SHIMADZU
Excellence in Science

150 YEARS ANNIVERSARY

secrets of science
magazine

02/2025

Giving the future a familiar taste
The science behind making plant-based meats (PBMs) as good as the original

The future belongs to the brave
Shimadzu is and remains an innovative partner in the scientific arena

Following the scent to scientific discovery
Investigating how the chemical process of heat affects the volatile ingredients of e-cigarettes

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Discover more about our products and applications as well as current topics of interest.

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Explore the frontiers of science: new applications and fields of use for our systems and new configurations for applications.

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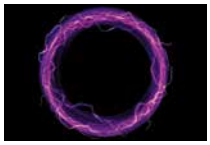
Think big – purity on a large scale

Preparative HPLC as the key to isolating active ingredients

Helping doctors more quickly treat hospital patients

Mass spectrometry is rapidly moving from research to real-life assistance at medical diagnostic lab



“There’s an easier way” – rethinking mass spectrometry

Innovative ion source overcomes limits in analysis

The perfect taste where sweet meets sour

HPLC methods for identifying and quantifying sugars and organic acids in tonic water and gin

Discovered quickly: Traces of heavy metals in raw plant materials

Robust and efficient – better consumer safety thanks to the ICP-OES and ICP-MS

Events

150 Years of Innovation

150 YEARS ANNIVERSARY

Milestones
in the company's history in this millennium

2003
World debut of the first cardiovascular X-ray imaging system with the "Flat Panel Detector" (FPD) that immediately provides a digital display of the image signal

The future belongs to the brave

Shimadzu is and remains an innovative partner in the scientific arena

The story of Shimadzu is one of tremendous ingenuity and great visions. In the end, the visions became reality – also (and even more so) in the Shimadzu Innovation Centers that have been established since 2015 as well. In this second and final part of our short series on the company's 150-year history, we're going to take a look at these think tanks that have redefined the phrase "close to the customer".

Shimadzu has always been close to its customers and focused on the needs of society: Right from the start, the company has been developing and producing innovations that advance research – and ultimately humanity. This was already the case during the first decades of the company under Genzo Shimadzu Sr. and Jr. The introduction of several Innovation Centers in the recent past gave product development an extra boost and redefined what it means to be close to the customer. In these centers, Shimadzu develops new devices and applications together with users.

Because Shimadzu knows: The world is full of diversity, and each customer has their own requirements. The Innovation Centers help when it comes to understanding these requirements even better and offering the right solutions. Here, academic expertise is combined with technical prowess. The four sites in Europe, China, Singapore and the USA have taken cooperation with important partners, such as universities, laboratories and private companies, to a whole new level. The importance of the hubs for research and development in the field of measurement and analysis technology cannot be emphasized enough.

→

Milestones

2005
Launch of MobileDaRt, the world's first fully digital mobile X-ray system

2006
***50th anniversary** of gas chromatography from Shimadzu*

2010

2010
Shimadzu launches the LCMS-8030, Japan's first triple quadrupole LC mass spectrometer

2012
***60th anniversary** of UV spectroscopy from Shimadzu*

2015
Shimadzu Innovation Centers are opened in the USA and China

New solutions for the future

The European Innovation Center (EUIC) in Duisburg, Germany, is one of these innovation-led think tanks. It unites Shimadzu's state-of-the-art technologies with forward-facing concepts for markets and science. The goal is always the same: coming up with new solutions for the future!

Launched in 2017, it is a real success story. Shimadzu and its partners focus on five areas in the EUIC:

– Clinical
– Food
– Imaging
– Composites
– Green Transformation (GX)

Highly respected scientists from prestigious European universities contribute their research expertise to the European Innovation Center and in turn benefit from the opportunities to collaborate with Shimadzu.

Faster inspections lead to greater food safety

One example is Prof. Erich Leitner from Graz University of Technology, Austria. In 2018, the food safety specialist, who had been a customer of Shimadzu for a long time already, joined forces with the technology experts: The goal was to jointly develop standardized methods for monitoring mineral oil components (MOSH and MOAH) in processed foods and packaging.

Shimadzu went on to build automated chromatography and mass spectrometry systems that reduce the amount of human effort and thus user error, while Leitner contributed his expertise in the areas of sample preparation and analytical protocols, optimizing the devices. The automated system eventually allowed Leitner to analyze 50 samples per day, whereas previous methods could take up to two days to analyze just a few samples. This was progress made possible by bringing together expertise and resources in the EUIC.

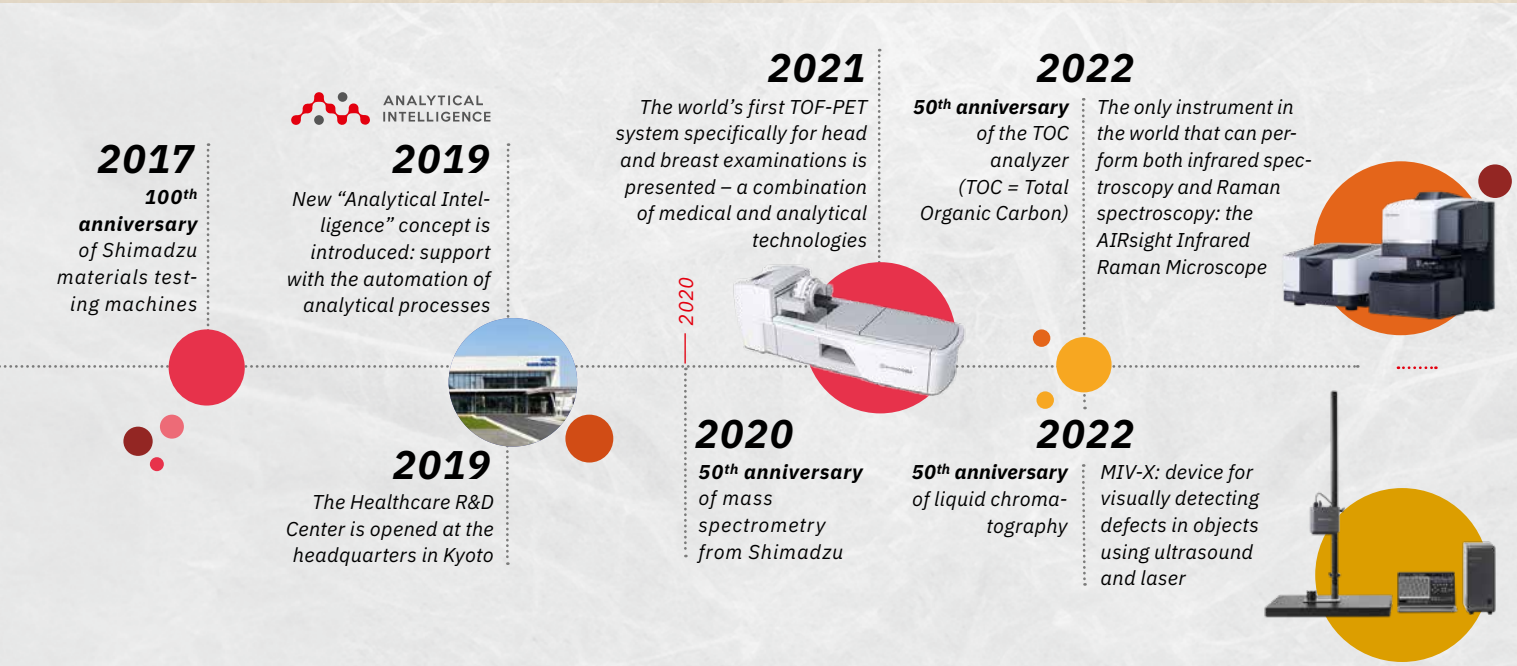
Working together saves lives

The network of knowledge provides selected customers with opportunities to take part in developing or updating Shimadzu devices, something that was previously unimaginable.

This collaboration paves the way for medical research, for example. Higher chances of surviving liver cancer – or even recognizing the presence of Alzheimer's and Parkinson's disease

»Through the European Innovation Center, Shimadzu is the first company who proposes us an actual and effective collaboration. This is a win-win and exciting partnership.«

Prof. Franck Saint-Marcoux, University Hospital of Limoges (France)



before symptoms appear: These are just a few examples of what has now become a reality thanks to methods developed at the EUIC. *"For a researcher, having a prototype and [being] the first to try something is a desire your whole life,"* says mass spectrometry expert Dr. Enrico Davoli from the Mario Negri Institute in Milan, Italy. Collaborating with Shimadzu's EUIC gave him, along with many other academics, this valuable opportunity. Shimadzu also provides financial support for PhD students from the partner institutes through the EUIC and, last but not least, the Innovation Center establishes contacts between researchers, in this way acting as an important network.

"One of our goals is to identify key opinion leaders and form strong research relationships with them. We see partners, not customers. We work together to maximise their research and the performance of our analytical instruments," says Stéphane Moreau, who is both LCMS Product Manager at Shimadzu Europe and responsible for the company's partnerships. One example of a groundbreaking device made possible by the collaboration at the European Innovation hub was the ELEM-SPOT: In 2024, four partners – Shimadzu, TotalEnergies, the French Université de Pau et des Pays de l'Adour (UPPA) and the Spanish Universidad de Oviedo (UO) – unveiled the powerful and versatile device to the public.

»[...] for me, the collaboration with Shimadzu is based on trust and a long-term relationship. This is quite different from other companies. I must say that this is the most fruitful collaboration I have had and still have.«

Prof. Christophe Hirtz, University of Montpellier (France)

Huge time savings

It all began with a problem we are facing today: Although biofuels are a key part of making our world a carbon-neutral place, they can contain undesirable oxygen compounds. Recognizing these is difficult. Experts were amazed when the solution was presented in the form of the ELEM-SPOT – after three years of joint research work: A GCMS was coupled with a special combustion unit that can detect compounds that contain either oxygen or nitrogen – with high sensitivity. →

Milestones

2023
OAD-TOF system, the world's first system for chemical structure analysis

2024
The first device worldwide able to detect compounds that contain oxygen and nitrogen: with the element-selective GCMS "ELEM-SPOT"

2025

2025
***20th anniversary** of the HPV high-speed camera*

This reduces the time it takes to detect oxygen compounds in biofuels by 80 percent!

The Shimadzu Innovation Centers are part of a line of tradition that goes right back to Genzo Shimadzu Sr. and Jr. *"To contribute to a society changing at a dizzying pace, we broke new ground,"* says Yasunori Yamamoto, President and CEO of Shimadzu Corporation, referring to the company's history. *"In every instance, the challenges we faced were by no means easy. Nevertheless we pressed forward, encouraged by the voices of uncompromising scientists and researchers who shared our goals, accumulating technology and delivering solutions."*

A pioneer and reliable partner

Of course, nobody knows exactly what the future holds. However, one thing is certain: Shimadzu remains a technological pioneer and a reliable partner. Yasunori Yamamoto believes that humanity is facing unprecedented challenges: *"[...] the expectations placed on science and technology are higher than ever."* The solution: *"As we move forward, we must pool our strength with even more scientists and researchers than before."* The Shimadzu Innovation Centers will play their part here.

As was true 150 years ago, the same goes for today: The future belongs to the brave, and Shimadzu is certainly that.

Note
For more information and references, please refer to the digital version of this edition.

»Shimadzu is an innovative company for academia and industries – and open for developments to fulfil future demands.«

Prof. Frank Walther,
TU Dortmund University
(Germany)

Think big – purity on a large scale

Preparative HPLC as the key to isolating active ingredients

Dr. Martin Meyer, Shimadzu Europa GmbH

Medicines save lives, ease suffering and shape modern medicine in ways that almost no other achievement has. However, before an active ingredient can contribute to a cure, it must be developed, tested and produced with the highest levels of purity. This is due to the fact that effectiveness depends not only on the correct dosage and application but also on the purity of the ingredients. This is where preparative HPLC comes into play – a key technology that is decisive for the quality and efficacy of new medicines. This article will explore whether the technology is capable of meeting the strict requirements.

When developing drugs, researchers are working tirelessly to develop new medicines that make it possible to fight infections, manage chronic diseases and improve the quality of life of millions of people. These include passionate chemists, researching promising new active substances that might even have the potential to treat rare but devastating diseases.

That being said, isolating an active substance doesn't come without challenges. The chemists have to deal with what is often a complex and demanding process in which there is always a risk that residues from the starting compound will remain in the end product or that unwanted by-products will be created.

These impurities could not only impair the effectiveness of the medicine itself but also cause toxic reactions or trigger unexpected side effects in the people taking them. A huge responsibility, since there's a fine line between a cure and a poison.

