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Dear Readers,

Masami Tomita

General Manager,
Analytical & Measurement Instruments Division

I am Masami Tomita, the new General Manager of the Analytical and Measuring Instruments Division. I have replaced Yoshiaki Mase, who was appointed Senior Executive this April.

Prior to becoming General Manager of the Analytical & Measuring Instruments Division, from 2012 to 2020, I led the Liquid Chromatography (LC) Business Unit. In this position, I was involved in the development of cutting-edge LC-related technologies and products from a customer perspective, and engaged in business activities aimed at supporting global customer operations and contributing to society. From 2020 to 2023, I served as the Deputy General Manager in charge of development and manufacturing of the Analytical & Measuring Instruments Division. During this time, I worked to build partnerships with customers, improve product development and technical capabilities, and ensure a stable and efficient supply of high-quality products.

My tenure as Deputy General Manager coincided with the Covid-19 pandemic. In the face of this unprecedented situation, we developed a rapid test reagent for Covid-19 using our innovative genetic testing reagent technology and also launched AutoAmp, a fully automatic genetic analyzer that enables rapid testing at clinics in the city. This achievement reflects well on how we aim to realize our company motto, "Contribute to society through science and technology," by responding quickly to social concerns.

As the world's population ages, the importance of healthy life expectancy will increase. In addition, we will be required to proactively address environmental issues by developing more environmentally friendly technologies and new energy sources to create a sustainable society. To address these social issues, we will be more active than ever in joint research with researchers from around the world.

I believe that analytical measurement technology is the basis of all industries by "making the invisible visible and the unknown understandable." We have launched an initiative called "Analytical Transformation (AX)" to make it easier to know what we want to know by incorporating the latest AI and other technologies, and we will promote innovative development that can revolutionize customers' workflows.

For our new medium-term management plan, which started this fiscal year, we have adopted the basic policy of "becoming an innovative company that solves social issues together with our partners around the world." In addition, we are promoting contributions to the realization of "human health" and "global health" under our corporate motto of "contributing to society through science and technology." Toward the realization of these goals, we will be more active in our interactions with you; this journal serves as just one resource to introduce contents that will be beneficial to you.

This issue features a special section on "Forensics / Toxicology", an area where science and technology are particularly important and needed. We introduce researchers working on the front lines and highlight applications that make full use of innovative technologies.

First, Dr. Jose Luiz Costa, Professor of Toxicology and Head of Campinas Poison Control Center, University of Campinas, talks about the concept of green toxicological analysis (GAT) and new psychoactive substances in Brazil. Next, Dr. Michelle Peace, a professor at Virginia Commonwealth University, speaks about the broad implications of vaping on public safety issues and developing methods for analyzing new THC isomers and derivatives.

In addition to the interviews, we introduce related applications using our latest technologies, including detection and differentiation of synthetic cannabinoids, qualitative screening of drugs in whole blood, and human hair cross-section analysis. Furthermore, we highlight recent initiatives related to Forensics / Toxicology, new partnerships, the 20th anniversary of the Koichi Tanaka Mass Spectrometry Research Laboratory, and a unique new product (AIRsight: Infrared and Raman Spectroscopy).

We hope that this journal provides you with ideas for solving issues now and in the future. Your generous feedback is always appreciated.

Yours Sincerely,

Forensics / Toxicology Issue2

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Interview 1 Interview with Dr. Jose Luiz Costa

"A trusted partnership."

We interviewed Dr. Jose Luiz Costa, Professor of Toxicology and Head of Campinas Poison Control Center, University of Campinas (UNICAMP, Brazil).

Dr. Jose Luiz Costa, thank you very much for spending some time for this interview. At first, How did you become familiar with Shimadzu?

My first contact with Shimadzu equipment was back in 2002, when I assumed the position of Forensic Expert in the Technical-Scientific Police of São Paulo, Brazil. At that time, I worked with a GC-17A for determination of cocaine and adulterants in seized drugs. I also worked a UV-Vis spectrophotometer to analyze pharmaceuticals forms (tablets, pills), and atomic absorption spectroscopy to analyze some metals of forensic interest.

Over time, I began to work with LC-MS/MS in forensic toxicology, for the screening of drugs of abuse in biological samples (postmortem and antemortem). When I came to the University of Campinas, we continued to work with Shimadzu equipment (LC-MS/MS, LC-QTOF GC-MS/MS, HS-GC-FID) in toxicological tests, now for research and diagnosis of intoxications at the university hospital.

Could you outline the research you have been doing and let us know what discovery and achievement have been made so far?

One of the research lines of our group is the development of bioanalytical methods using the concept of green toxicological analysis (GAT). The concept of GAT is very similar to green analytical chemistry, where there is interest in analytical processes that generate less waste, use less energy, less toxic solvents and reagents, etc. In the case of toxicology, there is also the interest in using smaller biological sample volumes, or even using dried samples such as dried blood spots. The use of smaller amounts of samples is important,

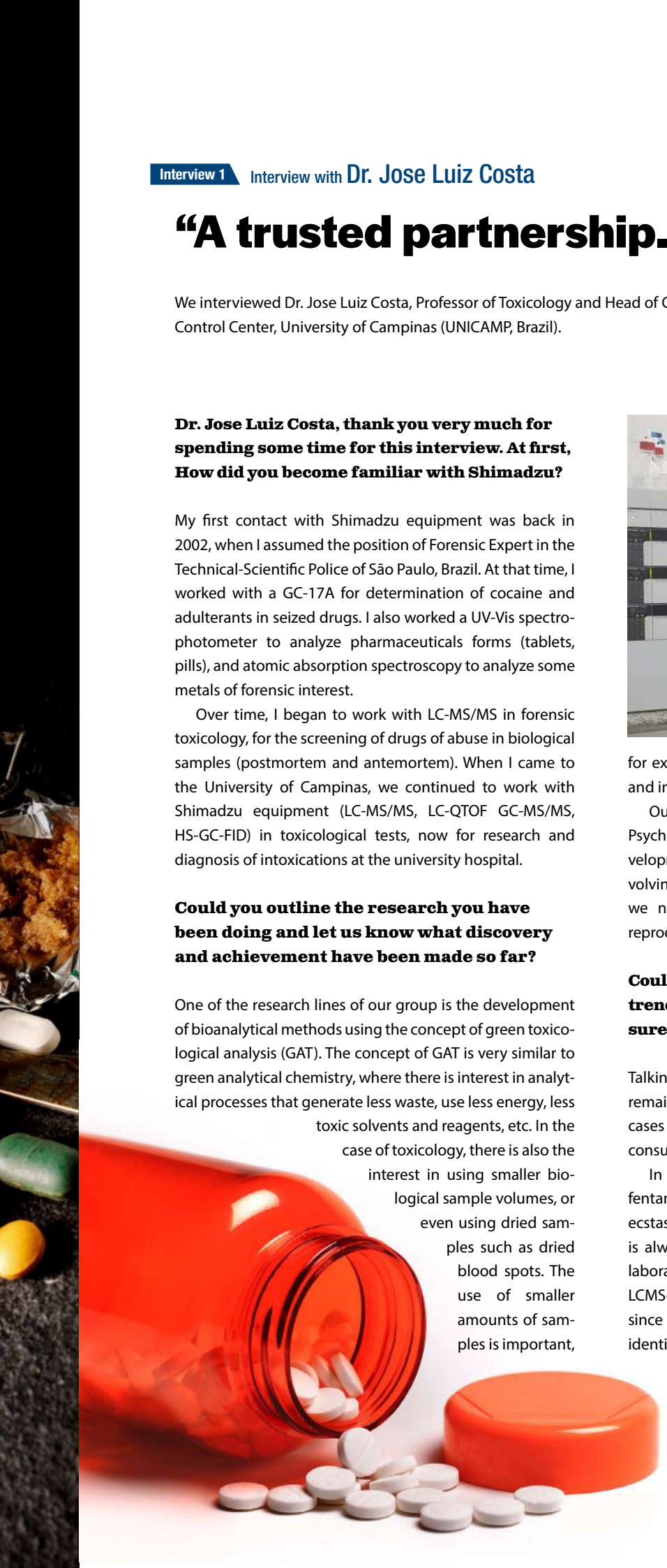
for example, in tests performed on newborns or children, and in pharmacokinetic studies using laboratory animals.

Our group has also been dedicated to research with New Psychoactive Substances in Brazil, working on method development, case reports and epidemiological studies involving this group of drugs of abuse. In both research fields, we need robust equipment with great sensitivity and reproducibility.

Could you give us a brief introduction to any trends in illicit drugs and regional countermeasures against them in your country or region?

Talking about illicit drugs, the biggest challenge in Brazil remains cocaine (mainly as crack cocaine). We rarely have cases of methamphetamine intoxication, and heroin consumption in our country is practically zero.

In recent years we have seen some cases of abuse of fentanyl, sold in the forms of white powder, pills (similar to ecstasy) and blotter paper (similar to LSD). Identifying NPS is always a challenge for forensic and clinical toxicology laboratories. We have a screening method using the LCMS-8060 with a regularly updated MRM catalog, and since July/2022 we have been using the LCMS-9030 to identify new cases of NPS poisoning.



Dr. Jose Luiz Costa

Congratulations to you on being received the TIAFT Achievement Award In 2021. Could you share in brief more about this achievement?

The TIAFT Achievement Award is bestowed upon TIAFT members who are recognized for their outstanding achievements in forensic toxicology through their scientific activities and outputs. The recipient should be a TIAFT member under 46 years of age by December 31st of the year that the award is given and have been an active member of the Association. The list of previous awardees is shown at TIAFT, TIAFT Achievement Award.

What are the main struggles in working with biological samples for toxicological analysis and how are Shimadzu instruments (HPLC, GC, GC-MS and LC-MS) helping you in both your research and your laboratory routine analysis?

Biological samples for analytical toxicology are always complex matrices, with huge amount of interferents (lipids, proteins, ions), requiring elaborate sample preparation in order to obtain reproducible results. Another problem is the fact that many toxicants are present in biological samples in very low concentrations (sometimes on the order of pg/mL), requiring that the sample preparation process has a high concentration factor. Using sensitive equipment, such as the LCMS-8060 and GCMS-TQ8050, we can detect toxicants in this order of magnitude, without the need for a large sample concentration factor. This makes sample preparation simplified, uses reduced volumes (of samples and solvents) and it is faster, increasing laboratory productivity.

Dr. Jose Luiz Costa

Could you tell us why you chose Shimadzu as your partner when you started this project?

My experience as a laboratory analyst (Forensic Expert) has always been very good when working with Shimadzu equipment, which has always been very robust, simple to operate and easy to maintain. When I started coordinating projects, I saw that in addition to these fundamental technical characteristics, I also had good support from the sales and post-sales team here in Brazil. This made me choose Shimadzu as a partner in the projects.

