

the **Cannabis Scientist**

S P E C I A L
S E R I E S :

*C a n n a b i s
T e s t i n g S a f e t y*



IN MY VIEW

Green Machine

Could automated testing technologies take the cannabis market to the next level?

Around the world, legal medicinal and recreational cannabis use is growing rapidly. A global trend that has continued to rise despite the COVID-19 pandemic, especially in the US, where states and territories with legal cannabis markets deemed the sector an essential industry. But it has not all been plain sailing.

The pandemic has fueled staffing challenges in cannabis testing, with labs struggling to find the skilled staff that they need. This and the desire for the industry to break into new geographies and market segments at the same time, is also leading to the need for more intuitive technologies to ensure reliable testing and analysis which is vital for providing processors with confidence in their developing supply chains.

The cannabis industry is no stranger to innovative testing technologies but, especially for a young field struggling with human resources, automated analysis appears to be a clear front runner in helping meet the challenges and opportunities within the growing sector. With sensitive, accurate and easy-to-use semi- or fully- automated testing technologies, labs and processors are able to meet regulatory and customer demands without the need to source scores of highly trained scientists and operators.

Automated mycotoxin and pesticide testing solutions provide streamlined sample prep, increased throughput, decreased cost per sample and feature “set it and forget it” functionality for all stages of the testing workflow. Prebuilt cannabis analysis methods that have been optimized for leading state regulations can also be used in concert to help increase efficiency and reproducibility, all while decreasing time and resource requirements.

In addition to the technology itself, cannabis testing can also generate a lot of data. With manual analysis proving both laborious and training-intensive, automated systems can help deliver accurate and consistent results to clients or relevant regulatory frameworks. Combining easy-to-use automated systems with powerful yet intuitive software can help ensure that the right data is easily collected, accessed, analyzed, and accurately reported.

Additionally, ensuring any implemented software is open-source, the ability to connect and rapidly analyze data from multiple, varied instruments, will further simplify analysis. Such benefits will help labs future-proof their efforts against growing sample volumes and regulatory demands as the industry continues its rapid expansion into the food and beverage sector.

So, what now? I’d argue that the ever-expanding cannabis market requires automated workflows on an open-source platform to help accommodate any future pesticide or mycotoxin targets that might be added to state or country regulations as producers work to keep pace. In my mind, education around regulations and best practices for implementing the newest generation of automated cannabis testing technologies is a great place to start.

But regardless of how the cannabis industry evolves and the regulations in this industry change, automation has the potential to allow the industry to not only keep up with demand, but also to advance, innovate, and thrive.

Toby Astill is the Global Market Manager for Cannabis and Hemp at PerkinElmer, Inc.



