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NEWS 03 2019

Better Prep!

New Nexera Prep LC for a preparative workflow

High-speed characterization of candle wax quality

SALDI-MS with etched silver substrates for analysis of complex lipid mixtures

Red Dot Design Awards

Awards for two Shimadzu instruments

High-speed characterization of candle wax quality

SALDI-MS with etched silver substrates for analysis of complex lipid mixtures

When the days are getting shorter, it is the time to create a warm and nice atmosphere and light some candles. Cosiness, flickering lights, a pleasant glow. But what are the candles made of? Their raw materials are beeswax, paraffin or stearin, which can also be mixed.

The content of beeswax in candles is an important quality criterion often used in marketing as a sales reason. Already in the Middle Ages during the time of the Hanseatic League, the quality of beeswax was controlled after counterfeited products emerged. Due to its high price, beeswax today is often replaced by cheaper alternatives, e.g. petroleum-like paraffin wax.

Stearin is seen as a renewable and therefore green alternative to paraffin, as it is made of plant materials. The remains of stearin candles can be composted. To check product authenticity and marketing claims, the main components of beeswax and stearin can be detected analytically due to the characteristic profile of wax compounds produced by bees or plants.

New method, quick and easy-to-use

Shimadzu has developed a new surface-assisted laser desorption/ionization mass spectrometry (SALDI-MS) method that is very fast and easy-to-use (figure 1):

Figure 1: Workflow: Apply wax directly from candle to etched surface → Analyze in MALDI mass spectrometer → Match in statistical software

Wax can be applied directly from the candle on the silver substrate and analyzed using the MALDI-8020 benchtop mass-spectrometer. Due to its wide range of applications, it can also be used for lipids.

No time-consuming dissolving step or chromatographic separation of the sample is necessary. The new eMSTAT statistical software helps to determine main components of the candle wax so that even people without deeper analytical knowledge can execute the analysis.

For etched silver substrates, silver foil was cut, washed with pentane, acetone, methanol and water, flattened and etched in nitric acid (23 %) at 50 °C until the surface appearance changed to grey. Finally, substrates were washed with water and fixed with conductive tape on a MALDI target [1, 2]. The nano-structured surface replaces the matrix, and matrix-assisted LDI (MALDI) becomes surface-assisted LDI (SALDI).

Wide range of lipid classes detectable

The fast sample stage and short pump time of the MALDI-8020 (figure 2) make the instrument especially suitable for high throughput analysis and method development. Due to its benchtop design, it provides outstanding performance parameters. With a compact footprint, it needs just a small space in the lab.

The compounds of candles are detected as Ag^+-adducts. Due to the natural abundance of silver, the spectrum shows duplets with almost identical signal heights. The range of lipid classes that can be observed by this method even covers alkanes, although these fully saturated hydrocarbons do not have any functional group.

To characterize the method, a GC-standard of alkanes with different chain-lengths was analyzed. Their detection is limited only by the vapor pressure of these volatile compounds. Alkanes with 23 or more carbon atoms can be detected. Even shorter chain-lengths are observable in some spectra, if the sample is analyzed directly after introduction into the vacuum of the mass spectrometer (figure 3).

Profiles of beeswax, stearin and paraffin

The natural origin of beeswax can be verified by the characteristic profile that is specific for these insects (figure 4a, page 4). It consists essentially of wax esters with even number of carbon atoms [1, 3] and of saturated or monounsaturated hydrocarbons with odd number of carbon atoms [1, 4].

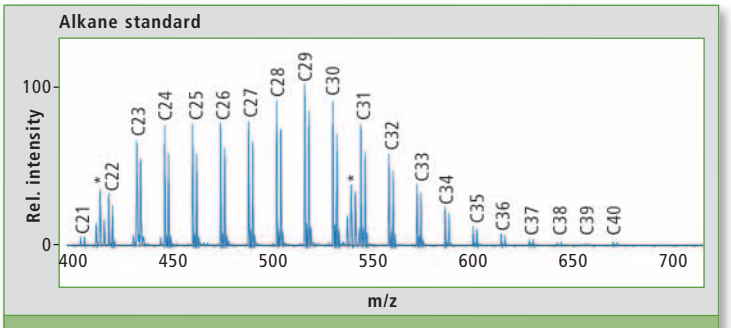

Figure 3: SALDI-MS spectrum of alkanes (GC-standard, same mass of each component)

Figure 2: The linear benchtop mass spectrometer MALDI-8020 shows a great performance on a minimum footprint. Typical applications for the MALDI-8020 are the analysis of proteins/peptides, lipids, or hydrocarbons in life science or quality control of polymers.

Stearin candles are made of vegetable or animal fat after saponification. They show a characteristic profile dominated by two free fatty acids (FFA): Palmitic and Stearic acid (figure 4b, page 4).

Paraffin is the cheapest and therefore most common resource for production of candles. Due to their origin in petroleum, alkanes with all different chain lengths of the fraction used are present in the mass spectrum (figure 4c, page 4).

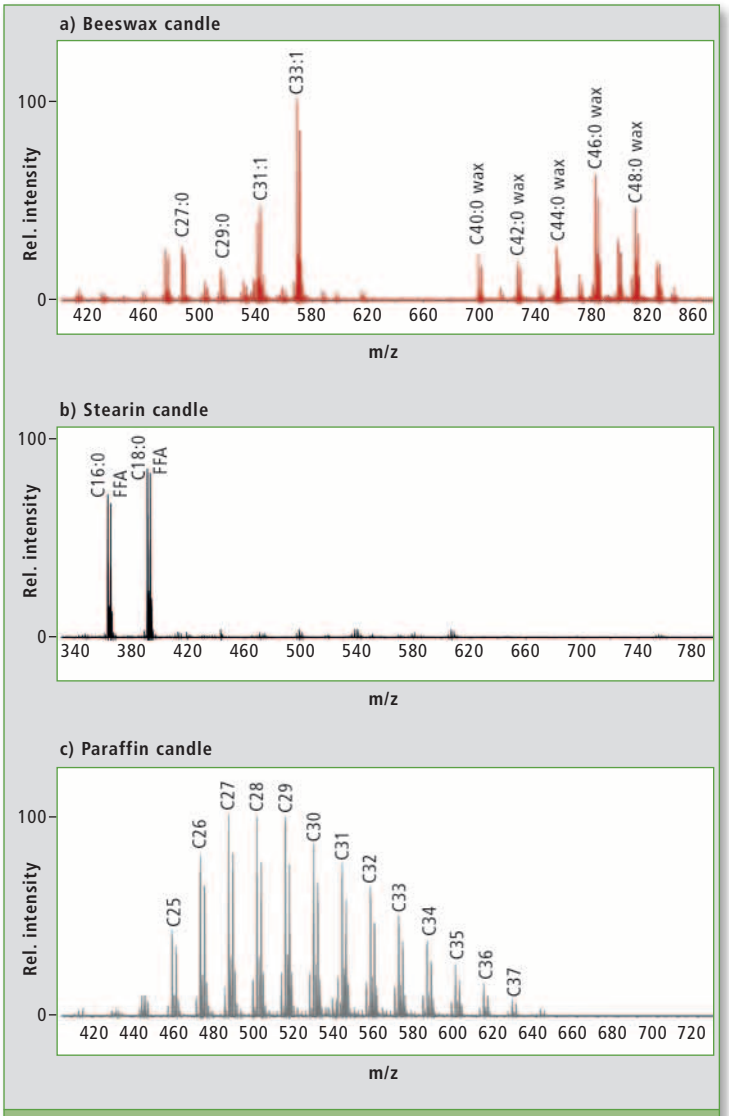

Figure 4: SALDI-MS spectra of different candles: a) Beeswax candle (already described [1, 3, 4] components annotated), b) Stearin candle (Palmitic acid [C16 FFA] and Stearic acid [C18 FFA]), c) Paraffin candle (alkanes from C25-C37).

High potential for complex lipid mixtures

These three examples show the large range of different lipid classes that can be analyzed with SALDI-MS using etched silver foil as substrate:

- Alkanes without any functional group which are analyzed classically via GC and
- more polar and less volatile lipids like FFA and wax esters that are therefore commonly not recommended to be analyzed via GC without derivatization.

As no chromatographic separation is necessary, the SALDI-MS method is much faster.

This application shows the potential of the method to analyze various complex lipid mixtures that contain both hydrocarbons and less volatile compounds that are challenging to detect with GC-MS. Often more than one method was used in the past to characterize such complex lipid mixtures.

eMSTAT simplifies data interpretation

The eMSTAT statistical software helps to evaluate MALDI, DPiMS and other full scan data sets. In Statistical Analysis mode, it is easy to differentiate samples and identify marker peaks with the implemented univariate and multivariate analysis tools.

For example, the score plot visualizes the groups of similar samples (figure 5). These discoveries can be used in Discriminant Analysis mode to assign unknown samples. A score is given to rate the similarity to the reference data. In this way, even people with limited analytical knowledge can perform the analysis.

Finding marker peaks to differentiate food, plant or other biological samples or to monitor the quality of polymers after identifying typical degradation products are just a few examples of the extensive number of eMSTAT applications.

Conclusion

The characterization of candle waxes shows the potential of SALDI-MS as a high-speed screening method for complex lipid mixtures. SALDI-MS with etched silver substrates can be used to analyze typical GC-MS analytes such as alkanes as well as less volatile lipids with polar functional groups such as waxes or free fatty acids. Analysis time is saved because no derivatization or chromatographic separation is necessary. In addition, pump time of MALDI-8020 is decreased and the speed of the sample stage is increased compared to previous instruments.

Literature

[1] Schnapp et al., Methods, 2016, 104, 194-203.
[2] Bien et al., Anal Bioanal Chem, 2019, 411 (13), 2981-2993.
[3] Fröhlich et al., J Chem Ecol, 2000, 26, 123-137.
[4] Ferreira-Caliman et al., J Chem Ecol, 2012, 38, 418-426.