With this in mind, it's important that chemists use a process capable of efficiently isolating the main substance and separating the unwanted compounds at the same time. Various methods such as crystallization, filtration and distillation are at their disposal here. →

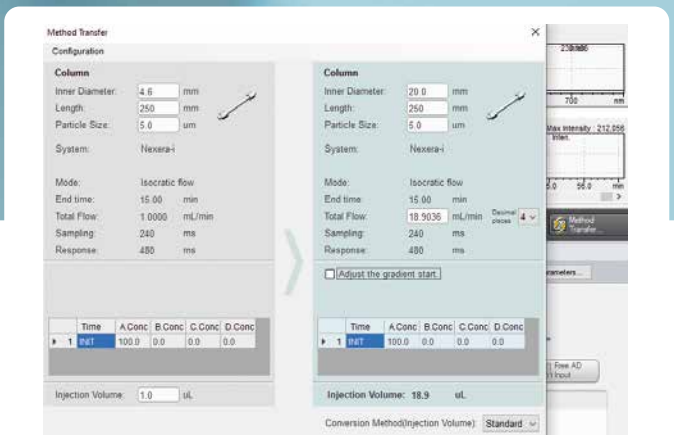


Figure 1: Scaling with the Method Transfer function in the Shimadzu software

However, a technique that not only separates the existing substances but also identifies them would be particularly valuable in the development process. High-performance liquid chromatography (HPLC) makes this possible. It provides chemists with new ways to precisely isolate and analyze their target compounds.

HPLC is an analytical technique that is widely used in the chemical and pharmaceutical industries. It allows complex mixtures to be separated and analyzed, which is essential for quality control and research.

Going from analytical to preparative HPLC

HPLC is usually optimized to be able to detect extremely small concentrations of substances. However, when it comes to isolating larger quantities of an active ingredient, it is necessary to select significantly larger dimensions. Both the device components and the method itself must be scalable here.

A critical component in determining how much of a substance can be applied to a chromatographic system is the separation column. Generally speaking, separation columns for analytical applications have an internal volume of 0.1 to 3 mL and can separate around 3–20 mg of substance. In contrast, preparative columns have an internal volume of 20 to 300 mL and can achieve separation capacities of 300 to 2,000 mg.

Due to the larger volume of the preparative columns, the flow rates of the liquid must also be adjusted, meaning that solvent consumption can be 20 to 100 times higher than in analytical applications.

For this reason, it's important to carry out preparative HPLC ideally in combination with already established methods in order to minimize solvent consumption.

Figure 2: Shimadzu columns: UHPLC column (2 mm I.D.), standard analysis column (4.6 mm I.D.), prep column (20 mm I.D.), prep column (50 mm I.D.) (from bottom to top)

As most experienced analysts know, method development is one of the most time-consuming parts of analytics. This is why it's better to first develop the method for separating the active ingredient from by-products on an analytical scale and then scale it up to a preparative scale. This scaling process is relatively straightforward and can be fully automated using software from Shimadzu (Figure 1).

For upscaling to work successfully, it is essential that both the analytical and preparative columns are very similar in terms of their separation behavior. Using the same series of columns is therefore recommended.

With the Shim-pack G and the Shim-pack Scepter series, Shimadzu is offering two column ranges that are fully available from small analytical dimensions to large preparative columns (Figure 2).

Going from salicylic acid to Aspirin®

Upscaling and isolation using preparative HPLC can be demonstrated using the example of one of the world's best-known active ingredients: acetylsalicylic acid (ASA) – Aspirin®.

The starting material for ASA is salicylic acid, which comes from a variety of plants. However, salicylic acid is not as well tolerated, is less effective and is poorly absorbed by the body compared to Aspirin® (acetylsalicylic acid). Aspirin® is synthesized by the acetylation of salicylic acid with acetic anhydride.

Nevertheless, it's possible for residues of salicylic acid to remain in the end product during synthesis. These unwanted residues can be effectively separated using preparative HPLC, which guarantees the purity of the end product (Figure 3). ⟶

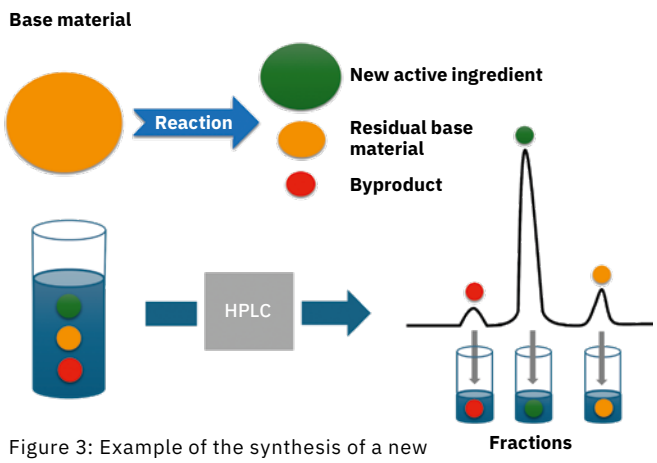
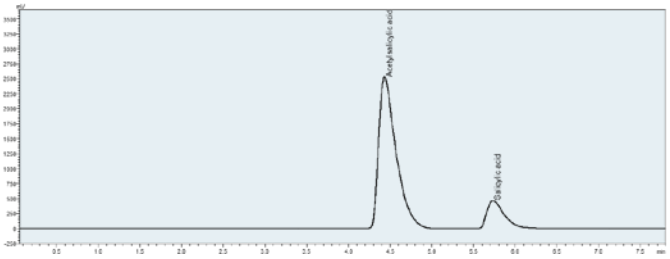


Figure 3: Example of the synthesis of a new active ingredient and its separation and isolation using preparative HPLC

To demonstrate this, a method was developed to establish the retention times for Aspirin® and salicylic acid through the use of standards (analytical parameters can be found in Table 1). Next, a sample of the synthesized Aspirin® was examined. The findings show the presence of salicylic acid next to the main product (Figure 4).

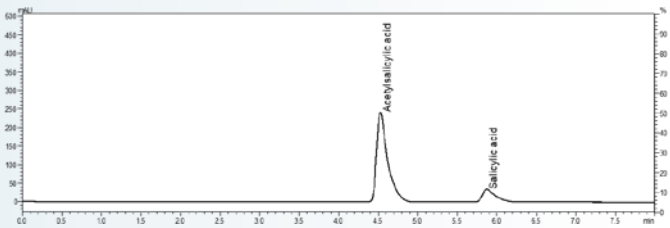


▲ Figure 4: Aspirin® sample contaminated with salicylic acid on an analytical column

Analytical method	
System	Nexera Prep/LH-40
Column	Shim-pack GIST 5 µm 250 x 4.6 mm
Mobile phase	Water 50 %/Acetonitrile 50 %/ 0.5 % phosphoric acid
Program	Isocratic
Run time	10 min
Flow rate	1 mL/min
Injection volume	1 µL
Detector	SPD-40 (standard cell) 200 nm

◄ Table 1: Parameters of the analytical measurement

The parameters were then transferred to the preparative dimensions (Table 2). A measurement was carried out with this method to ensure that both methods yield similar results.



▲ Figure 5: Measurement with preparative dimensions based on scaling of the analytical values

Preparative method	
System	Nexera Prep/LH-40
Column	Shim-pack GIST 5 µm 250 x 20 mm
Mobile phase	Water 50 %/Acetonitrile 50 %/ 0.5 % phosphoric acid
Program	Isocratic
Run time	10 min
Flow rate	19 mL/min
Injection volume	20 µL/1,000 µL
Detector	SPD-M40 (prep cell) 200 nm

◄ Table 2: Parameters of the preparative measurement

Although the column dimensions are substantially different and the flow rate was increased by 20 mL, separation remained almost identical. Based on this verification, the fractionation was set so that the system starts collecting the compounds at the right times (Figure 6). On top of this, the amount of material was greatly increased to ensure maximum yield of the substances.

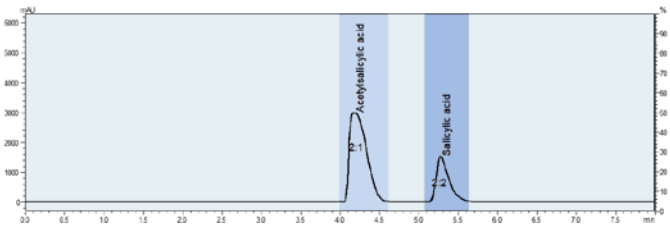


Figure 6: Preparative measurement with fractionation. The first fraction is acetylsalicylic acid, the second fraction is salicylic acid.

The fractions obtained can be tested for purity in another step.

As shown in Figure 7, salicylic acid is no longer detectable in fraction 1, indicating that the active ingredient has been successfully isolated.

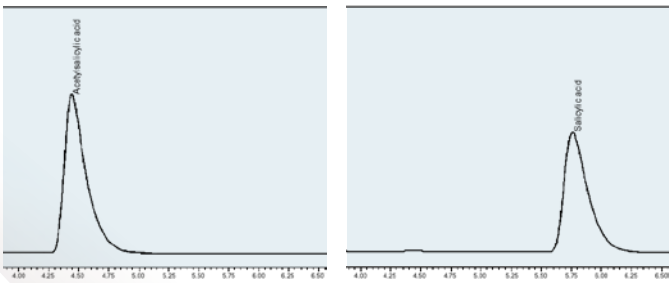


Figure 7: Comparison of the fractions of acetylsalicylic acid and salicylic acid

However, preparative liquid chromatography is not only used in the pharmaceutical sector but also plays a key role in the food industry, biotechnology, natural product chemistry and the cosmetics industry in that it contributes to the isolation and purification of valuable compounds.

Versatile technology for better patient safety

Scaling up analytical HPLC columns to preparative HPLC columns is an essential step in chemical synthesis and analysis. The synthesis of Aspirin® from salicylic acid was used to demonstrate how preparative HPLC from Shimadzu effectively removes impurities and produces a pure product that guarantees patient safety. This technique is not only relevant for Aspirin® synthesis but can also be applied to numerous other chemical compounds, which highlights its versatility and importance in a number of industrial sectors.

Note
For more information and references, please refer to the digital version of this edition.

E-cigarettes have become increasingly popular in recent years. Much testing has been done on the raw ingredients used in creating the vapor produced by e-cigarettes. Less research has been done on what happens to those ingredients through the process of heating. A recent set of experiments using gas chromatography/mass spectrometry (GC/MS) looked into the effects of the heating process on flavor.

The result was a clever new method to better understand and predict how to create and maintain better quality control for vaping flavors. Of additional interest, the new method also revealed the outline of a new way to test for consumer safety in the rapidly developing market for e-cigarettes.

Vaping – the use of e-cigarettes – has provoked heated discussion since commercialized electronic cigarettes first appeared over 20 years ago. Proponents have argued that e-cigarettes are a pleasant and effective way for consumers to wean themselves off of tobacco cigarettes.

At the same time, vaping opponents have argued that the health risks of e-cigarettes have not been adequately tested and that further research needs to be done.

Following the scent to scientific discovery

Investigating how the chemical process of heat affects the volatile ingredients of e-cigarettes

Waldemar Weber, Shimadzu Europa GmbH

Fascinated by flavors

Meanwhile, several lab researchers were dealing with a different vaping issue. E-liquids for e-cigarettes are designed to have a specific flavor. But how do you ensure that the flavor of the vapor produced is the same as the flavor promised by the liquid? They began to run tests using the world-class assortment of Shimadzu scientific instrumentation that they had at their disposal.

The focus on these tests was not on the chemicals themselves but on the chemical process at the heart of vaping. Basically, vaping uses a power source (usually a battery) to run an atomizer – a heating element – that creates an aerosol of vapor out of e-liquid in a small tank which is then inhaled. Relatively little work has been done on the effects of heating on the base chemicals, and the researcher began to look at how the raw ingredients change through the process of heating the e-liquid.

Taking advantage of state-of-the-art testing equipment

The vaporization ratio of aroma compounds in e-liquids changes with the temperature, since the vapor pressure of each aroma compound is different. Therefore, the flavor of an e-liquid is expected to change depending on the

→

temperature. Gas chromatography/mass spectrometry (GC/MS) analysis is ideal for objectively evaluating the correlation between flavors and aroma compounds.

What eventually became an effective new method started with this experiment: The aroma compounds of the e-liquid were exposed to a simple pretreatment and then analyzed in an environment close to actual use conditions. A flavored e-liquid was employed for the sample, of which 1 mg was directly weighed in a crimp vial for a headspace sampler, using a heat-resistant crimp cap for the vial cap and a highly heat-resistant septum.

An HS-20 NX headspace sampler was connected to a GCMS-QP2020 NX gas chromatograph/mass spectrometer, and the progress mode of a connected HS-20 NX was selected. Finally, analytical conditions specific to the Smart Aroma Database were used. During batch analysis, the oven temperature was changed step by step by selecting the progress mode, running analyses at 20 °C-increments at temperatures ranging from 150 °C to 270 °C.