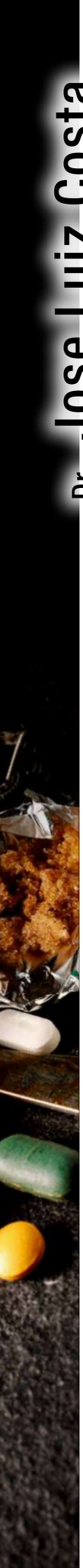
Shimadzu's strengths are the service provided by the sales and post-sales team, who are always very attentive, serving us quickly. And, of course, the very competitive costs of equipment and maintenances.

Finally, could you share any requests that you have with respect to analytical and measuring instrument vendors?

Analytical equipment is becoming more and more modern and technological, and today few people are trained to carry out minor interventions and maintenance. I would say that the company could invest in more user maintenance training, enabling them to carry out a greater number of procedures without having to request support from a specialized technician. I understand that this would be beneficial for both the user and the company's service team.

It was significant to know what you think of us and our collaboration. We will strive to meet your expectation more than ever. Thank you very much.

Dr. Jose Luiz Costa



Recent publications using Shimadzu instruments

Rodrigues, L. C., Kahl, J. M., de Chinaglia, K. O., de Campos, E. G., Costa, J. L. (2022). Dispersive liquid-liquid microextraction of 11-nor-Δ9-tetrahydrocannabinol-carboxylic acid applied to urine testing. *Bioanalysis*, 14(2), 87–100.

da Cunha, K. F., Kahl, J. M. M., Fiorentin, T. R., Oliveira, K. D., Costa, J. L. (2022). High-sensitivity method for the determination of LSD and 2-oxo-3-hydroxy-LSD in oral fluid by liquid chromatography–tandem mass spectrometry. *Forensic toxicology*, 40(2), 322–331.

de Araujo, K. R. G., Fabris, A. L., Neves Júnior, L. F., de Carvalho Ponce, J., Soares, A. L., Costa, J. L., Yonamine, M. (2023). The mystery behind the apprehensions of the selective cannabinoid receptor type-2 agonist BZO-HEXOXIZID (MDA-19) as a drug of abuse. *Forensic toxicology*, 41(1), 142–150.

Chinaglia, K. O., Arantes, A. C. F., Cunha, K. F. D., Campos, E. G., Kahl, J. M. M., Rodrigues, L. C., Costa, J. L. (2022). Development of analytical method for the determination of methylphenidate, the analog ethylphenidate and their metabolite ritalinic acid in oral fluid samples by micro-QuEChERS and liquid chromatography-tandem mass spectrometry. *Journal of chromatography. B*, Analytical technologies in the biomedical and life sciences, 1205, 123330.

Arantes, A.C.F., da Cunha, K.F., Cardoso, M.S., Oliveira, K. D., Costa, J. L. (2021) Development and validation of quantitative analytical method for 50 drugs of antidepressants, benzodiazepines and opioids in oral fluid samples by liquid chromatography–tandem mass spectrometry. *Forensic Toxicol 39*, 179–197.

Kahl, J. M. M., da Cunha, K. F., Rodrigues, L. C., Chinaglia, K. O., Oliveira, K. D., Costa, J. L. (2021). Quantification of amphetamine and derivatives in oral fluid by dispersive liquid-liquid microextraction and liquid chromatography-tandem mass spectrometry. *Journal of pharmaceutical and biomedical analysis*, 196, 113928.

Marilia S Cardoso, Rafael Lanaro, Raul C Dolores, Damila R Morais, Ana Carolina Furiozo Arantes, Karina Diniz Oliveira, Jose Luiz Costa, (2022) Determination of Drugs of Abuse in Hair by LC–MS-MS: Application to Suicide Attempts Investigation, *Journal of Analytical Toxicology*, 46(5), 577–581.

Taís B Rodrigues, Damila R Morais, Victor A P Gianvecchio, Elvis M Aquino, Ricardo L Cunha, Marilyn A Huestis, Jose Luiz Costa, (2021) Development and Validation of a Method for Quantification of 28 Psychotropic Drugs in Postmortem Blood Samples by Modified Micro-QuEChERS and LC–MS-MS, *Journal of Analytical Toxicology*, 45(7), 644–656.

Rodrigues de Morais, D., Francisco da Cunha, K., Betoni Rodrigues, T., Lanaro, R., de Melo Barbosa, L., Jardim Zacca, J., Nogueira Eberlin, M., Costa, J. L. (2020). Triple quadrupole-mass spectrometry protocols for the analysis of NBOMes and NBOHs in blotter papers. *Forensic science international*, 309, 110184.

da Cunha, K. F., Rodrigues, L. C., Huestis, M. A., Costa, J. L. (2020). Miniaturized extraction method for analysis of synthetic opioids in urine by microextraction with packed sorbent and liquid chromatography-tandem mass spectrometry. *Journal of chromatography. A*, 1624, 461241.

da Cunha, K. F., Oliveira, K. D., Huestis, M. A., Costa, J. L. (2020). Screening of 104 New Psychoactive Substances (NPS) and Other Drugs of Abuse in Oral Fluid by LC-MS-MS. *Journal of analytical toxicology*, 44(7), 697–707.

Costa, J. L., Cunha, K. F., Lanaro, R., Cunha, R. L., Walther, D., Baumann, M. H. (2019). Analytical quantification, intoxication case series, and pharmacological mechanism of action for N-ethylnorpentylone (N-ethylpentylone or ephylone). *Drug testing and analysis*, 11(3), 461–471.

▶ Graduated in Biochemical-Pharmacy (2001), Master's degree in Toxicology and Toxicological (2004), PhD in Analytical Chemistry (2008). Post-doctorate at the National Institute on Drug Abuse (NIDA-NIH, 2013-2014). Forensic Toxicologists at the Superintendence of the Technical-Scientific Police of São Paulo (2002-2016). Past-President of the Brazilian Society of Toxicology (SBTox, 2012-2013). In 2021, received the TIAFT Achievement Award in recognition of his contribution to forensic toxicology. Currently, Associate Professor at the Faculty of Pharmaceutical Sciences, University of Campinas and Executive-Coordinator of the Campinas Poison Control Center.

Interview 2 Interview with Dr. Michelle Peace

"We share a core principle of being caretakers of each other and our earth that drives our collaborations and relationship."

We interviewed Dr. Michelle Peace, Professor at Virginia Commonwealth University, on her research and projects in the Forensic Science program.

Thank you very much for spending some time for this interview. At first, could you outline the research and let us know what discovery and achievement have been made so far?

My pleasure – I appreciate the platform because I love to talk about what the research team has accomplished! We have a grant from the National Institute of Justice that supports evaluating the broad implications of vaping on public safety issues. The research has also supported public health education.

Early on, my team had to figure out the fundamentals of vaping – from the device construction to e-liquid formulations – to then postulate and monitor the marketplace for changes that allow for the inhalation of drugs other than nicotine. So, to the best of my knowledge, my team was the first to scholastically publish on the e-cig device evolution in a manuscript about an overdose from Blue Lotus using a dripping device (Poklis, J. L et al. 2017a).

We were also out front about the quality of nicotine e-liquid formulations (Poklis, J. L. et al. 2017b; Peace, M. R et al. 2018; Holt, A. K. et al. 2021a) in the United States, before there were any federal regulations. We've been vocal about the chemicals used in the formulations that are considered Generally Regarded As Safe (GRAS) to eat, but not to inhale (Holt, A. K., et al. 2021b). And, our most recent research is in evaluating the impact of vaping ethanol on roadside impairments evaluations, the breath tests, and on the formation of ethanol biomarkers. We have received dozens of emails and calls about people claiming they don't drink but are failing ethanol-based drug tests. So, we are developing a unified method to evaluate 6 ethanol biomarkers in blood, urine, and oral fluid. We also know that people charged with DUI are claiming that they were vaping. They claim that the roadside impairment tests are skewed. According to our clinical study, this is likely not the case. The manuscript describing this study is under review.

We also do a lot of work in the cannabis space, developing methods for analyzing these new THC isomers and derivatives (Holt, A. K., et al. 2022a; Holt, A. K., et al. 2022b) that are poisoning thousands of people nationwide. And, we have several other projects that have significant public health implications, that I am particularly proud of, not the least of which is a study to evaluate whether or not physicians can predict if a newborn child is at risk of neonatal abstinence syndrome (Gesseck, A. M., et al. 2021).

So, we have a lot going on – and I have a great team who is passionate about these questions.

Dr. Michelle Peace

How are Shimadzu instruments helping you in your research?

My lab is predominantly a Shimadzu lab. We have 2 GC-MSs, a GC-FID, and an LC-MS/MS. So, we use every one of them for different kinds of analyses. We have developed a really robust untargeted method on the GC-MSs, we do some quantitation work on the GC-MS, but really use the LC-MS/MS for that work because of its sensitivity and ease of sample prep. And, of course, we use the GC-FID for the volatiles analysis to identify ethanol and other solvents in products and in tissue. I'm really fortunate to have be able to explore all these issues in-house.

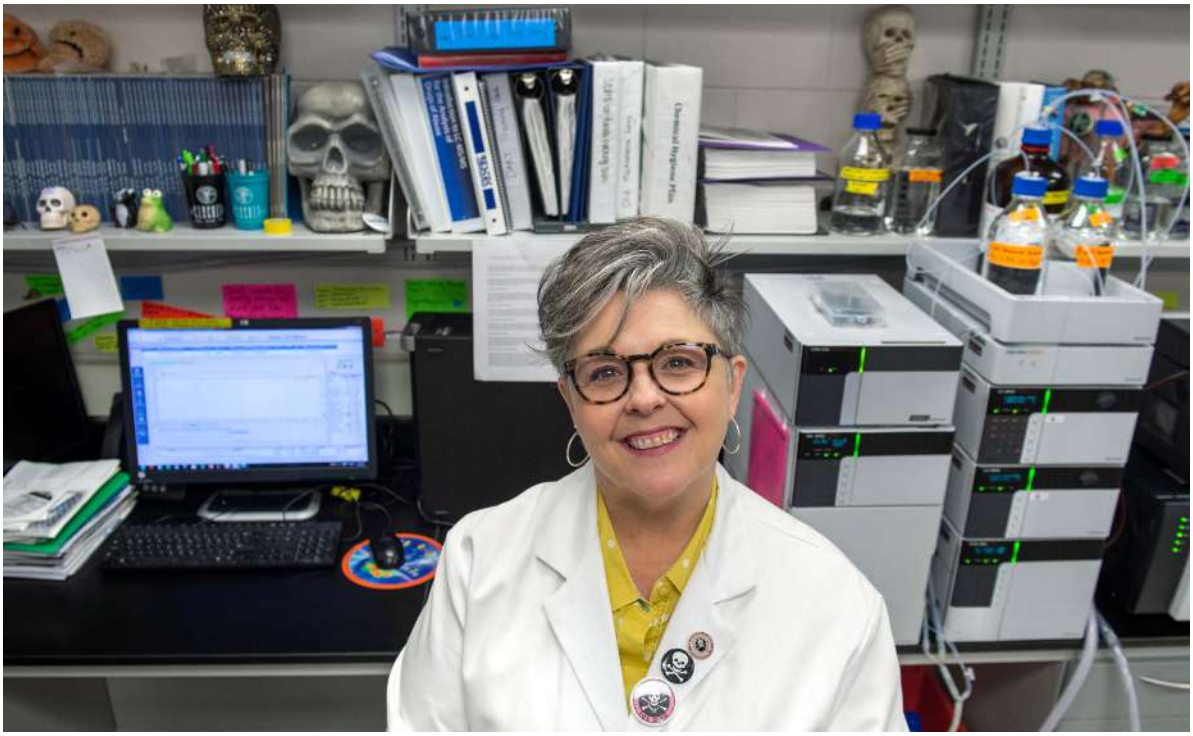
Could you tell us why you chose Shimadzu as your partner when you started this project?