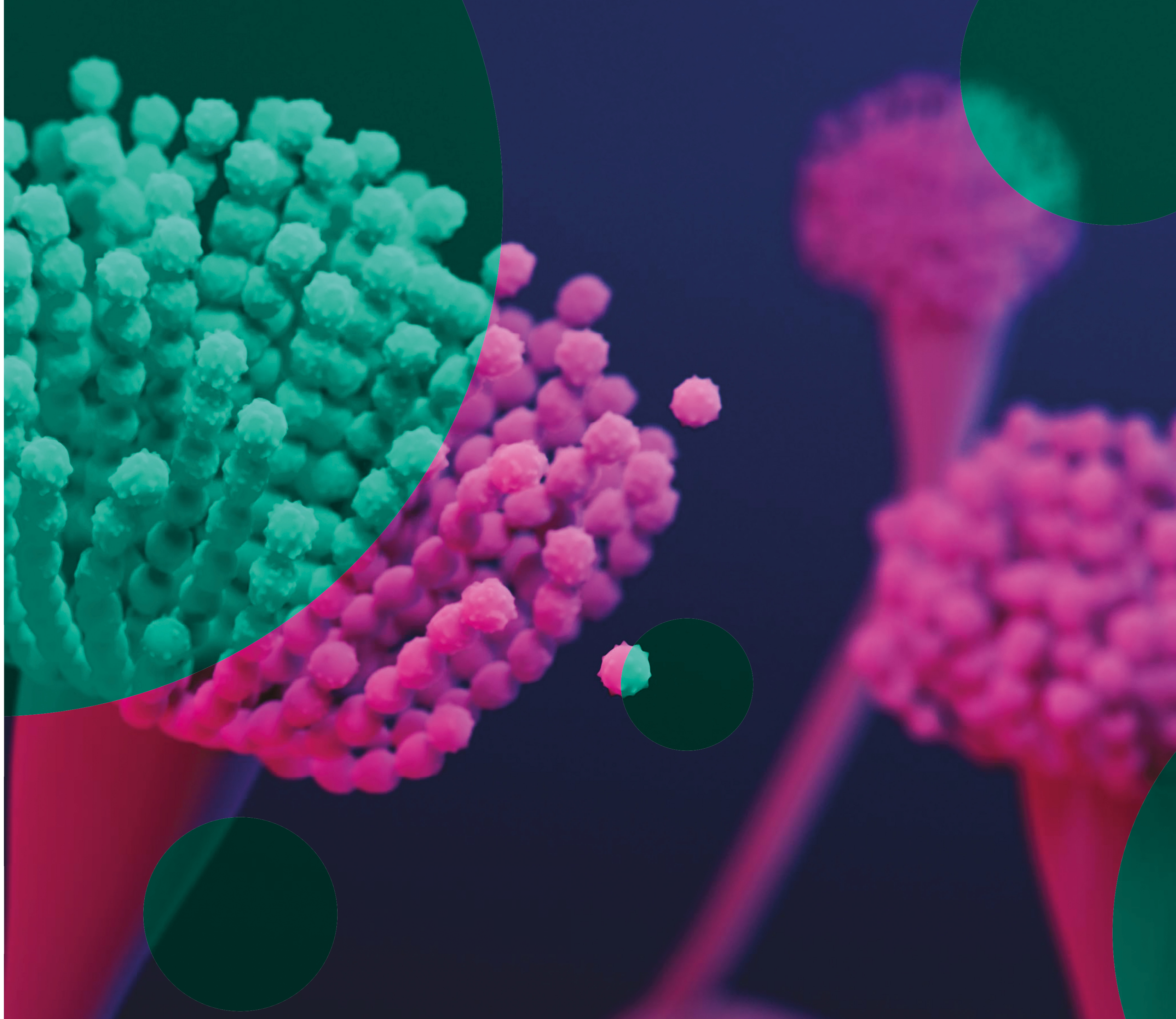
TESTING & PROCESSING

Tainted Bud

Surprising findings from the first study to look at mycotoxin contamination in illegal cannabis samples

Mycotoxins – such as ochratoxin A (OTA) and aflatoxins (AF) – are a class of compounds produced by some species of fungi that, at certain levels, are toxic to humans and animals. They are known to contaminate a wide range of agricultural and food products, including grains, coffee, and wine. Detecting and quantifying the levels of these toxins in medical cannabis is crucial to ensuring the safety of consumers – especially immunocompromised patients. However, there is very little research available on mycotoxin contamination in illegal cannabis samples. In fact, the authors of a recent paper report that they couldn't find a single study looking at mycotoxin contamination in illegal cannabis (1). This is particularly worrying because illegal cannabis is not subject to the same good agricultural practices expected of medical cannabis growers and could therefore harbor even higher levels of contaminants.

To rectify this, a team from the Laboratoire National de Santé analyzed 142 samples of illegal cannabis, seized from the Luxembourg market by police in 2016 and 2017, for the presence of AF and OTA. High-performance liquid chromatography coupled to fluorescence detection was the method of choice because of its low limits of detection. Surprisingly, no AF were detected in any of the 142 samples ($>0.004 \mu\text{g/kg}$). However, OTA was found in around one third of the samples at concentrations below $20 \mu\text{g/kg}$ – comparable to levels found in regulated food samples. Based on the European Food Safety Authority's risk assessment in food, these levels shouldn't present a significant risk to human health with moderate cannabis consumption – but larger studies are needed to confirm these findings.



TESTING & PROCESSING

Fake It Till You Vape It?

Inaccurate labeling is rife among delta-8 THC vaporizers, with many containing unlabeled adulterants and unintended byproducts

Despite the lack of information around their safety, e-cigarettes and vaporizers containing hemp-derived delta-8 THC continue to rise in popularity. A number of studies have cast doubt on the lab testing of these products (check out our [feature with Chris Hudalla for more on the elusive delta-8 THC “unicorn”](#)); few would disagree that more data on the health and safety implications are needed.

