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Forensics / Toxicology and more…

Director’s note

Dear Reader,

Launched in October 2013, Shimadzu Journal has become a dynamic resource highlighting various collaborative research projects as well as technical reports and applications from our library. I am very proud of it. Previous issues have concentrated on the fields of food safety, pharmaceuticals, clinical research and material science, and have introduced outstanding results from collaborations with leading experts in each field.

Our corporate philosophy: "Contributing to Society through Science and Technology", guides us in our effort to meet customers’ needs in a wide variety of fields all over the world. Furthermore, we strive to listen to our customers’ requirements and to offer valuable solutions with a sincere and earnest attitude in accordance with our corporate slogan of this year, “Best for our customers: Challenge without limits.” We, as a manufacturer, believe that collaboration with researchers should generate innovative development and create valuable solutions that will deliver true contribution to the world.

The Analytical and Measuring Instruments Division offers state-of-the-art solutions in a wide variety of fields that contribute to people's health and well-being. Our diverse product lineup, which achieves the top rank in the industry, includes mass spectrometers, chromatographs, life science instruments, spectrophotometers, surface analytical instruments, microscopes, environmental monitors of exhaust gas and water, strength and fatigue testing machines, X-ray inspection devices, balances, and thermal analyzers.

This latest issue focuses on forensics / toxicology and contains results from a collaboration with Professor Pierre MARQUET of University Hospital of Limoges, France. He and his team use our state-of-the-art mass spectrometry and have achieved great results. In addition, this issue contains much information on other applicable topics, as well as the latest news and applications.

We desire to establish a good partnership with you. We continuously make an effort to exceed your expectations with the highest technological capabilities and most meaningful solutions. We hope this journal will be of great help to all of you.

Yours Sincerely,

Teruhisa UEDA, PhD.

General Manager, Analytical & Measurement Instruments Division

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Featuring on Forensics / Toxicology

Professor Pierre MARQUET of University Hospital of Limoges

We interviewed Professor Pierre MARQUET, head of the Pharmacology, Toxicology and Pharmacovigilance department at the University Hospital of Limoges, France. His research area is pharmacology and toxicology. Since 2007, he has been the head of the INSERM research unit UMR 850 in "Pharmacology of immunosuppressive drugs in transplantation" (INSERM is the French National Institute of Medical and Health Research).
Professor MARQUET and Shimadzu started a collaborative project in 2013 that has already yielded several achievements.

Shimadzu:

Professor MARQUET, thank you very much for taking some time for this interview. First of all, could you tell us about the background of this collaborative research? Why did you choose Shimadzu?

Prof. MARQUET

The Laboratory of Pharmacology and Toxicology of the University Hospital of Limoges is one of the largest in France. It is divided into transplantation research activities (INSERM unit created in 2007) and clinical activities. In 2013, Shimadzu proposed to set up collaboration with a one-year loan of a triple quadrupole LCMS-8040. Due to the good results obtained, we decided to buy this year a triple quad LCMS-8050. The collaboration is currently ongoing with the loan of another LCMS-8050 system. This will help us meet our desires to develop new methods and work with two identical devices and to have a backup system.
Our most urgent development needs were in clinical and forensic toxicology. So, the LCMS-8050 was installed in this lab in order to develop techniques for drugs of abuse detection and determination. This collaboration helped us to take the plunge and use liquid chromatography-triple quadrupole mass spectrometry (LC-MS/MS) for the detection of illicit drugs, where we used to employ gas chromatography - mass spectrometry (GC-MS), which requires considerable sample preparation and analysis time. Other labs had already taken the step but we did not have enough LC-MS/MS instruments to dedicate one (or most of one of them) to illicit drug analyses.

Shimadzu:

Then could you outline your aims and let us know what methods have been developed so far?

Prof. MARQUET

In the early part of this collaboration, our aim was to establish four methods during the first year, but we have fallen behind. This can be explained both by a difficult start with the system configuration and the limited time we have been able to dedicate to such developments. Today, we have some pretty good results. Three of the four techniques we planned are currently being validated and the 4th is under development.
We have developed methods for the detection of drugs (cocaine and metabolites, opiates and opioids, amphetamines and analogs), a large number of anticonvulsants, and anticoagulants (including new oral anticoagulants). A method for cannabinoids is being optimized because we are facing a memory effect in the on-line extraction columns.
We had hoped to use online sample preparation systematically, as is already the case in our pharmacology lab. However, it is not working as well as we hoped, probably because we handle many heterogeneous molecules with different acid-base properties and/or polarities. Therefore, it has been difficult to find a single solid-phase extraction condition for all these molecules.

Shimadzu:

Why are you interested in such developments? What is your goal?

Prof. MARQUET

For most of these newly developed methods, the LCMS-8050 replaces more than one GC-MS. The latter requires long but also manual sample preparation. Budget restrictions being a strong reality in French hospitals, the lack of technicians is sorely felt. This technological switch allows us to maintain and develop our activity despite fewer technicians, while reporting the results faster. Another focus that we have in mind when doing new developments is the introduction of new illicit or therapeutic drugs to our panels of tests.

Shimadzu:

How are our instruments helping you?

Prof. MARQUET

When I think of Shimadzu instruments, sensitive and robust are the first two adjectives that come to my mind.
We use the QuEChERS preparation method, that is to say liquid extraction by salting effect. This preparation induces a dilution of the sample, when until recently we had to purify and then concentrate the samples prior to the analysis. Thus, the Shimadzu instrument's sensitivity saves much time, as it is not necessary to concentrate the samples any more. Also, dilution reduces matrix effects, which is a good thing.
Moreover, thanks to UHPLC and the system speed (run-time reduction), we have optimized our analysis times. Where in the past we needed 2 GC-MS systems, one LC-MS/MS system is now sufficient and there is time left for other analyses.

Shimadzu:

What are Shimadzu's strengths compared to other vendors?
(not limited to the instruments)

Prof. MARQUET

Apart from this specific collaboration, the "Pharmacology, Toxicology and Pharmacovigilance" department and Shimadzu are longtime collaborators. A strong relationship based on trust has been established and there are many reasons for this.
First of all, as I said earlier, the instruments are robust and sensitive, which is why there are so many Shimadzu HPLC and GC-MS systems in our department. In our laboratory, where many routine tests are carried out, it is important to have robust systems well maintained over time. Your good and reliable after-sale service distinguishes you from some of your competitors.
We are in a specific situation: we have a large analytical park but we cannot objectively renew it regularly. So we have to make it work as long as possible. Shimadzu is characterized by not planning system obsolescence and provides long-term support, which are very valuable assets.
Furthermore, our lab technicians can easily use the different instruments because of the common software for HPLC, GC-MS and LC-MS/MS.

Shimadzu:

Finally, could you please share any requests that you have with respect to instrument vendors?

Prof. MARQUET

The main suggestion I would make to scientific instrument vendors is not to neglect support and development assistance to customers. In a world where everyone is increasingly pressed for time, method implementation is a very important asset to stand out from other vendors.

Shimadzu:

It is important to know what you think of us and our collaboration. We will strive to meet your requests more than ever. Thank you very much.

Research Activities:

With the ultimate goal of treatment personalization in organ transplant recipients, the INSERM unit U850 pursues a translational research strategy to: (i) identify the pharmacokinetic, pharmacogenetic and pharmacodynamic factors influencing the response and tolerance to immunosuppressive drugs (ISD) and regimens; (ii) discover early, non-invasive biomarkers of graft lesions; (iii) and to set up treatment individualization tools, validate them clinically and transfer them to physicians. The unit also sets up cohort studies to measure the impact of treatment personalization on patient and graft survival, patients' quality of life and healthcare expenses.

Pierre MARQUET, Jean-Michel GAULLIER, Denis RAFFIER (from left to right)

Recent publications:

Pharmacokinetics

1. Woillard JB, Lebreton, Neely M, Turlure P, Girault S, Debord J, Marquet P, Saint-Marcoux F. Pharmacokinetic tools for the dose adjustment of cyclosporine in Hematopoietic Stem Cell transplant patients. *Br J Clin Pharmacol.* 2014 Oct;78(4):836-46.
2. Woillard JB, Bader-Meunier B, Salomon R, Ranchin B, Decramer S, Fischbach M, Berard E, Guigonis V, Harambat J, Dunand O, Tenenbaum J, Marquet P, Saint-Marcoux F. Pharmacokinetics of mycophenolate mofetil in children with lupus and clinical findings in favour of therapeutic drug monitoring. *Br J Clin Pharmacol.* 2014 Oct;78(4):867-76.