Well, when I first started evaluating which instruments to purchase, I evaluated all the major manufacturers. We all know there are pros and cons to each platform, but I needed a relationship. And, while this may seem strange, a corporate philosophy and code of ethics mean something to me. When I learned that the corporate mission was embedded all the way to their employee evaluations, this felt important in helping me do what I needed to do in my personal mission to support public safety and health. When I started working with Shimadzu, I really felt like they were approaching my needs like a partner would. And, they worked hard with me to get the necessary functionality that enabled me to dig deeper while not poking giant holes in my very shallow pockets, for which I am deeply grateful. Admittedly, my lab operates fairly independently, so, when I need some help and ask, I really need it and there's usually a multi-faceted tactic to get me online again or help me in developing a method. I also have a lot of student-researchers and they call for a lot of help – and I always appreciate that my students are always taken care of – that the service at Shimadzu is done in a teaching spirit.

This is not to say that the instruments are not great. We have been very successful is leveraging the Shimadzu technology to make major strides in discoveries and there are definitely Shimadzu tools that I know exist and I say "wow, if only a had some cash…" For instance, the effort to minimize contamination on the front end of an LC-MS/MS is such a critical feature, and the fast switching between positive and negative ion modes is known to reduce run times. These are important considerations whether you are working in a research lab or a production lab.

Could you share your partnership between you and Shimadzu?

Well, what I appreciate are the relationships. Frankly, I feel like I'm pretty small potatoes – meaning, I'm not buying a new instrument every 2-3 years. BUT, they treat me and my students and my research questions like we've got $5M budget every year. When I think a widget on an



instrument could be better, they take that into consideration – they listen to my team and ask questions. When I have an issue, they unpack the problem and call in others if necessary. We've asked some crazy questions and requested things that I thought were not workable – and they've figured that out. That's a great collaborator.

It was significant to know what you think of us and our collaboration. We will strive to meet your expectation more than ever. Thank you very much.

Related publications using Shimadzu instruments

Poklis, J. L., Mulder, H. A., Halquist, M. S., Wolf, C. E., Poklis, A., & Peace, M. R. (2017a). The Blue Lotus Flower (Nymphea caerulea) Resin Used in a New Type of Electronic Cigarette, the Re-Buildable Dripping Atomizer. *Journal of psychoactive drugs*, 49(3), 175–181.

Poklis, J. L., Wolf, C. E., 2nd, & Peace, M. R. (2017b). Ethanol concentration in 56 refillable electronic cigarettes liquid formulations determined by headspace gas chromatography with flame ionization detector (HS-GC-FID). *Drug testing and analysis*, 9(10), 1637–1640.

Peace, M. R., Mulder, H. A., Baird, T. R., Butler, K. E., Friedrich, A. K., Stone, J. W., Turner, J. B. M., Poklis, A., & Poklis, J. L. (2018). Evaluation of Nicotine and the Components of e-Liquids Generated from e-Cigarette Aerosols. *Journal of analytical toxicology*, 42(8), 537–543.

Gesseck, A. M., Peace, M. R., Nanco, C. R., Wolf, C. E., Hendricks-Muñoz, K. D., Xu, J., & Poklis, J. L. (2021). Neonatal Exposure to Tramadol through Mother's Breast Milk. *Journal of analytical toxicology*, 45(8), 840–846.

Holt, A. K., Poklis, J. L., Cobb, C. O., & Peace, M. R. (2021a). Identification of Gamma-Butyrolactone in JUUL Liquids. *Journal of analytical toxicology*, 45(8), 892–900.

Holt, A. K., Poklis, J. L., & Peace, M. R. (2021b). A Retrospective Analysis of Chemical Constituents in Regulated and Unregulated E-Cigarette Liquids. *Frontiers in chemistry*, 9, 752342.

Holt, A. K., Karin, K. N., Butler, S. N., Ferreira, A. R., Krotulski, A. J., Poklis, J. L., & Peace, M. R. (2022a). Cannabinoid-based vaping products and supplement formulations reported by consumers to precipitate adverse effects. *Drug testing and analysis*, 10.1002/dta.3253. Advance online publication.

Holt, A. K., Poklis, J. L., & Peace, M. R. (2022b). Δ8-THC, THC-O Acetates and CBD-di-O Acetate: Emerging Synthetic Cannabinoids Found in Commercially Sold Plant Material and Gummy Edibles. *Journal of analytical toxicology*, 46(8), 940–948.

▶ Dr. Peace is a Professor for the FEPAC-accredited Department of Forensic Science at VCU and is one of the founding faculty for the Department. She served as Associate Chair and Chair for nearly a decade. Dr. Peace has been funded by the National Institute of Justice since 2014 to study the efficacy of electronic cigarettes, particularly as they pertain to substance use and abuse. Dr. Peace has testified to the Food and Drug Administration regarding issues of quality assurance, public health, and public safety with the emerging cannabis industry. She has been featured in the New York Times, Consumer Reports, and AARP. The American Chemical Society and Discover Magazine recognized her research contributions in 2018 and 2019 as addressing some of the most salient and vexing issues in the nation.

Forensics / Toxicology

Detection and Differentiation of Positional and Structural Isomers of Synthetic Cannabinoids Using Gas Chromatography Product Ion Spectrometry

Cynthia Lahey[1], Chua Chun Kiang[1], Yuki Sakamoto[2]

[1] Shimadzu (Asia Pacific) Pte Ltd.
[2] Shimadzu Corporation

Introduction

Forensic chemists face the challenge of identifying new psychoactive substances (NPS), whereby the general structures of controlled drugs are modified to evade legislative banning. Hence, a plethora of synthetic cathinones and cannabinoids has been available to the public, causing a global social problem. It is therefore crucial that analytical methods are developed for identifying and differentiating new analogues of synthetic drug substances, to prevent potential trading and abuse. Additionally, drug legislation is made more challenging with the use of synthetic cannabinoid containing products, typically marketed as “herbal mixtures”, which consists of analogues of synthetic cannabinoids. In this study, simultaneous multi-reaction monitoring (MRM) and product ion scan (PIS) acquisition methods have been developed for detection and differentiation of isomeric synthetic cannabinoids.

Experimental

Methods and Materials

Data were acquired using a GC-TQMS system (GCMS-TQ8050 NX, Shimadzu Corporation, Japan) in electron ionization mode. Separation was achieved using a SH-Rxi-5Sil MS capillary column (30 m × 0.25 mm × 0.25 µm). Two classes of synthetic cannabinoids were analysed. They are a mixture of JWH-018 (1-pentyl-3-(1-naphthoyl)indole) and its seven structural isomers (Figure 2), and a mixture of four positional isomers of fluoro-PB-22 (Quinlin-8-yl 1-pentyfluoro-1H-indole-3-8-carboxylate) (Figure 4). 10 µg/ml synthetic cannabinoids standards were used for method development and stability tests.

Figure 1. GCMS-TQ8050 NX

Results and Discussion

A. Method Development for JWH-018 Isomers

A-1. Identification Points of JWH-018 Isomers

JWH-018 and its seven structural isomers were identified and differentiated using the identification points below:

1. **1 target MRM transition**
2. **2 reference MRM transitions**
   - ○ MRMs should consist of a distinctive precursor and/or product ion
3. **Product Ion Scan (PID) mass spectra**
   - ○ PIS was acquired from m/z 341 at an optimized single collision energy (10 V)
   - ○ Mass spectra should consist of 1 target ion and 1 or more reference ion(s), and the ion ratio% of the reference ions should fall within the tolerance range of the set ion ratio%
   - ○ Similarity to PIS mass spectrum registered be 80% (i.e. similarity index% ≥ 80)

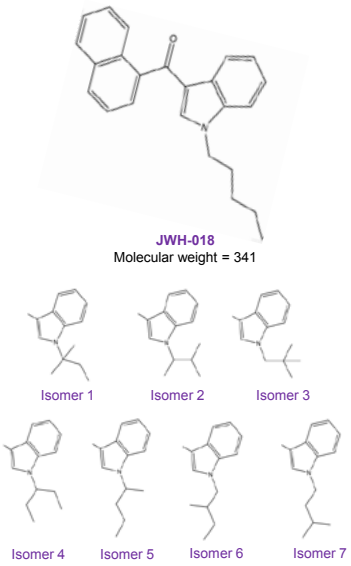


Figure 2. Molecular structure of JWH-018 and sub-structures of isomers

Table 1. MRM transitions of JWH-018 structural isomers

No.	Target	Target MRM	Ref MRM (1)	Ref MRM (2)
1	JWH-018	341 >284	341 >324	284 >167
2	Isomer 1	341 >254	341 >312	312 >155
3	Isomer 2	298 >155	341 >298	298 >170
4	Isomer 3	341 >284	284 >155	284 >167
5	Isomer 4	341 >312	312 >155	312 >254
6	Isomer 5	341 >298	298 >155	298 >170
7	Isomer 6	284 >167	284 >155	341 >284
8	Isomer 7	341 >284	284 >167	284 >254