To dig into the issue a little deeper, Irfan Rahman and Jiries Meehan-Atrash from the Department of Environmental Medicine at the University of Rochester, New York, analyzed 27 products from 10 brands using a combination of nuclear magnetic resonance spectroscopy (NMR), gas chromatography-mass spectrometry (GC-MS), and inductively-coupled plasma-mass spectrometry (ICP-MS). What did they find? None of the products they analyzed showed accurate delta-8 THC labeling. On top of this, all of them contained reaction side-products (including Δ^9 -THC), heavy metals, and a previously undescribed cannabinoid – and 11 had unlabeled cutting agents (1). We spoke to Irfan and Jiries to find out more.

What was the motivation behind your research?

New products emerge on the vaping market all the time, but large trends like delta-8 THC aren't as frequent. In the shadow of the e-cigarette or vaping use-associated lung injury (EVALI) outbreak, we felt it was something that needed to be investigated further. EVALI is a lung disease caused by e-cig/vaping and known to be associated with THC products including vitamin E acetate and other toxicants. The fact that these products are of synthetic origin is doubly interesting.

Could you elaborate on the analytical approaches you used in the study?

We primarily used ^1H -NMR spectroscopy because of its proven utility for characterizing natural products, and Jiries' research background involved developing NMR methods for the analysis of e-cigarettes. NMR offered fantastic insight into the major components of the e-cigarettes and vaporizers in an omics sense, which uncovered further details about the origins of some products. When we added GC-MS and manual column chromatography to the toolbox, we were able to account for nearly all the components in each product.

Can you walk us through the main findings?

The main finding was that the reported lab test values were all inaccurate – likely due to a lack of optimization in the HPLC-UV methods used by the various labs for testing. We also found a number of unlabeled additives, such as triethyl citrate and medium chain triglyceride oil – this was concerning, but not particularly surprising. What was particularly striking was the diverse mix of cannabinoids in the products. Someone consuming traditional cannabis would not be exposed to these, and we simply have no idea what impact they might have on the brain or respiratory system.

People that use delta-8 THC vaporizer (or those curious) should take these findings as a stark warning. Do you really want to inhale something when you aren't totally sure what's in there? Our study also highlights the potential problems with the existing cannabis lab-testing infrastructure; if

regulators don't enforce strict certification of testing labs, policies around product potency and composition won't be enforced.

You also identified a new cannabinoid... Please tell us more!

Several interesting signals in the ^1H -NMR spectra of all the delta-8 THC vapor products suggested the presence of many cannabinoids other than delta-8 THC, so manual column chromatography was used to fractionate the sample. One fraction had a peculiar ^1H -NMR spectrum in that it contained an isopropyl group, but it still displayed the 21 signal on the ^{13}C spectrum, meaning it had to be isomeric with THC. After many 2D experiments and GC-MS, which are all available for viewing in the supporting information, a structure was proposed and confirmed. A scifinder search shows that a similar structure was proposed in 1975 by a group in Milan, Italy. However the structures were not named, and they lacked the double bond. This is the first full characterization of a tricyclic cannabinoid that contains an isopropyl group.

What are the next steps for your research?

Working on cannabinoid products presents many regulatory challenges, but we must be vigilant about emerging trends. We hope that policies at the federal level loosen for academic institutions in the future, and that funding opportunities become available for this emerging field. In terms of next steps, there are several THC isoforms that are sold in the market as a vaping product. We would like to analyze the chemistry, toxicity, and human health effects of these products.



TESTING & PROCESSING

Pesticide Analysis at Pace

Application chemist Kirk Jensen tells us how a low-pressure gas chromatography kit and short collision cell technology helped him measure 244 pesticides in 11 minutes

Speed is king in the world of pesticide analysis; as many lab managers know, being able to process more samples in a shorter time frame – while maintaining data quality – can be invaluable in high-throughput applications. Current gas chromatography-tandem mass spectrometry (GC-MS/MS) methods are certainly sensitive, but they require longer analysis times to effectively separate complex mixtures. Feeling the need for speed, Kirk Jensen, Robert “Chip” Cody, and John Dane from JEOL decided to test an approach using a low-pressure GC (LPGC) kit (Restek) with the enhanced selected reaction monitoring (SRM) switching speed of the short collision cell in a GC-triple quadrupole MS system (JMS-TQ4000GC, JEOL) (1).

The result? Three transitions for each of 244 pesticides were measured in a standard mixture in just 11 minutes. We spoke to Kirk Jensen to find out a little more about his work.

What prompted this study?