Further information on this article:

- Application: High-speed characterization of candle waxes using SALDI-MS with etched silver foil as substrates

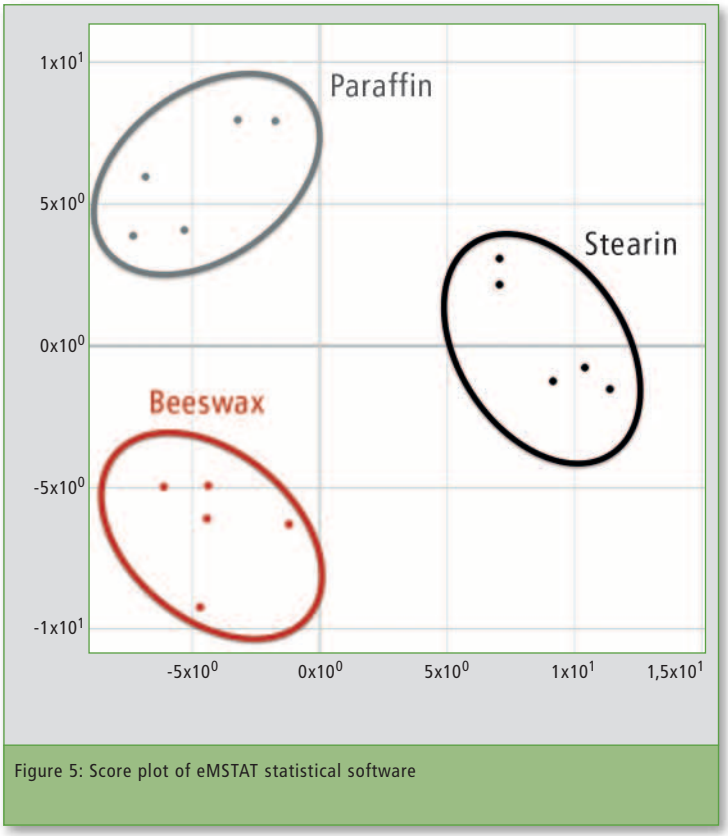

Figure 5: Score plot of eMSTAT statistical software

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1988 - 1999

2000 - 2012

2013 - 2019

Drug metabolization in plants

Method development for detection of environmentally relevant trace levels

Due to steady population growth, increasing chronic illnesses and advances in medical science, the consumption of drugs increases continuously. For example, in Germany an increase of 40 - 65 % of current demand is expected by 2045. [1]

As a negative effect, more and more drug residues are being introduced into the environment. The main source of contamination are sewage treatment plants. Excretion of pharmaceuticals not absorbed by the body, washing off of externally applied medical products (e.g. ointments or creams) and also the improper disposal of substances are ways that medicines end up in municipal sewage.

Although wastewater treatment plants purify the effluents, they are often unable to completely remove the various pharmaceutically active substances from the water. When the treated waters are returned to surface waters, the environment will inevitably be contaminated. Antibiotics, non-steroidal anti-rheumatics and antiepileptic drugs are detected frequently, occurring in purified waters in the ng/L up to the low µg/L range [2].

Interactions of medicinal products with plants

Due to climate change and increasing drought, purified waters are now reused directly for irrigation in agriculture, e.g. in countries such as Israel. Although this helps to preserve water resources, interactions between (pharmaceutical) residues in the water and plants can not be excluded. Purified water and sewage sludge used as fertilizer therefore cause food safety concerns [2].

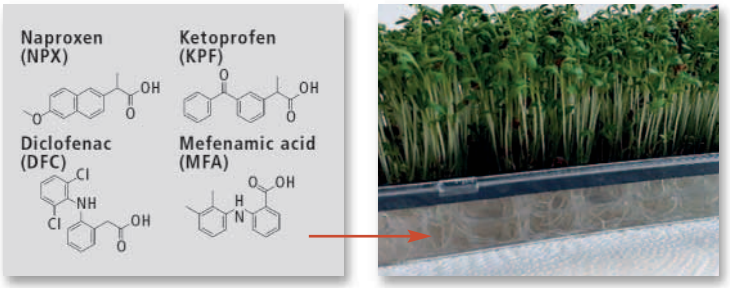


Figure 1: Investigated nonsteroidal anti-inflammatory drugs

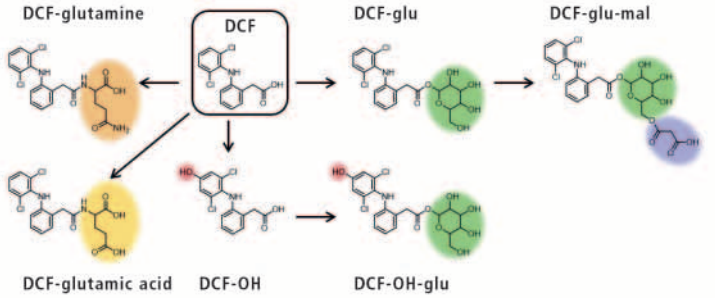


Figure 2: Schematic representation of the metabolization of DCF with structural proposals of the metabolites

Numerous studies have presented methods for trace analysis of drugs and have showed that various plants (such as lettuce, tomato, cucumber, spinach etc.) take up pharmaceutically active substances from their environment and transport them within the plant [2].

Based on these findings, it is possible that pharmaceutically active substances may be converted or metabolized within the plants into new compounds during detoxification. Initial studies with cell cultures or hydroponics showed that hydroxylation and conjugation with sugars and amino acids of the drugs can take place (based on the three-phase model) [3].

The identification of metabolites is essential in order to fully describe and elucidate the uptake of medicinal products by plants in the environment. Focussing on active substances only could lead to an underestimation of the extent of drug uptake, simply because metabolites formed (and possibly present in high concentrations) are not covered by the methods used so far.

Identification of metabolites

In this research project, the uptake and metabolization of pharmaceuticals in the plant specimen cress (*Lepidium sativum*) was investigated. The plants were exposed to four different non-steroidal anti-inflammatory drugs (NSAIDs): diclofenac (DCF), naproxen (NPX), ketoprofen (KPF) and mefenamic acid (MFA), (figure 1).

The plants were hydroponically cultured, harvested and finally extracted with a suitable mixture of solvents. To identify potential metabolites, the extracts were separated by RP-HPLC (reversed phase) followed by analysis with a high-resolution mass spectrometer (here a time-of-flight mass spectrometer).

Careful evaluation of the mass spectra obtained and comparison with untreated plants led to identification of 16 metabolites with proposed structures. These were hydroxylation products (OH) or conjugates with glucose (glu), malonic acid (mal), glutamine and glutamic acid (see figure 2). For these experiments, the plants were treated with high concentrations of drugs (> 1 mg/L) to facilitate the identification of the metabolites [4].

After this succeeded, the next goal was to develop a highly sensitive and selective method allowing detection of the four NSAIDs and their metabolites when plants were exposed to very low environmentally relevant concentrations. A first step was the adaptation of the sample preparation, enabling the plant extracts to be concentrated.

Furthermore, a triple-quadrupole mass spectrometer in MRM (multiple reaction monitoring) mode was used as a detector to increase the sensitivity. However, the performance of the available analytical instruments was not sufficient to advance into the desired concentration range. This could finally be achieved by coupling HPLC with the latest generation of triple quadrupole mass spectrometers (LCMS-8060).

LCMS-8060 for the development of a highly sensitive method

The objective was to develop a highly sensitive and selective method allowing the detection of

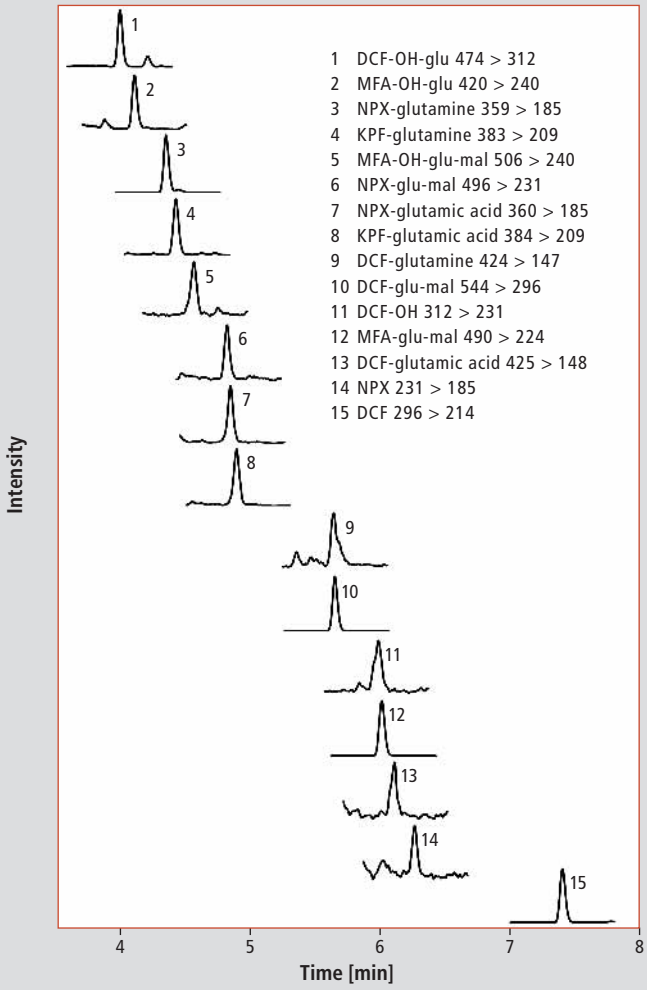


Figure 3: HPLC-MS/MS chromatograms of a root extract after treatment of cress with 1 µg/L per NSAID

the drugs, and in particular all of the identified metabolites, when plants are exposed to very low environmental concentrations (≤ 1 µg/L). The extracts were separated on an Atlantis T3 column (3 µm, 150 mm x 2.1 mm) from Waters using a water/acetonitrile gradient (+ 0.1 % formic acid) at a flow rate of 0.3 mL/min.