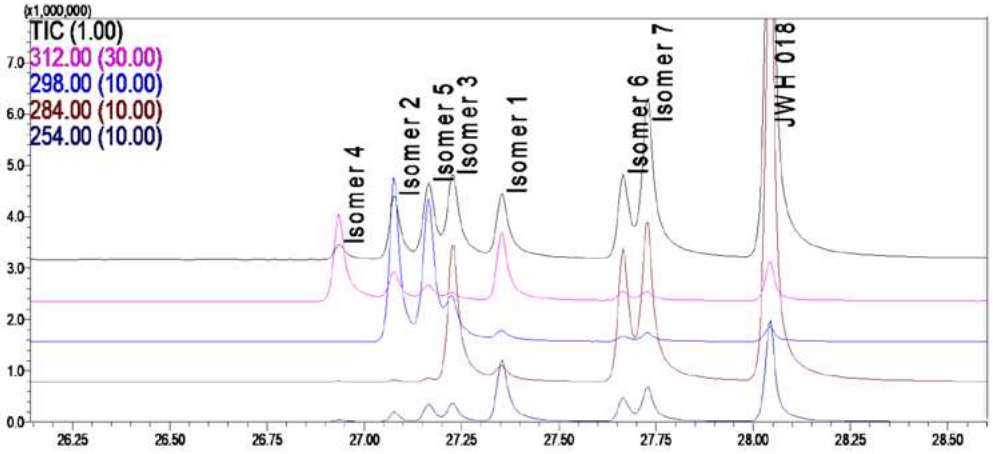
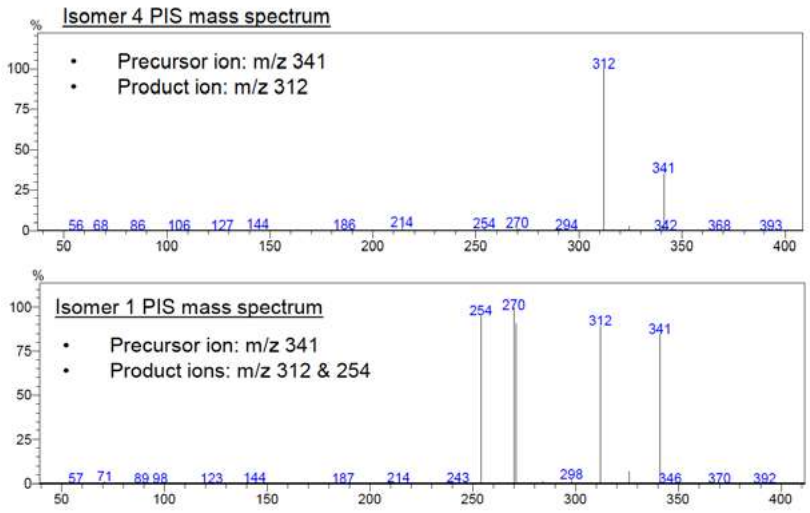
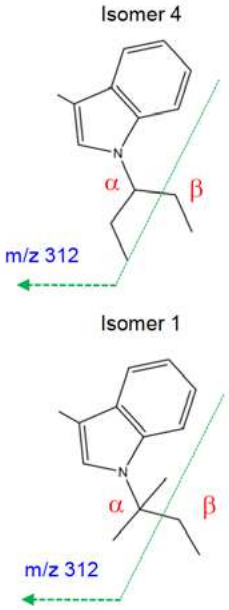


Figure 3. TIC profile of JWH-018 & isomers

E.g. Differentiation of isomers 4 & 1 via PIS





After the Ca-C_b bond cleavage, stability of the resulting carbocation resulted in different product ions, i.e. distinctive PIS mass spectra.

B. Method Development for Fluoro-PB-22 Isomers

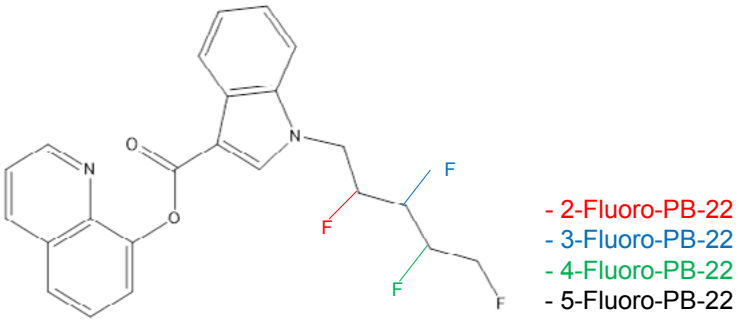


Figure 4. Molecular structures of Fluoro-PB-22 positional isomers

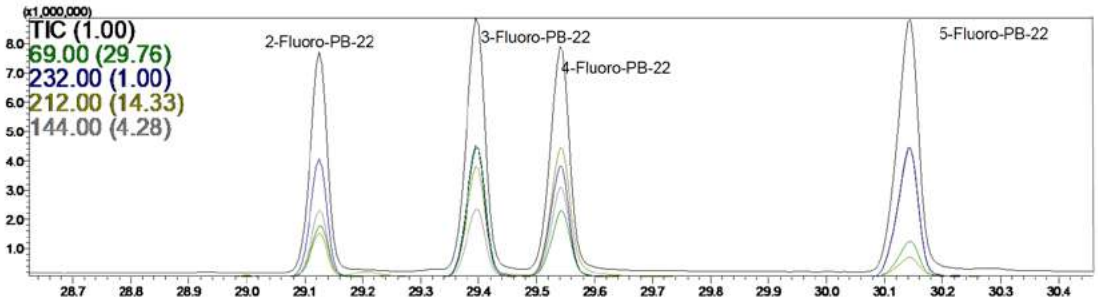


Figure 5. TIC profile of Fluoro-PB-22 positional isomers

B-1. Identification Points of Fluoro-PB-22 Isomers

Fluoro-PB-22 positional isomers were identified and differentiated using the identification points below:

1. **1 target MRM transition**
2. **2 reference MRM transitions**
3. **Product Ion Scan (PIS) mass spectra**
   - ○ PIS was acquired from m/z 232 at an optimized single collision energy (14V)
   - ○ Mass spectra should consist of 1 target ion and 1 or more reference ion(s), and the ion ratio% of the reference ions should fall within the tolerance range of the set ion ratio%
   - ○ Similarity to PIS mass spectrum registered be ≥ 80% (i.e. similarity index% ≥ 80)

Unlike the JWH-018 isomers, the Fluoro-PB-22 isomers did not produce distinctive product ions after ionization.Therefore the %RSD of monitoring ions (from the PIS mass spectra) is crucial to method reliability. Details of monitoring ions are listed in Table 3.

Table 2. MRM transitions of Fluoro-PB-22 positional isomers

Target MRM	Ref MRM (1)	Ref MRM (2)
232 >144	144 >116	116 >89

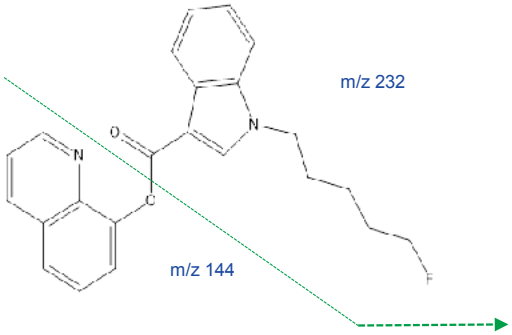
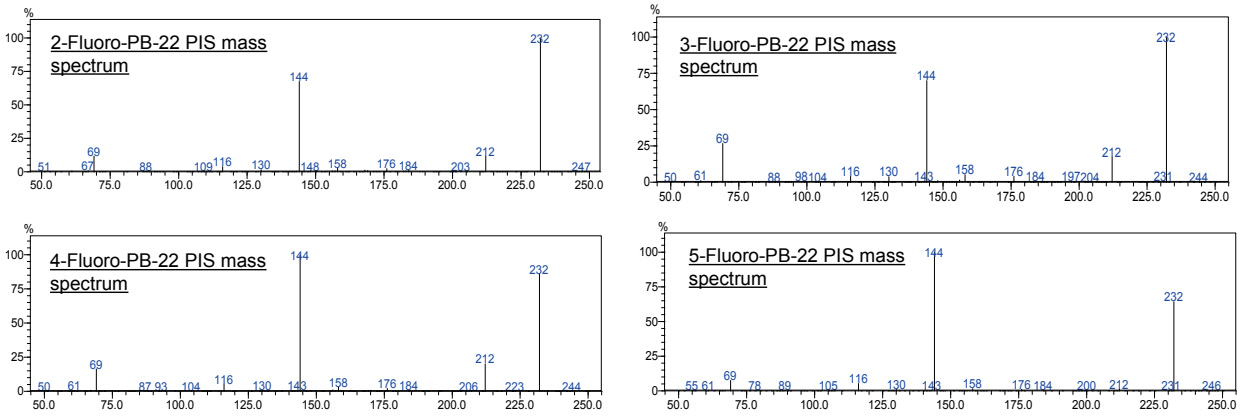


Table 3. PIS monitoring ions of Fluoro-PB-22 positional isomers

		2-Fluoro-PB-22	3-Fluoro-PB-22	4-Fluoro-PB-22	5-Fluoro-PB-22
Type	m/z	Set ion ratio% (area count relative to target ion)			
Target	232	100	100	100	100
Ref 1	114	80.00	81.17	72.73	58.66
Ref 2	69	14.80	31.05	16.93	8.13
Ref 3	212	12.01	16.73	18.30	1.60

Differentiation of Fluoro-PB-22 positional isomers via PIS



B-2. Method Validation

To ensure method stability and reliability, intra- and inter-day stability tests were done for a period of 3 consecutive days. The %RSD of PIS monitoring ions and similarity index% were monitored. In a day, 7 replicate analyses of 10 µg/ml standards were performed for each set of isomers. Each set of isomers was analysed separately. For JWH-018 isomers, the highest intra-day %RSD of monitoring ions ratio% and similarity index were 5.38% and 0.80%, respectively. The highest inter-day %RSD of monitoring ions ratio% and similarity index were 1.78% and 0.41%, respectively. For Fluoro-PB-22 isomers, the highest intra-day %RSD of monitoring ions ratio% and similarity index were 5.55% and 0.80%, respectively. The highest inter-day %RSD of monitoring ions ratio% and similarity index were 0.68% and 0.22%, respectively.

C. Method Application

Subsequently, the MRM/PIS methods of each set of isomers were combined into a single acquisition method. In this way, samples which may contain mixtures of synthetic cannabinoids can be analysed efficiently within a single run. With high similarity match to standard PIS mass spectra, JWH-018 and 5-Fluoro- PB-22 were detected (Figures 6 & 7).

Conclusion

Comprehensive detection and differentiation of structural and positional isomers of JWH-018 and Fluoro-PB-22, respectively, was achieved using simultaneous MRM and PIS with GC-TQMS. The method developed was tested to be stable and reliable for real NPS samples.