My colleague, Chip Cody, discovered that Restek were offering a preassembled low-pressure gas chromatography (LPGC) kit. Now, this is not new technology – but the implementation of it is new. The kit uses a restrictor column connected to the analytical column to calculate pressure correctly. In theory, you could just buy two different columns and set this up yourself, but it can be very time consuming and the connections don't always work. The LPGC kit makes this entire process a lot simpler.

The kit was of interest because we were looking for ways to increase throughput in pesticide testing labs – any way we can figure out how to do GC in less time is a boon for the industry. The idea with LPGC is to find a way to move more things through the column faster with similar separation efficiency. With a wider column, you should be able to push more things through. A wide-bore column combined with the MS vacuum reduces the pressure within the column, decreases carrier gas viscosity and increases optimum linear velocity. The whole idea is to increase your optimal linear velocity while minimizing the plate height to maximize efficiency. MS plays a key role in this process because the vacuum helps evacuate the column, meaning more shift in the optimal linear velocity. We were inspired to use the LPGC kit with our own triple quadrupole MS to see if we could push more pesticides through faster, but separate them in a similar fashion.

Why is the triple quad MS so pertinent to this type of research?

When analyzing pesticides in particular, but also for other compounds like PFAS, it's inevitable that some ions are going to co-elute. With triple quad MS, or tandem MS, you take a single fragment ion and you break it apart further (with a collision gas for example) and measure that mass spectrum. This means that even if two pesticides are coming out at the same time, you should be able to measure one or two qualifying ions as well which enable you to distinguish between the different pesticides. The other reason a triple quad is so important to cannabis analysis is due to the complexity of the matrix. You get a lot of different substances that co-elute with the pesticides, meaning a lot of interference ions and a messy chromatogram. With a triple quad, the ion you fragment is very specific and you can see the individual peaks quite clearly – it doesn't mean you won't ever get an overlap, but you're increasing your ability to be able to tell the two things apart.

Could you tell us about the short collision cell technology used?

The short collision cell incorporates two different patented technologies that allow it to perform differently compared with other systems on the market. The first technology accumulates all the ions in a small volume, and then produces a single ejection. So rather than the ions coming in a stream and being fragmented, it traps the ions for a short duration (<1 ms) ➡



“Clearly, pesticides are not limited to cannabis, so I’d love to see how those doing routine testing of vegetables or other food products could benefit from our work.”

while it’s fragmenting them, and then it pushes the whole packet out. The longer accumulation time increases sensitivity and decreases the number of interference ions – while the pesticide is trapped there, all the other ions are being sent off into the vacuum and lost. The second technology relates to highly specific timing. While the pesticide is trapped in the cell, nothing is hitting the detector in theory – so we simply shut it off! Because of this, we are able to significantly lower the noise and, in turn, increase sensitivity.

These two technologies working together allow us to do a couple of things. The most important for LPGC is that it enables us to switch between ions faster – the maximum switching speed is 1000 SRMs per second (the highest currently on the market). The JEOL JMS-TQ4000GC also has high pumping capacity and a good vacuum, meaning more penetration into the column, better linear velocity, and therefore higher efficiency.

What was the biggest challenge you faced?

The number one challenge was that all these different transitions have to be developed for every single pesticide. So anytime there’s a pesticide that isn’t in our library, we have to figure it out. We have tools built into our software to do this, but the real obstacle came when pesticides had very similar structures because they fragment the same and have similar ions. For these pesticides, instead of using the most intense transition, I often had to pick a more selective transition – something that was unique to one pesticide over the other. Sometimes these would be very

low intensity but highly specific ions – and that’s when we must rely on the sensitivity of the triple quad to pick them up.

You used a standard mixture in this work; do you have any plans to test your approach with real-world samples?

Yes! The next thing I’d like to explore is how this works for real-world cannabis samples. Can I still measure all these pesticides with different matrices? Cannabis testing labs have different jurisdictional pesticides they are looking for – and they want to know if our approach can measure a specific list of pesticides in that particular matrix. They don’t need to know about all 244 pesticides.

Clearly, pesticides are not limited to cannabis, so I’d love to see how those doing routine testing of vegetables or other food products could benefit from our work. The USDA and EPA are concerned about many more pesticides than the cannabis industry – these are the scientists who will actually care about the 244 pesticides we’ve managed to measure in our work! And that brings me to another hope for the future – I’d love to expand the pesticide capability on this instrument. I am almost certain there is scope to get more than 244 pesticides in 11 minutes, and the LPGC is so quick it’s possible to develop an SRM profile in less than a day. I can’t wait to explore the potential!

