SHIMADZU
Excellence in Science

TECHNOLOGY BRIEF | NO. MST-200

LC/MS – Direct injection – Illicit Drugs and Controlled Substances

Rapid Detection of Illicit Drugs and Psychoactive Plant Component in Sachet Powder, Beverage and Oil Samples by Green Technology DPiMS-8060

Written by:

Udi Jumhawan[1]

Saravana Kumar s/o Jayaram[2]

Ang May Yen[3]

Hazni bin Hashim[3]

Loo Lai Chin[1]

Sandhya Nargund[1]

[1]Shimadzu (Asia Pacific), Singapore

[2]Narcotics Division, Department of Chemistry Malaysia

[3]Customer Support Centre, Shimadzu Malaysia

Abstract

There has been substantial surge in the occurrence of illicit drug seizure worldwide. The seized drugs are found in various forms and matrices. This poses a serious concern 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 preparation is required for complicated matrices. Rapid method is tremendously needed for quick tracing and to expedite litigation. 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, DPiMS-8060 (direct probe ionization mass spectrometry) using PESI (probe electrospray ionization) kit, was utilized to develop fast (1 min) and accurate screening of illicit drugs and controlled substances in complex matrices.

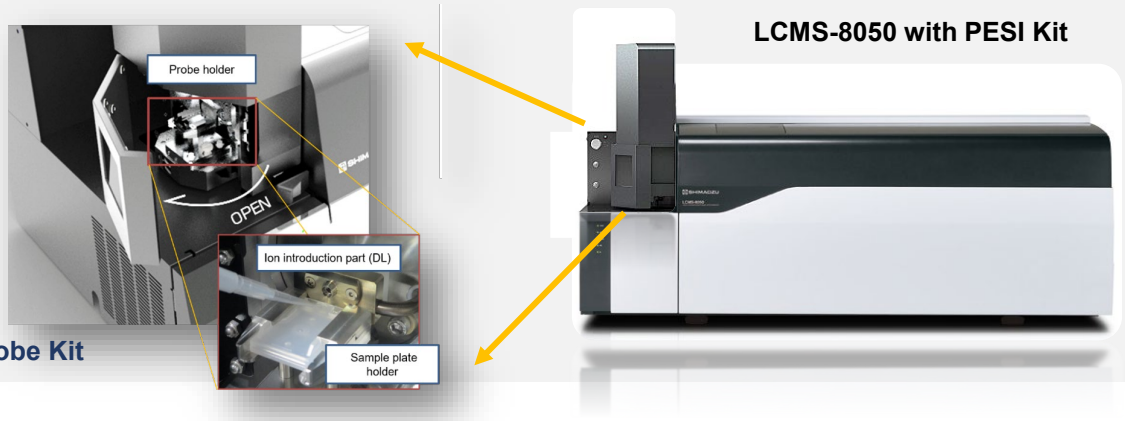
Rapid detection solutions needed to monitor illicit substances such as Kratom plant (left) in beverages

Keywords:
PESI, Direct Injection, Illicit Drugs, Controlled Substances

Highlights

- Rapid screening of illicit drugs and controlled substances with direct injection technology 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 sachet powders

Technologies Featured



1. INTRODUCTION

In addition to illicit substances, the abuse of ketum or kratom (Mitragyna speciosa), especially, has received significant attention. Kratom (Mitragyna speciosa) (Figure 1) has been originally utilized by local community as traditional medicine to combat fatigue and as energy supplement. However, its primary active alkaloids, mitragynine, has opium properties and stimulant-like effect. There have been numerous cases of patients with heroin/opiate withdrawal symptoms from consumption of kratom drink.

Figure 1. Kratom plant

Kratom is still regulated under Poison act in most ASEAN countries and thus categorized as controlled substance. Currently, conversations to group kratom into illicit substance have been reported in USA and ASEAN countries. Illicit drugs and controlled substances are often found in various forms and mixed into complex matrices to cloak the presence. 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. In this study, we reported development of accurate screening for illicit drugs and controlled substance using ambient ionization mass spectrometry, DPiMS-8060. DPiMS utilizes direct injection system and thus reduces the use of organic solvents significantly. This ultrafast method (1 min) was proven to effectively monitor the presence of multiple drugs and controlled substance in complex matrices using fast and easy sample pre-treatment.