Pharmacogenetics

3. Woillard JB, Picard N, Thierry A, Touchard G, Marquet P; DOMINOS study group. Associations between polymorphisms in target, metabolism, or transport proteins of mycophenolate sodium and therapeutic or adverse effects in kidney transplant patients. *Pharmacogenet Genomics.* 2014 May;24(5):256-62.

Pharmacodynamics & PKPD

4. Carr L, Gagez AL, Essig M, Sauvage FL, Marquet P, Gastinel LN. Calcineurin activity assay measurement by liquid chromatography-tandem mass spectrometry in the multiple reaction monitoring mode. *Clin Chem.* 2014 Feb;60(2):353-60.
5. Noceti OM, Woillard JB, Boumediene A, Esperón P, Taupin JL, Gerona S, Valverde M, Touriño C, Marquet P. Tacrolimus Pharmacodynamics and Pharmacogenetics along the Calcineurin Pathway in Human Lymphocytes. *Clin Chem.* 2014 Oct;60(10):1336-45.
6. Daher-Abdi Z, Lavau-Denes S, Premaud A, Urien S, Sauvage FL, Martin J, Leobon S, Marquet P, Tubiana-Mathieu, Rousseau A. Pharmacokinetics and exposure/effect relationships of capecitabine in elderly patients with breast or colorectal cancer. *Cancer Chemother Pharmacol.* 2014 Jun;73(6):1285-93.
7. Daher Abdi Z, Prémaud A, Essig M, Alain S, Munteanu E, Garnier F, Le Meur Y, Marquet P, Rousseau A. Exposure to mycophenolic acid better predicts immunosuppressive efficacy than exposure to calcineurin inhibitors in renal transplant patients. *Clin Pharmacol Ther.* 2014 Oct;96(4):508-15.

Clinical trials & clinical cases

8. Gauthier T, Piver P, Pichon N, Bibes R, Guillaudeau A, Piccardo A, Pesteil F, Tricard J, Gardet E, Laskar M, Lalloué F, Marquet P, Aubard Y. Uterus retrieval process from brain dead donors. *Fertil Steril.* 2014 Aug;102(2):476-82.
9. Monchaud C, Marin B, Estenne M, Preux PM, Marquet P; the eDelphi-Lung Transplant Group. Consensus Conference on a Composite Endpoint for Clinical Trials on Immunosuppressive Drugs in Lung Transplantation. *Transplantation.* 2014 Jun 20. [Epub ahead of print]

Determination of opiates, amphetamines and cocaine in whole blood, plasma and urine by UHPLC-MS/MS using a QuEChERS sample preparation

Sylvain DULAURENT[1], Mikaël LEVI[2], Jean-michel GAULIER[1], Pierre MARQUET[1,3] and Stéphane MOREAU[2]
[1] CHU Limoges, Department of Pharmacology and Toxicology, Unit of clinical and forensic toxicology, Limoges, France ;
[2] Shimadzu France SAS, Le Luzard 2, Boulevard Salvador Allende, 77448 Marne la Vallée Cedex 2
[3] Univ Limoges, Limoges, France

*Part of this work was presented in a poster session of the 62th ASMS Conference, 15 - 19 June, 2014, Baltimore.

1. Introduction

The determination of drugs of abuse (opiates, amphetamines, cocaine) in biological fluids is still an important issue in toxicology, in cases of driving under the influence of drugs (DUID) as well as in forensic toxicology. At the end of the 20th century, the analytical methods able to determine these three groups of narcotics were mainly based on a liquid-liquid-extraction with derivatization followed by GC-MS. Then LC-MS/MS was proposed, coupled with off-line sample preparation. Recently, on-line Solid-Phase-Extraction coupled with UHPLC-MS/MS was described, but in our hands it gave rise to significant carry-over after highly concentrated samples. We propose here another approach based on the QuEChERS (acronym for Quick, Easy, Cheap, Effective, Rugged and Safe) sample preparation principle, followed by UHPLC-MS/MS.

2. Methods and Materials

This method involves 40 compounds of interest (13 opiates, 22 amphetamines, as well as cocaine and 4 of its metabolites) and 18 isotopically labeled internal standards (designed with *) (Table1). To 100 µL of sample (urine, whole blood or plasma) were added isotopically labeled internal standards (in order to improve method precision and accuracy) at 20 µg/L in acetonitrile (20 µL), and 200 µL of acetonitrile. After a 15 s shaking, the mixture was placed at -20°C for 10 min. Then approximately 50 mg of QuEChERS salts ($MgSO_4$/NaCl/Sodium citrate dehydrate/Sodium citrate sesquihydrate) were added and the mixture was shaken again for 15 s and centrifuged for 10 min at 12300 g. The upper layer was diluted (1/3; v/v) with a 5 mM ammonium formate buffer (pH 3). Finally, 5 µL were injected in the UHPLC-MS/MS system. The whole acquisition method lasted 5.5 min.

Cocaine and metabolites	Amphetamines or related compounds	Opiates
-Anhydroecgonine methylester	-2-CB	-6-monoacetylmorphine*
-Benzoylecgonine*	-2-CI	-Dextromethorphan
-Cocaethylene*	-4-MTA	-Dihydrocodeine*
-Cocaine*	-Ritalinic acid	-Ethylmorphine
-Ecgonine methylester*	-Amphetamine*	-Hydrocodone
	-BDB	-Hydromorphone
	-Ephedrine*	-Methylmorphine*
	-MBDB	-Morphine*
	-m-CPP	-Naloxone*
	-MDA*	-Naltrexone*
	-MDEA*	-Noroxycodone*
	-MDMA*	-Oxycodone*
	-MDPV	-Pholcodine
	-Mephedrone	
	-Metamphetamine*	
	-Methcathinone	
	-Methiopropamine	
	-Methylphenidate	
	-Norephedrine	
	-Norfenfluramine	
	-Norpseudoephedrine	
	-Pseudoephedrine	

Table 1 list of analyzed compounds with their associate internal standard (*)

UHPLC conditions (Nexera MP system, Fig. 1)

Column: Restek Pinnacle DB PFPP

50×2.1 mm 1.9 µm

Mobile phase A: 5mM Formate ammonium with 0.1% formic acid in water

B: 90% CH_3OH/ 10% CH_3CN (v/v) with 0.1 % formic acid

Flow rate: 0.474 mL/min

Time program: B conc. 15% (0-0.16 min) - 20% (1.77 min) - 90% (2.20 min) – 100%(4.00 min) – 15% (4.10-5.30 min)

Column temperature: 50 °C

MS conditions (LCMS-8040, Fig. 1)

Ionization: ESI, Positive MRM mode

Ion source temperatures: Desolvation line: 300°C

Heater Block: 500°C

Gases: Nebulization: 2.5 L/min

Drying: 10 L/min

MRM Transitions: 2 Transitions per compound were dynamically scanned for 1 min except pholcodine (2 min)

Pause time: 3 msec

Loop time: 0.694 sec (minimum 17 points per peak for each MRM transition)

Fig. 1 Shimadzu UHPLC-MS/MS Nexera-8040 system

3. Results

Chromatographic conditions

The analytical conditions allowed the chromatographic separation of two couples of isomers: norephedrine and norpseudoephedrine; ephedrine and pseudoephedrine (Fig. 2). A typical chromatogram of the 58 compounds is presented in Fig. 3.(qualifier), respectively.