After the adaptation and optimization of HPLC and the triple quadrupole method, it was evident that detection limits of the four NSAIDs could be reduced by a factor of 25. In the analysis of the plant extracts, where cress was exposed to 1 µg/L per NSAID, 15 analytes (i.e. 75 % of the analytes) could be detected in the roots of the plants (for chromatograms see figure 3). In the upper part of the plant, nine analytes were found at this concentration level. At a drug concentration of only 0.1 µg/L per NSAID, seven analytes were detected in the cress roots using the developed method.

SFC an alternative complementary separation method?

Due to the possibilities in the Laboratory World at Shimadzu Europe, an alternative method could be developed separating the analytes by means of supercritical fluid chromatography (SFC). Different columns were tested and the parameters of the SFC (type and flow rate of the modifier and make-up flow) as well as the mass spectrometer were optimized. Finally, the extracts were separated on a Shim-pack UC-Diol (3 µm, 4.6 mm x 150 mm) column. As mobile phase, supercritical CO_2 was used, with methanol (5 - 45 %) as a modifier with a flow rate of 3 mL/min. A make-up flow was added post-column for better ionization.

Compared to HPLC, SFC showed a complementary elution behavior of the analytes, and the more apolar NSAIDs eluted at shorter retention times. Figure 4 shows the SFC-MS/MS chromatograms of a root extract (cress treated with 0.1 mg/L per NSAID). Interestingly, three analytes (KPF-glutamine, DCF-OH and KPF-glu-mal) showed two peaks in the SFC (in contrast to HPLC). This is a potential indication of the presence of two structural isomers. However, this assumption could not be verified within the project.

Conclusion

Using the LCMS-8060, a highly sensitive LC-MS/MS method could be developed allowing detection of trace levels of NSAIDs and their metabolites, as present when plants are exposed to environmentally relevant concentrations. Additionally, with the SFC, an alternative separation method could be tested and used for the separation of the analytes.

Author

Lisa Emhofer, Institute of Analytical Chemistry, Johannes Kepler University, Linz, Austria

Literature

[1] Civity Management Consultants (Hrsg.): Arzneimittelverbrauch im Spannungsfeld des demografischen Wandels, Berlin, 2017

[2] Wu X., Dodgen L.K., Conkle J.L., Gan J., Science of the Total Environment, 536 (2015) 655-666.

[3] Klampfl C.W., Trends in Analytical Chemistry, 111 (2019) 13-26.

[4] Emhofer L., Himmelsbach M., Buchberger W. Klampfl C.W., Journal of Chromatography A, 1491 (2017) 137-144.

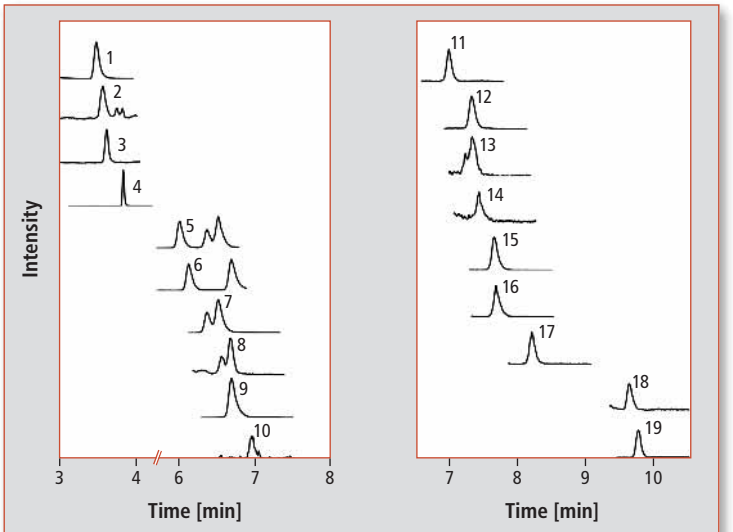
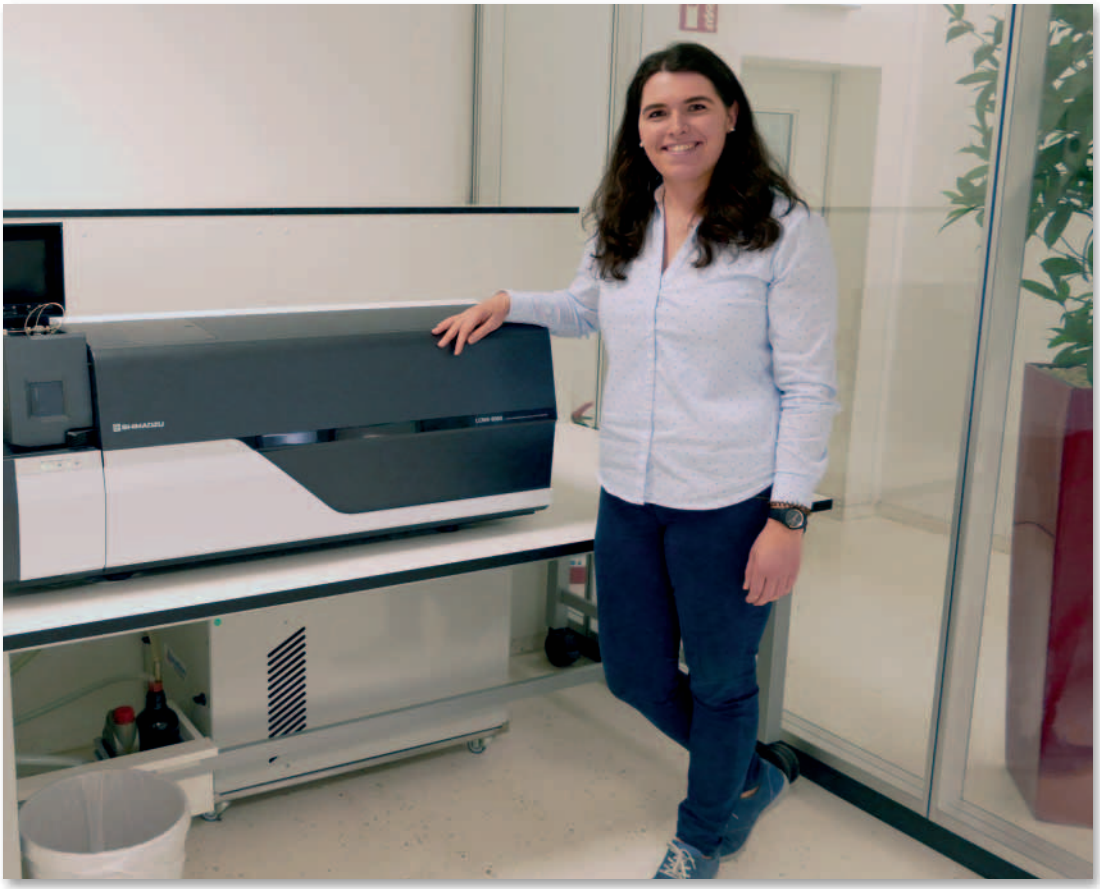


Figure 4: Separation of a root extract (treatment with 0.1 mg/L per NSAID) by means of SFC-MS/MS

Lab4you – an opportunity for young scientists



Lisa Emhofer, Institute of Analytical Chemistry, Johannes Kepler University, Linz, Austria

Shimadzu's Lab4you program is intended for young scientists from all over Europe. For their thesis and dissertation, they can apply for laboratory space to carry out measurements supporting their research.

The state-of-the-art "Shimadzu Laboratory World" at the European headquarters in Duisburg, Germany provides the latest generation of analytical instruments guaranteeing best analytical results. On 1,500 sqm, they cover HPLC/UHPLC, SFC and GC as well as mass spectrometry, MALDI, spectroscopy and material testing technology.

In 2018, Lisa Emhofer from the Institute of Analytical Chemistry at the Johannes Kepler University in Linz, Austria was selected by an internal jury to come to Duisburg.

Lisa Emhofer: "In addition to achieving scientific results, the Lab4you program is a unique opportunity for young scientists to develop in a scientific and personal way. After intensive training on the equipment by the very helpful product specialists, I could focus totally on my research topic and use all the equipment of the Laboratory World. I was always encouraged and supported in the implementation of new ideas that emerged during my research stay."

The Lab4you program for young scientists is linked to the Shimadzu European Innovation Center (EUIC). Together with universities across Europe, the EUIC explores new solutions for tomorrow, such as new methods, tools, techniques and software solutions.

Over the past four years, Shimadzu has hosted Lab4you candidates from Austria, Poland and Germany to conduct their research in the company's Laboratory World. The Lab4you program is in its fifth year.

European Innovation Center

Choose wisely!

Influence of column and method selection on Simulated Distillation results in compliance with ASTM D-2887

"Simulated distillation" (SIMDIS) is a gas chromatographic analytical method that simulates traditional distillation. With this procedure, it is possible to determine the composition of a petroleum sample according to the boiling point distribution. SIMDIS is a useful tool enabling fast analysis of the composition of petroleum products.

With the standard method ASTM-D-2887, low petroleum fractions can be analyzed. This method includes all fractions with boiling points in the range from 55 °C to 538 °C (up to C44).

Use of the right column and method becomes critical for accurate values and good peak resolution during simulated distillation measurements. In the following example, it can be seen how choosing appropriate column dimensions and adjusting method parameters can clearly improve results and obtain the desired information from the sample analyzed.

