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Ultrafast qualitative screening of mitragynine, MDMA, and THC in complex matrices by green technology direct probe ionization mass spectrometry

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1. Overview

- Rapid screening of illicit drugs and controlled substances with direct injection analysis coupled to highly sensitive mass spectrometry
- Environmentally sustainable technology to reduce usage of organic solvents significantly
- Minimal sample preparation of complex matrices including oil, beverage and drug sachets

2. Introduction

There has been substantial surge in the occurrence of illicit drug seizure worldwide. The seized drugs are found in various forms and matrices. This makes it inevitable for authorities to consider more advanced, versatile and rapid detection solutions. Mass spectrometry is the gold standard in forensic drug analysis and amongst the most discriminatory technique. However, extensive sample preparation is required for complicated matrices. Recently, development of Ambient ionization Mass Spectrometry (AMS), which allows samples to be investigated in open air and often with limited sample preparation, has been reported. Shimadzu's AMS technology, Direct Probe Ionization Mass Spectrometry (DPiMS), was utilized to develop fast (1 min) and accurate screening for mitragynine, MDMA, and THC in complex matrices such as kratom drink, oil, and drug sachets.

3. Experimental

3.1 Instrumentation, sample information, and sample pre-treatment

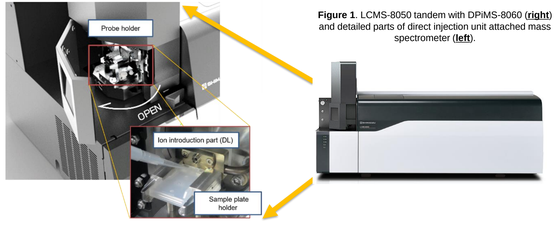

Figure 1. LCMS-8050 tandem with DPiMS-8060 (**right**) and detailed parts of direct injection unit attached mass spectrometer (**left**).

14 real case samples including, 1) six street drug sachets, 2) seven beverages, 3) one cannabis oil were analyzed by using DPiMS-8060 system. Conventional sample pre-treatment for beverage, drug sachet, and oil samples, and simple sample pre-treatment for direct injection were compared and displayed in **Figure 2**. Analysis method was set using scheduled MRM with 0.1 min window for each MRM. Five MRM transitions were used for detection of each drug. Total analysis time per sample is 1 min inclusive of 0.05 min for flushing, as shown in **Figure 3**.

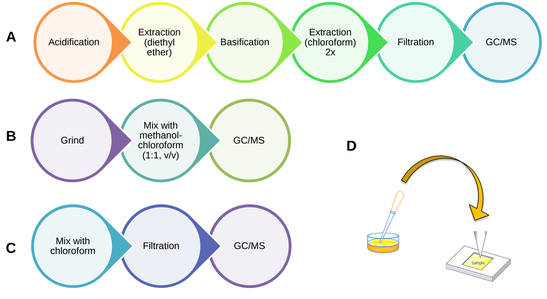

Figure 2. Conventional sample pre-treatment for (**A**) beverage, (**B**) drug sachet, and (**C**) oil samples. Sample pre-treatment for DPiMS analysis is simple and easy as follows: mix with solvent, put into sample plate and slide in into plate holder (**D**).

A fast screening method was established for synthetic, semi-synthetic and plant-based illicit drugs using LCMS-8050 tandem with DPiMS-8060. In this study, the method combines analysis of synthetic and plant-based drugs: ephedrine, MDA, MDMA, ketamine, methamphetamine, 2C-B (2,5-dimethoxy-4-bromophenethylamine), nimetazepam, mitragynine, and THC. Fast screening method for semi-synthetic drugs will be the subject for another study. Chromatogram of mixed drugs on DPiMS is shown in **Figure 4** and used to estimate the limit of detection (LOD). Sensitivity vary to each drug. Identification was conducted using absolute reference ion ratio with 20% allowance relative to quantitative ion (the most intense ion). The LOD was determined based on the lowest concentration at which five MRM transitions were observed and ranged from 10 to 45 ppb for each drug/substance.

No	Compound name	Scheduled MRM (time)
1	Flushing (positive scan)	
2	MDMA	
3	Ketamine	
4	MDA	
5	Methamphetamine	
6	Ephedrine	
7	Nimetazepam	
8	2C-B	
9	THC	
10	Mitragynine	
11	Flushing (negative scan)	

0.05 min 0.1 min

Figure 3. Schematic of scheduled MRM method (total running time 1 min).