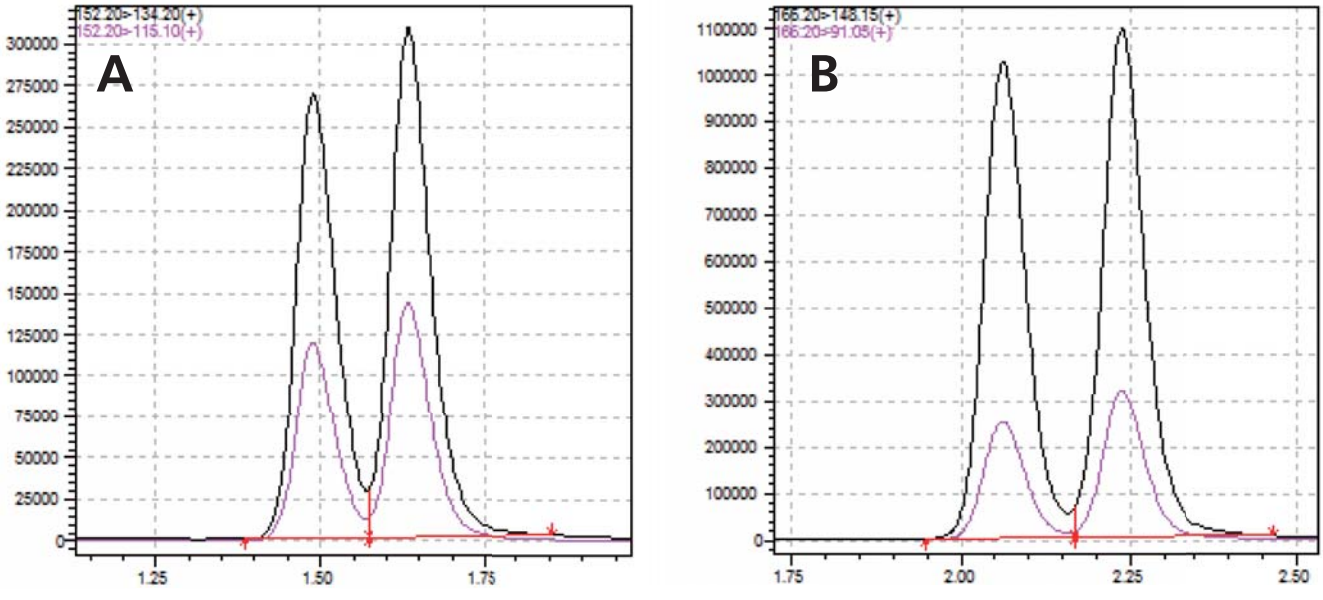

Fig. 2 Chromatograms obtained after an injection of a 5 µL whole blood extract spiked at 200 µg/L.
Order of retention - A: norephedrine and norpseudoephedrine /B: ephedrine and pseudoephedrine

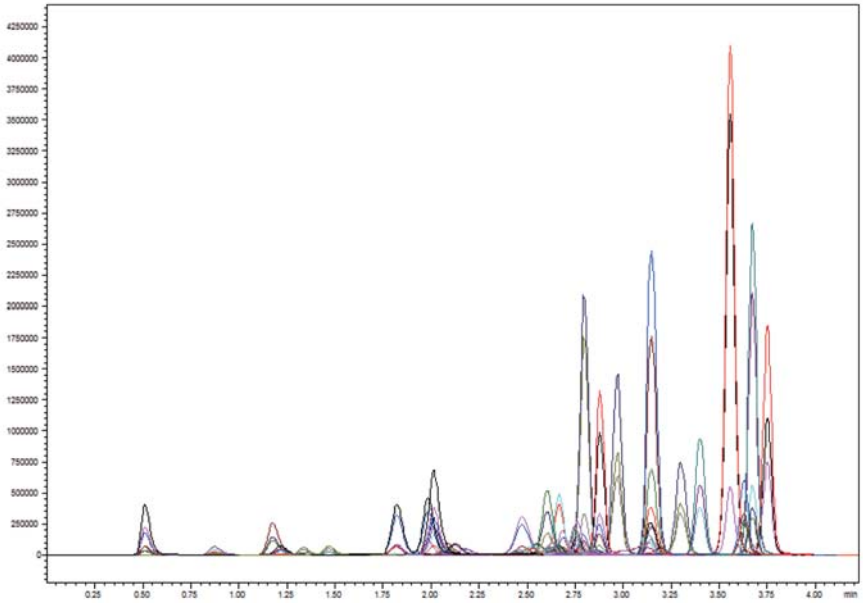

Fig. 3 Chromatogram obtained after an injection of a 5 µL whole blood extract spiked at 200 µg/L

Extraction conditions

As described by Anastassiades et al. J. AOAC Int 86 (2003) 412-31, the combination of acetonitrile and QuEChERS salts allowed the extraction/partitioning of compounds of interest from matrix. This extraction/partitioning process is not only obtained with whole blood and plasma-serum where deproteinization occurred and allowed phase separation, but also with urine as presented in Fig. 4.

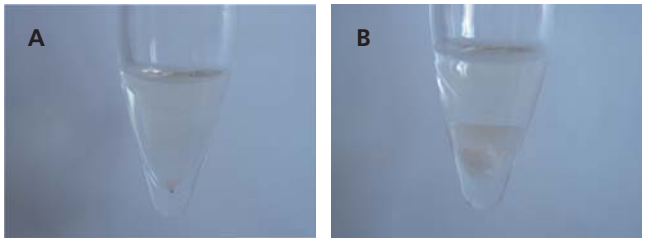

Fig. 4 influence of QuEChERS salts on urine extraction/partitioning: A: acetonitrile with urine sample lead to one phase / B: acetonitrile, QuEChERS salts and urine lead to 2 phases.

Validation data

Among the 40 analyzed compounds, 38 filled the validation conditions in term of intra- and inter-assay precision and accuracy were less than 20% at the lower limit of quantification and less than 15% at the other concentrations.

Despite the quick and simple sample preparation, no significant matrix effect was observed and the lower limit of quantification was 5 µg/L for all compounds, while the upper limit of quantification was set at 500 µg/L. The concentrations obtained with a reference (GC-MS) method in positive patient samples were compared with those obtained with this new UHPLC-MS/MS method and showed satisfactory results.

Contrary to what was already observed with on-line Solid-Phase-Extraction, no carry-over effect was noted using the present method, even when blank samples were injected after patient urine samples with analytes concentrations over 2000 µg/L.

4. Conclusions

- Separation of two couples of isomers with a run duration less than 6 minutes and using a 5 cm column,
- Quick sample preparation based on QuEChERS salts extraction/partitioning, almost as short as on-line Solid Phase Extraction,
- Lower limit of quantification compatible with determination of DUID,
- No carry over effect noticed.

CHU
Centre hospitalier universitaire
Limoges

A Closer Look at Cannabis Testing

Scott Kuzdzal, Ph.D., Bob Clifford, Ph.D., Paul Winkler and Will Bankert (Shimadzu Scientific Instruments)

Introduction – Current US Cannabis Research, Policy & Law

Cannabis has demonstrated health benefits since ancient times. While less than 6% of today's studies on marijuana analyze its medical properties, publications to date indicate that cannabis shows great promise for the treatment of many diseases and symptoms (Table 1). However, patients with cancer or severe pain, for example, have been blocked from these benefits since the mid-20th century when federal regulations were enacted that prohibited the use, sales and distribution of marijuana due to its psychoactive properties. The US Drug Enforcement Agency (DEA) stated in 2011 that marijuana has "no accepted medical use" and should therefore remain illegal under federal law.
Strict scheduling and law enforcement actions have made it more difficult for researchers to obtain marijuana samples for scientific studies than LSD, MDMA, heroin and cocaine. In June, 2014, the Drug Policy Alliance and the Multidisciplinary Association for Psychedelic Studies released a report titled "The DEA: Four Decades of Impeding and Rejecting Science." Citing case studies from 1972 to the present, this report claims that the DEA suppressed research on the positive benefits of marijuana for medicinal use.

More recently, thirty members of the US Congress sent a letter to the Health and Human Services Secretary demanding an end to the federal monopoly on marijuana research so that more studies can be performed by US researchers.

Mainstream acceptance of cannabis has increased steadily over the past decade in the United States. Twenty-two states and the District of Columbia have legalized or decriminalized marijuana in some form. Colorado and Washington have legalized marijuana for recreational use, with Oregon soon to follow suit. Maryland has approved bills making medical marijuana accessible to patients and decriminalizing possession of limited amounts of the drug. As the medical and recreational uses of cannabinoids increases both in the United States and globally, the need for improved quality control testing also increases.

On a recent tour of medicinal marijuana businesses in the State of Oregon, we learned all aspects of the cannabis industry and key differences between recreational and medical marijuana grow operations.

Appears to have powerful anti-tumor properties	Improves symptoms associated with Lupus
Reduces pain associated with chemotherapy	Shows promise in eliminating Crohn's disease
Treats glaucoma by lowering intraocular pressure	Reduces pain in multiple sclerosis patients
Decreases symptoms of epileptic seizures	Helps fight obesity by increasing metabolism
Reduces brain damage after a stroke	Reduces frequency and severity of concussions
Relieves discomfort from arthritis	Helps reduce muscle spasms
Lessens side effects from hepatitis C treatments	Reverses the carcinogenic effects of tobacco use
Treats inflammatory bowel disease	Decreases anxiety and improves appetite
Slows the progression of Alzheimer's and other neurodegenerative diseases	

Table 1 Partial listing of reported health benefits of cannabis in scientific literature and news reports (see suggested reading at the end of this article).