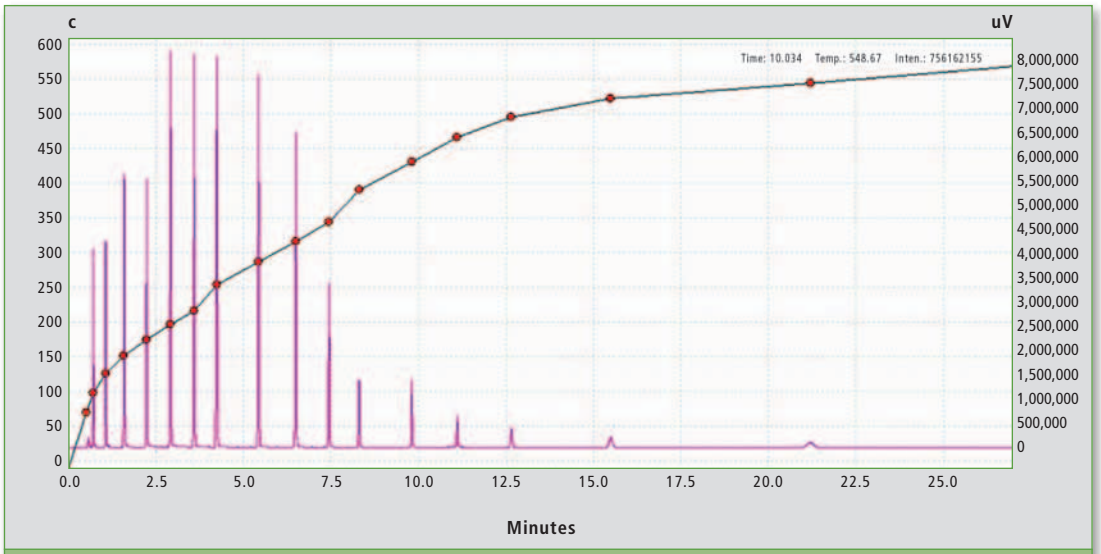


Figure 1: BP-RT calibration curve for column 1

Selecting the correct column and method

A GC-2030 instrument with FID detector was chosen for the

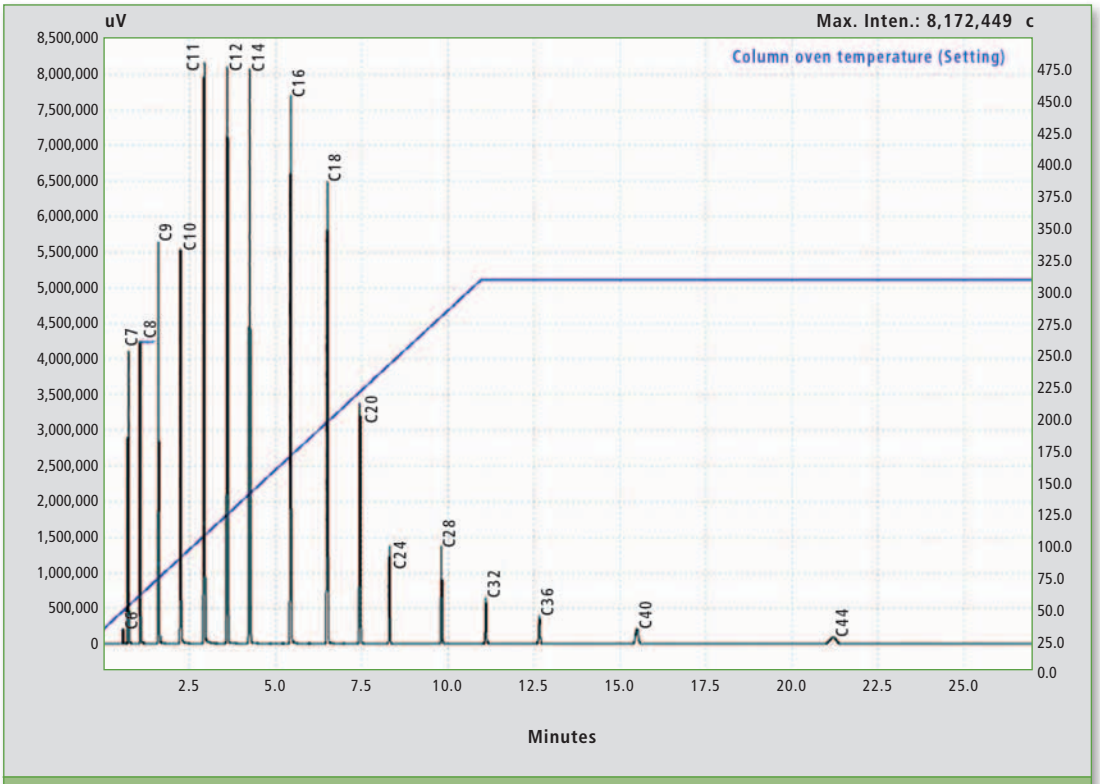


Figure 2: Peak retention times with column oven temperature profile for column 1

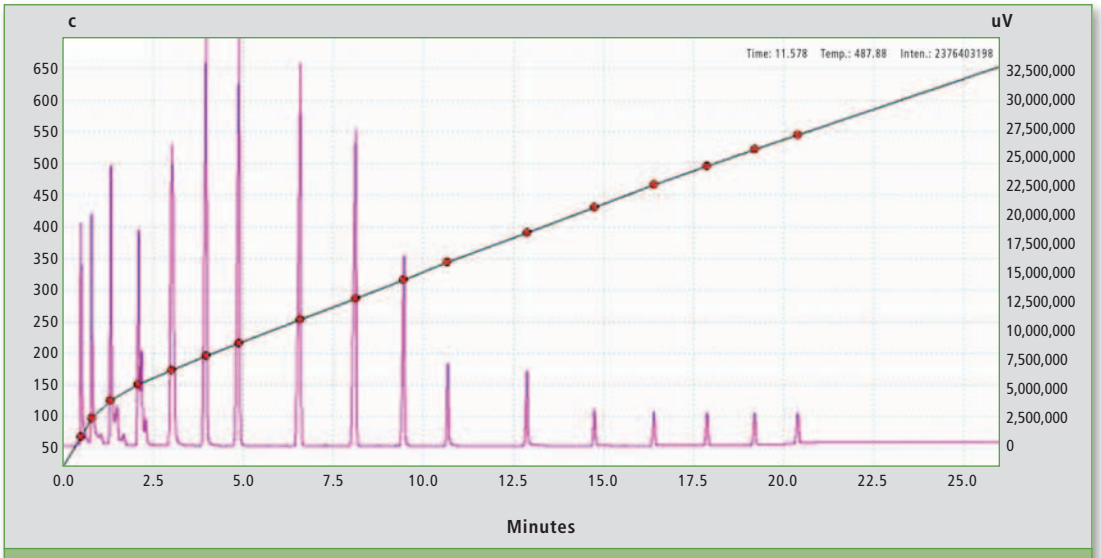


Figure 3: BP-RT calibration curve for column 2

measurements. First, a non-polar phase column (Column 1; # 221-75731-15; 15 m, 0.53mm; 1 µm) was installed and the method parameters summarized in table 1 were used.

An alkane standard C6-C44 was measured to obtain the BP-RT calibration curve and also to evaluate the effectiveness of the method and column selected.

As shown in figure 1 (page 9), high deviations in the BP-RT calibration curve arose. It could also be seen that the latest peaks from heavier compounds eluted the column at high retention times, already in the isothermal segment of the oven heating (figure 2).

This late elution and poor resolution of the last peaks were most likely the cause of poor linearity of the initial BP-RT curve. It was concluded that the length of the column could generate the discrepancies in the results. Although the temperature program was adjusted, it was not possible to improve resolution of the latest peaks.

Testing of a new column

In order to corroborate the real influence of the column length and heating program, a new non-polar column (column 2; # 980-23987; 10 m; 0.53 mm; 0.9 µm) was installed. Furthermore, new heating programs (table 2) in the OCI and column oven were introduced in order to achieve better results.

The same alkane standard C6-C44 was used for these measurements. A clear improvement of the linear-

ity of the BP-RT calibration curve was observed (figure 3) by using column 2 and the new method parameters.

In the case of column 2, all compounds eluted the column while the GC oven was still in heating process, improving the resolution of the latest peaks (figure 4).

Using the shorter column 2 (10 m) and lower heating rates directly influenced the results obtained. These factors can therefore be considered as key to obtaining satisfactory results with good resolution and linearity.

Analysis of Reference gas oil (RGO)

Finally, after the optimal experimental conditions were determined, it was possible to analyze a certified gas reference oil sample and obtain correct values of the reference check results (table 3). These good results were only possible when column 2 and the new heating programs were used.

Conclusions

Choosing the right column dimensions and heating program becomes crucial for best results with the simulated distillation method. By replacing the initial column which was for this purpose less than ideal, and setting the right heating program, it was possible to improve initial results and to define the best conditions for accurate analysis of the reference gas oil sample.