2. EXPERIMENT

2.1 Experiment Condition

A total of 14 real case samples including, 1) six sachets, 2) seven beverages, 3) one oil were analyzed by using PESI kit (P/N: 225-32900-58) installed on LCMS-8050. Analytical conditions are described on Table 1. Conventional method by using GC/MS and straightforward method for DPiMS were compared and displayed in Figure 2. Extensive sample preparation is naturally applied for beverage samples to remove sugar content (Figure 2A). By utilizing DPiMS, samples were simply mixed with methanol. Samples were vortexed and filtered with 0.22 µm PTFE filter (when necessary).

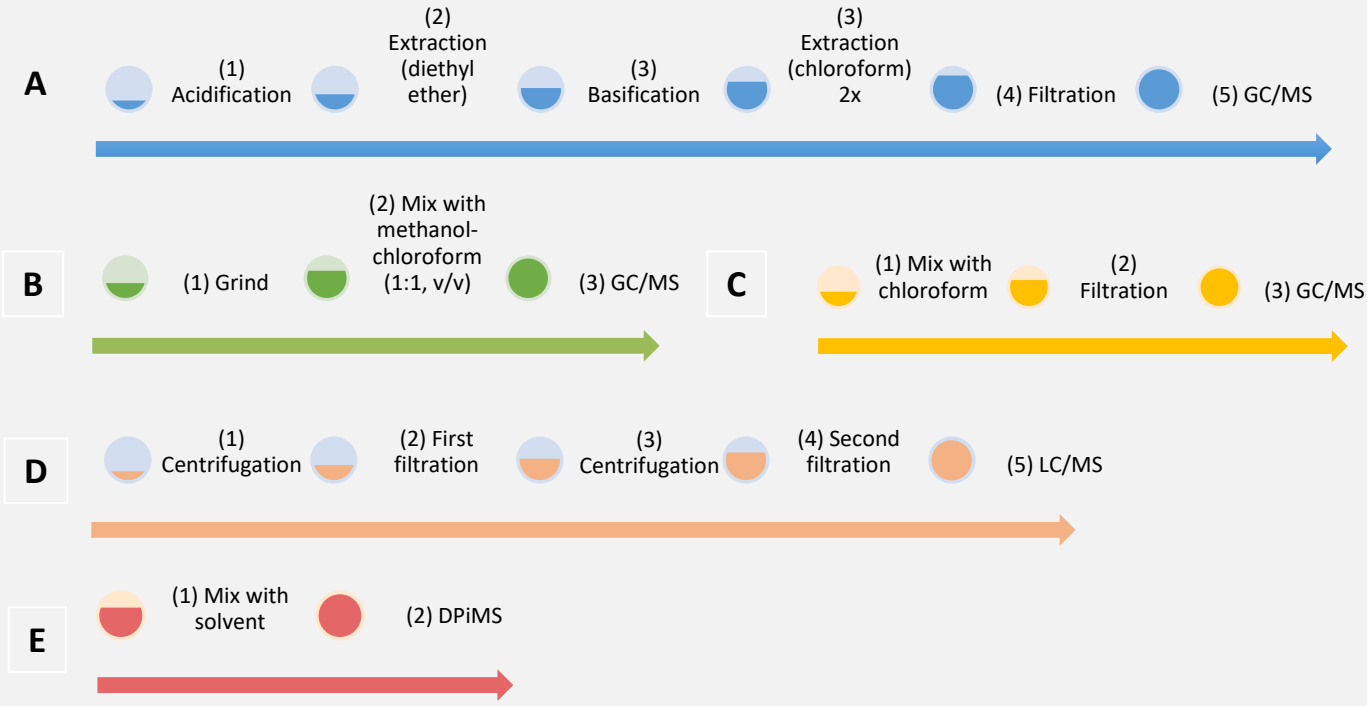


Figure 2. Conventional sample pre-treatment for (A) beverage, (B) sachet, (C) oil samples by GC/MS and (D) for detection of rape drug in beverage by LCMS. (E) Sample pre-treatment for DPiMS analysis is fast and easy as follows: mix with solvent, put into sample plate and slide in into plate holder

2.2 Analytical Setup

Analysis method was set using scheduled MRM with 0.1 min window for each analyte. Total analysis time per sample for nine target analytes is 1 min inclusive of 0.1 min for flushing, as shown in Figure 3.