REFERENCE AVAILABLE ONLINE



Meet Kirk Jensen

After graduating with a Bachelor’s in chemistry from the University of Northern Colorado, I worked in the pharmaceutical industry for a while. I soon decided I wanted more of a challenge, so I went back to grad school at Colorado School of Mines where I studied under Kent Voorhees – a big name in the MS sphere. I worked on a variety of projects; from combustion of biofuels to detecting *Bacillus anthracis* with phage amplification. I then took up a position as an invited researcher at Osaka University in Japan where I was looking at non-invasive ways of measuring stress markers in saliva. In my third year there, I was promoted to assistant professor and I was studying time-of-flight MS – specifically a closed loop kind of technology that used a figure of eight (or “infinite”) flight path.

Eventually, I moved back to the US and took up a position as an applications chemist at JEOL. Now, my job primarily involves helping customers with their application ideas, and providing them with guidance on how to make their ideas a reality. My secondary role is to find applications for our own systems. So I work on projects with our mass spectrometers and I try to disseminate this information as best I can.

FEATURE

We Believe in Unicorns (and Delta-8)

Contaminated product, negligent testing, consumer safety concerns... Why is the industry turning a blind eye to the hazards of synthetic delta-8 THC?

Delta-8 is one of the hottest topics in the US right now. The problem: Delta-8 does not exist – at least, not in the form you might think. Everybody is arguing about unicorns. Everyone believes a unicorn should be treated humanely but the problem is that unicorns, like delta-8-THC, don't exist – certainly not in the commercial market. What do exist are heavily contaminated delta-8 products – mixtures of synthetic chemicals with impurity levels of up to 47 percent. By shifting the focus of the conversation onto the legality of delta-8, we are obscuring the real argument that it doesn't even exist yet. So how did we get here?

The 2018 Farm Bill defines hemp as “the plant species *Cannabis sativa* L. and any part of the plant, including the seeds thereof and all derivatives, extracts, cannabinoids, isomers, acids, salts, and salts of isomers, whether growing or now, with a delta-9 tetrahydrocannabinol concentration of not more than 0.3 percent on a dry weight basis.” It is easy to see the industry's thought process. CBD extracted from hemp is natural and legal. Trace levels of delta-8 have been observed in biomass; therefore, delta-8 is a natural product. And since delta-8 is naturally occurring, a derivative pathway from CBD for production is legal.

But here's the catch: The conversion of CBD to delta-8 is not a natural process. Many of the isomers and byproducts formed during the conversion are not naturally occurring, produced in the ➔



synthetic reaction to isomerize CBD to THC, which leads to both legal and consumer safety issues arising from what are essentially unknown contaminants. Synthesis is not a singular chemical reaction, but rather a system of parallel competing reactions, resulting in multiple synthetic outcomes. Many of the isomers and byproducts formed are not found in nature and have not been tested for safety or efficacy. In fact, we have no real understanding of many of these compounds. Without safety studies, and with their toxicity unknown, we cannot say they are not a health risk. As such, it would be irresponsible to recommend these products for human consumption.

I remember the first time I saw delta-10 THC gummies submitted to our laboratory. I thought: “This is cool. People are thinking outside the box. I love to see innovation.” The next thing I did was consult the literature. What do we know about the toxicity of delta-10-THC? What is the metabolic fate of the delta-10-THC molecule? Does it clear the liver? Will it cause cancer with repeated long-term exposure? Will use of these products trigger a positive drug test? Might it interact with other pharmaceutical drugs that a person may be taking? Will these compounds cause birth defects if consumed during pregnancy? What about some of the other THC isomers formed in the process? What about other synthetic byproducts? What about residual synthetic reagents left over in the product? There are lots of unanswered questions here.

Why do isomers matter?

Many people in the US have never heard of the drug thalidomide – and luckily so. US pharmacologists at the FDA turned down several requests from the distributing company because they did not provide clinical evidence to refute reports of patients developing nerve damage in their limbs after long-term use. And that prevented the drug from ever being approved for use in the US. Unfortunately, this wasn’t the case in Europe, Canada, and Australia. First marketed in 1957 in West Germany, the drug was promoted for the treatment of anxiety, sleep disorders, tension, and morning sickness in pregnant women. It took five years for

researchers to realize that the drug was affecting the development of the fetus 20–37 days after conception. It is estimated that over 10,000 babies were affected by the drug worldwide. Around half died within months of being born. The thalidomide babies who survived – and their families – live with the side effects, which include issues with limbs, brain, eyesight, and hearing. Can we say with certainty that the synthetic compounds and isomers found in delta-8 products won’t do the same?