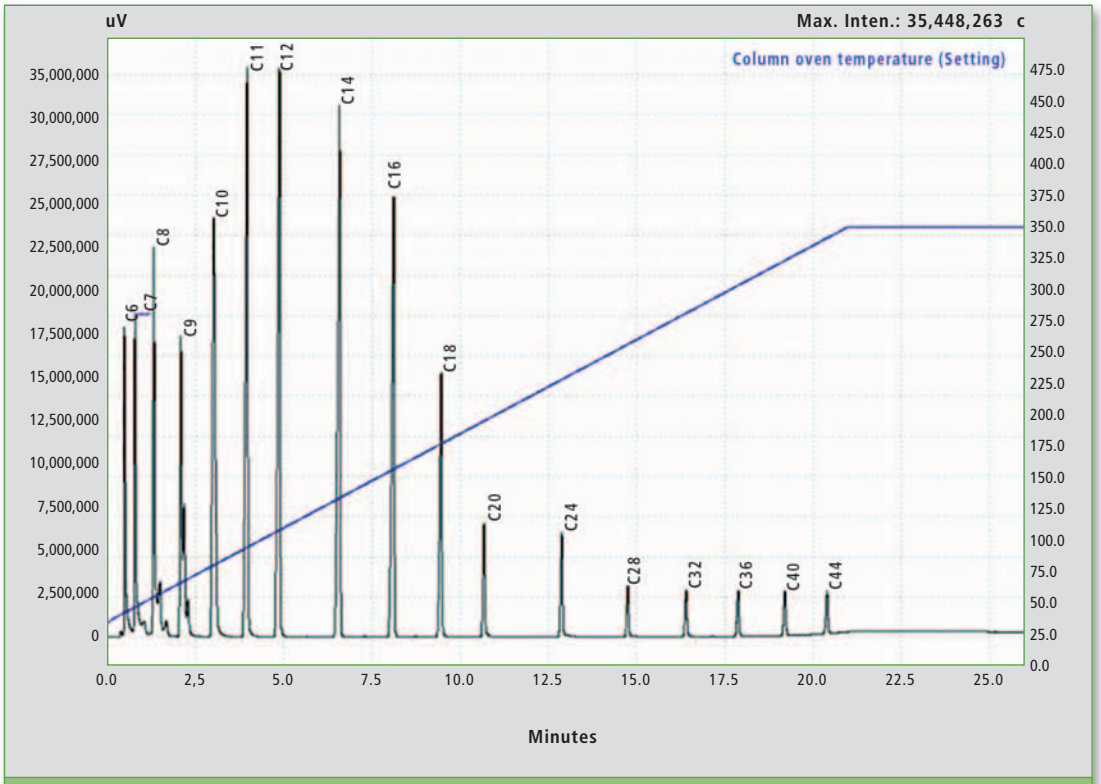


Figure 4: Peak retention times with column oven temperature profile for column 2

OCI temperature programm	50 °C, 0 min, 35 °C/min, 310 °C, 19.57 min
Injection volume	0.1 µL
Column oven program	35 °C, 0 min, 25 °C/min, 310 °C, 16 min
Column pressure	24.3 kPa (Pressure control mode)
FID temperature	320 °C

Table 1: Method parameters for the Simulated Distillation analysis with the ASTM-D2887 method on column 1

OCI temperature programm	50 °C, 0 min, 25 °C/min, 350 °C, 14 min
Column oven program	35 °C, 0 min, 15 °C/min, 350 °C, 5 min

Table 2: New heating ramps for the OCI and column oven for column 2

Recovery [w/v]	Temperature [C]	BP criteria [C]	Difference [C]	Check result
IBP	114.1	115	-0.9	Pass
10	176.9	176	0.9	Pass
30	260.2	259	1.2	Pass
50	311.2	312	-0.8	Pass
70	352.5	354	-1.5	Pass
90	404.8	407	-2.2	Pass
FBP	474.3	475	-0.7	Pass

Table 3: Reference check results for RGO sample

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Red Dot Design Awards for two Shimadzu instruments

The role of design in capital goods business

reddot award 2019
winner

Figure 1: Groundbreaking technology regarding intelligence, efficiency and design: the awarded Nexera LC-40 series.

The new Nexera UHPLC series LC-40 and UV-1900 UV-Vis spectrophotometer have been recognized with the Red Dot Design Award 2019 in the product design category. The award ceremony was held in Essen, Germany in July 2019. An actual Nexera series instrument and an explanatory panel showing the UV-1900 will be displayed in the city's Red Dot Museum for the next year.

The Red Dot Design Award is one of the three major design awards in the world, alongside the German iF Design Award and the US IDEA Award. Manufacturers and designers from 55 countries submitted their works in the product design category.

Based on excellent design and innovation, functionality, quality, ergonomics and durability, a jury of experienced designers judged more than 5,500 products. Red Dot represents the best in design and business. The award covers the areas of product design, communication design and design concepts.

The role of design in capital goods business

In the last years, Shimadzu systems have been recognized nine times with Red Dot as well as iF Design-Awards, e.g. for the AIM-9000 Infrared Microscope, the IRSpirit Fourier Transform Infrared Spectrophotometer series and the Q-TOF LCMS-9030 time-of-flight mass spectrometer.

Besides functional aspects, design also has a communication task – through its shape, appearance and look. The design of a product is voice as well as content talking to the user. Design is not only visually striking based on appearance, it also is a signal for technological innovation.

Users get their first impression through design. A new look of a product differentiates at first glance from former versions, attracting attention and calling the users for a closer look. In contrast, technological innovation in former versions' housings would be wasting a business opportunity due to a lack of visual novelty and messaging.

»Excellence in Science« translated into products

Beyond specifications and performance parameters, how does "Excellence in Science" translate into products and solutions? Or vice versa: how can a product speak "Excellence in Science"?

Just a brief look at the UV-1900 designed by Masakuni Tachi and Ryo Takegawa: the system fea-

tures technological innovation such as the ultra-fast scanning function. It provides operational convenience, with for example the on-screen user interface with easy-to-see icons on a black background displaying instrument settings at a glance. Regarding ergonomics, the control panel design is based on these principles and is positioned at the very best viewing angle for the user. These functionalities and innovations are expressed through "distinctive design, which is characterized by light-dark contrasting and skillfully draws attention to the touchscreen", as the Red Dot Award jury stated.

A technological innovation alone does not guarantee commercial success. The design needs to bridge the communicative gap to the users. For product development this means that design as an innovation signal should be an integral part of the product and its construction process. The best of both worlds is the fit between functional innovation and new design.

This way, design is a decisive part of the commercial success.

Figure 2: Red Dot Design Award ceremony in Essen (Germany) on July 8, 2019

Figure 3: Distinctive design, ergonomic principles: the awarded UV-Vis spectrophotometer UV-1900.

Experience New Benchmarks: the Nexera UHPLC LC-40 series

HPLC systems are able to quantitatively analyze substances in mixtures containing multiple ingredients by separating and detecting target substances. The "Nexera Series" applies groundbreaking technology in terms of intelligence, efficiency and design. By incorporating Internet of Things (IoT), Artificial Intelligence (AI) capabilities and sensor technology, the instrument's users benefit from simplified workflows and increased laboratory efficiency. With its compact exterior, the design is adaptable to a variety of laboratory environments. The proportions of the modules have been optimized and designed to lend an attractive appearance to both the individual modules and the overall system.

Statement by the Jury

The design of Nexera combines straightforward lines with open asymmetries, giving rise to a very clear arrangement of the modules.

In-house design: Hyeri Kang, Ryo Takegawa

www.shimadzu.eu/awards-of-shimadzu

Better Prep!

New Nexera Prep LC for a simplified and highly efficient preparative workflow

The new Nexera Prep series of preparative and purification LC systems improves productivity tremendously via efficient preparative work using application-specific LC or LC-MS methodology. It offers ease-of-operation in a flexible set-up and enables customer- and application-specific solutions, supported by a wide choice of equipment, accessories, detectors and efficient process automation. Nexera Prep provides better prep processes for drug discovery and purification of functional components in pharmaceutical, chemical and food industries.

The typical preparative workflow follows several steps that can be streamlined using the latest technology:

1. Development and optimization of separation conditions in analytical scale

In order to isolate different analytes from a mixture of components, separation of the compounds of interest must be ensured. Analysis and fractionation parameters have to be carefully optimized. Since method development in preparative scale would waste a lot of sample and eluent, the analytical scale Method Scouting system for automated column screening with a variety of mobile phases is the ideal tool for this purpose.

Nexera preparative LC system

2. Upscaling from analytical to preparative LC conditions

After optimization of separation conditions in analytical scale, upscaling from analytical to preparative LC conditions can be calculated using the dedicated "Method Transfer" tool. The dimensions and particle size of the preparative separation column should be selected according to the required amount of purified compound or injection volume as shown in table 1. Column dimensions dictate the flowrate range and the appropriate system configuration can be determined based on mobile phase flow required, target number of fractions and fraction volume.

3. Optimization of fraction conditions for preparative work

LabSolutions software offers precise fractionation simulation, where a peak segment in the pre-preparative results can be specified, and fractionation parameters are set automatically in the system, thereby reducing time and effort significantly. Signals from up to four channels of a variety of detectors enable most selective and sensitive identification of target compounds.

4. Re-analysis of collected compounds to confirm purity

With the new LH-40 Liquid Handler for re-injection of isolated fractions, purity of target compounds can be confirmed using a dedicated analytical flow path of the same versatile system.

Type	Loading	Column i.d.	Flow rate	Purpose of preparation
Analytical scale	~ 20 mg	4 - 6 mm	1 - 5 mL/min	Structural analysis and biochemical fractionation
Semi prep	~ 300 mg	10 - 20 mm	10 - 50 mL/min	Structural analysis and biochemical fractionation
Lab scale prep	~ 2,000 mg	30 - 50 mm	50 - 150 mL/min	Purification and pretreatment

Table 1: Typical loading, column dimensions and flow rate in different scale LC analysis

Senna powder: Nexera Prep in an application example

Preparative purification of sennoside A and sennoside B from senna powder and confirmation of purity in a single system.

Sennoside A and sennoside B are the active components in senna leaf extract powder, commonly used as a natural laxative. In order to isolate the target compounds, a HPLC separation was developed in analytical scale and transferred to semi-preparative conditions. After successful fractionation of the single analytes, the samples collected were subjected to re-analysis to confirm the purity of each compound.