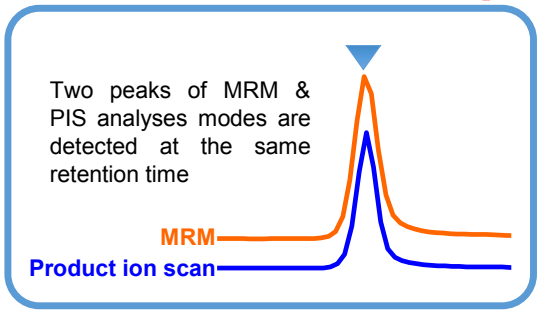
ID#	Name	SI	Ret.Time
1	JWH 018 N-(1-ethylpropyl) isomer; Isomer4	No peak is detected.	
2	Isomer 4 PIS	Ratio of reference ion does not match.	
3	JWH 018 N-(1,2-dimethylpropyl) isomer; Isomer2	No peak is detected.	
4	Isomer 2 PIS	Ratio of reference ion does not match.	
5	JWH 018 N-(1-methylbutyl) isomer; Isomer5	No peak is detected.	
6	Isomer 5 PIS	Ratio of reference ion does not match.	
7	JWH 018 N-(2,2-dimethylpropyl) isomer; Isomer3	No peak is detected.	
8	Isomer 3 PIS	Ratio of reference ion does not match.	
9	JWH 018 N-(1,1		
10	Isomer 1 PIS		not match.
11	JWH 018 N-(2-m		/Band range.
12	Isomer 6 PIS		not match.
13	JWH 018 N-(3-methylbutyl) isomer; Isomer7	No peak is found in Window/Band range.	
14	Isomer 7 PIS	Ratio of reference ion does not match.	
15	JWH 018	68	27.403
16	JWH018 PIS	99	27.399

Positive detection of JWH018 in sample A

Figure 6. Positive detection of JWH-018 with 99% PIS mass spectrum similarity match to standard PIS mass spectrum.

17	2-Fluoro-PB-22	Ratio of reference ion does not match.	
18	2-Fluoro-PB-22 PIS	No peak is found in Window/Band range.	
19	3-Fluoro-PB-22 PIS	No peak is found in Window/Band range.	
20	3-Fluoro-PB-22	Ratio of reference ion does not match.	
21	4-Fluoro-PB-22 PIS	No peak is found in Window/Band range.	
22	4-Fluoro-PB-22	Ratio of reference ion does not match.	
23	5-Fluoro-PB-22 PIS	97	29.304
24	5-Fluoro-PB-22	69	29.306

Figure 7. Positive detection of 5-Fluoro-PB-22 with 97% PIS mass spectrum similarity match to standard PIS mass spectrum.



Forensics / Toxicology

Qualitative Screening of Drugs in Whole Blood by DPiMS QT installed LCMS-9030

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*The affiliation is those at the time of writing.

User Benefits

- Screening of drugs in biological samples is possible with simple sample preparation.
- Separation using a column is not necessary, and a comprehensive qualitative analysis can be conducted in a measurement time of 3 min.
- *iDIA* which has narrower *m/z* window, and makes it possible to comprehensively acquire MS/MS spectra.

Introduction

A simpler and faster technique for identification of the relevant drugs in acquired samples has been required in analyses of drugs and poisons in forensic medicine and scientific criminal investigations.

This Application News introduces a new analysis technique combining the DPiMS QT which is a probe kit of electrospray ionization unit and an LCMS-9030 quadrupole time-of-flight mass spectrometer (Fig. 1) for screening of drugs in human whole blood. The DPiMS QT makes it possible to conduct direct analysis and minimize the time required from sample preparation to analysis. Use of the newly-developed *iDIA* measurement method makes it possible to comprehensively acquire MS/MS spectra for all ionized compounds.

Fig. 1. Appearance of DPiMS™ QT and LCMS™-9030

Analysis Technique

In the DPiMS QT, the attached probe repeatedly carries out sampling from the sample plate, and simultaneously ionizes the sample material adhering to the probe surface by applying a voltage to the probe tip. Then, the ionized samples are introduced directly into the mass spectrometer. In this study, a spiked human whole blood sample (500 ng/mL) was prepared by spiking human whole blood with 17 drug compounds. After diluting 10 µL of the spiked human whole blood sample with 90 µL of water, the solution was mixed with 100 µL of ethanol. The mixtures were then centrifuged, and 10 µL of the supernatant was dripped on the sample plate.

The *iDIA* method, which is realized by a combination of the DPiMS QT and LCMS-9030, was used in qualitative screening of the spiked human whole blood sample. *iDIA* is a technique for acquiring MS/MS spectra which are set to minimize the range of precursor ions to the limit. Here, MS/MS spectra were acquired comprehensively for a window width of 1 Da, and a search of the MS/MS spectra acquired by PESI-Q-TOFMS using the DPiMS QT was conducted using a spectrum library constructed in advance by LC-ESI-Q-TOFMS using standard substances of the various drugs. Table 1 shows the analysis conditions.

Table 1. Analysis Conditions

Mass spectrometer	
System	: DPiMS QT+LCMS-9030
Polarity	: Positive
DL temp	: 250 ˚C
Heat block temp	: 50 ˚C
Interface Voltage	: 3.5 kV
TOF-MS	: m/z 120-770
Precursors of MS/MS	: m/z 140-770 (Fixed window size 1 Da)
MS/MS	: 20-780 m/z
Collision energy ramp	: 10-50 V
Measurement Time (TOF-MS)	: 3 min
Measurement Time (MS/MS)	: Each group within 0.1 min (Total 30 groups)

Analysis of Spiked Human Whole Blood Sample

Table 2 shows the 17 drug compounds spiked in the human whole blood and the library scoring results for each drug. All of the spiked drugs received library scores of 84 to 100, demonstrating that extremely good identification results could be obtained with simple sample preparation and a high-speed analysis with a measurement time of 3 min.

Fig. 2 shows the MS/MS spectra when each drug was compared with the spectrum library. Because the MS/MS spectra are acquired with a window width of 1 Da, it is possible to reduce the effects of contaminant components and isotopic ions.

Table 2. Library Scores of Drugs (500 ng/mL) in Human Whole Blood

#	Compounds	Formula	[M+H]+	Library Score
1	7-Aminonitrazepam	C15H13N3O	252.1132	97
2	Aconitine	C34H47NO11	646.3222	100
3	Blonanserin	C23H30FN3	368.2497	95
4	Carbamazepine	C15H12N2O	237.1023	84
5	Clotiazepam	C16H15ClN2OS	319.0667	95
6	Colchicine	C22H25NO6	400.1755	100
7	Dextromethorphan	C18H25NO	272.2009	100
8	Donepezil	C24H29NO3	380.2221	100
9	Dosulepin	C19H21NS	296.1468	87
10	Escitalopram	C20H21FN2O	325.1711	95
11	Lidocaine	C14H22N2O	235.1805	94
12	Methylphenidate	C14H19NO2	234.1489	97
13	Mosapramine	C28H35ClN4O	479.2572	98
14	Propericiazine	C21H23N3OS	366.1635	96
15	Temazepam	C16H13ClN2O2	301.0739	99
16	Trazodone	C19H22ClN5O	372.1586	96
17	Zolpidem	C19H21N3O	308.1758	96

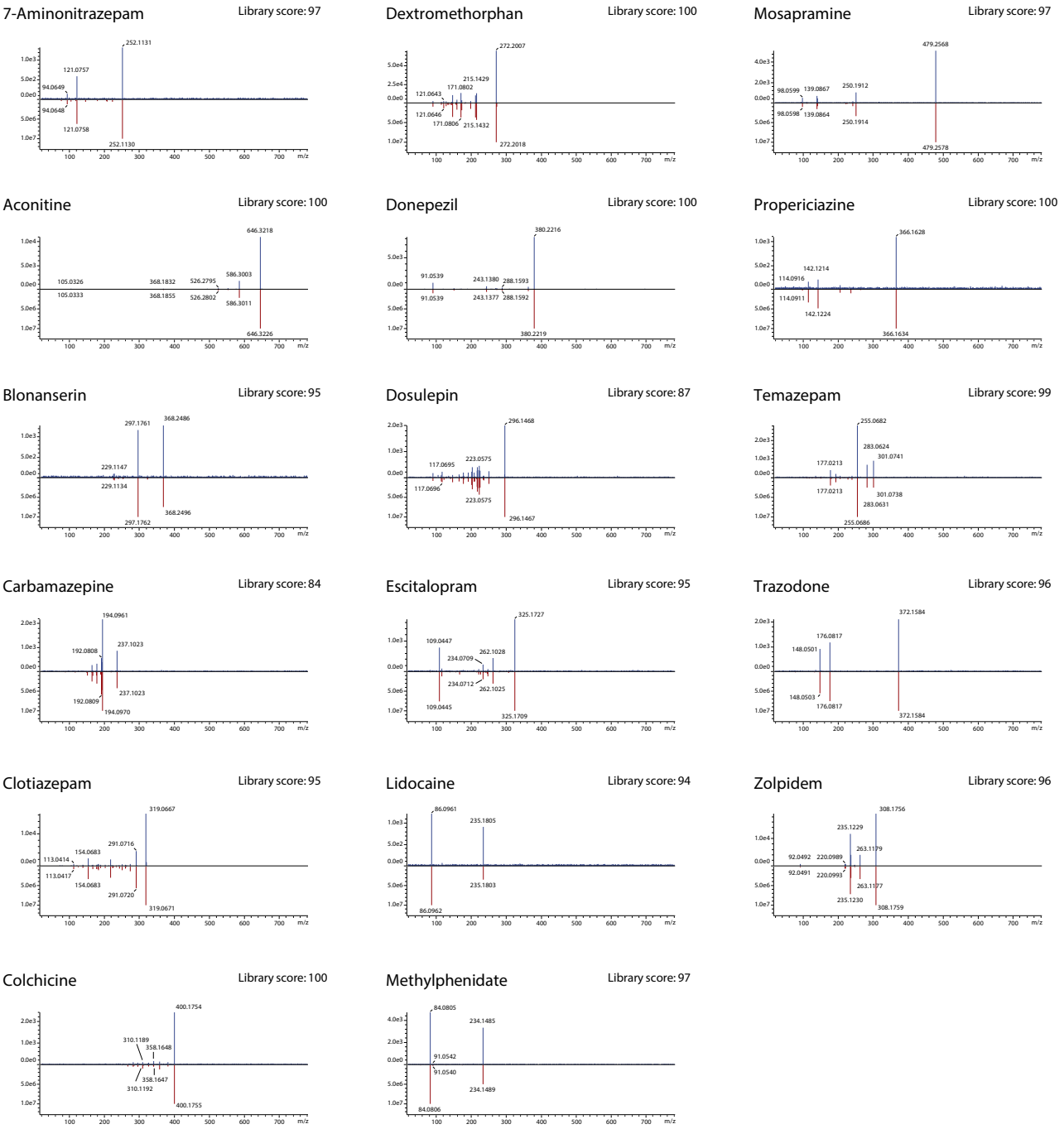


Fig. 2. (Top) MS/MS Spectra and Library Scores of Drugs (500 ng/mL) in Human Whole Blood Acquired Using *iDIA* and (Bottom) MS/MS Spectra of Standard Substances of Drugs Acquired by LC-ESI-Q-TOFMS

Conclusion

The iDIA measurement method for comprehensively acquiring the MS/MS spectra of all ionized components in a sample was developed by using the DPiMS QT and LCMS-9030. Extremely good results were obtained as a result of screening of 17 drug compounds spiked in human whole blood, as the library scores for all drugs were from 84 to 100.