Heating things up

As a result of this, 47 aroma compounds were identified by the Smart Aroma Database. Next, in order to investigate the correlation between the peak area of each aroma compound and the temperature, the area value was standardized, and cluster analysis was performed using the “R” statistical analysis software. The heat map obtained as the result of the cluster analysis is shown in Figure 2. Here, it is apparent that the vapor pressure of e-liquid increases with rising temperature. Therefore, the peak area value in Figure 2 is corrected by the dilution rate with the pressurized gas. The dilution rate by the pressurized gas was calculated based on the measured internal pressure of the vial.

Figure 2 also shows the correlation between the area value of each compound and the oven temperature. As one can see, the correlation can be confirmed at a glance. Overall, it can also be observed that the amount of aroma compounds in the generated gas tends to increase with rising oven temperature. In particular, there is a significant tendency for this to increase from 210 °C. On the other hand, the tendency of the area of aroma compounds to change depends on the variety of compounds when viewed in detail.

Changes in aroma characteristics

Figure 3 shows the temperature dependence of the quantitative ion peak areas of raspberry ketone and benzonitrile. These two compounds are shown in the red frame in Figure 2. The area values in Figure 3 have been corrected to take into consideration the dilution ratio of the pressurized gas, as in the case of Figure 2. As shown in Figure 3, the peak area of raspberry ketone increases with temperature, but the tendency decreases from around 210 °C. On the other hand, the peak area of benzonitrile does not change much in the low-temperature range, but the peak area value rapidly increases from 250 °C. These results show that the increasing tendencies of the area values of the two compounds are quite different.

The Smart Aroma Database contains sensory information about numerous aroma compounds. According to the sensory information, for example, raspberry ketone smells like raspberry, and benzonitrile smells rancid. From the results shown in Figure 2 and Figure 3, it can be inferred that the raspberry-like scent intensifies until 210 °C, and the rancid smell increases rapidly from around 250 °C.

To sum it all up: Investigating the correlation between aroma compounds of e-liquid vapor and heating temperature using a GCMS-QP2020 NX and an HS-20 NX revealed that, by linking changes in aroma compounds with sensory information, a new method was created that can be applied to improve strategic scent design and evaluation.

The rest of the story ...

As noted, a new method was developed that offers researchers the opportunity for more efficient design and evaluation of e-cigarette aromas and flavors. But – even more interestingly – it also points the way towards a better way to test e-cigarettes for safety. Investigating the effects of heating on e-liquids for one thing – aromas – can also be used for investigating another thing: unplanned harmful compounds created by the chemical process of heating. But that, as they say, is another story. Perhaps even one for a future issue of the Secrets of Science. →

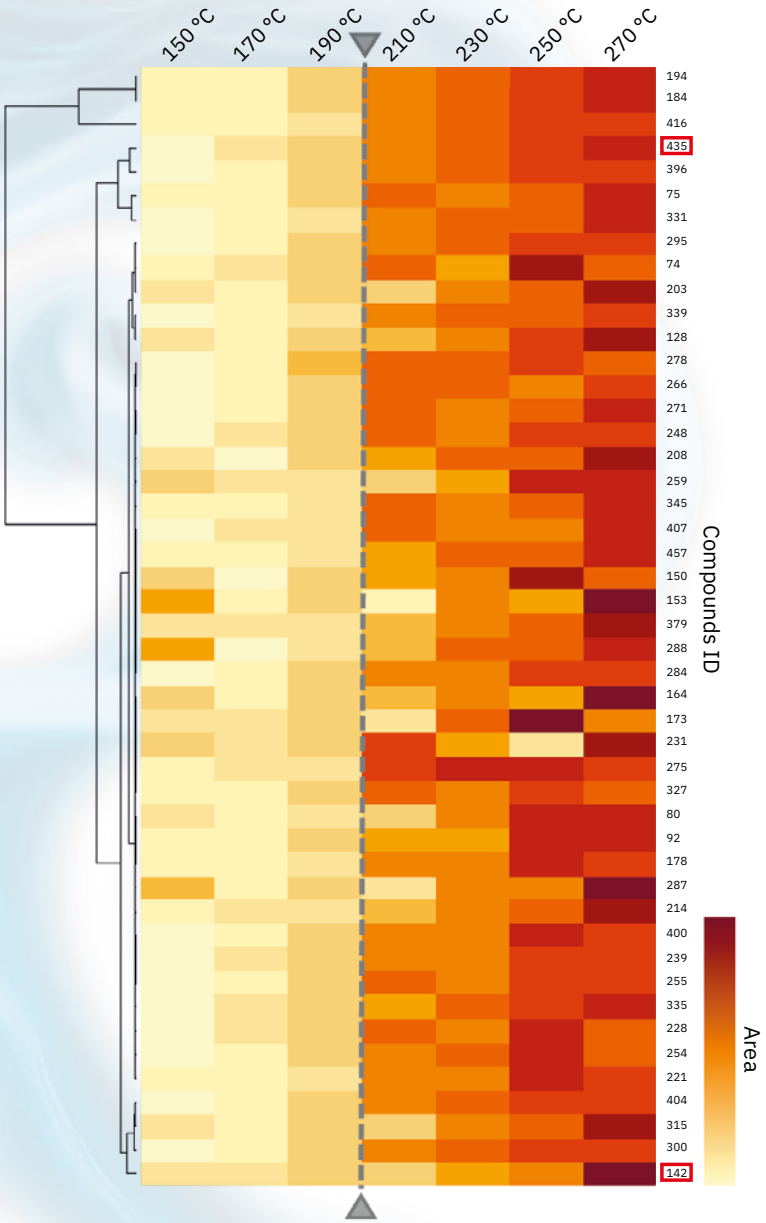


Figure 2: Correlation between area value of aroma compounds and oven temperature

Figure 1: Shimadzu GCMS-QP2020 NX with HS-20 NX

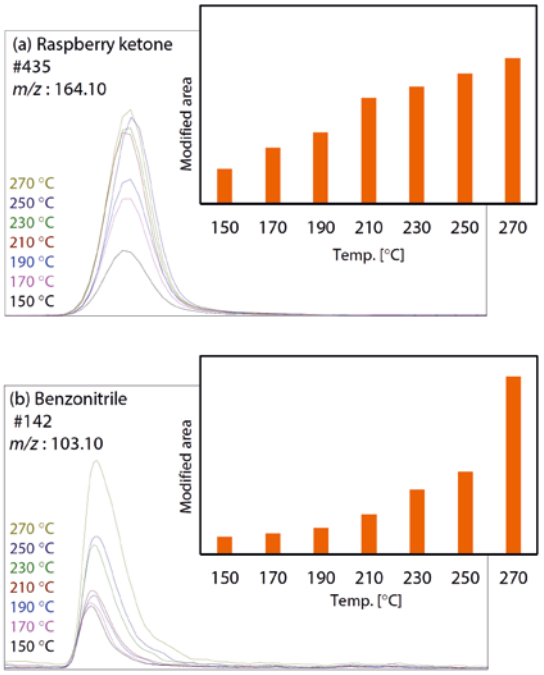


Figure 3: Correlation between temperature and quantitative ion peak area of raspberry ketone and benzonitrile

The science of discovery

This article highlights an important aspect of scientific inquiry. That is, that one thing does truly lead to another. From looking into flavors to improving consumer safety is not necessarily a linear move. Science hops and jumps and sometimes leads from A to Z while bypassing all of the letters in between. Science leads to discovery, and sometimes we discover things that we didn't even know were there.

Shimadzu salutes the creativity and dedication of scientific researchers everywhere and commits its research to ensuring that laboratories worldwide have the best tools available to follow science –wherever it leads.

The recommended analytical hardware and software are listed below.
Main unit: Nexis GC-2030 with GCMS-QP2020 NX: gas chromatograph plus mass spectrometer detector
Accessory: HS-20 NX headspace sampler
Main consumable: SH-I-5Sil MS
Software: GCMSsolution and GCMS Lab Solutions Insight Software

A picture of the instruments used, including the main unit and the accessory, can be seen in Figure 1.

Note
For more information and references, please refer to the digital version of this edition.

Helping doctors more quickly treat hospital patients

Mass spectrometry is rapidly moving from research to real-life assistance at medical diagnostic lab

Ewa Gawrylak-Dryja, Tomasz Czerner,
University Clinical Hospital in Opole

Until recently, mass spectrometry (MS) has primarily been associated with highly specialized research and university laboratories. These days, however, it is increasingly saving time and adding precision to the field of medical diagnostics – serving real-life patients and their doctors.

Mass spectrometry offers the additional advantage of allowing for the study of not only basic substances but also their metabolites. And, thanks to its ultra-high measurement sensitivity and precision selectivity and resolution, it is now the technique of choice in the routine analysis of blood, urine, physiological fluids, saliva and even hair. Secrets of Science recently spoke with an expert in medical diagnostics about the advantages of MS in his daily work.

Figure 1: Part of the team at USK's Department of Laboratory Diagnostics: Maria Przystajko, Tomasz Czerner

Science needs scientists, and the University Clinical Hospital (Uniwersytecki Szpital Kliniczny – USK) in Opole, Poland, has many of them. Among them are several specialists in medical laboratory diagnostics working at the Department of Laboratory Diagnostics, including: Ewa Gawrylak-Dryja, MSc, head of the department, Maria Przystajko, MSc and Tomasz Czerner, MSc – currently specializing in Laboratory Medical Toxicology. We asked Tomasz Czerner to tell us a bit about the lab:

Shimadzu: Good morning. What can you tell us about the University Clinical Hospital?

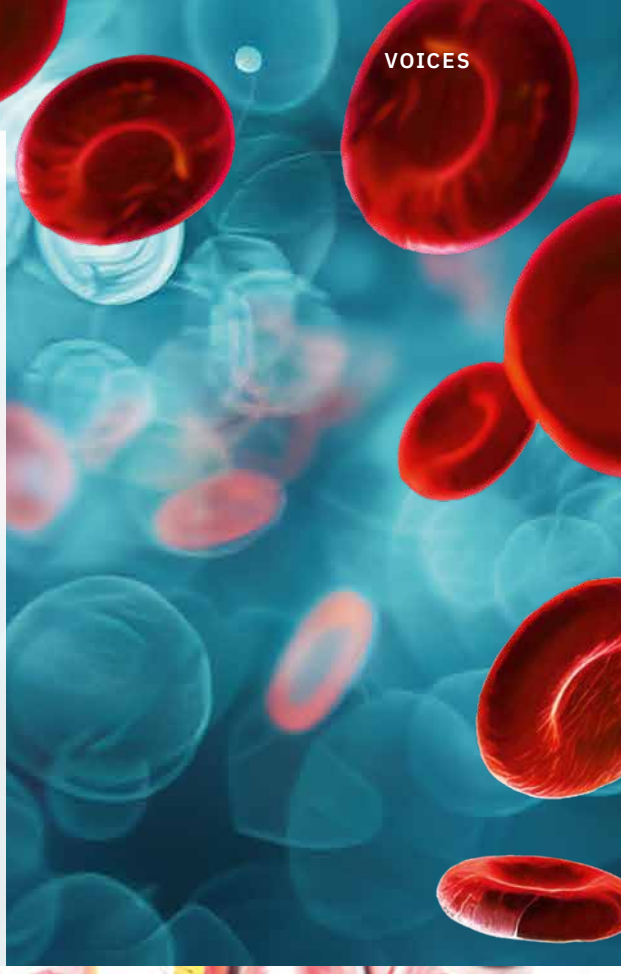
Tomasz Czerner: Good morning to you! The University Clinical Hospital (USK) is an independent public healthcare facility. We are a big multi-specialty hospital, operating 24 hours a day. As a result, we treat about 250,000 patients every year!

Shimadzu: That's a lot! Can you say more about USK's areas of specialization?

Tomasz Czerner: The hospital is active in most of the medical service specialties, cooperating with and participating in a number of national and international organizations for the promotion of healthcare in particular areas. For example, our Center for Pediatric Diabetes belongs to the International Society for Pediatric and Adolescent Diabetes (ISPAD) as well as to the SWEET initiative. And our Allergy Center belongs to the international network GA²LEN (Global Allergy and Asthma European Network) Urticaria Centers of Reference and Excellence (UCARE).

Shimadzu: That sounds impressive! Now, what can you tell us about your actual part of that: the diagnostic facilities and labs?

Tomasz Czerner: Our Laboratory Diagnostics Department has one of the largest laboratories in Poland! Naturally, we use all of the traditional analytical techniques in our work. But several years ago, we realized that we needed to implement more cutting-edge separation techniques such as gas chromatography (GC) and high-performance liquid chromatography (HPLC) coupled with tandem mass spectrometry (MS).



Shimadzu: Why did you do that?

Tomasz Czerner: Of course, the traditional techniques worked better than the ones they replaced. However, they still weren't always precise enough. And they sometimes produced cross-reactions as well as a multitude of false positive or negative results. These drawbacks led the entire medical field to look for new solutions offering better results. Mass spectrometry turned out to be such a solution.