I had a client who was in ICU for 10 days after using a counterfeit THC vape product – which turned out to be a mixture of delta-8-THC with vitamin E acetate – that caused her lungs to collapse. Though it is most likely it was the vitamin E acetate that landed her in the ICU, she almost lost her life because of an unregulated product, distributed illegally. Already, National Poison Control has received around 600 exposure cases, 77 percent of which involved minors. Eighteen percent required hospitalization, with some children treated in the ICU. Are these the statistics of a safe product? And this rise in adverse events has seen key industry groups release statements. The Centers for Disease Control and Prevention (CDC) have reported that delta-8 intoxication is similar to that of delta-9, resulting in lethargy, slurred speech, low blood pressure, difficulty breathing, sedation, and coma. The United States Pharmacopeia (USP) said, “The prevalence of synthetically derived delta-8 THC raises safety and quality concerns related to both identity and purity – given the unknown and untested nature of the synthetic analogs and the remaining compounds.” The US Hemp Authority has also distanced itself from hemp products marketed for their intoxicating effects, including delta-8. The Hemp Industry Association has taken a different tack, advocating for safer production methods and FDA regulation of delta-8 THC, along with CBD and other hemp compounds. The FDA, on the other hand, has released a carefully worded warning letter in which they don’t explicitly say that delta-8 is a hazard, but that the products associated with delta-8 represent a hazard. And from what we see in the products submitted to our lab for testing, I agree with this position. The problem is not delta-8, but the unregulated distribution of synthetic, contaminated products. ➡



“There are no two ways about it, 100 percent of delta-8 products that have been tested by our lab are heavily contaminated with synthetic byproducts.”

At least Walter White was a chemistry teacher

So, why don't we just remove these synthetic compounds? Removal of these contaminants can be costly and time consuming, resulting in increased production costs. And that means reduced profits. In addition, the synthesis uses toxic chemicals and organic solvents. The resulting mixtures, in addition to non-natural isomers and synthetic byproducts, can contain residuals of these toxic reagents. Most producers are not testing for acids, residual solvents, neutralizing bases, and heavy metals. How adept are producers at removing these residual reagents from their process? Without more testing, we'll never know. And that brings us to another problem: The DEA has said multiple times that synthetic cannabinoids are illegal – but who is willing to say delta-8 is synthetic? Not politicians, lawyers, or regulators, who are focused on the legality of delta-8. Not law enforcement who are afraid to enforce sanctions, arrest people or confiscate products. To make matters worse, much of the product is found via the internet, in which the producer may be nebulous – and difficult to hold accountable. All this ambiguity has created a huge window of opportunity for producers – and, of course, delta-8 has become a money printing machine, which nobody wants to disrupt. But given that many of the isomers formed do not exist naturally, they can only be classified as synthetic.

Another issue: Producers are oftentimes unaware that they are distributing crude mixtures of synthetic contaminants. Right now, most laboratories providing cannabinoid testing for these producers are using HPLC as their

primary methodology. But these methods were optimized for cannabinoids found in the cannabis plant, and as such, are incapable of resolving many of the synthetic cannabinoids and synthetic byproducts. It's like using a screwdriver to pound a nail; though I love screwdrivers, it's just not the right tool for the job. And so there are often multiple chromatographic peaks hiding behind the delta-8 signal. Recorded retention times of these peaks do not match exact cannabinoid reference standards, so their presence is often omitted from laboratory reports. Without chromatographic resolution of these chemical compounds, these contaminants are often integrated into the delta-8 signal. Consequently, products that claim to be 90 percent delta-8 typically contain contaminants that have been erroneously attributed to the delta-8 signal. Many of the cannabinoids have similar retention and UV absorbance, making it difficult to distinguish individual isomers. The similarity of these structures is part of the reason why they are so challenging to resolve in a singular chromatographic method. The use of orthogonal analytical methodologies, such as gas chromatography or supercritical fluid chromatography, can be used to separate some of the chemical contaminant signals from the delta-8 signal, but this takes extra time and extra resources.