The effects of contaminant components and isotopic ions contained in biological samples can be reduced by acquiring MS/MS spectra with the width of the precursor ion window set to 1 Da. Quick and comprehensive qualitative screening of drugs in biological samples is possible with simple sample preparation and a measurement time of 3 min.

Forensics / Toxicology

Human Hair Cross-Section Analysis Using the AIM-9000 Infrared Microscope

Shoko Iwasaki

Solutions COE, Analytical & Measuring Instruments Division, Shimadzu Corporation

Introduction

A wide variety of samples are required to identify items left at a crime scene. These analyses are conducted from multiple angles using a variety of analytical instruments. Many of the samples are very small, and it is necessary to select the appropriate equipment to analyze them according to their size, condition, and the components attached to them.

The AIM-9000 infrared microscope enables visualization of component distributions in minute areas. This article introduces an example of analyzing cross sections of human hair using the AIM-9000. The cross sections of human hair were prepared using a microtome manufactured by Leica Biosystems.

AIM-9000 Infrared Microscope with Mapping Program

Minute areas of samples can be analyzed in detail by combining the AIM-9000 infrared microscope with the optional mapping program. Fig. 1 shows the instruments used for analysis. The mapping program is capable of both area mapping measurement for analyzing the in-plane distribution of sample components, and line mapping measurement which is effective for analysis at regular intervals along straight lines. In addition to mapping measurement in the standard transmission and reflectance modes, ATR mapping measurement that uses the optional ATR objective mirror and pressure sensor is also available.

Fig. 1. IRTracer™-100 Fourier Transform Infrared Spectrophotometer (Left) and AIM-9000 Infrared Microscope (Right)

Preparation of Human Hair Sections

Untreated black hair and permed/bleached hair were prepared as samples of human hair.

A Leica Biosystems fully automatic rotary microtome was used to prepare the sample sections. Fig. 2 shows the HistoCore NANOCUT R which is the latest model. The cutting method on the HistoCore NANOCUT R can be switched between automatic and manual modes and the cutting thickness can be set from 0.25 to 300 µm. In this example, 3 µm thick sections were created through vitreous ice-embedding using the EF-13 electronic sample freezing device.

Fig. 2. Leica Biosystems HistoCore NANOCUT R
Fully Automatic Rotary Microtome

Analysis of Human Hair Cross Sections

Mapping measurement was performed using the infrared microscope. The human hair sections were placed on a diamond cell and measured using transmission microspectroscopy. The aperture was set to 10 µm × 10 µm and the measurement interval was set to 5 µm. Table 1 lists the measurement conditions and Fig. 3 shows the representative infrared spectra of untreated black hair and permed/bleached hair.

The spectra show an amide I peak (C=O stretching vibrations) in the vicinity of 1650 cm^{-1} and a peak originating from cysteic acid (S-O stretching vibrations), which is an indicator of hair damage, in the vicinity of 1040 cm^{-1}. The cysteic acid peak only appears for the permed/bleached hair.

Table 1 Measurement Conditions

Instrument	: IRTracer-100, AIM-9000
Resolution	: 8cm^{-1}
Accumulation	: 10
Apodization function	: Sqr-Triangle
Aperture size	: 10 µm × 10 µm
Measurement interval	: 5 µm
Detector	: MCT

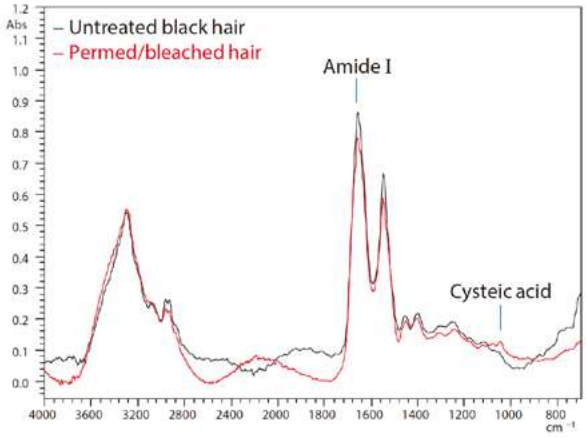


Fig. 3. Representative Infrared Spectra of Untreated Black Hair and Permed/Bleached Hair

Chemical Images of Hair Cross Sections

Observation images of untreated black hair and permed/bleached hair were acquired and chemical images were created from the mapping measurement results.

Chemical images were created from the results of mapping measurement using peak height and area, multivariate analysis (PCR/MCR), and the degree of similarity with target spectra. By this, component distributions that cannot be confirmed visually were successfully visualized. Mapping measurement is widely used for defect analyses as well as analysis of industrial materials and biological samples.

Fig. 4 (a) shows chemical images derived from amide I (peak correction area values near 1650 cm^{-1}). Amide I is widely distributed from the surface to the interior of the hair for both the untreated black hair and permed/bleached hair, and both favorably agree with their observation image counterparts.

Fig. 4 (b) shows chemical images derived from cysteic acid (peak correction area values near 1040 cm^{-1}). Compared to the untreated black hair, cysteic acid is distributed throughout the permed/bleached hair, which is assumed to be the result of hair damage.

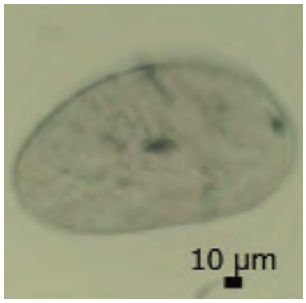
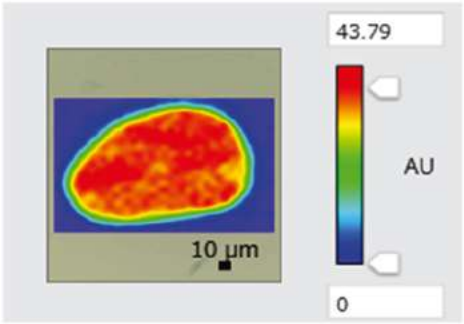
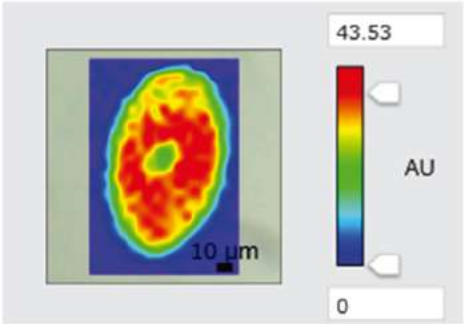
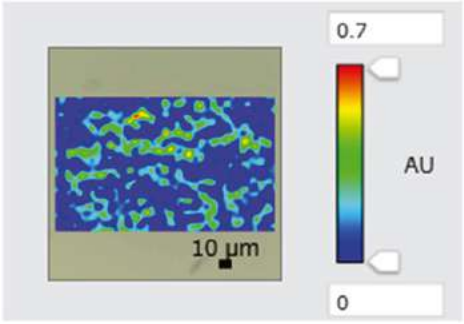
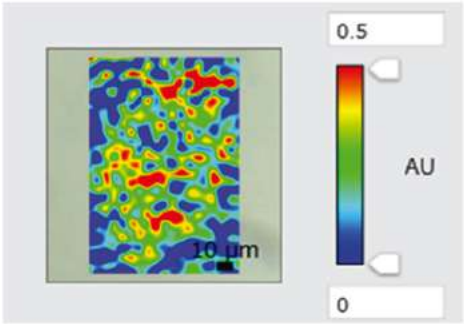
	Untreated Black Hair Measurement Area: 180 µm Horizontal, 110 µm Vertical	Permed/Bleached Hair Measurement Area: 90 µm Horizontal, 130 µm Vertical
Observation image		
(a) Amide I distribution Peak correction area values in vicinity of 1650 cm^{-1}		
(b) Cysteic acid distribution Peak correction area values in vicinity of 1040 cm^{-1}		

Fig. 4. Chemical Images of Hair Cross Sections (Untreated Black Hair, Permed/Bleached Hair)

Conclusion

This article introduced an analysis of human hair cross sections using the AIM-9000 infrared microscope. We were able to demonstrate the changes in composition of internal proteins resulting from hair damage. FTIR makes it easy and quick to assess samples brought in from the scene of an incident or accident by observing the internal components of the hair and changes due to damage.

Acknowledgments

We would like to thank Leica Microsystems GmbH for their cooperation in the cutting of samples.

References

1. Satoshi Inamasu et al., “Analysis of Human Hair Cross Section Using Infrared Microspectroscopy”
J. Soc. Cosmet. Chem. Jpn. Vol.50, No.3 2016 P.209-217

Shimadzu Selection

This is a selection of articles by Shimadzu relating to Forensics and Toxicology. From posters presented at the international conferences to e-books, they include everything from the latest applications to the latest publications. In these articles, you will find a variety of applications of our instruments as well as cutting-edge technologies. Please obtain the articles of your interest by clicking on the titles.

Screening Analysis of Steroid Profiles and Qualitative Doping Substances by GC-MS/MS

WADA-accredited laboratories around the world pursue to fight against doping in sports. Shimadzu GCMS-TQTM 8050 NX was selected as an instrument of choice for an anti-doping testing at international sports games held in 2021. The method developed for the games analyzed 180 substances, encompassing both quantitative and qualitative substances with one injection. The sensitivity, the linearity, and the robustness of the instrument were demonstrated with endogenous steroids quantified for steroid profiling. The sensitivity in qualitative analysis of target substances was also proved to be sufficient, and chromatograms were provided for a dozen of such substances as an illustration in this article. A document on the rest of the data is available specifically for those working in the WADA-accredited doping control laboratories. The readers interested in the document are encouraged to contact Shimadzu Corporation, or its oversea branches.