Shimadzu: But surely MS has been around for a while? What was holding you back?

Tomasz Czerner: A good question! Yes, techniques like GC-MS and LC-MS are not completely new and are used extensively in research. But it has only been recently that clinical labs have started to realize how beneficial these techniques can be in routine testing. LC-MS, for example, improves the sensitivity of diagnostic testing, disease screening and therapeutic drug monitoring.

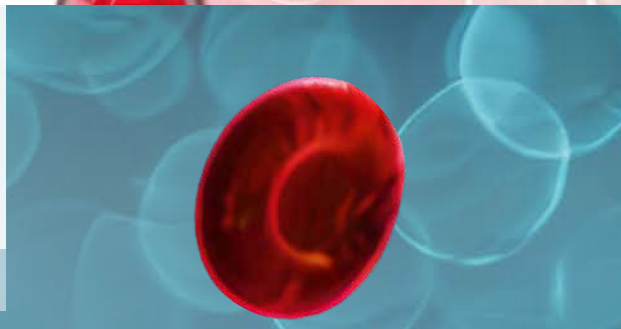
Shimadzu: That sounds important.

Tomasz Czerner: In a hospital, it is very important! And it also gives labs like ours the ability to both reduce costs and to more rapidly provide doctors and patients with much-needed test results.

Shimadzu: That sounds like a win-win situation for everyone! So methods are important, right?

Tomasz Czerner: Indeed they are. Like most scientists, we place great emphasis on achieving the highest quality of certainty in our work and research and want to use the best means available. We rigorously ensure that our procedures are compliant with the latest requirements.

So-called consumables are helpful in that regard. That is why in most tests we use ready-made kits with IVD certificates, preferably IVDR. We generally try to respond to the current needs of our patients and work closely with our doctors to listen to their needs. →



Shimadzu: All of that is really interesting. Can you give me a recent example of your lab at work?

Tomasz Czerner: Sure. We were asked by some of our doctors about the possibility of determining statins in human blood plasma. Statins, by the way, are lipid-lowering agents.

Shimadzu: Tell me more. Are these natural or synthetic drugs? And where do they come from?

Tomasz Czerner: If I remember correctly, the story begins with mevastatin. It was the first substance with properties that lowered cholesterol and LDL lipoprotein and was isolated from the fungus Penicillium citrinum in 1973 by Japanese biochemist Akira Endō. Then, in 1979, Endō patented the first statin: monacolin K obtained from the mold Monascus ruber. Later, studies proved that monacolin K and mevinolin are the same compound: Their current name is lovastatin.

Shimadzu: Do we know the mechanism of action of statins?

Tomasz Czerner: Yes. To sum it up, these drugs are useful in preventing coronary artery disease as well as in inhibiting its development and reducing complications related to atherosclerosis, such as heart attack or stroke. Statins also prevent the recurrence of these complications.

Shimadzu: I believe you are using a new method in testing statins in your laboratory? How did that come about?

Tomasz Czerner: To put it simply, we had a problem and needed a solution. As I said, our doctors – a lot of doctors! – were increasingly asking us to test for the determination of statins in plasma samples. The conventional analyzers that we had did not allow for such determinations, and it was beginning to feel overwhelming. In desperation, we mentioned this to our friends at SHIM-POL, who are the exclusive representatives of Shimadzu in Poland. They sent over an expert to spend the day with us observing and asking questions. A few days later, SHIM-POL made some suggestions for how we could overcome the challenges we faced. I took those ideas back to my colleagues, and we liked what we saw ...

Shimadzu: What did you like?

Tomasz Czerner: We realized that the only truly sensible technique for such difficult analyses is mass spectrometry. As luck would have it, we had had the answer for years, sitting right under our noses! Specifically, we used our ultra-high performance liquid chromatograph Nexera X2, coupled to an LCMS-8050 mass spectrometer with UFMS technology. Using the combined talents of these instruments, we were able to achieve high resolution and selectivity and, above all, high sensitivity in detecting and fully quantifying several statins in plasma samples from our patients. This significantly streamlined the process of diagnosis and treatment of our patients.

Shimadzu: With your new solution, how many statins were you able to test for? Did you also determine their metabolites?

Tomasz Czerner: Together with the experts from SHIM-POL, we were able to determine four statins in plasma and their metabolites. The analysis took less than 10 minutes! We then spent several days on optimization. That was not always easy, but in the end we were more than fully satisfied with the outcome. And we are even discussing how we can shorten the analysis time even further. Because for both our patients and our doctors, time is very valuable!

Shimadzu: Tell me: What are your most important goals for the coming years?

Tomasz Czerner: Time will tell. Our team is developing dynamically and we hope to significantly expand the profile of our research. For instance, we are thinking a lot about the determination of antiepileptic drugs in serum and steroids in plasma. And we naturally intend to deepen our knowledge of MS with the aim of implementing further methods using this advanced technique.

Shimadzu: Do you face any obstacles to achieving your goals?

Tomasz Czerner: Only that we have a huge amount of daily work to do! But we have a solution for that, too. We would like to add another HPLC instrument to our laboratory to increase our capacity – some of our existing instrumentation is simply too slow!

Shimadzu: Any final words of wisdom to offer?

Tomasz Czerner: Only to repeat that the use of mass spectrometry in clinical medicine is a rapidly evolving technique that offers lower (i.e. more precise) detection capabilities as well as excellent identification of compounds in a very short period of time. Altogether, this means that we can do faster and more detailed work, which allows clinicians to make better decisions and to provide quicker treatment regimens for our patients. Shimadzu's promise for the future is that we can use a sample with a single drop of blood to quickly identity hundreds of clinical markers for disease!

Shimadzu: Thank you very much for your time and for your insights from the front lines of healthcare.

Tomasz Czerner: It was a pleasure!

The long tail of innovation

We often think about innovation as a singular moment: something new or better or faster is suddenly created, and that's the important part. In reality, innovation is only the beginning. It needs to be used and, through that process, its benefits fully understood. Often, the potential applications of an innovation extend well beyond the original rationale or purpose of its conception.

In the case of mass spectrometry – already a go-to method for research labs around the world – the ability of people like the dedicated staff at USK's Department of Laboratory Diagnostics to adapt, utilize and continue to probe the potential of this innovative tool is impressive. And to do it in direct service to medical patients and practitioners is inspiring. Shimadzu is proud to play a role in their vital work by providing tools and expertise that allow them to follow their curiosity wherever it may lead.

Figure 2: Tomasz Czerner in the lab

Note

For more information and references, please refer to the digital version of this edition.

Giving the future a familiar taste

The science behind making plant-based meats (PBMs) as good as the original

Dr. Jan Peter Mayser, Shimadzu Europa GmbH

New products often only gain acceptance by emphasizing how much they resemble older products. This applies in particular to conceptually innovative or disruptive products. A classic example is the automobile, which was originally called the "horseless carriage" to make it seem familiar – even though it was actually a revolutionary new invention that would change the world forever.

One of today's innovative new products are plant-based alternatives to meat. The potential market is huge. So companies are investing heavily in giving these new foods the look, feel, smell, taste and texture of real meat as well as in meeting various other regulatory and consumer demands. How exactly are they doing all that?

Plant-based meats (PBMs) are becoming increasingly popular. More and more consumers are opting to go meat-free, whether out of concerns for animal welfare, personal health, their carbon footprint or in support of more sustainable agricultural practices (Figure 1). Or perhaps because of all of the above: By reducing or eliminating meat from their diets, individuals can decrease their risk of chronic heart disease and cancer, help mitigate deforestation and greenhouse gas emissions associated with the livestock industry and align their values with a more compassionate approach to food consumption. ⟶

Environmental footprints of dairy and plant-based milks

Impacts are measured per liter of milk. These are based on a meta-analysis of food system impact studies across the supply chain which includes land use change, on-farm production, processing, transport and packaging.

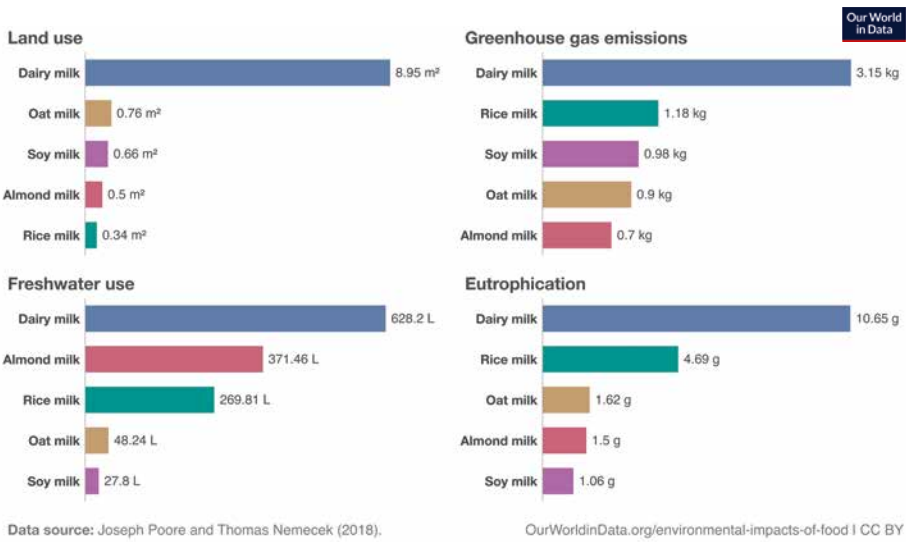


Figure 1: Environmental impact of different protein sources

They can also help ensure global food security. Not only is the world's population rising, but numerous climaterelated and other factors are expected to affect how well we will be able to feed one another in the years ahead. To put it another way: Expanding the development of plant-based meats satisfies many different appetites.

Gaining acceptance through analysis

Despite the many reasons why a consumer might desire to buy a plant-based meat substitute, whether they actually do so will depend on several factors. For instance, further increasing the popularity of plant-based alternatives requires that these foods better imitate their traditional meat counterparts. At the same time, plant-based foods must be reliably tested in areas ranging from protein and fat content to the presence of pesticides, herbicides and allergens.

Sensory testing: The human touch

One of the ways that manufacturers of PBMs use to ensure that their products replicate the end-user experience of real meat is sensory testing. Human sensory evaluation involves the testing of a product's sensory characteristics by trained panelists. For plant-based meat alternatives, sensory testing is important, as it provides information on how the product will be perceived by consumers. By obtaining feedback from a panel of trained sensory evaluators, manufacturers can make adjustments to improve the user experience of their PBMs.

Sensory testing by expert instruments

In addition to testing by human experts, sensory testing is also being carried out by precision lab instruments. Figure 2 shows an example of sensory testing by instrumentation in which a plant-based meat is compared with an organic beef sample. A gas chromatograph is obtained for each of the samples and compared. The gas chromatograph run shows the more volatile

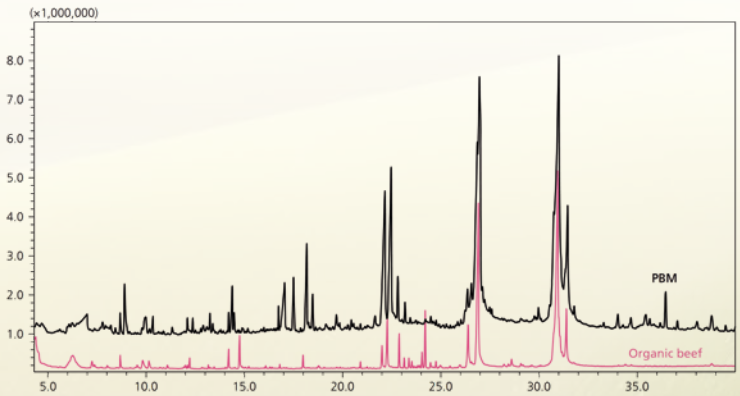


Figure 2: Overlaid representative chromatograms for PBM (black) and organic beef (pink) at 10-min extractions with the SPME Arrow

and semi-volatile compounds within the food sample. The comparison of the chromatograms shows that there is already a large overlap in odor-active compounds between the samples. This suggests that they have a similar taste profile, while clear differences can still be seen. This analysis and sample preparation was conducted on a Shimadzu GCMS-TQ8050 NX in combination with an AOC-6000 sample preparation station (Figure 5).

Allergen testing: Safety, compliance and quality

While plant-based foods are often thought of as inherently safer than animal products, the reality is that many common allergens, such as nuts, soy and wheat, can be present in these products. Therefore, it is essential that food manufacturers conduct thorough allergen testing to ensure the safety of consumers with food allergies.

Cross-contamination: One of the primary reasons why allergen testing is crucial for plant-based meat alternatives is the risk of cross-contamination during the manufacturing process. Many plant-based meat alternatives are produced in facilities that also process allergenic ingredients, increasing the risk of accidental contamination.