Figure 1 shows typical chromatograms of a) 50 µg/mL mixed standard solution of sennosides A and B and b) senna powder extract in methanol. For preparation of the extract sample, 100 mg senna powder was extracted for 30 min in an ultrasonic bath with 10 mL of a 70 % aqueous solution of methanol, centrifuged and the supernatant was filtered before HPLC analysis. Because of the large amount of contaminating components in the extracted powder sample, the column had to be rinsed thoroughly with 100 % organic solvent after elution of the separated target components.

Analytical separation conditions

Column: Shim-pack Scepter C18, 150 x 4.6 mm, 5 µm
Mobile phase A: 0.1 mol/L ammonium acetate in water (pH 6.9)
Mobile phase B: Acetonitrile
Gradient: 5 % B → 12 % B (0 - 15 min)
12 % B → 100 % B (15.01 - 20 min)
100 % B → 5 % B (20.01 - 30 min)
Flow rate: 1 mL/min
Temperature: Ambient
Detection: UV 340 nm
Inj.Vol.: 2 µL

The LabSolutions method transfer calculator and fractionation simulator were used to convert the method to preparative scale and to specify the peak segments, for the scan system to automatically determine the appropriate parameters required for successful target fractionation.

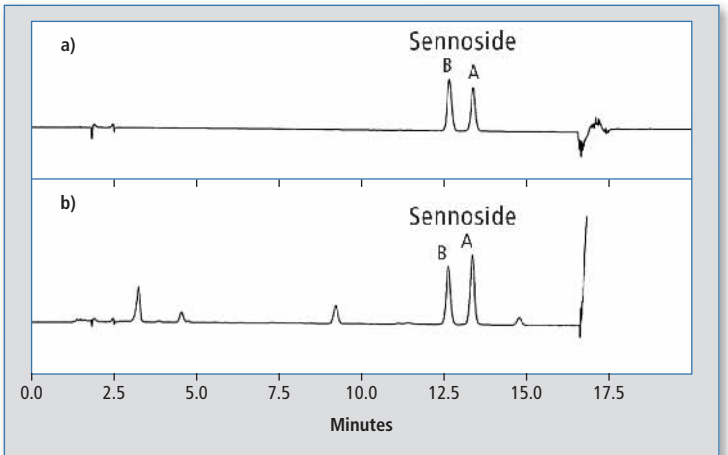


Figure 1: Typical chromatograms of a) 50 µg/mL mix standard solution of sennosides A and B and b) senna powder extract in methanol

Preparative separation conditions

Column: Shim-pack Scepter C18, 150 x 20 mm, 5 µm
Mobile phase A: 0.1 mol/L ammonium acetate in water (pH 6.9)
Mobile phase B: Acetonitrile
Gradient: 5 % B → 12 % B (0 - 15 min)
12 % B → 100 % B (15.01 - 20 min)
100 % B → 5 % B (20.01 – 30 min)
Flow rate: 19 mL/min
Temperature: Ambient
Detection: UV 340 nm
Inj.Vol.: 500 µL
Fractionation: 13.09 - 13.63 min (Sennoside B)
13.88 - 14.48 min (Sennoside A)

A typical chromatogram of the separation of sennosides A and B in preparative scale showing the color-coded fractionation segments can be seen in figure 2.

Conclusion

The Nexera Prep system for fractionation and purity confirmation was applied successfully to separate and isolate sennosides A and B from a mixed extract of senna powder. The system was equipped with the LH-40 Liquid Handler, to re-inject the collected fractions in a separate analytical flow path in the same system for confirmation of purity. The chromatograms obtained from re-analysis in analytical scale only showed the single peak for sennoside A and sennoside B respectively (figure 2).

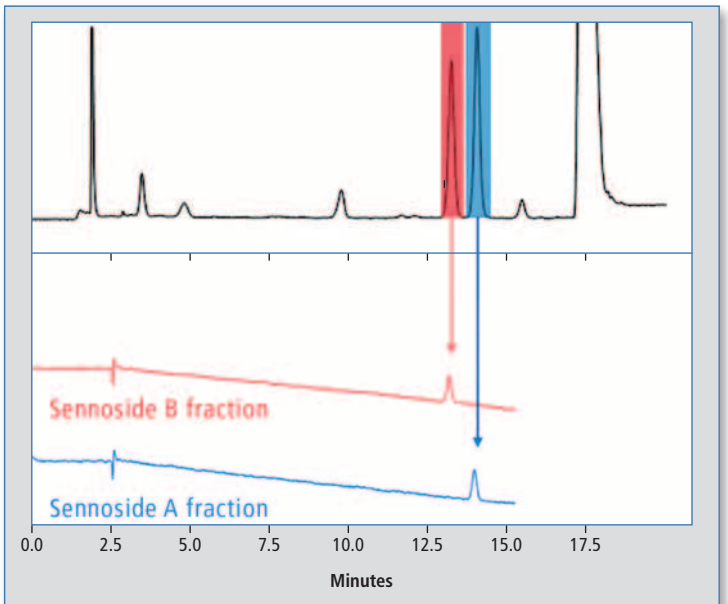


Figure 2: Typical chromatograms of the separation of sennosides A and B in preparative scale and re-analysis of single fractions

Implant contaminated?

TOC analysis in the production of orthopedic implants

Mankind explores the vastness of the cosmos and sends telescopes into space. Humans also explore the microcosm; with a particle accelerator, they break down matter into its components in order to uncover the big bang of the universe. 50 years ago, the first astronaut set foot on the moon, brought there by a lunar module with new electronic control technology. Hardly any comparison to today's powerful devices, which allow access to enormous knowledge at the touch of a finger and connect people all over the world. These are amazing masterpieces of human ingenuity.

But often, the human body, one of the greatest miracles, falls out of sight. From a single cell an organism grows which has still not been fully understood in its entirety, although it has hardly changed over recent generations. And yet, life expectancy is increasing constantly due to better living conditions such as nutrition, hygiene, social stability and especially due to advances in medicine, such as diagnostics, drugs and medical devices.

Balancing benefits and risk

Medical devices today are key to support or even enable the recovery of patients from a variety of ailments, from bone fractures and joint damage to heart diseases and spinal injuries.

However, bringing foreign substances as implants into the organism is not possible without considerable potential risks for the patient – post-operative infections or long-term damage caused by heavy metal poisoning would be a catastrophe. It must therefore be ensured that so-called "biocompatibility" is always achieved, so that the benefit for the patient outweighs the potential risks. In the distribution and production of medical devices, manufacturers are therefore confronted with consistently strict quality requirements under regulatory supervision.

The new EU Medical Device Regulation MDR 2017/745

The European Parliament has passed the new medical device regulation MDR 2017/745 and transitional periods for product certification will already expire for manufacturers in May 2020. It replaces the previous Medical Device Directive MDD 93/42 / EEC and the Directive on Active Implantable Medical Devices 90/385 / EEC. Manufacturers of

medical devices will be exposed to major changes, including stricter clinical post-marketing surveillance. Unannounced audits and product inspections are intended to help reduce the risk of unsafe medical devices.

Sample	TOC [mgC/L]	TOC minus BV [mgC/L]	TOC per implant [mgC]
Ultrasonic bath – blank value (BV)	0.64	—	—
Clean implant	1.98	1.34	0.335
Contaminated by glucose	3.46	2.82	0.705
Contaminated by touch	2.48	1.84	0.46

Table 1: Results of the extraction experiments

Risk reduction through implant purity

Besides the actual material, hygiene and purity are key factors in achieving the biocompatibility of an implant. The international standard ISO 19227 "Cleanliness of Orthopedic Implants – General Requirements" is a guideline to assist manufacturers in addressing this issue. It covers general requirements from risk assessment and validation of cleaning methods to sampling, and prescribes a series of tests to demonstrate cleanliness throughout the entire production process. These include test methods to identify inorganic and particulate contaminants, organic contaminants and systematic visual checks. The TOC parameter is one way of determining the total organic contamination.

Validation of purity by TOC analysis

TOC (Total Organic Carbon) analysis records the total carbon from organic compounds in one step and is therefore particularly suited to determining contamination by organic components. Carbon content of the sample is oxidized to CO_2 and analyzed with a NDIR (non-dispersive IR) detector. The parameter is common practice in cleaning validation for pharmaceutical production plants.

TOC measurement does not identify contamination, but does reflect the total organic contamination caused by by-products of the manufacturing process such as grease or lubricants, detergents and disinfectants as well as natural organic matter (biological contaminants). Aqueous samples after extraction can thus be analyzed quickly and easily (analysis time: approx. 4 min). A prerequisite is good water solubility of the substances to be tested. With the TOC analyzer of the TOC-L series, Shimadzu offers a very suitable tool for validating the cleanliness of orthopedic implants after liquid extraction.

Examination of a knee implant

Using the femoral component of a knee prosthesis as shown in figure 1, organic impurities on the surface of the sample were examined. Two beakers, each containing 250 mL ultrapure water were prepared, the previously cleaned implant being placed in one for actual extraction and the other used for blank value determination. Both containers were left in a tempered ultrasonic bath for one hour for extraction. The extraction solutions of both containers were then filled into autosampler vials and analyzed in the TOC-L.

To simulate different types of contamination, the implant was placed in a glucose solution containing 50 mg/L TOC for one hour. In a second experiment, an employee briefly touched the cleaned part with unprotected fingers. Both times, extraction solutions were produced and analyzed according to the above scheme.

The results in table 1 show that the organic contamination on the surface of the implant could be detected and confirmed quickly and precisely. ISO 19227 recommends a TOC limit of 0.5 mg per implant if historical data is not available. However, this is only an orientation – the actual limits should always be determined after a risk assessment, taking into account factors such as the size of the component, detergents used and potential sources of hazard.

Alternatively, entire components such as smaller plates and screws for surgery as a whole could be examined for organic contamination in the TOC solid sampling module. In order to track down substances that are not water-soluble, analysis by means of GC-FID after extraction in non-polar solvents is a suitable method.