There are no two ways about it, 100 percent of delta-8 products that have been tested by our lab are heavily contaminated with synthetic byproducts. Most labs are not telling producers that they have found synthetic isomers and/or contaminants whose signals cannot be resolved from delta-8. With labs not reporting what they are seeing, producers are being led to believe that they have high quality delta-8

distillate. Naturally, they go on to make that distillate into vapes, edibles, and so on, and carry those contaminants along in the process.

Why do so many labs ignore the presence of these compounds? Are they just not able to understand what the chromatography is telling them? Are they afraid of losing the testing business from these producers? Our lab has lost significant testing revenues based on our policy for delta-8 samples, which includes noting the presence of these contaminants on our Certificate of Analysis (COAs). Nobody wants to send me a second vape cartridge for analysis when my first report came with a warning: *No toxicity data is available for these unknown compounds, and as such would not be recommended for human consumption.*

Although labs are part of the problem, they are not the only guilty party. Producers can plead ignorance because labs have not been forthcoming with the truth – or incompetent with their testing. But when I show producers what is really in their sample, they don't stop making it, they don't stop distributing it – they just go to another lab who will not acknowledge the contaminants found. Few other labs in the US will call attention to contaminants in the products we test, providing a clear warning that a product may not be safe or recommended for human consumption. And when consumers are provided with test results to confirm safety, at least against agricultural contaminants of concern, they are misled by the omission of data indicating contaminants that would be of a synthetic nature and therefore of concern. In reality, we ➔

cannot say these contaminants are harmful for human consumption, but – more importantly to me – I also cannot say they are safe. The scientific community, for the most part, has been very supportive of our stance on consumer safety – but few people are stepping up to take a public stance against synthetic delta-8 products and the associated contaminants.

The solution

So, what do we do about it? The answer is to look to industries dedicated to manufacturing and testing synthetic compounds for human consumption. How is Viagra manufactured? Trained people put chemicals together, perform several synthetic reaction steps, and finally get to the desired compound – but never with 100 percent yield. And that could mean a multitude of synthetic reaction byproducts. Those unintended synthetic compounds are treated one of two ways: i) They are either removed through a purification step – like chromatographic isolation, or ii) these compounds are studied to ensure they are safe for consumption, to ensure their presence in a final drug product will not cause harm. Nobody that I know of is doing that for delta-8.

In fact, we haven't even identified many of the resulting compounds from delta-8 synthesis. Each producer or each batch that uses different acids, different temperatures, or different reaction times creates a different mixture of contaminants – so contamination profiles in these products can differ greatly. But we do see some common foreign signals in many of the products, and with the application of multiple analytical techniques, we are starting to get bits and pieces of information. In one sample, the mass spec isotopic ratios observed are indicative of a chlorinated molecule, with the mass of hexahydrocannabinol. We don't have the complete picture, but chlorinated cannabinoids are probably not a good thing. Recently, researchers have published studies using nuclear magnetic resonance spectroscopy, along with chromatography and mass spectroscopy, to identify some of the structures they found in selected consumer products. Several of the structures found, including one compound that has not been previously identified, have not yet been studied for safety or toxicity.

We have been working collaboratively with multiple equipment manufacturers that provide instrumentation capable of the necessary isolation or purification of chemical compounds, like delta-8. These collaborations demonstrate that there is hope for legitimate delta-8 products. I have presented much of our data and concerns at conferences, and while much of the data is not favorable for delta-8 product lines, I like to end my presentation with examples from these collaborations of what delta-8 could look like. That is, what delta-8 should look like. And yet, I'm left somewhat amazed after my presentations. I present an alternative to the current contaminant-produced products, but do not get asked for additional follow up information on the conditions, equipment or collaborators which were capable of producing a purified product. It seems that most producers just are not interested because of the additional resources necessary to pursue this alternate route.

And make no mistake, it will take time to gain clarity on these compounds. They all need to be purified, isolated, and characterized. If they cannot be removed by purification, then they need to be studied for biological safety. Unfortunately, my lab doesn't have the equipment to purify and study all these contaminants. But even for researchers that have access to this equipment, it will take years to get the full picture and understand these complex mixtures completely. With the unregulated, non-standardized industry, the contaminating compounds are part of a shifting landscape; as noted, every time we see variation in the process, there are subtle (or major!) differences in resulting contaminant profile. And as long as people continue to change their processes, there will be new contaminants and new risks. No wonder it takes millions of dollars to bring a regulated drug to market...