4. Results and discussion

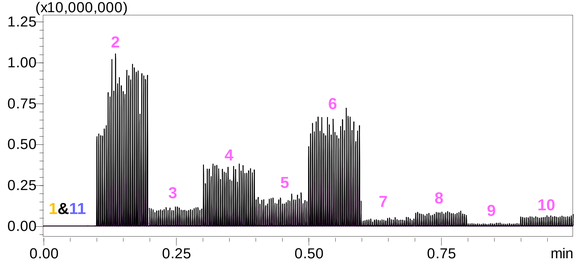

Figure 4. MRM chromatogram of mix standards (concentration vary from 10 to 100ppb) by scheduled MRM on DPiMS. Numbers represent each analysis window: 1) flushing (positive scan), 2) MDMA, 3) Ketamine, 4) MDA, 5) Methamphetamine, 6) Ephedrine, 7) Nimetazepam, 8) 2C-B, 9) THC, 10) Mitragynine, and 11) flushing (negative scan).

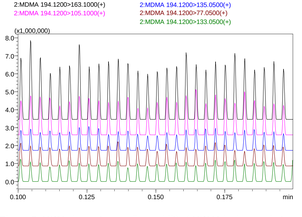

Figure 5. MRM chromatogram (base shift) of MDMA in drug sachet sample by DPiMS. Multiple peaks represent number of needle probe movement during ionization.

Five MRM transitions were used for detection of each drug/substance based on automatic MRM optimization program. The use of MRM transition and scheduled MRM program will enhance selectivity and sensitivity of analysis tremendously. This is in line with Shimadzu's UFMS (Ultra-Fast Mass Spectrometry) ability that provide measurement up to 555 MRM/sec without compromising its sensitivity.

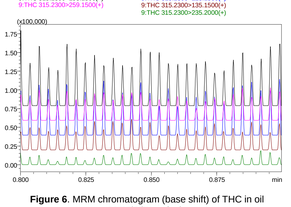

Figure 6. MRM chromatogram (base shift) of THC in oil sample by DPiMS.

Detection of three drugs (MDMA in drug sachets, mitragynine in beverages, and THC in cannabis oil) was feasible in all real case samples and matched to that of GC/MS system (**Figure 5-7**, **Table 1**). In comparison to conventional method, DPiMS cuts down the overall analysis time (sample pre-treatment and running time) significantly. Conventional GC/MS method requires extensive sample pre-treatment and much longer running time (30 min).

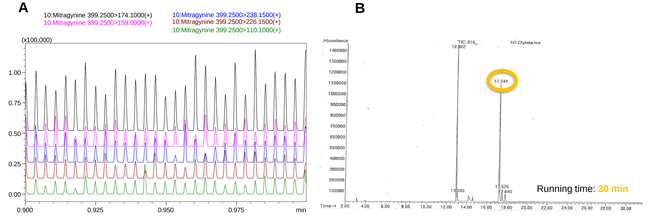

Figure 7. MRM chromatogram (base shift) of mitragynine in beverage sample by DPiMS (**A**) and GC/MS chromatogram of conventional method (**B**). Mitragynine peak was eluted at 17.24 min in conventional GC/MS method. Identification was carried out by comparing to mass spectral database.

Table 1. Screening results of 14 real case samples. Identification was performed based on five MRM transitions for DPiMS and comparison to in-house mass spectral database for GC/MS.

Sample	DPiMS detection	GCMS detection	Sample	DPiMS detection	GCMS detection
Drug sachet 1	MDMA	MDMA	Beverage 1	Mitragynine	Mitragynine
Drug sachet 2	MDMA	MDMA	Beverage 2	Mitragynine	Mitragynine
Drug sachet 3	MDMA	MDMA	Beverage 3	Mitragynine	Mitragynine
Drug sachet 4	MDMA	MDMA	Beverage 4	Mitragynine	Mitragynine
Drug sachet 5	MDMA	MDMA	Beverage 5	Mitragynine	Mitragynine
Drug sachet 6	MDMA	MDMA	Beverage 6	Mitragynine	Mitragynine
Cannabis oil	THC	THC	Beverage 7	Mitragynine	Mitragynine

5. Conclusions

An ultra fast method for qualitative screening of illicit drugs and controlled substances was developed by using Shimadzu direct injection technology, DPiMS-8060 coupled to LCMS-8050. Detection of drugs in various samples was achieved using minimal sample preparation and thus reduce the use of organic solvent significantly. It cuts down analysis time tremendously compared to conventional GC/MS method. DPiMS demonstrates practicality for analyzing multigroup illicit drugs and presents as an alternative green technology for rapid forensic analysis.

References

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