Summary

Shimadzu's TOC-L series TOC analyzers are reliable companions in monitoring the production of implants and medical devices. Software packages and services additionally enable validated work within GxP-compliant data integrity. For many other test methods listed in ISO 19227, such as ICP-MS/OES, GC-FID, FTIR and particle determination, Shimadzu offers high-performance solutions.

Figure 1: Knee implant

Further information on this article:

- Application: »LAAN-A-TC-E049 074 – Cleanliness Evaluation of Orthopedic Implants using TOC«
- Application: »LAAN-A-TC-E045 – Quality Evaluation of Medical Devices using TOC Solid Sample Measurement System«

Food laboratory from the future's perspectives

Shimadzu and Merck: Education Seminars in food analysis

By 2050, world population will have grown to over nine billion people. This development will be one of the major challenges for mankind: how to ensure the supply of safe food and clean water, how to increase agricultural yields and how to develop additional food sources. Experts estimate that general food production will need to be doubled compared to today.

How can the safety and quality of food be guaranteed in the future? There are many laws and regulations within the EU and beyond the borders of Europe. Analytical instrumentation has become an indispensable tool for monitoring the safety and quality of food and beverages as well as consumer goods.

It detects residues from fertilizers and pesticides, and emissions that enter groundwater, lakes, and rivers – and migrate from there into the human food chain. Furthermore, it contributes to secure supply and manufacturing chains in food production, starting with raw materials and ingredients, their treatment, processing and all the way to packaging. Each ingredient or material could contain prohibited or dangerous substances and pollutants.

Food analysis is challenging due to complex matrices. Moreover, the challenges for analytics and laboratory staff are increasing constantly, for instance through qualitative and quantitative methods with ultra-fast detection in the ultra-trace range.

New applications, tips and tricks for the food laboratory

For several years, the companies Shimadzu and Merck have been

Exhibition of instruments at the »KUBUS« location in Leipzig, Germany

offering seminars on this subject. They have introduced new applications as well as tips and tricks for use in the food laboratory. These training forums are aimed at all analytical chemists responsible for food monitoring and analysis. In addition to the extensive lecture program, they provide an excellent platform for dialogue and exchange between experts in food production, control and research & development.

Training forums in seven European cities

The idea for this event was launched in 2016 and implemented in the same year at the Shimadzu European headquarters in Duisburg, and at the Merck corporate headquarters in Darmstadt. After meanwhile four years, the seminars have become so popular that in 2019, a total of seven events will take place at European locations. Alongside Leipzig, Darmstadt and Paris in the first half of 2019, Vienna, Rotterdam, Bologna and Milton Keynes are on the calendar for the second half of the year.

The following is an overview of the lectures. In the second half of the year, guest speakers will complement the agenda with current topics:

Coupling of LC-GC (MS) for MCPD, cholesterol and PAH determination
Dr. Stephan Schröder, Shimadzu Germany

Unique selectivity & capabilities of ionic liquid GC capillary columns, including water determination with GC
Klaus Buckendahl, Merck/ Sigma-Aldrich Chemistry

The suitable quality of ultrapure water for your application in the Food & Bev laboratory
Ekkehart Berndt, Merck

What's in my grocery bag? Latest LC/LCMS technology for food analysis
Dr. Klaus Bollig, Shimadzu Germany

The Shimadzu Laboratory World in Duisburg, Germany


Food seminar in Paris, France


Lecture presentation at Shimadzu in Duisburg, Germany

Fast, efficient and cost-effective chromatographic solutions for HPLC in the food & beverage industry
Dr. Martin Finkbeiner, Merck

Use of atomic spectroscopy for the determination of heavy metals in food and food packaging
Uwe Oppermann, Shimadzu Europa

Sample preparation for fatty and complex food matrices, using solid phase extraction & QuEChERS for pesticide analysis
Dr. Martin Finkbeiner, Merck

Filtration and Particle-Monitoring in the F&B Lab & Sample Preparation for instrumental Analytics
Uwe Wagner, Merck

Size matters – particle size distribution in the food industry
Sascha Hupach, Shimadzu Germany

Pursuing food quality with global partnership

Professor Leitner's scientific work and Shimadzu's technological expertise meet in the European Innovation Center

Professor Erich Leitner, Graz University of Technology, Austria in one of his laboratories

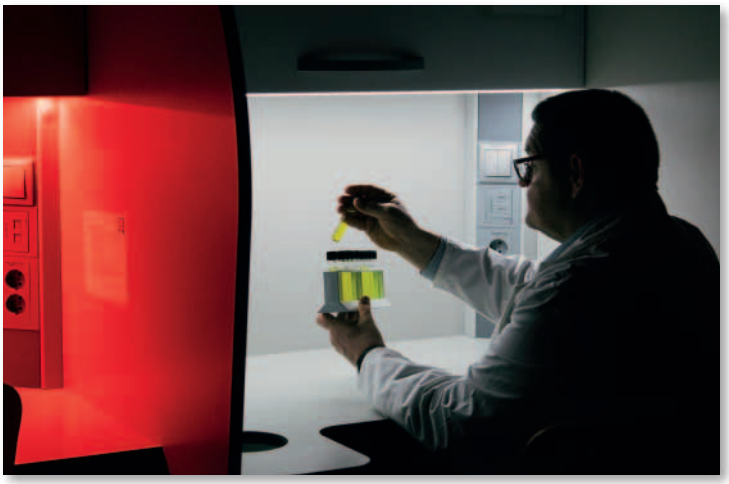
For nearly 150 years, the Shimadzu Corporation has been "contributing to society through science and technology" by building analytical and measuring instruments. As part of this endeavor, Shimadzu has established Shimadzu Innovation Centers (SICs) in China, Singapore, the United States, and Europe. The European Innovation Center (EUIC) works with leading academic institutions to translate university innovation into large-scale scientific solutions. Here we highlight a project between EUIC and an academic institution that will advance food quality.

Food safety standards

Professor Erich Leitner is a leading expert on food quality at the Graz University of Technology in Austria. He is a major node in the local food network, having strong relations with local food producers and farmers in the region. Leitner has been using Shimadzu chromatography systems and mass spectrometers for over a decade to study food. To him, scents and chromatograms are the same.

»When I smell a substance, I can see the structure of the molecules«, he says.

Identification of odor active substances by nose after separation with GC-2010 Plus ...



... and final judgement in the organoleptic laboratory with all the senses

However, Leitner takes as strong an interest in the packaging food comes in as the food itself. Companies invest an enormous amount of time and money to insure their foods have the right food chemistry for the best flavor. All that effort can be lost, however, by the food packaging. Be it pasta in paper boxes, sugar in plastic bags, or chocolate in foil wrapping, the quality of all foods is vulnerable to molecules leaking from the packaging. Preservation can be an extremely challenging problem when considering that some foods are kept in their packaging for months or even years. Contamination can sometimes be recognized by a change in taste or aroma, but not all contaminants can be detected by our senses. That is the case for mineral oil saturated hydrocarbons (MOSH) and mineral oil aromatic hydrocarbons (MOAH). MOSH is known to accumulate in the body, and MOAH is associated with potentially carcinogenic substances.

This year or next, the European Commission is expected to set strict guidelines on the amount of MOSH and MOAH acceptable in foods. What has delayed these guidelines is the lack of standardized methods. Besides contributing to food safety, such a method would assist in troubleshooting which stage in the manufacturing the contamination occurs.

»We monitor from the raw product to the final product. The more you process a food, the higher the risk of contamination«, Leitner explains.

Loyal partnerships

EUIC and Leitner have teamed together to solve this problem. Shimadzu is building automated chromatography and mass spectrometry systems that reduce the amount of human handling and thus errors by the experimenter, while Leitner is bringing his expertise on sample preparation and analysis protocols to optimize the instruments. The automated system allows Leitner to test 50 samples per day. In comparison, previous methods could require as long as two days to test some samples. When daily production is measured in tons, any reduction in time can translate into huge savings.

Science is teamwork

Leitner has been working with Shimadzu so long and on so many projects that he cannot remember who first proposed the MOSH/MOAH study. Either way, there was little doubt he would join.

»Many people think they can do analytical measurements by buying equipment. But that's half the story. You need good people«, he says. Leitner has been convinced those people are at Shimadzu ever since they loaned him two engineers for days to configure his first Shimadzu instrument.

»I was able to test the instrument (multi-dimensional gas chromatography mass spectrometry system with additional sniffing port) exclusively for two days with two experts. I was impressed by the performance and the customer service.«

Working with EUIC has allowed Leitner to explore the problems that most interest and inspire him, namely, food quality. **»I'm absolutely crazy about quality«**, he says. **»I'm one of the luckiest people in the world. My job is my hobby.«**

*The information including affiliates and titles of the persons in this article are current as of the time of interviewing (August 2019).

SHIMADZU GLOBAL INNOVATION SUMMIT 2019

Pioneering partnerships for advanced healthcare

Leading scientists at the 2nd Global Innovation Summit in Kyoto, Japan

New Healthcare R&D Center

Over 95 leading scientists from all over the world attended the second Shimadzu Global Innovation Summit. Two days in July focused on "Pioneering Partnerships for Advanced Healthcare – Synergy between Analytical & Medical." This topic deals with collaborative improvement of methods for early detection of diseases, addressing both natural scientists and physicians.

Shimadzu, being one of the few manufacturers of both Analytical Measurement Technology and Medical Technology, has for years created synergistic effects between analytical instrumentation and the health sector, for example through highly developed analytical systems for medical research. However, the synergies from the technological integration of medical technology as well as analytics can be taken even further. They offer great potential to provide solutions for diseases that pose the greatest challenges today, such as the diagnosis and treatment of cancer, dementia and endocrine disorders.