Novel ingredients: The use of novel ingredients in plant-based meat alternatives, such as pea protein or seitan, may also pose a risk for individuals with allergies to these ingredients. While they are generally considered safe for the majority of consumers, individuals with specific allergies must be cautious and rely on accurate allergen testing to determine if a product is safe for consumption.

Regulatory compliance: In addition to the safety concerns for consumers with food allergies, proper allergen testing is also essential for regulatory compliance. Failure to accurately test for allergens and disclose this information can result in serious legal consequences for food companies.

Quality control: Allergen testing can also help food manufacturers optimize their production processes and prevent costly recalls. By implementing robust allergen testing procedures, companies can identify and eliminate potential allergen contaminants early in the production process, reducing the risk of contaminated products reaching consumers.

Cross-reactivity: Cross-reactivity occurs when proteins in one type of food trigger an allergic reaction in individuals who are allergic to different foods. By conducting comprehensive allergen testing, food manufacturers can identify potential cross-reactive allergens and take appropriate steps to address and label these in their products. →

A new, time-saving method of allergen testing

Allergen testing for PBMs can be challenging due to their complex nature. Plant-based meat alternatives often contain a wide range of ingredients, some of which may have been processed in different ways or come from different sources.

A new method – recently developed by Shimadzu – compensates for this complexity by providing a time-saving, holistic analytical solution. Figures 3 and 4 detail how LC-MS/MS was used to check for 13 different food allergens in a single run. The method is capable of identifying the eight allergens FALCPA recommends as well as the expanded list recommended by EFSA. A total of 245 transitions were set to monitor 50 peptides selected from 21 proteins. Allergens were found in both raw foods and cooked foods, proving that the new method can identify allergens from different food matrices.

This ability to check for multiple allergens within a single run is particularly important for PBM producers. Producers need to be able to quickly and easily check for multiple allergens from multiple sources, because when developing recipes for these alternative meats, they need to combine ingredients from many different bases to achieve the desired results in taste and in smell. If something in the mix is not working right, they need to know quickly so they can adjust the recipe.

Analytical instrumentation is also used to test for composition, nutritional content and overall quality. Instrumental analysis reveals important information about the product, such as its protein content, fat content and the presence of any harmful substances. Manufacturers use these tests to ensure that their PBMs meet the desired nutritional profile and are safe for consumption. By combining these tests with others, such as sensory testing, manufacturers can look forward to a very appetizing future for their plant-based meats.

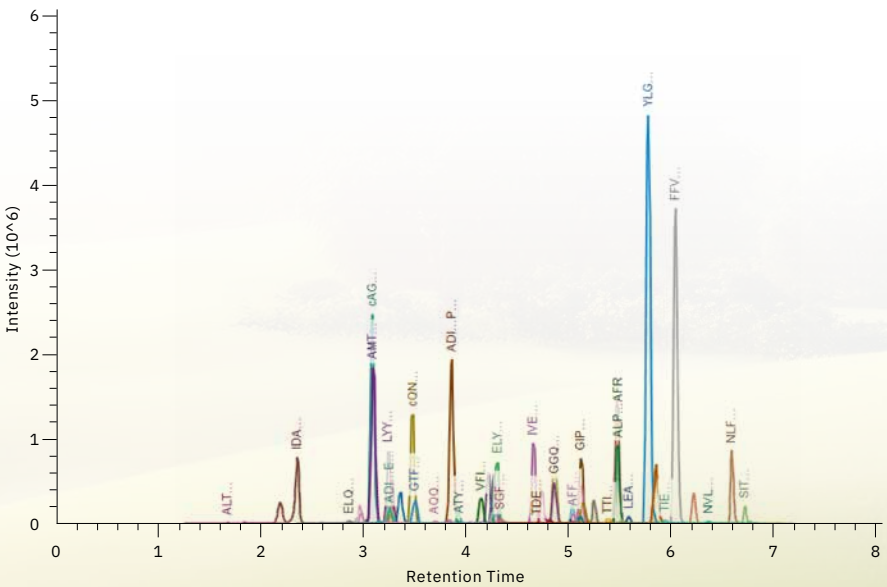


Figure 3: Chromatogram of a mixture of milk, eggs, cod, shrimp, lobster, almonds, Brazil nuts, cashew nuts, hazelnuts, walnuts, peanuts, wheat and soybeans

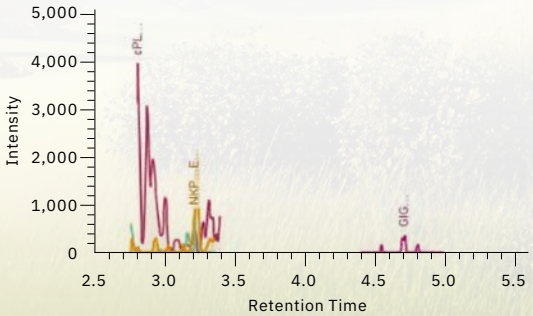


Figure 4: Allergen-containing soybeans in frozen pasta

Making progress safe – and palatable

Sensory and allergen testing are just two of the many strategies being used to help expand the acceptance of plant-based alternative foods. Greater acceptance offers benefits ranging from the personal to the global level, as well as financial benefits for the companies able to meet the increasing consumer demand. Shimadzu instruments deliver the capability to fast and efficiently perform most of the necessary tests for this growing industry. We know there is a hunger and no time to waste.

Planet Earth – and humanity – will face a number of challenges in the coming years. Many say that we are already facing them today. However you look at it, the solution is simple: science. Using the best science and the best technological tools, together we can rise to meet the challenges.

Figure 5: Sensory tests were conducted on a GCMS-TQ8050 NX + AOC-6000

Note
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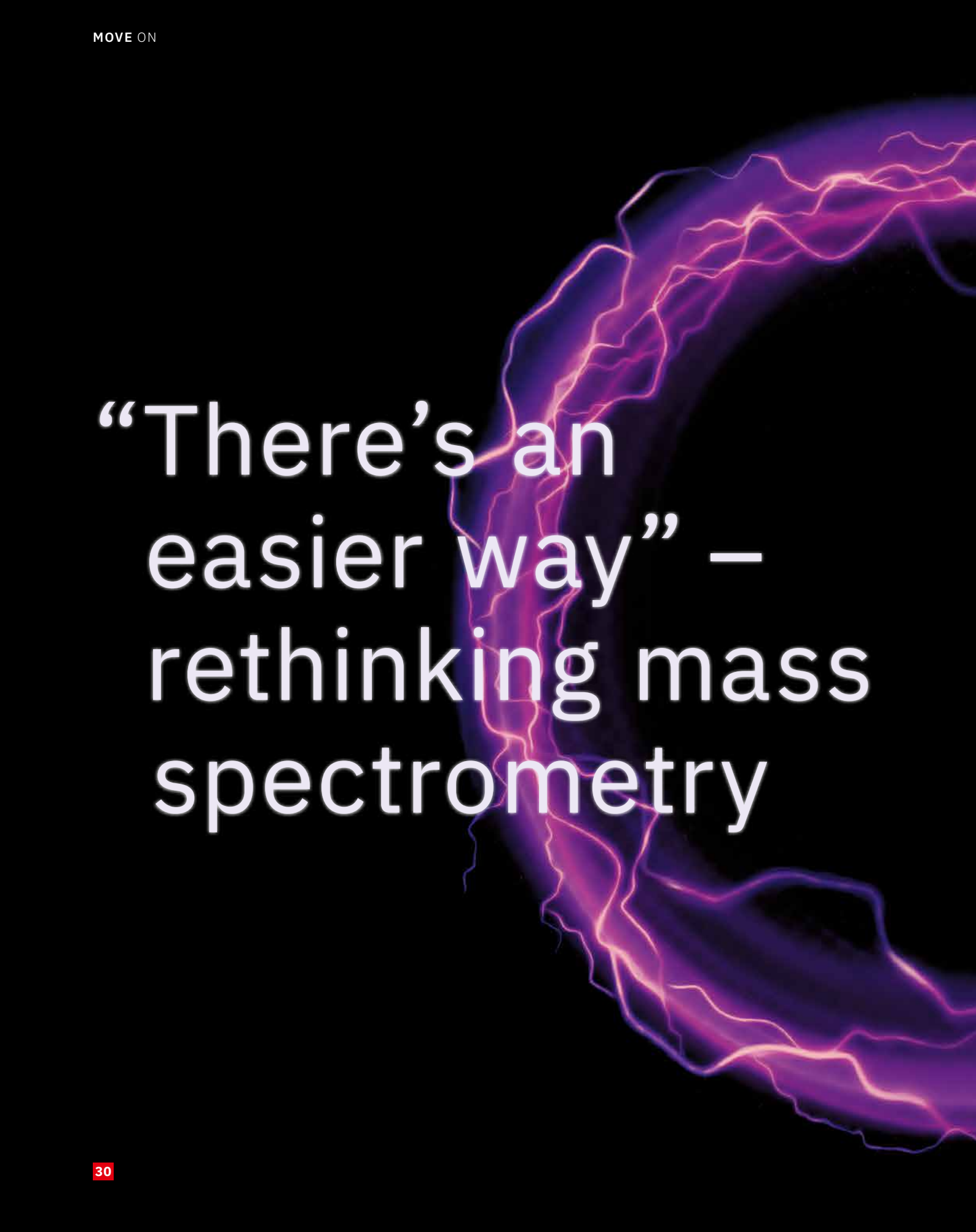


“There’s an easier way” – rethinking mass spectrometry

Innovative ion source overcomes limits in analysis

Petra Romero, Plasmion GmbH

Jan-C. Wolf, founder of Plasmion GmbH, was driven by the idea of making mass spectrometry more accessible, simpler and more efficient as early as his university days. He has made huge strides in this area with the development of the SICRIT® ion source: This universal innovation makes mass spectrometry more user-friendly, more powerful and more sustainable.

The vision of more accessible mass spectrometry

Even back when he was studying at the TU Munich, Jan-C. Wolf was already heavily involved in developing instruments and methods, particularly mass spectrometers. He quickly realized that the specific dependencies between separation and MS-based detection, i.e. the historically driven technical delimitation between GC-MS and LC-MS, result in a complexity that makes laboratory processes laborious and time-consuming. Wolf was convinced: “There must be an easier way!” This conviction stayed with him into his postdoctoral years at ETH Zurich. There he worked with Prof. Renato Zenobi on developing what’s called an ambient ion source. The aim was to create a technology that allows volatile organic compounds (e.g. fragrances, flavorings or chemical warfare agents) to be analyzed on-site.

With the SICRIT® (Soft Ionization by Chemical Reaction in Transfer) technology, Wolf has developed an almost universal ion source for mass spectrometry. The business idea for Plasmion was born.