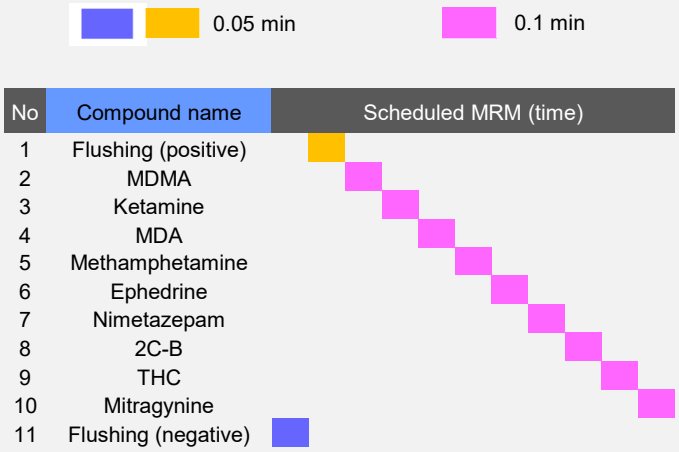


Figure 3. Schematic of scheduled MRM method

Table 1. Analytical conditions for detection of illicit drugs and controlled substance on LCMS-8050 tandem with DPiMS-8060

Acquisition mode	Scheduled MRM with 5 transitions for each target analyte
Ionization mode	Positive mode
Injection volume	10µL
Measurement time	1 min
Dwell time	1 msec
Pause time	1 msec
Interface voltage	2.45 kV
DL temp.	250˚C
Heat block tem.	30˚C
CID gas	270 kPa

3. RESULTS AND DISCUSSION

A fast screening method was established for synthetic drugs and plant-based substances using LCMS-8050 tandem with DPiMS-8060 as follows: ephedrine, nimetazepam, mitragynine, ketamine, MDA (3,4-Methylenedioxyamphetamine), MDMA (3,4-Methylenedioxymethamphetamine), methamphetamine, 2C-B (2,5-dimethoxy-4-bromophenethylamine**)** and THC (Tetrahydrocannabinol). Chromatogram of mixed drugs and substances on DPiMS is shown in Figure 4 and used to estimate the limit of detection (LOD).