A biomedical cannabis grow operation in Oregon. This facility prefers natural sunlight for mature plant growth and reduces environmental stresses on the plants to ensure that the most natural, homeopathic medicines are produced.

Chemistry and Biomedical Properties of Cannabis

Cannabis plants contain more than 480 compounds that have been identified to be unique to cannabis, including over 66 cannabinoids. Cannabis also contains approximately 140 terpenes, which are more widespread in the plant kingdom. While tetrahydrocannabinol (THC) is the most abundant active component in cannabis, cannabidiol (CBD) and cannabinol (CBN), a degradation product of THC, are commonly measured in cannabis samples. CBD, a non-psychoactive compound, has been shown to reduce convulsions, inflammation, nausea and anxiety, and has even eradicated tumors in some patients.

Fig. 1 provides partial listing of cannabinoid pharmacological characteristics. Recreational marijuana growers, primarily interested in high THC content are less concerned with the "CBX profiles", whereas these compounds may be beneficial to biomedical marijuana patients with specific diseases or symptoms.

Cannabis Consumption & Delivery

Smoking is an expedient method of consuming marijuana, but some experts argue that smoking can cause lung and respiratory problems and reduce the bioavailability of some constituents. Marijuana plants naturally contain the acid forms of THC and CBD known as THCA and CBDA. During smoking, heat converts the THCA and CBDA into their more potent, non-acid forms, THC and CBD. This is referred to as decarboxylation.

Vaporizers have provided a means of more gently heating the cannabis. Doing so releases more medicinal components of the marijuana and reduces the amount of noxious chemicals. Due to the volatility of cannabinoids, they vaporize at a temperature much lower than the combustion temperature of plant matter. Vaporization usually heats the sample to 150-200 C. This is sufficient to evaporate off the cannabinoids and terpenes but not combust the sample into more

	Antibiotic	Antifungal	Anti-inflammatory	Analgesic	Anxiolytic	Antioxidant	Antispasmodic	Antiemetic	Sedative	Euphoriant
Cannabigerolic Acid (CBGA)	✓									
Cannabigerol (CBG)	✓	✓	✓	✓						
Cannabichromene (CBC)	✓	✓	✓	✓						
Cannabidiolic Acid (CBDA)	✓									
Cannabidiol (CBD)			✓	✓	✓	✓	✓			
Δ-9-THC			✓	✓		✓		✓		✓
Δ-9-THCV				✓						✓
Cannabinol (CBN)	✓		✓						✓	

Fig. 1 Cannabis constituents and partial listing of pharmacological characteristics.

carcinogenic compounds like benzopyrene. It is important to note that when marijuana products are smoked, combustion sterilizes cannabis from various mold and bacterial spores (including Aspergillus, Penicillium, Cladosporium, Alternaria, Yeasts, and E.Coli). Migration to vaporization, however, puts immuno-compromised cancer and HIV patients at increased risk for bacterial infections.

The majority of patients prefer to consume edibles or beverages that have been created using butters and oils derived from plant extracts. The effects of cannabis ingestion differ significantly from smoking or vaporizing, and the time it takes for therapeutic benefits to begin takes much longer. This delayed onset, coupled with high THC concentrations present in some edibles puts consumers at a greater risk of THC overdosing. There are also growing concerns over infants and children gaining access and overdosing on THC-infused edibles that look identical to candy.

Medical marijuana dispensaries offer many forms of cannabis products, including the orange slices, pretzels, granola bites and hard candy products shown here. Brownies, beverages, chocolates and sublingual oils are also popular.

Towards Personalized Cannabis Therapies

The premium products in medical marijuana dispensaries are products high in THC. But as described previously, it is actually the various CBX compounds that appear to have enhanced health benefits. As research into cannabis treatments grows, much more will be known about the mechanisms of action of cannabinoids and terpenes. G.I. Grow, an organic biomedical farm, is pioneering new approaches for natural cannabis remedies (www.GIGrow.us). They continuously nurture cannabis and reformulate CBX oil blends in response to patient outcomes, delivering a personalized cannabis treatment approach for each individual patient.

There are growing numbers of cannabis oil success stories, including Elkan, now 10 years old, living in Oregon. Elkan suffered from severe autism, including Attention Deficit Disorder (ADD), Attention Deficit Hyperactivity Disorder (ADHD), Pervasive Developmental Disorder (PDD) and Sensory Processing Disorder (SPD). Elkan also had trouble speaking, suffered intense Leaky Bowel Syndrome symptoms and needed to be physically restrained 3-4 times per week because he would start flailing around. In a recent interview with Elkan's mother, Laura, she commented that, "Elkan's doctors were not sure why all pharmaceuticals other than Ritalin were showing no benefit whatsoever." Nothing seemed to work and most pharmaceuticals only exacerbated his symptoms. Elkan began taking a blend of natural CBD oils from G.I. Grow just months ago and after just 3 months taking cannabis oil, he can now speak, does not experience Leaky Bowel Syndrome symptoms and does not need to be restrained.

A breeding pair consisting of a female Purple Heart G.I. (pre98 Bubba Kush female x Purple Thai trainwreck) and a male Mendo Express (Mendo Purps female x E32 Arcata Trainwreck), left, and a high-CBG strain Black Trainwreck (Oregon Trinity X Purple Thai Trainwreck), right, at G.I. Grow's Biomedical Farm.

Cannabis Analytical Testing

Cannabis growers and dispensaries benefit tremendously from testing performed at independent laboratories. This testing determines potencies, reduces the risk of contamination and improves product quality. In the following paragraphs we will more closely examine cannabis testing. Routine cannabis testing services include cannabinoid potency, and screening/determination of terpenes, aflatoxins, heavy metals, molds, bacteria, pesticides, herbicides and residual solvents.

Cannabinoid Potency Testing

A critical test associated with cannabis testing is cannabinoid potency. Most labs quantitate levels of at least three major cannabinoids: THC, CBD and CBN and their different forms (carboxylated vs decarboxylated). Some labs employ gas chromatography (GC), in which the sample is vaporized under heat. Both GC-FID and GC-MS are commonplace. Because intense heating is used in GC, any THCA present in the natural sample is converted to THC and labs report this value as "THC Total". Other labs use HPLC to determine the amount of cannabinoids present. Because HPLC does not require heating, testing by this method provides a more accurate determination of the actual amounts of carboxylated or decarboxylated forms present in the sample. Potency testing accompanied with proper product labeling is needed to ensure that customers know exactly how much of the cannabinoids they are consuming.

THC, CBD and CBN potency testing by HPLC (left and middle) and Rose City Labs (www.RoseCityLabs.com) advertisement (Blueberry Kush potency of 20.41% THC, right).

Typical THC potency ranges from 5 to 25 % in plant materials and edibles, but can run much higher for concentrated oils. There are no established standard methods for chopping samples, homogenizing them and performing extractions. Therefore, variations in cannabis potency can easily exceed 20%. Potency testing will improve as chemical standards of known potency become more readily available.

Shimadzu integrated HPLC systems, including the new i-Series, are ideally suited to meet the challenges of cannabis potency testing. The i-Series touchscreen, graphical user interfaces between system and workstation, allows intuitive operations regardless of experience level.

Pesticides, Herbicides and Residual Solvent Screening

The analytical detection of pesticides in cannabis remains a challenge. Pesticides are used in commercial cannabis grow operations to kill mites that thrive on cannabis plants. Female mites lay over 2,000,000 eggs per day at 90° Fahrenheit (32.2° Celsius). Also, they are mutating throughout the cannabis industry with resistance to some pesticides. Thrips (tiny, slender insects with fringed wings), aphids, and root gnats are common indoor pests. Spider mites, caterpillars, grasshoppers threaten greenhouse grows. Halyomorpha halys, also known as the brown marmorated stink bug, is a voracious eater and has an affinity for cannabis plants.