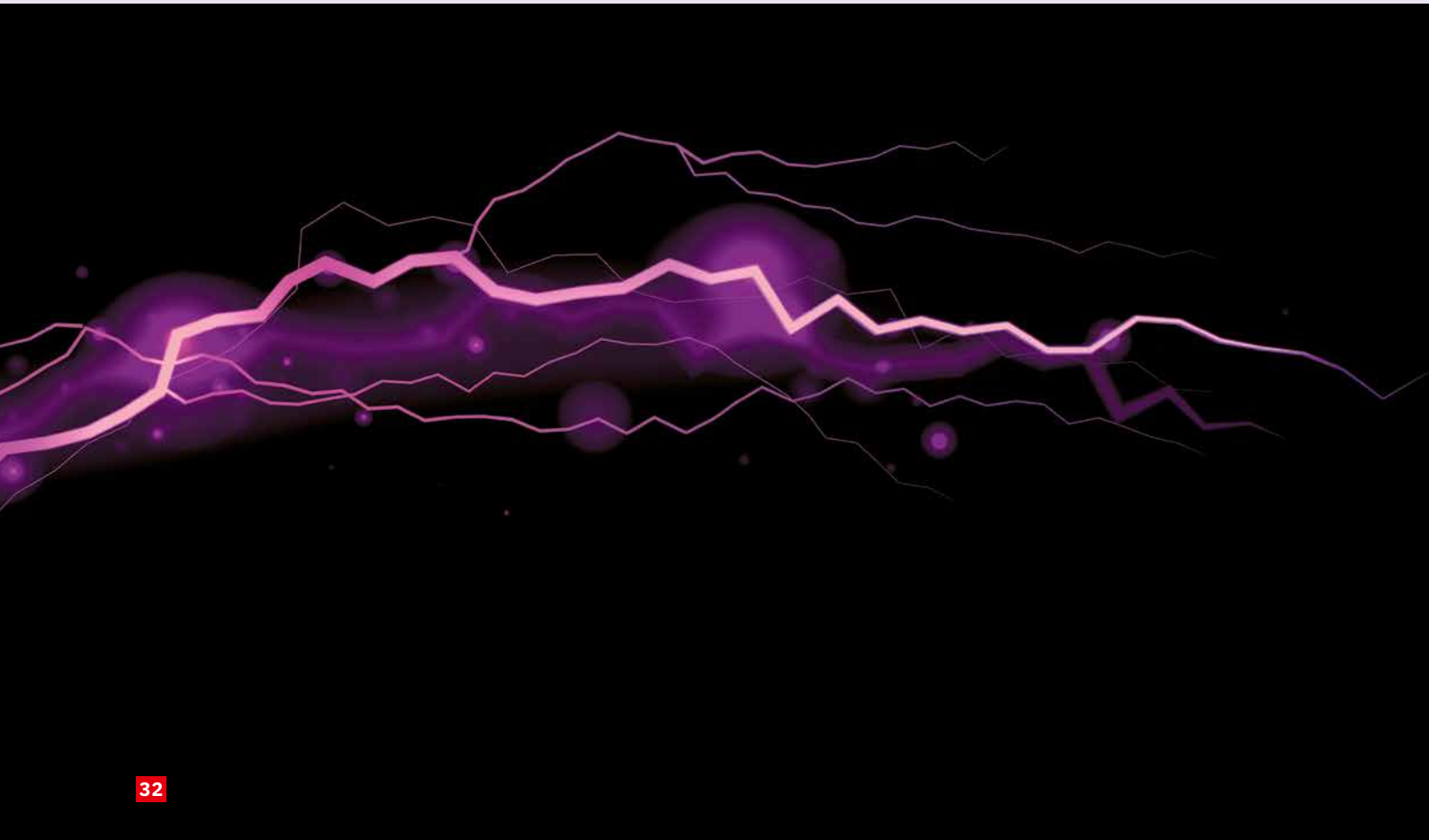
How the SICRIT® ion source works

The principle of the SICRIT® ion source is very simple: The source is mounted directly on the atmospheric pressure inlet of the (LC) mass spectrometer in just a few simple steps (plug & play). During mounting, the existing source is removed, a special adapter is attached to the inlet of the mass spectrometer and the source is simply “clicked on” with a ball lock, creating a gas-tight connection between the source and the device’s vacuum. Volatile or vaporized substances are drawn in by the vacuum and ionized on their way into the system by means of a cold plasma ring in the source. This form of ionization is efficient, comparably soft as electrospray ionization, but covers almost the entire chemical polarity range (from amino acids to alkanes), since SICRIT® can ionize both non-polar (typical GC) and polar (typical LC) analytes thanks to its unique ionization mechanism. →

However, this technology has one limitation: What cannot be vaporized or transferred into the gas phase cannot be measured. This includes very large molecules such as proteins. Another aspect that hinders the analysis of large molecules is the fact that this form of ionization does not generate multiple charges on the analyte: In contrast, in electrospray ionization, the standard ionization method for large molecules, several charges are formed and "attached" to the analyte via atomization. This reduces the analyte with the exemplary mass of 100,000 *m/z* and 20 attached charges to the *m/z* value of 5,000, thereby bringing it within the detectable mass range of the mass spectrometer.

Numerous combination options

A major advantage of the SICRIT® ion source is its versatility. In addition to direct MS measurement, various modules enable all common chromatographic methods, such as gas chromatography (GC), liquid chromatography (LC) and supercritical fluid chromatography (SFC), to be combined with one (LC-)MS device.



Certain analyses that previously had to be carried out using different chromatographic methods and dedicated MS instruments can now be performed on a single LC-MS device, which to some extent, removes the traditional separation between LC-MS and GC-MS markets.

Users benefit from high-resolution GC-MS – combining an LCMS-9030 Q-TOF with a GC (Figure 2), for example, creates one of the most powerful analysis systems on the market: A system that brings together the strengths of a GC (non-polar analytes and high separation performance) with those of an LC-MS (higher resolution, polar analytes). In this setup, the SICRIT® ion source acts as a link that connects the two analysis methods via the ionization range (non-polar/polar) and softness. This system has the potential to rethink mass spectrometry in terms of making chemical analyses easier and more sustainable with better results. →

Figure 2: Shimadzu GC with SICRIT® plug & play coupling of a Shimadzu LCMS-9030 Q-TOF

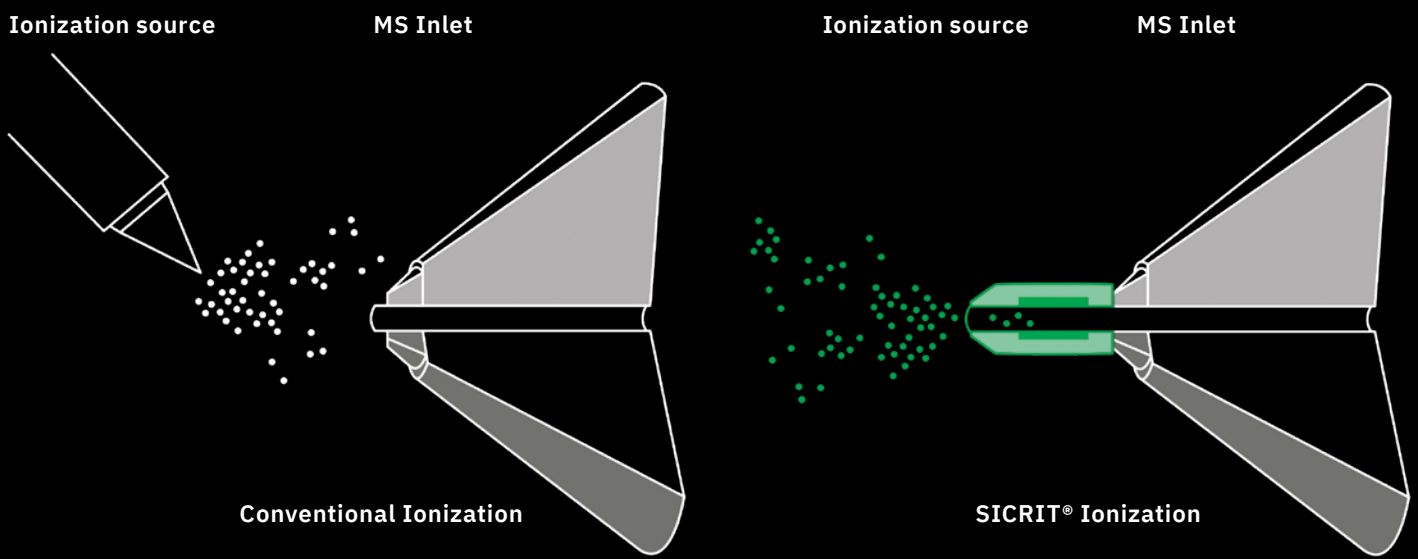


Figure 1: How the SICRIT® ion source works

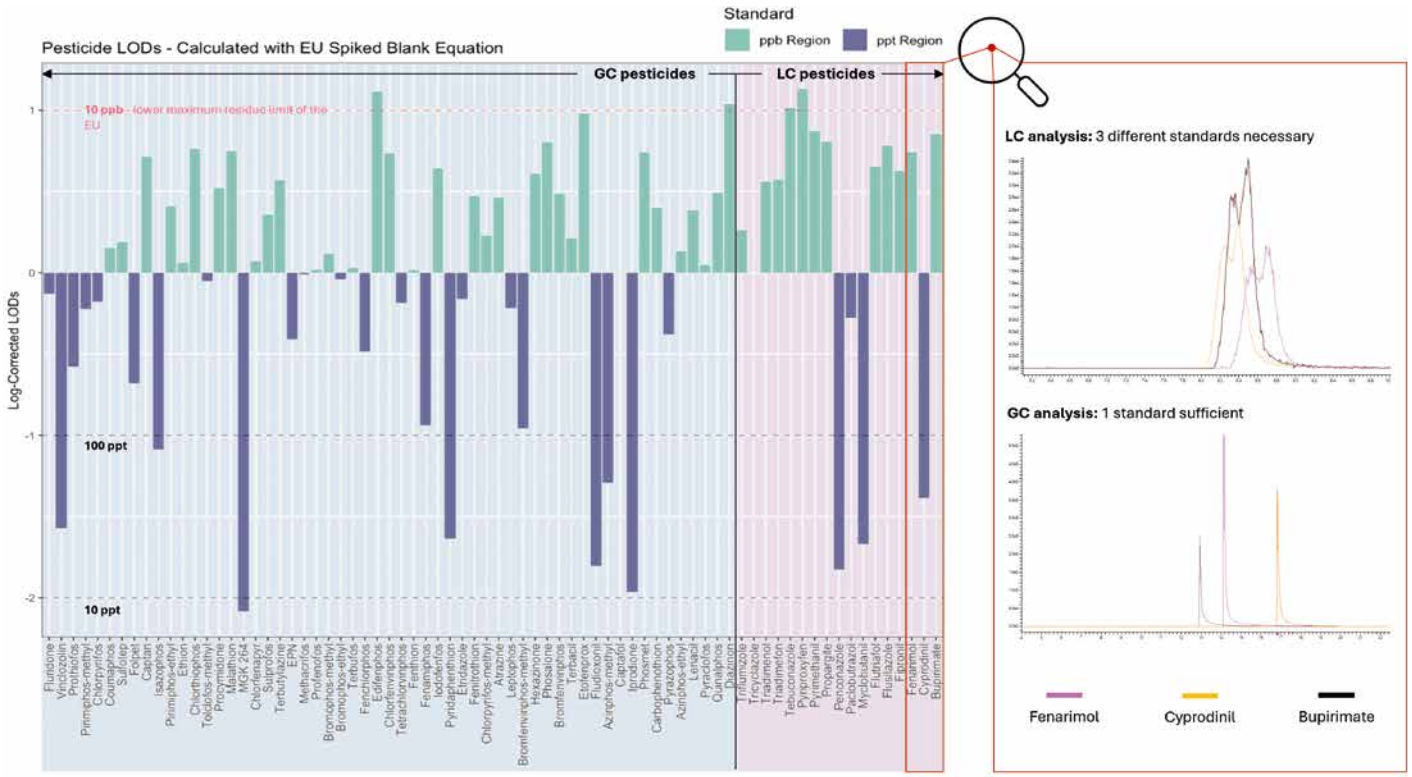
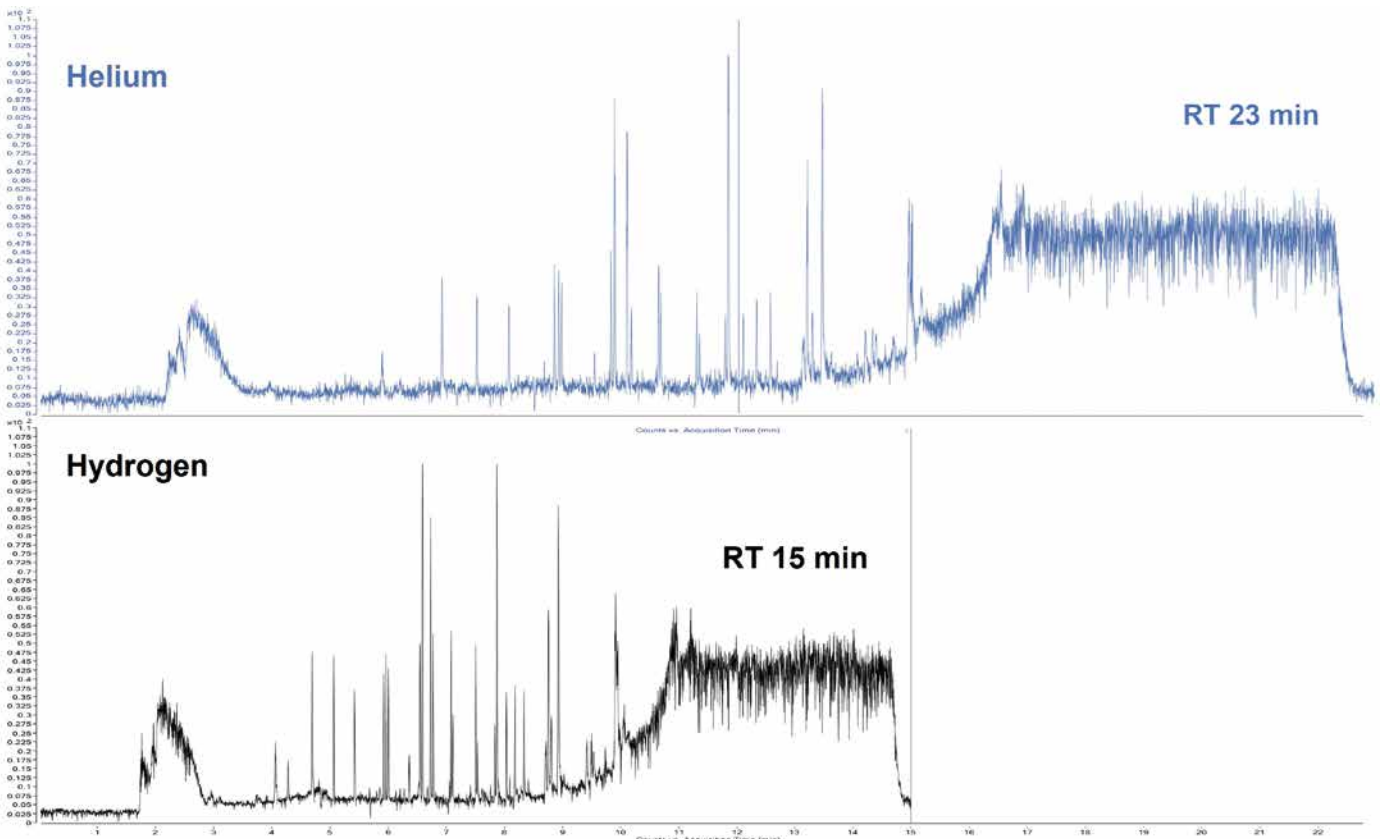


Figure 3: LODs of a GC-SICRIT®-Q-TOF analysis of Restek, pesticide standards #1, #5 and #8 (left), calculated according to EU guidelines. Comparison of LC and GC cycles for three exemplary LC pesticides, measured using LC-SICRIT®-Q-TOF (top right) and GC-SICRIT®-Q-TOF (bottom right).