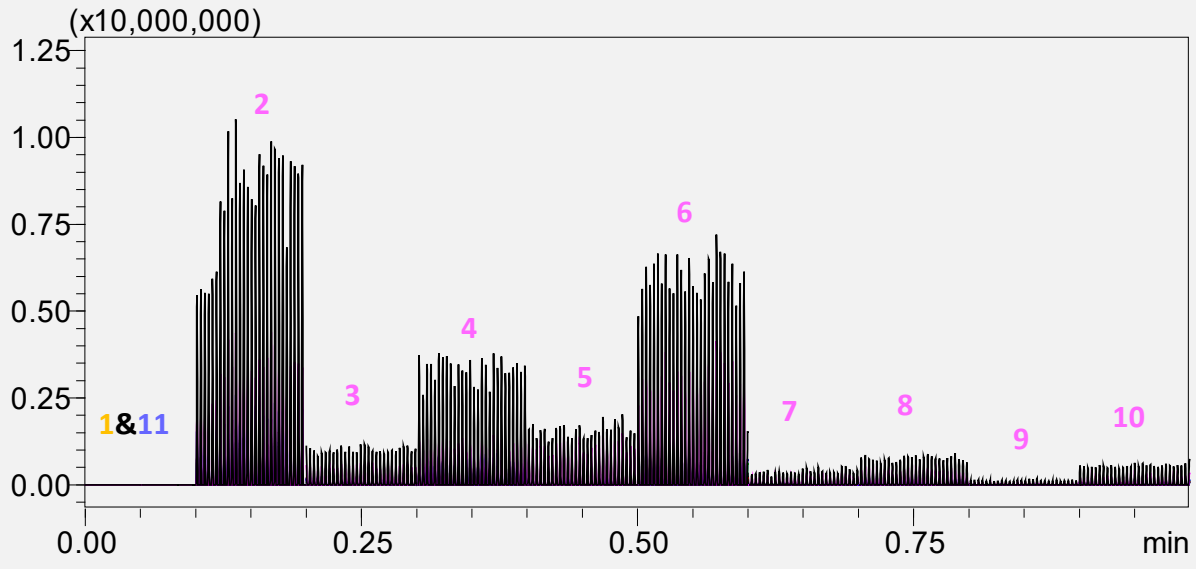


Figure 4. MRM chromatogram of mix standards (concentration vary from 10 to 100ppb) by scheduled MRM on DPiMS. Numbers represent each analysis window: 1) flushing (positive scan), 2) MDMA, 3) Ketamine, 4) MDA, 5) Methamphetamine, 6) Ephedrine, 7) Nimetazepam, 8) 2C-B, 9) THC, 10) Mitragynine, and 11)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

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.

Five MRM transitions were used for detection of each drug/substance based on Shimadzu LC/MS/MS Forensic Toxicology Database (P/N: 225-31175-92) or auto MRM optimization program. The use of MRM transition and scheduled MRM program enhances 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.

Detection of two drugs and one controlled substance (MDMA in sachet powder, mitragynine in beverages, and THC in oil) was feasible in all real case samples and matched to that of GC/MS system (Figure 5A-5D, Table 2). 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).