An enormous number of pesticides are available in the commercial marketplace, and no lab can test for all of them. GCMS is the preferred instrumentation platform for such testing. While there are currently no guidelines for residual pesticide screening in cannabis, most labs test for the most common pesticides employed during cannabis cultivation: organophosphates, carbamates, pyrethroids and avermectins. MRX Labs in Portland, OR, is leading the way in pesticide analytical testing services, offering a panel of 40 pesticides. MRX Labs uses Shimadzu GCMS-QP2010 Ultra instruments, which enhance lab productivity and sample throughput. The ecology mode saves power and carrier gas consumption allowing for a lower cost of ownership and less environmental stress. Another laboratory, G.O.A.T. Labs (www.GOATLabs.us) in Vancouver, WA, utilizes a GCMS-QP2010 SE. Herbicides are also reported using both of these platforms. Residual solvent testing is performed on a headspace GC such as with Shimadzu's GC-2010 Plus with HS-20 Headspace Sampler similar to monograph "USP <467> for Residual Solvents".

Shimadzu GCMS (top) and LC (bottom) instrumentation at MRX Labs in Portland, Oregon (www.MRXLabs.com).

Additional Cannabis Laboratory Tests

The moisture content of a variety of cannabis samples can be measured using Shimadzu MOC63u (and MOC-120H) balances. The MOC63u is applicable to a variety of cannabis products and its' long-life and high power halogen heater provides quick and accurate measurement. Medical marijuana dispensaries require National Type Evaluation Program (NTEP) approved scales for use in legal trade.

Additional testing of contaminants, including heavy metals, mycotoxins and microorganisms are also important to cannabis labs. The ideal conditions for cannabis growth are also ideal for the growth of potentially harmful bacteria and fungi including yeast and molds. Recreational and medical cannabis must be properly screened for microbial contamination that poses health risks to consumers and immunocompromised individuals. Traditional mold and bacteria testing with petri dishes is being replaced with qPCR platforms. MALDI based microorganism identification may be useful as a qualitative technique to certify the presence or absence of various microorganisms. MALDI could also compete with genomics testing for cannabis strain typing.

Mycotoxins (aflatoxin) can be detected using Shimadzu LC and LCMS systems. Heavy metals analyses generally include the big four of lead (Pb), mercury (Hg), cadmium (Cd), and arsenic (As), which can be tested by Shimadzu's AA-7000 with GFA-7000 or ICPE-9800. Alternatively, ICP-MS may be employed.

Considerations for Future Cannabis Testing

The cannabis industry and cannabis testing are in their infancies. As the need for better quality control continues and standardization is introduced, it is likely that lower limits for the various cannabis contaminants will be established and regulations will be introduced. Mass spectrometry will likely play a greater role in quantitation as detection levels are lowered and confirmatory tests are required. The health benefits of terpenes present in cannabis will also provide a fertile area of scientific research. CBD, CBG and other compounds appear to have a synergistic relationship with each other as well as with various THC forms and terpenes. This field needs much more investigation to determine mechanisms of action, bioavailability and health benefits.

With an increase in cannabis product consumers there comes an increase in public safety concerns, such as "drugged driving". Law enforcement will need new, low-cost methods for rapid salivary, breath-based and/or finger-stick screening of individuals that appear to be under the influence of marijuana. Also, better product packaging and labeling will be needed to reduce accidental infant exposures, especially to candy-like, medicinal marijuana edibles.

Cannabis testing is not just a growing US market. Sativex™ a synthetic, pharmaceutical version of cannabis, has been approved for use in 25 countries as a treatment for muscle spasm pain in multiple sclerosis patients. Marinol®, a synthetic THC product, has been FDA approved to treat nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional treatments. The FDA also approved Marinol® to treat appetite loss associated with weight loss in people with AIDS. Idrasil™ is a physician prescribed "medical cannabis in a pill". Unlike Marinol, which is a synthetic form of a single cannabinoid (THC) only, Idrasil is an all-natural cannabis

plant extract containing the full spectrum of naturally occurring cannabinoids from cannabis. CBD oils can be purchased legally from Amazon.com and many other sources.

As more cannabis-based or synthetic cannabinoid drugs and homeopathic medicines enter the marketplace, and as more states legalize medical and/or recreational marijuana, the need for cannabinoid testing and standardization will continue to grow. The US cannabis industry is projected to be an $8 Billion industry by 2017, with rapid growth expected in all aspects of cannabis businesses (production, quality control, informatics, packaging, labeling, security, etc.). In our estimation, as cannabis research moves forward, biological insights into the health benefits of cannabis, including personalized cannabis oil therapies, will be unlocked and many more people will benefit from the natural healing benefits of cannabinoids.

Suggested Reading:

1. An archaeological and historical account of cannabis in China. Econ Bot 1974. 28:437-8.
2. Marijuana and Medicine: Assessing the Science Base (1999). Janet E. Joy, Stanley J. Watson, Jr., and John A. Benson, Jr., Editors, Division of Neuroscience and Behavioral Health Institute of Medicine, National Academy Press, Washington, D.C.
3. "DEA Blatantly Blocks Medical Marijuana Research" by Scott Morgan, January 2009. Blog from StoptheDrugWar.org.
4. Chemstry and Analysis of Phytocannabinoids and Other Cannabis Constituents, Chapter 2 in Forensic Science and Medicine: Marijuana and the Cannabinoids. Rudolf Brenneisen. Edited by M.A. ElSohly, Humana Press, Inc.
5. American Herbal Pharmacopoeia (2013). Cannabis Inflorescence, Standards of Identity, Analysis and Quality Control.
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8. 23 Health Benefits of Marijuana. Business Insider (2014). Jennifer Welsh and Kevin Loria. http://www.businessinsider.com/health-benefits-of-medical-marijuana-2014-4?op=1
9. Sativex for relieving persistent pain in patients with advanced cancer (SPRAY III). ClinincalTrials.gov (2011).

Businesses featured in this article:

G.I. Grow
www.GIGrow.us
G.I. Grow Farm's utilizes sustainable cultivation practices to enhance our environmental quality and the natural resource base and soil nutrients used for growing. They are a single source, local Oregon grown, organic farm that strictly adheres to and abides by the OMMP – Oregon Medical Marijuana Program rules and regulations.

Ole World Oils
www.CamelinaGold.com
Ole World Oils manufactures Camelina Gold oil, which is a natural source of fiber, proteins, chlorophyll, essential minerals and vitamins and can be used as a carrier for CBX oils.

G.O.A.T. Labs LLC – Genesis Organic Assurance Testing
www.GOATLabs.us
G.O.A.T. Labs is a Full Service Laboratory. G.O.A.T. Labs is the brainchild of Dana Luce. He was joined by 4 other members from A/Co 158th Avn, 101st Airborne. All of the Founders were Crew Members (pilots or door gunners) on UH-1 Huey Helicopters in Vietnam.

Rose City Laboratories LLC
www.RoseCityLabs.com
Rose City Laboratories was established in April 2012. Their staff is dedicated, highly skilled and has years of experience in both the medical marijuana industry and analytic testing. Rose City Laboratory utilizes state-of-the-art high performance liquid chromatography, gas chromatography, and mass spectrometry equipment.

MRX Labs Analytical Testing Services
www.MRXLabs.com
MRX Labs is a state-of-the-art laboratory located in Portland, Oregon, offering a full range of analytical testing services.

Viridian Sciences
www.ViridianSciences.com
Viridian offers a wide array of services, including implementation, configuration, training, prompt support, custom reporting and other ancillary professional services to clients. Their mission is to help businesses grow by providing the world's leading enterprise resource planning technology while helping companies adhere to government regulations with complete legal compliance.

[Disclaimer]

Shimadzu products mentioned in this article are for Research Use Only and are not for use in diagnostic procedures. Shimadzu Scientific Instruments is not condoning the use of recreational nor medical marijuana, we are merely being solicited by customers for cannabis testing at their facilities and are herein providing a market summary of the cannabis industry.

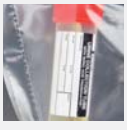
Posters from Recent Conferences

The following posters were presented at recent international conferences in 2014, such as ASMS 2014, ISCC 2014 and TIAFT 2014. Click the title URLs to download the posters of interest.

Poster 1 **Food Safety**

Highly sensitive and rapid simultaneous method for 45 mycotoxins in baby food samples by HPLC-MS/MS using fast polarity switching

Mycotoxins are toxic metabolites produced by fungal molds on food crops. Depending on the potency of the mycotoxin and the use of the food, the maximum allowed level is defined by legislation. Baby food is particularly critical. Therefore, a sensitive method to assay mycotoxins in complex matrices is mandatory. In this study, we tested three kinds of samples: baby milk powder, milk thickening cereals (flour, rice and tapioca) and a vegetable puree mixed with cereals.