Overcoming limits for easier analysis

An obvious example of this is pesticide analysis, as the complexity of their chemical composition means pesticides have to be analyzed using both GC-MS and LC-MS. Therefore, laboratories need to employ several devices and workflows for an overall picture. At present, the Plasmion team is leveraging the unique ionization range of SICRIT® to develop a comprehensive GC-based pesticide method that reduces this effort in the future. The most important prerequisite for such a consolidated method is that it must be able to comply with the specified limit values (LODs). For this purpose, 74 LC-compatible pesticides from three standards (Restek GmbH) – organophosphorus compounds, organonitrogen compounds and hydramethylnon – were analyzed in a first set using GC-SICRIT®-Q-TOF (Shimadzu LCMS-9030) (Figure 3). The results show that the GC-SICRIT® method enables reliable detection of pesticides that are highly problematic in LC-MS, such as Folpet, while adhering to the specified LODs of the European Union.

Improved sustainability thanks to combined benefits

SICRIT® is based on mass spectrometers with atmospheric pressure inlet (AP-MS), which have more powerful pumps compared to conventional GC-MS systems. This allows considerably higher flow rates (up to 200 mL/min) of hydrogen to be used in GC coupling. As with the development of UHPLC, this now allows analysis times to be significantly reduced. Switching from helium to hydrogen alone already provides a speed advantage of 40 % (Figure 4). By using higher flow rates, the analysis time can be reduced by more than 80 %. The hydrogen can be produced directly from water and electricity using a generator, making it much more sustainable than helium, which is now a scarce resource.

Out-of-the-box thinking for better results

Coupling GC with LC-MS also brings advantages in the areas of pharmaceutical quality control. The sensitive ionization, together with the excellent separation performance of gas chromatography, enables the direct identification of impurities in pharmaceuticals as well as ultra-trace detection of carcinogenic compounds such as nitrosamines. A respective application using an LCMS-9030 SICRIT®-GC coupling has shown to be one of the most sensitive nitrosamine applications on Shimadzu LC-MS instruments. The unusual coupling makes the results difficult to compare with existing analyses. Comparing them to a corresponding analysis published by Shimadzu, which was carried out on the same device but with an APCI source (the standard ionization method for nitrosamines) and an LC, this unusual coupling via the SICRIT® source increases sensitivity up to a factor of 40, though.

Efficiency meets sustainability – a paradigm shift in the laboratory world

The efficient use of our resources and the application of more climate-friendly analytics are challenges that every laboratory, from quality assurance to research and routine analysis, will have to face in the future. The SICRIT® ion source offers the opportunity to rethink and redesign established processes - not only to improve analytical efficiency but also to enhance sustainability by reducing analysis times, savings on equipment, and replacing scarce resources such as helium. This represents a real benefit not only for laboratories but also for the environment and ultimately for us all.

In the spirit of the inventor Jan-C. Wolf:
“There’s an easier way.” – and it’s actually better.

◄ Figure 4: GC-SICRIT®-MS chromatogram of an aroma standard with direct switch from helium to hydrogen

Note
For more information and references, please refer to the digital version of this edition.

The perfect taste where sweet meets sour

HPLC methods for identifying and quantifying sugars and organic acids in tonic water and gin

Dr. Brigitte Bollig, Shimadzu Europa GmbH

This article provides a detailed description of the application of HPLC analysis for determining sugars and organic acids – in tonic water especially. By analyzing these components in detail, insight into the factors that influence the taste and quality of a gin and tonic can be gained.

The gin and tonic: a refreshing beverage with a history as long as the glass it's served in that's hugely popular across the world. Sales of tonic water, which is also enjoyed neat, are just as high: One market analysis company estimated the global market at USD 1.29 billion in 2024, and this is anticipated to rise to USD 1.85 billion within five years, with the largest growth expected in the Asia-Pacific region.

Product developers at beverage companies are always coming up with new flavors in the hope that they will appeal to consumers' tastes: For example, the market analysts highlight the varieties of "Raspberry Rhubarb", "Wild Elderflower" and "Damask Rose", some of which are made with dandelion instead of quinine.

Once the tonic water of choice is placed in the shopping cart and later in the refrigerator, then it's traditionally mixed with gin: Gin and tonic – the combination of gin, a distilled alcoholic beverage mainly characterized by its juniper note, and tonic water, a carbonated drink with a bitter edge – owes its unique taste to a variety of chemical components. Sugar and organic acids are some of these chemical components that play a significant role since they contribute to the taste profile and sensory experience of the beverage to a large extent. This text shows analysis methods for certain components of tonic water and gin samples, important for manufacturers, test laboratories and consumer protection companies. Precise measuring procedures are necessary to ensure that consumers get a tasty and safe beverage. →

Determination of sugars

Gin and tonic can contain different types of sugar such as glucose, fructose and sucrose, each of which has varying levels of sweetness and sensory properties. These sugars not only affect the taste but also the texture and the mouthfeel of the drink. The exact composition and concentration of the sugars can be precisely determined using analytical methods such as high-performance liquid chromatography (HPLC).

In nine of the ten tonic water samples that were tested, sucrose was declared as the sweetener. Only one tonic water gets its sweetness from a combination of fructose and stevia.

Sucrose, also known as granulated sugar, is a disaccharide made up of equal parts of the monosaccharides fructose and glucose. As a result of the low pH value in the tonic water, the sucrose is hydrolyzed into the monosaccharides. That's why only the monosaccharides fructose and glucose are determined for quantifying sugars in tonic water, the sum of which giving the sucrose content.

The chromatographic determination of sugars presents two challenges. On the one hand, saccharides cannot be separated using conventional reversed-phase HPLC due to their high polarity, and on the other hand, sugars do not have any chromophoric groups, which is why it's not possible to detect them using UV-Vis.

However, a good alternative to chromatographic reversed-phase separation of sugars is HILIC (hydrophilic interaction chromatography). A polar column with typical reversed-phase solvents such as acetonitrile and water is used for this. The elution strength of the solvents is reversed compared to traditional reversed-phase chromatography. In HILIC, water is the stronger solvent for the elution of substances from the column compared to acetonitrile. The column material mostly consists of modified polymers, and the column material used here is a polymer with functional amino groups.

The RID-20A refractive index detector from Shimadzu is used as an alternative to a UV-Vis detector. This works based on the change in the refractive index between the pure liquid and the analyte. The exact analysis conditions are laid out in Table 1.

Standard and sample preparation

To quantify fructose and glucose, solutions in the concentration range 0.25–1.25 mg/mL and 0.25–1.0 mg/mL respectively were prepared in the mobile phase (Figure 1). The sample solutions were diluted with the mobile phase at a ratio of 1:50.

Results of the sugar determination

The calibration curves of the sugars that were tested, fructose and glucose, are very good with a regression value of $R^2 > 0.999$.

In the nine tonic waters that were declared as containing sucrose, this was also found in the stated quantity. The results all turned out very similar and range between 7.1 and 8.8 g of sucrose per 100 mL tonic water (Figure 2 and Table 2). The tonic water that was sweetened only with fructose contains the same amount of fructose as the other nine tonic waters. These were all sweetened with sucrose, which means they also contain glucose. The lack of sweetness from not using glucose in that tonic water was compensated for by adding stevia instead (content according to LC-MS analysis: 0.1 mg/mL).

Neither fructose nor glucose could be detected in the gin samples.

Organic acids

The organic acids usually found in gin and tonic are citric acid, malic acid and ascorbic acid. These acids are not only important when it comes to the taste but also play a role in the stability and shelf life of the drink. HPLC analysis makes it possible to precisely determine the concentrations of these acids in samples of tonic water and non-alcoholic gins.

Citric acid was found in all ten tonic water samples tested. This is an organic tricarboxylic acid that belongs to the group of fruit acids. Citric acid fulfills several functions in tonic water, including changing the taste and lowering the pH value, which then reduces the growth of microorganisms. →

System	Nexera-i
Column	Shodex HILICpak VG-50 4E (4.6 mm x 250 mm)
Guard column	Shodex HILICpak VG-50G 4A (4.6 mm x 10 mm)
Flow rate	1 mL/min
Mobile phase	Water/Acetonitrile 20/80
Column temperature	40 °C
Injection volume	5 µL
Detection	RID-20A (Refractive Index Detection)
Run time	12 minutes

Table 1: Analytical conditions for the determination of sugars

Tonic water	Glucose [g/100 mL]	Fructose [g/100 mL]	Sucrose (calculated) [g/100 mL]
1	3.7	4.5	8.2
2	3.3	3.9	7.1
3	3.4	4.1	7.4
4	–	4.3	–
5	3.2	3.8	7.1
6	4.1	4.8	8.8
7	3.3	4.0	7.3
8	4.0	4.8	8.7
9	3.9	4.7	8.6
10	3.9	4.8	8.7

Table 2: Results of the sugar determination in ten tonic water samples

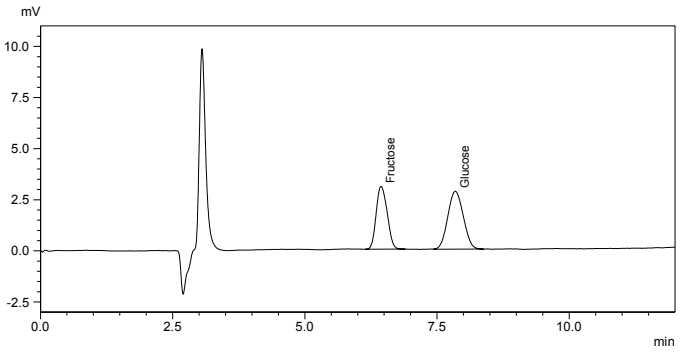


Figure 1: Chromatogram of a reference standard for sugar determination

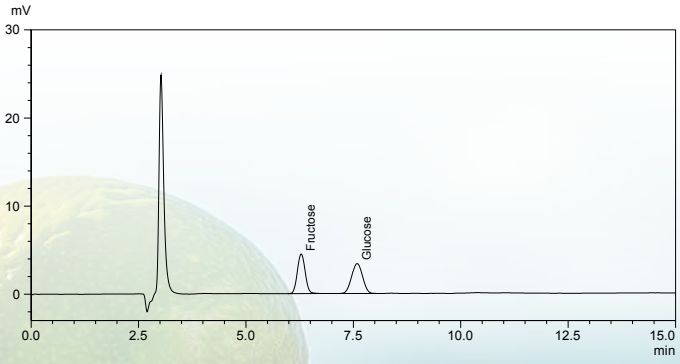


Figure 2: Chromatogram of a tonic water sample for sugar determination

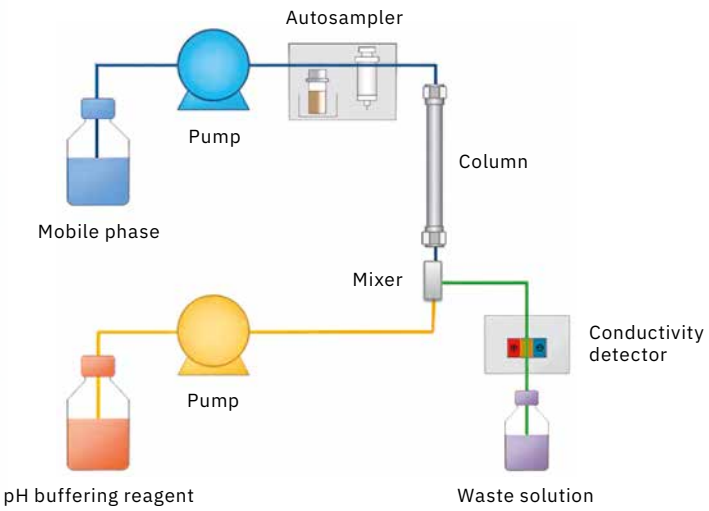


Figure 3: Flow diagram Nexera analysis system for organic acids

In two tonic waters, ascorbic acid and malic acid were declared in addition to citric acid. Ascorbic acid is used as an antioxidant in food.