Self-regulate or die

I want the industry to self-regulate so outside organizations don't have to shut it down. But I don't see that happening... Many in the industry instead are trying to move regulation of delta-8 under the US Farm Bill so it is treated and regulated like hemp. But this delta-8 is not an agricultural ➡



“We certainly have the means to produce a clean, uncontaminated delta-8 with proper post-synthesis isolation and purification.”

product. I am frustrated when producers present a COA which includes pesticide screening results. Pesticides are contaminants of agricultural concern. As soon as the added acid starts changing the chemical structure of CBD, it leaves the world of agriculture and enters the realm of synthetic chemistry – but farmers are not synthetic chemists. And neither are cultivators, extractors, nor most processors. If delta-8 should be regulated, it should be overseen by the same organizations that regulate other synthetic chemistry products intended for consumption: In the US, most likely the FDA. But FDA regulation of CBD, and with it, delta-8, would be challenging because it would mean producers would have to follow legitimate processes to produce their goods. These processes, which would include GMP production, are neither easy nor inexpensive to implement and maintain. FDA-regulation means audits, paperwork, manufacturing practice guidelines, as well as safety and stability studies. The bureaucracy associated with an FDA-regulated program would crush most current CBD and delta-8 producers, inevitably forcing consumers to the black market. But without any regulatory oversight, many states have already started to shut delta-8 products down. At the last count, 17 US states had outlawed delta-8 products – with no oversight, no responsibility, and no integrity – driving producers and consumers underground. And that’s especially disappointing because delta-8 (without the contaminants) has legitimate therapeutic potential.

The silver lining

Raphael Mechoulam was one of the first researchers to see the therapeutic potential of delta-8. It has significant neuroprotective

properties. It is also an appetite stimulant – and it has analgesic properties in terms of neuropathic and inflammatory pain, as well as anxiolytic properties, binding to CB1 and potentially CB2 receptors. Its antiemetic effects have been studied with pediatric chemotherapeutic treatment in the reduction of nausea to great success. In fact, delta-8 has an almost identical therapeutic profile to delta-9, but with only 20 percent of the psychoactivity. If prepared without contaminants and used correctly, it could allow healthcare providers to treat the most vulnerable with cannabinoids, without getting them high.

From a commercial perspective, delta-8 is relatively easy to produce from CBD (at least without regulatory oversight) – and that’s currently in overabundance. It requires minimal capital investment for production equipment and supplies, making it incredibly attractive to suppliers – especially in our turbulent economy. With the exception of purification, delta-8 can be produced inexpensively. So once we find a way to scale the purification process, those costs will also be reduced. And because the oversupply of CBD isolate has resulted in lower margins for manufacturers, conversion to THC represents a significant financial opportunity and provides salvation for investors waiting for FDA approval of CBD. These are all incredible benefits, but they must be treated with caution.

It worries me that the synthetic version of delta-8 has become so palatable to the cannabis industry. So much so that the industry is now comfortable moving forward with additional chemical modifications. In the last few months, we have seen hexahydrocannabinol (HHC), THCP, delta-8 THC acetate, and delta-9 THC acetate (THCO) – synthetic

cannabinoids that aren’t even pretending to be phytocannabinoids. And yet these are being sold as legal hemp derivatives, “Farm Bill compliant,” which, according to lawyers, is lawful. To put that into context, if you could find a synthetic pathway to convert CBD into methamphetamine or heroin, that synthetic process would make those products legal – after all, it would still be a hemp derivative. Really?

As long as I feel that consumers need to be warned about the risks associated with delta-8 products, and as long as regulators and health care professionals need to understand what these are, I will continue to be a mouthpiece for unpopular opinions. I cannot deny that I am also driven by scientific curiosity; it is very frustrating to say that I’ve found compounds or chemical signals that I cannot identify, and include that note on our certificate of analysis. But the laboratories who are not prepared to acknowledge these unknown compounds are doing no benefits to producers and consumers.

We certainly have the means to produce a clean, uncontaminated delta-8 with proper post-synthesis isolation and purification. It will take time, money, research, and regulation, but it will be worth it. I just need more people – preferably the whole industry – to see the light.

In the meantime, I still want to believe, so I will keep watching for legitimate delta-8 (and unicorns).

Christopher Hudalla is the President and Chief Scientific Officer of ProVerde Laboratories, US