Poster 2 **Forensics**

Development and Validation of Direct Analysis Method for Screening and Quantitation of Amphetamines in Urine by LC/MS/MS

The new guidelines of SAMHSA under U.S. Department of Health and Human Services, effective as of Oct. 2010, allowed the use of LC/MS/MS for screening, confirmation and quantitation of illicit drugs, including amphetamines. The objective of this study was to develop a fast LC/MS/MS method for direct analysis of amphetamines in urine without sample pre-treatment (except dilution with water) on UFMS.

Poster 3 **Food**

Quantitative analysis of anabolic steroids in control samples from food-producing animals using a column-switching LC-HESI-MS/MS assay

The use of natural and synthetic hormones to increase the weight of meat-producing animals is prohibited in the European Union in order to protect consumers from the harmful effects of digesting hormone residues and their metabolites. In this poser, we present an online-SPE method that was developed to considerably shorten the pre-treatment time. In addition to optimisation of the extraction method, chromatographic separation was optimised to decrease ion-suppression and isobaric interference.

Poster 4 **Forensics**

The application of UHPLC and Ultrafast-LCMSMS to the analysis of small volume biological samples for drug residues

The analysis of specimens such as blood spots, hair and saliva for the presence of drug residues is limited by the sample size and the need to perform both screening and confirmatory analyses. Sample preparation techniques for such samples benefit from micro-scaled approaches that minimise the exposure of the sample to diluents and possible contaminants, poor recovery and the increased processing time associated with scale. We couple Noviplex cards for the isolation of small molecules from hydrolysed urine, with UHPLC and Ultrafast-LCMSMS (UFMS) to detect low-level drug residues and metabolites in small-volume biological specimens with subsequent identification of unknowns using MS scan events.

Poster 5 **Pharmaceutical**

Highly sensitive quantitative estimation of genotoxic impurities from API and drug formulation using LC/MS/MS

The toxicological assessment of Genotoxic Impurities (GTI) and the determination of acceptable limits for such impurities in Active Pharmaceutical Ingredients (API) are difficult issues. Dronedarone is a drug mainly used for indications of cardiac arrhythmias. GTI of this drug have been quantitated here. A method was optimized for simultaneous analysis of DRN-IA, DRN-IB and BHBNB.

Poster 6 **Food Safety**

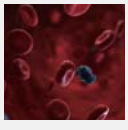
Characterization of metabolites in microsomal metabolism of aconitine by high-performance liquid chromatography/quadrupole ion trap/time-of-fight mass spectrometry

Aconitine (AC) is a bioactive alkaloid from plants of the genus Aconitum, some of which have been widely used as medicinal herbs for thousands of years. AC is also well known for its high toxicity, which induces severe arrhythmias leading to death. The study of metabolic pathways is very important for efficacy of therapy and evaluation of toxicity for those with narrow therapy windows. The aim of our work was to obtain the metabolic pathways of AC by the human liver microsomes.

Poster 7 **Forensics**

Simultaneous Screening and Quantitation of Amphetamines in Urine by On-line SPE-LC/MS Method

The new SAMHSA guidelines, implemented in Oct 2010, allow the use of LC/MS and LC/MS/MS for the screening, confirmation and quantitation of illicit drugs, including amphetamines. The objective of this study was to develop an on-line SPE-LC/MS method for analysis of five amphetamines in urine without sample pre-treatment except dilution with water.



Poster 8 **Forensics**

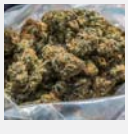
Simultaneous analysis for forensic drugs in human blood and urine using ultra-high speed LC-MS/MS

The simultaneous analysis of drugs of abuse in clinical and forensic laboratories requires highly specific system. Conventional procedures to analyze drugs in complex matrices like whole blood involve tedious, time-consuming, expensive, and complex steps, and possible sample loss and contamination problems are not unusual. The developed system in this study contained not only optimized MRM transition parameters with product ion scanning, which is automatically triggered once an MRM exceeds a specified threshold, but also sample preparation utilizing modified QuEChERS extraction.

Poster 9 **Forensics**

Determination of Δ9-tetrahydrocannabinol and two of its metabolites in whole blood, plasma and urine by UHPLC-MS/MS using QuEChERS sample preparation

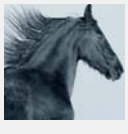
Cannabis is the most widely used illicit drug. Δ 9-tetrahydrocannabinol (THC) and two of its metabolites are regularly investigated in biological fluids. Historically, the concentrations of these compounds were determined using a time-consuming extraction procedure and GC-MS. We propose here a highly sensitive UHPLC-MS/MS method with straightforward QuEChERS sample preparation.



Poster 10 **Forensics**

Comprehensive Analysis of Naphthoylindole-type Synthetic Cannabinoids by GC-MS/MS

Recently, the abuse of synthetic cannabinoids (SCs) in the form of so-called herbal smoking powders has become increasingly common. However, for a class of compounds such as SCs that is undergoing rapid chemical evolution, detection of new analogs is limited by the lack of available standards. In this study, a GC-MS/MS method for the identification of Naphthoylindole-type SCs (NISCs) using simultaneous scan, MRM and precursor ion scanning simultaneous scan, MRM and precursor ion scanning was evaluated.



Poster 11 **Forensics**

Analysis of doping agents using ultrafast LC-MS/MS with scheduled MRM

In horse racing, for example, terms such as negative doping, which is doping to defeat, are an issue. In the past, the attitude "Allowed is, what is not found" predominated. Nowadays, improved analytical methods allow the detection of even the slightest traces of doping agents in blood and urine. Thus, the analytical possibilities of the different labs are crucial for the detection of a substance. Here we show the advantage of an ultrafast MS technique with excellent sensitivity when analyzing horse doping agents.

Drugs and Poisons Involved in Criminal Cases: Recent Tendency in Japan and Analytical Strategies

Hitoshi TSUCHIHASHI, Division of Preventive and Social Medicine, Department of Legal Medicine, Osaka Medical College, JAPAN

Increasing numbers of criminal cases involving drugs and poisons have been reported in Japan. Sleeping pills are frequently used in atrocious crimes, such as murder and sexual assault. There have also been many cases where foreign substances, such as agrochemicals or poisons, are mixed into food or drinks. Moreover, the wide spread of newly-encountered drugs, in addition to classical illicit drugs such as methamphetamine, has become a serious social problem. Thus, analyses of drugs and poisons in various specimens, as well as determination of drugs and metabolites in biological specimens are becoming increasingly important in criminal investigations.

Recently, newly-encountering so-called recreational drugs (which are actually, often more potent or toxic than classical narcotics) are causing serious problems. To combat with such drugs, we presume drugs that may appear on the streets in the near future, synthesize standards of such drugs in advance, and collect their analytical data using GC/MS, GC-MS/MS, and LC-MS/MS.[1-3] We construct the libraries in order to quickly identify such new-type drugs, and to share such valuable data with many colleagues around the world. We have also investigated their metabolic pathways by carefully analyzing urine specimens from drug users, using newly-synthesized standards of their possible metabolites, which may be important analytical targets in forensic drug analyses. Such newly-encountered drugs usually have a number of isomers, and the isomers often vary in regulation status. To clearly distinguish such analogs, we have developed useful GC-MS/MS and LC-MS/MS procedures.[4] For instance, a simultaneous analysis system, including elucidation of chemical structures, has been established for synthetic cannabinoids and cathinones, using GC-MS/MS in the scan/MRM/product ion mode.

Hair analysis for drugs has drawn much attention, owing to its longer window of detection. We have established single-hair MALDI-MS imaging of drugs incorporated into hair, and for the first time succeeded in the visualization of methamphetamine (MA) on the longitudinal section of hair specimens from MA users.[5,6] This new approach provides much more detailed information about drug use history, when compared with conventional LC-MS/MS procedure after extraction of the drug in segmented hair samples. In addition, this methodology will help reveal the route and mechanism of drug incorporation into hair tissue.

Due to their high metabolisms, the detection of hypnotics in urine quickly becomes impracticable after intake. For supposed drug-facilitated sexual assaults, we have developed an effective analytical procedure to determine hypnotics/metabolites incorporated into hair, for proving such an unusual single exposure to a hypnotic drug. Zolpidem was readily detectable in a one-cm-sectioned single hair specimen sampled one month after a single administration of a sleeping pill (10 mg zolpidem/tablet).