Organic acids are highly hydrophilic compounds that are difficult to determine with the C18 columns often used in HPLC analysis. The disadvantage of organic acids in UV detection is that they only absorb in the non-selective low wavelength range, which can lead to contamination caused by impurities and the absorption of solvents. That's why ingenuity is needed both when it comes to choosing a solvent and a column and for the detection method in order to perform analyses with high levels of sensitivity and selectivity.

The Nexera organic acids analysis system uses "post-column pH buffering with electrical conductivity detection". Organic acids are separated by ion exclusion chromatography with an acidic solvent and then mixed with a pH-buffering reagent to increase detection sensitivity (Figure 3). The system is optimized for the analysis of organic acids, and since the retention times are very stable, it's also possible to provide a qualitative estimation of the organic acids contained in unknown samples.

Standard and sample preparation

As the concentration ranges of the organic acids were not known, screening was carried out with all gins and tonic waters. The samples were injected without dilution for this. The acids and concentrations identified in the screening were then used to create calibration curves for quantification (Table 3).

Results of the determination of organic acids

Calibration curves were created for citric acid and malic acid in the range of 1.0–5.0 mg/mL. The calibration curves of the acids that were tested, citric acid and malic acid, are very good with a regression value of $R^2 > 0.999$. According to the declaration, all ten tonic water samples contained citric acid (Figure 4), the content of which amounted to between 3.3 and 5.0 mg/mL (Table 4). Ascorbic acid could not be detected in any sample, despite being declared in one sample. Acetic acid was detected instead. Since ascorbic acid is used as an antioxidant, it can be assumed that the ascorbic acid has degraded through oxidation.

In the gin samples, the only significant results were found for the non-alcoholic gin varieties. The acids contained here are citric, acetic, tartaric and phosphoric acid (Table 5).

Suitable for identification and quantification

The analyses have revealed which specific sugars and acids are present. The only surprise was one of the samples of tonic water: It was supposed to contain ascorbic acid, but this could not be detected. The methods described here – such as HILIC (hydrophilic interaction chromatography) and "post-column pH buffering with electrical conductivity detection" – are obviously suitable for identifying and quantifying sugars and organic acids in beverages.

In the next issue: Analysis of gin samples

The third and final part of the series on the ingredients in a gin and tonic covers other options for analyzing gin and tackles the question of which gin goes best with which tonic water.

Note

For more information and references, please refer to the digital version of this edition.

System	Nexera Organic Acid Analysis System
Column	2 x Shim-pack SCR-102H (300 mm × 8.0 mm I.D., 7 µm)
Guard column	Shim-pack SCR-102H (50 mm × 6.0 mm I.D.)
Flow rate	0.8 mL/min
Mobile phase	5 mmol/L p-toluene sulfonic acid
pH buffer reagent	5 mmol/L p-toluene sulfonic acid 20 mmol/L bis-tris 1 mmol/L EDTA
Column temperature	40 °C
Injection volume	10 µL
Detection	CDD (Conductivity Detection)

Table 3: Analytical conditions for the determination of organic acids

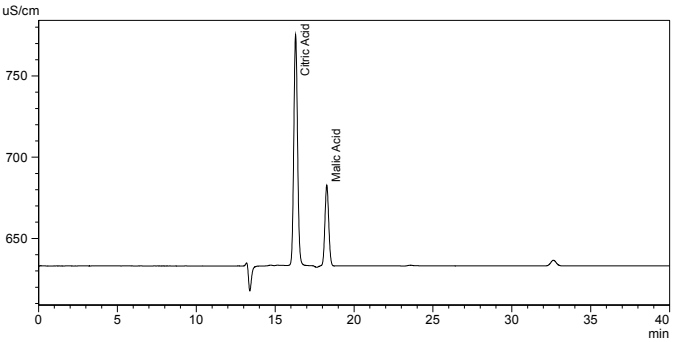


Figure 4: Chromatogram of a tonic water sample for the determination of organic acids

Tonic water	Citric acid [mg/mL]	Ascorbic acid [mg/mL]	Malic acid [mg/mL]	Acetic acid [mg/mL]
1	3.9	declared but not found	–	found but not declared, approx. 0.1 mg/mL
2	3.9	–	–	–
3	3.8	–	–	–
4	5.0	–	–	–
5	3.3	–	1.0	–
6	4.4	–	–	–
7	3.9	–	–	–
8	4.2	–	–	–
9	3.9	–	–	–
10	3.9	–	–	–

Table 4: Results of the determination of organic acids in ten tonic water samples

Alcohol-free gin	Citric acid [mg/mL]	Acetic acid [mg/mL]	Tartaric acid [mg/mL]	Phosphoric acid [mg/mL]
1	0.13	0.01	0.88	–
2	1.81	0.97	–	–
3	0.13	0.01	0.37	0.32

Table 5: Results of the determination of organic acids in three alcohol-free gins

Discovered quickly: Traces of heavy metals in raw plant materials

Robust and efficient – better consumer safety thanks to the ICP-OES and ICP-MS

Nico Gilles, Shimadzu Deutschland

Some are important, some are toxic: Heavy metals are a natural part of the earth's crust and also accumulate in plants through the absorption of water and nutrients. As a result, they can also end up in food, pharmaceuticals, cosmetics and other plant-based products. That's why continuously monitoring raw plant materials is extremely important in order to prevent contamination and damage to health caused by toxic heavy metals. Both the ICP-OES and ICP-MS are fast, robust techniques.

Raw plant materials have always been the foundation of many different products, and "going plant-based" is in trend at the moment. Especially when it comes to gentle cosmetics or health products, consumers are turning back to the power of nature more and more. Plant-based products convey the idea of natural care and purity. However, the natural ingredients can literally have these heavy metals "in them", as they accumulate in plants through the absorption of water and nutrients and eventually enter the human body. While some metals such as manganese and iron are essential for us as trace elements, others – such as cadmium or mercury – are toxic and can lead to long-term damage if ingested on a regular basis.

Heavy metals are everywhere. They occur in the soil and enter the environment through natural processes such as weathering, but human influences play a role here too. Usually, when heavy metals occur naturally in fields and bodies of water, the amount is so low that they pose no danger.

It is precisely the man-made deposits of heavy metals that lead to harmful contamination. They can enter the soil in various ways. For example, centuries-old mining and metallurgical waste, i.e. slag or ash, can still cause problems as contaminated sites. Since heavy metal pollution does not break down naturally, even this waste – despite being buried for hundreds of years – is just as dangerous today as it ever was. ⟶

Figure 1: The ICPE-9820 from Shimadzu

The use of sewage sludge as a fertilizer can also lead to contamination – chromium is one example here. There are legal regulations governing the use of sewage sludge as a fertilizer with regard to its composition and the maximum quantity that may be applied. However, if this type of fertilizer is continually used, then it can accumulate in the soil and become a long-term source of contamination.

Contamination with toxic heavy metals, even in small traces, can have dangerous effects. That's why raw plant materials must undergo heavy metal analysis before being processed further. This places a variety of demands on laboratories and the respective measuring instruments, since the limit values are very low. The ICP-OES and ICP-MS techniques are perfect for this.

The ICP-OES, the all-rounder

Inductively coupled plasma optical emission spectrometry (ICP-OES) is a widely used method in element analysis and is primarily set apart by its speed and robustness. Up to 60 elements can be analyzed at the same time, covering a wide range from the ppb to the % range. This makes the ICP-OES technique one of the most widely used measurement techniques in the field of heavy metal analysis. By automatically switching between axial and radial measuring modes, macroelements such as calcium and magnesium can be measured together with trace elements such as cadmium in a single measuring cycle.

On top of this, the ICP-OES has the huge advantage of always being able to measure the entire spectrum, meaning qualitative measurements can also be carried out.

Raw plant materials must first be converted into a liquid measuring solution for analysis. The easiest way to do this is by microwave digestion, where 0.5 g of dried sample is mixed with 7.5 mL nitric acid (HNO_3) and 0.5 mL hydrochloric acid (HCl). Then the solution is topped up to 25 mL.

As an example, six plants whose raw materials are used in naturopathy and in the food and cosmetics industry were analyzed for their trace element (heavy metal) content. As well as this, the macro elements were also determined in one example, the ICPE-9820 from Shimadzu being used (Figure 1).

On the one hand, quantitative measurements of trace elements were taken using the calibration line method and, on the other, qualitative measurements for various macroelements such as magnesium, potassium and phosphorus. These are also particularly interesting to know about in relation to raw plant materials, for example as a quality feature in the food supplement and pharmaceutical industries.

The fact that both can be combined in a single measuring process is a huge advantage here. The complete spectrum from 167 nm to 800 nm is always recorded, so that qualitative evaluations can be made later.

The quantitative analysis of arsenic, cadmium, chromium, copper and lead showed that the samples of raw plant materials that were tested did not exceed the maximum levels recommended by the World Health Organization (WHO) (Table 1). In the EU, there are different limit values for raw plant materials depending on where they are used, which must be taken into account and which are set out in EU Regulation 2023/915, for example. →

	As [ppm]	Cd [ppm]	Cr [ppm]	Cu [ppm]	Pb [ppm]
Cardamom	< 0.2	0.06	< 0.02	5.4	0.3
Cinnamon	< 0.2	< 0.007	0.4	6.6	0.6
Goat weed	0.4	0.13	2.8	4.5	1.5
Carrot	< 0.2	0.03	0.04	5.0	< 0.1
Rehmannia root	< 0.2	< 0.007	0.4	3.8	< 0.1

Table 1: Results of the quantitative analysis of trace elements in raw plant materials

	Ca [wt%]	K [wt%]	Mg [wt%]	Na [wt%]	P [wt%]	S [wt%]
Goat weed	3.7	1.1	0.35	0.008	0.31	0.45

Table 2: Qualitative analysis of macroelements in goat weed

The qualitative measurement (Table 2) is suitable for internal quality controls and checks. It is also often used to detect unknown contamination, which can then be quantified.

The ICP-MS, for maximum sensitivity

Depending on the requirements, the sensitivity of ICP-OES technology may not be sufficient, which is why inductively coupled plasma mass spectrometry (ICP-MS) is becoming more and more important when it comes to monitoring raw plant materials.

Monitoring heavy metal residues in cannabis is a very topical issue here. The so-called Big Four (cadmium, lead, mercury and arsenic) are currently monitored with strict limits to protect consumers from health risks.

The high sensitivity of the ICP-MS enables detection/analysis limits down to the ppt range (parts per trillion). The large linear operating range extends into the sub-ppm range. As with the ICP-OES, both purely quantitative measurements and qualitative screening can be carried out.

Samples are also prepared using microwave digestion with the addition of a nitric acid-hydrochloric acid mixture. The ICPMS-2050 LF from Shimadzu was used (Figure 2).

The results in Table 3 were generated from the exemplary analysis of a cannabis sample.

Figure 2: The ICPMS-2050 LF from Shimadzu

On the one hand, this shows that the legal limits were not exceeded, on the other hand, the traces of heavy metals found in low concentrations prove just how sensitive the ICP-MS is.

Rest assured thanks to sensitive measuring methods

Raw plant materials are the foundation of many different products and are currently in particularly high demand due to the trend towards more natural ingredients. But just because something is a natural ingredient doesn't mean it is always healthy and pure. Contamination with trace amounts of heavy metals can have dangerous effects on humans and the environment.

The ICP-OES and ICP-MS techniques offer very user-friendly and at the same time sensitive measurement techniques for testing both legal and internal requirements with regard to heavy metal contamination in raw plant materials. These can also be important tools when it comes to identifying sources of contamination.

	As [ppm]	Cd [ppm]	Pb [ppm]	Hg [ppm]
Untreated cannabis	< 0.04	0.13	0.138	< 0.015
Legal limit value	0.2	0.2	0.5	0.1

Table 3: Example analysis of cannabis

Note
For more information and references, please refer to the digital version of this edition.

Euroanalysis
Barcelona, Spain
August 31–September 4, 2025

ExTech
Mülheim an der Ruhr, Germany
September 8–11, 2025

POWTECH TECHNOPHARM
Nuremberg, Germany
September 23–25, 2025

SFC Europe
Basel, Switzerland
October 5–7, 2025

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Düsseldorf, Germany
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