDMA | QC-Low | 125 | 9 | 126.0 | 9.3 | 100.8 |
| | Qc-Med | 500 | 9 | 491.9 | 7.1 | 98.4 |
| | Qc-High | 2500 | 9 | 2502.2 | 5.1 | 100.1 |
| MDA | QC-Low | 125 | 9 | 131.7 | 6.8 | 105.3 |
| | Qc-Med | 500 | 9 | 538.4 | 5.5 | 107.7 |
| | Qc-High | 2500 | 9 | 2550.0 | 7.7 | 102.0 |
| MDEA | QC-Low | 125 | 9 | 128.6 | 8.9 | 102.8 |
| | Qc-Med | 500 | 9 | 531.0 | 8.0 | 106.2 |
| | Qc-High | 2500 | 9 | 2565.6 | 4.9 | 102.6 |

**Table 2:** Inter-run precision and accuracy

| | | Conc. (ng/mL) | N | Mean (ng/mL) | %RSD | %Nom |
|---|---|---|---|---|---|---|
| MDMA | L L O Q | 50 | 3 | 49.7 | 7.8 | 99.5 |
| | QC-Low | 125 | 3 | 121.7 | 8.1 | 97.3 |
| | Qc-Med | 500 | 3 | 502.7 | 9.7 | 100.5 |
| | Qc-High | 2500 | 3 | 2450.0 | 4.6 | 98.0 |
| | U L O Q | 5000 | 3 | 5003.3 | 2.5 | 100.1 |
| | | Conc. (ng/mL) | N | Mean (ng/mL) | %RSD | %Nom |
| MDA | L L O Q | 50 | 3 | 51.0 | 4.7 | 102.1 |
| | QC-Low | 125 | 3 | 124.3 | 9.5 | 99.5 |
| | Qc-Med | 500 | 3 | 553.0 | 1.8 | 110.6 |
| | Qc-High | 2500 | 3 | 2600.0 | 10.2 | 104.0 |
| | U L O Q | 5000 | 3 | 5013.3 | 8.3 | 100.3 |
| MDEA | L L O Q | 50 | 3 | 48.1 | 11.8 | 96.3 |
| | QC-Low | 125 | 3 | 123.0 | 7.1 | 98.4 |
| | Qc-Med | 500 | 3 | 557.7 | 8.0 | 111.5 |
| | Qc-High | 2500 | 3 | 2646.7 | 4.5 | 105.9 |
| | U L O Q | 5000 | 3 | 4896.7 | 4.5 | 97.9 |

**Table 3:** Intra-run precision and accuracy

### Recovery

Recovery at 5,000 ng/mL of concentration for each drug is reported in **Table 4** (N=3).

| | MDMA | MDEA | MDA |
|---|---|---|---|
| Recovery (%) | 93 | 100 | 90 |

**Table 4:** Recovery results for all drugs

### Stability Verification

Following the SPE extraction process, all samples were stored at 4°C to evaluate the wet stability of the drugs. After 96h, all samples were re-spotted and analyzed. Linearity, precision and accuracy were evaluated to determine the stability. **Table 5** shows that a wet stability of 96h is obtained with good precision and accuracy of LOQ standard.

The stability of dry samples in LazWell plate was also determined. All standards and QCs are spotted, dried and kept at room temperature for 24h. Then, standards and QCs were analyzed and the linearity, precision and accuracy are verified. **Table 5** shows the dry stability results and the storage conditions of the LazWell.

| | Wet Stability | | | Dry in LazWell (RT) | | |
|---|---|---|---|---|---|---|
| Time (h) | 96 | | | 24 | | |
| Temp. (°C) | 4°C | | | RT | | |
| Conc. (ng/mL) | 50 | | | 50 | | |
| N | 3 | | | 3 | | |
| Drug | MDA | MDEA | MDMA | MDA | MDEA | MDMA |
| Mean (ng/mL) | 50.6 | 46.8 | 49.2 | 44.7 | 45.7 | 53.2 |
| %RSD | 16.1 | 14.2 | 15.6 | 1.2 | 8.6 | 9.2 |
| %Nom | 101.1 | 93.6 | 98.4 | 89.3 | 91.3 | 106.5 |

**Table 5:** Stability Results for MDEA, MDA and MDMA

## Conclusions

The sample solid extraction using **Silia*Prep* CleanDrug** SPE cartridges ensures accurate and precise results with a linear standard curve ($r^2 > 0.99$) for all three drugs.

A fast analysis can be reach using LDTD-MS/MS system. This system allows a total sample-to-sample analysis time of **8 seconds**.

Phytronix Technologies
Parc Technologique du Québec métropolitain
4535, boul. Wilfrid-Hamel, suite 120 Québec, (QC), Canada
www.phytronix.com

SiliCycle
2500, boul. Du Parc-Technologique, Québec, (QC), Canada
Tel: 1 418-874-0355 Toll-free: 1 877-SILICYCLE (North America)
www.SiliCycle.com