For cases of agrochemicals or poisons mixed into frozen foods, rapid identification of the causative agent is required for saving victims and prompt arrestment of the criminal to prevent recurrences. We have made efforts to establish rapid and reliable GC-MS/MS and LC-MS/MS procedures by combining with a newly developed user-friendly sample pretreatment method and automated library search and quantitation systems.[7-11]

A wide range of numerous drugs and chemicals should be considered in the forensic drug analysis. However, specimens are usually not in ideal conditions; samples are often insufficient or contaminated, metabolisms and decomposition obscure the identity of the parent drug. Thus, we should make full efforts to learn the latest studies and share useful techniques, for the advancement in the fields of forensic toxicology and criminal investigations.

1) Zaitsu, K.; Katagi, M.; Kamata, H.; Kamata, T.; Shima, N.; Miki, A.; Tsuchihashi, H. and Mori, Y.:Determination of the metabolites of the new designer drugs bk-MBDB and bk-MDEA in human urine. *Forensic Sci. Int.*, 188, 131–139 (2009).

2) Katagi, M.; Zaitsu, K.; Shima, N.; Kamata, T.; Kamata, H.; Nakanishi, K.; Nishioka, H.; Miki, A. and Tsuchihashi, H.: Metabolism and Forensic Toxicological Analyses of the Extensively Abused Designer Drug Methylone. *TIAFT Bull.*, 40, 30-35 (2010).

3) Shima, N.; Katagi, M.; Kamata, H.; Matsuta,S.; Nakanishi, K.; Zaitsu, K.; Kamata, T.; Nishioka, H.; Miki, A.; Tatsuno, M.; Sato, T.; Tsuchihashi, H. and Suzuki, K. : Urinary excretion and metabolism of the newly encountered designer drug 3,4-dimethylmethcathinone in humans. *Forensic Toxicol.*, 31, 101-112 (2013).

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6) Miki, A.; Katagi, M.; Shima, N.; Kamata, H.; Tatsuno, M.; Nakanishi, T.; Tsuchihashi, H.; Takubo, T. and Suzuki, K. : Imaging of methamphetamine incorporated into hair by MALDI-TOF mass spectrometry. *Forensic Toxicol.*, 29, 111-116 (2011).

7) Matsuta, S.; Nakanishi, K.; Miki, A.; Zaitsu, K.; Nishioka, H.; Katagi, M.; Tatsuno, M.; Tsuboi,K.; Tsuchihashi, H. and Suzuki, K.: Development of a simple one-pot extraction method for metabolites of forensic interest in blood by modifying the method. *Forensic Sci. Int.*, (2013).

8) Minohata, T.; Kudo, K.; Usui, K.; Shima, N.; Katagi, M.; Ikeda, N.; Tsuchihashi, H. and Suzuki, K.: The Application of Ultra-Fast Triple Quadrupole LC-MS/MS to Forensic Analysis, *Shimadzu Review*, Vol.70[3・4](2013).

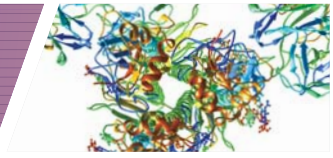
9) Tsuchihashi, H.: Automatic Identification and Semi-quantitative Analysis of Psychotropic Drugs in Serum Using"GC/MS Forensic Toxicological Database," *Shimadzu GC/MS Technical Report* (2012)

10) *GC/MS Forensic Toxicology Screening System,* Shimadzu Corporation (2012)

11) *LC/MS/MS Rapid Toxicology screening System,* Shimadzu Corporation (2013)

For Research Use Only.

Collaboration between Shimadzu Corporation and the MacCoss Lab of Biological Mass Spectrometry, University of Washington



Shimadzu seeks to redefine quantitative proteomics by enabling powerful Skyline software support on its ultra-fast mass spectrometry platforms

Shimadzu Corporation released the new mutual support between the Skyline quantitative proteomics software and Shimadzu's high-sensitivity triple quadrupole LC/MS/MS platform.

As mass spectrometry-based proteomics technologies continue to play an ever-increasing role in biomarker discovery, validation and translation for biological and clinical applications, advances in throughput and multiplexing are necessary to improve quantitation of biomarkers in this emerging field referred to as quantitative Clinical Chemistry Proteomics (qCCP). To bring qCCP applications closer to clinical laboratories, Shimadzu has integrated its ultra-fast LC/MS/MS platforms with the powerful, freely available Skyline quantitative proteomics software.

Skyline software can be used to design, refine and optimize Selected Reaction Monitoring (SRM) / Multiple Reaction Monitoring (MRM) and Full Scan MS and MS/MS quantitative methods based on protein sequences and user-defined rules. Skyline software not only integrates results with method optimization; it is also described as a common framework for quantitative proteomics for researchers to adopt and to standardize to.

"Shimadzu has been an excellent collaborator to work with. Their effort to complete the integration with Skyline in such a rapid time scale has been impressive," said Brendan MacLean, Software Project Manager for Skyline at the University of Washington, School of Medicine, Department of Genome Sciences.

Dr. Michael MacCoss, Professor at the University of Washington, School of Medicine, Department of Genome Sciences, said: "Skyline is a community effort in the field of quantitative proteomics. It is important to foster a broad sharing of both methods and results across instrument platforms. By including Shimadzu's high-sensitivity triple quadrupole platforms into Skyline, it enables the proteomics community to work with far-reaching technologies."

"We are now excited to redefine the quantitative proteomics market in collaboration with the MacCoss Lab and their outstanding software. MacCoss Lab has brought together Shimadzu's class-leading mass spectrometry platforms and Skyline software to help enhance quantitative proteomics workflows. We will continue our effort to develop and provide the best solutions to our customers," said Kozo Miseki, Corporate Officer, Deputy General Manager of Analytical & Measuring Instruments Division, Shimadzu Corporation.

About Skyline

Skyline is an open source software project, started in 2008 by the MacCoss lab at the University of Washington. It is now the leading software application for building Selected Reaction Monitoring (SRM)/Multiple Reaction Monitoring (MRM), Parallel Reaction Monitoring (PRM - Targeted MS/MS and DIA/SWATH) and targeted DDA with MS1 quantitative methods and analyzing the resulting mass spectrometer data. For more information visit skyline.maccosslab.org.

EDX-7000/8000 Receives 2014 IBO Industrial Design Gold Award for Analytical Instrument Industrial Design

The EDX-7000/8000 won the 2014 IBO Industrial Design Awards – Gold Award for Analytical Instrument Industrial Design on August 15, 2014.

The Award is promoted by Instrument Business Outlook, the newsletter issued by Strategic Directions International, Inc. (SDi, USA), which implements market surveys on analytical and life science-related instruments. Awards are given to superior products from among the industrial products released during that year, considered from the perspectives of cutting-edge design, functionality, and user experience (the concept of expressing the experience of users in terms of level of satisfaction and impression when using the instruments).

The EDX-7000 and EDX-8000 energy dispersive X-ray fluorescence spectrometers, released in September 2013, present a different exterior to the square, heavy formats of other similar instruments. Their round, streamlined exterior makes them user-friendly in a wide variety of circumstances. In addition, the coloring and compact sizes made them extremely popular with the judges.

Instrument Business Outlook said, "The system's round front and streamlined profile set it apart from the boxier and heavier-looking designs of other benchtop ED-XRF systems, making the system approachable and distinctive." For further details of the Award, click here.

Energy dispersive X-ray fluorescence spectrometers detect fluorescent X-rays discharged by irradiating a sample with X-rays, thereby allowing the qualitative and quantitative analysis of elements included within the sample. They are used in a wide range of industries and settings, for everything from ensuring compatibility to environmental regulations such as the EU's RoHS Directive to materials analysis for research purposes.

Shimadzu intends to further expand sales of the EDX series throughout North America as a result of this Award. We will continue to further improve the quality of the products through improvements to their functionality, design, and ease of use.

For further details on the EDX-7000/8000, click here.