Toxicology Screening of Human Blood using Quadrupole-Time of Flight (QTOF) Mass Spectrometry

This method focuses on the use of high-resolution mass spectrometer for screening blood samples for commonly abused drugs using data independent analysis and library matching Initial toxicology screening is performed on all toxicology samples to screen for the presence of certain drug classes and compounds. Traditionally, toxicology screening has been done using immunoassay which is limited to specific drug classes and can result in false positives. With the addition of many new novel psychoactive substances and unknown compounds, the demand to identify these unknown compounds has increased. To meet the increasing demand for a more rapid and effective toxicology screening method, a high-resolution accurate mass quadrupole-time of flight (Q-TOF) mass spectrometer with a comprehensive library was used to develop a screening workflow. A method was developed on a Q-TOF to screen toxicologically significant compounds in blood extracts.

Multi-Method LCMS Assay Multiplexing with Advanced Intelligence Capabilities to Increase Laboratory Throughput

Increased throughput is one of the greatest interest in multi-sample processing in clinical laboratories. Multiplex analysis offers significant advantages with respect to time, reagent cost, sample requirements, and the amount of data that can be generated. In high-volume assays, the same analytical method is usually assigned to all streams of a multiplex system to accelerate sample processing. However, there are also middle to low volume assays, and there is a need to combine these assays to run multiple methods on a single LC in order to maximize LCMS utilization.
The Nexera QX Multiplexing LCMS system is the next generation LCMS platform that can alleviate many of the commonly associated problems with existing high throughput LCMS assays. Using QX Solution software, a seamless control of the system can be achieved even while multiplexing multiple assays within a single batch, allowing a single instrument ultimate method flexibility.

Best Poster Award Participant

Separating Cannabinoid Stereoisomers Utilizing LabSolutions MD with an Analytical Quality by Design (AQbD) Approach

The cannabis market has been rapidly growing with the list of identified cannabinoids constantly increasing. Analytical methods for detecting over 25 cannabinoids by means of HPLC (High Pressure Liquid Chromatography) analysis have been explored and currently there are methods to separate 21 cannabinoids in a single run. Expanding the list of cannabinoids is possible, however stereoisomers challenge the current methods and, therefore, further method optimization is needed. Shimadzu's new analytical method development software, LabSolutions MD (Method Development) alleviates the tedious task of testing, analyzing, and comparing all the individual runs. LabSolutions MD uses "Analytical Quality by Design (AQbD)" concepts to determine the optimal method for cannabinoid separation. Experimental design during the entire method development process, identification of the most robust analytical conditions, and predicted of chromatograms, provide the user with the power to automate the development of robust analytical methods. This software can be an asset to many fields and will be used in this study to efficiently separate cannabis stereoisomers.

Confirmation of Synthesis of Sparingly Soluble Compounds by Accurate MALDI-TOF Mass Spectrometry

The MALDI method is tolerant to various characteristics of samples, and thus, for example, can be used to perform mass spectrometry of poorly soluble compounds that are difficult to measure with LC-MS. For the analysis of less polar compounds, an ionizing agent is sometimes added to the sample and matrix to promote ionization. They must be mixed and dissolved, and then spotted and dried on a sample plate to form cocrystals. Therefore, it is necessary to dissolve all components in the same solvent. Meanwhile, for highly accurate mass measurement in MALDI-TOF MS analysis, it is desirable to perform mass calibration using internal standards. However, calibrants with similar physical properties and molecular weight to the sample compound may not be easily found.

Solutions for Forensic Toxicology

At Shimadzu, we have the analytical tools necessary for your forensic toxicology laboratory to be accurate, efficient, and confident with your results. Our products cover anything from sample preparation to screening, identification and confirmation. In addition, our wide range of instrumentation can be used with a variety of sample types, such as whole blood, urine, plasma, oral fluids, postmortem, tissues, etc.

Micro Volume QuEChERS Kit for LC/MS

This pretreatment kit for human biological samples is intended for the field of forensic medicine. Salt precipitation via QuEChERS extraction salts is adopted as the method* for extracting toxicants in blood and urine. The sample volume has been scaled down to 100 µL, so biological samples can be pretreated even if an ample sample volume cannot be ensured. Samples pretreated with this kit can be measured with high sensitivity using LC/MS/MS.

Rapid pharmacokinetic analysis of small drugs by mass spectrometry imaging combined with product ion analysis

Comprehensive information of administered drugs in biological tissues or organs is of paramount importance to understand their clinically-relevant properties, efficacy, potential side effects, and toxicity. Mass spectrometry imaging (MSI) is a labelfree and highly sensitive imaging technique that offers accurate visualization of drugs and their metabolites in the tissue sections. Among several tools of MSI, matrix-assisted laser desorption/ionization MSI (MALDI-MSI) is most commonly used for mapping of drugs, their metabolites, and other analytes present in the sample. In this study, we are using a newly developed MALDI-MSI tool known as iMScopeTM QT for rapid pharmacokinetics analysis of imipramine and chloroquine.

Detection of THC Metabolites in Urine by LCMS8050 with Supported Liquid Extraction Method

Despite its role as recreational and medicinal drug, cannabis can potentially lead to dependence and behavior disturbances affecting a person's daily duties as long-term effects. This concern has prompted authorities to consider advanced technique to trace the track of cannabis intake especially in biological fluids. Urine is among the biological fluid frequently used for routine cannabis tracing. Mass spectrometry is the gold standard in forensic and clinical analysis for its sensitivity and selectivity. In this report, liquid chromatography mass spectrometry-triple quadrupole system (LCMS-8050) was employed for measuring THC metabolites in urine samples.

Multi-target Screening of Toxicological Compounds in Blood on A Fully-automated Platform Consisting of Sample Preparation Module CLAM and LC-MS/MS

Multi-target screening by LC/MS/MS has been widely adopted in detection and quantitation of drugs of abuse (DoA) in forensic investigation and toxicological research. Usually, a wide range of targets are screened in such analysis, including illicit drugs, narcotics, psychotropics, antipsychotics, pharmaceuticals and other toxic compounds in urine, serum/plasma and whole blood samples. Sample preparation is often a bottleneck due to the tedious steps. It is also a factor responsible for inaccurate or false negative results. We describe a solution by using an automated sample preparation module CLAM-2000™ connected with LC/MS/MS system (LCMS-8060) for multi-target screening of 61 drugs in whole blood. A ready-to-use method package Rapid Toxicology Screening (Shimadzu) was used to set up the screening method with human whole blood (frozen) spiked sample without efforts in LC and MRM method development.

Latest topics 1

Expanding the Clinical Testing Business Based on Synergies between Analytical and Measuring Instruments and Culture Media/Reagents

Making Nissui Pharmaceutical a Wholly-Owned Subsidiary

In November 2022, Shimadzu Corporation used the prerogative from a stock merger to make Nissui Pharmaceutical Co., Ltd. (with Head Office at Taito-ku, Tokyo, and President Tokuya Ono) a wholly-owned subsidiary. Nissui Pharmaceutical Co., Ltd., has changed its trade name to Shimadzu Diagnostics Corporation (hereinafter "SDC") since April 1, 2023.

Given that analytical and measuring instruments are Shimadzu's strongest product segment, adding SDC, which has extensive sales channels in clinical markets and a wealth of technology and expertise related to reagents, as a wholly-owned subsidiary will increase the corporate value of Shimadzu Corporation by generating synergies in the following three business areas.

- **Clinical diagnostics**: Offer solutions that combine SDC's reagents with Shimadzu's liquid chromatograph mass spectrometers (LCMS), PCR testing systems, and other products.
- **Clinical microbial testing**: Newly enter the clinical microbial testing market by advancing product development with SDC's commercial distribution and technological capabilities in the field.
- **Cellular analysis**: Use SDC's culture media and Shimadzu cell testing systems to create culture medium-related businesses.

Investing in Biotech Venture MiCAN Technologies: Expanding Clinical Business by Focusing on Cell-Related Business

In April 2023, SDC invested approximately 50 million yen in MiCAN Technologies, Inc. (Head Office: Kyoto City, hereinafter "MiCAN"), a biotechnology venture specializing in regenerative medicine, in addition to approximately 20 million yen invested in MiCAN in 2019.

In 2019, MiCAN developed Mylc cells, the world's first white blood cells from humans that can be grown in culture. Developed from blood or iPS cells, Mylc cells offer high sensitivity to stimuli (suited to drug response testing), a homogeneous cell population with identical genetic information, and low production costs.

Pyrogen testing is essential to regenerative medicine. The test determines whether pharmaceutical products and vaccines are free of contamination by fever-inducing substances (pyrogens) found in bacteria. Laws in many countries require pyrogen testing on every production batch before shipment. Pyrogen testing is currently performed by animal testing in rabbits, but this practice is expected to be replaced by a cell-based test (the monocyte activation test, hereinafter "MAT") based on forthcoming pharmacopoeia revisions and other regulatory changes in Europe and Japan. In 2021, MiCAN developed a MAT procedure using Mylc cells (MylcMAT method). With this additional investment, MiCAN will establish a stable production system for Mylc cells. SDC and MiCAN will commercialize a simple MylcMAT kit consisting of Mylc cells, test reagents, and cell culture media. They will jointly market this kit in Japan and Europe.

Shimadzu Group will continue to focus on cell-related business and work with MiCAN to expand global sales of test kits based on Mylc cell technology. In the clinical diagnostics business, Shimadzu Group is also exploring working with MiCAN to develop infectious disease test reagents. These are used in PCR testing systems and liquid chromatograph mass spectrometers.

Shimadzu Diagnostics Corporation

MiCAN Technologies, Inc.

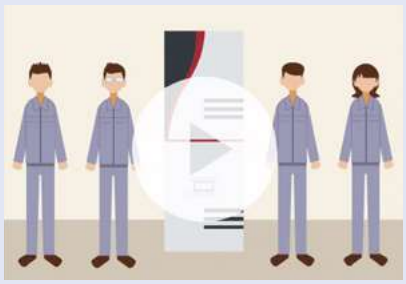
Latest topics 2

Celebrating 20 Years of Koichi Tanaka Mass Spectrometry Research Laboratory

The Koichi Tanaka Mass Spectrometry Research Laboratory was established on January 1, 2003 with Koichi Tanaka, who received the Nobel Prize in Chemistry in 2002, as General Manager. Since then, the laboratory has engaged in research into structural analysis methods for biomolecules, and the development of next-generation mass spectrometry systems, with the aim of ultra-early detection of diseases from blood droplet samples. 2023 marks the 20th anniversary of this laboratory.

Initiatives by the Koichi Tanaka Mass Spectrometry Research Laboratory

With matrix-assisted laser desorption/ionization mass spectrometry (MALDI-MS) as the core technology, the laboratory engages in early detection of protein related diseases, research into structural analysis methods for sugar chains and other biomolecules, and the development of next-generation mass spectrometry systems.