Two examples: The combination of an angiography system with LC-MS can be used to diagnose primary aldosteronism, a cause of high blood pressure. Furthermore, the NIR-Pit (Near Infrared Photoimmune Therapy) can be used in cancer therapy. This new method is based on a near-infrared camera system combined with an LC-MS system.

The fact that the Summit was opened by Dr. Teruhisa Ueda, President and CEO of Shimadzu, is not only a sign of the significance of this event but also demonstrates that the implementation of the corporate philosophy of "contributing to society through science and technology" has become a standard for research and development.

At the same time as the Innovation Summit, the openings of the Healthcare R&D Center and KYOLABS were announced. Shuzo Maruyama, Director of the Analytical & Measuring Instrument Division, used a short presentation and video to give participants their first impression. With the KYOLABS, Shimadzu offers an environment in which companies can conduct applied research on their own or together with Shimadzu – always striving to achieve healthcare synergies with medical technology and analytics.

Koichi Tanaka (General Manager Mass Spectrometry Research Laboratory, Shimadzu Corporation)

Group photo of participants in the Global Innovation Summit 2019

The speakers, lectures and poster topics would make some organizers of other events envious. Furthermore, the open exchange of results and the dialog between analysts and physicians showed the potential of this event and highlighted the importance and synergistic effects inherent in both disciplines.

The importance of cooperation for science and industry

The keynote speakers were Kevin Schug (University of Texas, USA) and Alex R. Rai (Columbia University, USA), who have been working together since the first Innovation Summit in 2017. Kei Takase (Tohoku University, Japan) with his topic "Development of Interventional Radiological Treatment of Primary Aldosteronism Utilizing Rapid Aldosterone Analysis" emphasized that analytics and medicine are equally important for high-tech medicine.

Mark Horrigan (Austin Health, University of Melbourne, Australia) reported on the existing cooperation between Austin Health and the Shimadzu Medical Division. He was followed by Philipp Scherer (UT Southwestern, USA) who spoke on the use of LC-MS for the analysis of metabolites and the detection of critical metabolites from tissue samples, especially from adipose tissue.

Poster presentations expand the summit's topics

The lunch speech was given by Prof. Maeda-Yamamoto of the National Agriculture and Food Research Organization on the healing and invigorating power of green teas. Afterwards, Shosaku Murayama of iPS Portal Inc. added greater emphasis to the laboratory of the future. In the afternoon, Koichi Tanaka, Nobel Laureate in Chemistry 2002, joined the participants and discussed their posters and research.

An overview of the individual posters revealed a number of new applications. With the further development of mass spectrometry as a detection technique for liquid or gas chromatography, and the considerable increase in knowledge in biochemistry and protein chemistry, a large number of new applications have been developed. They enable the determination and evaluation of biomarkers for numerous serious diseases and their early detection, as well as the deduction of a targeted therapy. The journey to the often-invoked personalized medicine seems to be shortening.

Colin Masters (University of Melbourne, Australia)

Mass spectrometry in particular has long been established in a wide range of applications and is now an indispensable tool in research. Moreover, classical methods have neither lost their place nor their importance in research routine.

Dr. Teruhisa Ueda, President and CEO, Shimadzu Corporation

Instrumental analytics in medical applications

The last session of the day was once again a topical attraction. Teo Eng Kiong (Changi General Hospital Singapore) gave an interesting insight into the use of analytical methods in high-performance medicine. Stanley Hazen (Cleveland Clinic, USA) reported on the use of MS in biomedical research for the diagnosis of cardiovascular diseases. Finally, Colin Masters (University of Melbourne, Australia) spoke on the subject "The Molecular Origins of Alzheimer's Disease: When does it Start and What Strategies for Primary Prevention?"

It is important to detect Alzheimer's disease as early as possible in order to start appropriate therapy approaches in time. A number of renowned researchers and institutions are working on this subject, and there are opportunities for progress in the near future. With Colin Masters' presentation, the current state of research in Alzheimer's detection was clearly described, and a multitude of open questions were highlighted that could be discussed during the Summit.

Networking & event, poster-awards

Akira Nakamoto, Chairman of the Board of Shimadzu, welcomed to the gala dinner and encouraged dialog between scientists and Shimadzu Research & Development staff to benefit from each other's inspiration and technology.

Ai Takaoka, a famous calligraphy artist, celebrated the creation of the characters for "Synergy/Co-Creation", a small but impressive insight into the host's tradition and culture.

One of the highlights of the evening was the selection of the winner of the poster award. From the numerous posters, the jurors chose six, including two from Europe: Silvia Giordano from Italy and Tiffany Porta Siegel from the Netherlands. All award winners were invited to present their research topic in a short presentation the following day.

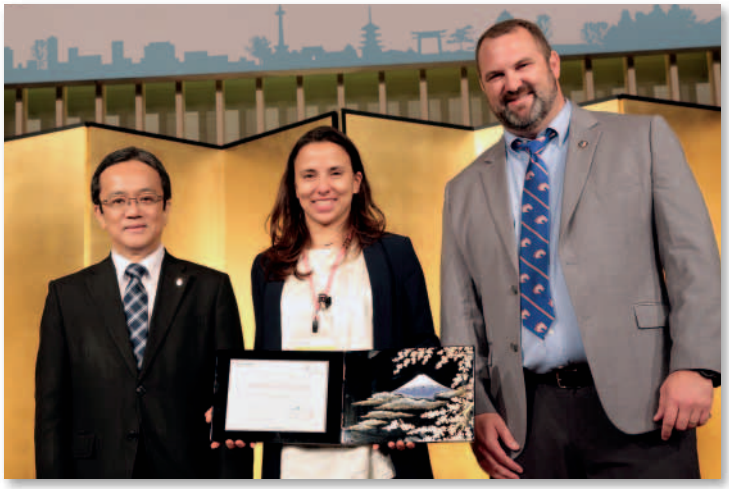
Ai Takaoka, a famous calligraphy artist, celebrated the creation of the characters for 'Synergy/Co-Creation', a small but impressive insight into the host's tradition and culture

Excellence in Science

The second day started with "Excellence in Science Workshops": Giancarlo la Marca (Meyers Children's Hospital, Italy) started with the topic "Next Generation of Disease Biomarkers", with focus on newborn diagnostics; Yi Chen (Chinese Academy of Science, China) followed with the topic "Towards the Intelligence of Analytical Instruments."

The third workshop "Neuroimaging with NIRS – Fundamentals to Hyperscanning with Emerging New Directions for Autism" by Joy Hirsch (Yale School of Medicine, USA), Ilias Tachtsidis (University College of London, UK) and Jung Li (South China Normal University) was a vivid, multi-national presentation. They showed the basics, possibilities and chances of fNIRS technology and presented results of their investigations. fNIRS is short for Near-Infrared Spectroscopy, an imaging technology that visualizes brain functions.

Wasan Udayachalerm (King Chulalongkorn Memorial Hospital, Thailand) emphasized the importance of cardiac catheters for minimally invasive procedures and the opportunities for closer interaction between analytics (LCMS) and medical technology (Trinias Unity, an image processing technology for highly complex surgical procedures). The lunch break was reserved for presentations from Research & Development, providing another opportunity to speak directly to the engineers and to gain insight into current projects.



Silvia Giordano (Mario Negri Institute, Milan, Italy) with her Poster Award

The closing words came from Kunimasa Ito, General Manager of the Medical Division. After a visit to the production facilities and the Shimadzu Science Plaza, all participants met in the Heian Jingu Shrine Hall for another networking dinner to establish and strengthen contacts.

The third day was reserved for a visit to the Shimadzu Memorial Hall, the Okura Sake Museum and the Byodin Temple. Hence, the participants could visit a (certainly too small) part of Kyoto, the former capital, and get an impression of Japanese culture and tradition, providing an incentive for some to visit again.

Byodin Temple Kyoto, Japan

Silvia Giordano and Enrico Davoli (Mario Negri Institute, Milan, Italy) at the Networking Dinner

What remains beyond the Global Summit?

Participants are often asked: what remains and what do they take away? A comprehensive answer is complex.

Technical developments thrive on being triggered by inspiration and exchange, as well as on recognizing necessities and possibilities. This requires direction and structure – both framework conditions as set out in the Global Innovation Summit. The willingness to collaborate in the search for new approaches for clinical research and diagnostics and to think beyond the existing barriers between classical analytics and medical technology was evident among all participants.

In addition, professional and personal encouragement plays an important role in this context: the feeling of being part of a global community and of this truly international event is inspiring. Rarely could so many discussions be experienced beyond the boundaries of areas of expertise. New contacts have been made and many projects will be followed up.

The synergies between analytics and medical technology are obvious. Many of the presentations demonstrate successful cooperation between the two areas, whose opportunities and potential are already concrete and are more than just a vague idea.

Shimadzu as a global company follows a long tradition of analytics and medical technology and continues the innovative spirit of its founder and visionary Genzo Shimadzu. With its current developments and projects, Shimadzu as a company occupies a top position in many areas and has the ability to actively shape the growth market.

Working together with customers and with leading scientists as partners, new requirements arise for Research & Development to create new "Excellence in Science" technologies and solutions in order to continuously "contribute to society through science and technology."

Shimadzu live

RAFA
Prague,
Czech Republic
November 5 - 8, 2019
rafa2019.eu/

Analytical Cannabis Expo
London, United Kingdom
November 11, 2019
expo.analyticalcannabis.com/london-2019

Job Vector Career Day
Düsseldorf, Germany
November 15, 2019
jobvector.de/karrieremesse/duesseldorf/

EBF
Barcelona,
Spain
November 20 - 22, 2019
bcn.e-b-f.eu/

Shimadzu & Merck Food Seminar
Milton Keynes, United Kingdom
November 6, 2019
shimadzu.eu/food-seminars-2019

HTC
Ghent,
Belgium
January 29 - 31, 2020
kuleuvencongres.be/htc16

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