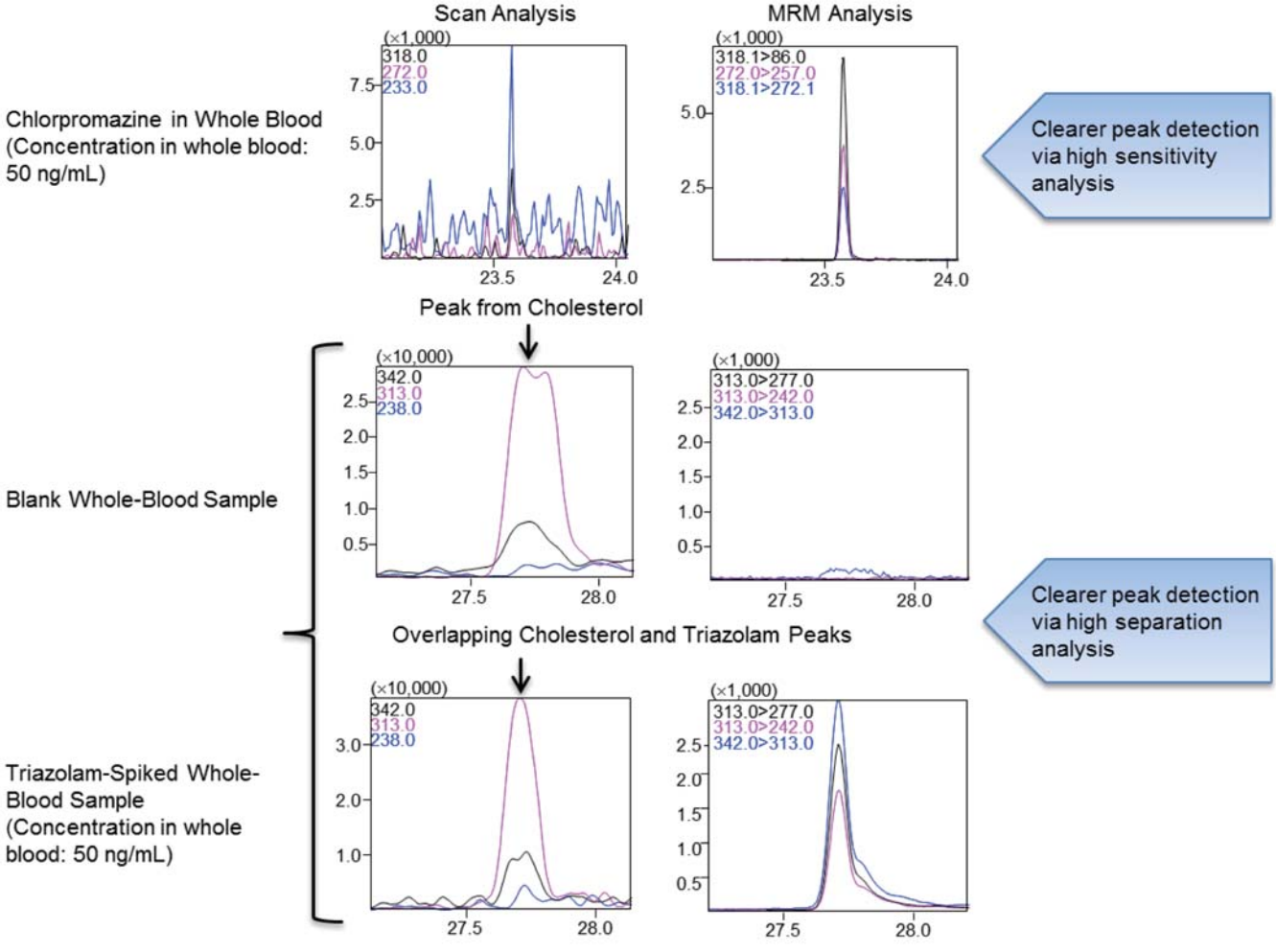
Shimadzu Releases its Smart Forensic Database for GC-MS/MS Analysis

Shimadzu has released its Smart Forensic Database for GC-MS/MS Analysis. This database supports the creation of MRM methods for forensic toxicological substances.
High mass separation of background impurities from biological samples and high-sensitivity, high-selectivity MRM (Multiple Reaction Monitoring) play a key role in forensic toxicological analysis. With its preset MRM transitions of 201 forensic toxicological substances, which often cause poisonings, the Smart Forensic Database allows users to start analysis without any complex transition settings.

Features

1. Supports Creation of MRM Methods for Forensic Toxicological Analysis Using GC-MS/MS

The database is registered with a total of 201 forensic toxicological substances often involved in poisonings, such as drugs of abuse, psychotropic drugs, pharmaceuticals and pesticides, and includes 1200 MRM transitions. For all registered compounds, it contains information on MRM transitions, collision energies, and confirmation ion ratios, so there is no need to configure complicated analysis conditions. Furthermore, retention indices are registered for all of the components, enabling easy updating of retention times via the AART (Automatic Adjustment of Retention Time) function.



2. Provides Improved Selectivity and Sensitivity via MRM

With GC-MS/MS MRM mode, mass separation is performed in 2 stages, so background interferences from biological samples are easily separated from the target compounds, and the forensic toxicological substances are detected with improved sensitivity. Thus, it is easy to determine whether biological samples contain forensic toxicological substances, and data analysis times are substantially reduced.

3. Creates Optimal MRM Methods Automatically

The Smart MRM program creates MRM methods automatically. In multicomponent simultaneous analysis, it is difficult to configure the dwell, event, and loop time-measurement settings in the MRM program. Smart MRM, however, automatically determines the optimal time-measurement settings, and creates a high-sensitivity method. The MRM method is created based on the retention time information for target compounds, using the AART function.

Extensive support for creating MRM methods

4. Combination with the GC/MS Forensic Toxicological Database in Simultaneous Scan/MRM Measurement

Scan data obtained with simultaneous Scan/MRM measurements can be analyzed using the GC/MS Forensic Toxicological Database, which is used to screen for forensic toxicological substances. MRM data can be used for trace quantity analyses of toxicological substances often involved in poisonings, which are registered in the Smart Forensic Database, while the scan data can be used to screen for drugs of abuse using the GC/MS Forensic Toxicological Database, which includes many designer drugs.

Application Data Sheet

Analysis of Toxicological Substances in Whole Blood Using the Smart Forensic Database (1)

Analysis of Toxicological Substances in Whole Blood Using the Smart Forensic Database (2)

Shimadzu has also released a new version of its LC/MS/MS Rapid Toxicology Screening System. For more information, visit: http://www.shimadzu.com/an/lcms/toxicology.html

Remarks and Precautions

1. Shimadzu makes no warranty regarding the accuracy of information included in the database or the usefulness of information obtained from using the database.
2. Be sure to perform tests using standards to confirm qualitative and quantitative information obtained with the given system.
3. To reliably identify registered substances using this database, measure samples using the instrument parameters specified in the method template files included in the product.
4. This database is for research purposes. It cannot be used for clinical diagnostic applications.

For Research Use Only. Not for use in diagnostic procedures.

New Products

Comprehensive 2D Chromatography e-Series

New Systems Enable Detailed Analysis of Structural Analogs and Other Complex Samples

The new systems maximize the uppermost features of chromatography, separation performance, and detection, and achieve high-resolution analysis, even for structurally similar compounds. The e-Series consists of the Nexera-e LC×LC system and the Ultra-e GC×GC system. Dedicated ChromSquare software is used for data analysis.

Features

- Excellent performance for enhanced separation and high-speed analysis
- Systems based on Ultra Fast Mass Spectrometry (UFMS) technology
- Easy Analysis

Note: ChromSquare is a product of Chromaleont S.r.l., Italy.

iMScope *TRIO*

Advanced Imaging Technology Platform Brings Together Innovative Mass Spectrometry and High Resolution Morphological Images

The iMScope *TRIO* is the world's first imaging technology that supports high-resolution morphological imaging from an optical microscope overlaid with molecular distribution images generated by high mass accuracy mass spectrometry with a spatial resolution of 5 µm.

Features

- Global Leader in high spatial resolution mass spectrometry imaging
- Integration of optical and mass spectrometry images
- High-level qualitative analysis via the IT-TOF function

Sales area: all areas excluding North America

ICPE-9800 Series

Shimadzu's New Simultaneous ICP Atomic Emission Spectrometers Achieve Stable Analysis with Low Operating Costs

Featuring user-friendly software, a proprietary design, Eco mode, and enabling high-speed simultaneous analysis of multiple elements, the ICPE-9810 and ICPE-9820 improve throughput and reduce operating costs.

Features

- Lower operating costs thanks to eco mode
- Faster rinse time and reduced memory effects increase analytical throughput
- Simultaneous acquisition for all wavelengths and easy reanalysis with ICPEsolution control software

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