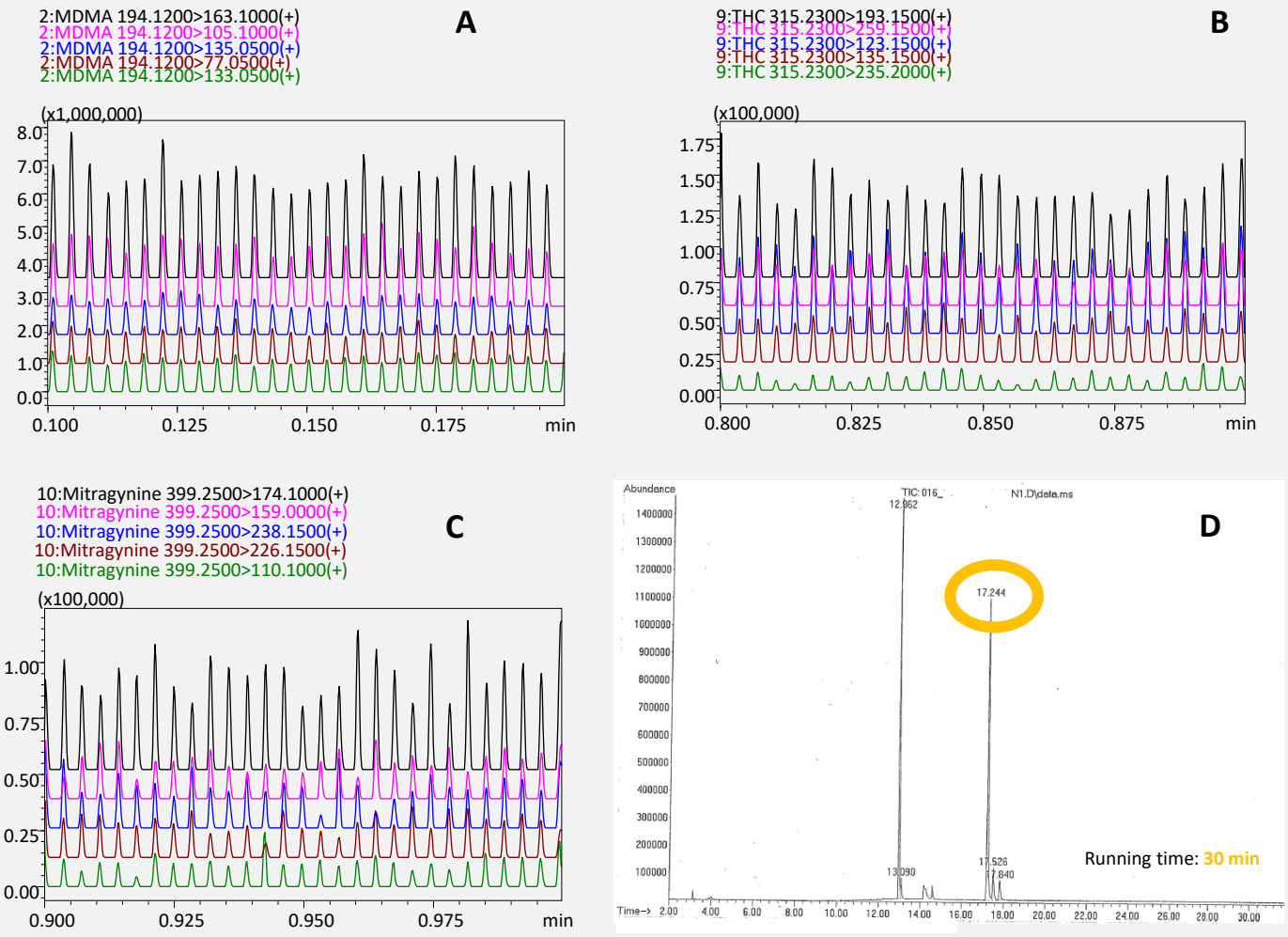


Figure 5. MRM chromatogram (base shift) of MDMA in sachet powder (A), THC in oil (B), mitragynine in beverage (C) by DPiMS. GC/MS chromatogram shows mitragynine peak in same beverage sample in figure 7C (D). Mitragynine peak was eluted at 17.24 min in conventional GC/MS method. Identification was carried out by comparing to GC/MS mass spectral database

Sample	DPiMS detection	GC/MS detection	Sample	DPiMS detection	GC/MS detection
Sachet powder 1	MDMA	MDMA	Beverage 1	Mitragynine	Mitragynine
Sachet powder 2	MDMA	MDMA	Beverage 2	Mitragynine	Mitragynine
Sachet powder 3	MDMA	MDMA	Beverage 3	Mitragynine	Mitragynine
Sachet powder 4	MDMA	MDMA	Beverage 4	Mitragynine	Mitragynine
Sachet powder 5	MDMA	MDMA	Beverage 5	Mitragynine	Mitragynine
Sachet powder 6	MDMA	MDMA	Beverage 6	Mitragynine	Mitragynine
Oil	THC	THC	Beverage 7	Mitragynine	Mitragynine

Table 2. Screening results of real case samples. Identification was performed based on five MRM transitions for DPiMS and comparison to in-house mass spectral database for GC/MS

4. CONCLUSION

An ultra fast method for qualitative screening of illicit drugs and plant-based controlled substances was developed by using Shimadzu direct injection technology, DPiMS-8060 coupled to LCMS-8050. Detection of MDMA, THC, and mitragynine was achieved in complicated matrices 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.

5. REFERENCES

- Harper, L. et al. An overview of forensic drug testing methods and their suitability for harm reduction point-of-care services. *Harm Reduct J*. (2017), 14:52.
- Chiang, C. et al. Using ambient mass spectrometry and LC-MS/MS for the rapid detection and identification of multiple illicit drugs. *J Food and Drug Anal*. (2019), 27(2), 439-450.
- Vetri, C. et al. Current perspective on the impact of Kratom use. *Substance Abuse and Rehab*. (2019), 10. 23-31.
- Albright, JA. Et al. Detecting ketamine in beverage residues: Application in date rape detection. *Drug Test Anal*. (2012). 4(5), 337-341.
- DPiMS-8060 (Direct Probe Ionization Mass Spectrometer Kit) https://www.shimadzu.com/an/ms/dpims/8060/index.html.
- Shimadzu LC/MS/MS Forensic Toxicology Database. https://www.shimadzu.com/an/lcms/forensic_toxicology-database/index.html.