Introduction to Koichi Tanaka Mass Spectrometry Research Laboratory

While maintaining contact with the world at large, the laboratory is producing results, which in turn have an impact on the world at large, causing a chemical reaction that fosters new possibilities for mass spectrometry. The aim is to develop science and technology and contribute to society by functioning as a site for collaborative creation sparked by this virtuous cycle.

20th Anniversary Lecture

A 20th anniversary lecture was held in Kyoto in February of this year. A number of researchers participated including Professor Shinya Yamanaka at Kyoto University, who received the Nobel Prize in Physiology or Medicine in 2012, and who was invited as a special lecturer. In the Tanaka Fellow commemorative lecture, he described the history of the laboratory, which has resulted in the publication of approximately 150 research articles over a 20 year period, and gave examples of the research.

The Koichi Tanaka Mass Spectrometry Research Laboratory, which was started to commemorate Tanaka's Nobel Prize win, continues to take on challenges both in terms of facilitating research activities, and promoting and popularizing science and technology.

Koichi Tanaka Mass Spectrometry Research Laboratory

Latest topics 3

Release of AIRsight Infrared Raman Microscope

World's Only Instrument Capable of Performing Both Infrared Spectroscopy and Raman Spectroscopy

Shimadzu announces the release of the AIRsight infrared Raman microscope. This product is the world's only microscope on the known market that allows two different analytical techniques, infrared spectroscopy and Raman spectroscopy, to be performed with one instrument. It is useful for the analysis of trace contaminants, quality control in the chemical, electrical, electronic, machinery, and transportation equipment fields, and for research into microplastics.

An infrared microscope combines an infrared spectroscopy analytical instrument and an optical microscope. Since a comprehensive qualitative analysis database is available, this microscope is widely used to detect impurities. In contrast, a Raman microscope is a combination of instruments that detect the spectra acquired using Raman spectroscopy and an optical microscope. This type of microscope shows its effectiveness when analyzing aqueous solutions, inorganic substances, and microscopic samples, which are difficult to analyze using an infrared microscope.

This product brings to reality a microscope that employs two different analytical techniques: infrared spectroscopy and Raman spectroscopy. It is the only microscope capable of acquiring infrared spectra and Raman spectra from the same position in an extremely small section. The combination of two analytical techniques provides complementary information. Without moving the sample, spectra can be acquired from the same stage. Moreover, it requires less space compared to a setup where both an infrared microscope and a Raman microscope are installed. Additionally, since the same software can be used for control of both techniques, operability is enhanced. Note that to use this product, a Fourier transform infrared (FTIR) spectrophotometer needs to be connected.

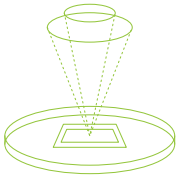
By continuously providing even more precise analytical data for a broad variety of applications, Shimadzu contributes to solving challenges in society, such as the analysis of contaminants and microplastics.

Note 1: The following three FTIR models can be connected to this product: IRTracer-100, IRXross, and IRAffinity-1S. IRSpirit, a compact FTIR model, cannot be connected.
Note 2: AIRsight, IRTracer, IRXross, IRAffinity, and IRSpirit are registered trademarks of Shimadzu Corporation.

Features

1. Both Infrared and Raman Measurements Possible without Moving the Sample

Once the sample has been set on the infrared Raman microscope stage, both infrared spectra and Raman spectra can be acquired from the same position in an extremely small section, without moving the sample. It eliminates the time required to search for the measurement position when performing analyses using

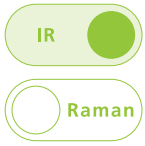


Same position
is measured by IR and Raman

two instruments. This product is equipped with Shimadzu's proprietary wide-view camera, infrared microscope camera, and Raman-use objective lens. The wide-view camera not only enables observations up to a 10 × 13 mm area, but it also supports variable digital zooming. Additionally, it shares positional information with the infrared microscope camera and Raman-use objective lens, which ensures that the target of interest is observed. The infrared microscope camera can be used to observe areas as small as 30 × 40 µm, and the Raman-use 100 × objective lens to observe areas as small as 7.5 × 10 µm.

2. Both Infrared and Raman Measurements and Analysis Possible with One Software

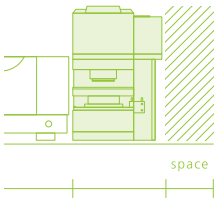
The type of spectra to be acquired can be switched using the AMsolution control software. The software can also overlay and search infrared and Raman spectra, create libraries, and so on.



Smart software controls IR and Raman

3. Information Provided for Organic and Inorganic Substances with One Microscope

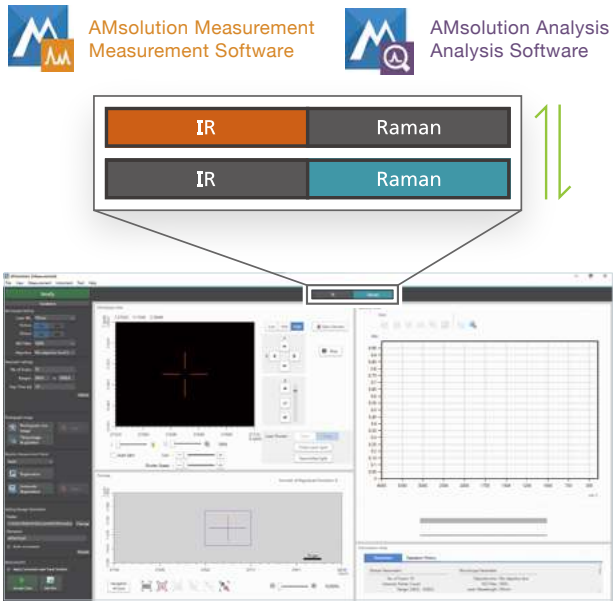
Though infrared microscopes are useful for analyzing organic substances, they have difficulty obtaining information for some inorganic substances. On the other hand, Raman microscopes can obtain information about inorganic substances, such as titanium oxide and carbon. By using this product, it is possible to analyze the main organic substances as well as any inorganic additives using a single microscope.



Single system saves space

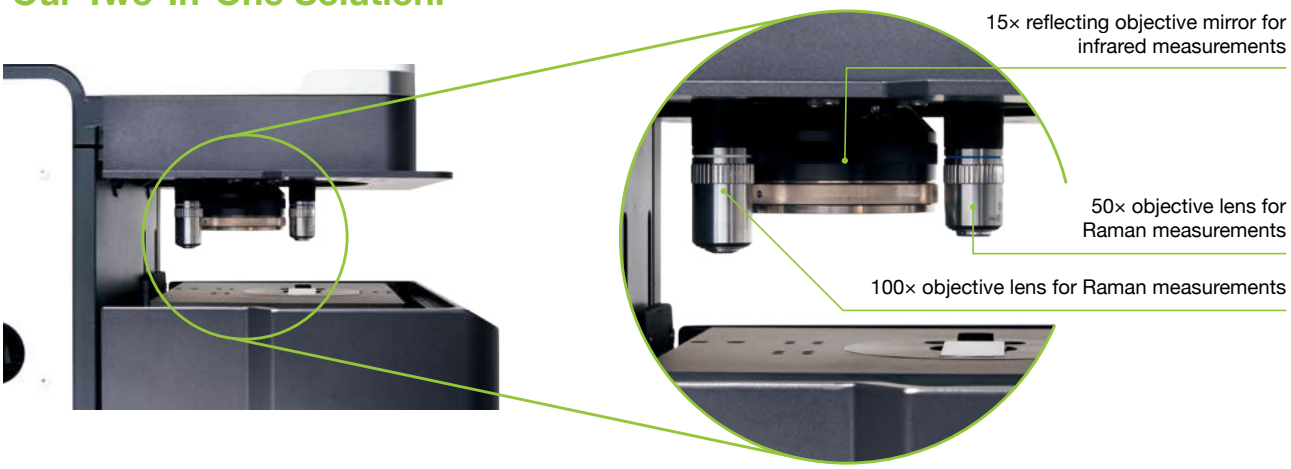
4. AMsolution Control Software Includes a Length Measurement Function

Using the AMsolution control software, the length of the targeted object can be measured. Simply clicking the start and end points for the measurement displays the measurement length in the window. Also, length measurement results can be output with a single button click. This function is convenient for measuring the diameter of microplastic particles.



For more details, visit AIRsight

Our Two-In-One Solution!



RELEASED

New Products

LCMS-2050

ANALYTICAL INTELLIGENCE

High-Performance Liquid Chromatograph Mass Spectrometer

The LCMS-2050 single quadrupole mass spectrometer combines the user-friendliness of an LC detector with the excellent performance of MS to provide a complete package of easy to use high-level performance and compactness. To make it accessible to all users, the system is enhanced with technology and functions to ensure that even technicians unfamiliar with mass spectrometers can easily and efficiently perform analysis.

Learn more

Nexera lite inert

ANALYTICAL INTELLIGENCE

Application Specific LC Systems

Nexera lite inert is a robust HPLC system that eliminates the risk of corrosion by high-salt mobile phases and sample adsorption onto metal surfaces. It improves the data quality of protein analysis in biological samples with superior reproducibility, without any special considerations for stable and long-term use.

Learn more

CLAM-2040

Fully Automated Sample Preparation Module for LCMS

CLAM-2040 is an online automated sample preparation module that brings LC/MS smoothly into your laboratory. The CLAM-2040 accompanies you on most of the analytical workflow and improves your overall throughput by drastically reducing the sample preparation time. Simply place the blood tubes in position and the CLAM-2040 performs the next steps automatically, from sample extraction, up to the LCMS analysis and data processing.

Learn more

High Resolution Accurate Mass Library for Forensic Toxicology

Application Specific LC-MS Systems

The High Resolution Accurate Mass (HRAM) Library includes two MS/MS spectral libraries. Each library is built using two different separation conditions and is suitable for targeted or non-targeted screening of drugs of abuse, psychotropic drugs, pharmaceuticals, pesticides, and other compounds of toxicological interest.

Learn more

AIRsight

Infrared/Raman Microscope

AIRsight is an Infrared and Raman Microscope Based on a Combination of Two Analytical Techniques to Provide Complementary Molecular Information. This simple system improves the efficiency of analytical operations by making it easy to perform all process steps from sample observation to data analysis.

Learn more

Benchtop MALDI-TOF Imaging Starter Kit

MALDI Imaging Solutions

The Benchtop MALDI-TOF Imaging Starter Kit provides a complete MALDI imaging application solution to your existing Shimadzu MALDI-8020 and MALDI-8030 benchtop MALDI-TOF instruments. The kit has been developed and robustly tested to the highest quality standards to provide reliable imaging mass spectrometry results.

Learn more

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