FIND OUT MORE

READ MORE

LC/MS/MS Forensic Toxicology Database (P/N: 225-31175-92)

❖ **MRM & Spectral Library database contains information on more than 2,500 compounds**

The spectral library database is built using two separation conditions (ODS and Biphenyl). Both methods have information on clinical and forensic compounds of interest in routine analysis. The ODS method contains information on 1,250 compounds and the Biphenyl method contains 1,281 compounds. Compound datasheet includes monoisotopic mass, RT, CAS number, formula and compound class. This package provides Synchronized Survey Scan parameters (MRM parameters, MRM intensity threshold and triggered product ion scan parameters) optimized for screening analysis.

❖ **Simplified Acquisition and Identification**

The Forensic Toxicology Database includes optimized LC-MS/MS data acquisition parameters and a library database to help clinical and forensic researchers build screening and quantitation methods quickly, simplifying method development.

❖ **Enhanced identification by merged spectrum**

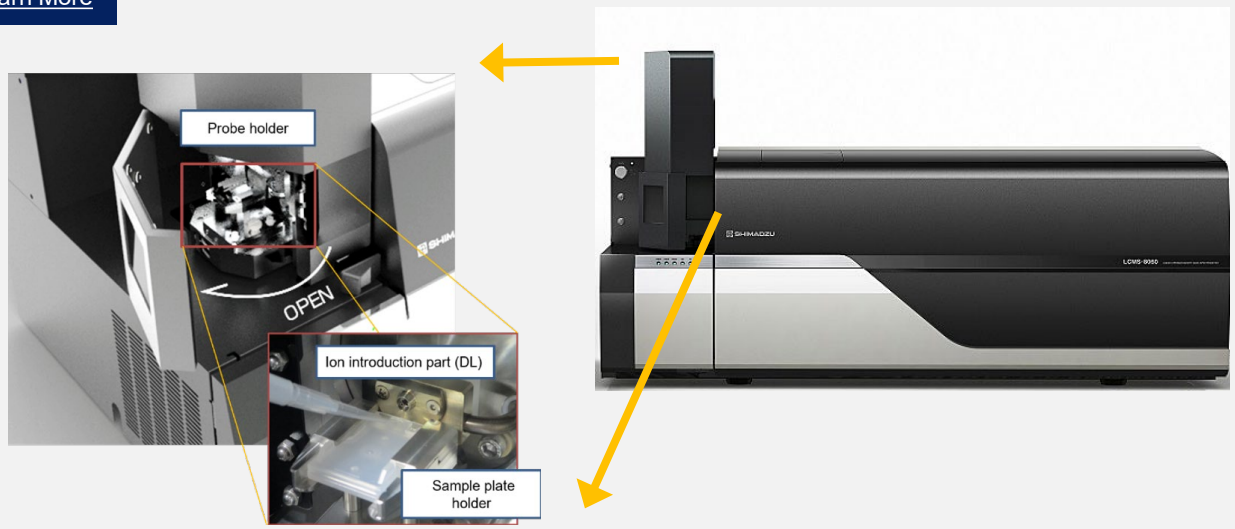
Each certified reference material was acquired with three different collision energies to generate an information-rich merged-CE spectrum which can be used in library matching and compound verification. Matching with a merged-CE spectrum library can be a powerful tool to identify compounds with a library score.

Learn More

DPiMS-8060 (P/N:225-32900-58)

DPiMS-8060 Kit for Direct Probe Ionization Mass Spectrometer uses a probe to extract a micro quantity of liquid and inject it into the MS unit of triple quadrupole mass spectrometer. This was achieved by using an ultrafine needle/probe to sample an extremely small volume of sample on its surface and subsequently applying high voltage to the needle to imitate an ESI probe. DPiMS can be a robust solution for the routine analysis of high-complexity matrices, such as plasma or food extract, as contamination of MS hardware can be perfectly mitigated. Moreover, direct sampling from solid samples causing minimal destruction might enable new applications such as real-time analysis of live tissues or cells.

Learn More



SHIMADZU

Shimadzu (Asia Pacific) Pte. Ltd
www.shimadzu.com.sg